Developing and Evaluating a Patient Decision Aid for Managing Early Surgical Menopause

by

Tasneem Siyam

A thesis submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Pharmacy Practice

Faculty of Pharmacy and Pharmaceutical Sciences
University of Alberta

ABSTRACT

Background: Early surgical menopause results in severe and prolonged health consequences due to early estrogen deprivation. Hormone therapy (HT) is a recommended treatment when no contraindications exist, yet it is poorly utilized by women with early surgical menopause. Given women perceived uncertainty about HT risks, a situation of complex decision-making ensues when deciding if HT is a suitable option. Other barriers to effective decision-making inherent in early surgical menopause are the abrupt presentation of severe menopausal symptoms, the long-term health sequelae and the need to make a decision on a short timeline. Patient decision aids (PDAs) are useful interventions when patients are faced with complex therapy decisions. No peer-reviewed, evidence-based PDAs currently exist to support women who go through early surgical menopause. Considering the complexity of decision-making about HT and the paucity of decision support strategies for early surgical menopause, we systematically developed and evaluated an evidence-based, self-administered PDA to help women make HT decisions for managing early surgical menopause.

Methods: The PDA development was guided by the Ottawa decision support framework (ODSF) and the International Patient Decision Aid Standards (IPDAS) and involved: (1) assessing the need and feasibility of developing a PDA; (2) exploring the decision support needs of the target population; and (3) developing the PDA and evaluating for acceptability in a non-clinical setting. In phase one, a scoping review was completed to identify the nature and extent of research done in the area of decision aids for surgical menopause. A systematic review to assess the effect of HT in a sub-population of women who go through early surgical menopause was also completed to assess for feasibility of development. In phase two, the decisional needs of the target population were identified from five focus groups completed as part of a descriptive

qualitative study to explore the process of decision-making about menopausal therapies in a sample of women who have had an early surgical menopause. As well, a narrative review to identify the decisional needs in a broader population of women with surgical menopause was conducted. In phase three, findings from phases one and two were used to inform the PDA development. The PDA was then evaluated in a cross-sectional mixed method study to elicit evidence on acceptability. To draft the PDA, relevant guidelines were targeted to gather information on surgical menopause, HT and evidence on risks and benefits. For outcome probabilities, systematic reviews addressing the risks and benefits of HT in surgical/natural menopause were searched. Data on HT outcome probabilities were evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE). The development of the PDA was driven by a steering committee consisting of a multidisciplinary group of researchers, clinicians and patient partners to ensure women priorities were met. For the focus groups and the mixed method study, women were recruited from two menopause clinics in Edmonton, Alberta. The PDA was assessed against the IPDAS quality criteria for conformity with internationally recognized standards.

Results: Informed by identified decisional needs and findings from the scoping and systematic reviews, a prototype of the SheEmpowers PDA was developed. The PDA focuses on five domains: information on surgical menopause and HT, outcomes and resources for menopausal support; HT outcome probabilities; patient stories; explicit values clarification; and guidance in deliberation. Clinician and patient experts from the steering committee provided positive feedback about the PDA and suggested improvements were implemented. Participants in the evaluation phase perceived the tool as acceptable and offered useful suggestions for targeted modifications. The tool met 39 of the 46 IPDAS quality criteria for content and development.

Conclusion: Through our adopted, systematic, evidence-based and multidisciplinary approach the SheEmpowers PDA was developed that aims to help women overcome deterrents to decision-making related to lack of knowledge, decision-making skills and involvement in therapy decisions, for an ultimate goal of attaining informed and value-based decisions about HT, and a long-term goal of optimizing medication use among women of the target population. The effectiveness of the tool in terms of achieving those outcomes is yet to be assessed. The practice implications of such tools are of specific significance to health care professionals, particularly pharmacists, being the most accessible and trusted front-line healthcare professionals, as they support women in shared, informed and value-based decision-making for optimal medication use and health outcomes.

PREFACE

This thesis is an original work by Tasneem Siyam. A research project which is part of this thesis received ethics approval from the University of Alberta Research Ethics Board. The project is entitled "Perspectives and Decision-Making about Menopausal Therapies in Women Who Had Bilateral Oophorectomy (BO)", ID# Pro00054435, date of ethics approval October 5, 2016.

Some of the research conducted for this thesis constitute part of a research collaboration, led by my supervisor, Dr. Nese Yuksel at the University of Alberta. Our collaborators included my co-supervisor Dr. Sue Ross from the Faculty of medicine and dentistry, University of Alberta; a member of my supervisory committee, Dr. Dean T. Eurich from the School of Public Health, University of Alberta; clinician and patient experts from the Lois Hole Hospital for Women (LLHW) and the Grey Nuns Community Hospital (GNCH) in Edmonton, Alberta; Pharmacy students and Pharm D candidates at the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta; and librarians from the John W. Scott Health Sciences Library, University of Alberta.

Chapter 3 of this thesis has been published as T. Siyam, H. Sultani, S. Ross, T. Chatterley, N. Yuksel, Evaluating the content and development of decision aid tools for the management of menopause: A scoping review, Maturitas 106 (2017) 80-86. For this work, I was responsible for the study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, and administrative, technical or material support. Chapter 4 of this thesis has been published as T. Siyam, S. Ross, S. Campbell, D.T. Eurich, N. Yuksel, The effect of hormone therapy on quality of life and breast cancer risk after risk-reducing salpingo-oophorectomy: a systematic review, BMC Womens Health 17(1) (2017) 22. My contribution to this work also

involved study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, and administrative, technical or material support. Chapter 5 of this thesis has been published as T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause 25(7) (2018) 795-802. In this study, I was responsible for the study concept and design, data collection and analysis as well as the manuscript preparation. Chapter 6 of this thesis has been accepted for publication as T. Siyam, J. Carbon, S. Ross, N. Yuksel, Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy (BO): A Narrative Review, Maturitas, on November 8, 2018. My contribution to this study involved study concept and design, data collection and analysis as well as manuscript composition. Our collaborators contributed variably to the published work as part of this thesis. Their contributions involved assistance with study concept, design, conduct and/or data analysis and interpretation; critical revision of the manuscript for important intellectual content; and approval of final version of the manuscript.

DEDICATIONS

To my loving and caring Mom, Naeima Salem and Dad, Abdemageed Siyam for their unconditional love and support

To my sisters and brothers for making me always feel special and supported

To my supervisors, Nese Yuksel and Sue Ross for supporting me all along and being an excellent role model for guidance and mentorship.

ACKNOWLEDGEMENTS

I owe my deepest gratitude to my supervisors, Nese Yuksel and Sue Ross for their ongoing guidance and support. I am fortunate to have had the chance to work under their supervision and learn from their expertise. I am forever indebted to them for all the time and effort they have dedicated to guiding me through my thesis projects.

I am very appreciative to the support of members of my supervisory committee, Dr. Afsaneh Lavasanifar and Dr. Dean T. Eurich for the great ideas they brought to our supervisory meetings and meaningful feedback which contributed significantly to the work presented.

I am sincerely grateful to the SheEmpowers steering committee including clinicians: Tami Shandro, Shelly Hagen and Lori Battiochio as well as patients: Wendy Campbell, Sue Hopgood and Kyla Sorel for their outstanding work in reviewing our tool and providing valuable feedback and suggestions for improvement. Our clinician stakeholders were also our research partners for both the exploratory and evaluation phases of development, without their passion and exceptional support the implementation of these phases would not have been possible.

My thanks also go out to all of our research collaborators including clinicians and staff members at both the Lois Hole Hospital for Women (LLHW) and the Grey Nuns Community Hospital (GNCH) menopause clinics for their assistance in the conduct of the exploratory phase of development.

I also wish to sincerely thank all the women who contributed to our research findings by participating in either the exploratory or evaluation phases of the study. Their shared experiences and feedback were key for the development and revision of our tool.

I also would like to acknowledge the role of my dear sister and best friend, interior designer, Aya Siyam in designing and developing the tool and logo. Her creative insights and exceptional technical skills were major contributors to the development of the SheEmpowers tool.

It's with great pleasure that I also give credit to all the pharmacy and Pharm D students that have contributed to the work presented in this thesis. Through working closely under the supervision of Dr. Nese Yuksel and I these students assisted in the conduct of several projects involved in

developing the SheEmpowers PDA. This includes pharmacists: Julia Kwan, Jenny Carbon, Arianne Bayot, Humirah Sultani, and Lisa Zhou, as well as Pharm D candidate, Alisha Shivji.

My sincere regards extend to my qualitative mentors and research advisors, Megan Lefebvre and Tatjana Alvedij for supporting me in the design, conduct and analysis of the qualitative component of my research projects.

I am also thankful for the support I received from Librarians, Sandra Campbell and Trish Chatterley in designing and implementing the literature search of different projects involved in this thesis.

I also would like to recognize the research support we got from Alberta's Strategy for Patient Oriented Research (AB-SPOR), with specific mention to Yazid N. Al Hamarneh, Robin Laczy and Meghan Sebastianski from the research consultation, patient engagement, and knowledge translation platforms, respectively.

My sincere thanks go out to editors from the Academic Success Centre, Debbie Waldman for editing the SheEmpowers tool and Kelly Parkatti for editing chapters one and two of my thesis.

I also would like to acknowledge the role of the Women and Children's Health Research Institute (WCHRI) in funding our exploratory and evaluation phases of development. Only through the generous support of WCHRI was this research work possible.

At last, my utmost gratitude goes out to my loving parents and family for their overwhelming love, care, support, and endless prayers. Without their love and trust, attaining this milestone in my personal and research growth would not have been possible.

TABLE OF CONTENTS

1 CHAPTER 1. INTRODUCTION 1

1.1 RATIONALE 1

2 CHAPTER 2. BACKGROUND 11

2.1 NATURAL MENOPAUSE 11
2.2 INDUCED MENOPAUSE: SURGICAL MENOPAUSE 11
2.3 EPIDEMIOLOGY OF SURGICAL MENOPAUSE 12
2.4 SYMPTOMS OF SURGICAL MENOPAUSE 13
2.5 LONG-TERM RISKS 14
2.6 MANAGING SURGICAL MENOPAUSE 16
2.7 HORMONE THERAPY (HT) AND COMPLEX DECISION-MAKING 18
2.8 SHARED DECISION-MAKING (SDM) 19
2.9 PATIENT DECISION AIDS (PDAS) 20
2.10 ROLE OF PDAS IN SURGICAL MENOPAUSE 22
2.11 DECISION AIDS DEVELOPMENT BEST PRACTICE 23
2.11.1 Theoretical framework 23
2.11.2 Theories 24
2.11.3 Decision aid components 25
2.11.3.1 Presenting information 25
2.11.3.2 Personal stories 27
2.11.3.3 Values clarification methods 28
2.11.3.4 Guidance in deliberation 29
2.11.3.5 Other considerations 30
2.11.3.5.1 Conflict of interest 31
2.11.3.5.2 Mode of delivery 31
2.11.3.5.3 Plain language 31
2.12 CONCLUSION 32

3 CHAPTER 3. EVALUATING THE CONTENT AND DEVELOPMENT OF DECISION AID TOOLS FOR THE MANAGEMENT OF MENOPAUSE: A SCOPING REVIEW 33

3.1 INTRODUCTION 34
3.2 METHODS 35
3.2.1 Eligibility criteria 35
3.2.2 Data sources 36
3.2.3 Selection process 36
3.2.4 Data extraction and synthesis 36
3.3 RESULTS 38
3.3.1 DATs characteristics 38
3.3.2 DAT content evaluation 39
3.3.3 DAT development evaluation 40
3.3.4 Qualification and certification standards of DATs from grey literature 40
3.3.5 Effectiveness trials of DATs 41
3.4 DISCUSSION 41
3.5 CONCLUSION 44
3.6 REFERENCES 44

4 CHAPTER 4. THE EFFECT OF HORMONE THERAPY ON QUALITY OF LIFE AND BREAST CANCER RISK AFTER RISK-REDUCING SALPINGO-OOPHORECTOMY: A SYSTEMATIC REVIEW 67

4.1 BACKGROUND 68
4.2 METHODS 70
4.2.1 Eligibility criteria 70
4.2.2 Outcome measures 70
4.2.3 Data sources and search strategy 70

4.2.4 Study selection *71*
4.2.5 Data extraction and quality assessment *71*
4.2.6 Data synthesis *72*
4.3 RESULTS 72
4.3.1 Study characteristics *72*
4.3.2 Synthesis of results *73*
4.3.2.1 Quality of life 73
4.3.2.2 Breast cancer 73
4.3.2.3 Other outcomes 74
4.3.2.3.1 Vasomotor symptoms 74
4.3.2.3.2 Sexual function 74
4.3.2.3.3 Vulvovaginal Atrophy (VVA) 74
4.3.2.3.4 Prevention of bone loss 75
4.4 DISCUSSION 75
4.5 CONCLUSION 78
4.6 REFERENCES 79

5 CHAPTER 5. PERSPECTIVES AND DECISION-MAKING ABOUT MENOPAUSAL THERAPIES IN WOMEN WHO HAD BILATERAL OOPHORECTOMY (BO) 118

5.1 INTRODUCTION 119
5.2 METHODS 120
5.2.1 Design and participants *120*
5.2.2 Data collection and management *121*
5.2.3 Interview guide *121*
5.2.4 Data analysis *121*
5.3 RESULTS 122
5.3.1 Perceptions of surgical menopause experience *122*
5.3.1.1 Experience worse than expectations 122
5.3.1.2 Experience of menopausal symptoms 122
5.3.1.3 Emotional repercussions 123
5.3.1.4 Menopause and life overlap 124
5.3.2 Perceptions of received support *124*
5.3.2.1 Perceptions of timely support 124
5.3.2.2 Perceptions of symptoms management (role of menopausal therapies) 124
5.3.2.3 Role of family and friends 125
5.3.2.4 Perceptions of medical support 126
5.3.2.4.1 Lack of patient-centered care and patient engagement in decision-making 126
5.3.2.4.2 Lack of interest in menopausal concerns 127
5.3.2.4.3 Lack of knowledge about menopause and hormones 127
5.3.2.4.4 Lack of clear messages about menopausal therapies 127
5.3.3 Be my own advocate *128*
5.3.3.1 Seeking help from within health care system and outside 128
5.3.3.2 Searching the internet for information and communal support 128
5.3.3.3 Empowering myself and others 129
5.3.3.4 Negotiating competing expectations 129
5.3.3.4.1 Quality of life 129
5.3.3.4.2 Long-term risks of surgical menopause 130
5.3.3.4.3 Health risks of HT 130
5.3.3.4.4 Other reasons 130
5.3.4 Concept of adequate support *131*
5.3.4.1 Be prepared 131
5.3.4.2 Have the information and resources 132
5.3.4.3 Have the social support 132
5.3.4.4 Tailored multidisciplinary care 133
5.3.4.5 Research on women with surgical menopause 133
5.4 DISCUSSION 133
5.5 CONCLUSION 137
5.6 REFERENCES 137

6 CHAPTER 6. DETERMINANTS OF HORMONE THERAPY UPTAKE AND DECISION-MAKING IN BILATERAL OOPHORECTOMY (BO): A NARRATIVE REVIEW....146

6.1 INTRODUCTION....147
6.2 METHODS....148
6.2.1 Search strategy....148
6.2.2 Inclusion and exclusion criteria....148
6.2.3 Screening for eligibility and data abstraction....149
6.2.4 Developing of a model of patient decision-making....149
6.3 RESULTS....149
6.3.1 Characteristics of the studies....149
6.3.2 Factors affecting use and decision-making about HT....150
6.3.2.1 Women-related factors....150
6.3.2.1.1 Individual characteristics....150
6.3.2.1.2 Perceptions, beliefs and values....151
6.3.2.1.2.1 Perceptions of HT....151
6.3.2.1.2.2 Perceived susceptibility of risks....152
6.3.2.1.2.3 Beliefs on menopause....152
6.3.2.1.2.4 Perceived need for treatment....152
6.3.2.1.2.5 Perceived control over actions....153
6.3.2.1.2.6 Perceived complexity of therapy decisions....153
6.3.2.1.2.7 Value placed on present versus the future....153
6.3.2.1.3 Knowledge on menopause and HT....153
6.3.2.1.4 Experiences with surgical menopause and HT....154
6.3.2.2 External factors....154
6.3.2.2.1 Physician's recommendation....154
6.3.2.2.2 Information sources....155
6.3.2.2.2.1 Media, family and friends....155
6.3.2.2.3 Evidence about HT....155
6.4 DISCUSSION....156
6.5 CONCLUSION....160
6.6 REFERENCES....161

7 CHAPTER 7. DEVELOPING AND EVALUATING A PATIENT DECISION AID FOR MANAGING SURGICAL MENOPAUSE: THE STORY BEHIND THE "SHEEMPOWERS" PATIENT DECISION AID 175

7.1 INTRODUCTION....176
7.2 METHODS....177
7.2.1 Development framework....177
7.2.2 Steps for developing PDA....178
7.2.2.1 Scope and purpose....178
7.2.2.2 Steering committee and roles....178
7.2.2.3 Assessment of decisional needs (exploratory phase)....180
7.2.2.4 Drafting the PDA....180
7.2.2.4.1 Development of content....181
7.2.2.5 Review of the PDA with steering committee (evaluation phase)....181
7.2.2.6 Acceptability testing (evaluation phase)....182
7.2.2.6.1 Participants and recruitment....182
7.2.2.6.2 Data collection....182
7.2.2.6.3 Data collection tools....183
7.2.2.6.4 Data Analysis....183
7.2.3 Assessing PDA quality against IPDAS checklist....183
7.3 RESULTS....184
7.3.1 Women's decisional needs....184
7.3.2 Components of the PDA....184
7.3.3 Feedback from the steering committee....186
7.3.4 Evaluation of PDA (alpha testing)....186
7.3.4.1 Results of quantitative analysis....187
7.3.4.2 Results of qualitative analysis....187

7.3.4.2.1 Strengths of PDA 187
7.3.4.2.1.1 Value of the tool 188
7.3.4.2.1.2 Context of use and dissemination 189
7.3.4.2.2 Suggestion for improvement 190
7.3.4.2.2.1 Symptoms of surgical menopause 190
7.3.4.2.2.2 Hormone therapy 190
7.3.4.2.2.3 Other areas 191
7.3.4.2.3 Other expectations of support 192
7.3.5 Quality assessment against IPDAS criteria 192
7.4 DISCUSSION 193
7.4.1 Implemented modifications 193
7.4.2 Challenge of incorporating other suggestions 194
7.4.3 Strengths and limitations 195
7.5 CONCLUSION 197
7.6 PRACTICE IMPLICATIONS 197
7.7 REFERENCES 197
8 CHAPTER 8. GENERAL DISCUSSION AND RECOMMENDATIONS 294
8.1 GENERAL DISCUSSION 294
8.2 FUTURE RECOMMENDATIONS FOR THE DECISION AID 304
8.2.1 Beta testing 304
8.2.2 Evaluation of effectiveness 305
8.2.3 Implementation and dissemination 306
8.2.3.1 Implementation plans 307
8.2.3.2 Dissemination plans 308
8.3 OTHER FUTURE RECOMMENDATIONS 311
8.3.1 Guidance for PDA developers 311
8.3.2 More research in surgical menopause 312
8.3.3 Unmet support needs 312
8.4 CONCLUSION 313
REFERENCES 316

LIST OF TABLES

CHAPTER 3. Evaluating the Content and Development of Decision Aid Tools for the Management of Menopause: A Scoping Review

TABLE 3.1. MANUSCRIPT CHARACTERISTICS (PEER-REVIEWED ARTICLES) 52
TABLE 3.2. POPULATION CHARACTERISTICS (PEER-REVIEWED ARTICLES) 54
TABLE 3.3. DAT CHARACTERISTICS (PEER-REVIEWED LITERATURE) 55
TABLE 3.4. DAT CHARACTERISTICS (GREY LITERATURE) 56
TABLE 3.5. DAT CONTENT EVALUATION BASED ON IPDAS QUALITY CRITERIA 58
TABLE 3.6. DAT DEVELOPMENT EVALUATION BASED ON IPDAS QUALITY CRITERIA 60
TABLE 3.7. RESULTS OF QUALIFICATION AND CERTIFICATION SCREENING OF IDENTIFIED DATS FROM GREY LITERATURE 62

CHAPTER 4. The Effect of Hormone Therapy on Quality of Life and Breast Cancer Risk After Risk-Reducing Salpingo-oophorectomy: A Systematic Review

TABLE 4.1. STUDY CHARACTERISTICS 90
TABLE 4.2. INTERVENTION CHARACTERISTICS 92
TABLE 4.3. OUTCOME DATA FOR INDIVIDUAL STUDIES: HT USERS VERSUS NON-USERS 93

CHAPTER 5. Perspectives and Decision-Making about Menopausal Therapies in Women Who Had Bilateral Oophorectomy (BO)

TABLE 5.1. PARTICIPANTS CHARACTERISTICS 143

CHAPTER 6. Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy (BO): A Narrative Review

TABLE 6.1. SUMMARY TABLE OF STUDY CHARACTERISTICS 168
TABLE 6.2. DETAILED TABLE OF STUDY CHARACTERISTICS 169

CHAPTER 7. Developing and evaluating a patient decision aid for managing surgical menopause: The story behind the "SheEmpowers" patient decision aid

TABLE 7.1. PARTICIPANTS CHARACTERISTICS 208
TABLE 7.2. VIEWS ON ACCEPTABILITY OF SECTIONS OF THE PDA 209
TABLE 7.3. ACCEPTABILITY VIEWS ON OTHER ASPECTS OF THE PDA 210
TABLE 7.4. EVALUATION OF CONTENT AND DEVELOPMENT OF THE SHEEMPOWERS PDA AGAINST THE IPDAS QUALITY FRAMEWORK 212

LIST OF FIGURES

Chapter 1. Introduction

FIGURE 1.1. A DIAGRAM DELINEATING THE DIFFERENT PROJECTS CULMINATING INTO THE DEVELOPMENT OF A REVISED PROTOTYPE OF THE SHEEMPOWERS PDA AND FUTURE EVALUATION AND IMPLEMENTATION PLANS....10

CHAPTER 3. Evaluating the Content and Development of Decision Aid Tools for the Management of Menopause: A Scoping Review

FIGURE 3.1. FLOW CHART FOR STUDY IDENTIFICATION AND SCREENING FOR INCLUSION 51

CHAPTER 4. The Effect of Hormone Therapy on Quality of Life and Breast Cancer Risk After Risk-Reducing Salpingo-oophorectomy: A Systematic Review

FIGURE 4.1. FLOW CHART FOR STUDY IDENTIFICATION AND SELECTION 89

CHAPTER 6. Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy (BO): A Narrative Review

FIGURE 6.1. EXPLANATORY MODEL OF FACTORS CONTRIBUTING TO DECISION MAKING ABOUT HT IN SURGICALLY MENOPAUSAL WOMEN BASED ON SCIENTIFIC LITERATURE.....167

CHAPTER 7. Developing and evaluating a patient decision aid for managing surgical menopause: The story behind the "SheEmpowers" patient decision aid

FIGURE 7.1. FLOW CHART OF THE DEVELOPMENT MODEL OF THE SHEEMPOWERS PDA 206
FIGURE 7.2. FLOW CHART OF PATIENTS' RECRUITMENT 207

LIST OF APPENDICES

CHAPTER 3. Evaluating the Content and Development of Decision Aid Tools for the Management of Menopause: A Scoping Review

APPENDIX 3.1. SEARCH STRATEGY – SCOPING REVIEW OF DATS FOR MENOPAUSE....63

CHAPTER 4. The Effect of Hormone Therapy on Quality of Life and Breast Cancer Risk After Risk-Reducing Salpingo-oophorectomy: A Systematic Review

APPENDIX 4.1. SEARCH STRATEGY FOR ELECTRONIC BIBLIOGRAPHIC DATABASES....100

APPENDIX 4.2. SEARCH STRATEGY FOR GREY LITERATURE: AN UPDATE....108

APPENDIX 4.3. THE EFFECT OF HORMONE THERAPY ON QUALITY OF LIFE AND BREAST CANCER RISK AFTER RISK REDUCING SALPINGO-OOPHORECTOMY: META-ANALYSIS OF POOLED STUDIES....109

APPENDIX 4.4. FULL-TEXT SCREENING TABLE....112

APPENDIX 4.5. COMPLIANCE WITH MOOSE GUIDELINE....116

CHAPTER 5. Perspectives and Decision-Making about Menopausal Therapies in Women Who Had Bilateral Oophorectomy (BO)

APPENDIX 5.1. CHECKLIST SUMMARIZING COMPLIANCE WITH COREQ GUIDELINES....144

CHAPTER 7. Developing and evaluating a patient decision aid for managing surgical menopause: The story behind the "SheEmpowers" patient decision aid

APPENDIX 7.1. CLINICIAN STAKEHOLDERS' INVITATION LETTER....216

APPENDIX 7.2. PATIENT STAKEHOLDERS' INVITATION LETTER....217

APPENDIX 7.3. THE METHODS FOLLOWED TO IDENTIFY, SCREEN AND EVALUATE SCIENTIFIC EVIDENCE INFORMING THE CONTENT OF THE SHEEMPOWERS PDA....218

APPENDIX 7. 4. CRITERIA FOR RATING EVIDENCE OF RISK ESTIMATES REPORTED IN SHEEMPOWERS PDA BASED ON THE GRADE APPROACH FOR RATING QUALITY OF EVIDENCE AND FORMULATING RECOMMENDATIONS....220

APPENDIX 7. 5. INTERVIEW GUIDE....223

APPENDIX 7.6. ACCEPTABILITY QUESTIONNAIRE....224

APPENDIX 7.7. QUALITATIVE ANALYSIS – REVIEWER 1 (AS)....227

APPENDIX 7.8. QUALITATIVE ANALYSIS – REVIEWER 2 (TS)....234

APPENDIX 7.9. GRADE EVIDENCE TABLE FOR SURGICAL MENOPAUSE OUTCOMES WITH NO HT....267

APPENDIX 7.10. GRADE EVIDENCE TABLE FOR SURGICAL MENOPAUSE OUTCOMES WITH HT....268

APPENDIX 7.11. GRADE EVIDENCE TABLE FOR BREAST CANCER OUTCOME WITH ET....269

APPENDIX 7.12. GRADE EVIDENCE TABLE FOR BREAST CANCER OUTCOME WITH EPT....270

APPENDIX 7.13. GRADE EVIDENCE TABLE FOR CARDIOVASUCULAR OUTCOMES....271

APPENDIX 7.14. QUALITATIVE EVALUATION OF PDA BY STEERING COMMITTEE....272

APPENDIX 7.15. QUALITATIVE EVALUATION OF PDA BY STEERING COMMITTEE – SUGGESTIONS FOR IMPROVEMENT....277

CHAPTER 8. General Discussion and recommendations

APPENDIX 8.1. PDF VERSION OF THE SHEEMPOWERS PDA....315

LIST OF ABBREVIATIONS

SDM	Shared Decision-Making
PDA	Patient Decision Aids
HT	Hormone Therapy
CVD	Cardiovascular Diseases
WHI	Women's Health Initiative
RCT	Randomized Controlled Trials
VTE	Venous Thromboembolism
EPT	Estrogen-Progestogen Therapy
ET	Estrogen Therapy
HCPs	Health Care Providers
RRSO	Risk-Reducing Salpingo-oophorectomy
POF	Premature Ovarian Failure
POI	Primary Ovarian Insufficiency
BO	Bilateral Oophorectomy
ACOG	American College of Obstetrics and Gynecology
QOL	Quality of Life
BMD	Bone Mineral Density
CEE	Conjugated Equine Estrogen
ODSF	Ottawa Decision Support Framework
IPDAS	International Patient Decision Aid Standards
GRADE	Grading of Recommendations Assessment, Development and Evaluation
VCMs	Values Clarification Methods
DAT	Decision Aid Tools
CHD	Coronary Heart Diseases
MeSH	Medical Subject Headings
OHRI	Ottawa Health Research Institute
MAU	Multi-Attribute Utility Model
CHESS	Comprehensive Health Enhancement Support System
FIDM	Foundation of Informed Decision-Making
MOOSE	Meta-Analyses and Systematic Reviews of Observational Studies
VVA	Vulvovaginal Atrophy
NOS/NCOS	Newcastle-Ottawa Scale
BMI	Body Mass Index
FACT-ES	Functional Assessment of Cancer Therapy-Endocrine Score
SF-36	Short-form Health Survey
MSL	Menopause Symptoms List
MENQOL-I	Menopause-Specific Quality of Life-Intervention tool
MRS	Menopause Rating Scale
OR	Odds Ratio
HR	Hazard Ratio
SAQ	Sexual Activity Questionnaire
FSFI	Female Sexual Function index

FSDS	Female sexual Distress Scale-revised-
DXA	Dual X-ray Absorptiometry
PROSPERO	International Prospective Register of Systematic Reviews
CI	Confidence Interval
WMD	Weighted Mean Differences
LLHW	Lois Hole Hospital for Women
GNCH	Grey Nuns Community Hospital
GPs	General Practitioners
COREQ	Consolidated Criteria for Reporting Qualitative Research
OB-GYN	Obstetrics and Gynecology
ESHRE	European Society of Human Reproduction and Embryology
NAMS	North Americal Menopause Society
SOGC	Society of Obstetricians and Gynecologist in Canada
NICE	National Institute for Health and Care Excellence
AACE	Americal Association of Clinical Endocrinologists
EMAS	European Menopause and Andropause Society
SIGMA	Canadian Menopause Society
IMS	International Menopause Society

1 Chapter 1. Introduction

1.1 Rationale

"It's not hard to make decisions when you know what your values are." **Roy E. Disney**

Shared decision-making (SDM) is a widely recommended practice which recognizes the need to involve patients in health care decisions.[1] Although many conceptual definitions of SDM exist,[2] at its essence SDM is viewed as a collaborative process in which clinicians and patients share clinical and experiential knowledge when faced with decision-making about options in the context of treating, screening, or preventing a health condition.[1, 3] SDM involves more than clinicians being attentive to patient needs and concerns.[3] It demands adjustments to the asymmetrical power balance typically seen in patient-clinician interactions, in which clinicians decide on what works best for patients with minimal contribution from patients on how this aligns with their preference or what matter most to them.[3]

Involving patients in SDM depends to a great extent on having an informed patient; that is, ensuring that patients are adequately informed about options and are therefore empowered to contribute to the decision-making process.[4] Despite the growing social, legislative, and policy imperatives to adopt SDM and assist people in making health care decisions that reflect individual preferences, SDM has poor clinical implementation.[5, 6] Several barriers to effective implementation have been cited in the literature, many of which are related to health care professionals' inadequate knowledge and competency to accomplish SDM.[4, 7] Another commonly identified barrier is the lack of resources designed for patient use.[8] All patients have a right to be involved in their own health care decisions; however, not all patients are capable or willing to participate. Involving patients in their health requires the availability of objective and evidence-based tools that are relevant to the clinical situation and that can facilitate the initiation

of SDM discussions.[9] These tools should provide sufficient knowledge about available options, the associated outcomes, and other factors that patients might consider when making their decisions, including risk and benefit probabilities. An example of such tools is patient decision aids (PDAs). PDAs are powerful patient-targeted interventions for promoting and implementing SDM.[10] They help patients participate in decision-making about health care options and promote patient-centered care through integrating the best available evidence with patients' values, preferences, and expectations.[11]

PDAs are of value in situations where complex health care decisions are involved, specifically when no "single best option" exists and patients are faced with options of a comparable nature, with each option posing its own health risks and being valued differently by different people.[9] In this context, decisions are driven by patients' values and preferences.[12] When patients lack knowledge about available options and clarity of values associated with features of options, such decisions can lead to decisional uncertainty. Such is the case for women who decide on hormone therapy (HT) for managing early surgical menopause.

Early surgical menopause is menopause induced by the surgical removal of both ovaries before age 45. The clinical manifestation of surgical menopause includes an abrupt onset of severe menopausal symptoms, such as vasomotor and urogenital symptoms, sexual dysfunction, sleep disturbances, impaired concentration, mood symptoms, and a decreased sense of well-being that can greatly compromise quality of life.[13] These women often experience an extreme presentation of the symptoms that women undergoing natural menopause normally experience. Long-term manifestations include a high risk of osteoporosis, cardiovascular diseases (CVD), cognitive impairment, and premature death.[14] Many of these health consequences can be effectively managed by HT. Current practice guidelines recommend the long-term use of HT in

early menopause until the average age of menopause (51 years), when no contraindications exist.[15-17]. Yet, HT is greatly underutilized among women with early surgical menopause.[18]

Following the publication of the initial results of the Women's Health Initiative (WHI), the routine acceptance of HT among menopausal women has been challenged. The large-scaled randomized clinical trials (RCTs) that aimed to assess the long-term effects of HT in naturally, asymptomatic postmenopausal women showed an increased risk of invasive breast cancer, CVD, venous thromboembolism (VTE), and stroke with the use of the estrogen-progestogen therapy (EPT) arm.[19] These findings were accompanied by a rapid decline in HT use.[20] The results of the WHI estrogen therapy (ET) arm (women who have had a hysterectomy) showed no increased risk of breast cancer or CVD,[21, 22] but the use of HT continued to decline.[23] Even though these risks were only seen in older postmenopausal women and should not be transposed to younger age cohorts affected by early menopause, the decision to use HT is still a subject of uncertainty and fear among younger women.This fear may have been shaped primarily by the extensive negative framing of WHI findings in media coverage,[24] as well as the lack of reliable and consolidated messages about HT relayed through different communication platforms, such as media outlets and popular press.[25] While other factors may potentially contribute to poor uptake of HT among menopausal women, such as poor tolerance for side-effects,[26] presence of co-morbidity,[27, 28] and cost of therapy, [29] following the publication of the WHI, the perceived uncertainty of HT risks seems to be the major deterrent to HT use.[30]

In early surgical menopause, the complexity of decision-making about HT is essentially viewed in light of women's perceived uncertainty of the benefit-harm ratio of HT. [31] In such cases, when making therapy decisions, these women rely on subjective perceptions and inferences from sought information sources, which may trigger feelings of decisional conflict and limit their

participation in SDM about available treatment options.[32] Furthermore, women with surgical menopause often present with abrupt and severe symptomology and long-term risks, which necessitates timely and long-term access to treatment. It is likely that feelings of decisional conflict are heightened by the physical and emotional burden of early surgical menopause and the need to make a difficult decision on a short timeline due to the sudden occurrence of symptoms. In a cross-sectional telephone interview completed previously by members of our study group to identify practice patterns with HT in women who have undergone surgical menopause, the majority of women were not on HT after a surgical menopause and many were still experiencing frequent and severe vasomotor symptoms.[18] The study highlighted the suboptimal use of HT among women with surgical menopause and the need for targeted patient education to improve symptoms and long term risks management. An editorial in Maturitas emphasized the importance of our finding as follows *"It is of concern that over 2/3rd of women were not taking HT after a surgical menopause despite the majority having no contraindications. This has implications not only with the management of menopausal symptoms but also the long term health consequences of untreated early menopause..."*[33]

PDAs are powerful tools for targeted education and decision support. PDAs support adequate decision-making through making the decision involved more explicit; providing balanced, accurate, and patient-tailored information about options and their outcomes; helping patients clarify and communicate values associated with treatment options and their outcomes and building or reinforcing patient engagement skills for SDM with health care providers (HCPs). No peer-reviewed, evidence-based PDAs currently exist to support women who go through early surgical menopause.[34]

Given the complexity of therapy decisions that women with early surgical menopause face, and the paucity of decision support strategies for SDM, and building on findings from the previous cross-sectional study completed, we felt it was important to develop an evidence-based PDA to help support these women in their treatment decisions and with the long-term goal of optimizing medication use among women who go through early surgical menopause. The practice implications of such tools are of specific significance to health care professionals, particularly pharmacists being the most accessible and trusted front-line healthcare professionals, as they support women in shared, informed and value-based decision-making for optimal medication use and health outcomes.

Outline and objectives

This thesis is divided into three phases (Figure 1.1). In phase one, we searched, reviewed, and evaluated current evidence on decision aids for managing menopause and the effect of HT in a sub-population of women who go through early surgical menopause. Two review papers were completed: a scoping review summarizing the content and development of decision aids for managing menopause with a special focus on surgical menopause, and a systematic review evaluating the evidence on the safety and efficacy of HT for BRCA mutation carriers who experience early surgical menopause due to risk-reducing oophorectomy. In phase two, we explored the decision support needs of surgical menopausal women. Two studies were completed. The first was a descriptive qualitative research study that explored the process of decision-making about menopausal treatments among a sample of women who have had an early surgical menopause. The second was a narrative review completed to determine factors influencing HT uptake and decision-making among a broader sample of women with surgical menopause. In the third and final phase, findings from studies completed in phases one and two

were used to inform the development of a PDA, which was then evaluated in a cross-sectional mixed method study to elicit evidence on acceptability. Each chapter of the thesis illustrates information on the background, objectives, methods, results, and discussion of each project completed in the different phases outlined above.

A summary of the specific objectives of each of the thesis chapters are listed below:

Chapter 1. Introduction

This chapter presents the key argument behind developing a patient decision aid for surgical menopause, which is the primary objective of this thesis. It also includes an outline of the different projects involved in the thesis and an overview of the primary objectives of each project completed as part of the overarching thesis project.

Chapter 2. Background

This chapter presents information on surgical menopause, risk outcomes, management protocols, and the complexity of decision-making around HT. It provides a detailed description of PDAs, the potential benefits PDA's have in complex health care decisions, and the potential role of PDA's in surgical menopause. An explanation of best practices in the development of PDAs is also included to give readers a sense of appreciation and understanding of the content presented in the subsequent chapters.

Chapter 3. Evaluating the Content and Development of Decision Aid Tools for the Management of Menopause: A Scoping Review

This chapter discusses a scoping review completed as part of the primary phase of the thesis. The objectives of the scoping review were to identify and evaluate the development and content of decision aids used for managing menopause in the published and unpublished literature, and specifically in the context of surgical menopause. The choice to include decision aids targeting

menopause in general (as opposed to limiting the inclusion criteria to surgical menopause) was driven by prior knowledge in the field and the limited number of tools focused strictly on early surgical menopause. Also, many of the decision aids designed for menopause targeted a broad population of menopausal women, including those with early surgical menopause. Findings from the scoping review highlight the gap in knowledge around decision aids for surgical menopause and the need for decision support strategies to aid women in making therapy decisions about managing surgical menopause.

Chapter 4. The Effect of Hormone Therapy on Quality of Life and Breast Cancer Risk After Risk-Reducing Salpingo-oophorectomy: A Systematic Review

This chapter is also part of the first phase of the thesis project. It is a systematic review to evaluate the effect of HT on quality of life and breast cancer risk in BRCA mutation carriers who experience surgical menopause because of risk-reducing salpingo-oophorectomy (RRSO) for breast and ovarian cancer risk reduction. Ensuring the availability of evidence-based information about viable options and their outcomes is key to assessing the feasibility of developing a PDA for the decision of interest. Current guidelines on the use of HT for early natural and surgical menopause are available but the safety of using HT in the specific population of BRCA mutation carriers who go through surgical menopause due to RRSO is unclear. Therefore, for the systematic review the focus was on women of the high-risk population (BRCA 1 or 2 mutation carriers) who go through early surgical menopause as a result of risk reducing surgeries. These women have a higher baseline risk of breast cancer compared to non-carriers and the decision to take HT for their symptoms is greatly controversial. The results of our systematic review were used to develop the content of the PDA that targets women of the high-risk population (BRCA mutation carriers) to help guide in decision making.

Chapter 5. Perspectives and Decision-Making about Menopausal Therapies in Women Who Had Bilateral Oophorectomy (BO)

This chapter is the first project of phase two, where we explored the decisional needs of our target population. This was a descriptive qualitative research study using focus groups. The objectives of this study were to understand experiences of surgical menopause and the use of menopausal therapies for managing early surgical menopause, as well as to explore the process of decision-making about menopausal treatments in affected women. The target population was comprised of women who have had an early surgical menopause (≤45years); however, it was necessary to revise the inclusion criteria to include surgical menopause "at or below age 50" to achieve an adequate number of eligible women for the focus group study. Findings from this study were used to inform the content and design of the decision aid.

Chapter 6. Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy

To get a broader sense of the decision support needs of women with surgical menopause in different settings, the scientific literature was reviewed for relevant studies about therapy decision-making in the context of surgical menopause. To increase the sensitivity of the search and locate all relevant literature and decisional needs the inclusion criteria included studies that included both natural and surgical menopause population. This chapter includes a narrative review completed to identify and describe factors influencing the uptake of and decision-making about hormone therapy in a broader sample of women who have had surgical menopause.

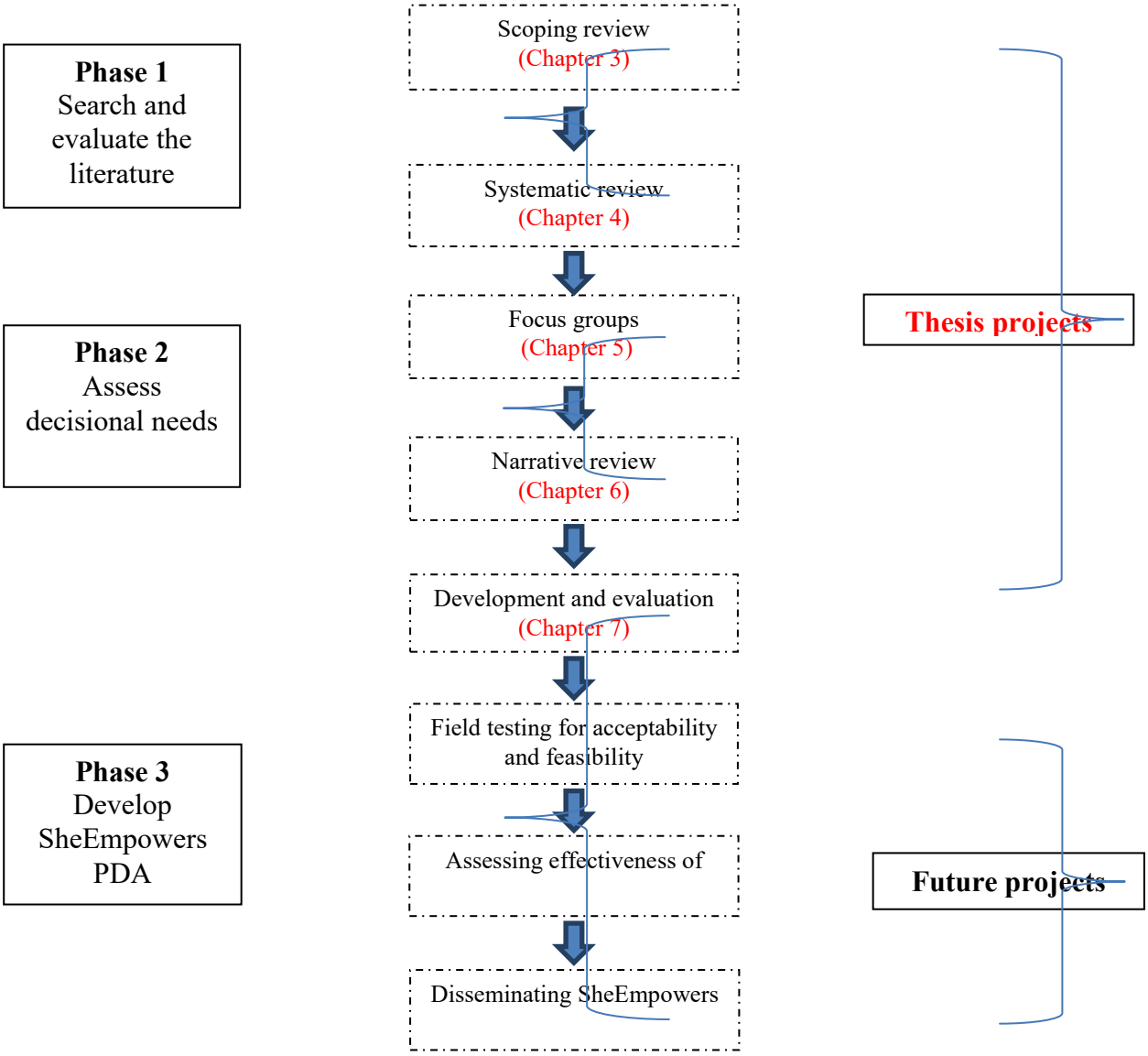
Chapter 7. Development and Evaluation of a Patient Decision Aid (PDA) for Managing Early Surgical Menopause: The Story Behind the SheEmpowers PDA

In chapter 7, the systematic approach used to develop the PDA is discussed. It includes details of the theoretical framework chosen to inform development of the PDA, as well as the characteristics of the steering committee overseeing the development process. The evaluation process for evidence of PDA acceptability is also included. Women recruited for the evaluation phase were identified from the cohort of women who have participated in the earlier focus groups.

Chapter 8. Overall summary and practice implications

This chapter summarizes the key findings of the individual chapter in the thesis and the overall conclusion of the thesis. Practice and research implications of the developed PDA for patients with early surgical menopause are discussed. The chapter ends with a discussion of future directions.

Figure 1.1. A diagram delineating the different projects culminating into the development of a revised prototype of the SheEmpowers PDA and future evaluation and implementation plans.



2 Chapter 2. Background

2.1 Natural menopause

Natural menopause is defined as the cessation of menses for 12 or more consecutive months in the absence of a pathological or surgical cause.[35] In Canada and the United States, the mean age of natural menopause is 51 years (with a range of 40-58 years).[36] The hypothalamus-pituitary-ovarian axis controls the menstrual cycle in a woman's body. As the ovaries control the menstrual changes in the endometrium, the cessation of ovarian function results in a cessation of menses.[13] Natural menopause is a gradual process involving the gradual loss of ovarian hormones as ovarian functions decline over time. Some women experience premature menopause or early natural menopause at ages well before the mean age of natural menopause.[36] Premature menopause, which is used synonymously with premature ovarian failure (POF), primary ovarian insufficiency (POI), or premature/primary ovarian dysfunction, is defined as amenorrhea, delayed or absent menarche or menopause before age 40.[37] Early menopause refers to menopause that occurs at or before the age of 45.[38]

2.2 Induced menopause: surgical menopause

Menopause can be induced before the onset of natural menopause through surgical or medical procedures. Chemotherapy and radiation therapy can both lead to damage to the ovaries and therefore a loss of their function which triggers menopausal symptoms.[39] The surgical removal of both ovaries is known as bilateral oophorectomy (BO) and almost always immediately induces menopause. This is referred to as surgical menopause.[36] BO may be performed for several reasons. It can be used as a surgical intervention for managing a malignant or benign ovarian condition.[13] It can also be performed electively at the time of a benign hysterectomy to reduce the risk of ovarian cancer.[40] In women who have a genetic predisposition for ovarian

cancer and breast cancer, BO is performed prophylactically to reduce the risk of cancer.[41] Surgical menopause may also occur inadvertently as a consequence of unilateral oophorectomy, ovarian cystectomy, hysterectomy, or uterine artery embolization.[42] Surgical menopause that occurs before age 45 is known as “early surgical menopause.”

2.3 Epidemiology of surgical menopause

BO at the time of a hysterectomy is a common procedure due to the potential benefit of reducing ovarian cancer risk, which is the leading cause of death from gynecologic cancer among women.[41, 43] However, elective BO could be undertaken for reasons other than prevention of ovarian cancer, such as to reduce the need for future gynecological procedures, particularly in women with ovarian pathologies related to endometriosis, pelvic inflammatory disease, and chronic pain.[41, 44] In the US, in the period between the year 2000 and 2010, 50% of women who had undergone a hysterectomy also had a concurrent BO. This rate was as high as 40% in women younger than 45 years.[45] In the UK, 85 to 90% of physicians recommend BO for women undergoing a hysterectomy.[46] In Canada, hysterectomy is one of the 10 most performed surgeries and the second most performed in women,[47] however no statistics are available for the rates of concurrent BO. In the last decade, indications for BO were made more stringent as women who experience early surgical menopause were shown to have an increased risk of premature morbidity and mortality.[16, 48-54] The American College of Obstetrics and Gynecology (ACOG) recommend the conservation of ovaries at the time of hysterectomy in premenopausal women without an increased risk of ovarian cancer and their removal for postmenopausal women regardless of their ovarian cancer risk.[41] For women who have a strong family history of ovarian cancer or who are carriers of BRCA mutations, prophylactic or

risk-reducing BO is recommended before age 40 for BRCA1 carriers and between the ages of 40 and 45 for BRCA2 carriers.[55]

2.4 Symptoms of surgical menopause

Surgical menopause is associated with short- and long-term health consequences. These effects are more pronounced in women who undergo the surgery before age 45.[56] Surgical menopause results in sudden and acute loss of ovarian sex hormones including estrogen, progesterone and testosterone, which often correlates with sudden and intense menopausal symptoms.[13] These symptoms include vasomotor and urogenital symptoms, sexual dysfunction, sleep disturbances, cognitive changes, mood symptoms, and a decreased sense of well-being.[57] In contrast to natural menopause, early surgical menopause is more detrimental with long-term implications, such as bone loss, cardiovascular disease (CVD), cognitive impairment, and early or premature mortaility.[14, 38]

Quality of life (QOL) can be greatly compromised in surgical menopause.[58] Ovarian sex hormones have been associated with the maintenance of normal function of several health domains pertaining to QOL, such as mental health, sexual function, body image, and general well-being.[59-62] In a prospective cohort that compared health-related QOL outcomes in premenopausal women who underwent BO to women who conserved their ovaries at the time of hysterectomy, women who underwent BO had less improvement in the mental and body image domains of health-related QOL within the first 6 months following hysterectomy.[63] Similarly, a cross-sectional study assessed body image and sexuality in women who had BO and found that satisfaction with body image was significantly poorer in the BO group compared to their non-surgical counterparts.[62]

Sexual function is an important determinant of QOL, especially in younger women.[42, 64, 65] In women, sexual function is regulated by sex hormones such as estrogen and androgens. Estrogen mediates vaginal lubrication and elasticity while testosterone promotes desire and arousal.[66] Since surgical menopause leads to a rapid and immediate loss of these hormones, sexual dysfunction is commonly experienced.[66] Several studies have shown the impact of BO on various aspects of sexual dysfunctions such as pleasure, discomfort, and habit.[64, 67-70]

2.5 Long-term risks

In the long term, early surgical menopause has been shown to increase the risk of osteoporosis, [71] cardiovascular disease (CVD), [48] cognitive impairment, [53] and premature mortality.[52].

The effect of menopause-induced estrogen loss on bone mineral density (BMD) is well established.[15] The earlier in life that estrogen loss happens, the greater the loss in BMD will be later in life.[72] Bone loss in early surgical menopause was found to be higher than natural menopause by more than two-fold.[73] In a cross-sectional study that studied the effect of age and type of menopause on BMD, early surgical menopause was associated with a lower vertebral BMD compared to natural menopause between the ages of 45 to 50.[74] Two long-term cohorts looked at fracture risk with early surgical menopause compared to natural menopause.[75, 76] One study found an increase in distal wrist fracture and vertebral fracture.[75] The other study did not find a risk increase in non-vertebral fractures after two decades of follow-up.[76]

Several studies associate surgical menopause with increased risk of CVD and CVD-related mortality.[51, 77-80] A meta-analysis by Atsma and colleagues showed an increased risk of CVD with early menopause compared to natural menopause; however, the greatest risk was seen

in women with early surgical menopause.[81] A few studies have showed a correlation between surgical menopause and several risk factors for CVD such as atherosclerosis,[82] obesity,[83] metabolic syndrome,[84] and dyslipidemia.[85] The direct effect of surgical menopause on CVD and CVD-related mortality was shown in large prospective cohorts. [51, 78] After following close to 30,000 women who had either hysterectomy or hysterectomy with concurrent BO for 28 years, Parker et al. reported that women who had an early BO and never used ET had an increased incidence of fatal and non-fatal coronary heart diseases[78] and CVD-related mortality than women who preserved their ovaries.[86] Similarly, in a long-term prospective cohort by Rivera et al, women who had early surgical menopause experienced an increased risk of CVD-related mortality.[51]

The effect of surgical menopause on cognition has been assessed in three long term studies.[53, 87, 88] Rocca et al. showed an almost doubling of long-term risk of cognitive impairment or dementia in women who underwent BO before menopause.[53] The risk of cognitive impairment and dementia increased with younger age at the time of surgery and no ET. Phung et al. also reported that women who underwent BO had an increased risk of early dementia with onset before age 50.[87]. Recently, Bove et al. showed that earlier age at surgical menopause was associated with a faster decline in global cognition, specifically in the domains of episodic memory and semantic memory and with an increased burden of Alzheimer's disease neuropathology.[88]

In long-term observational studies, early surgical menopause has been associated with increased risk of mortality.[52, 79, 86, 89] Rocca and colleagues found that BO undertaken before age 45 was associated with increased all-cause mortality.[52] Likewise, in a retrospective analysis of the English Hospital Episode Statistics Database, Mytton and colleagues showed that women who

underwent BO before age 45 had a higher risk of all-cause mortality than women who preserved their ovaries.[89]

2.6 Managing surgical menopause

Menopausal hormone therapy (HT) is the most effective treatment for menopausal symptoms,[16] and has also been shown to offset some of the long-term effects of early surgical menopause on the bones,[90] cardiovascular system,[78] cognition,[91] and survival.[52]. HT is composed of systemic ET, with or without progestogen.[17, 92] Vaginal estrogen is also available for vaginal symptoms. Estrogen only therapy is used for hysterectomized women. Combined estrogen plus progestogen therapy are for women who have a uterus. The progestogen, which is a term used to refer to both synthetic progestins and progesterone, is added to reduce the risk of estrogen-induced endometrial hyperplasia or endometrial cancer. The estrogen in commercially available HT formulations often include bio-identical forms, like 17β-estradiol and conjugated estrone sulphate. Other types of estrogen such as conjugated equine estrogens (CEE) that come from animal sources are also commercially available in various Health Canada approved HT products. HT comes in different formulations and is delivered to the body through various routes. In Canada, HT is available in the form of tablets, skin patches, creams, gels or a vaginal ring. In many HT products, the estrogen and progestogen are combined in the same product; however, they can also be taken or used separately. Doses of HT are often individualized to woman's symptom burden and tolerability.[93]

Current practice guidelines recommend long-term HT use in early menopause until the average age of menopause (51 years) in the absence of contraindications.[15-17] Yet, HT is greatly underutilized in women with surgical menopause.[18, 26, 94] In a cross-sectional chart review with telephone follow-up survey completed at an academic teaching facility in Edmonton,

Alberta, Canada, to identify current practice patterns with HT in women who have undergone surgical menopause, 40% of women were started on ET after a surgical menopause (hysterectomy and BO) and only 33% had continued taking HT post-surgery (mean of 10 months).[18] The prevalence of moderate to severe hot flashes was significantly higher among women who were not on HT.[18] Similarly, Chen et al. captured the use of ET following surgical menopause in Taiwanese women in a cross-sectional survey and found that only 31% of the women in their study population were either current or past users of ET. [26]

The acceptance of HT has been greatly challenged among menopausal women ever since the initial findings of the WHI EPT arm were published in 2002. This trial showed an increased risk of invasive breast cancer, CVD, VTE, and stroke with the use of EPT in naturally postmenopausal women (average age 63 years).[19] As a result, a drastic decline in HT use was seen worldwide.[20, 23] The results of the WHI ET arm (women who have had a hysterectomy) showed no increased risk of breast cancer or CVD, however, the rate of use of HT (both EPT and ET) continued to decline.[21, 22]

The state of confusion and controversy typically associated with HT among women and their HCPs has primarily stemmed from the extensive and inaccurate representation of the initial WHI findings in the general and scientific press.[24, 95, 96] The misleading representation of findings ensued essentially from media reports highlighting outcomes as relative risks and reporting risk outcomes for the entire studied population, rather than for separate age groups as defined in the study's own protocols, which magnified the negative perception of HT risks.[19, 96, 97] Experts in the field commented on the abrupt and poor way in which the premature termination of the EPT arm was planned, and the dramatic nature of the early announcement of findings, which together set the tone for an exaggerated media response and a confused public perception of

HT.[96, 98] Currently, the confusion is further exacerbated by the consistent lack of consolidated messages about HT risks and benefits in information sources commonly sought by menopausal women.[25] In a recent content analysis that examined information about HT in three information sources used by clinicians and patients, including medical review journal articles, physician surveys, and news media coverage, varied views about HT harms and benefits were reported.[25] This, as the authors explained, has led to limited certainty about the actual risks and benefits of HT among menopausal women and a state-of-the-science gap. A state-of-the-science-gap was described by the authors as *"a condition when the evaluation of a medical condition or therapy ascertained by the highest standards of investigation is incongruent with the science-in-practice such as physician recommendations and patient actions."* [25]

Despite the fact that risks attributed to HT were only seen in older postmenopausal women who were asymptomatic and should not be transposed to younger age cohorts with early menopause, including those with surgical menopause, the decision to use HT is still a subject of uncertainty among younger women.[31, 32, 99-101]

2.7 Hormone therapy (HT) and complex decision-making

Decision-making about menopause can be complex, given the mixed messaging with HT. Several studies have captured perspectives about HT and factors influencing treatment decision-making during menopause; however, these studies were mainly in women who experienced natural menopause.[31] Factors that influenced decision-making about HT included women socio-demographics[102-105] and psychological characteristics related to beliefs on HT and attitudes about menopause,[32, 102, 106, 107] as well as physicians' beliefs and attitudes about HT.[108] Perceived benefits and risks of HT were viewed as the strongest predictors of decision-making about HT.[30, 102] In the mid and late 1990s, perceived benefits with HT use was the

stronger predictor of decision-making. Following the release of the WHI, the role of perceived risks became more prominent.[30] In surgical menopause, decisions about HT are also driven by women's perceptions of risks and benefits. A study published after the WHI showed that close to 60% of surgical menopausal women discontinued HT due to fear of cancer. In the same study, half the women claimed they were willing to use HT if they could be convinced that its benefits outweighed the risks.[26]

As women rely on their risk-benefit perceptions of menopausal treatments for decision-making, they are often challenged by the value-laden nature of the decision to manage their menopausal symptoms.[31] Women who go through early surgical menopause are specifically challenged as they may experience severe symptoms associated with the abrupt decline in hormones and may have long-term health sequelae.

2.8 Shared decision-making (SDM)

In complex health decisions in which people associate different values and preferences with different options or features of an option, SDM ensures the provision of care is consistent with patients' preferences and values.[109] SDM is a joint process of decision-making, allowing patients and HCPs to collaborate when making health care decisions. It integrates the clinical perspective of HCPs with the experiential perspective of the patient to help patients develop informed preferences and health care decisions.[110, 111] SDM has potential benefits for patients, HCPs, and the health care system. SDM has been associated with improved patient decisional outcomes such as knowledge, engagement in decision-making, and making quality health decisions that are personalized to their values and beliefs.[112] Implementation of SDM was also shown to benefit HCPs and health care systems by reducing anxiety over the care process, providing consistency in deliverance of care, and reducing health care costs.[113, 114]

Despite these benefits, SDM has not been widely adopted in clinical practice.[5, 6] Its adoption depends to a great extent on the degree to which involved stakeholders support core principles of SDM, such as respecting patients' right of autonomy and self-determination.[4, 115] Common barriers to effective SDM implementation are mostly specific to HCPs and include lack of knowledge and skills to adopt SDM in clinical encounters, holding views that patients do not want decisional responsibility when facing difficult decisions, lack of trust or agreement with tools for promoting SDM among patients, and lack of practicality of SDM due to time demands for implementation.[6] Reported patient-specific barriers were the lack of resources for patients' use and the patients' lack of capacity to engage in SDM.[110, 116] The implementation of SDM in clinical practice can be facilitated by the use of PDAs.[117]

2.9 Patient decision aids (PDAs)

Decision aids are decision support interventions that facilitate SDM between patients and clinicians facing complex, value-laden health care decisions.[111, 118] These tools are of great value when a potential health care strategy is considered a guideline or an option as opposed to a standard of care. In such cases, the evidence about outcomes of interventions is known but there is more perceived uncertainty among patients and clinicians about the benefit-harm ratio of available options. Consequently, these decisions are mostly driven by patients' values.[12] Decision aids vary from usual health education materials in that they provide detailed and precise information on options and outcomes to prepare people for decision-making in a certain clinical context.[119] Conversely, health education materials are not decision-focused, but instead provide information for a broader purpose of helping people better understand their diagnosis, treatment, and management,[12] and therefore, do not necessarily support patients in decision-making.[120] Decision aids can target various health decisions related to screening, treatment, or

prevention.[118] Content in decision aids can be presented in booklets, audio-visuals, computers, and other formats.[121] They can be used before, during, or after a clinical encounter and target different populations of patients or HCPs.[122] Decision aids that specifically target patients are called patient decision aids (PDAs). PDAs are known as tools that *"communicate evidence on treatment options to patients in ways that encourage them to engage with their practitioners to choose an intervention that is consistent with the evidence and with their personal values."*[10] They help patients participate in decision-making about health care options and promote patient-centered care through integrating the best available scientific evidence with patients' values, preferences, and expectations.[11] These tools support effective decision-making by presenting accurate and balanced information about options and outcomes, aiding in values clarification and enhancing skills in deliberation and collaboration.[12, 123]. PDAs are not designed to direct patients towards one option over another, nor do they replace a clinician's consultation.[119] Instead, they serve to empower patients with the information, resources, and skills to manage complex decision-making.[124]. The influence PDAs can have on the quality of decisions and the decision-making process is significant.[120] In the most recent Cochrane Collaboration review to assess the effects of PDAs for people facing treatment and screening decisions, PDAs were superior to usual care in: (1) improving people's knowledge about options, (2) reducing decisional conflict related to feeling uninformed and unclear about personal values, (3) stimulating people to take a more active role in decision-making, (4) improving accuracy and comprehension of risk information, and (5) improving congruency between the chosen option and the patient's values.[120]

2.10 Role of PDAs in surgical menopause

In general, the value of PDAs is grounded on ethical and moral principles that respect rights to patients' autonomy and informed choice.[4, 115, 125] While these form reasonable grounds to support the use of PDAs in any decision context, essentially it is the complex decision involved in choosing HT to manage surgical menopause which forms the key argument behind the value of a PDA for surgical menopause. Women with surgical menopause are vulnerable and face many challenges as they decide on a suitable treatment for their symptoms. The uncertainty about the benefit-harm ratio of HT,[31] and the severe symptomology and long-term risks associated with surgical menopause which often warrant timely and long-term access to treatments are a few to mention.[14, 57] The need to rationally negotiate between competing expectations to come to a treatment decision is also a main challenge to consider.[126] These women tend to rely on their emotions and personal life experiences to develop risk perceptions which often influence their ability to logically choose between given options.[32] Making treatment decisions based on un-informed, unrealistic, and emotionally-biased risk perceptions can translate into poor decisional and patient health outcomes. In surgical menopause, a PDA can help address these challenges. It can offer decisional support in the form of educating women about facts, improving comprehension of risk information, guiding the process of rational risk trade-off, and encouraging collaboration with HCPs for SDM. This, in turn, can help women develop informed risk perceptions, and ultimately, informed and value-based treatment decisions.

PDAs for surgical menopause are lacking. In 2011, a systematic review of the effectiveness of menopausal symptoms management decision aids reported several decision aids created for managing menopause.[34] The review identified 15 trials that assessed the effectiveness of

decision aids mostly geared towards the use of HT. Decision aids targeted natural menopause and included broad indications for use, such as symptom management, prevention of heart disease, and prevention of osteoporosis. Many of the decision aids were developed prior to the WHI and the publication of International Patient Decision Aid Standards (IPDAS), and therefore had several inadequacies related to the lack of completeness and currency of evidence on presented options. None of these decision aids targeted surgical menopause.[34]

2.11 Decision aids development best practice

The science of developing PDAs is broad and warrants the careful consideration of many aspects pertaining to development. A review of best practices in developing decision aids is imperative when approaching the development of an evidence-based PDA.

2.11.1 Theoretical framework

Decision aids produce desirable effects when developed based on recognized quality criteria that avoid bias and use valid evidence sources.[118, 127] However, not all decision aids are developed with reference to theoretical frameworks.[128] In an analysis conducted to evaluate the extent to which theoretical frameworks guided decision aid development, only one-third of identified decision aids were based on theoretical frameworks.[129] Available theoretical frameworks for decision aid development include the Ottawa Decision Support Framework (ODSF);[130] Dutch Institute for Healthcare Improvement;[131] Cardiff University;[132] Informed Decision Making Foundation;[133] and Mayo Clinic.[134] These frameworks are outlined by different organizations, each presenting a development process guided mostly by theory and experiential knowledge. The models vary in comprehensiveness, with some providing more guidance and addressing more areas pertaining to development than others; however, models typically include three main elements of development: (1) scoping and design, (2)

developing a prototype, and (3) evaluating the aid for acceptability and effectiveness. A recent review provided an overview of theoretical frameworks available for decision aid developers and accordingly presented a model of a development process that aims to integrate the best of available frameworks.[128] The described process is guided by quality dimensions of the international patient decision aid standards (IPDAS) that focus on development. IPDAS is a widely accepted quality framework established in 2003. IPDAS was developed by a group of over 100 stakeholders including practitioners, researchers, patients, and policy makers from different parts of the world, through a web-based Delphi consensus and synthesis of evidence. The IPDAS goal is to enhance the quality of developing and evaluating decision aids.[127] The authors of the review explained that elements outlined in the recommended development process are pragmatic rather than evidence based.[128] In summary, decision aids should be developed in reference to a transparent and systematic development framework that aims to minimize bias and improve quality. Several frameworks are available, but most are founded on pragmatic and theoretical underpinnings. There is little empirical evidence to provide guidance on the best development frameworks. IPDAS presents one of the most comprehensive development models that aims to integrate the best of available frameworks while considering areas that are seldom addressed in current models, such as describing a distribution strategy, health literacy standards, and reviewing and synthesizing evidence on options and outcomes.

2.11.2 Theories

The use of theory to guide decision aid development is a recommended practice.[12] Theoretical underpinnings of decision aids range from traditional decision theories to intuitive choice models.[121, 135, 136] Yet, some argue that theories are abstract and do not offer much guidance on how to best present evidence to assist in knowledge gains and values

clarification.[137] In such cases, adopting guidelines and recommendations that are informed by theory and empirical evidence to aid in development can be more helpful.[127]

2.11.3 Decision aid components

For an intervention to qualify as a decision aid, Joseph-Williams and colleagues proposed a "qualifying" criteria which state that a decision aid has to describe the health condition or problem for the index decision; explicitly state the decision under consideration; describe the options available for the index decision; and describe the positive and negative features of each option to allow for values clarification.[138] Decision aids are expected to include an information section which presents details about the decision involved and relevant information on the respective health condition, available options, and associated outcomes. Besides presenting information, many aids will include a values clarification component to help patients contemplate the desirability of options within a specific decision context, as well as provide guidance in deliberation to facilitate and support a self-guided approach to the process of decision-making.[139, 140]

2.11.3.1 Presenting information

Presenting information is an important aspect to consider when developing decision aids. The competency of patients in decision-making depends to a great extent on the comprehension of presented information and development of knowledge.[120] The IPDAS recommends that information presented in decision aids be complete, up-to-date, evidence based, relevant, balanced, and evaluated for certainty.[141-143] Information presented should be gathered from up-to-date, evidence-based resources that address all valid options and are validated by patient and clinician experts for relevancy.[142, 144]

Providing a balanced presentation of information is key to enabling patients to process relevant information without bias. One way to ensure an unbiased presentation of available options is by displaying information side by side.[141] A linear presentation of health options was shown to affect patients' perceptions of the importance of options.[141, 143] Framing information on outcomes in a positive or negative context can also affect patients' perceptions of outcomes.[145] Using more than one method, such as numbers and visual depictions, to display outcome information can help reduce biases due to the framing effect. [145] Evidence on the use of visuals for outcome presentation is mixed. Visual displays like infographics or bars are perceived as easier to understand by patients.[145] However, the ability to read and comprehend visual displays depends on patients' graph literacy.[146] The graph literacy level of the target population should be carefully considered when developing a decision aid. The use of numbers to present information on outcomes is recommended over words.[145] When using numbers, the same denominator should be used across options and throughout the decision aid to help with comparisons.[145] Risks should be presented in absolute rather than relative terms, as absolute terms are easier to comprehend.[145]

To help users understand the strength of evidence and degree of confidence in outcome information that is presented, phrases, symbols, or numbers should be used to display evidence on uncertainty.[142] However, evidence on the best way to present uncertainties is unclear. The choice of tools to assess evidence on uncertainty should also be considered. An effective tool recommended by IPDAS is the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[142, 147] This approach defines quality of evidence in light of the likelihood of bias, likelihood of reporting bias, inconsistency in results across studies, imprecision in effect estimates, and the degree of applicability to the target population. GRADE

is mainly used to formulate clinical practice guidelines and has been adopted as quality assessment criteria by over 20 international organizations.[147]

In summary, evidence on the best practice to present information in a decision aid is limited. The length and method of presenting information should be tailored to present options and outcomes to the informational needs of the target population.

2.11.3.2 Personal stories

The use of personal stories in decision aids is debatable. Personal stories are shared experiences of others who have made the same health decision.[148] They are used to facilitate the communication of health information and guide patients on how to make decisions.[148] Patient stories can be presented in the form of testimonials, documentaries, scripted narratives, or interactions between patients and practitioners.[148] Cognitive learning theories support the use of personal stories in decision aids and suggest that they improve the processing and retrieval of health information by patients.[149] Yet, some concerns have been raised about the potential bias shared stories can have on patients' decisions.[148]

Patient stories can be outcome based, describing the choice made; experience based, describing the whole experience; or process based, describing the decision-making process.[149] Process-based stories are more likely to lead patients to search for more information, whereas experience-based stories help patients better imagine their health experience.[149] It is suggested that outcome-based stories should not be included in a decision aid as they may inadvertently influence patients' decisions.[149]

Patients perceive patient stories as valuable as these stories help them better comprehend factual information and better cope with the challenges they face as they make health decisions.[148]

Learning the stories of others is of particular value to patients with lower literacy. However, there is insufficient evidence on their effectiveness in a decision aid. Guidelines suggest that if patient stories are included in a decision aid, they should include stories that explore the benefits and harms of all presented options to avoid biases in information.[148, 149]

In summary, patient stories are viewed positively by patients and may aid in the comprehension of presented information. However, the type of stories and aim of presenting stories should be carefully considered so that these are not biased towards certain options, but rather reflect the full spectrum of available options.

2.11.3.3 Values clarification methods

Values clarification methods (VCMs) are defined as *"strategies that are intended to help an individual patient evaluate the desirability of options or attributes of options within a specific decision context, in order to identify which option he/she prefers."*[135] VCMs can be explicit or implicit. Explicit methods require patients to actively engage in and complete an exercise which can be completed alone or with the support of others, such as HCPs.[97] Explicit VCMs include pros and cons lists, utility assessments, and rating scales, among other methods. In implicit methods no interactive exercises are involved; values clarification is intuitively achieved through patient testimonials and descriptive stories.[135] It is unclear if explicit VCMs are superior to intuitive approaches.

Evidence on the value of VCMs in improving decision-making and decision quality is mixed.[135, 139] VCMs were shown to improve preparedness for decision-making, agreement with the decision, and decision regret.[97, 135] Similarly, patients using decision aids with VCMs were more likely to choose a treatment that was consistent with their values.[118] In contrast, VCMS were shown to confer no benefit on decisional conflict.[150, 151]

Empirical evidence to guide the development of VCMs in a decision aid are lacking.[135, 139] Data from a recent review showed that VCMs were mainly used in treatment decision contexts (46%). They were designed to be completed on paper (50%) and the majority were presented after the information section (85%). Close to 40% were developed based on a theory or framework that was different from the one informing the overarching decision aid. Most studies in the review reported the development process of VCMs, which mainly included literature reviews (42%), expert reviews (51%), or testing (80%). They also reported the individuals involved in development, which mostly included HCPs (53%), academic experts (31%), and patients (38%). The review discussed how the role of VCMs in SDM is not fully understood.

In summary, more research is required to elicit clarity on the development of VCMs and the value they contribute to a decision aid. Yet, given the empirical grounds that VCMs are not associated with worse decisional outcomes, there seems to be a consensus among decision aid developers and experts in the field on the inclusion of VCMs in decision aids. A review by Witteman et al. recommend that developers consider theory and previous designs when incorporating a VCM. The authors also recommend transparency in reporting the VCM development, design, and rationale for design choice, which will aid in developing an evidence base to guide future developers in the field.[139]

2.11.3.4 Guidance in deliberation

Guidance in deliberation is an explicit component embedded within a decision aid to facilitate and support a self-directed approach to the process of decision-making.[140] It was first introduced by ODSF to address modifiable decisional needs contributing to decisional conflict, through structuring and outlining the decision-making process and encouraging patients to communicate their informed preferences with others involved in the decision (e.g. practitioner,

family, and friends).[152] Guidance in deliberation can include one or more of the following features: (1) a systemic approach for making a decision; (2) a worksheet to help patients clarify and express their values; (3) an invitation for patients to identify questions to ask the practitioner; and/or (4) a generated summary of the patients' preferences and decisional needs that can be given to the patient and shared with others involved in the decision. These features aim to provide support in decision-making by improving patients' deliberation and communication skills, helping patients follow through on a chosen option, and managing patients' emotional distress.[140]

In a review of evidence on the use of guidance in deliberation in decision aids, 63 of 98 reviewed decision aids incorporated some sort of explicit guidance in deliberation.[140] The review showed that decision aids that included one or more elements of guidance in deliberation produced higher gains in knowledge, more realistic expectations, and greater consistency between patients' values and their chosen option.[140] However, the independent effect of explicit guidance in deliberation is lacking.

In summary, evidence on the effectiveness of various elements of guidance in deliberation is limited. However, given the potential benefit of this component on decisional outcomes, developers should consider explicitly incorporating it in a decision aid. Development should mostly be informed by theoretical frameworks, users' needs, and previous work in the field.

2.11.3.5 Other considerations

The use of plain language, disclosure of conflict of interest, and the mode of delivery are other aspects that developers should thoughtfully consider when developing a decision aid.

2.11.3.5.1 Conflict of interest

Since financial ties to organizations can influence how users perceive the quality and usefulness of a decision aid, disclosing all potential conflicts of interest is recommended.[127] Guidelines recommend that developers state explicitly and in plain language any funding or financial support received from commercial or for-profit organizations, affiliations of decision aid developers, and the loss or gain attained by developers when patients make a choice on the options.[153] Guidelines state that "*disclosure is necessary but not sufficient*" and that no funds should be received from commercial organizations that sell any of the options discussed in the decision aid.[153]

2.11.3.5.2 Mode of delivery

Decision aids can be delivered via various modes, such as paper, video, audio, computer, or smartphone applications. Evidence supporting the use of one mode over the other is lacking.[154] When deciding on the mode of delivery, developers should consider the needs of the target population, setting of use, and other factors related to the aid's dissemination and update policy.

2.11.3.5.3 Plain language

The impact decision aids can have on a patient depends on the user's health literacy. It is recommended that decision aids are written in plain language for patients across the spectrum of health literacy.[155] Consequently, guidelines recommend that information be presented at a Grade 6 to 8 reading level and evaluated for readability among patients of the target population.[155]

2.12 Conclusion

The need for a decision support intervention such as a PDA is recognized, due to the complexity of therapy decision-making around managing early surgical menopause, as well as the lack of tools and resources to help support women going through this decisional dilemma. PDA development is a rapidly growing and evolving field. Despite this, several areas in the PDA development process are yet to be informed by scientific evidence. Determining the need for a PDA is an important aspect to consider when approaching decision aid development. Developing an evidence-based PDA that poses minimal risk of bias for end users, requires following a standardized procedure that allows for transparent and systematic development. Special consideration for the decisional needs of the target population when designing the components of a PDA is key for development. As well, it should be considered to apply practices informed by evidence, expert opinion, and/or scientific consensus when addressing the presentation of information, the use of patient stories, the development of values clarification, and strategies for guidance in deliberation.

3 Chapter 3. Evaluating the Content and Development of Decision Aid Tools for the Management of Menopause: A Scoping Review[a]

Tasneem Siyam[1], BScPharm, MSc; Humirah Sultani[2], BScPharm, ACPR; Sue Ross[3], PhD; Trish Chatterley[4], MLIS; Nese Yuksel[5], BScPharm, PharmD, FCSHP, NCMP

[1]PhD candidate
Faculty of Pharmacy and Pharmaceutical Sciences
3-015 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
tsiyam@ualberta.ca

[2]Pharmacist
Tom Baker Cancer Centre
1331 29 Street NW, Calgary, AB T2N 4N2
humirah.sultani@ahs.ca

[3]Cavarzan Chair in Mature Women's Health Research
Department of Obstetrics & Gynecology
Rm 5S131 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada, T5H 3V9
Sue.Ross@albertaheatlhservices.ca

[4]Public Services Librarian
John W. Scott Health Sciences Library,
2K3.28 Walter C. Mackenzie Health Sciences Centre,
University of Alberta,
Edmonton AB, Canada, T6G 2R7
trish.chatterley@ualberta.ca

[5]Professor (corresponding author)
Faculty of Pharmacy and Pharmaceutical Sciences
3-171 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
nese.yuksel@ualberta.ca
Tel: (780)492-4442; Fax: (780)492-121

[a] T. Siyam, H. Sultani, S. Ross, T. Chatterley, N. Yuksel, Evaluating the content and development of decision aid tools for the management of menopause: A scoping review, Maturitas 106 (2017) 80-86.

3.1 Introduction

Decision-making at menopause can be complex given the variability in the risk-benefit perceptions of treatment options, such as hormone therapy (HT). The use of HT declined dramatically after the initial publication of the Women's Health Initiative (WHI) Estrogen-Progestin (EPT) trial showed an increased risk of coronary heart diseases (CHD), stroke, venous thromboembolism (VTE) and breast cancer with HT and raised concerns over its safety.[1, 2] As participants in the WHI on average were in their 60s and were not symptomatic, the same risks may not apply to younger symptomatic women.[3] Other treatment options are available for managing menopausal symptoms, however HT is the most effective treatment. In light of the controversy with HT, menopausal women are often challenged by the value-laden nature of the decision to manage their menopausal symptoms. Women who go through early surgical menopause (<45 years) are specifically challenged as they may experience severe symptoms associated with the abrupt decline in hormones and may have long-term health sequelae.

Decision aid tools (DATs) are patient-targeted interventions to help patients facing value-laden decisions. DATs are shown to be superior to standard measures in improving patients' knowledge, expectations about treatment outcomes, decision quality, shared decision-making, and decisional conflict.[4-6] DATs support shared decision-making and informed, value-based decisions when developed based on a recognized quality criteria and valid evidence sources.[7, 8] On the contrary, poorly developed DATs have the potential to cause harm and are less likely to advocate shared decision-making.[9] The International Patient Decision Aid Standards (IPDAS) provides a framework of evidence-based quality criteria that serves as a reference for developing and/or evaluating the quality of DATs.[7]

In 2011, a systematic review of the effect of menopausal symptoms management decision aids reported several DATs created for managing menopause.[10] None of these DATs targeted surgical menopause. This review highlighted several inadequacies of identified DATs mostly related to the lack of completeness and currency of evidence on presented options.[11-26] However, this review did not include the grey literature, and focused only on trials evaluating the effectiveness of DATs in menopause. We decided to undertake a scoping review which would allow us to broadly examine the extent, range and nature of research activity associated with the development of DATs for menopause to identify gaps in existing literature, with no restrictions on the type and source of studies that can be incorporated (e.g. both peer-reviewed and grey literature) as opposed to a systematic review. The objectives of our scoping review were to identify and evaluate the development and content of DATs used for managing menopause in the published and unpublished literature, and specifically in the context of surgical menopause.

3.2 Methods

We conducted a scoping review based on the stages proposed by Arksey and O'Malley for performing scoping reviews.[27] The systematic approach involved in identifying, extracting and summarizing relevant scientific evidence in scoping reviews reduces the risk of introducing bias during any of these steps.

3.2.1 Eligibility criteria

Studies on the development and evaluation of DATs for managing natural or surgical menopause, with no restriction to the target population of women or treatment modalities discussed in the DAT were eligible for inclusion. Unpublished DATs for managing menopause, found in the grey literature also qualified for inclusion. We excluded: review papers; studies on

DATs created for conditions other than menopause management; studies on determinants or predictors of decisions; and studies published in languages other than English.

3.2.2 Data sources

A systematic literature search was conducted by a librarian (TC) to identify all relevant published and unpublished studies. We searched electronic bibliographic databases including: Ovid MEDLINE (1946 to March 2017), Ovid EMBASE (1974 to March 2017), CINAHL (inception to March 2017), Ovid PsycINFO (1806 to March 2017), and HAPI (1985 to October 2015), to identify studies reporting the development of DATs for managing surgical or natural menopause (Appendix 3.1). Grey literature[b] searches were conducted in SCOPUS, ProQuest Dissertations and Theses, and Google web from inception to March 2017. Search terms were searched as MeSH headings or keywords and were derived from two main concepts: menopause and DATs. We hand searched reference lists of relevant review papers and relevant articles for additional studies. We limited our search to English language and human.

3.2.3 Selection process

Search results from relevant sources were exported to one RefWorks account and close duplicates were removed. Eligibility screening was completed independently by two reviewers (HS and LM) and disagreements were resolved by a third investigator (TS). Titles and abstracts were initially screened, followed by full-text review of articles to confirm eligibility.

3.2.4 Data extraction and synthesis

Data extraction was completed by two independent reviewers (HS and LM) and discrepancies were resolved by a third reviewer (TS). Data extracted included: manuscript characteristics, population characteristics, DAT characteristics and data on DATs content and development

[b] Grey literature refers to unpublished efforts or materials produced outside the context of traditional commercial or academic publishing channels (e.g. government reports, conference proceedings, policy documents, theses and dissertations, newsletters, magazine articles, unpublished manuscripts, etc.)

evaluation in reference to the IPDAS quality checklist.[7] We chose the IPDAS checklist as a judging criteria because it is comprehensive, evidence-based and developed by an international collaboration of experts in the field of DATs. IPDAS has also been used as a quality reference in several systematic reviews,[28, 29] and is currently embraced as a DAT evaluation criteria by the Ottawa Health Research Institute (OHRI). The OHRI aims at educating the public about DATs and promotes their use in different health decision contexts.[30] The IPDAS criteria address three dimensions of quality: content, development and effectiveness. Since DAT effectivness was previously addessed by Carpenter et al, our scoping review focuses on the content and development dimensions.[10] Each DAT was evaluated with respect to four content quality criteria including: 1) provides information about options in sufficient detail for decision making; 2) presents probabilities of outcomes in an unbiased and understandable way; 3) includes methods for clarifying and expressing values; and 4) includes structured guidance in deliberation and communication. Development was evaluated with respect to five development quality criteria: 1) presents information in a balanced manner; 2) has a systematic development process; 3) includes up to date scientific evidence that is cited in a reference section or technical document; 4) discloses conflicts of interest; and 5) uses plain language. Descriptive analysis was used to describe the evaluation of the content and development of DATs. Peer-reviewed and grey literature were discussed separately. To determine the qualifying and certifying potential of identified DATs we screened them against features of qualification and certification as proposed by Joseph-Williams et al.[31] The proposed "qualifying" criteria for an intervention to qualify as a decision aid included: describes health condition or problem for which index decision is required; explicitly states decision under consideration; describes the options available for the index decision; and describes the positive and negative features of each option. Additionally, the

following DAT "certified" criteria were proposed to prevent harm to a patient: shows the negative and positive features of options in equal detail; provides citations to the evidence selected; provides a production/ publication date; provides an update policy; provides information about the levels of uncertainty around event or outcome probabilities; and provides the funding source used for development. Each DAT must meet all the proposed criteria to be classified as "qualified" and "certified".

3.3 Results

The results of our search and screening process are included in Figure 3.1. Our search yielded 18,801 records, of which 44 full-text records were retrieved and assessed for eligibility. Of these, 26 were included in the review. Twenty articles were located in the peer-reviewed literature which discussed 12 unique DATs. The remaining 6 records were found in the grey literature each representing a unique DAT.

Table 3.1 lists the main characteristics of peer-reviewed articles discussing DATs for managing menopause. Articles were mainly from the US (55%), and Canada (40%). The majority were evaluation studies (85%), of which 88% were randomized controlled trials (RCTs). Only 3 of the studies were on DAT development and included data on evaluation.[14, 32, 33] Over 50% were published before the WHI publication, and 70% published before the release of IPDAS. All studies focused on natural menopause. One study targeted menopausal women with disabilities.[19] The age range of women across studies was 40-75 years and the mean sample size was 177 (range 24-463) (Table 3.2).

3.3.1 DATs characteristics

Characteristics of peer-reviewed and grey literature DATs are summarized in Table 3.3 and 3.4, respectively.

Twelve unique DATs were identified from the peer-reviewed literature. None targeted women with surgical menopause. All DATs were patient-targeted interventions for women who had natural peri- or post menopause. The majority were developed to be administered before consultation with a health care provider (75%). Close to 60% were computer/web-based interventions, and 42% were paper-based. Most DATs discussed only HT as a treatment option (83%), and half were informed by the Ottawa Decision Support Framework (ODSF).

Six DATs were found in grey literature.[34-39] Of these, four were developed for natural menopause, one for both natural and surgical menopause,[39] and one for surgical menopause only.[37] All 6 DATs targeted patients, and four were developed for prior consultation use.[35-38] All DATs were web/computer or smart-phone-based. All DATs in the grey literature were developed post-WHI and IPDAS except one.[38] Four of the DATs focused primarily on HT as a treatment modality.

3.3.2 DAT content evaluation

Table 3.5 describes the results of DATs' content evaluation.

Peer-reviewed DATs met most items listed under the quality criterion for "providing information in sufficient details for decision-making", yet only one-third included the option of doing nothing.[12, 18, 22, 26] Only a few DATs met several aspects of the criterion about "presenting probabilities of outcomes in an unbiased and understandable way".[20, 22, 25, 26] In the criterion for "methods for clarifying and expressing values," less than half described the procedures & outcomes to help patients imagine the physical, emotional and social effects of the option for values clarification.[14, 17, 20, 25, 26] The criterion for "structured guidance in deliberation and communication" included very few DATs that explicitly presented the steps involved to make a therapy decision to support guidance in deliberation (17%).[12, 14]

On a similar note, most DATs found in the grey-literature met several items under criteria for "providing information in sufficient details for decision-making", "methods for clarifying and expressing values" and "structured guidance in deliberation and communication". Yet, almost all failed to report many items for "presenting probabilities of outcomes".[35-37, 39]

3.3.3 DAT development evaluation

Table 3.6 summarizes the results of DATs' development evaluation. For peer-reviewed DATs, only 3 reported the full development process of the corresponding DAT.[14, 32, 33] Less than half of DATs performed a needs assessment to identify the decisional needs of their target population and their health providers.[12, 14, 20, 22, 25] Only one DAT was field tested with practitioners.[15] None of the DATs reported the steps involved in finding, appraising and summarizing the scientific evidence included in DAT. Similarly, none reported how often the tool is updated.

Several quality features of development were lacking in DATs found in the grey literature. For example, all DATs failed to report steps for finding and appraising scientific data, and evidence on needs assessments and field-testing were lacking for all identified DATs.

3.3.4 Qualification and certification standards of DATs from grey literature

Table 3.7 summarizes the results of DATs screening for qualification and certification. Of the 6 available DATs, only 3 met all qualification standards and therefore were classified as "qualified" DATs. However, none of the DATs were considered "certified" and fully met the proposed certification criteria. It's important to note that only 6 DAT's were available for us to evaluate and these were all from grey literature. None of the DATs from the peer review literature were available for review, as these were not published with the development or evaluation trials.

3.3.5 Effectiveness trials of DATs

The most common study design for assessing the effectiveness of DATs was an RCT (88%). Prevalent outcomes captured in these peer-reviewed evaluation studies include: decisional conflict (68%), knowledge (58%), decisional satisfaction (52%), accuracy of risk expectations (32%), DAT acceptability (16%) and decisional confidence (16%). The efficacy of DATs in terms of improving these decisional outcomes varied across studies. Many showed significant improvements from baseline with respect to several decisional outcomes. However, fewer showed significant improvements when compared to alternative procedures (e.g. standard care). Evaluating the effectiveness of DATs was beyond the scope of this review.

3.4 Discussion

We report that among the 18 DATs identified from the peer-reviewed and grey literature, only one DAT focused on surgical menopause and one targeted natural and surgical menopause. Both of these DATs were found in the grey literature.[37] Overall, the highest quality criteria for DATs was in content evaluation such as providing information about HT and menopause and including explicit methods for values clarification. Yet, several limitations were identified. Very few studies reported the full development of the DAT involved, and less than half of DATs were informed by a needs assessment to identify the decisional needs of their target population. Most DATs primarily focused on HT as a treatment option and did not provide a comprehensive account of all other options. None of the DATs reported the steps involved in finding, appraising and summarizing scientific content of the tool and only two reported how often the DAT is updated.[36, 37]

DATs for surgical menopause were only found in the grey literature with no published evidence of development and evaluation.[37, 39] These DATs lacked several measures of quality related

to the presentation of outcome probabilities and/or the quality of scientific evidence informing content. Also, there were no reports that the tools' development was informed by a needs assessment. In terms of qualification and certification, one tool did not qualify as a DAT, and both tools were not "certified" and may potentially pose a risk of harmful bias. While these standards are fairly new and have not been validated, they still suggest that available DATs for surgical menopause may not be adequate for use by patients.

More than half of published DATs were published before the WHI and have not been updated since. These DATs do not reflect recent evidence and recommendations on HT. Even the DATs published after the WHI are now at least 7 years old and may not align with current treatment guidelines. None of the identified DATs reported criteria of updating the DAT and only 1 published DAT reported the date of last update. Another factor to consider is the lack of information on the clinical uptake of these DATs. Despite established benefits of DATs in general including knowledge gains by patients and improvement in the quality of decision and decision-making, it has been shown that DATs are often poorly adopted in clinical settings.[40] In our review, none of the identified reports discussed dissemination and implementation plans to promote clinical utilization. Strategies to implement and evaluate DATs into routine clinical setting should be considered. For example, health providers' knowledge, attitudes and behaviors toward DATs have been identified as barriers to successful implementation in clinical settings.[41-43] One approach to overcome this barrier and improve clinical relevance is to involve health care providers during the DAT development. Additionally, health providers' views and interest in adopting tools into a clinical setting need to be considered.

Similar to the review by Carpenter et al, we found that none of the identified DATs discussed a full range of available menopausal treatment options or resources to allow for an informed value-

based treatment decision.[11] Most tools focused only on HT decision making and very few included other available treatment options. Furthermore, many tools did not provide a clear presentation of HT outcome probabilities. To help women make informed preferences and therefore informed decisions, it is important to clearly present them with all valid options and their subsequent risks and benefits. The length, depth and form of information presented should be informed by a needs assessment on the population of choice and their respective health providers.

To our knowledge this is the first scoping review to evaluate the quality of content and development of DATs for managing menopause. Our search strategy was comprehensive and aimed to target both published and unpublished work in the field. We also followed a strict process to reduce the risk of inaccuracy and bias in articles screening, data extraction and evaluation. A few limitations should be noted. Very few studies reported the development of a DAT, therefore most of the data on development was based on what was reported in the evaluation trials which may have not included a detailed account of the tool's development. Since most were developed before the IPDAS the need to transparently disclose the systematic process of the tools' development may not have been recognized. Similarly, many of the DATs from the peer-reviewed literature were inaccessible and therefore certain features, such as disclosure of conflict of interests, developers' credentials or qualifications, and references to evidence used, may not have been accurately captured from supporting documents. However, we were able to evaluate most other features that were included in the published reports. We also limited our search to English language. Findings from our review may have also been affected by publication bias due to the tendency of publishing interventions with significant findings. To

reduce the possible influence of publication bias in our study, we searched the grey literature for unpublished work.

3.5 Conclusion

Our scoping review has identified limitations in the quality of available DATs for menopause that may affect the decisional effectiveness as well as clinical utility of the DAT. This review especially highlighted the lack of DATs addressing the complex decision involved with managing surgical menopause and its long-term implications. Essentially, a tool to help women suffering from symptoms with surgical menopause should be considered.

3.6 References

[1] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, J. Ockene, Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial, JAMA 288(3) (2002) 321-33.

[2] J.J. Hillman, I.H. Zuckerman, E. Lee, The impact of the Women's Health Initiative on hormone replacement therapy in a Medicaid program, J Womens Health (Larchmt) 13(9) (2004) 986-92.

[3] A.F. Pinkerton J, Blake J, Cosman F, Hodis H, Hoffstetter S, Kaunitz A, et al, The 2017 hormone therapy position statement of The North American Menopause Society, Menopause 24 (2017) 1-26.

[4] A.M. O'Connor, D. Stacey, V. Entwistle, H. Llewellyn-Thomas, D. Rovner, M. Holmes-Rovner, V. Tait, J. Tetroe, V. Fiset, M. Barry, J. Jones, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev (2) (2003) CD001431.

[5] S. Molenaar, M.A. Sprangers, F.C. Postma-Schuit, E.J. Rutgers, J. Noorlander, J. Hendriks, H.C. de Haes, Feasibility and effects of decision aids, Med Decis Making 20(1) (2000) 112-27.

[6] C. Estabrooks, V. Goel, E. Thiel, P. Pinfold, C. Sawka, I. Williams, Decision aids: are they worth it? A systematic review, J Health Serv Res Policy 6(3) (2001) 170-82.

[7] G. Elwyn, A. O'Connor, D. Stacey, R. Volk, A. Edwards, A. Coulter, R. Thomson, A. Barratt, M. Barry, S. Bernstein, P. Butow, A. Clarke, V. Entwistle, D. Feldman-Stewart, M. Holmes-Rovner, H. Llewellyn-Thomas, N. Moumjid, A. Mulley, C. Ruland, K. Sepucha, A. Sykes, T. Whelan, Developing a quality criteria framework for patient decision aids: online international Delphi consensus process, BMJ 333(7565) (2006) 417.

[8] D. Stacey, F. Legare, N.F. Col, C.L. Bennett, M.J. Barry, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, J.H. Wu, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev 1 (2014) CD001431.

[9] A. Coulter, D. Stilwell, J. Kryworuchko, P.D. Mullen, C.J. Ng, T. van der Weijden, A systematic development process for patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S2.

[10] J.S. Carpenter, J.L. Studts, M.M. Byrne, A systematic review of menopausal symptom management decision aid trials, Maturitas 69(1) (2011) 11-21.

[11] J.S. Carpenter, M.M. Byrne, J.L. Studts, Factors related to menopausal symptom management decisions, Maturitas 70(1) (2011) 10-5.

[12] F. Legare, S. Dodin, D. Stacey, A. Leblanc, S. Tapp, Patient decision aid on natural health products for menopausal symptoms: randomized controlled trial, Menopause Int 14(3) (2008) 105-10.

[13] P. Menard, D. Stacey, F. Legare, K. Woodend, Evaluation of a natural health product decision aid: a tool for middle aged women considering menopausal symptom relief, Maturitas 65(4) (2010) 366-71.

[14] A.M. O'Connor, P. Tugwell, G.A. Wells, T. Elmslie, E. Jolly, G. Hollingworth, R. McPherson, H. Bunn, I. Graham, E. Drake, A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation, Patient Educ Couns 33(3) (1998) 267-79.

[15] F. Legare, A.M. O'Connor, I.D. Graham, G.A. Wells, M.J. Jacobsen, T. Elmslie, E.R. Drake, The effect of decision aids on the agreement between women's and physicians' decisional conflict about hormone replacement therapy, Patient Educ Couns 50(2) (2003) 211-21.

[16] H.D. Clark, A.M. O'Connor, I.D. Graham, G.A. Wells, What factors are associated with a woman's decision to take hormone replacement therapy? Evaluated in the context of a decision aid, Health Expect 6(2) (2003) 110-7.

[17] A. Rostom, A. O'Connor, P. Tugwell, G. Wells, A randomized trial of a computerized versus an audio-booklet decision aid for women considering post-menopausal hormone replacement therapy, Patient Educ Couns 46(1) (2002) 67-74.

[18] T.J. Deschamps MA, Neubauer SL, Whitings S, Green K, Impact of pharmacist consultation versus a decison aid on decision making regarding hormone replacement therapy., Int J Pharm Pract (12) (2004) 21-8.

[19] H. Becker, A.K. Stuifbergen, S.L. Dormire, The effects of hormone therapy decision support for women with mobility impairments, Health Care Women Int 30(9) (2009) 845-54.

[20] L.A. Bastian, C.M. McBride, L. Fish, P. Lyna, D. Farrell, I.M. Lipkus, B.K. Rimer, I.C. Siegler, Evaluating participants' use of a hormone replacement therapy decision-making intervention, Patient Educ Couns 48(3) (2002) 283-91.

[21] M.L. Rothert, M. Holmes-Rovner, D. Rovner, J. Kroll, L. Breer, G. Talarczyk, N. Schmitt, G. Padonu, C. Wills, An educational intervention as decision support for menopausal women, Res Nurs Health 20(5) (1997) 377-87.

[22] N.F. Col, L. Ngo, J.M. Fortin, R.J. Goldberg, A.M. O'Connor, Can computerized decision support help patients make complex treatment decisions? A randomized controlled trial of an individualized menopause decision aid, Med Decis Making 27(5) (2007) 585-98.

[23] E. Murray, H. Davis, S.S. Tai, A. Coulter, A. Gray, A. Haines, Randomised controlled trial of an interactive multimedia decision aid on hormone replacement therapy in primary care, BMJ 323(7311) (2001) 490-3.

[24] B.G. Saver, D. Gustafson, T.R. Taylor, R.P. Hawkins, N.F. Woods, S. Dinauer, S. Casey, A. MacLaren-Loranger, A tale of two studies: the importance of setting, subjects and context in two randomized, controlled trials of a web-based decision support for perimenopausal and postmenopausal health decisions, Patient Educ Couns 66(2) (2007) 211-22.

[25] M.M. Schapira, M.A. Gilligan, T. McAuliffe, G. Garmon, M. Carnes, A.B. Nattinger, Decision-making at menopause: a randomized controlled trial of a computer-based hormone therapy decision-aid, Patient Educ Couns 67(1-2) (2007) 100-7.

[26] M. Holmes-Rovner, J. Kroll, D.R. Rovner, N. Schmitt, M. Rothert, G. Padonu, G. Talarczyk, Patient decision support intervention: increased consistency with decision analytic models, Med Care 37(3) (1999) 270-84.

[27] H. Arskey, L. O'Malley, Scoping studies: towards a methodological framework, International Journal of Social Research Methodology 8(1) (2005) 19-32.

[28] D. Stacey, C.L. Bennett, M.J. Barry, N.F. Col, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, F. Legare, R. Thomson, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev (10) (2011) CD001431.

[29] A.M. O'Connor, C. Bennett, D. Stacey, M.J. Barry, N.E. Col, K.B. Eden, V. Entwistle, V. Fiset, M. Holmes-Rovner, S. Khangura, H. Llewellyn-Thomas, D.R. Rovner, Do patient decision aids meet effectiveness Criteria of the international patient decision aid standards collaboration? A systematic review and meta-analysis, Medical Decision Making 27(5) (2007) 554-574.

[30] The Ottawa Hospital Research Institute. Patient Decision Aids. https://decisionaid.ohri.ca/eval.html (accessed 26.08.2016). https://decisionaid.ohri.ca/eval.html. (Accessed August 26, 2016.

[31] N. Joseph-Williams, R. Newcombe, M. Politi, M.A. Durand, S. Sivell, D. Stacey, A. O'Connor, R.J. Volk, A. Edwards, C. Bennett, M. Pignone, R. Thomson, G. Elwyn, Toward Minimum Standards for Certifying Patient Decision Aids: A Modified Delphi Consensus Process, Med Decis Making 34(6) (2014) 699-710.

[32] M.M. Schapira, M.A. Gilligan, T.L. McAuliffe, A.B. Nattinger, Menopausal hormone therapy decisions: insights from a multi-attribute model, Patient Educ Couns 52(1) (2004) 89-95.

[33] F. Legare, D. Stacey, S. Dodin, A. O'Connor, M. Richer, F. Griffiths, A. LeBlanc, J.L. Rousseau, S. Tapp, Women's decision making about the use of natural health products at menopause: a needs assessment and patient decision aid, J Altern Complement Med 13(7) (2007) 741-49.

[34] H. Currie, Menopause Matters. Decision Tree. http://www.menopausematters.co.uk/tree.php (accessed 14.12.2016).

[35] Mayo Clinic Staff. Hormone therapy: Is it right for you? http://www.mayoclinic.org/diseases-conditions/menopause/in-depth/hormone-therapy/art-20046372 (accessed 10.02.2017).

[36] Healthwise Staff. Menopause: Should I Use Hormone Therapy (HT)? https://www.healthwise.net/cochranedecisionaid/Content/StdDocument.aspx?DOCHWID=aa114076. (accessed 14.12.2016).

[37] Healthwise staff. Hysterectomy and Oophorectomy: Should I Use Estrogen Therapy? https://www.healthwise.net/cochranedecisionaid/Content/StdDocument.aspx?DOCHWID=tn9713 (accessed 14.12.2016).

[38] D.N. Kerner, Impact of a decision aid videotape on young women's attitudes and knowledge about hormone replacement therapy, Clinical Psychology, University of California, San Diego, 1998, p. 180.

[39] J.E. Manson, J.M. Ames, M. Shapiro, M.L. Gass, J.L. Shifren, C.A. Stuenkel, J.V. Pinkerton, A.M. Kaunitz, D.T. Pace, R. Kagan, P.F. Schnatz, S.A. Kingsberg, J.H. Liu, H. Joffe, G. Richard-Davis, S.R. Goldstein, I. Schiff, W.H. Utian, Algorithm and mobile app for menopausal symptom management and hormonal/non-hormonal therapy decision making: a clinical decision-support tool from The North American Menopause Society, Menopause 22(3) (2015) 247-53.

[40] G. Elwyn, I. Scholl, C. Tietbohl, M. Mann, A.G. Edwards, C. Clay, F. Legare, T. van der Weijden, C.L. Lewis, R.M. Wexler, D.L. Frosch, "Many miles to go ...": a systematic review of

the implementation of patient decision support interventions into routine clinical practice, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S14.

[41] D.L. Frosch, K.J. Singer, S. Timmermans, Conducting implementation research in community-based primary care: a qualitative study on integrating patient decision support interventions for cancer screening into routine practice, Health Expect 14 Suppl 1 (2011) 73-84.

[42] S. Feibelmann, T.S. Yang, E.E. Uzogara, K. Sepucha, What does it take to have sustained use of decision aids? A programme evaluation for the Breast Cancer Initiative, Health Expect 14 Suppl 1 (2011) 85-95.

[43] D. Stacey, S.K. Chambers, M.J. Jacobsen, J. Dunn, Overcoming barriers to cancer-helpline professionals providing decision support for callers: an implementation study, Oncol Nurs Forum 35(6) (2008) 961-9.

Figure 3.1. Flow chart for study identification and screening for inclusion

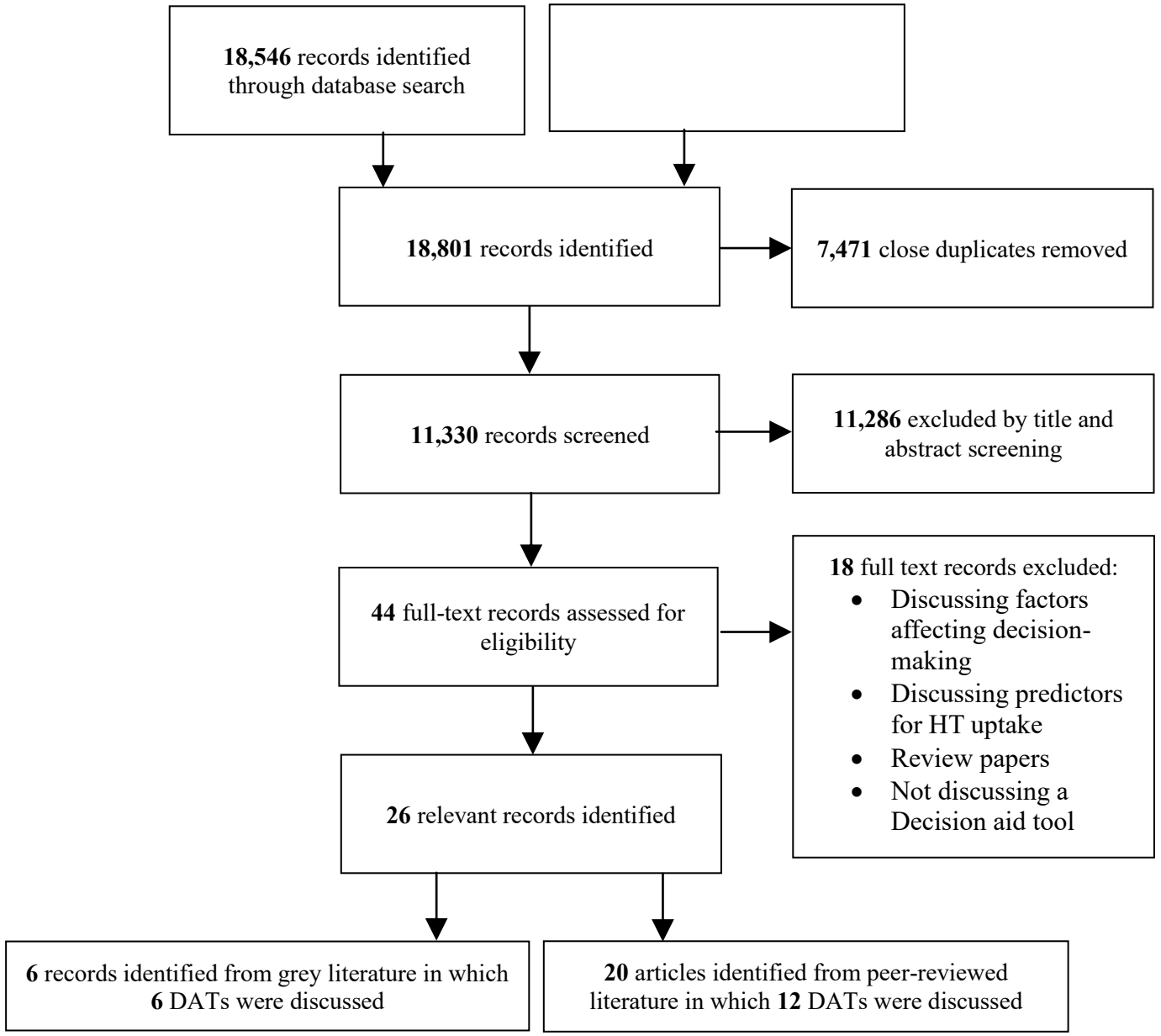


Table 3.1. Manuscript Characteristics (Peer-reviewed articles)

Manuscript Characteristic	**N (%)** **(N = 20)**
Year of Publication	
1995-1999	4 (20%)
2000-2004	8 (40%)
2005-2009	7 (35%)
2010-2014	1 (5%)
Country of origin	
USA	11 (55%)
Canada	8 (40%)
UK	1 (5%)
Setting of recruitment	
Community-based	6 (30%)
Clinic Based	10 (50%)
Both	4 (20%)
Study design	
Development & evaluation	3(15%)
Qualitative (Focus groups)	2 (67%)
Decision analysis model	1 (33%)
Evaluation only	17 (85%)
RCT	15 (88%)
Other (e.g. pre-post)	2 (12%)
Timing of study relative to WHI	

Before	11 (55%)
During/After	5 (25%)
Unknown	4 (20%)
Timing of study relative to IPDAS	
Before	14 (70%)
After	3 (15%)
Unknown	3 (15%)

Table 3.2. Population Characteristics (Peer-reviewed articles)

Population Characteristic	**N (%) or mean** **(N = 20)**
Age Range	40 – 75 years
Average Sample size	177 (Range 24-463)
Type of menopause	
Natural (Peri and/or post)	19 (95%)
Natural and surgical	1 (5%)
Special population	
Mobile disability	1(5%)

Table 3.3. DAT Characteristics (Peer-reviewed literature)

DAT Characteristic	**N (%)** **N = 12**
Target population	
Patient	11(92%)
Patient and clinician	1 (8%)
Nature of DAT	
Paper based/paper +audio	5 (42%)
computer-based/web-based	7 (58%)
Decision coach with aid	1 (8%)
Treatment modality presented	
HT	10 (83%)
HT and other available menopausal treatments	1 (8%)
Natural health products	1 (8%)
Timing of administration	
Prior to consultation	9 (75%)
Prior and during consultation	3 (25%)
Theoretical framework informing development [a]	
Ottawa decision support framework (ODSF)	6 (50%)
Decision analysis risk model (e.g. Markov model and multi-attribute utility (MAU) model)	4 (33%)
International Patient Decision-Aid Standards (IPDAS)	1 (8%)
Comprehensive Health Enhancement Support System (CHESS)	1 (8%)
Foundation for Informed Medical Decision Making	1 (8%)

[a]An aid can have more than 1 informing theory, hence proportions do not add up to 100

Table 3.4. DAT characteristics (Grey Literature)

DAT Characteristic	**N (%)** **N = 6**
Target population	
Natural	4 (67%)
Natural and surgical	1 (17%)
Surgical only	1 (17%)
Timing of DAT update relative to WHI	
Post	5 (83%)
Pre	1 (17%)
Timing of DAT update relative to IPDAS	
Post	5 (83%)
Pre	1(17%)
Target population	
Patient	5 (83%)
Patient and clinician	1 (17%)
Nature of DAT	
Web-based	4 (67%)
Tablet/mobile application	1 (17%)
Video-based	1 (17%)
Treatment modality presented	
HT	4 (67%)
HT and other available menopausal treatments	2 (33%)
Timing of administration	
Prior to consultation	4 (67%)

Prior and during consultation	2 (33%)
Theoretical framework informing development [a]	
Ottawa decision support framework (ODSF)	2 (33%)
International Patient Decision-Aid Standards (IPDAS)	2 (33%)
Foundation of informed decision-making (FIDM)	1 (17%)

[a]An aid can have more than 1 informing theory, hence proportions do not add up to 100%)

Table 3.5. DAT content evaluation based on IPDAS quality criteria

Content Criterion	**N(%) N = 12 (Peer-reviewed)**	**N(%) N = 6 (Grey-literature)**
Provide information about options in sufficient detail for decision making		
Describes the condition	9 (75%)	5 (83%)
List the treatment options	12 (100%)	6 (100%)
List the option of doing nothing	4 (33%)	4 (67%)
Describes the natural course	8 (67%)	5 (83%)
Describes positive features	11 (92%)	6 (100%)
Describes negative features	12 (100%)	6 (100%)
Include chances of positive and negative outcomes	7 (58%)	2 (33%)
Present probabilities of outcomes in an unbiased and understandable way		
Use event rates specifying the population & time period	4 (33%)	2 (33%)
Compare outcome probability using the same denominator & time period	4 (33%)	2 (33%)
Describe uncertainty around probabilities	4 (33%)	0 (0%)
Use visual diagrams	7 (58%)	2 (33%)
Use multiple methods to view probabilities	5 (42%)	2 (33%)
Allow a patient to select a way of viewing probabilities	3 (25%)	1 (17%)
Allow a patient to view probabilities based on their own situation	9 (75%)	0 (0%)
Place probabilities in context of other events	8 (67%)	3 (50%)
Use both positive and negative frames	5 (42%)	2 (33%)
Include methods for clarifying and expressing values		
Describe the procedures & outcomes to help patients	5 (42%)	4 (67%)

Ask patient to consider which positive or negative features matter most	8 (67%)	5 (83%)
Suggest ways for patients to share what matters most with others	8 (67%)	4 (67%)
Include structured guidance in deliberation and communication		
Provide steps to make a decision	2 (17%)	2 (33%)
Suggest ways to talk about the decision with a health professional	7 (58%)	6 (100%)
Include tools [worksheet, question list] to discuss options with others	10 (83%)	4 (67%)

Table 3.6. DAT development evaluation based on IPDAS quality criteria

Development Criterion	**N(%) N = 12 (Peer-reviewed)**	**N(%) N = 6 (Grey-literature)**
Present information in a balanced manner		
Able to compare positive or negative features of options	8 (67%)	6 (100%)
Shows negative/positive features with equal detail	1 (8%)	4 (67%)
Have a systematic development process		
Include developers' credentials or qualifications	12 (100%)	5 (83%)
Finds out what users need to discuss options	5 (42%)	0 (0%)
Peer reviewed by patients and experts in the field	9 (75%)	3 (50%)
Field tested with users (patients and/or practitioners)	12 (100%)	0 (0%)
Use up to date scientific evidence that is cited in a reference section or technical document		
Provides references to evidence used	6 (50%)	5 (83%)
Report steps to find, appraise, summarize evidence	0 (0%)	0 (0%)
Report date of last update	1 (8%)	4 (67%)
Report how often patient decision aid is updated	0 (0%)	2 (33%)
Describe the quality of scientific evidence	2 (17%)	1 (17%)
Uses evidence from studies of patients similar to those of target audience	5 (42%)	4 (67%)
Disclose conflicts of interest		
Report source of funding to develop and distribute the patient decision aid	10 (83%)	3 (50%)
Report whether authors of decision aid stand to gain or lose by choices made by patients using decision aid tool	4 (33%)	5 (83%)

Use plain language		
Written at a level that can be understood by majority of patients	7 (58%)	5 (83%)
Written at grade 8 equivalent or less	6 (50%)	0 (0%)
Provide ways to help patients understand information other than reading	7 (58%)	1 (17%)

Table 3.7. Results of qualification and certification screening of identified DATs from grey literature

Dimension	Item		1	2	3	4	5	6	Total number of DATs fulfilling the criterion (N = 6) N(%)
Qualifying Criteria									
Information	1	DAT describes health condition or problem for which index decision is required		x	x	x	x	x	5 (83%)
	2	DAT explicitly states the decision that needs to be considered (index decision)		x	x		x		3 (50%)
	3	DAT describes the options available for the index decision	x	x	x	x	x	x	6 (100%)
	4	DAT describes the positive features (benefits/advantages) of each option	x	x	x	x	x	x	6 (100%)
	5	DAT describes the negative features (harms, side effects, or disadvantages) of each option	x	x	x	x	x	x	6 (100%)
Number of items met			3	5	5	4	5	4	
Certifying criteria									
Information	1	DAT shows the negative and positive features of options in equal detail (using similar fonts, sequence, and representation of statistical information)		x	x		x	x	4 (67%)
Evidence	2	DAT (or associated documentation) provides citations to the evidence selected	x	x	x	x	x		5 (83%)
	3	DAT (or associated documentation) provides a production or a publication date	x					x	2 (33%)
	4	DAT (or associated documentation) provides information about the update policy		x	x				2 (33%)
	5	DAT provides information about the levels of uncertainty around event or outcome probabilities							0 (0%)
Disclosure	6	DAT (or associated documentation) provides information about the funding source used for development		x	x		x		3 (50%)
Number of items met			2	4	4	1	3	2	

1. MenoPro App (NAMS); **2**. Menopause: Should I Use Hormone Therapy (HT)? (Healthwise); **3**. Hysterectomy and Oophorectomy: Should I Use Estrogen Therapy (ET)? (Healthwise) **4**. Interactive decision tree (menopause matters); **5**. Hormone therapy: Is it right for you? (Mayo clinic); **6**. Impact of a decision aid videotape on young women's attitudes and knowledge about hormone replacement therapy. (Kerner, David)

Appendix 3.1. Search strategy – Scoping review of DATs for menopause

scoping review search terms

RefWorks Account: ScopingReview2015/////scopingreview2015
Ovid Account: ScopingReview2015/////scope15
EBSCOhost: ScopingReview2015/////ScopeReview2015

PSYCINFO

Database: PsycINFO <1806 to October Week 1 2015> updated Mar 9, 2017
1 (menopaus* or premature menopaus* or peri-menopaus* or perimenopaus*).mp. or exp Menopause/ (4914)
2 (postmenopaus* or post-menopaus* or pre-menopaus* or premenopaus*).mp. (3070)
3 (ovariectom* or ovarectom*).mp. or exp Ovariectomy/ (3383)
4 surgical menopaus*.mp. or exp Hysterectomy/ (497)
5 (salpingo-oophorectom* or oophorectom* or salpingo-ovariectom* or salpingectom* or hysterectom*).mp. (845)
6 (RRSO or BPSO).mp. (13)
7 (estrogen replacement therap* or hormone replacement therap* or progesterone replacement therap*).mp. or exp Hormone Therapy/ (2227)
8 or/1-7 (10654)
9 exp Decision Support Systems/ or decision support technique*.mp. (2505)
10 decision making.mp. or exp Decision Making/ (100830)
11 (decision support or decision tree* or decisional tree*).mp. (4944)
12 (decision adj2 process).mp. (8567)
13 exp Treatment Guidelines/ or practice guidelines.mp. (7105)
14 (clinical protocol* or critical pathway* or clinical pathway*).mp. (628)
15 consumer health information.mp. (59)
16 (inform* adj2 (choice* or decision*)).mp. (6655)
17 (patient* adj2 (choice* or preference* or value*)).mp. (4318)
18 ((choose or choice) adj2 treatment).mp. (2727)
19 (pamphlet* or brochure* or handout* or booklet* or leaflet*).mp. (6120)
20 exp Algorithms/ or (medical algorithm* or clinical algorithm*).mp. (12666)
21 or/9-20 (137423)
22 8 and 21 (302)
23 Humans/ (0)
24 Animals/ (6168)
25 23 not (23 and 24) (0)
26 22 not 25 (302)
27 limit 26 to english language (292) + updated search (44)

MEDLINE

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to October Week 1 2015> updated Mar 9, 2017
1 exp Menopause, Premature/ or exp Menopause/ or menopaus*.mp. (68837)
2 (postmenopaus* or post-menopaus*).mp. or exp Postmenopause/ (58665)
3 (premenopaus* or pre-menopaus*).mp. or exp Premenopause/ (19166)
4 (peri-menopaus* or perimenopaus*).mp. or exp Perimenopause/ (4070)
5 exp Ovariectomy/ or surgical menopaus*.mp. (22429)
6 hysterectomy/ or hysterectomy, vaginal/ or hysterectom*.mp. (39584)
7 (ovarectom* or ovariectom* or salpingo-ovariectom* or salpingo-oophorectom* or oophorectom* or salpingectom*).mp. (39635)
8 (RRSO or BPSO).mp. (115)
9 hormone replacement therapy/ or estrogen replacement therapy/ (22102)
10 (hormone replacement therap* or estrogen replacement therap* or progesterone replacement therap*).mp. (27720)
11 or/1-10 (172099)
12 exp Decision Support Techniques/ (65636)
13 exp Decision Support Systems, Clinical/ or exp Decision Making/ (138435)
14 exp Decision Making, Computer-Assisted/ or decision support technology.mp. (108566)
15 (decision aid* or decision-making or decision making or decision support).mp. (160634)
16 exp Decision Trees/ or (decisional tree* or decision tree*).mp. (12326)
17 (decision adj2 process).mp. (11010)
18 Practice Guidelines as Topic/ or practice guideline*.mp. (117035)
19 Clinical Protocols/ or Critical Pathways/ (26743)
20 (clinical protocol* or clinical pathway* or critical pathway*).mp. (31403)
21 Pamphlets/ or (pamphlet* or brochure* or handout* or booklet* or leaflet*).mp. (29039)
22 exp Algorithms/ (198126)

23 (medical algorithm* or clinical algorithm*).mp. (893)
24 (inform* adj2 (choice* or decision*)).mp. (12591)
25 (patient* adj2 (choice* or preference* or value*)).mp. (32897)
26 ((choose or choice) adj2 treatment).mp. (32107)
27 or/12-26 (752237)
28 11 and 27 (5732)
29 Animals/ (5621674)
30 Humans/ (14470519)
31 29 not (29 and 30) (4035570)
32 28 not 31 (5593)
33 limit 32 to english language (4930) + updated search (773)

EMBASE

Database: Embase <1974 to 2015 October 16> Updated Mar 10, 2017
1 (menopaus* or premature menopaus* or peri-menopaus* or perimenopaus*).mp. or exp early menopause/ or exp menopause/ (84622)
2 (post menopaus* or post-menopaus*).mp. or exp postmenopause/ (55864)
3 exp premenopause/ or (pre-menopaus* or premenopaus*).mp. (26450)
4 (ovarectom* or ovariectom*).mp. or exp ovariectomy/ (40639)
5 surgical menopaus*.mp. or exp estrogen therapy/ (22107)
6 (salpingo-oophorectom* or salpingo-ovariectom* or oophorectom* or salpingectom*).mp. or exp salpingooophorectomy/ (19112)
7 hysterectomy/ or abdominal hysterectomy/ or vaginal hysterectomy/ or hysterectom*.ti,ab. (60093)
8 (RRSO or BPSO).mp. (209)
9 (progesterone replacement therap* or hormone replacement therap* or estrogen replacement therap*).mp. or exp hormone substitution/ (54623)
10 or/1-9 (250010)
11 decision support technique*.mp. or exp decision support system/ (16215)
12 decision making.mp. or exp decision making/ (296164)
13 (decision adj2 process).mp. (14699)
14 exp medical decision making/ or (decision aid* or decision support).mp. (92829)
15 "decision tree"/ or (decisional tree* or decision tree*).mp. (10630)
16 practice guideline*.mp. or practice guideline/ or clinical pathway/ or clinical protocol/ or consensus development/ or nursing protocol/ (348636)
17 (critical pathway* or clinical pathway* or clinical protocol*).mp. (84862)
18 (pamphlet* or brochure* or handout* or booklet* or leaflet*).mp. (31612)
19 exp algorithm/ or (medical algorithm* or clinical algorithm*).mp. (214625)
20 (inform* adj2 (choice* or decision*)).mp. (16530)
21 (patient* adj2 (choice* or preference* or value*)).mp. (48814)
22 ((choose or choice) adj2 treatment).mp. (44535)
23 or/11-22 (961900)
24 10 and 23 (10385)
25 exp animal/ (20903604)
26 human/ (16316588)
27 25 not (25 and 26) (4587016)
28 24 not 27 (10301)
29 limit 28 to english language (9256) + updated search (1995)

HEALTH AND PSYCHOSOCIAL INSTRUMENTS

Health and Psychosocial Instruments <1985 to July 2015>
1 exp Menopause, Premature/ or exp Menopause/ or menopaus*.mp. (231)
2 (postmenopaus* or post-menopaus*).mp. or exp Postmenopause/ (199)
3 (premenopaus* or pre-menopaus*).mp. or exp Premenopause/ (104)
4 (peri-menopaus* or perimenopaus*).mp. or exp Perimenopause/ (23)
5 exp Ovariectomy/ or surgical menopaus*.mp. (8)
6 hysterectomy/ or hysterectomy, vaginal/ or hysterectom*.mp. (82)
7 (ovarectom* or ovariectom* or salpingo-ovariectom* or salpingo-oophorectom* or oophorectom* or salpingectom*).mp. (26)
8 (RRSO or BPSO).mp. (0)
9 [hormone replacement therapy/ or estrogen replacement therapy/] (0)
10 (hormone replacement therap* or estrogen replacement therap* or progesterone replacement therap*).mp. (80)
11 or/1-10 (495)
12 [exp Decision Support Techniques/] (0)
13 [exp Decision Support Systems, Clinical/ or exp Decision Making/] (0)
14 exp Decision Making, Computer-Assisted/ or decision support technology.mp. (0)
15 (decision aid* or decision-making or decision making or decision support).mp. (1888)

16 exp Decision Trees/ or (decisional tree* or decision tree*).mp. (5)
17 (decision adj2 process).mp. (91)
18 Practice Guidelines as Topic/ or practice guideline*.mp. (49)
19 [Clinical Protocols/ or Critical Pathways/] (0)
20 (clinical protocol* or clinical pathway* or critical pathway*).mp. (38)
21 Pamphlets/ or (pamphlet* or brochure* or handout* or booklet* or leaflet*).mp. (182)
22 [exp Algorithms/] (0)
23 (medical algorithm* or clinical algorithm*).mp. (0)
24 (inform* adj2 (choice* or decision*)).mp. (57)
25 (patient* adj2 (choice* or preference* or value*)).mp. (171)
26 ((choose or choice) adj2 treatment).mp. (14)
27 or/12-26 (2301)
28 11 and 27 (12)
29 [Animals/] (0)
30 [Humans/] (0)
31 29 not (29 and 30) (0)
32 28 not 31 (12)
33 limit 32 to english language (10)

CINAHL

Original search <1965 to 2015 October 1> Updated Mar 9, 2017	
S21	s9 and s19 >> (1003) + updated search (254)
S20	s9 and s19
S19	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18
S18	((choose or choice) N2 treatment)
S17	(patient* N2 (choice* or preference* or value*))
S16	(inform* N2 (choice* or decision*))
S15	decision N2 process
S14	"clinical protocol" OR "critical pathway" OR "clinical pathway"
S13	(MH "Pamphlets") OR pamphlet* OR brochure* OR handout* or booklet* or leaflet*
S12	(MH "Decision Trees") OR "decision tree*" OR "medial algorithm*" OR "decision aid*"
S11	(MH "Decision Support Systems, Clinical") OR (MH "Decision Support Techniques+") OR "decision support"
S10	(MH "Decision Making+") OR "decision making" OR (MH "Decision Making, Patient+") OR (MH "Decision Making, Clinical")
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S8	"RRSO" OR "BPSO"
S7	(MH "Hormone Replacement Therapy+") OR "hormone replacement therap*" OR "estrogen replacement therap*" OR "progesterone replacement therap*"
S6	(MH "Salpingectomy") OR "salpingectomy" OR "salpingo-oophorectom*" OR "salpingo-ovariectom*" OR "salpingo-ovarectom*"
S5	(MH "Hysterectomy+") OR "hysterectom*"
S4	(MH "Oophorectomy") OR "oophorectom*"

S3	"perimenopaus*" OR "peri-menopaus*" OR "post menopaus*" OR "postmenopaus*" OR " post-menopaus*" OR "pre menopaus*" OR "premenopaus*" OR "pre-menopause"
S2	(MH "Menopause, Premature") OR "premature menopaus*" OR "surgical menopaus*"
S1	(MH "Menopause+") OR "menopaus*" OR (MH "Menopause, Premature") OR (MH "Premenopause") OR (MH "Postmenopause") OR (MH "Perimenopause")

PROQUEST DISSERTATION AND THESES

Original search performed June 13 2016 (96) Updated March 9, 2017 (71)

all(menopaus* OR perimenopaus* OR premenopaus* OR postmenopaus* OR oopherectom* OR ovariectom* OR ovarectom* OR hysterectom* OR "hormone replacement therapy") AND all(("decision support" OR "decision tree*" OR "medical algorithm*" OR "decision aid*" OR pamphlet* OR brochure* OR handout* or booklet* or leaflet* OR "clinical protocol" OR "critical pathway" OR "clinical pathway" OR (inform* NEAR/2 (choice OR decision*)) OR ((choose or choice) NEAR/2 treatment) OR (patient* NEAR/2 (choice* or preference* or value*))))

scopus

Original search performed June 13 2016 (196) Updated March 9, 2017 (179)

((TITLE-ABS-KEY (menopaus* OR perimenopaus* OR premenopaus* OR postmenopaus* OR oopherectom* OR ovariectom* OR ovarectom* OR hysterectom* OR "hormone replacement therapy") AND TITLE-ABS-KEY ("decision support" OR "decision tree*" OR "medical algorithm*" OR "decision aid*" OR pamphlet* OR brochure* OR handout* OR booklet* OR leaflet* OR "clinical protocol" OR "critical pathway" OR "clinical pathway"))) OR ((TITLE-ABS-KEY (menopaus* OR perimenopaus* OR premenopaus* OR postmenopaus* OR oopherectom* OR ovariectom* OR ovarectom* OR hysterectom* OR "hormone replacement therapy") AND TITLE-ABS-KEY ((inform* W/2 (choice OR decision*)) OR ((choose OR choice) W/2 treatment) OR (patient* W/2 (choice* OR preference* OR value*))))) AND (LIMIT-TO (DOCTYPE , "cp"))

4 Chapter 4. The Effect of Hormone Therapy on Quality of Life and Breast Cancer Risk After Risk-Reducing Salpingo-oophorectomy: A Systematic Review[c]

Tasneem Siyam[1], BScPharm, MSc; Sue Ross[2], Ph.D.; Sandra Campbell[3], MLS; Dean T. Eurich[4], Ph.D.; Nesé Yuksel[5], PharmD

[1]Ph.D. Candidate
Faculty of Pharmacy and Pharmaceutical Sciences
3-015 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
tsiyam@ualberta.ca

[2]Cavarzan Chair in Mature Women's Health Research
Department of Obstetrics & Gynecology
Rm 5S131 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada, T5H 3V9
Sue.Ross@albertaheatlhservices.ca

[3]Public Service Librarian
2K4.01 WC Mackenzie Health Science Center
University of Alberta
Edmonton, AB
Canada T6G 2R7
sandra.campbell@ualberta.ca

[4]Associate Professor
School of Public Health
2-040 Li Ka Shing HRIF
University of Alberta
Edmonton, AB, Canada, T6G 2E1
deurich@ualberta.ca

[5]Professor (corresponding author)
Faculty of Pharmacy and Pharmaceutical Sciences
3-171 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
nese.yuksel@ualberta.ca
Tel: (780)492-4442; Fax: (780)492-121

[c] T. Siyam, S. Ross, S. Campbell, D.T. Eurich, N. Yuksel, The effect of hormone therapy on quality of life and breast cancer risk after risk-reducing salpingo-oophorectomy: a systematic review, BMC Womens Health 17(1) (2017) 22.

4.1 Background

BRCA mutations are associated with an increased risk of breast and ovarian cancer. In women with mutations of BRCA1 genes, the average cumulative risk for breast cancer by age 80 years is 67% and for ovarian cancer 45%.[1-4] In BRCA2 carriers, the average cumulative risks are 66% and 12%, respectively.[1-4] Risk-reducing saplingo-oophorectomy (RRSO) offers reduction in the risk of ovarian cancer of approximately 80%, among BRCA1 and 2 carriers, and of 50 % for breast cancer.[5] However, more recent evidence suggests that breast cancer-risk reduction with RRSO may not be significant, particularly for BRCA1 carriers.[6, 7] Since cancer risk estimates for BRCA carriers are age-dependent and tend to be higher in younger age populations,[7] current guidelines recommend RRSO for BRCA carriers before age 40 years or after completion of child-bearing.[8-11]

An immediate consequence of RRSO in premenopausal women is surgical menopause. Surgical menopause is associated with symptoms that can significantly affect a woman's quality of life (QOL), including vasomotor and urogenital symptoms, sexual dysfunction, sleep disturbances, and mood changes.[12] Furthermore, these women are at risk of long-term sequelae such as osteoporosis, cardiovascular diseases, and cognitive impairment.[13-15] In women with early menopause, who have no contraindications to hormone therapy (HT), current guidelines recommend the use of HT until the average age of menopause.[15-18] As BRCA mutation carriers would ideally undertake RRSO at an earlier age than women who perform it for other benign reasons or who go through early natural menopause, guidelines specific to BRCA mutation carriers suggest the consideration of short-term HT use due to the unknown nature of long-term safety.[10]

The concern in women with BRCA mutations is that HT may further increase breast cancer risk following a RRSO. The Women's Health Initiative (WHI) randomized trials found an increased risk of breast cancer with estrogen plus progestin, although not with estrogen alone.[19] Data from short-term observational studies assessing the risk of breast cancer with HT use after RRSO are inconsistent, and at this time it is unclear if HT increases breast cancer risk following a RRSO.[20, 21]

Carriers of BRCA mutations and women at high risk for breast cancer are often challenged by the decision to undertake RRSO due to the health consequences associated with surgical menopause, and the need for HT that may further increase their breast cancer risk. In 2014, Marchetti et al addressed this important topic in a narrative review, but the lack of details of the literature review method lead to concern about the rigor and completeness of the review.[22] Similarly, in early 2016, Birrer et al published a review of evidence about the safety of HT in women with BRCA mutations.[23] Even though they reported in their title and methods that they conducted a systematic review, the study lacked the main elements of a systematic review, such as a comprehensive literature search, an assessment of the methodological quality of studies included, and transparency in reporting the methods and findings.[23]

We, therefore, performed a systematic review to assess the effect of HT on QOL and breast cancer risk in women who have BRCA mutations and who also underwent RRSO for breast and ovarian cancer risk reduction. The effect of HT on other short and long-term outcomes was also evaluated.

4.2 Methods

Our study was designed and conducted in accordance with the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies [24].

4.2.1 Eligibility criteria

Eligible studies included women who had BRCA1/2 mutations or who had a high risk of breast and ovarian cancer (as defined by the original study authors) but had not undergone genetic testing, and who had undergone RRSO for cancer risk reduction. Studies comparing the effect of HT (with no restriction on type, dose, regimen, or route of administration) to placebo, non-exposed group or baseline, qualified for inclusion. All controlled trials and observational studies (including prospective and retrospective cohort studies, case-control studies, and cross-sectional studies) were included. Review papers were screened for cited articles. Exclusion criteria included qualitative studies, hypothetical decision analysis, editorials and studies that did not assess the effect of HT on outcomes of interest.

4.2.2 Outcome measures

Primary outcomes were QOL (general and menopause-specific) and breast cancer risk. Secondary outcomes included: vasomotor symptoms, vulvovaginal atrophy (VVA), sexual function, mood, sleep disturbance, bone loss, cardiovascular disease, stroke, venous thromboembolism, and mortality**.**

4.2.3 Data sources and search strategy

A systematic literature search was conducted by a librarian (SC) to identify all relevant published and unpublished studies. Searches using both controlled vocabulary and natural language were performed in databases including MEDLINE (1946 to March 7, 2016), EMBASE (1974 to March 7, 2016), and CINHAL (inception to March 7, 2016) (Appendix 4.1). Natural language

search terms were derived from three main concepts: 1) RRSO, 2) BRCA mutations or high risk of breast and ovarian cancer, and 3) HT. Grey literature searches were conducted in SCOPUS, Web of Science, Google Scholar, Proquest, Dissertations and Theses and clinical trials registries, from inception to July 22, 2016 (Appendix 4.2) Other searches included hand searches of the reference list of review papers; and citation search of studies included in the systematic review. To increase the sensitivity of our search no language or date restrictions of publications were applied.

4.2.4 Study selection

Two-step screening for eligibility was performed independently by 2 reviewers (TS and NY), with disagreements resolved by consensus. First, titles and abstracts were screened to select articles eligible for further review. Second, full-text of relevant articles was reviewed for eligibility. Reviewer agreement for confirmation of eligibility was 100%.

4.2.5 Data extraction and quality assessment

Data extraction was completed independently by two reviewers (TS, AB), and discrepancies resolved by a third reviewer (NY). Data elements extracted included: manuscript characteristics; study design and settings; population characteristics; interventions; comparators; outcomes; and adjustments for potential confounders. The risk of bias assessment was conducted independently by two reviewers (TS, NY) and discrepancies resolved by consensus. The quality of studies was evaluated using the Jadad scale for RCTs,[25] and relevant versions of the Newcastle-Ottawa scale (NOS) for observational studies [26]. Cut off scores of ≥ 4 for Jadad scale and ≥ 7 for NOS were used to distinguish study quality.[27] Quality assessment scores were used to inform sensitivity analyses to evaluate its effect on pooled measure(s) of effect. Corresponding authors were contacted when data on outcomes were not available.

4.2.6 Data synthesis

Outcome data were synthesized by tabulating together all studies reported on specific outcomes. For each study, the outcomes reported were grouped by HT users versus non-users, with mean differences or measures of association as relevant. Descriptive analysis was used for each outcome.

When sufficient homogeneity was demonstrated, outcome data were pooled quantitatively via a meta-analysis (as only two or three papers could be pooled for each outcome variable the details of the meta-analysis can be found in Appendix 4.3).

4.3 Results

Our search identified 1,059 records of which 51 full-text articles were retrieved and assessed for eligibility, and 13 were included. The most common reasons for exclusion are listed in Figure 4.1. Appendix 4.4 lists all 51 studies reviewed for eligibility and the reason for exclusion whenever this may apply.

4.3.1 Study characteristics

Table 4.1 lists the main characteristics of the studies and their methodological quality. No RCTs were identified. The mean age of women across studies was 49.87 years (range 33-83), however, 6 studies did not report the participants' age.[21, 28-32] The mean age at RRSO surgery was 45.54 years (range 24-80). Studies included both BRCA1 and 2 carriers, except for 2, which included only BRCA1 carriers.[21, 31] In addition to BRCA mutation carriers, 6 studies included women who had high risk of breast and ovarian cancer with no confirmed genetic diagnosis.[29, 32-36] Other variables, such as time since RRSO, body mass index (BMI), smoking status, history of breast cancer and hysterectomy were reported in some but not all studies. Intervention characteristics are listed in Table 4.2.

4.3.2 Synthesis of results

The outcomes reported for individual studies are shown in Table 4.3.

4.3.2.1 Quality of life

Six studies assessed the effect of HT on menopause-specific QOL.[29, 32-34, 37, 38] Tools of QOL assessment varied and included Functional Assessment of Cancer Therapy-Endocrine Score (FACT-ES)[33, 34]; Menopause Symptoms List (MSL)[37], Menopause-Specific Quality of Life-Intervention tool (MENQOL-I),[32, 38] and Menopause Rating Scale (MRS).[29] Where reported, the mean age of women was 46 years or older in these studies.[33, 34, 37, 38] Studies differed with respect to the menopausal status at the time of RRSO surgery: 4 included pre and postmenopausal women, [29, 32, 37, 38] 2 included only pre-menopausal women.[33, 34] In one study including both pre and postmenopausal women, QOL was analyzed in the pre-menopausal group only.[38] Of the 6 studies evaluating QOL, 3 studies showed improvement in QOL,[32, 34, 38] and 3 showed no change.[29, 33, 37] One study evaluated the effect of HT on general QOL using the Short-form Health Survey (SF-36).[32] The use of systemic HT improved only the pain domain of the SF-36 survey but none of the other domains.

4.3.2.2 Breast cancer

Four studies looked at breast cancer risk with HT use.[20, 21, 28, 31] One study was an update of a previous analysis done by Eisen et al.[21, 31] All 4 studies included women, with confirmed BRCA mutations, of comparable mean age at the time of RRSO surgery and with no personal history of breast cancer. Two studies included BRCA1 and 2 mutations, with BRCA1 carriers, represented ≥60% in both.[20, 28] The remaining 2 studies included only BRCA1 carriers.[21, 31] All studies included ET and EPT users. The mean duration of HT use was 3.83 years (range

0.05-25). The mean duration of follow-up for the only prospective study was 2.6 years (range 0.1-19.1).[20] Breast cancer risk did not change with HT use in any of the 4 studies.

Only 2 studies reported the effect of HT regimen on breast cancer risk.[20, 28] In Gabriel et al, 3 women on ET developed breast cancer (OR 0.48; 95% CI, 0.1-2.1), with no cases in women on EPT.[28] Rebbeck et al reported that compared to ET users the risk of breast cancer with EPT was higher but not significant (HR 2.56; 95% CI, 0.08-78.13).[20] The effect of HT duration of use on breast cancer was reported in one study.[31] Compared to never use, breast cancer risk did not change with greater than 3 years of HT use post RRSO.

4.3.2.3 Other outcomes

4.3.2.3.1 Vasomotor symptoms

Vasomotor symptoms were assessed in 4 studies.[32-34, 38] HT reduced the prevalence and/or severity of hot flashes in all studies.

4.3.2.3.2 Sexual function

Sexual function was measured in 5 studies as part of the QOL instruments (MENQOL, and FACT_ES), or using the Sexual Activity Questionnaire (SAQ), Female Sexual Function index (FSFI) or Female Sexual Distress Scale – revised (FSDS).[29, 32, 34, 36, 38] Two studies showed an improvement in sexual function with HT, using the sexual domain of MENQOL (Table 4.3).[32, 38] The only aspect of sexual activity that consistently improved with HT use across studies was discomfort/pain.[32, 36, 38] Other aspects of sexual activity, such as pleasure, habit, satisfaction and libido showed no improvement.

4.3.2.3.3 Vulvovaginal Atrophy (VVA)

Four studies measured the effect on VVA.[32-34, 38] In 2 studies, vaginal dryness was included as a component of sexual function: taking HT improved vaginal dryness and reduced the risk of

lubrication difficulty with intercourse.[32, 38] Two studies measured the effect of taking HT on VVA, separate from sexual function, and did not find improvement.[33, 34]

4.3.2.3.4 Prevention of bone loss

Three studies evaluated the effect of HT on bone loss.[30, 33, 37] Two studies included the time frame of DXA screening post-RRSO (6.3 years [33] and 1.25 years [30]). HT users had less bone loss compared to non-users in 2 studies.[33, 37]

4.4 Discussion

In our rigorously conducted systematic review, women with BRCA mutations who had RRSO had improvements in overall menopause-specific QOL with the use of HT, as well as reduction in vasomotor symptoms and VVA. The association of HT with breast cancer risk is still unclear due to the lack of long-term quality studies.

QOL after RRSO is an important consideration for women who elect to have RRSO. QOL in this population is comparable with the general population,[39, 40] though menopause-specific QOL may be compromised.[34, 40-43] Several studies show that HT improves menopause-specific QOL in symptomatic women who have gone through natural or surgical menopause.[44-46] Our cumulative results are consistent with these findings, as HT improved menopause-specific QOL following RRSO. Although 3 of the studies that assessed QOL showed no change with HT use, findings from these studies were more prone to bias due to confounding than studies that showed improvement in QOL.[29, 33, 37]

The risk of breast cancer is the greatest concern women in the general population have when considering HT.[47, 48] This fear stems from the results of the WHI, which showed an increased risk of breast cancer in women on EPT for 5 or more years.[19, 49] These results are often

extrapolated to younger surgically menopausal women, even though the WHI participants mean age was 63 years at the time of study recruitment. In contrast, the use of ET alone in the WHI in younger women who have had a hysterectomy showed no increase in breast cancer risk.[19, 50, 51] Unfortunately we were unable to further explore the relative impact of ET versus EPT on breast cancer or other outcomes, as few studies reported the outcomes by specific treatment [20, 21] and not all specified the type of HT.[29, 30, 35, 37]

Several recently published narrative reviews evaluated whether HT counteracts the breast cancer risk-reducing effects of RRSO.[12, 22, 23, 52] However, with newer evidence suggesting the lack of breast cancer risk-reducing benefits from RRSO, the clinical inquiry that rather needs to be addressed is whether HT further increases the risk of breast cancer following a RRSO. These review papers concluded that HT seems to be safe in the short-term. We argue that given the scarcity and methodological limitations of the available evidence, no firm conclusions can be drawn, in the short or long term. None of the reviews critically appraised the included studies to assess their risk of bias. In our systematic review, we identified several limitations in the studies assessing breast cancer risk. All studies were affected by recall bias as HT was self-reported. Three of the studies were not designed to capture breast cancer incidence.[21, 28, 31] The only prospective study that captured this outcome had a relatively short follow-up (mean 2.6 years).[20], as well there was selection bias due to lost to follow-up.[20] Furthermore, in this study, breast cancer events within each group were relatively small which may have limited the estimate's precision and validity.

Among the other outcomes we studied, our systematic review found that HT was associated with a reduction in vasomotor symptoms. The benefits of HT on vasomotor symptoms is already well established.[53] VVA was also shown to improve with systemic HT in the pooled findings from

the two relevant studies in our meta-analysis (Appendix 4.3). This aligns with established evidence in the literature.[54] However, in the individual studies, there was no significant improvement in VVA with HT. Unfortunately, information on vaginal estrogen use was not provided in these studies. The one study that reported and evaluated the effect of vaginal estrogen use on vaginal dryness showed a reduction in the severity of the symptom and its risk.[32] Sexual discomfort improved for women taking systemic or local HT, while other sexual dimensions were not found to be significantly different between groups.[32, 36, 38] Sexual function is more complex than hormone levels alone, and other factors such as emotional satisfaction, psychological status, physical health and relationship status also need to be considered.[55] Androgen levels are reduced in surgical menopause[56], and may contribute to low libido[57, 58] However, in the studies that looked at sexual function in our review, only one study analyzed the effect of androgen levels on sexual desire and arousal and found no association.[32] The effect of testosterone on sexual function was outside the scope of this review.

There are several limitations associated with our study, mainly related to the limitations of the included studies. First, all of the studies included in this review were observational with a small sample size. Evidence from these studies cannot be considered as robust as those from RCTs. Second, very few studies provided sufficient outcome data suitable for meta-analysis limiting the value of these analyses (Appendix 4.3). Third, several studies in this review did not control for the effect of baseline QOL score and menopause status at the time of RRSO which are considered confounders. The only study that controlled for baseline score showed a significant improvement in QOL with HT.[38] Fourth, we could not assess the effect of HT regimens (ET vs. EPT) on different outcomes as these were poorly reported in most studies. Conclusions from

our systematic review may also be affected by publication bias. The preferential publication of studies, with statistically significant treatment effects, may overestimate the effect of HT. Our search strategy aimed to locate both published and unpublished work. We were unable to locate any unpublished efforts.

Despite the limitations, our systematic review possesses several strengths that differentiate it from previous less-structured reviews on this topic.[12, 22, 23] Our review was executed in compliance with MOOSE guidelines (Appendix 4.5) and based on a pre-specified protocol (PROSPERO registration number: 42014012997). We believe that the rigorous protocol and clear description of our method allow clinicians and RRSO patients to be confident that our findings are as rigorous as they can be based on the relative paucity of good evidence to answer the important questions that RRSO patients are asking.

4.5 Conclusion

Cumulative evidence from our review highlights the benefits of HT in improving QOL and managing common menopausal symptoms induced by RRSO. However, no conclusions can be drawn about the safety of HT, as far as breast cancer risk is concerned. There are too few well-designed long-term studies to draw firm conclusions to guide women and their clinicians in their decision-making about HT. Future well-designed RCTs are needed. In the absence of clear evidence to inform the use of HT post RRSO, clinicians and patients must carefully discuss the potential benefits of HT as well as non-hormonal therapies in improving QOL, in the context of the unknown risk of breast cancer in this population. However, this may not be of concern for women who opt for risk-reducing bilateral mastectomy since the risk of breast cancer in this population is negligible.

4.6 References

[1] L.C. Hartmann, N.M. Lindor, The Role of Risk-Reducing Surgery in Hereditary Breast and Ovarian Cancer, N Engl J Med 374(5) (2016) 454-68.

[2] A.C. Antoniou, A.P. Cunningham, J. Peto, D.G. Evans, F. Lalloo, S.A. Narod, H.A. Risch, J.E. Eyfjord, J.L. Hopper, M.C. Southey, H. Olsson, O. Johannsson, A. Borg, B. Pasini, P. Radice, S. Manoukian, D.M. Eccles, N. Tang, E. Olah, H. Anton-Culver, E. Warner, J. Lubinski, J. Gronwald, B. Gorski, L. Tryggvadottir, K. Syrjakoski, O.P. Kallioniemi, H. Eerola, H. Nevanlinna, P.D. Pharoah, D.F. Easton, The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions, Br J Cancer 98(8) (2008) 1457-66.

[3] N. Mavaddat, S. Peock, D. Frost, S. Ellis, R. Platte, E. Fineberg, D.G. Evans, L. Izatt, R.A. Eeles, J. Adlard, R. Davidson, D. Eccles, T. Cole, J. Cook, C. Brewer, M. Tischkowitz, F. Douglas, S. Hodgson, L. Walker, M.E. Porteous, P.J. Morrison, L.E. Side, M.J. Kennedy, C. Houghton, A. Donaldson, M.T. Rogers, H. Dorkins, Z. Miedzybrodzka, H. Gregory, J. Eason, J. Barwell, E. McCann, A. Murray, A.C. Antoniou, D.F. Easton, Cancer risks for BRCA1 and BRCA2 mutation carriers: results from prospective analysis of EMBRACE, J Natl Cancer Inst 105(11) (2013) 812-22.

[4] R.M. Brohet, M.E. Velthuizen, F.B. Hogervorst, H.E. Meijers-Heijboer, C. Seynaeve, M.J. Collee, S. Verhoef, M.G. Ausems, N. Hoogerbrugge, C.J. van Asperen, E. Gomez Garcia, F. Menko, J.C. Oosterwijk, P. Devilee, L.J. van't Veer, F.E. van Leeuwen, D.F. Easton, M.A. Rookus, A.C. Antoniou, Breast and ovarian cancer risks in a large series of clinically ascertained families with a high proportion of BRCA1 and BRCA2 Dutch founder mutations, J Med Genet 51(2) (2014) 98-107.

[5] T.R. Rebbeck, N.D. Kauff, S.M. Domchek, Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers, J Natl Cancer Inst 101(2) (2009) 80-7.

[6] J. Kotsopoulos, T. Huzarski, J. Gronwald, C.F. Singer, P. Moller, H.T. Lynch, S. Armel, B. Karlan, W.D. Foulkes, S.L. Neuhausen, L. Senter, N. Tung, J.N. Weitzel, A. Eisen, K. Metcalfe, C. Eng, T. Pal, G. Evans, P. Sun, J. Lubinski, S.A. Narod, Bilateral Oophorectomy and Breast Cancer Risk in BRCA1 and BRCA2 Mutation Carriers, J Natl Cancer Inst 109(1) (2017).

[7] B.A. Heemskerk-Gerritsen, C. Seynaeve, C.J. van Asperen, M.G. Ausems, J.M. Collee, H.C. van Doorn, E.B. Gomez Garcia, C.M. Kets, F.E. van Leeuwen, H.E. Meijers-Heijboer, M.J. Mourits, T.A. van Os, H.F. Vasen, S. Verhoef, M.A. Rookus, M.J. Hooning, Breast cancer risk after salpingo-oophorectomy in healthy BRCA1/2 mutation carriers: revisiting the evidence for risk reduction, J Natl Cancer Inst 107(5) (2015).

[8] J.L. Walker, C.B. Powell, L.M. Chen, J. Carter, V.L. Bae Jump, L.P. Parker, M.E. Borowsky, R.K. Gibb, Society of Gynecologic Oncology recommendations for the prevention of ovarian cancer, Cancer 121(13) (2015) 2108-20.

[9] S. Paluch-Shimon, F. Cardoso, C. Sessa, J. Balmana, M.J. Cardoso, F. Gilbert, E. Senkus, Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening, Ann Oncol 27(suppl 5) (2016) v103-v110.

[10] M.B. Daly, R. Pilarski, J.E. Axilbund, M. Berry, S.S. Buys, B. Crawford, M. Farmer, S. Friedman, J.E. Garber, S. Khan, C. Klein, W. Kohlmann, A. Kurian, J.K. Litton, L. Madlensky, P.K. Marcom, S.D. Merajver, K. Offit, T. Pal, H. Rana, G. Reiser, M.E. Robson, K.M. Shannon, E. Swisher, N.C. Voian, J.N. Weitzel, A. Whelan, M.J. Wick, G.L. Wiesner, M. Dwyer, R.

Kumar, S. Darlow, Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2.2015, J Natl Compr Canc Netw 14(2) (2016) 153-62.

[11] M.B. Daly, J.E. Axilbund, S. Buys, B. Crawford, C.D. Farrell, S. Friedman, J.E. Garber, S. Goorha, S.B. Gruber, H. Hampel, V. Kaklamani, W. Kohlmann, A. Kurian, J. Litton, P.K. Marcom, R. Nussbaum, K. Offit, T. Pal, B. Pasche, R. Pilarski, G. Reiser, K.M. Shannon, J.R. Smith, E. Swisher, J.N. Weitzel, Genetic/familial high-risk assessment: breast and ovarian, J Natl Compr Canc Netw 8(5) (2010) 562-94.

[12] A. Finch, S.A. Narod, Quality of life and health status after prophylactic salpingo-oophorectomy in women who carry a BRCA mutation: A review, Maturitas 70(3) (2011) 261-5.

[13] J.C. Gallagher, Effect of early menopause on bone mineral density and fractures, Menopause 14(3 Pt 2) (2007) 567-71.

[14] W.H. Parker, M.S. Broder, E. Chang, D. Feskanich, C. Farquhar, Z. Liu, D. Shoupe, J.S. Berek, S. Hankinson, J.E. Manson, Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study, Obstet Gynecol 113(5) (2009) 1027-37.

[15] W.A. Rocca, B.R. Grossardt, L.T. Shuster, Oophorectomy, estrogen, and dementia: a 2014 update, Mol Cell Endocrinol 389(1-2) (2014) 7-12.

[16] A. Finch, G. Evans, S.A. Narod, BRCA carriers, prophylactic salpingo-oophorectomy and menopause: clinical management considerations and recommendations, Womens Health (Lond Engl) 8(5) (2012) 543-55.

[17] T.J. de Villiers, M.L. Gass, C.J. Haines, J.E. Hall, R.A. Lobo, D.D. Pierroz, M. Rees, Global Consensus Statement on menopausal hormone therapy, Maturitas 74(4) (2013) 391-2.

[18] R. Reid, B.L. Abramson, J. Blake, S. Desindes, S. Dodin, S. Johnston, T. Rowe, N. Sodhi, P. Wilks, W. Wolfman, M. Fortier, L. Graves, B. Guthrie, A. Khan, Managing menopause, J Obstet Gynaecol Can 36(9) (2014) 830-8.

[19] J.E. Manson, R.T. Chlebowski, M.L. Stefanick, A.K. Aragaki, J.E. Rossouw, R.L. Prentice, G. Anderson, B.V. Howard, C.A. Thomson, A.Z. LaCroix, J. Wactawski-Wende, R.D. Jackson, M. Limacher, K.L. Margolis, S. Wassertheil-Smoller, S.A. Beresford, J.A. Cauley, C.B. Eaton, M. Gass, J. Hsia, K.C. Johnson, C. Kooperberg, L.H. Kuller, C.E. Lewis, S. Liu, L.W. Martin, J.K. Ockene, M.J. O'Sullivan, L.H. Powell, M.S. Simon, L. Van Horn, M.Z. Vitolins, R.B. Wallace, Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials, JAMA 310(13) (2013) 1353-68.

[20] T.R. Rebbeck, T. Friebel, T. Wagner, H.T. Lynch, J.E. Garber, M.B. Daly, C. Isaacs, O.I. Olopade, S.L. Neuhausen, L. van 't Veer, R. Eeles, D.G. Evans, G. Tomlinson, E. Matloff, S.A. Narod, A. Eisen, S. Domchek, K. Armstrong, B.L. Weber, Effect of short-term hormone replacement therapy on breast cancer risk reduction after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers: the PROSE Study Group, J Clin Oncol 23(31) (2005) 7804-10.

[21] A. Eisen, J. Lubinski, J. Gronwald, P. Moller, H.T. Lynch, J. Klijn, C. Kim-Sing, S.L. Neuhausen, L. Gilbert, P. Ghadirian, S. Manoukian, G. Rennert, E. Friedman, C. Isaacs, E. Rosen, B. Rosen, M. Daly, P. Sun, S.A. Narod, Hormone therapy and the risk of breast cancer in BRCA1 mutation carriers, J Natl Cancer Inst 100(19) (2008) 1361-7.

[22] C. Marchetti, R. Iadarola, I. Palaia, V. di Donato, G. Perniola, L. Muzii, P.B. Panici, Hormone therapy in oophorectomized BRCA1/2 mutation carriers, Menopause 21(7) (2014) 763-8.

[23] N. Birrer, C. Chinchilla, M. Del Carmen, D.S. Dizon, Is Hormone Replacement Therapy Safe in Women With a BRCA Mutation?: A Systematic Review of the Contemporary Literature, Am J Clin Oncol (2016).

[24] D.F. Stroup, J.A. Berlin, S.C. Morton, I. Olkin, G.D. Williamson, D. Rennie, D. Moher, B.J. Becker, T.A. Sipe, S.B. Thacker, Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group, JAMA 283(15) (2000) 2008-12.

[25] A.R. Jadad, R.A. Moore, D. Carroll, C. Jenkinson, D.J. Reynolds, D.J. Gavaghan, H.J. McQuay, Assessing the quality of reports of randomized clinical trials: is blinding necessary?, Control Clin Trials 17(1) (1996) 1-12.

[26] J.P. Nolan, M.F. Hazinski, J.E. Billi, B.W. Boettiger, L. Bossaert, A.R. de Caen, C.D. Deakin, S. Drajer, B. Eigel, R.W. Hickey, I. Jacobs, M.E. Kleinman, W. Kloeck, R.W. Koster, S.H. Lim, M.E. Mancini, W.H. Montgomery, P.T. Morley, L.J. Morrison, V.M. Nadkarni, R.E. O'Connor, K. Okada, J.M. Perlman, M.R. Sayre, M. Shuster, J. Soar, K. Sunde, A.H. Travers, J. Wyllie, D. Zideman, Part 1: Executive summary: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations, Resuscitation 81 Suppl 1 (2010) e1-25.

[27] S.K. Myung, W. Ju, D.D. McDonnell, Y.J. Lee, G. Kazinets, C.T. Cheng, J.M. Moskowitz, Mobile phone use and risk of tumors: a meta-analysis, J Clin Oncol 27(33) (2009) 5565-72.

[28] C.A. Gabriel, J. Tigges-Cardwell, J. Stopfer, J. Erlichman, K. Nathanson, S.M. Domchek, Use of total abdominal hysterectomy and hormone replacement therapy in BRCA1 and BRCA2 mutation carriers undergoing risk-reducing salpingo-oophorectomy, Fam Cancer 8(1) (2009) 23-8.

[29] L. Heiniger, P.N. Butow, J. Coll, T. Bullen, J. Wilson, B. Baylock, B. Meiser, M.A. Price, Long-term outcomes of risk-reducing surgery in unaffected women at increased familial risk of breast and/or ovarian cancer, Fam Cancer 14(1) (2015) 105-15.

[30] C. Garcia, L. Lyon, C. Conell, R.D. Littell, C.B. Powell, Osteoporosis risk and management in BRCA1 and BRCA2 carriers who undergo risk-reducing salpingo-oophorectomy, Gynecol Oncol 138(3) (2015) 723-6.

[31] J. Kotsopoulos, T. Huzarski, J. Gronwald, P. Moller, H.T. Lynch, S.L. Neuhausen, L. Senter, R. Demsky, W.D. Foulkes, C. Eng, B. Karlan, N. Tung, C.F. Singer, P. Sun, J. Lubinski, S.A. Narod, Hormone replacement therapy after menopause and risk of breast cancer in BRCA1 mutation carriers: a case-control study, Breast Cancer Res Treat 155(2) (2016) 365-73.

[32] P.E. Tucker, M.K. Bulsara, S.G. Salfinger, J.J. Tan, H. Green, P.A. Cohen, The effects of pre-operative menopausal status and hormone replacement therapy (HRT) on sexuality and quality of life after risk-reducing salpingo-oophorectomy, Maturitas 85 (2016) 42-8.

[33] J. Challberg, L. Ashcroft, F. Lalloo, B. Eckersley, R. Clayton, P. Hopwood, P. Selby, A. Howell, D.G. Evans, Menopausal symptoms and bone health in women undertaking risk reducing bilateral salpingo-oophorectomy: significant bone health issues in those not taking HRT, Br J Cancer 105(1) (2011) 22-7.

[34] J.B. Madalinska, M. van Beurden, E.M. Bleiker, H.B. Valdimarsdottir, J. Hollenstein, L.F. Massuger, K.N. Gaarenstroom, M.J. Mourits, R.H. Verheijen, E.B. van Dorst, H. van der Putten,

K. van der Velden, H. Boonstra, N.K. Aaronson, The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women after prophylactic salpingo-oophorectomy, J Clin Oncol 24(22) (2006) 3576-82.

[35] T.M. Michelsen, S. Tonstad, A.H. Pripp, C.G. Trope, A. Dorum, Coronary heart disease risk profile in women who underwent salpingo-oophorectomy to prevent hereditary breast ovarian cancer, Int J Gynecol Cancer 20(2) (2010) 233-9.

[36] N. Johansen, A.H. Liavaag, T.G. Tanbo, A.A. Dahl, A.H. Pripp, T.M. Michelsen, Sexual activity and functioning after risk-reducing salpingo-oophorectomy: Impact of hormone replacement therapy, Gynecol Oncol 140(1) (2016) 101-6.

[37] J.S. Chapman, C.B. Powell, J. McLennan, B. Crawford, J. Mak, N. Stewart, L.M. Chen, Surveillance of survivors: follow-up after risk-reducing salpingo-oophorectomy in BRCA 1/2 mutation carriers, Gynecol Oncol 122(2) (2011) 339-43.

[38] A. Finch, K.A. Metcalfe, J.K. Chiang, L. Elit, J. McLaughlin, C. Springate, R. Demsky, J. Murphy, B. Rosen, S.A. Narod, The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation, Gynecol Oncol 121(1) (2011) 163-8.

[39] L. Elit, C. Charles, I. Gold, A. Gafni, S. Farrell, S. Tedford, D. Dal Bello, T. Whelan, Women's perceptions about treatment decision making for ovarian cancer, Gynecol Oncol 88(2) (2003) 89-95.

[40] M. Robson, M. Hensley, R. Barakat, C. Brown, D. Chi, E. Poynor, K. Offit, Quality of life in women at risk for ovarian cancer who have undergone risk-reducing oophorectomy, Gynecol Oncol 89(2) (2003) 281-7.

[41] L. Elit, M.J. Esplen, K. Butler, S. Narod, Quality of life and psychosexual adjustment after prophylactic oophorectomy for a family history of ovarian cancer, Fam Cancer 1(3-4) (2001) 149-56.

[42] J.B. Madalinska, J. Hollenstein, E. Bleiker, M. van Beurden, H.B. Valdimarsdottir, L.F. Massuger, K.N. Gaarenstroom, M.J. Mourits, R.H. Verheijen, E.B. van Dorst, H. van der Putten, K. van der Velden, H. Boonstra, N.K. Aaronson, Quality-of-life effects of prophylactic salpingo-oophorectomy versus gynecologic screening among women at increased risk of hereditary ovarian cancer, J Clin Oncol 23(28) (2005) 6890-8.

[43] S. Ozdemir, C. Celik, H. Gorkemli, A. Kiyici, B. Kaya, Compared effects of surgical and natural menopause on climacteric symptoms, osteoporosis, and metabolic syndrome, Int J Gynaecol Obstet 106(1) (2009) 57-61.

[44] M.A. Limouzin-Lamothe, N. Mairon, C.R. Joyce, M. Le Gal, Quality of life after the menopause: influence of hormonal replacement therapy, Am J Obstet Gynecol 170(2) (1994) 618-24.

[45] K. Kotz, J.L. Alexander, L. Dennerstein, Estrogen and androgen hormone therapy and well-being in surgically postmenopausal women, J Womens Health (Larchmt) 15(8) (2006) 898-908.

[46] R. Buzgova, J. Kaniokova, [The influence of hormone replacement therapy on the quality of life of women in menopause], Ceska Gynekol 78(5) (2013) 420-6.

[47] V.L. Zimmerman, S.C. Smeltzer, Hormone therapy and breast cancer, Clin Excell Nurse Pract 4(1) (2000) 30-4.

[48] M.A. Gerend, L.S. Aiken, M.J. Erchull, A. Lapin, Women's use of hormone therapy before and after the Women's Health Initiative: a psychosocial model of stability and change, Prev Med 43(3) (2006) 158-64.

[49] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, J. Ockene, Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial, JAMA 288(3) (2002) 321-33.

[50] M.L. Stefanick, G.L. Anderson, K.L. Margolis, S.L. Hendrix, R.J. Rodabough, E.D. Paskett, D.S. Lane, F.A. Hubbell, A.R. Assaf, G.E. Sarto, R.S. Schenken, S. Yasmeen, L. Lessin, R.T. Chlebowski, Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy, JAMA 295(14) (2006) 1647-57.

[51] V. Beral, Breast cancer and hormone-replacement therapy in the Million Women Study, Lancet 362(9382) (2003) 419-27.

[52] F. Guidozzi, Hormone therapy after prophylactic risk-reducing bilateral salpingo-oophorectomy in women who have BRCA gene mutation, Climacteric (2016) 1-4.

[53] A.H. Maclennan, J.L. Broadbent, S. Lester, V. Moore, Oral oestrogen and combined oestrogen/progestogen therapy versus placebo for hot flushes, Cochrane Database Syst Rev (4) (2004) CD002978.

[54] J. Suckling, A. Lethaby, R. Kennedy, Local oestrogen for vaginal atrophy in postmenopausal women, Cochrane Database Syst Rev (4) (2006) CD001500.

[55] L. Dennerstein, J.L. Alexander, K. Kotz, The menopause and sexual functioning: a review of the population-based studies, Annu Rev Sex Res 14 (2003) 64-82.

[56] C.L. Hughes, Jr., L.L. Wall, W.T. Creasman, Reproductive hormone levels in gynecologic oncology patients undergoing surgical castration after spontaneous menopause, Gynecol Oncol 40(1) (1991) 42-5.

[57] J.L. Shifren, Androgen deficiency in the oophorectomized woman, Fertil Steril 77 Suppl 4 (2002) S60-2.

[58] B.B. Sherwin, M.M. Gelfand, The role of androgen in the maintenance of sexual functioning in oophorectomized women, Psychosom Med 49(4) (1987) 397-409.

[59] J.P.T. Higgins, S. Green, Cochrane Collaboration., Cochrane handbook for systematic reviews of interventions, Wiley-Blackwell, Chichester, England ; Hoboken, NJ, 2008.

Figure 4.1. Flow chart for study identification and selection

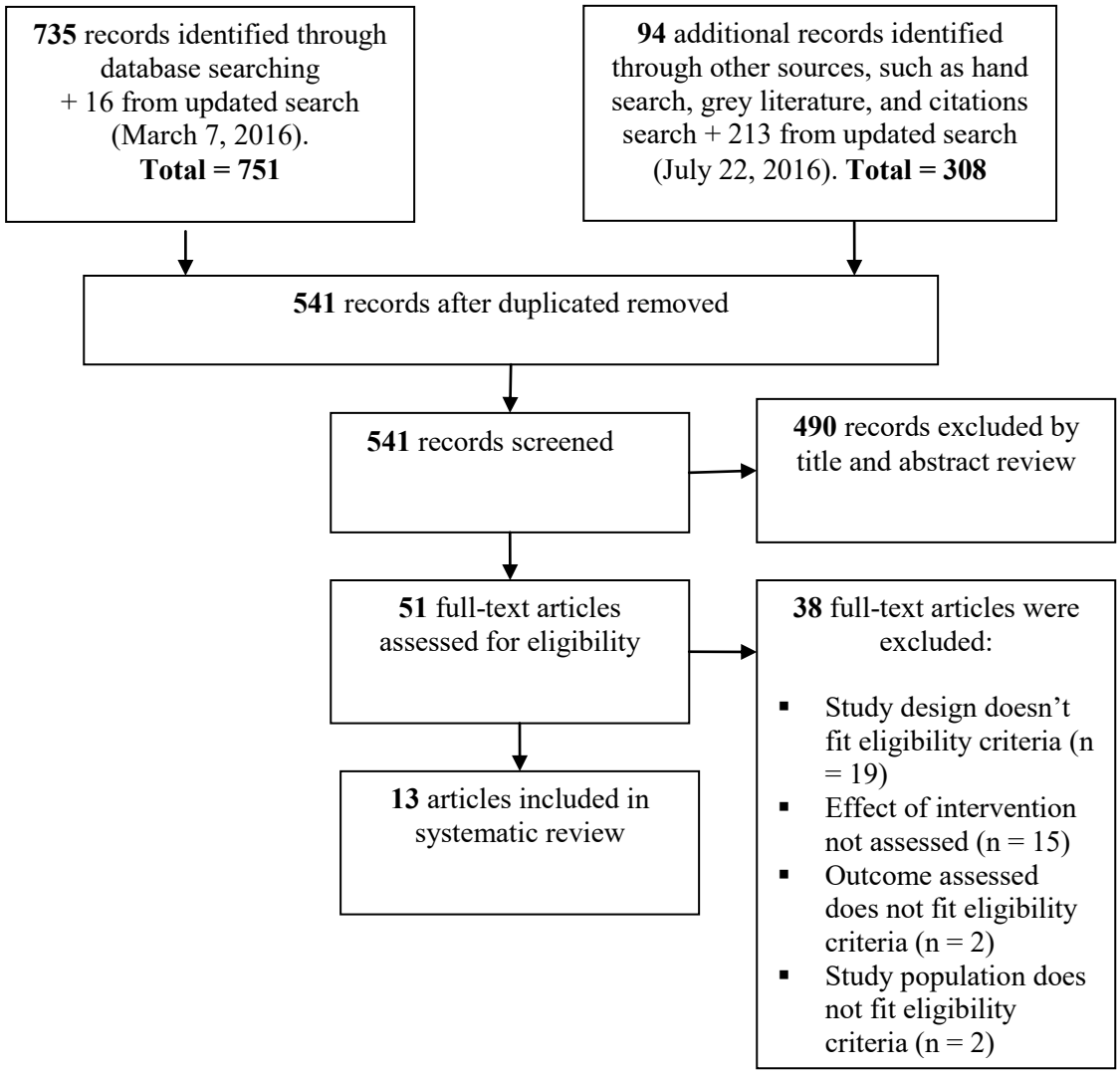


Table 4.1. Study characteristics

First author, year of publication	Study design	Sample size	Sample size for RRSO	Age at time of study[a], mean (range/SD)[b]	BRCA status (%)	Menopause status at time of RRSO (%)	Age at RRSO surgery, mean(range/SD)[b]	Comparator	Quality rating
Challberg, 2011[25]	Cross-sectional survey design	212	212	50(36-77)	BRCA1 & BRCA2 (58%)	Premenopausal (100%)	41.20 (24-48)	Non-exposed and previous users	Low
Chapman, 2011[29]	Cross-sectional survey design	51	51	49 (36-54)	BRCA1 (63%) & BRCA2 (37%)	Premenopausal (47%) & Postmenopausal (53%)	46 (31–68)	Non-exposed	Low
Eisen, 2008[14]	Matched case control study	472	136	NS	BRCA1 (100%)	Premenopausal (100%)	42.45 (28 – 52)[c]	Control (no outcome)	High
Finch, 2011[30]	Prospective cohort study	114	114	53(42-74)	BRCA1 (51%) & BRCA2 (49%)	Premenopausal (66%) & Postmenopausal (34%)	47.50 (35-69)	Non-exposed, baseline	Low
Gabriel, 2008[20]	Retrospective cohort study	73	73	NS	BRCA1 (64%) & BRCA2 (38%)	Premenopausal (NS) & Postmenopausal (NS)	42 (29.5-59.2)	Non-exposed	Low
Garcia, 2015[22]	Retrospective chart review	225	225	NS	BRCA1 & 2 (100%)	Premenopausal (NS) & Postmenopausal (NS)	50 (31-80)	Non-exposed	Low
Heiniger, 2014[21]	Matched prospective cohort design	233	38	NS	BRCA1 & 2 (16.7%)	Premenopausal (NS) & Postmenopausal (NS)	NS	Non-exposed and previous users	Low
Johansen, 2016[28]	Retrospective cohort study	1522	294	54(33-83)	NS[d]	Premenopausal (NS) & Postmenopausal (NS)	48(31-76)	Non-exposed	Low

Kotsopoulos, 2016[23]	Matched case control study	864	210	NS	BRCA 1 (100%)	Premenopausal (NS) & Postmenopausal (NS)	42.75(28-53)[c]	Control (no outcome)	Low
Madalinska, 2006[26]	Cross-sectional survey design	450	450	46±6 (range34-59)	BRCA1 & 2 (48%)	Premenopausal (100%)	43±6	Non-exposed	High
Michelsen, 2009[27]	Cross-sectional survey design	1956	326	54.4(8.9)	BRCA1 & 2 (20%)	Premenopausal (NS) & Postmenopausal (NS)	48±7.8	Non-exposed	High
Rebbeck, 2005[13]	Prospective cohort study	462	155	42.7(37-78)	BRCA1 (70%) & BRCA2 (30%)	Premenopausal (NS) & Postmenopausal (NS)	NS	Non-exposed	High
Tucker, 2016[24]	Cross-sectional survey design	119	119	NS	BRCA1 (8.40%) & BRCA2 (11.70%)	Premenopausal (43%) & Postmenopausal (57%)	50(33-69)	Non-exposed	Low

NS = Not specified; RRSO = Risk reducing salpingo-oophorectomy; [a] for RRSO cohort only; [b]based on the measure of variance reported in the primary study; [c]average age at surgery among cases and controls; [d]BRCA status is captured in the questionnaire but not reported in paper

Table 4.2. Intervention characteristics

First author	Type of HT	Dose of ET	Route of ET	Duration of HT[a]-mean (range/SD)[b]
Challberg[25]	ET, EPT and tibolone	NS	NS	3.4 (0.1-19)
Chapman[29]	NS	NS	NS	6 (0.75-9)
Eisen[14]	ET and EPT	NS	NS	3.85[c] (NS)
Finch[30]	ET and EPT	NS	NS	NS
Gabriel[20]	ET and EPT	NS	NS	2.79 ±3.22
Garcia[22]	NS	NS	Systemic HT (60%)	NS
Heiniger[21]	NS	NS	NS	NS
Johansen[28]	ET, EPT and tibolone	NS	Systemic HT (39.28%) & local/vaginal HT (6.54%)	NS
Kotsopoulos[23]	ET and EPT	NS	NS	4.35(0.05-25)[c]
Madalinska[26]	EPT and tibolone	NS (standard)	Systemic HT (Oral/transdermal)	3 ±2.3
Michelsen[27]	NS	NS	Systemic (Oral/transdermal)	NS
Rebbeck[13]	ET and EPT	NS	NS	NS
Tucker[24]	ET	NS	Systemic HT (20% - oral and transdermal) & local/vaginal HT (8%)	NS

HT = Hormone therapy; ET = Estrogen therapy; EPT = Estrogen progesterone therapy; NS = Not specified
[a]in years; [b]based on the measure of variance reported in the primary study; [c]average duration of use among cases and controls

Table 4.3. Outcome data for individual studies: HT users versus non-users

Outcome	First author	Tool of assessment	N of analysis	Mean difference[ab]	Measure of association (95% CI)[c]	P value	Duration of follow-up
General quality of life	Tucker[24]	Short form Health Survey (SF-36) - total	108	Systemic HT = 1.76	-	0.57	NA
			93	Local HT = 3.3	-	0.86	
		SF-36 – pain	108	Systemic HT = 14.64	-	**<0.01**	
			93	Local HT = 4.85	-	0.75	
		SF-36 – physical	108	Systemic HT = 7.15	-	0.38	
			93	Local HT = 5.34	-	0.52	
		SF-36 – emotional	108	Systemic HT = -0.50	-	0.50	
			93	Local HT = -5.5	-	0.27	
		SF-36 – social	108	Systemic HT = -3.67	-	0.82	
			93	Local HT = 3.66	-	0.92	
		SF-36 – energy	108	Systemic HT = 0.6	-	0.42	
			93	Local HT = 3.66	-	0.87	
		SF-36 – general health	108	Systemic HT = 4.55	-	0.55	
			93	Local HT = 3.37	-	0.96	
Menopause specific quality of life	Challberg[25]	Self-reported-FACT-ES[d]-Total	141	3.1	-	0.09	NA
	Chapman[29]	Self-reported-MSL[e] - Total	51	-1.1	-	0.06	NA

	Finch[30]	Self-reported-MENQOL Intervention[e] – total	73	-3.37[f]	-	**<0.01**	13.6 months (10.8–21.8)
		MENQOL – vasomotor	73	-3.4	-	**<0.01**	
		MENQOL – physical	73	-0.38	-	0.28	
		MENQOL – psychosocial	73	-0.07	-	0.89	
		MENQOL – sexual	73	-1.22	-	**0.02**	
	Heiniger[21]	Self-reported-MRS[e]	38	NS	-	>0.05	3 years[g]
	Madalinska[26]	Self-reported-FACTES[d] - Total	164	3.4	-	**0.03**	NA
	Tucker[24]	Self-reported MENQOL[e] – total	108	Systemic HT = -2.76[f]	-	**<0.01**	
			93	Local HT = -2.23[f]	-	**<0.01**	
		MENQOL – vasomotor	108	Systemic HT = -1.08	-	**0.02**	
			93	Local HT = -1.04	-	0.22	
		MENQOL – physical	108	Systemic HT = -0.74	-	**0.03**	
			93	Local HT = -0.54	-	0.38	
		MENQOL – psychosocial	108	Systemic HT = -0.1	-	0.36	
			93	Local HT = -0.1	-	0.91	

		MENQOL – sexual	108	Systemic HT = -0.84	-	**0.03**	
			93	Local HT = -0.55	-	0.74	
Breast cancer	Eisen[14]	Self-reported[h]	124	-	OR = 0.48(0.19-1.21)	0.12	NA
	Kotsopoulos[23] *Same study as Eisen but an updated analysis*	Self-reported	210	-	OR = 1.06(0.58-1.96)	0.85	NA
					OR = 1.06(0.52-2.18) - *Breast cancer risk with HT use of ≤3 years vs. never use*	0.87	
					OR = 1.06 (0.41-2.71) - *Breast cancer risk with HT use of >3 years vs. never use*	0.91	
	Gabriel[20]	Self-reported[h]	60	-	OR = 0.31(0.09-1.04)[f]	>0.05	NS
					OR = 0.48(0.1-2.1) - *Breast cancer risk with ET only (no cases with EPT)*	>0.05	
	Rebbeck[13]	Medical records, operative notes, and pathology reports	155	-	HR = 3.93(0.51-30.50)[i]	>0.05	2.6 years (0.1-19.1)
					HR = 2.56(0.08-78.13) *Breast cancer risk with EPT vs. ET*	>0.05	
Vasomotor symptoms	Challberg[25]	Self-reported - FACT-ES[j]	141	-	Hot flashes OR = 0.55(0.23-1.28)[f]	>0.05	NA
					Night sweats OR = 0.28(0.11-0.76)[f]	**<0.05**	
	Finch[30]	Self-reported	73	-	Hot flashes OR = 0.27(0.09-0.80)[f]	**0.03**	13.6 months (10.8–21.8)
	Madalinska[26]	Self-reported-FACT-ES[j]	164	-	Hot flashes OR = 0.34(0.17-0.70)[f]	**<0.01**	NA
					Night sweats OR = 0.51(0.26-1.00)[f]	**0.04**	

Sexual function	Finch[k30]	Self-reported-SAQ[d]	61	Pleasure = 1.22		0.50	13.6 months (10.8–21.8)
				Discomfort = 1.92		**0.03**	
				Habit = 0.19		0.10	
	Heiniger[21]	Self-reported-SAQ[d]	38	NS for all 3 dimensions	-	>0.05	
	Johansen[28]	Self-reported SAQ[l]	157	Pleasure systemic HT (both ET and EPT) = 0.9	-	>0.05	
			102	Pleasure local HT = -1.5	-	>0.05	
			116	Pleasure systemic ET = 0.8		>0.05	
			111	Pleasure systemic EPT = 0.5		>0.05	
			112	Pleasure systemic tibolone = 1.5		>0.05	
			157	Discomfort systemic HT (both Et and EPT) = -1.2		**<0.01**	
			102	Discomfort local HT = -0.7		0.2	
			116	Discomfort systemic ET = -1.1		**0.04**	
			111	Discomfort systemic EPT = -1.2		**0.02**	

			112	Discomfort systemic tibolone = -1.39		**<0.01**	
	Madalinska[26]	Self-reported-SAQ[d]	164	Pleasure = 0.4		0.70	NA
				Discomfort = 0.4		0.17	
				Habit = 0.1		0.45	
	Tucker[24]	Self-reported-Female Sexual Function index (FSFI)[dm]- total	108	Systemic HT 5.36	OR = 0.40(0.12-1.31); P = 0.130 *Risk of FSD with systemic HT*	0.14	NA
			93	Local HT 7.61	OR = 0.22(0.05-0.95); P = **0.043** *Risk of FSD with local HT*	0.07	
		FSFI – desire[n]	108	Systemic HT 0.09	OR = 0.77(0.23-2.52) P = 0.66 *Risk of HSDD with systemic HT*	0.83	
			93	Local HT 0.52	OR = 0.29(0.07-1.28); P = 0.10 *Risk of HSDD with local HT*	0.25	
		FSFI – arousal	108	Systemic HT 0.57	-	0.63	
			93	Local HT 1.35	-	0.09	
		FSFI – lubrication[o]	108	Systemic HT 1.39	OR = 0.38(0.12-1.19); P = 0.10 *Risk of lubrication difficulty with systemic HT*	**0.04**	
			93	Local HT 1.84	OR = 0.29(0.05-1.53); P = 0.14 *Risk of lubrication difficulty with local HT*	**0.03**	
		FSFI – pain[o]	108	Systemic HT	OR = 0.16(0.03-0.81);	**<0.01**	

				1.97	P = **0.03** *Risk of dyspareunia with systemic HT*		
			93	Local HT 1.55	OR = 0.99(0.22-4.47); P = 0.99 *Risk of dyspareunia with local HT*	0.05	
		FSFI – orgasm[o]	108	Systemic HT 0.71	OR = 0.35(0.10-1.21); P = 0.10 *Risk of orgasm difficulty with systemic HT*	0.40	
			93	Local HT 1.47	OR = 0.57(0.10-3.15); P = 0.52 *Risk of orgasm difficulty with local HT*	0.13	
		FSFI – satisfaction[o]	108	Systemic HT 0.62	OR = 0.36(0.11-1.14); P = 0.08 *Risk of dissatisfaction with sex life with systemic HT*	0.25	
			93	Local HT 0.86	OR = 0.88(0.19-4.06); P = 0.87 *Risk of dissatisfaction of sex life with local HT*	0.36	
		Female sexual distress scale – revised (FSDS)[p]	108	Systemic HT -4.07	OR = 0.36(0.16-1.13); P = 0.08 *Risk of sexual distress with systemic HT*	0.07	
			93	Local HT -2.34	OR= 1.28(0.30-5.41); P = 0.74 *Risk of sexual distress with local HT*	0.94	
Loss of interest in sex	Challberg[25]	Self-reported - FACT-ES[j]	141		OR = 0.68(0.34-1.37)[f]	>0.05	NA
	Madalinska[26]	Self-reported- FACT-ES[j]	164		OR = 0.66(0.30-1.47)[f]	0.35	NA
Vaginal dryness	Challberg[25]	Self-reported - FACT-ES[j]	141		OR = 0.48(0.20-1.16)[f]	>0.05	NA
	Finch[30]	Self-reported – MENQOL	73	-1.22		**0.02**	13.6 months (10.8–21.8)

		Intervention[e]					
	Madalinska[26]	Self-reported-FACT-ES[j]	164	-	OR = 0.47(0.21-1.07)[f]	>0.05	NA
	Tucker[24]	MENQOL – sexual	108	Systemic HT = -0.84	-	**0.03**	
			93	Local HT = -0.55	-	0.74	
		FSFI – lubrication[o]	108	Systemic HT 1.39	OR = 0.38(0.12-1.19); P = 0.10 *Risk of lubrication difficulty with systemic HT*	**0.04**	
Bone loss prevention	Challebrg[25]		93	Local HT 1.84	OR = 0.29(0.05-1.53); P = 0.14 *Risk of lubrication difficulty with local HT*	**0.03**	NA
	Chapman[29]	DXA scan	31	-	OR = 0.41(0.07-2.41)[fi]	>0.05	NA
	Garcia[22]	DXA scan	198		OR = 0.84(0.26-2.74)	>0.05	NA
Cardiovasc-ular disease	Michelsen[27]	Physical measurements, blood samples and self-administered questionnaire	326	-	NS	>0.05	NA

Bold values indicate statistical significance; CI = confidence interval; FACT-ES = 18-item functional assessment of cancer therapy-endocrine score; NA = Not applicable (due to cross-sectional nature of data); MSL = menopause symptoms list; MENQOL = menopause-specific quality of life; MRS = Menopause rating scale; SAQ = Sexual activity questionnaire; FSFI = Female Sexual Function index; FSD = Female sexual dysfunction; FSDS-R = Female sexual distress scale- revised; HSDD = Hypoactive sexual desire disorder; [a]mean score of users minus the mean score of non-users; [b]continuous outcome; [c]discrete outcome; [d]higher score indicates improvement of symptoms; [e]higher score indicates worsening of symptoms; [f]measures of effect not reported in primary study but calculated from reported data(unadjusted); [g] menopausal symptoms and sexual activity were measured only once in the follow-up interview, no baseline assessment for these variables were performed; [h]diagnosis confirmed through medical records and pathology reports; [i]authors contacted for measure of effect and 95% CI as not reported in published paper; [j]individual symptoms of the FACT-ES scale were dichotomized (symptom present was considered to be a response in either of the two highest categories, "very much" and "quite a bit"); [k]standard deviation for sexual activity questionnaire domains was not reported in study, values were imputed from Madalinska et al. for meta-analysis[52]; [l]a higher pleasure score indicates high pleasure and a higher discomfort score indicates higher discomfort; [m]FSFI- total score is dichotomized to identify risk of FSD with those scoring ≤26.55 considered likely to have FSD; [n]FSFI-desire sub-score is dichotomized to identify the risk of HSDD with those scoring ≤5 having a high likelihood of HSDD; [o]dichotomization criterion of these sub-scores was not reported in the primary study; [p] a cutoff score of ≥11 on the FSDS-R was used to indicate high levels of sexual distress

Appendix 4.1. Search strategy for electronic bibliographic databases

Systematic searches were conducted in a variety of databases including MEDLINE, EMBASE, CINAHL, Proquest Dissertations and Theses, SCOPUS, LILACS, PsycINFO, and Cochrane Library by an expert searcher (SC), between February 25, 2014 and March 21, 2014 and updated in March, 2016. Searches were conducted using controlled vocabularies (eg: MeSH and EMTREE) and key words representing the concepts: (bcra1 or bcra2) and (oopherectomy) and (hormone replacement therap*). No limits were applied. Search strategies are available in Appendix 1.

Grey literature searches were conducted in SCOPUS, Web of Science, Google Scholar, Proquest, Dissertations and Theses and clinical trials registries, between February 25, 2014 and March 21, 2014 and updated in July 2016. Other searches included hand searches of reference list of review papers; and citation search of studies included in the systematic review

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

---

1 exp Genes, BRCA2/ or exp Genes, BRCA1/ or brca1.mp. (10753)

2 exp BRCA2 Protein/ or brca2.mp. (6557)

3 hereditary breast cancer*.mp. (781)

4 (HEREDITARY BREAST and OVARIAN CANCER SYNDROME).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (157)

5 exp BRCA1 Protein/ (3477)

6 "breast cancer 1".mp. (488)

7 "breast cancer 2".mp. (271)

8 genetic predisposition.mp. or exp Genetic Predisposition to Disease/ (93864)

9 exp Breast Neoplasms/ or (ovarian carcinoma* or breast carcinoma* or ovarian cancer* or ovarian neoplasm* or breast cancer* or breast neoplasm*).mp. (314845)

10 8 and 9 (6302)

11 1 or 2 or 3 or 4 or 6 or 7 or 10 (16245)

12 ((family history or familial*) adj1 (ovarian carcinoma* or breast carcinoma* or ovarian cancer* or ovarian
neoplasm* or breast cancer* or breast neoplasm*)).mp. [mp=title, abstract, original title, name of substance word,subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1317)

13 11 or 12 (16671)

14 (hormone adj2 therap*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (26211)

15 exp Hormone Replacement Therapy/ (20628)

16 exp Progesterone Congeners/ or exp Estrogens/ or hrt.mp. (180437)

17 exp Progesterone/ or (progesterone adj1 (replacement* or therap*)).mp. (63082)

18 14 or 15 or 16 or 17 (204693)

19 exp Ovariectomy/ (20317)

20 (oophorectom* or ovariectom* or oophorotom* or ovarectom* or ovariotom* or ovarotom* or ovary amputation* or ovary resection* or salpingooophorectom*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (35698)
21 (female adj castration*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (27)
22 (BPSO or BOO or BSO or BPO or RRSO).mp. (3518)
23 19 or 20 or 21 or 22 (38969)
24 13 and 18 and 23 (72)
25 exp Genes, BRCA2/ or exp Genes, BRCA1/ or brca1.mp. (10753)
26 exp BRCA2 Protein/ or brca2.mp. (6557)
27 hereditary breast cancer*.mp. (781)
28 (HEREDITARY BREAST and OVARIAN CANCER SYNDROME).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (157)
29 exp BRCA1 Protein/ (3477)
30 ("breast cancer 1" or breast cancer type 1).mp. [mp=title, abstract, original title, name of substance word,
subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (516)
31 ("breast cancer 2" or breast cancer type 2).mp. (279)
32 genetic predisposition.mp. or exp Genetic Predisposition to Disease/ (93864)
33 exp Breast Neoplasms/ or (ovarian carcinoma* or breast carcinoma* or ovarian cancer* or ovarian neoplasm* or breast cancer* or breast neoplasm*).mp. (314845)
34 32 and 33 (6302)
35 25 or 26 or 27 or 28 or 30 or 31 or 34 (16254)
36 ((family history or familial*) adj1 (ovarian carcinoma* or breast carcinoma* or ovarian cancer* or ovarian
neoplasm* or breast cancer* or breast neoplasm*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1317)
37 35 or 36 (16680)
38 (hormone adj2 therap*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (26211)
39 exp Hormone Replacement Therapy/ (20628)
40 exp Progesterone Congeners/ or exp Estrogens/ or hrt.mp. (180437)
41 exp Progesterone/ or (progesterone adj1 (replacement* or therap*)).mp. (63082)
42 38 or 39 or 40 or 41 (204693)
43 exp Ovariectomy/ (20317)
44 (oophorectom* or ovariectom* or oophorotom* or ovarectom* or ovariotom* or ovarotom* or ovary amputation* or ovary resection* or salpingooophorectom*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept

word, rare disease supplementary concept word, unique identifier] (35698)
45 (female adj castration*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (27)
46 (BPSO or BOO or BSO or BPO or RRSO).mp. (3518)
47 43 or 44 or 45 or 46 (38969)
48 37 and 42 and 47 (72)

Database: Embase <1974 to 2014 Week 10>

Search Strategy:

---

1 exp BRCA2 protein/ or exp BRCA1 protein/ (10834)
2 (BCRA* or breast cancer type 1 or breast cancer type 2).mp. (381)
3 familial cancer/ or exp genetic predisposition/ (85814)
4 exp breast tumor/ (347062)
5 exp ovary cancer/ (73287)
6 ((hereditary or genetic predisposition* or familial or family history) adj1 (breast cancer* or breast neoplasm* or breast carcinoma* or ovar* cancer* or ovar* neoplasm* or ovar* carcinoma*)).mp. (8677)
7 (breast cancer* or breast neoplasm* or breast carcinoma* or ovar* cancer* or ovar* neoplasm* or ovar*
carcinoma*).mp. (393377)
8 3 and (4 or 5 or 7) (7590)
9 1 or 2 or 6 or 8 (21148)
10 hormone replacement therap*.mp. or exp hormone substitution/ (50266)
11 hormone substitution*.mp. (29283)
12 (progesterone adj1 (replacement* or therap*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (4418)
13 exp estrogen/ (223236)
14 exp progesterone/ (77616)
15 hrt.mp. (11036)
16 10 or 11 or 12 or 13 or 14 or 15 (285069)
17 exp ovariectomy/ (28267)
18 (oophorectom* or ovariectom* or oophorotom* or ovarectom* or ovariotom* or ovarotom* or ovary amputation* or ovary resection* or salpingooophorectom*).ti,ab. (34545)
19 (female adj castration*).ti,ab. (29)
20 (BPSO or BOO or BSO or BPO or RRSO).ti,ab. (4567)
21 17 or 18 or 19 or 20 (46318)
22 9 and 16 and 21 (204)

****

SCOPUS Searched Feb 25, 2014

(TITLE-ABS-KEY(**hrt** OR **"hormone therap*"** OR **"hormone substitution"** OR **"hormone replace*"** OR **progesterone*** OR **estrogen**)) AND ((TITLE-ABS-KEY(**bcra*** OR **"hereditary breast cancer"** OR **"breast cancer 1"** OR**"breast cancer type 1"** OR **"breast cancer 2"** OR **"breast cancer type 2"**)) OR ((TITLE-ABS-KEY((**"ovarian carcinoma*"** OR **"breast carcinoma*"** OR **"ovarian**

cancer*" OR **"ovarian neoplasm*"** OR **"breast cancer*"** OR **"breast neoplasm*") .**) AND TITLE-ABS-KEY(**"family history"** OR **familial** OR **"genetic predispos*"**))) OR ((TITLE-ABS-KEY(**bcra*** OR **"hereditary breast cancer"** OR **"breast cancer 1"** OR **"breast cancer type 1"** OR **"breast cancer 2"** OR **"breast cancer type 2"**)) OR ((TITLE-ABS-KEY((**"ovarian carcinoma*"** OR **"breast carcinoma*"** OR **"ovarian cancer*"** OR **"ovarian neoplasm*"** OR **"breast cancer*"** OR **"breast neoplasm*"**) AND TITLE-ABS-KEY(**"family history"** OR **familial** OR **"genetic predispos*"**)))))) AND ((TITLE(**bpso** OR **boo** OR **bso** OR **bpo** OR **rrso**)) OR (TITLE(**oophorectom*** OR **ovariectom*** OR **oophorotom*** OR **ovarectom*** OR **ovariotom*** OR **ovarotom*** OR **"ovary amputation"**)) OR (TITLE-ABS-KEY(**"ovary resection*"** OR **salpingooophorectom***)) OR (TITLE-ABS-KEY(**"female castration*"**)))

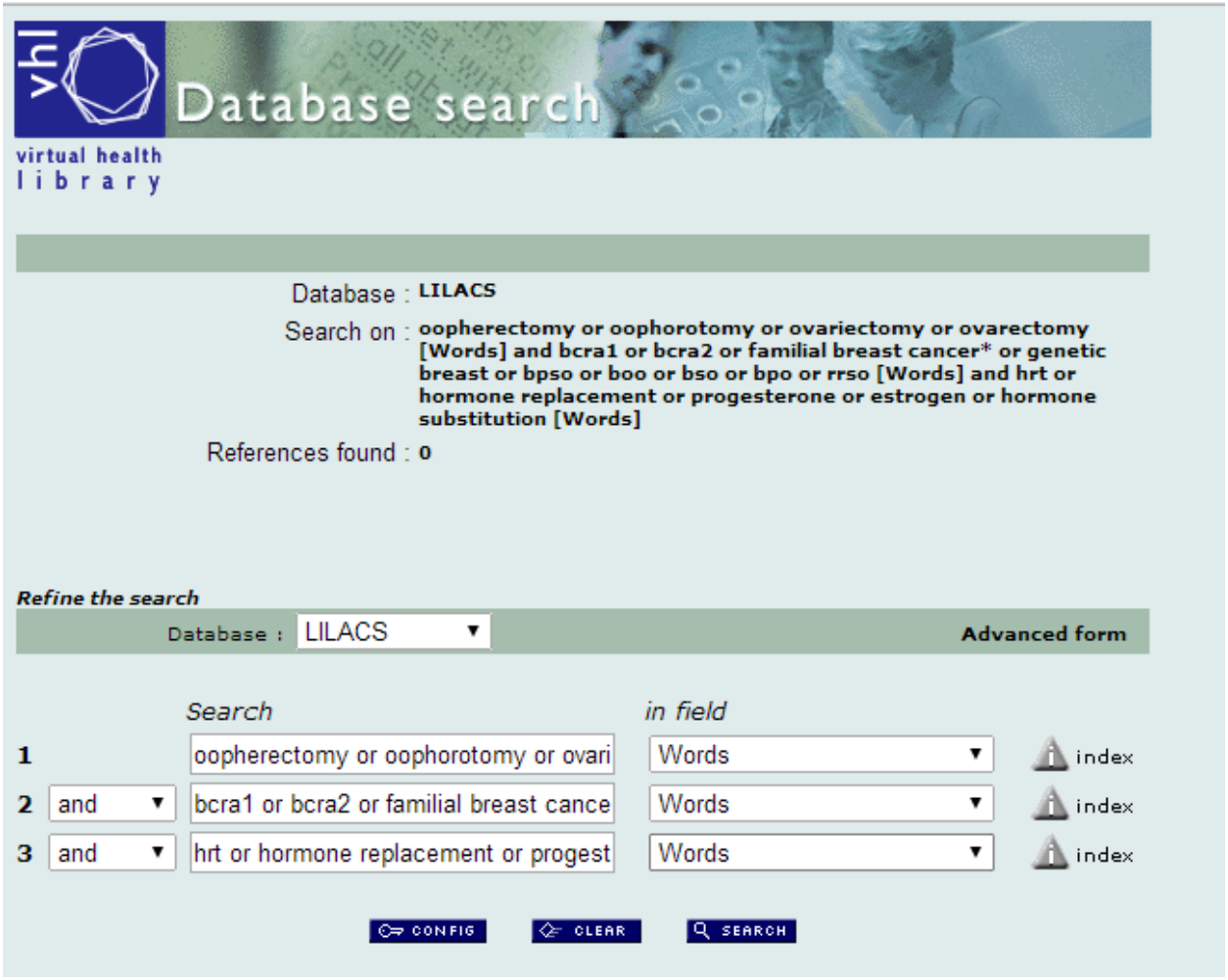
CINAHL March 21, 2014

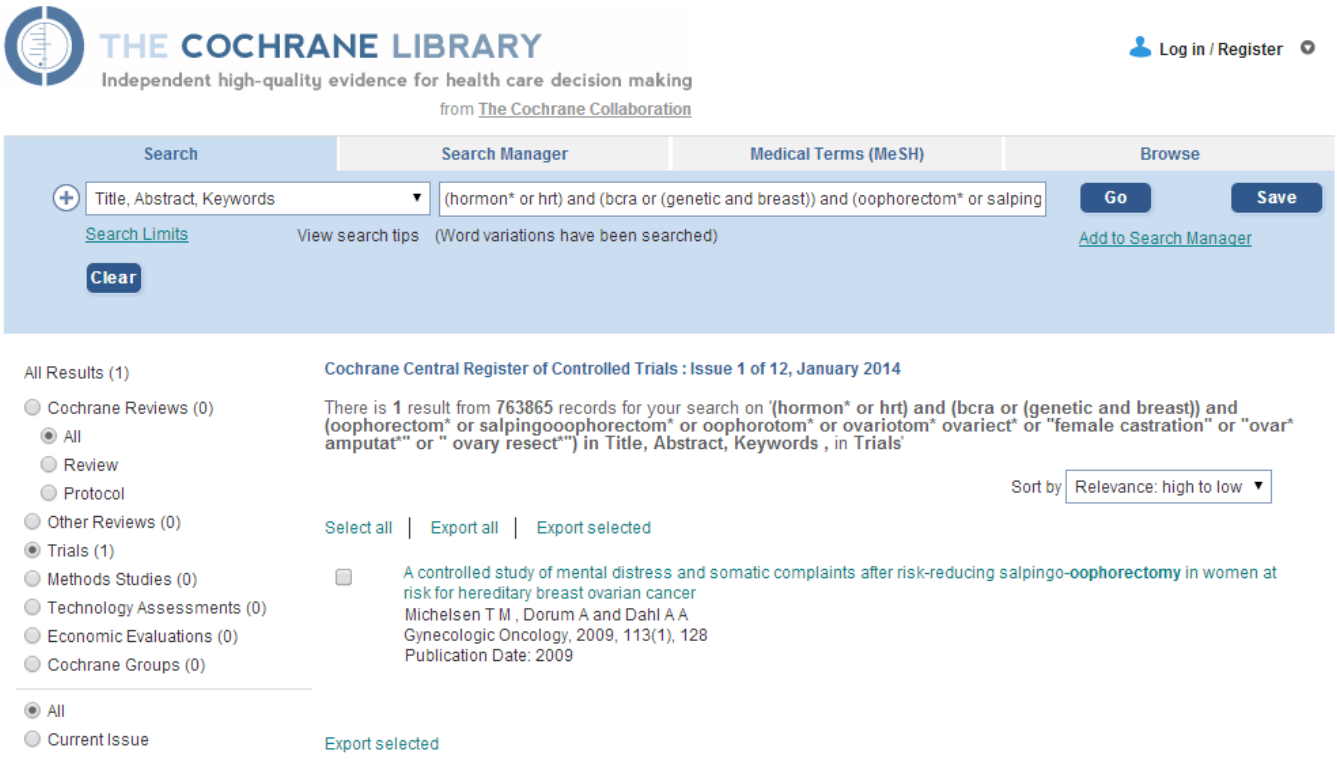
Friday, March 21, 2014 4:57:45 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S30	((S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28)) AND (S7 AND S15 AND S29)	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	28
S29	(S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28)	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2,071
S28	AB BPSO or BOO or BSO or BPO or RRSO	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	96
S27	TI BPSO or BOO or BSO or BPO or RRSO	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	39
S26	"female castration*"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1
S25	salpingooophorectom*	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	12
S24	"ovary resection*"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S23	"ovary amputation*"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S22	ovarotom*	Search modes - SmartText Searching	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S21	ovarotom*	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S20	ovarectom*	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	4
S19	oophorotomy	Search modes - SmartText Searching	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S18	oophorotom*	Search modes - SmartText Searching	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S17	oophorectom*	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,883
S16	"ovariectomy" OR (MH "Oophorectomy")	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,641
S15	(S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14)	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	22,638
S14	progesterone n1 replacement	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	19
S13	"estrogen" OR (MH "Estrogens+")	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	13,012
S12	(MH "Progesterone+")	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2,932
S11	progesterone	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,268
S10	hrt	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,443
S9	hormone n2 therap*	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	11,507
S8	(MH "Hormone Replacement Therapy") OR (MH "Hormone Therapy")	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	9,035
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,055

S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,055
S6	((hereditary or "genetic predisposition*" or familial or "family history") n1 ("breast cancer*" or "breast neoplasm*" or "breast carcinoma*" or "ovar* cancer*" or "ovar* neoplasm*" or "ovar* carcinoma*"))	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2,366
S5	MH "Hereditary Breast and Ovarian Cancer Syndrome"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	21
S4	Hereditary Breast and Ovarian Cancer Syndrome	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	58
S3	"breast cancer type 2"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1
S2	"breast cancer type 1"	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2
S1	(MH "Genes, BRCA")	Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	951

Lilacs Searched March 21, 2014





Proquest Dissertations and Theses Searched March 21, 2014

all(bpso OR boo OR bso OR bpo OR rrso OR oophorectom* OR ovariectomy* OR oophorotom* OR ovariectomy* OR ovariotomy* OR ovariotomy* OR "ovary amputation" OR "ovary resection*" OR salpingooophorectom* "female castration*") OR all((("ovarian carcinoma*" OR "breast carcinoma*" OR "ovarian cancer*" OR "ovarian neoplasm*" OR "breast cancer*" OR "breast neoplasm*") AND ("family history" OR familial OR "genetic predispos*"))) AND all(bcra* OR "hereditary breast cancer" OR "breast cancer 1" OR "breast cancer type 1" OR "breast cancer 2" OR "breast cancer type 2") AND all(hrt OR "hormone therap*" OR "hormone substitution" OR "hormone replace*" OR progesterone* OR estrogen*) = 1

PsycINFO Searched March 21, 2014
Database: PsycINFO <1987 to March Week 3 2014>
Search Strategy:
---
1 bcra.mp. (1)
2 (("ovarian carcinoma*" or "breast carcinoma*" or "ovarian cancer*" or "ovarian neoplasm*" or "breast cancer*" or "breast neoplasm*") adj2 ("family history" or familial or "genetic predispos*")).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (233)
3 ("hereditary breast cancer" or "breast cancer 1" or "breast cancer type 1" or "breast cancer 2" or "breast cancer type 2").mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (98)
4 1 or 2 or 3 (328)
5 (bpso or boo or bso or bpo or rrso or oophorectom* or ovariectom* or oophorotom* or ovarectom* or ovariotom* or ovarotom* or "ovary amputation" or "ovary resection*" or salpingooophorectom* or "female castration*").mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (2413)
6 (hrt or "hormone therap*" or "hormone substitution" or "hormone replace*" or progesterone* or estrogen*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] (8247)
7 4 and 5 and 6 (1)

Appendix 4.2. Search Strategy for grey literature: an update

SCOPUS Update search July 22, 2016
(((TITLE (**bpso** OR **boo** OR **bso** OR **bpo** OR **rrso**)) OR (TITLE (**oophorectom*** OR **ovariectom*** OR **oophorotom*** OR **ovarectom*** OR **ovariotom*** OR **ovarotom*** OR **"ovary amputation"**)) OR (TITLE-ABS-KEY (**"ovary resection*"** OR **salpingooophorectom***)) OR (TITLE-ABS-KEY (**"female castration*"**)))) AND ((((TITLE-ABS-KEY (**hrt** OR **"hormone therap*"** OR **"hormone substitution"** OR **"hormone replace*"** OR **progesterone*** OR **estrogen**))) AND ((TITLE-ABS-KEY (**bcra*** OR **"hereditary breast cancer"** OR **"breast cancer 1"** OR **"breast cancer type 1"** OR **"breast cancer 2"** OR **"breast cancer type 2"**)))) OR (((TITLE-ABS-KEY (**"ovarian carcinoma*"** OR **"breast carcinoma*"** OR **"ovarian cancer*"** OR **"ovarian neoplasm*"** OR **"breast cancer*"** OR **"breast neoplasm*"**))) AND ((TITLE-ABS-KEY (**"family history"** OR **familial** OR **"genetic predispos*"**)))) OR ((((TITLE-ABS-KEY (**bcra*** OR **"hereditary breast cancer"** OR **"breast cancer 1"** OR **"breast cancer type 1"** OR **"breast cancer 2"** OR **"breast cancer type 2"**))) OR ((TITLE-ABS-KEY (**"ovarian carcinoma*"** OR **"breast carcinoma*"** OR **"ovarian cancer*"** OR **"ovarian neoplasm*"** OR **"breast cancer*"** OR **"breast neoplasm*"**)))) AND ((TITLE-ABS-KEY (**"family history"** OR **familial** OR **"genetic predispos*"**)))))) 87 from 2014 – 2016)
ProQuest dissertation
(all(bpso OR boo OR bso OR bpo OR rrso OR oophorectom* OR ovariectomy* OR oophorotom* OR ovariectomy* OR ovariotomy* OR ovariotomy* OR "ovary amputation" OR "ovary resection*" OR salpingooophorectom* "female castration*") OR all((("ovarian carcinoma*" OR "breast carcinoma*" OR "ovarian cancer*" OR "ovarian neoplasm*" OR "breast cancer*" OR "breast neoplasm*") AND ("family history" OR familial OR "genetic predispose*")))) AND all(bcra* OR "hereditary breast cancer" OR "breast cancer 1" OR "breast cancer type 1" OR "breast cancer 2" OR "breast cancer type 2") AND all(hrt OR "hormone therapy*" OR "hormone substitution" OR "hormone replace*" OR progesterone* OR estrogen*) = 2 (but neither from 2014 or later so not exported)
Clinicaltrials.gov
(hrt or hormone*) or (bpso or boo or bso or bpo or itso or oophorect* or ovariect*) and ("breast cancer*" or BCRA or famil* or genetic*) =0
Web of Science
(bpso OR boo OR bso OR bpo OR rrso OR oophorectom* OR ovariectomy* OR oophorotom* OR ovariectomy* OR ovariotomy* OR ovariotomy* OR "ovary amputation" OR "ovary resection*" OR salpingooophorectom* "female castration") *AND* **TOPIC:**(BCRA or (("ovarian carcinoma" OR "breast carcinoma*" OR "ovarian cancer*" OR "ovarian neoplasm" OR "breast cancer" OR "breast neoplasm") and (hereditary or famil* or genetic))) *AND* **TOPIC:** (hrt OR "hormone therapy" OR "hormone substitution" OR "hormone replace" OR progesterone* OR estrogen*) = 14
Google Scholar -
brca oophorectomy* "hormone replacement" 2014 – 2016 Selected 107 titles

Appendix 4.3. The effect of hormone therapy on quality of life and breast cancer risk after risk reducing salpingo-oophorectomy: meta-analysis of pooled studies

Data synthesis

Studies addressing the same outcome were assessed qualitatively for clinical and methodological heterogeneity. In case of inconsistencies, data were synthesized using evidence summaries or tables. When sufficient homogeneity was demonstrated, outcome data were pooled quantitatively via a meta-analysis. DerSimonian-Laird random effects model (accounting for part of the unexplained heterogeneity between studies) was used to calculate the pooled odds ratio (OR) and 95% confidence interval (CI) for discrete variables and weighted mean differences (WMD) and 95% CI for continuous variables. Heterogeneity in results of individual studies was assessed statistically using the I^2 statistic, with an I^2 >50% considered evidence for significant heterogeneity. Effect estimates were pooled irrespective of the extent of statistical heterogeneity. All statistical analyses were conducted using Review manager software (RevMan version 5.3.4; Copenhagen, Nordic Cochrane Centre, Cochrane Collaboration, 2008). Assessment to identify the risk of bias across studies was not performed because of the small number of studies included.

Results

Quality of life (QOL)

The WMD for the two homogenous studies showed improved QOL associated with HT use. The pooled estimate of WMD from random effect model was 3.27 (95% CI, 0.88-5.65, P <0.01, I2 = 0%)[1, 2]

Breast cancer

For this variable, no sufficient qualitative homogeneity was demonstrated across relevant studies to justify pooling of estimates; hence no meta-analysis was performed.

Vasomotor symptoms

The pooled OR for three studies showed that HT reduced the prevalence of hot flashes (OR = 0.38; 95%CI, 0.23-0.62, P<0.01, I2 = 0%).[1-3]The pooled OR for two studies that reported night sweats showed a reduction with HT (OR = 0.42; 95%CI, 0.24-0.74, P<0.01, I2 = 0%).[1, 2]

Sexual function

Pooled estimates failed to show improvement with HT in any of the measured aspects of sexual activity (pleasure, discomfort, habit or libido) in the two homogenous studies that reported this outcome.[2, 3] WMD for pleasure was 0.62; 95%CI, -0.27-1.51, P = 0.17, I2 = 0%. WMD for discomfort was 1.12; 95%CI, -0.36-2.61, P = 0.14, I2 = 0%. WMD for habit was 0.12, 95%CI, -0.02-0.27, P = 0.09, I2 = 0%. OR for libido was 0.67; 95%CI, 0.40-1.14, I2 = 0%.

Vaginal dryness

Pooled analysis showed a lower prevalence of vaginal dryness in women taking HT, in contrast to the two individual studies (OR = 0.48; 95%CI, (0.26-0.87), P = 0.02, I2 = 0%).[1, 2]

Bone Loss

HT users had less bone loss compared to non-users in the 3 studies included in the pooled analysis (OR = 0.45; 95%CI, 0.23-0.86, P = 0.02, I2 = 0%).[1, 4, 5]

References

1. Challberg J, Ashcroft L, Lalloo F, Eckersley B, Clayton R, Hopwood P, et al. Menopausal symptoms and bone health in women undertaking risk reducing bilateral salpingo-oophorectomy: significant bone health issues in those not taking HRT. Br J Cancer. 2011 Jun 28;105(1):22-7.
2. Madalinska JB, van Beurden M, Bleiker EM, Valdimarsdottir HB, Hollenstein J, Massuger LF, et al. The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women after prophylactic salpingo-oophorectomy. J Clin Oncol. 2006 Aug 1;24(22):3576-82.
3. Finch A, Metcalfe KA, Chiang JK, Elit L, McLaughlin J, Springate C, et al. The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation. Gynecol Oncol. 2011 Apr;121(1):163-8.
4. Garcia C, Lyon L, Conell C, Littell RD, Powell CB. Osteoporosis risk and management in BRCA1 and BRCA2 carriers who undergo risk-reducing salpingo-oophorectomy. Gynecol Oncol. 2015 Sep;138(3):723-6.

5. Chapman JS, Powell CB, McLennan J, Crawford B, Mak J, Stewart N, et al. Surveillance of survivors: follow-up after risk-reducing salpingo-oophorectomy in BRCA 1/2 mutation carriers. Gynecol Oncol. 2011 Aug;122(2):339-43.

Appendix 4.4. Full-text Screening table

Ref work ID	First Author	Decision	Reason for exclusion
191-3	Alanbay	0	Study design doesn't meet eligibility criteria (Book review)
234-1	Antoine	0	Study design doesn't meet eligibility criteria (Review paper)
50-1	Armstrong	0	Study design doesn't meet eligibility criteria (Markov decision analysis)
152-3	Barlin	0	Study design doesn't meet eligibility criteria (Review paper)
696-1	Barry	0	Study design doesn't meet eligibility criteria (Review paper)
128-3	Breda	0	Study design doesn't meet eligibility criteria (Review paper)
212-1	Castiqlione	0	Study design doesn't meet eligibility criteria (Review paper)
10-1	Challberg	1	
167-1	Chang-Claude	0	Effect of HT on risk of breast cancer not assessed. Only studied effect of age at menarche; time of breast mitotic activity from menarche till first pregnancy and menopause; age at menopause; menopause status; and type of menopause on breast cancer risk among carriers of BRCA1/2 mutations
9-1	Chapman	1	
104-3	Cibula	0	Study design doesn't meet eligibility criteria (Meta-analysis). Also, study population doesn't fit eligibility criteria – no RRSO performed
107-3	Cui	0	Study population doesn't fit eligibility criteria (No BRCA carriers and not all surgically menopausal women are high risk)
731-1	Domchek	0	Effect of HT on mortality among BPSO not assessed (Intervention BPSO and comparator non-BPSO)
623-1	Dorum	0	Effect of HT on Metabolic syndrome and Framingham risk score among BPSO not assessed (Intervention BPSO and comparator non-BPSO)
766-1	Eisen	1	

268-1	Eltabbakh	0	Outcome doesn't meet eligibility criteria (Bleeding with HT)
11-1	Finch	1	
802-1	Foulkes	0	Effect of HT on risk of breast cancer not assessed. Studied effect of mutation, age and type of breast cancer on estrogen receptor status of breast cancer.
22--1	Gabriel	1	
1-2	Garcia	1	
153-3	Guidozzi	0	Study design doesn't meet eligibility criteria (Review paper)
777-1	Haile	0	Effect of oral contraceptive on breast cancer among BPSO patients not assessed (population included BRCA 1 and 2 mutations not necessarily had BPSO)
672-1	Hallowell	0	Study design doesn't fit eligibility criteria (Editorial)
48-1	Hallowell	0	Study design doesn't meet eligibility criteria (Descriptive/qualitative)
3-2	Heiniger	1	
133-3	Johansen	1	
753-1	King	0	Effect of BPSO and HT on risk of breast cancer not assessed (looked at lifetime risk of breast cancer among BRCA 1 and 2 mutations and effect of multiple family history of risk increase…as well as other non-genetic predispositions to breast cancer risk increase
270-1	Kontoravids	0	Outcome doesn't meet eligibility criteria (Rates of ovarian cancer following hysterectomies and oophorectomies)
134-3	Kotsopoulos	1	
765-1	Laki	0	Study design doesn't fit eligibility criteria (non-analytical no comparator). Also effect of HT on breast cancer risk not assessed
33-3	Levy-Lahad	0	Study design doesn't meet eligibility criteria (Review paper)
119-3	Lorenz	0	Effect of HT on sexual activity post RRSO was not assessed. HT was included in the statistical model to control for its potential

			confounding effect on sexual activity and other psychosocial variables
34-1	Madalinska	1	
774-1	Madalinska	0	Effect of HT on quality of life not assessed. (BPSO is intervention and comparator is gynecologic screening)
61-1	Meiser	0	Study design doesn't meet eligibility criteria (Qualitative study)
798-1	Metcalfe	0	Effect of HT on breast cancer not assessed. Effect of HT on contralateral breast cancer not assessed
796-1	Metcalfe	0	Effect of HT on breast cancer not assessed. Only looked at predictors of risk of contra-lateral breast cancer (effect of HT not assessed though)
132-1	Michelsen	0	Effect of HT on anxiety and depression among BPSO patients not assessed-analysis done for whole group (RRSO and controls (non-BPSO)
119-1	Michelsen	1	
669-1	Moller	0	Effect of HT on breast cancer risk not assessed (only survival with stage at diagnosis, BRCA status, and oophorectomy)
800-1	Narod	0	Effect of oral contraceptives on breast cancer was assessed for BRCA mutation carriers only. Type of menopause (natural/BPSO) was not measured or looked at.
67-1	Pines	0	Study design doesn't meet eligibility criteria (Case report)
42-1	Rebbeck	1	
727-1	Rebbeck	0	Effect of HT on risk of breast cancer among BPSO patients not assessed
735-1	Roukos	0	Study design doesn't meet eligibility criteria (Editorial)
178-3	Schrijver	0	Study design doesn't meet eligibility criteria (Review paper)
168-3	Schuler-Toprak	0	Study design doesn't meet eligibility criteria (Systematic review)

729-1	Struewing	0	Effect of HT on risk of breast cancer among BPSO patients not assessed. Only looked at incidence of breast cancer post-oophorectomy
761-1	Tiller	0	Study design doesn't meet eligibility criteria (Qualitative study)
159-3	Tucker	1	
801-1	Ursin	0	Effect of oral contraceptives on breast cancer was assessed for BRCA mutation carriers only. Type of menopause (natural/BPSO) was not measured or looked at

Exclude "0" Include"1"

Legend:

	Study design doesn't meet eligibility criteria
	Effect of intervention not assessed
	Outcome doesn't fit eligibility criteria
	Study population doesn't fit eligibility criteria

Appendix 4.5. Compliance with MOOSE guideline

Reporting background should include	
Problem definition	Yes
Hypothesis statement	Yes
A statement of objectives that include the study population, the condition of interest, the exposure or intervention, and the outcome(s) considered	Yes
Reporting of search strategy should include	
Qualifications of searches (e.g. librarians and investigators)	Yes
Search strategy, including time period included in the synthesis and keywords	Yes
Effort to include all available studies, including contact with authors	Yes
Databases and registries searched	Yes
Search software used, name and version, including special features (appendix)	Yes
Use of hand searching (e.g. reference lists of obtained articles) – also electronic citation search	Yes
List of citations located and those excluded including justification	Yes
Method of addressing articles published in languages other than English	N/A
Method of handling abstracts and unpublished studies	None found
Description of any contact with authors	Yes
Reporting methods should include	
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Yes
Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Yes
Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Yes
Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	Yes
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Yes
Assessment of heterogeneity	Yes
Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Yes
Provision of appropriate tables and graphics	Yes
Reporting of results should include	
Graphic summarizing individual study estimates and overall estimate	Yes
Table giving descriptive information for each study included	Yes
Results of sensitivity testing (e.g., subgroup analysis)	N/A
Indication of statistical uncertainty of findings	Yes
Reporting of discussion should include	
Quantitative assessment of bias (e.g., publication bias)	N/A
Justification for exclusion (e.g., exclusion of non–English-language citations)	Yes
Assessment of quality of included studies	Yes

Reporting of conclusions should include	
Consideration of alternative explanations for observed results	Yes
Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)	Yes
Guidelines for future research	Yes
Disclosure of funding source	Yes

5 Chapter 5. Perspectives and Decision-Making about Menopausal Therapies in Women Who Had Bilateral Oophorectomy (BO)[d]

Tasneem Siyam[1], BScPharm, MSc; Sue Ross[2], PhD; Tami Shandro[3], MD, CCFP, FCFP, NCMP; Shelly Hagen[4], RD, NCMP; Lori Battochio[5], RN, NCMP, Nese Yuksel[6], BScPharm, PharmD, FCSHP, NCMP

[1]PhD Candidate,
Faculty of Pharmacy and Pharmaceutical Sciences,
3-015 Edmonton Clinic Health Academy (ECHA)
University of Alberta, Edmonton, AB, Canada,
tsiyam@ualberta.ca

[2]Cavarzan Chair in Mature Women's Health Research,
Department of Obstetrics & Gynecology
Rm 5S131 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada,
sue.ross@albertahealthservices.ca

[3]MD, Assistant Professor
Women's Health and Sleep Medicine Clinics
Lois Hole Hospital for Women & Grey Nuns Community Hospital
University of Alberta, Edmonton, AB, Canada,
Tami.Shandro@albertahealthservices.ca

[4]RD/Health Educator,
Women's Wellness Program
Grey Nuns Community Hospital,
1100 Youville Dr W Northwest, Edmonton, AB, Canada,
shelly.hagen@covenanthealth.ca

[5]RN/Health Educator,
Women Menopause Clinic,
Rm GS146 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada; Edmonton, AB, Canada,
lori.battochio@albertahealthservices.ca

[5]Professor (Corresponding author),
Faculty of Pharmacy and Pharmaceutical Sciences, 3-171 Edmonton Clinic Health Academy (ECHA), University of Alberta, Edmonton, AB, Canada, T6G 1C9,
nese.yuksel@ualberta.ca, Tel: (780)492-4442; Fax: (780)492-1217

[d] T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause 25(7) (2018) 795-802.

5.1 Introduction

Menopause can be induced before the onset of natural menopause through the surgical removal of both ovaries (bilateral oophorectomy).[1] Bilateral oophorectomy (BO) may be performed for several reasons. It can be used as a surgical intervention for treating an existing malignant or benign ovarian condition.[2] It can also be performed electively at the time of benign hysterectomy to reduce the risk of ovarian cancer or prophylactically in women who have a genetic predisposition for ovarian and/or breast cancer.[3, 4] BO is associated with immediate menopausal symptoms,[2] which include vasomotor instability, urogenital atrophy, sexual dysfunction, sleep disturbances, and mood effects, which can severely affect a woman's quality of life.[5, 6] In the long term, early surgical menopause, as a result of BO, increases the risk of osteoporosis, cardiovascular disease, cognitive impairment and mortality.[6-9] In women with early menopause and without contraindications to hormone therapy (HT), current guidelines recommend the use of HT (estrogen therapy (ET) for women without an intact uterus and estrogen-progestin therapy (EPT) for women with an intact uterus) until the average age of menopause, not only for symptom management but also to prevent long-term health consequences.[10-13] Other options for vasomotor symptoms include antidepressants, clonidine, and gabapentin, however, HT is the most effective treatment.[14]

A decline in HT use was seen worldwide in 2002, after the initial results of the Women's Health Initiative (WHI) showed an increased risk of breast cancer and cardiovascular disease (CVD), with the use of estrogen and progestin in postmenopausal women.[15-19] Even though the WHI results should not be extrapolated to younger, symptomatic women with early surgical menopause, the use of HT in this patient population is still underutilized.[20, 21] In a cross-sectional study completed in Edmonton by our research group, 40% of women were started on

HT after a surgical menopause, and only 33% had continued taking HT post-surgery (mean 10 months).[21] The prevalence of moderate to severe hot flashes was also significantly higher among women who were not on HT.

Given the variability in women's risk-benefit perceptions of HT and other treatment options, decision-making after surgical menopause can be complex.[22, 23] Patient decision aid (PDAs) can foster informed decision-making through incorporating women's preferences, values, and decisional needs.[24] The International Patient Decision Aid Standards (IPDAS) recommends focus groups to assess patients' decisional and information needs prior to developing an effective PDA.[25] Although, several studies have captured perspectives about HT and factors influencing treatment-decision making during menopause, these were mainly in women with natural menopause.[26] Unfortunately, very little information is available on surgical menopausal women.[22, 27] This study is the first step in developing a PDA specific for surgical menopause. Our objectives were to understand the experiences with surgical menopause and the use of menopausal therapies for managing early surgical menopause, and explore the process of decision-making about menopausal treatments in these women.

5.2 Methods

5.2.1 Design and participants

This was a descriptive qualitative method using focus groups.[28] Our inclusion criteria consisted of women who had a surgical menopause (≤50 years), could converse in English and were willing to participate and physically attend a focus group meeting. Participants were recruited purposefully from the menopause clinics at the Lois Hole Hospital for Women (LLHW) and the Grey Nuns Community Hospital (GNCH), in Edmonton, Canada.

5.2.2 Data collection and management

The data was collected using focus groups which provided the opportunity for participants to interact and reflect on the topic.[29] Five focus groups were conducted (n = 37) with women across Edmonton and surrounding areas, between June 30 and July 21, 2016. Each focus group consisted of 6 – 10 participants and was led by an experienced facilitator (ML). One of the study investigators also attended as an assistant (TS) to record field notes on group dynamics and non-verbal communication. Focus groups lasted approximately 1.5 hours and were digitally audio-recorded and transcribed verbatim. Audiotapes were sent for verbatim transcription following each meeting. Transcripts were reviewed by study investigators and compared with the field notes for verification. Participants were also asked to complete a short questionnaire at the beginning of each focus group to collect data on: time and reason for surgery, hysterectomy status, HT or non-hormonal therapy use and use of non-drug measures for symptom control.

5.2.3 Interview guide

An interview guide was developed to provide direction for the conduct of the focus groups. Questions developed by the study team using previous literature as well as clinical experience were semi-structured with an open-ended focus, and responses were further explored using additional questions and probes. The questions were revisited and revised when necessary following each focus group to ensure that research objectives were captured.

5.2.4 Data analysis

Qualitative content analysis was used to organize data into meaningful segments (codes) and integrate segments into broader categories to generate themes.[30] Data analysis took place concurrently with data collection following each focus group to ensure that data saturation was reached (TS). No theoretical framework was used to inform data analysis. Data from each focus

group were analyzed separately and categories and themes were generated inductively based on consensus of shared experiences across the focus groups. Yet, to capture a range of experiences within surgical menopause, we also highlighted the less dominant views. Categories and themes were discussed as developed with research team members (SR, NY) to ensure they were representative of the findings. All qualitative data were coded and managed using Nvivo qualitative data analysis software package version11.

5.3 Results

Characteristics of participants are listed in Table 5.1. Overall, the areas women discussed and the concerns raised were consistent and reached saturation across the five focus groups. Four main themes identified were: "perceptions of surgical menopause experience", "perceptions of received support", "being my own advocate", and "concept of adequate support".

5.3.1 Perceptions of surgical menopause experience

5.3.1.1 Experience worse than expectations

Several women across the focus groups described their surgical menopause experience as an experience they were not prepared for and worse than any of their expectations. Some viewed it as a life-changing event and trying to adapt to its implications was an on-going struggle.

> *FG2F5: "So I joke to when I'm in a jokey place, it's like you know I feel like menopause seriously bitch slapped me right across the face. It's like boom and you're in full menopause. It's like getting hit by a truck. You have no clue what is coming your way, where traditionally you sort of ease into it over years. No, it hits you like a truck."*

5.3.1.2 Experience of menopausal symptoms

Women shared a variety of menopausal symptoms, but a common sentiment across the groups was distress accompanying the sudden and severe symptoms. Symptoms described include night

sweats, lack of sleep, mood swings, anxiety, depression, emotional numbness, vaginal itch and pain, low sex drive, pain during intercourse, urinary incontinence, weight gain, hair changes, arthritic pain, and fatigue. For some, hot flashes were the most debilitating, while for others, mood changes were quite significant and hard to manage. Some long-term implications were reported as well, such as memory and bone loss. Almost all women reported negative impacts on sexual well-being. Sleep was also a major concern for many women, with several still struggling with lack of sleep even years after their surgery. A few women felt they had aged rapidly after their surgery, reporting aging manifestations, such as weight gain and being more physically challenged.

5.3.1.3 Emotional repercussions

Many women across the sessions grieved the loss of their ovaries, yet women grieved different aspects of the loss. At times, grief was associated with the loss of fertility or femininity, but at other times, it meant the loss of an intimate relationship or the loss of time trying to find support for their menopausal health issues. After their surgical menopause experience, some women, in retrospect, pondered if they made the right decision of having their ovaries removed and others shared feelings of regret.

> *FG3F2: "But within menopause and relationships you do grieve. You grieve the loss of something you had, and it's not like your fairytale romance. It's a part of your relationship that will never ever, ever be the same again because you're never ever going to be the same again. And I don't know if [there's hormones] enough in the world to make you ever feel that way again, you don't have that same relationship."*

5.3.1.4 Menopause and life overlap

Women in two focus groups reported that physical and emotional symptoms of surgical menopause coincided with their underlying health issues, lifestyle, and work. For example, for some, surgical menopause correlated with the loss of a family member, separation or divorce, so that they were not sure whether their feelings of grief and depression were caused by menopause or other life stressors. Confused by their symptoms, some did not know when and what avenue of support to seek.

5.3.2 Perceptions of received support

Women across the focus groups shared several aspects of their perceptions of support received during their menopausal experience.

5.3.2.1 Perceptions of timely support

Time to support was a common concern across all the group sessions. Almost all women revealed they did not have a prompt access to support for their menopausal symptoms after their surgery. These women often fell through the cracks:

> *FG3F3: "Nobody ever said anything about therapy to me. Nobody ever suggested hormone therapy to me, nothing until, like I said, the symptoms got so bad that I went back to the gynecologist and went please help me, do something,[cause] this is all the symptoms of menopause that you said would come but you didn't tell me what to do about it."*

5.3.2.2 Perceptions of symptoms management (role of menopausal therapies)

Perceptions of symptom management and experiences with menopausal therapies were similar among focus groups. The majority of women were on HT for managing menopausal symptoms, which they expressed as helping with some but not all symptoms. Despite being on HT some

women still struggled with their symptoms especially the lack of sleep. A small proportion of women reported discontinuing HT (10%) because of side effects such as shakiness, dizziness, swollen legs, bloating, and emotional fluctuations. Some were intolerant to certain transdermal formulations and developed a skin allergic reaction. Many women continued to struggle with mood symptoms despite being on HT and also anti-depressants.

A few women were not on HT because of their history of a gynecological cancer. These women tried non-hormonal alternatives (e.g. gabapentin, duloxetine, and venlafaxine) for vasomotor symptoms and/or mood swings, which helped to a certain extent but did not quite meet their therapy expectations.

5.3.2.3 Role of family and friends

The importance of social support from spouses and families was commonly mentioned across the focus groups. Women shared several occasions of support from their spouse. For example, a woman shared:

> *FG2F3: "You know what my husband would do when I have hot flashes, I'd be in bed and I just be so cold, just shaking. So, he'd get the hair blower and go to the foot of the bed and blow the air. As soon as I had enough, he'd shut it off. He hardly even turned around that I'd be whipping the covers off."*

Yet, some women felt that even though their families were overall supportive, there was nothing further their families could have offered in terms of support. Women who did not have any social support, on the other hand, were severely distressed by the experience and shared feelings of hopelessness.

A few of the younger women indicated that friends of the same age could not relate to their menopausal experience and did not know how to support them. As a result, these women did not feel comfortable sharing their menopausal experience with their friends.

> *FG2F5: "And I found it difficult too like I'm 42 years old and going through menopause, my same age friends, they can't support me. They have no clue what to do to help or what to say. And I don't even talk to them about it because what's the point?"*

5.3.2.4 Perceptions of medical support

For menopausal concerns, women often referred to doctors (e.g. general practitioners (GPs), surgeons or gynecologists) for medical support. Women expressed that doctors were not always as understanding of their surgical menopause needs and shared several incidences of inadequate supports; these were categorized as follows:

5.3.2.4.1 Lack of patient-centered care and patient engagement in decision-making

Some women felt that their doctors had strong opinions about therapies and offered no room for discussion about treatments and/or engaging women in shared decision-making.

> *FG1F3: "When I had the surgery, you know, the surgeon said that I would need to have estrogen and I said okay, you know, not knowing a whole lot about it, until I started reading and oh, big mistake, you know, because then I asked questions. And he said no, you will go on this estrogen…."*

The women also expressed that they felt that GPs extrapolated findings from the WHI to their own situation, for example, a number of women reported the need to discontinue therapy after 5 or more years, regardless of their need for therapy or age. Other times women were given information about the pros and cons of therapies but were not guided on how to make therapy decisions.

5.3.2.4.2 Lack of interest in menopausal concerns

Some women explained that they felt their concerns were not taken seriously by their GP. A number of women also felt that male doctors may not be as understanding of their symptoms.

> *FG2F6: "I think family doctors have to realize this is an issue and it's not made up. And sometimes you get the mentality that you're just being a woman. This is part of your life."*

5.3.2.4.3 Lack of knowledge about menopause and hormones

A few women felt that doctors, especially GPs and surgeons, lacked knowledge about menopause, and so could not offer the kind of support that they were seeking.

5.3.2.4.4 Lack of clear messages about menopausal therapies

Many women were confused by the mixed messages they were hearing about HT from different sources. Women were hearing conflicting messages about HT safety and the need and duration of therapy. For instance, a woman shared:

> *FG1F7: "My surgeon made it sound like well there's all those risks and you risk this and you risk that and you risk that, so if you can live with that then do it. So, for me, it was just like well, why would I risk anything if I don't need to, right. And then when I went to the menopause clinic seven years later it was the opposite. It was this is all the stuff you're risking if you don't go on it, if you wait three more years then you're over that ten-year mark."*

Women with BRCA mutations were specifically caught in this dilemma and often received conflicting recommendations about HT. Women were also hearing different suggestions for the duration of HT. This caused significant uncertainty and frustration among a few.

5.3.3 Be my own advocate

Women across focus groups expressed the need to be one's own advocate to cope with menopausal health issues.

5.3.3.1 Seeking help from within health care system and outside

Women had to seek information and support from within the healthcare system and outside, to take control of their health. Many initially approached their GPs, surgeons and/or gynecologists for support but felt their needs were not adequately addressed and therefore continued to struggle with their symptoms. They turned to other forms of support. For instance, several women asked for referral to the menopause clinic for more focused care. Some sought a second opinion from within the healthcare system, while others turned to private clinics promoting compounded bio-identical HT. A few decided to try complementary and alternative medicine, such as naturopathy and acupuncture.

> *FG4F2: "And I had to fight my GP and actually switch GPs [because] nobody wanted to do a referral. And I went to a, they had an open house or something for…they had an information night about menopause. And there was actually doctors to help you and stuff like that."*

5.3.3.2 Searching the internet for information and communal support

A number of women used the internet as a primary information and support resource where they could find answers to their unresolved health problems and learn more about their health condition. Some found guidance in an online communal support group for women who had hysterectomies and oophorectomies. Here, women shared medical and experiential information about surgery and treatments.

FG1F2: "But there's a time that you just throw your hands up on the healthcare field and you try your best to find out for yourself what's going on….."

5.3.3.3 Empowering myself and others

Some women empowered themselves mentally by having positive insights about their body and health and by practicing relaxation techniques, and physically by implementing lifestyle changes including dietary changes and physical activity. Several women supported their friends who were going through menopause by sharing information and resources.

FG3F2: "And I gave her my whole package that was given to me with all the information and I gave it to her and I said read it, I said, let your husband read it, and I said don't stop until your family doctor makes you a referral because you need it."

5.3.3.4 Negotiating competing expectations

To make therapy decisions women recognized a need to negotiate between competing expectations. They shared several reasons for deciding on treatments, including the option of no treatment. The following motives for treatment decisions were expressed consistently across focus groups:

5.3.3.4.1 Quality of life

Many decided to take HT for their quality of life. After the surgery, these women struggled with their symptoms and felt that their quality of life was greatly compromised; they chose to take HT to manage their symptoms and feel the way they used to before the surgery. Although they knew about the long-term risks of HT, more value was placed on the present over the future and the risks it may bring.

FG5F5: "Yeah. Well, he [the doctor] said it's my choice, but then he said, "Do you know the risks after ten years of taking it [HT]?" And I said, "Well, I guess like heart and

stroke issues. Yeah." But it doesn't give me that. Well, the chip's [on the] 7-11 [convenience store] causes that too."

5.3.3.4.2 Long-term risks of surgical menopause

A few women who had early surgical menopause (<45 years) took HT as they were concerned about the long-term risks of surgical menopause, such as risk of osteoporosis and cardiovascular disease.

5.3.3.4.3 Health risks of HT

In contrast, some decided against HT because they were more worried about HT adverse effects. Despite their severe symptoms, these women were typically concerned about breast cancer risk with HT, and the impact on survival. Cardiovascular risks and blood clots also concerned a few.

FG2F5: "Nobody can really tell me what exactly my [risk level] – because if I had some percentages, I can make an educated decision. But it's just not there, so my decision was long term versus short term and I'm just trying to deal with now the best I can so that I'm here for my kids long-term."

5.3.3.4.4 Other reasons

Other women felt they did not need HT since they had minimal symptoms; they were not concerned about the long-term risks of surgical menopause. A few stopped HT because they were intolerant of its side-effects or because they experienced no improvement in their symptoms.

Women's decisions were sometimes influenced by others. A few indicated that their decision was mainly driven by their prescribing doctor. Doctor-driven decisions were either because women were not given the option to choose or because women relied on their doctor's choice of treatment. In other cases, women sought the advice of their family and friends. Sometimes

women did not seek the advice of a family member but their treatment decision was affected by how they perceived a friend's or a relative's past experience with surgical menopause, as emphasized below:

> *FG4F3: "[Cause] I look at my mom who, of course, had her hysterectomy same age as me but, you know, 25 years before, 1988. So she had no hormone therapy after, she has massive osteoporosis, she's just in the middle of treatment for A-fib, her heart's crapping out.."*

Given the abundance of available information and the need to negotiate between competing expectations, a few women shared feelings of decisional conflict and frustration related to decision-making.

> *FG5F3: "Sometimes there's so much information out there and it's so confusing. There's too much. You know, and then you're just like, "Now what do I do?" You know, it's like overwhelming trying to make a decision, because there's so much – so many different avenues."*

5.3.4 Concept of adequate support

Women's perception of adequate support was that it would prepare them for the surgical menopause experience with true and honest information before the surgery. Adequate support would also include information on available treatments and resources, adequate social support, and multidisciplinary care.

5.3.4.1 Be prepared

These women wanted facts about the short and long-term implications of surgical menopause before the surgery, so they can be prepared for the experience. They shared that this will help

them deal with any mental and physical health issues that may be exacerbated by surgical menopause.

> *FG4F1: "And so you need, you need I think the support and the true and honest information prior. Then you need support through it while you're at that kind of critical stage where you can't stop sweating, you can't stop crying, you're taking handfuls of hair out, you know, all those kinds of things."*

5.3.4.2 Have the information and resources

To make an informed decision about treatments post-surgery, women expressed a need to learn more about all available treatment options, including non-hormonal alternatives, herbal therapies, and other resources and avenues for support. Learning about available resources for support was especially important to women who had contraindications to HT. These women wanted to know what other avenues of support are available to help them cope with symptoms. For example, women wanted to learn about specialty clinics for menopausal women.

5.3.4.3 Have the social support

Women indicated that support groups are crucial for emotional and intellectual support for women who go through surgical menopause. Some women felt isolated and emotionally scarred by the menopausal experience and therefore needed a place to interact with other women who could relate to their experience.

Some women explained that hearing stories and testimonials of other women and how they approached therapy decisions about surgical menopause would have been a helpful guide for making treatment decisions.

FG2F4: "There are support groups for everything but nothing for this. And it's such an old-school hush hush, don't talk about it. It still seems to be in that mentality, like why are women not talking to each other about this that have gone through this?"

5.3.4.4 Tailored multidisciplinary care

The women thought it is essential to receive care tailored towards their menopausal needs and get in touch with specialists who understand and make them feel supported in their treatment decisions. Many women found the menopause clinic and its multidisciplinary team approach very supportive. However, they were frustrated with the long wait time and the lack of enough resources to support the demands of women with such menopausal needs. Ideally, these women would like to have an immediate access to the menopause clinic after their surgery.

FG1F1: "And then I finally got onto the menopause clinic and I always say this, and truly honestly, that I really just feel that that clinic saved my life in so many ways….and I think get more hours to this clinic."

5.3.4.5 Research on women with surgical menopause

A few women shared that information about HT is mainly gathered from studies on older women who have gone through natural menopause, and they cannot identify with the findings. Women felt it was important to gather long-term evidence on the safety of HT among women who have gone through early surgical menopause.

5.4 Discussion

From the shared accounts of women in our study, we learn that surgical menopause is a sudden and intense experience that greatly affects many aspects of a woman's physical, psychological and emotional health. Women in our sample also shared unique perceptions of inadequate support received before and during their menopausal experience. Perceptions such as lack of

adequate information prior to the surgery (and after), lack of guidance and engagement in decision-making and lack of social support, were viewed as modifiable deterrents to effective decision-making. These women had a clear view of what adequate support would involve. They believed they needed to be prepared for the short and long-term consequences of surgical menopause, by having the information about valid treatment options and available avenues of support before the surgery, having social support, and having prompt access to multidisciplinary care tailored to their needs. Several women also expressed a need for more research on women of their population for evaluating the long-term effects of certain treatments on their health.

In our study, women were not adequately prepared for surgical menopause and its short and long-term effects and therefore struggled to understand their symptoms and seek supportive measures. We could not find any previously published work on women with surgical menopause highlighting this outcome. However, similar findings have been seen in studies with women who had a hysterectomy.[31, 32] In the study by Wade and colleagues, women who had a hysterectomy reported having insufficient information about the surgery and adverse health effects that follow, consequently, these women shared a need for more education about hysterectomy and coping strategies for its implications, at the time of contemplating a hysterectomy. Current guidelines, such as the National Institute for Health and Care Excellence (NICE) also recommend women who are likely to go through a surgically induced menopause be offered information about menopause and HT before their surgery.[12]

Our cohort revealed feelings of decisional conflict and a general lack of guidance in decision-making about treatments. It is likely that these feelings were heightened by the physical and emotional burden of the experience and the need to make a difficult decision about managing symptoms on a short timeline.[33] Women in our study needed the early receipt of information

(i.e. before the surgery). Apart from facilitating the receipt of support, the early provision of information will help women consider therapy decisions before the surgery when they are not as emotionally and physically burdened.[34] Women can then weigh competing risks, seek guidance and support in decision-making and have less emotional biases to their treatment decision.

Women felt they did not get adequate medical support during their decision-making about treatment options. Empowering women with the information and the skills to support engagement in decision-making may enhance shared decision-making with healthcare professionals. For example, it may stimulate discussions about women's needs and values which may help healthcare professionals tailor care and engage in shared decision-making. This is particularly of value in a group of women who want to take an active role in making treatment decisions. For example, our cohort discussed several instances that highlighted their strength and determination in being responsible for their own health and healthcare decisions and their need to empower oneself and be one's own advocate.

Among women who want to be actively involved in their treatment choices, patient-targeted decision support interventions, such as patient decision aids (PDAs) might be powerful tools. Well-designed PDAs support adequate decision-making through making the decision involved more explicit; providing balanced, accurate and patient-tailored information about options and their outcomes; helping patients clarify and communicate values associated with treatment options and their outcomes, and building or reinforcing skills in engaging in decision-making and collaborating with healthcare providers for shared decision-making. These tools are not designed to direct patients towards one option over another, nor do they replace health care provider's consultation. Instead, they empower patients when making a decision about their

health and advocate informed value-based decisions that are often associated with better adherence to chosen treatment and better health outcomes.[24, 35-37]

Many of these women had strong connections with their spouses and family members, which served as a source of emotional and social support; however, they also expressed the need to connect with other women facing similar struggles. Women shared a need to participate in support groups not only to feel supported by others but also to help empower women with similar experiences. The importance of emotional support and the need for women specifically to exchange experiences and engage in interpersonal female discussions about their health when faced with an emotionally overwhelming medical experience was seen in other female populations, such as women who had a hysterectomy,[31, 32] BRCA mutation carriers contemplating an oophorectomy, [38] and women with breast cancer.[39]

Our study addressed an important phenomenon related to surgical menopause and the complexity of decision-making in this context. Through our strong research methodology with respect to participants' selection, and data collection and analysis, unique perceptions were discovered which improved our understanding, and ways with which we can provide interventions to support these women. [e] A few limitations should be recognized. Our limited sites of recruitment may not have shown the full spectrum of experiences and opinions among women who have had a surgical menopause. For example, women participating in the focus groups were all seen at the Menopause Clinic and had access to reliable information, tailored treatment and other forms of support through the clinic. The Menopause Clinic includes a multidisciplinary group of health care providers including physicians, pharmacists, dietitians and nurses.[40] Women in our

[e] See appendix 5.1 for checklist summarizing compliance with consolidated criteria for reporting qualitative research (COREQ) guidelines.

sample may not reflect women who did not receive a similar specialized care, nor are we able to identify how health care provider interactions may have influenced our findings. It also may be the case that these women had a more intense menopausal experience that warranted special care than women who did not attend the menopause clinic. Other limitations common to focus groups include the inability to generalize findings to a larger population. Yet, our study was exploratory in nature and the findings were not meant to represent the entire population of surgical menopause. The women we recruited in our study worked hard to get the resources they needed to cope with their symptoms and therefore were experts in that sense, this only added to the richness and quality of our data.

5.5 Conclusion

Despite being severely impacted by the experience, women who have had a surgical menopause have a strong sense of ownership towards their menopausal health and treatment decisions; although, at times, they may not have the adequate support to act upon this shared sense of ownership. Patient decision aids can serve as an ideal source of support and guidance to these women as it will offer them with the information, resources, and skills to manage decision-making. Most importantly, it may reinforce their sense of empowerment and engagement in therapy decisions and help them overcome perceived barriers to shared decision-making.

5.6 References

[1] W.H. Utian, D.F. Archer, G.A. Bachmann, C. Gallagher, F. Grodstein, J.R. Heiman, V.W. Henderson, H.N. Hodis, R.H. Karas, R.A. Lobo, J.E. Manson, R.L. Reid, P.J. Schmidt, C.A. Stuenkel, Estrogen and progestogen use in postmenopausal women: July 2008 position statement of The North American Menopause Society, Menopause 15(4 Pt 1) (2008) 584-602.

[2] S.L. Hendrix, Bilateral oophorectomy and premature menopause, Am J Med 118 Suppl 12B (2005) 131-5.

[3] W.H. Gotlieb, G.B. Baruch, E. Friedman, Prophylactic oophorectomy: clinical considerations, Semin Surg Oncol 19(1) (2000) 20-7.

[4] ACOG Practice Bulletin No. 89. Elective and risk-reducing salpingo-oophorectomy, Obstet Gynecol 111(1) (2008) 231-41.

[5] C.Y. Fang, C. Cherry, K. Devarajan, T. Li, J. Malick, M.B. Daly, A prospective study of quality of life among women undergoing risk-reducing salpingo-oophorectomy versus gynecologic screening for ovarian cancer, Gynecol Oncol 112(3) (2009) 594-600.

[6] A. Finch, K.A. Metcalfe, J. Chiang, L. Elit, J. McLaughlin, C. Springate, M.J. Esplen, R. Demsky, J. Murphy, B. Rosen, S.A. Narod, The impact of prophylactic salpingo-oophorectomy on quality of life and psychological distress in women with a BRCA mutation, Psychooncology 22(1) (2013) 212-9.

[7] W.H. Parker, M.S. Broder, Z. Liu, D. Shoupe, C. Farquhar, J.S. Berek, Ovarian conservation at the time of hysterectomy for benign disease, Obstet Gynecol 106(2) (2005) 219-26.

[8] W.H. Parker, M.S. Broder, E. Chang, D. Feskanich, C. Farquhar, Z. Liu, D. Shoupe, J.S. Berek, S. Hankinson, J.E. Manson, Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study, Obstet Gynecol 113(5) (2009) 1027-37.

[9] W.A. Rocca, B.R. Grossardt, L.T. Shuster, Oophorectomy, estrogen, and dementia: a 2014 update, Mol Cell Endocrinol 389(1-2) (2014) 7-12.

[10] L. Webber, M. Davies, R. Anderson, J. Bartlett, D. Braat, B. Cartwright, R. Cifkova, S. de Muinck Keizer-Schrama, E. Hogervorst, F. Janse, L. Liao, V. Vlaisavljevic, C. Zillikens, N.

Vermeulen, ESHRE Guideline: management of women with premature ovarian insufficiency, Hum Reprod 31(5) (2016) 926-37.

[11] The 2017 hormone therapy position statement of The North American Menopause Society, Menopause (2017).

[12] G. Sarri, M. Davies, M.A. Lumsden, Diagnosis and management of menopause: summary of NICE guidance, BMJ 351 (2015) h5746.

[13] R.J. Baber, N. Panay, A. Fenton, 2016 IMS Recommendations on women's midlife health and menopause hormone therapy, Climacteric 19(2) (2016) 109-50.

[14] J.L. Shifren, M.L. Gass, The North American Menopause Society recommendations for clinical care of midlife women, Menopause 21(10) (2014) 1038-62.

[15] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, J. Ockene, Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial, JAMA 288(3) (2002) 321-33.

[16] A. Morabia, M.C. Costanza, Recent reversal of trends in hormone therapy use in a European population, Menopause 13(1) (2006) 111-5.

[17] W.F. Huang, Y.W. Tsai, F.Y. Hsiao, W.C. Liu, Changes of the prescription of hormone therapy in menopausal women: an observational study in Taiwan, BMC Public Health 7 (2007) 56.

[18] J.A. Udell, M.A. Fischer, M.A. Brookhart, D.H. Solomon, N.K. Choudhry, Effect of the Women's Health Initiative on osteoporosis therapy and expenditure in Medicaid, J Bone Miner Res 21(5) (2006) 765-71.

[19] J.J. Hillman, I.H. Zuckerman, E. Lee, The impact of the Women's Health Initiative on hormone replacement therapy in a Medicaid program, J Womens Health (Larchmt) 13(9) (2004) 986-92.

[20] M.L. Stefanick, G.L. Anderson, K.L. Margolis, S.L. Hendrix, R.J. Rodabough, E.D. Paskett, D.S. Lane, F.A. Hubbell, A.R. Assaf, G.E. Sarto, R.S. Schenken, S. Yasmeen, L. Lessin, R.T. Chlebowski, Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy, JAMA 295(14) (2006) 1647-57.

[21] A. Chubaty, M.T. Shandro, N. Schuurmans, N. Yuksel, Practice patterns with hormone therapy after surgical menopause, Maturitas 69(1) (2011) 69-73.

[22] M. Crowe, B. Burrell, L. Whitehead, Lifestyle risk management--a qualitative analysis of women's descriptions of taking hormone therapy following surgically induced menopause, J Adv Nurs 68(8) (2012) 1814-23.

[23] B. Burrell, V. Valledor, M. Crowe, L. Whitehead, Negotiating competing discourses: the decision to take menopausal hormone therapy following surgical menopause, Women Health 50(6) (2010) 527-43.

[24] D. Stacey, F. Legare, N.F. Col, C.L. Bennett, M.J. Barry, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, J.H. Wu, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev 1 (2014) CD001431.

[25] A. Coulter, D. Stilwell, J. Kryworuchko, P.D. Mullen, C.J. Ng, T. van der Weijden, A systematic development process for patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S2.

[26] J.S. Carpenter, M.M. Byrne, J.L. Studts, Factors related to menopausal symptom management decisions, Maturitas 70(1) (2011) 10-5.

[27] R.J. Chen, T.C. Chang, S.N. Chow, Perceptions of and attitudes toward estrogen therapy among surgically menopausal women in Taiwan, Menopause 15(3) (2008) 517-23.

[28] M. Sandelowski, Whatever happened to qualitative description?, Res Nurs Health 23(4) (2000) 334-40.

[29] R. Barbour, Doing Focus Group. The Sage Qualitative Research Kit., Sage Publications Ltd., London, 2007.

[30] J. Creswell, Qualitative Inquiry and Research Design: Choosing Among Five Approaches, Sage publications Ltd., London, 2013.

[31] C. Mingo, C.J. Herman, M. Jasperse, Women's stories: ethnic variations in women's attitudes and experiences of menopause, hysterectomy, and hormone replacement therapy, J Womens Health Gend Based Med 9 Suppl 2 (2000) S27-38.

[32] J. Wade, P.K. Pletsch, S.W. Morgan, S.A. Menting, Hysterectomy: what do women need and want to know?, J Obstet Gynecol Neonatal Nurs 29(1) (2000) 33-42.

[33] K.S. MacDonald, K.R. Fowke, J. Kimani, V.A. Dunand, N.J. Nagelkerke, T.B. Ball, J. Oyugi, E. Njagi, L.K. Gaur, R.C. Brunham, J. Wade, M.A. Luscher, P. Krausa, S. Rowland-Jones, E. Ngugi, J.J. Bwayo, F.A. Plummer, Influence of HLA supertypes on susceptibility and resistance to human immunodeficiency virus type 1 infection, J Infect Dis 181(5) (2000) 1581-9.

[34] D.W. Scott, Anxiety, critical thinking and information processing during and after breast biopsy, Nurs Res 32(1) (1983) 24-8.

[35] D. Stacey, J. Kryworuchko, J. Belkora, B.J. Davison, M.A. Durand, K.B. Eden, A.S. Hoffman, M. Koerner, F. Legare, M.C. Loiselle, R.L. Street, Jr., Coaching and guidance with patient decision aids: A review of theoretical and empirical evidence, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S11.

[36] D. Feldman-Stewart, M.A. O'Brien, M.L. Clayman, B.J. Davison, M. Jimbo, M. Labrecque, R.W. Martin, H. Shepherd, Providing information about options in patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S4.

[37] A. Fagerlin, M. Pignone, P. Abhyankar, N. Col, D. Feldman-Stewart, T. Gavaruzzi, J. Kryworuchko, C.A. Levin, A.H. Pieterse, V. Reyna, A. Stiggelbout, L.D. Scherer, C. Wills, H.O. Witteman, Clarifying values: an updated review, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S8.

[38] R.H. Kenen, P.J. Shapiro, S. Friedman, J.C. Coyne, Peer-support in coping with medical uncertainty: discussion of oophorectomy and hormone replacement therapy on a web-based message board, Psychooncology 16(8) (2007) 763-71.

[39] M.T. Hoybye, C. Johansen, T. Tjornhoj-Thomsen, Online interaction. Effects of storytelling in an internet breast cancer support group, Psychooncology 14(3) (2005) 211-20.

[40] B.C. Sydora, N. Yuksel, N.L. Veltri, J. Marillier, C.P. Sydora, M. Yaskina, L. Battochio, T.M.L. Shandro, S. Ross, Patient characteristics, menopause symptoms, and care provided at an interdisciplinary menopause clinic: retrospective chart review, Menopause 25(1) (2018) 102-105.

Table 5.1. Participants Characteristics

Characteristic	**N(%) or Mean(range) N = 37**
Age at participation	50.78(27-77)
Recent Surgery (0-5 years)	13(35%)
Reason for bilateral oophorectomy	
Endometriosis/ovarian cysts	28(75%)
Cancer prevention	12(32%)
Concurrent Hysterectomy (concurrent to a bilateral oophorectomy)	36(97%)
HT users (mostly systemic)	26(70%)
Antidepressant users	15(41%)
Non-drug measures	
Vitamins and supplements	18(49%)
Exercise	16(43%)

Appendix 5.1. Checklist summarizing compliance with COREQ guidelines

COREQ (COnsolidated criteria for Reporting Qualitative research) Checklist

Topic	Item No.	Guide Questions/Description	Reported on Page
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	1*
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	1*
Occupation	3	What was their occupation at the time of the study?	1*
Gender	4	Was the researcher male or female?	N/A
Experience and training	5	What experience or training did the researcher have?	1*
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	N/A
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	N/A
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	N/A
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	120
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	121
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	121
Sample size	12	How many participants were in the study?	121
Non-participation	13	How many people refused to participate or dropped out? Reasons?	-
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	121
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	121
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	143
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	125
Repeat interviews	18	Were repeatinter views carried out? If yes, how many?	N/A
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	121
Field notes	20	Were field notes made during and/or after the interview or focus	125

Duration	21	What was the duration of the inter views or focus group?	121
Data saturation	22	Was data saturation discussed?	121
Transcripts returned	23	Were transcripts returned to participants for comment and/or	-
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	122
Description of the coding tree	25	Did authors provide a description of the coding tree?	122
Derivation of themes	26	Were themes identified in advance or derived from the data?	122
Software	27	What software, if applicable, was used to manage the data?	122
Participant checking	28	Did participants provide feedback on the findings?	-
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the	122-133
Data and findings consistent	30	Was there consistency between the data presented and the findings?	122-133
Clarity of major themes	31	Were major themes clearly presented in the findings?	122-133
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	122-133

*Refers to page numbers in published paper (T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause 25(7) (2018) 795-802.))

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

6 Chapter 6. Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy (BO): A Narrative Review[f]

Tasneem Siyam[1], BScPharm, MSc; Jenny Carbon[2], BScPharm, PharmD; Sue Ross[3], PhD; Nese Yuksel[4], BScPharm, PharmD, FCSHP, NCMP

[1]PhD candidate
Faculty of Pharmacy and Pharmaceutical Sciences
3-015 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
tsiyam@ualberta.ca

[2]Pharmacist
Cross Cancer Institute
11560 University Avenue
Edmonton, AB T6G 1Z2
carbon@ualberta.ca

[3]Cavarzan Chair in Mature Women's Health Research
Department of Obstetrics & Gynecology
Rm 5S131 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada, T5H 3V9
Sue.Ross@albertaheatlhservices.ca

[4]Professor (corresponding author)
Faculty of Pharmacy and Pharmaceutical Sciences
3-171 Edmonton Clinic Health Academy (ECHA)
University of Alberta
Edmonton, AB, Canada, T6G 1C9
nese.yuksel@ualberta.ca
Tel: (780)492-4442; Fax: (780)492-121

[f] T. Siyam, J. Carbon, S. Ross, N. Yuksel, Determinants of hormone therapy uptake and decision-making in bilateral oophorectomy (BO): A narrative review, Maturitas, Accepted for publication, November 8, 2018

6.1 Introduction

Bilateral oophorectomy (or surgical menopause) is associated with short and long-term clinical consequences. These effects are more pronounced in women who have a bilateral oophorectomy (BO) before age 45 years (early surgical menopause).[1] Menopausal symptoms associated with early surgical menopause, such as vasomotor and urogenital symptoms, sexual dysfunction, sleep disturbances, and mood swings can be sudden and severe. In the long term, these women are at a greater risk of osteoporosis, cardiovascular disease, cognitive impairment, and early mortality than women with natural menopause. [1-5]

In early surgical menopause, current guidelines recommend the use of hormone therapy (HT) until the average age of menopause (51 years) in women without HT contraindications.[6-8] Despite this, HT is often underutilized in this population.[9, 10] Findings from the Women's Health Initiative (WHI) randomized controlled trial showed an increased risk of breast cancer, cardiovascular disease (CVD), blood clots and stroke, with the use of estrogen and progestin when initiated in naturally postmenopausal women of older age (mean 63 years in the study).[11, 12] Unfortunately, these findings are often extrapolated to younger, symptomatic women who have had an early surgical menopause, even though this was not the population studied.[13] In contrast, the estrogen therapy (ET) arm of the WHI, involving more than 10,000 postmenopausal women who had undergone hysterectomies, ET had neutral effects on the incidence of heart disease and breast cancer.[14]

Managing menopause can be complex and the decision to start HT may be emotionally driven.[15] Women who go through early surgical menopause (<45 years) are specifically challenged as they may experience severe symptoms and long-term health risks [3, 4] Several

studies have captured determinants of HT uptake and factors influencing decision-making however all were in women who have gone through a natural menopause.[15] In this narrative review, we will discuss the factors that influence HT uptake and decision-making in surgical menopause.

6.2 Methods

For this narrative review, we followed a systematic search and review process that allows for the best available evidence synthesis in the researched area.[16]

6.2.1 Search strategy

Three databases were used in the search: Medline (1946 to April 2018), EMBASE (1946 to April 2018) and CINAHL (1937 to April 2018). The search terms were derived from 3 main concepts: 1) surgical menopause, 2) hormone therapy, and 3) decision-making. The search terms used for surgical menopause included 'surgical menopause', 'ovariectomy', 'oophorectomy', 'hormone substitution', and 'salpingo-oophorectomy'. The search terms used for HT included 'hormone replacement therapy', 'estrogen replacement therapy', 'progesterone replacement therapy', 'hormone therapy', and 'estrogen therapy'. The search terms used for decision-making included 'decision making', 'choice behavior', 'facilitator', 'barrier', 'obstacle', 'factor', 'determinant', 'predictor', 'decision', and 'hinder'. Search terms were searched as MeSH terms or keywords. For additional studies, reference lists of relevant review papers and eligible studies were hand searched. Limitations applied in this search were to English language, and human studies.

6.2.2 Inclusion and exclusion criteria

Eligibility criteria included qualitative and quantitative studies assessing determinants of HT use and decision-making in surgical menopause. Studies whose study populations included both surgical and natural menopausal women, and women contemplating BO and HT, were also

eligible for inclusion. Studies were excluded if the study population did not include surgical menopause. Conference proceedings, abstracts and review papers were also excluded.

6.2.3 Screening for eligibility and data abstraction

Titles and abstracts were initially screened by one reviewer (JC). Full-text of eligible articles was then assessed independently by two reviewers (JC and TS) for eligibility. Data abstraction was performed by 1 reviewer (JC) using a pre-developed extraction table and checked for accuracy by a second reviewer (TS). Data abstraction included: characteristics of manuscript (first author name, year of publication, timing of publication with respect to WHI); characteristics of study (study design, setting, objectives, sample size, and method of data collection); characteristics of study population (proportion of surgical menopause, definition of surgical menopause, age at time of study and/or time of surgery); and factors affecting uptake or decision-making.

6.2.4 Developing of a model of patient decision-making

Based on identified factors from relevant literature, a model of patient decision-making about HT in the context of surgical menopause was developed.

6.3 Results

The search yielded 947 articles from CINAHL, 596 from Medline, and 438 from EMBASE. Of these, 23 were eligible for inclusion.

6.3.1 Characteristics of the studies

Table 6.1 summarizes the characteristics of the studies included. For study details, please refer to table 6.2. Studies were mostly published before the WHI (61%), came from Europe (61%) and had a cross-sectional survey design (57%). Only 22% of studies were strictly on women who had surgical menopause. The mean age at the time of surgical menopause was 43.6 years (range 29-68). The use of HT was higher in women who had surgical menopause than natural menopause.

6.3.2 Factors affecting use and decision-making about HT

An explanatory model of factors affecting HT uptake and decision-making is shown in Figure 1. The model was informed by the health belief theoretical model (HBM). The HBM explains and predicts health behaviors given several psychosocial factors.[17] In surgical menopause, numerous factors in the literature were shown to influence the uptake of HT and decision-making. These factors were either women-related which included individual characteristics, perceptions, experiences with menopause and HT, and knowledge about menopause and HT or external factors which included physicians' recommendations, information sources and available evidence about HT.

6.3.2.1 Women-related factors

6.3.2.1.1 Individual characteristics

Individual characteristics included sociodemographic, medical & surgical history, reproductive factors, and health behaviors. Sociodemographic factors that were positively correlated with current use of HT were: younger age,[18-21] higher education,[19, 21-26] and higher income.[25] The effect of social class on HT use varied across studies, with some showing a higher HT uptake with higher social class,[21] while others suggesting a higher uptake with lower social class.[27]

A recent bilateral oophorectomy was strongly correlated with current and long-term HT use[22, 26] and also significantly predicted HT initiation in a longitudinal study.[28] Women having a history of hysterectomy,[20, 21, 29] and tubal ligation[21] were more likely to use HT than those who did not. Similarly, women who did not have a history of breast cancer,[21, 24] CVD,[19, 21, 24, 26] diabetes,[19, 21, 26] stroke or thromboembolic disease reported significantly higher rates of HT use than those who did.[21, 24] Having a history of osteoporosis was a significant

determinant of HT use in the late 90's but not after the publication of estrogen-progestin arm of WHI in 2002.[19]

Health behaviors also affected HT use. Women who had a lower BMI,[21, 24, 26] engaged in a regular physical activity,[21, 22, 25-27] performed regular medical care,[25] or attended gynecology clinics[18, 23] were more likely to be current HT users. Alcohol consumption was linked to current HT use.[18, 21, 25] The effect of smoking on HT use was mixed.[20, 21, 26] Past use of oral contraceptives was the only reproductive factor consistently associated with current HT use.[19, 21, 27] Effect of parity varied with settings with studies from France and the US suggesting a positive correlation with parity [18, 23] and studies from Italy linking HT use to nulliparous women.[19, 24]

6.3.2.1.2 Perceptions, beliefs and values

6.3.2.1.2.1 Perceptions of HT

Perceived benefits and risks of HT were the most cited factors in decision-making about HT. In several studies, women reported initiating HT because they believed it was effective in managing menopausal symptoms including vasomotor and psychological symptoms[9, 18, 20, 27-33] and maintaining quality of life.[34] Beliefs about long term benefits of HT in preventing osteoporosis and cardiovascular disease were also reported as reasons for initiating HT but mainly in studies published prior to the WHI.[18, 20, 27-29] Other perceived benefits included preservation of femininity and having a generally positive attitude towards HT.[30, 31, 33]

In contrast, perceived risks of HT hindered HT uptake and included fear of cancer,[9, 18, 20, 28, 31, 34-36] fear of side-effects [18, 20, 29, 31, 36, 37] and beliefs that HT is not natural. Of these,

the most prevalent were fear of cancer, particularly breast cancer, and fear of side-effects.[9, 34, 37, 38]

6.3.2.1.2.2 Perceived susceptibility of risks

Susceptibility of risks included the women's perceived susceptibility to breast cancer, to long-term risks of HT, and to risks of surgical menopause. Women who intended to take HT long-term had lower perceived susceptibility to breast cancer.[37, 39, 40] Women who preserved their ovaries following a hysterectomy had a higher perceived susceptibility to risks of HT and surgical menopause.[37] In qualitative studies exploring decision-making about HT, women who had a higher perceived susceptibility to HT risks were not using HT, whereas women who had a lower perceived susceptibility were using HT.[34, 40]

6.3.2.1.2.3 Beliefs on menopause

Beliefs on menopause influenced HT uptake.[20, 32, 38-40] Women who were never users of HT were more likely to view menopause as a natural event and believed that medications should be avoided. In contrast, adopting a medicalized philosophy about menopause, that is, perceiving it as a disease state promoted HT uptake.

6.3.2.1.2.4 Perceived need for treatment

Perceived need for treatment also affected HT uptake. [9, 20, 32] In one study, close to 80% of women who had oophorectomy believed that they needed treatment, and close to 50% had taken HT at some point in their life.[32] In other studies, women reported discontinuing HT because they believed they did not need it.[9, 20, 34] One study showed that beliefs about menopause and perceived need for treatment were inter-related; women who had their ovaries removed viewed themselves as physiologically deficient and believed others perceived them this way. Therefore, they believed in their need for HT treatment.[38]

6.3.2.1.2.5 Perceived control over actions

Women who felt a greater sense of responsibility or control over one's actions and decisions were more likely to be actively engaged in making a decision about HT and were less influenced by external factors.[35, 40] For example, some women felt they had so much control over their bodies and trust in their decision that it did not matter if it opposed the advice given by their doctors.[34, 35]

6.3.2.1.2.6 Perceived complexity of therapy decisions

Perceived complexity of therapy decisions was primarily seen in studies with women who were BRCA mutation carriers making decisions about prophylactic oophorectomy or HT.[35] These women felt overwhelmed by the enormity of the decision, given the lack of evidence about HT safety in their population. They sought medical and experiential knowledge as well as emotional and communal support to make a treatment decision.[35]

6.3.2.1.2.7 Value placed on present versus the future

The value women placed on the present versus the future and on the quality versus the quantity of life affected therapy decisions. Women who actively decided to take HT placed a higher value and preference for maintaining a good quality of life.[34, 35, 38, 40] On the contrary, some women chose to discontinue HT because of its long-term risks and relied on their own body to get them through menopause.[34, 35, 38]

6.3.2.1.3 Knowledge on menopause and HT

In a recent study, learning about menopause and menopausal therapies was strongly associated with taking HT.[26] Several studies showed that surgical menopausal women particularly do not receive adequate information about HT,[9, 31, 37] and surgical menopause[34, 37] either before or after BO. Women’s need for more accessible and reliable information on HT and menopause

was consistently emphasized across included studies. To make informed therapy decisions, women needed to learn about short and long term effects of surgical menopause; as well as, HT benefits, risks, duration of treatment, dosage forms, and doses. [34, 36, 37]

6.3.2.1.4 Experiences with surgical menopause and HT

HT uptake was influenced by women's experiences with surgical menopause and HT. Many women continued on HT because of the severity of their surgical menopausal experience and the impact the symptoms had on their physical and emotional wellbeing.[35, 38] The decision to continue or stop HT was also affected by personal experience with HT. A study showed that continued use of HT correlated with menopausal symptoms control.[30] On the other hand, the most cited reason for stopping HT was the experience of unfavorable side-effects such as nausea, weight gain, irregular bleeding, headaches, and sore breasts.[20, 28, 29, 31, 34] Other less common reasons include lack of complete alleviation of symptoms[29, 31] and development of a disease, such as thrombosis, breast cancer or hypertension.[29]

6.3.2.2 External factors

6.3.2.2.1 Physician's recommendation

Almost all studies in the review emphasized the role of physicians in influencing women's therapy decisions, risk perceptions and treatment preferences.[20, 26-28, 34-36, 38, 39] Physician advice had a positive or negative influence on HT uptake. In some studies, women reported starting HT because of their doctor's recommendations.[20, 27, 39] In other studies, physician advice was a reason for stopping or never initiating HT.[28]

Physician's advice affected women's risk perceptions about HT. One study highlighted that one way women assessed risks of treatment was through doctor's advice.[38] Another study reported

that 50% of never users said that they would take HT if their physician convinced them that the benefits of HT outweighed its risks.[9]

Treatment preferences were also influenced by physician's advice. In one study, women stated that their doctors had left the decision up to them, the content of their shared stories suggest that their physician's advice was strongly directional towards a particular therapy.[37] Furthermore, patient decisions were sometimes influenced by physician's specialty. Gynecologists appeared to favor the use of HT compared to family physicians and oncologists.[18]

6.3.2.2.2 Information sources

6.3.2.2.2.1 Media, family and friends

Several studies reported that mass media was a primary source of HT information (e.g. internet, magazines, journals, books, TV, and radio).[9, 20, 35, 36] In one study, women were confused and uncertain about HT because of the conflicting information delivered by the media and popular press.[36]

A few studies referenced family, friends and colleagues as main sources of information on HT, besides media outlets.[9, 20, 34, 37, 40] Friends' disapproval of HT stirred negative beliefs about its use among women who had surgical menopause. [20, 40] Therapy decisions were affected indirectly by how women perceived a friend's or a relative's past experience with HT and surgical menopause.[34]

6.3.2.2.3 Evidence about HT

Evidence about the safety of HT in BRCA mutation carriers who have had a prophylactic BO is lacking, and current literature is of limited relevance to these women. In one study, women were mainly concerned about their risk of breast cancer and how HT may counteract the benefits

conferred by prophylactic oophorectomy. They were also concerned that their short and long term quality of life may be compromised without it.[35]

6.4 Discussion

From identified factors in the literature, we proposed a model that aims to illustrate the decision-making process of surgical menopausal women as they make treatment decisions pertaining to HT. The model suggests that women go through a risk evaluation process where they weigh competing risks to make treatment preferences which in turn guide treatment decisions. It also proposes that women evaluate risks primarily according to emotional/subjective dimensions related to perceptions of HT risks and benefits, value placed on present versus future health, experiential knowledge, and inferences made from commonly sought information sources, such as media and popular press.

Our review particularly highlights the role of women's perceptions in informing treatment preferences. These mostly included perceptions related to HT risks and benefits as well as perceptions of susceptibility to HT risks, severity of surgical menopause, and control over treatment decisions. This finding is not specific to surgical menopause and was previously explained by Carpenter et al. for natural menopause.[15] It is rather a property of complex decisions where choice is mostly guided by risk perceptions due to uncertainty of treatment(s) outcomes.[41] In the general population of surgical menopause evidence supports the use of HT for managing short and long term symptoms; yet uncertainty about outcomes is still perceived among women. This-may have mostly been driven by conflicting messages about HT conveyed through various communication platforms, such as media outlets and physician's recommendations.

Physician's recommendation was shown as a main external influencer of decisions about HT. Physician's advice affected women's risk perceptions and treatment preferences. Physician's role in HT decisions may be attributed to the traditional belief some patients hold about relying on physician's advice for health care decisions.[42] It may be the case that women rely more on doctor's advice when overwhelmed by the uncertainty and contradictory messages about HT which was strongly captured in our review.

In our model, knowledge also contributed to decision-making about HT. However, the review showed that women in various decision settings, shared a common belief about the lack of adequate and reliable information about surgical menopause and HT when making treatment decisions. Research shows that laypeople tend to draw upon cognitive dimensions for developing risk perceptions when they have a good understanding of the subject involved.[43-45] In surgical menopause, the lack of a common message and understanding about HT and related outcomes, may undermine the use of cognitive dimensions in driving informed risk perceptions and treatment decisions. Instead, the role of emotional judgements about risks become accentuated.

In this review, factors like lack of knowledge about surgical menopause and HT; use of subjective, experiential reasoning in weighing risk perceptions; and limited patient involvement in therapy decisions were viewed as modifiable determinants of decision-making. These factors can be essentially modified by evidence-based decision support interventions such as patient decision aids that aims to foster decision-making through: (1) improving the understanding of surgical menopause, its short and long term outcomes and available treatment options; (2) enhancing the comprehension of risk information about HT and other options; (3) helping women develop realistic expectations of HT outcomes; (4) clarifying patient's values and

preferences; and (5) increasing patient's involvement in decision-making through stimulating communications with health care providers.

While decisions may still be guided by women's perceptions and experiences, an evidence-based patient decision aid may help create a fine balance between the integration of emotion and reason for effective decision-making. A decision aid can also modify physician's role in decision-making to a more collaborative approach, inclusive of women's values and informed preferences.

The model developed has implication for clinicians who care for women who have had or about to have a bilateral oophorectomy for prophylaxis or treatment. These implications include a greater understanding of the complexity involved in decision-making about treatments for surgical menopause and the value of clinical counselling as a decision support measure in addressing decisional complexities. The model highlights various factors involved in managing HT decisions in surgical menopause and the specific role of women perceptions and intuitive judgements in guiding decisions. With such awareness in mind, clinicians are encouraged to first, identify women's need for decision support. Second, screen for unresolved decisional needs with reference to factors highlighted in the model. And third, to tailor clinical counselling to unresolved decisional needs specific to each woman for effective decisional support. For example, based on identified decisional needs clinicians can focus their counselling on advising/educating women about evidence-based information, helping women make realistic expectations about suggested treatments, addressing values and treatment preferences, providing guidance in deliberation and/or engaging women in shared decision-making. Barriers to implementing effective clinical counselling as a decision support intervention include clinicians' lack of time and skills in promoting shared decision-making and/or lack of knowledge about

evidence-based therapies and associated outcomes. In such case the use of other decision support measures like patient decision aids and decision coaching may be of benefit.

To our knowledge, this is the first review paper to discuss factors affecting decision-making and HT uptake in surgical menopause. The review involved a comprehensive search of published literature, and a systematic process of screening and data extraction to provide an accurate and detailed textual narrative synthesis of factors affecting decision-making about HT. Though, it's important to note our limitations. An important limitation of this review is that most studies were published before the WHI and included both surgical and naturally menopausal women. Very few studies stratified analysis by menopause status. In a large study included in the review, patterns of current HT use according to medical history, lifestyle and use of other health related services were very similar in women who had surgical menopause and those who had natural menopause.[21] Additionally, none of the studies identified in the review analyzed data by age or age at time of surgery. Most studies included women of a wide age range. Among studies that included surgical menopausal women only the average age at surgery was 43.6 years. In two included studies were most women were of younger age (average age 38.3years), perceptions of HT risks and benefits also contributed to therapy decision-making.[31, 35] Furthermore, reported facilitators to HT uptake included perceived control over one's action, value placed on present versus future health and severity of menopausal symptoms. Reported barriers were perceived complexity of therapy decision and lack of knowledge about HT outcomes.[31, 35] Given the lack of information, we are unable to state specific age cut-offs to which evidence from the narrative review can be best inferred. In our review, only 3 studies were of longitudinal nature and hence captured patterns and correlates of use over time across and within individuals.[27, 28, 39] Most of the studies were cross-sectional and can only suggest causation through observed

correlations. Furthermore, in the qualitative studies, women provided a retrospective account of decision-making, which may differ from reflection at the time of decision-making. Definition of surgical menopause was not consistent among studies: for example, some studies considered hysterectomy as a cause of surgical menopause. Similarly, in one study women who reported having a cessation of menstrual period due to an operation without specifying type of operation were considered surgically menopausal. Moreover, not all studies reported age at surgical menopause and HT prevalence as we hoped, thus the reported average estimates of these characteristics may not accurately represent the target population parameters. This may also explain why in our review the reported drop in HT use before and after the WHI publication in both the general population of menopausal women and the specific population of surgical menopause was lower than the usage decline documented in the literature.[46] Last, while narrative reviews offer a good method of consolidating evidence from a wide range of peer-reviewed literature, with a special focus on the conceptual contribution of each reference in the relevant literature, an inherent limitation of narrative reviews is that their conclusions are more prone to bias, essentially due to the lack of an explicit and formal process of identifying, screening, and evaluating literature.[16] In our review, we attempted to limit this subjectivity through following a comprehensive and systematic approach for identifying, screening and analyzing relevant literature.

6.5 Conclusion

Women who go through surgical menopause are faced with a complex therapy decision related to HT due to the perceived uncertainty of its treatment outcomes. In such case, women tend to rely on subjective perceptions and inferences from sought information sources when making treatment decisions which may hamper their likelihood to make informed preferences and

treatment decisions. Patient decision aids may offer these women decision support in the form of improving their knowledge and understanding about HT and surgical menopause, improving risk comprehension and offering guidance in clarifying values and negotiating informed risk perceptions to arrive to an informed, value-based therapy decision. To support women in decision-making and reduce harm from misguided decisions, careful attention needs to be given in developing evidence-based patient decision aids that avoids bias and is based on recognized quality criteria.

6.6 References

[1] M.S. Hunter, Long-term impacts of early and surgical menopause, Menopause 19(3) (2012) 253-4.

[2] L.J. Melton, 3rd, C.S. Crowson, G.D. Malkasian, W.M. O'Fallon, Fracture risk following bilateral oophorectomy, J Clin Epidemiol 49(10) (1996) 1111-5.

[3] W.A. Rocca, J.H. Bower, D.M. Maraganore, J.E. Ahlskog, B.R. Grossardt, M. de Andrade, L.J. Melton, 3rd, Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause, Neurology 69(11) (2007) 1074-83.

[4] C.M. Rivera, B.R. Grossardt, D.J. Rhodes, R.D. Brown, Jr., V.L. Roger, L.J. Melton, 3rd, W.A. Rocca, Increased cardiovascular mortality after early bilateral oophorectomy, Menopause 16(1) (2009) 15-23.

[5] W.A. Rocca, B.R. Grossardt, M. de Andrade, G.D. Malkasian, L.J. Melton, 3rd, Survival patterns after oophorectomy in premenopausal women: a population-based cohort study, Lancet Oncol 7(10) (2006) 821-8.

[6] The 2017 hormone therapy position statement of The North American Menopause Society, Menopause 24(7) (2017) 728-753.

[7] T.J. de Villiers, M.L. Gass, C.J. Haines, J.E. Hall, R.A. Lobo, D.D. Pierroz, M. Rees, Global Consensus Statement on menopausal hormone therapy, Maturitas 74(4) (2013) 391-2.

[8] R. Reid, B.L. Abramson, J. Blake, S. Desindes, S. Dodin, S. Johnston, T. Rowe, N. Sodhi, P. Wilks, W. Wolfman, M. Fortier, L. Graves, B. Guthrie, A. Khan, Managing menopause, J Obstet Gynaecol Can 36(9) (2014) 830-8.

[9] R.J. Chen, T.C. Chang, S.N. Chow, Perceptions of and attitudes toward estrogen therapy among surgically menopausal women in Taiwan, Menopause 15(3) (2008) 517-23.

[10] A. Chubaty, M.T. Shandro, N. Schuurmans, N. Yuksel, Practice patterns with hormone therapy after surgical menopause, Maturitas 69(1) (2011) 69-73.

[11] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, J. Ockene, Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial, JAMA 288(3) (2002) 321-33.

[12] A. Morabia, M.C. Costanza, Recent reversal of trends in hormone therapy use in a European population, Menopause 13(1) (2006) 111-5.

[13] S. Torrealday, P. Kodaman, L. Pal, Premature Ovarian Insufficiency - an update on recent advances in understanding and management, F1000Res 6 (2017) 2069.

[14] G.L. Anderson, M. Limacher, A.R. Assaf, T. Bassford, S.A. Beresford, H. Black, D. Bonds, R. Brunner, R. Brzyski, B. Caan, R. Chlebowski, D. Curb, M. Gass, J. Hays, G. Heiss, S. Hendrix, B.V. Howard, J. Hsia, A. Hubbell, R. Jackson, K.C. Johnson, H. Judd, J.M. Kotchen, L. Kuller, A.Z. LaCroix, D. Lane, R.D. Langer, N. Lasser, C.E. Lewis, J. Manson, K. Margolis, J. Ockene, M.J. O'Sullivan, L. Phillips, R.L. Prentice, C. Ritenbaugh, J. Robbins, J.E. Rossouw, G. Sarto, M.L. Stefanick, L. Van Horn, J. Wactawski-Wende, R. Wallace, S. Wassertheil-Smoller,

Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial, JAMA 291(14) (2004) 1701-12.

[15] J.S. Carpenter, M.M. Byrne, J.L. Studts, Factors related to menopausal symptom management decisions, Maturitas 70(1) (2011) 10-5.

[16] M.J. Grant, A. Booth, A typology of reviews: an analysis of 14 review types and associated methodologies, Health Info Libr J 26(2) (2009) 91-108.

[17] I.M. Rosenstock, V.J. Strecher, M.H. Becker, Social learning theory and the Health Belief Model, Health Educ Q 15(2) (1988) 175-83.

[18] B.T. Levy, J.M. Ritchie, E. Smith, T. Gray, W. Zhang, Physician specialty is significantly associated with hormone replacement therapy use, Obstet Gynecol 101(1) (2003) 114-22.

[19] F. Parazzini, Trends of determinants of hormone therapy use in Italian women attending menopause clinics, 1997-2003, Menopause 15(1) (2008) 164-70.

[20] K.M. Newton, A.Z. LaCroix, S.G. Leveille, C. Rutter, N.L. Keenan, L.A. Anderson, Women's beliefs and decisions about hormone replacement therapy, J Womens Health 6(4) (1997) 459-65.

[21] Patterns of use of hormone replacement therapy in one million women in Britain, 1996-2000, BJOG 109(12) (2002) 1319-30.

[22] R. Lucas, H. Barros, Life prevalence and determinants of hormone replacement therapy in women living in Porto, Portugal, Maturitas 57(3) (2007) 226-32.

[23] V. Ringa, B. Ledesert, R. Gueguen, F. Schiele, G. Breart, Determinants of hormonal replacement therapy in recently postmenopausal women, Eur J Obstet Gynecol Reprod Biol 45(3) (1992) 193-200.

[24] F. Pansini, A.B. Bacchi Modena, D. de Aloysio, M. Gambacciani, M. Meschia, F. Parazzini, G. Sciacchitano, R. di Micco, E. Peruzzi, G. Maiocchi, Sociodemographic and clinical factors associated with HRT use in women attending menopause clinics in Italy, Climacteric 3(4) (2000) 241-7.

[25] R.M. Brennan, C.J. Crespo, J. Wactawski-Wende, Health behaviors and other characteristics of women on hormone therapy: results from the Third National Health and Nutrition Examination Survey, 1988-1994, Menopause 11(5) (2004) 536-42.

[26] N. Mendoza, C. Hernandez, M.J. Cornellana, A. Carballo, P. Llaneza, X. Harvey, S. Palacios, Factors determining the use of hormonal therapy and phytotherapy in Spanish postmenopausal women, Climacteric : the journal of the International Menopause Society 19(4) (2016) 375-80.

[27] D. Kuh, R. Hardy, M. Wadsworth, Social and behavioural influences on the uptake of hormone replacement therapy among younger women, BJOG 107(6) (2000) 731-9.

[28] C.B. Johannes, S.L. Crawford, J.G. Posner, S.M. McKinlay, Longitudinal patterns and correlates of hormone replacement therapy use in middle-aged women, Am J Epidemiol 140(5) (1994) 439-52.

[29] A. Koster, Hormone replacement therapy: use patterns in 51-year-old Danish women, Maturitas 12(4) (1990) 345-56.

[30] G. Khastgir, J. Studd, Patients' outlook, experience, and satisfaction with hysterectomy, bilateral oophorectomy, and subsequent continuation of hormone replacement therapy, Am J Obstet Gynecol 183(6) (2000) 1427-33.

[31] N. Hallowell, A qualitative study of the information needs of high-risk women undergoing prophylactic oophorectomy, Psychooncology 9(6) (2000) 486-95.

[32] D.H. Barlow, K.A. Grosset, H. Hart, D.M. Hart, A study of the experience of Glasgow women in the climacteric years, Br J Obstet Gynaecol 96(10) (1989) 1192-7.

[33] S.H. Pedersen, B. Jeune, Prevalence of hormone replacement therapy in a sample of middle-aged women, Maturitas 9(4) (1988) 339-45.

[34] T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause (2018).

[35] R.H. Kenen, P.J. Shapiro, S. Friedman, J.C. Coyne, Peer-support in coping with medical uncertainty: discussion of oophorectomy and hormone replacement therapy on a web-based message board, Psychooncology 16(8) (2007) 763-71.

[36] L.H. Lack, I., Post-surgical hormone replacement therapy: information needs of women Journal of Clinical Nursing (1) (1992) 323-327.

[37] V. Bhavnani, A. Clarke, Women awaiting hysterectomy: a qualitative study of issues involved in decisions about oophorectomy, BJOG 110(2) (2003) 168-74.

[38] M. Crowe, B. Burrell, L. Whitehead, Lifestyle risk management--a qualitative analysis of women's descriptions of taking hormone therapy following surgically induced menopause, J Adv Nurs 68(8) (2012) 1814-23.

[39] M.A. Gerend, L.S. Aiken, M.J. Erchull, A. Lapin, Women's use of hormone therapy before and after the Women's Health Initiative: a psychosocial model of stability and change, Prev Med 43(3) (2006) 158-64.

[40] B. Burrell, V. Valledor, M. Crowe, L. Whitehead, Negotiating competing discourses: the decision to take menopausal hormone therapy following surgical menopause, Women Health 50(6) (2010) 527-43.

[41] A.M. O'Connor, M.J. Jacobsen, Workbook on Developing and Evaluating Patient Decision Aids Ottawa Health Research Institute, Ottawa, 2003.

[42] D.S. Brody, The patient's role in clinical decision-making, Ann Intern Med 93(5) (1980) 718-22.

[43] P. Slovic, M.L. Finucane, E. Peters, D.G. MacGregor, Risk as analysis and risk as feelings: some thoughts about affect, reason, risk, and rationality, Risk Anal 24(2) (2004) 311-22.

[44] M. Watson, S. Lloyd, J. Davidson, L. Meyer, R. Eeles, S. Ebbs, V. Murday, The impact of genetic counselling on risk perception and mental health in women with a family history of breast cancer, Br J Cancer 79(5-6) (1999) 868-74.

[45] D. Stacey, F. Legare, N.F. Col, C.L. Bennett, M.J. Barry, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, J.H. Wu, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev (1) (2014) CD001431.

[46] P.I. Jewett, R.E. Gangnon, A. Trentham-Dietz, B.L. Sprague, Trends of postmenopausal estrogen plus progestin prevalence in the United States between 1970 and 2010, Obstetrics and gynecology 124(4) (2014) 727-33.

Figure 6.1. Explanatory model of factors contributing to decision making about HT in surgically menopausal women based on scientific literature

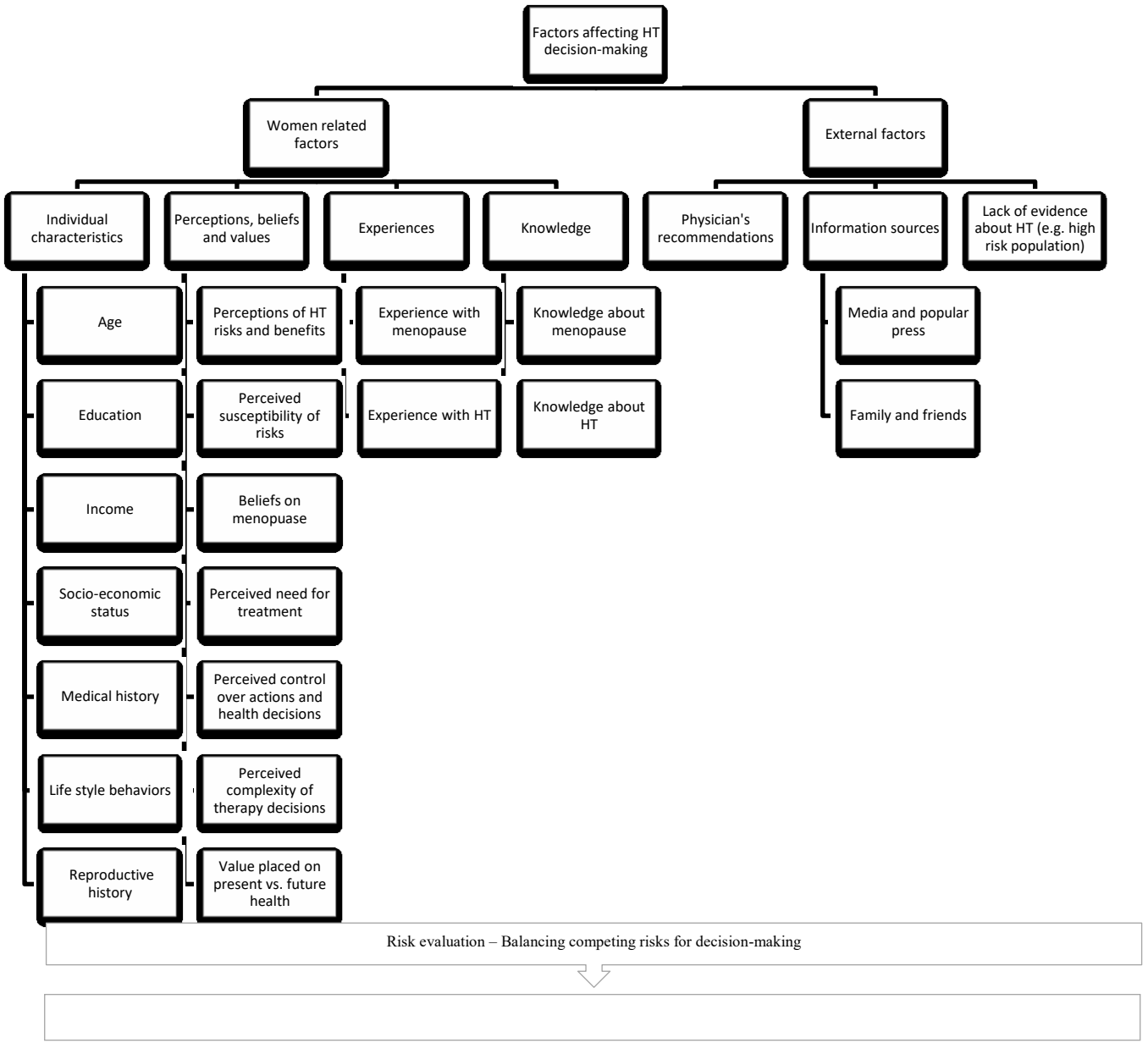


Table 6.1. Summary table of study characteristics

Characteristic	**Number of studies (%)** **N = 23**
Setting	
Europe	14 (61%)
USA	6 (26%)
Other	3 (13%)
Timing of publication with respect to WHI	
Before	14 (61%)
After	7 (30%)
Before and after	2 (9%)
Study design	
Quantitative	17 (74%)
Cross-sectional	13 (76%)
Longitudinal/Prospective cohorts	4 (24%)
Qualitative	6 (26%)
Study population	
Natural and surgical	15 (65%)
Surgical only	5 (22%)
Surgical and contemplate BO	1 (4%)
Contemplate BO only	1 (4%)
Hysterectomy and BO[a]	1 (4%)
Average proportion of surgical menopausal population[b]	17% (1.5-44)
Mean age at time of study – years (range)[c]	52.9 (27-86)
Mean age at time of surgery – years(range)[c]	43.6 (29-68)
HT prevalence overall[d]	
Before WHI	35.3%
After WHI	33.4%
HT prevalence among surgical menopausal population[d]	
Before WHI	43.2%
After WHI	31.6%

WHI = Women's Health Initiative; BO = Bilateral Oophorectomy; HT = Hormone Therapy; [a]83% of those who had hysterectomy had concurrent bilateral oophorectomy; [b]Proportion of surgical menopause in studies that included both natural and surgical menopausal women; [c]Not all studies reported average age and/or range; [d]Not all studies reported prevalence of HT use among study population or surgical menopausal population

Table 6.2. Detailed table of study characteristics

Author, year	Settings	Timing with respect to WHI	Objective(s)	Design	Sample size	Data collection	Study population	% of surgical	Age at study, mean, SD/range	Age at surgery, mean, SD/range	HT prevalence overall (%)	HT prevalence surgical (%)
Barlow et al., 1989	UK	Before	Describe women's experience with menopause	Quantitative – cross-sectional survey design	424	Questionnaire administered by interviewer	Natural & surgical	7.80%	40-60	NS[a]	7%	27.30%
Bhavnani et al., 2003	UK	After	Describe women thoughts about BO and the consequent need for HT	Qualitative	16	In-depth interviews	Contemplate BO	NA	NS	NA	NA	NA
Brennan et al., 2004	USA	Before	Study the prevalence of HT use and compare the demographics and health behaviors and indicators between users and non-users	Quantitative – cross-sectional survey design	3,673	Self-administered questionnaire	Natural & surgical	NS	≥40	NS	11.40%	NS
Burrell et al., 2010 & Crowe et al., 2011	New Zealand	After	Discuss the perceptions and experiences of women who had surgical menopause with HT and how they arrived to a decision about HT	Qualitative – based on Foucault's theoretical position and risk management theoretical approach	30	Semi-structured interviews	Surgical	100%	45-65	NS	NS	NS

Chen et al., 2008	Taiwan	After	Evaluate attitudes towards ET among surgically menopausal women	Quantitative – cross-sectional survey design	188	Self-administered questionnaire	Surgical	100%	48.3(35-53)	45.3(32-49)	22.30%	22.30%
Gerend et al., 2006	USA	Before and After	Examine factors underlying HT use before and after WHI	Quantitative – longitudinal	324	Questionnaire administered by interviewer	Natural & surgical	26.50%	61.2(NS)	NS[b]	Before WHI: 45%; After WHI: 15.1%	NS
Hallowell et al., 2000	UK	Before	Determine information needs of high-risk premenopausal women who had undergone PBO	Qualitative	23	In-depth interviews	Surgical	100%	44.4(32-62)	38.3(31-45)	40.90%	40.90%
Johannes et al., 1994	USA	Before	Examine Patterns of HT use over time and predictors of initiating or discontinuing use.	Quantitative – longitudinal	2,425	Questionnaire administered by interviewer (phone interviews)	Natural & surgical	6.50%	50.2(NS)	NS	12.30%	45%
Khastgir et al., 2000	UK	Before	Recognize patients' understanding of the indication, outlook in, acceptance, experiences of recovery, and extent of symptom relief, with hysterectomy, BO and	Quantitative – pre-post survey design	194	Self-administered questionnaire	Hysterectomy & surgical	83%	NS	(29-68)	97%	97%

			routine use of HT									
Kenen et al., 2007	USA	After	Explore psychosocial and physical concerns surrounding the choice of BO for risk-reduction and the processes involved in the decision to use HT	Qualitative	29	Online threads on message boards with relevance to HBOC community	Surgical & contemplate BO	NS	NS (most women were in their 30s)	NS	NS	NS
Koster et al.,1990	Denmark	Before	Describe prevalence and patterns of HT use in a nationally representative birth cohort in Denmark (women born in 1936)	Quantitative – cross-sectional survey design	526	Self-administered questionnaire	Natural & surgical	1.50%	51 years	NS	22%	NS
Kuh et al., 2000	England, Scotland and whales	Before	Determine social and behavioral influences on the uptake of HT among a nationally representative birth cohort in UK (younger women before age 50)	Quantitative – Longitudinal	1572	Self-administered questionnaire, medical records and home interviews	Natural & surgical	8.20%	<50	NS	45%	54%

Lack et al., 1992	UK	Before	Examine the feelings and thoughts of women who received HT after surgical menopause	Qualitative	14	Unstructured interviews	Surgical	100%	32-56	NS	NS	NS
Levy et al., 2003	USA	Before	Identify predictors of current HT use	Quantitative – cross-sectional survey design	426	Self-administered questionnaire	Natural & surgical	26.50%	58.5	NS	67%	NS
Lucas et al., 2006	Portugal	After	Survey the life prevalence and determinants of HT use in menopausal women in Portugal	Quantitative – cross-sectional survey design	908	Self-administered questionnaire	Natural & surgical	15.50%	62.3(9.6)	NS	26.50%	26.50%
Mendoza et al., 2016	Spain	After	Identify sociodemographic factors and other health related factors that are associated with the use of HT in Spanish postmenopausal women	Quantitative – cross-sectional survey design	3022	Self-administered questionnaire	Natural & surgical	16.90%	56.7 (5.6)	48.7(.37)	31.90%	20.40%
Million women study collaborators, 2002	England and Scotland	Before	Describe national patterns of use of HT in 1996–2000	Quantitative – cross-sectional survey design	1,091, 250	Self-administered questionnaire	Natural & surgical	27.80%	47.3(0.02)	23% had surgery before age 45	33%	66%
Newton et al., 1997	USA	Before	Describe women's reasons for initiating, discontinuing	Quantitative – cross-sectional survey design	1,082	Questionnaire administered by interviewer (phone interviews)	Natural & surgical	NS	50-80	NS	42.50%	NS

			or not initiating HT									
Pansini et al., 2000	Italy	Before	Find any association between the use of HT and sociodemographic and clinical factors among women attending menopause clinics in Italy.	Quantitative – cross-sectional survey design	17,851	Self-administered questionnaire	Natural & Surgical	19.80%	53.3(36-79)	NS	47.80%	21.90%
Parazzini et al., 2008	Italy	Before & After	Patterns of hormone therapy (HT) use among postmenopausal Italian women, before and after publication of results from the WHI.	Quantitative – cross-sectional survey design	106,784	Self-administered questionnaire	Natural & Surgical	3.40%	53(NS)	NS	Before WHI :17.6%; After WHI: 11.4%	Before WHI:31.7 % to After WHI: 18.7%
Pederson et al., 1988	Denmark	Before	Examine the use of HT during climacteric in middle-aged Danish women.	Quantitative – cross-sectional survey design	401	Self-administered questionnaire	Natural & Surgical	17%	40-59	42	33%	37%
Ringa et al., 1992	France	Before	Examine the prevalence of HT and determinants of HT use	Quantitative – cross-sectional survey design	1986	Self-administered questionnaire	Natural & Surgical	44%	51.4(2.8)	NS	8.10%	11%

Siyam et al., 2018	Canada	After	Explore the process of decision-making about menopausal treatments in women who had surgical menopause after BO	Qualitative	37	Focus groups	Surgical	100%	50.8 (27-77)	≤50	70%	70%

WHI, Women's Health Initiative; SD, Standard deviation; NS, Not specified; NA, Not applicable; BO, Bilateral Oophorectomy; PBO, Prophylactic Bilateral Oophorectomy; HBOC, Hereditary Breast and Ovarian Cancer; [a]20% had surgery before age 45; [b]71% had surgery before age 51

7 Chapter 7. Developing and Evaluating a Patient Decision Aid for Managing Surgical Menopause: The Story Behind The "SheEmpowers" Patient Decision Aid[g]

Tasneem Siyam[1], BScPharm, MSc; Alisha Shivji[2], Sue Ross[3], PhD; Dean T. Eurich[4], PhD, Afsaneh Lavasanifar[5], PhD; Nese Yuksel[6], BScPharm, PharmD, FCSHP, NCMP

[1]PhD candidate
Faculty of Pharmacy and Pharmaceutical Sciences
3-015 Edmonton Clinic Health Academy (ECHA)
University of Alberta, Edmonton, AB, Canada, T6G 1C9
tsiyam@ualberta.ca

[2]Pharm D Candidate
Faculty of Pharmacy and Pharmaceutical Sciences
University of Alberta, Edmonton, AB, Canada, T6G 1C9
ashivji@ualberta.ca.ca

[3]Cavarzan Chair in Mature Women's Health Research
Department of Obstetrics & Gynecology
Rm 5S131 Lois Hole Hospital/Robbins Pavilion Royal Alexandra Hospital
10240 Kingsway Ave, Edmonton, AB, Canada, T5H 3V9
Sue.Ross@albertaheatlhservices.ca

[4]Associate Professor
School of Public Health
2-040 Li Ka Shing HRIF
University of Alberta, Edmonton, AB, Canada, T6G 2E1
deurich@ualberta.ca

[5]Professor
Faculty of Pharmacy and Pharmaceutical Sciences
2-142F Katz building
University of Alberta, Edmonton, AB, Canada, T6G 2H1
afsaneh@ualberta.ca

[6]Professor (corresponding author)
Faculty of Pharmacy and Pharmaceutical Sciences
3-171 Edmonton Clinic Health Academy (ECHA)
University of Alberta, Edmonton, AB, Canada, T6G 1C9
nese.yuksel@ualberta.ca

[g] T. Siyam, A. Shivji, S. Ross, N. Yuksel, Developing and evaluating a patient decision aid for managing surgical menopause: The story behind the "SheEmpowers" patient decision aid. To be submitted to "Patient education and counselling"

7.1 Introduction

One of the consequences of bilateral oophorectomy (BO) when performed before natural menopause is surgical menopause. Surgical menopause, a form of induced menopause is commonly associated with several short and long term effects which are more pronounced in women who have had a BO before age 45 years (early surgical menopause).[1] Symptoms of surgical menopause include vasomotor and urogenital symptoms, sexual dysfunction, sleep disturbances, mood symptoms and a decreased sense of well-being.[2-4] In the long term, surgical menopause also predisposes to osteoporosis,[5] cardiovascular disease (CVD),[6] cognitive impairment,[7] and premature death.[8]

Hormone therapy (HT) is a recommended option for managing surgical menopause. Clinical guidelines advocate the use of HT in early menopause until the average age of natural menopause (51 years) when there are no HT contraindications.[9-11] Yet, studies have shown that HT is poorly utilized in women with surgical menopause.[12-14] Confusion may exist about the risks and benefits of HT among women and clinicians, as evidenced by a clear discrepancy between current guidelines and practice-based behaviors related to physician's recommendations and patient's actions.[15]

The nature of decision-making about HT is complex, given women perceived uncertainty of its outcomes.[13, 16, 17] In such case, decisions are driven by women subjective perceptions, experiences and preferences.[16] Preference-sensitive decisions can lead to feelings of decisional conflict.[18] Women with early surgical menopause might be particularly at risk due to their sudden and severe symptomology,[19] lack of information and medical support and the need to make a difficult therapy decision on a short timeline.[20-22]

Patient decision aids (PDAs) are powerful interventions in situations where patients are faced with a complex therapy decision.[23] They present facts and unbiased information about available options and outcomes and help patient make informed preferences and decisions.[24] PDAs are specifically helpful in surgical menopause as they help women develop realistic expectations about HT, clarify values and engage with clinicians for shared decision-making (SDM). This, may ultimately, result in reduced feelings of decisional conflict and quality therapy decision.[24]

No peer-reviewed, evidence-based PDAs are currently available to support women who go through early surgical menopause.[25, 26] In a scoping review recently published by our study group the lack of decision aids for managing early surgical menopause was emphasized.[25] Decision aids for surgical menopause were found only in the grey literature with no published evidence of development and evaluation, were not informed by a needs assessment and lacked several measures of quality related to the presentation of outcome probabilities.[27, 28] Given the lack of decision support intervention for early surgical menopause, we systematically developed and evaluated an evidence-based, self-administered PDA to help women make HT decisions for managing early surgical menopause.

7.2 Methods

7.2.1 Development framework

The PDA development was guided by the Ottawa Decision Support Framework (ODSF),[29, 30] and the International Patient Decision aid Standards (IPDAS) criteria.[31, 32] ODSF was chosen because of its relevance to preference-sensitive decisions that require careful deliberation and negotiation among given options.[29] The IPDAS is a comprehensive and widely accepted quality framework, established to enhance the quality of developing and evaluating decision

aids.[32] IPDAS criteria was followed to develop a PDA that is consistent with internationally recognized standards for quality.[31] Drawing on ODSF and recommendations from IPDAS,[29, 31] the following steps were implemented for developing the PDA:

1. Define scope and purpose
2. Assemble steering committee and define roles
3. Explore the decisional needs of target population (exploratory phase)
4. Draft PDA
5. Review PDA with steering committee (evaluation phase)
6. Evaluate PDA for acceptability (evaluation phase)

7.2.2 Steps for developing PDA

Figure 7.1 outlines the steps involved in developing and evaluating the PDA

7.2.2.1 Scope and purpose

The PDA is targeted at women who had or about to have an early surgical menopause (≤45 years) to offer decision support when making HT decisions. The aid has been developed to be self-administered, prior to a clinical encounter to prepare women for SDM about treatment options with their healthcare providers (HCPs). Because the tool aims to support women in decision-making by empowering them with information, resources and guidance in decision-making, we have named it the "SheEmpowers" PDA.

7.2.2.2 Steering committee and roles

The steering committee, composed of a multidisciplinary group of researchers, clinicians and patients who are experts in the field, guided the development of the tool. The SheEmpowers PDA steering committee consisted of:

- Patient partners (Women who have gone through early surgical menopause):

    - Kyla Sorel
    - Sue Hopegood
    - Wendy Miller
- Clinician Partners (Clinicians from the women's menopause clinics who have expertise in women's health and menopause):
    - Dr. Tami Shandro, Primary care physician at the Lois Hole Hospital for Women (LLHW) and the Grey Nuns Community Hospital (GNCH) menopause clinics.
    - Shelly Hagen, registered dietician and health educator at GNCH menopause clinic
    - Lori Battochio, registered nurse and health educator at the LLHW menopause clinic
- Research team:
    - Dr. Nese Yuksel, Professor at the Faculty of Pharmacy and Pharmaceutical Sciences and clinical pharmacist and menopause practitioner at the LLHW menopause clinic
    - Dr. Sue Ross, Professor at the Faculty of Medicine, Department of Obstetrics and Gynecology and Cavarzan Chair in Mature Women's Health Research at the LLHW
    - Tasneem Siyam, registered clinical pharmacist and PhD candidate

The role of the research team was to draft the initial prototype. The role of patient and clinician stakeholders were to review the tool drafts and provide feedback to enhance content and format.

Both researchers and stakeholders were involved in the exploratory and evaluation phases. See appendix 7.1 and 7.2 for stakeholders' invitation letter.

7.2.2.3 Assessment of decisional needs (exploratory phase)

Data on decisional needs were gathered from the literature and five focus groups on women who had early surgical menopause. The purpose of the focus groups was to explore the process of decision-making on menopausal therapies and identify decision support needs related to early surgical menopause. Thirty-five women were recruited in five focus groups between June 30 to July 21 of 2016. Methods and findings are described elsewhere.[20] To get a broader sense of the decisional needs of women with early surgical menopause, a comprehensive literature search and narrative synthesis of relevant peer-reviewed literature was completed to identify factors influencing the uptake of and decision-making about HT in surgical menopause.

7.2.2.4 Drafting the PDA

Based on the identified decisional needs, expert's opinion and best practices for decision aid development,[25, 33-39] five domains were considered necessary for therapy decision-making in early surgical menopause: (1) Information on surgical menopause, HT, outcomes and resources for menopausal support; (2) HT outcome probabilities; (3) patient stories; (4) explicit values clarification; and (5) guidance in deliberation and decision-making. For the first three domains, we searched, screened and evaluated relevant literature to develop the content (Appendix 7.3). The fourth and fifth domains were informed by expert's opinion within our steering committee and previous decision aids in the field of menopause.[25] The format of the PDA was informed by the Ottawa Personal Decision Guide.[40] The guide has been found to improve decision-making in various clinical domains.[41] Based on initial feedback from the focus groups, the PDA was developed as a print booklet.

7.2.2.4.1 Development of content

Relevant guidelines were specifically targeted to gather information on surgical menopause, HT and evidence on risks and benefits.[42-44] For outcome probabilities, we searched for systematic reviews addressing the risks and benefits of HT in surgical/natural menopause. When no systematic reviews were identified, we looked for long term primary studies. Targeted outcomes were mostly determined a priori based on our prior knowledge in the field and included long term outcomes of surgical menopause, particularly CVD, osteoporosis, cognitive impairment, and early death. Also, we targeted long term risks associated with HT, notably risk of breast cancer, CVD, blood clots and strokes. The quality of life outcome was targeted based on feedback from the focus groups. The reporting of these outcome probabilities however, was conditional on the availability of risk measures from peer-reviewed evidence sources. Reported probabilities were evaluated independently by two reviewers (TS and SR) using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Appendix 7.4).[35] Discrepancies were resolved by consensus.

7.2.2.5 Review of the PDA with steering committee (evaluation phase)

The PDA was reviewed in an iterative process by members of the steering committee. First, the research team revised the content for clarity, coherency and relevance to end users. The revised tool was then edited by a professional editor to ensure content is written in plain language and at a grade 8 reading level. Second, the tool was evaluated by patient and clinician stakeholders of the steering committee in face-to-face semi-structured interviews (n=6) to capture views on clarity, comprehensibility, biasness, relevancy, length and amount of information, and usefulness of PDA. This review process represents phase 1 of alpha testing the PDA on expert clinicians

and patients. Feedback from the interviews and suggestion for improvement were used to revise the PDA and enhance content and format.

7.2.2.6 Acceptability testing (evaluation phase)

The revised PDA was evaluated in a mixed method study design for acceptability. This type of evaluation represents phase 2 of alpha testing on patients. Ethics approval was received by the University of Alberta Human Research Ethics Board.

7.2.2.6.1 Participants and recruitment

A convenience sample of women who participated in the focus groups and had indicated interest in taking part in similar future studies, were approached via phone or email for participation. The target sample size was 10 participants.[45]

7.2.2.6.2 Data collection

Women who consented to participate were asked to attend a one-on-one semi-structured interview to review the tool and provide views on acceptability. A week before the scheduled date of the interview, participants received an email with an invitation letter, consent form, a PDF version of the decision aid, and the acceptability questionnaire to allow time to review the tool and complete the questionnaire. During the interview, women were given the chance to review a hard copy of the booklet and complete a demographics questionnaire. Women were then asked to share their overall impression of the PDA, views on acceptability and strengths and any suggestions for improvement. Questions were open ended and responses were further explored using additional questions and probes. A guide was developed to provide consistency and direction for the conduct of the interview (Appendix 7.5). The interviews lasted about one hour. All interviews were digitally audio-recorded and transcribed verbatim. Audiotapes were

sent for verbatim transcription following each interview. The interviews were completed between May 31 and July 19, 2018.

7.2.2.6.3 Data collection tools

A 9-item questionnaire adapted from the Ottawa acceptability tool was used to elicit views on acceptability (Appendix 7.6).[46] The tool captures views on acceptability of each section of the tool rated on a scale of 0-4 as poor, fair, good, or excellent. Additionally, the tool assesses participants' views on the length of the presentation, amount of information, presence of bias, ease of interpretation of risk outcomes, and suitability for decision making. Demographic information on participants' age, race, education and employment was also captured.

7.2.2.6.4 Data Analysis

All quantitative analyses were performed on SPSS25 (SPSS Inc., Chicago, IL). Descriptive statistics were used to characterize the cohort and summarize data on acceptability. Qualitative data were analyzed using qualitative content analysis. Written transcripts were analyzed independently by two coders to identify common themes (Appendix 7.7 and 7.8). Consensus on overall themes was agreed on by the research team. Qualitative data were managed using Nvivo qualitative data analysis software package version12.

7.2.3 Assessing PDA quality against IPDAS checklist

To ensure conformity with internationally recognized standards for quality, the PDA was assessed against 46 IPDAS quality criteria for content and development that were applicable to the PDA.[47]

7.3 Results

7.3.1 Women's decisional needs

Women from the focus groups shared unique perceptions of inadequate support received before and during their menopausal experience. Perceptions such as lack of adequate information prior to the surgery (and after), lack of guidance and engagement in decision-making and lack of social support, were viewed as modifiable deterrents to effective decision-making.[20] To make an informed decision about treatments post-surgery, these women expressed a need to learn more about the symptoms of surgical menopause, treatment options, resources for support and stories of similar experiences, preferably before the surgery. Modifiable determinants of decision making identified from the narrative review were the lack of knowledge about surgical menopause and HT, use of experiential reasoning to weigh competing risks, and limited patient involvement in therapy decisions.

7.3.2 Components of the PDA

The developed and revised PDA had 4 main sections:

1. A "know the facts" section which presents information on: (a) surgical menopause, symptoms, emotional impact and long-term outcomes, (b) HT doses, formulations, duration of use, benefits, and harms along with associated outcome probabilities (c) other management strategies, (d) relative and absolute contraindications of HT, and (e) patient stories.
2. A "clarify your values" section in which common reasons for choosing HT versus the no HT option were elicited using a 6-point importance rating scale (0 to 5).
3. An "identify what else you need to make a decision" section where women are asked to complete two self-assessments to identify other barriers to decision-making. Self-

assessments include: (a) a 5-item knowledge test and, (b) a validated 4-item sure test for assessing decisional conflict.

4. A “plan the next step” section in which women are offered suggestions that can help them proceed with their chosen course of action

Information on surgical menopause and HT were mainly gathered from the Guideline of the European Society of Human Reproduction and Embryology on the management of women with premature ovarian insufficiency (ESHRE).[42] Other guidelines used were: NAMS,[43] SOGC,[48] NICE,[49]AACE,[50] ACOG,[51] EMAS,[52] and the Endocrine Society.[53]Since guidelines in the field of menopause are updated every three to five years, a 5-year update policy of the tool is endorsed to reflect updates.

Patient stories were captured from shared experiences from the focus groups with women’s consent.[20] The aid was mainly focused on the HT versus the no HT option as much of the uncertainty in decision-making is associated with HT. However, other management strategies were briefly discussed.

An important section of the aid was the section on outcome probabilities. To help women develop realistic expectations and make informed risk trade-offs we presented probabilities for outcomes decided a priori and for which quantitative risk measures were available. Outcomes included were CVD-related mortality, cognitive impairment and early death with and without HT. For these outcomes, probabilities were gathered from long term observational studies.[7, 8, 54, 55] HT outcomes discussed in the aid were for: breast cancer, cardiovascular disease, blood clots and strokes. Risk measures were gathered from systematic reviews.[56, 57] All presented outcome probabilities were represented numerically in absolute risks measures and graphically in

the form of woman pictograms and bar graphs. Uncertainty around probabilities were evaluated using GRADE and presented for each outcome as very low, low, moderate or high. No discrepancies were identified between the independent evaluations. For GRADE evidence tables of reported outcome probabilities see appendix 7.9, 7.10, 7.11, 7.12 and 7.13.

Guidance in deliberation and decision-making was emphasized in several ways in the aid. The PDA provides a step-wise approach that walks women through the decision-making process. The approach is explicitly listed in the beginning of the aid and women are encouraged to follow for guidance. The PDA provides women with ways to consult and engage with their HCPs for shared decision-making. Work sheets are provided to guide women with questions and concerns, and communicate their knowledge, values, unresolved decisional needs and next steps with others. Tracking forms, a unique feature of the PDA, helps women track their symptoms and consider treatment decisions progressively with time along with their HCPs.

7.3.3 Feedback from the steering committee

Overall, clinician and patient experts provided positive feedback about the tool, yet several suggestions for improvement were disclosed (Appendix 7.14). Suggested and implemented changes are summarized in appendix 7.15. Important additions were a figure discussing the risk of breast cancer with HT relative to other risk factors; a section on ways to maintain health and reduce risks associated with surgical menopause and HT; and tracking forms to help women track changes in their menopausal symptoms. A few modifications were implemented to the values clarification exercise.

7.3.4 Evaluation of PDA (alpha testing)

Twelve women were recruited for the evaluation phase (Figure 7.2). Characteristics of participants are included in Table 7.1.

7.3.4.1 Results of quantitative analysis

Table 7.2 and 7.3 summarizes responses from the acceptability questionnaire. Overall, most participants rated the acceptability of different sections of the PDA as good or excellent (83%). Less than 10% rated sections of the PDA as fair. The length of the tool and the amount of information were rated as just right (92% and 83% respectively) and women did not feel that the tool was biased (83%). Majority of participants would have found this decision aid useful when making their decision about HT (92%).

7.3.4.2 Results of qualitative analysis

Themes related to the value of the tool, context of use, dissemination and other expectations of support were identified when women were asked to share views on strengths of PDA and areas for improvement.

7.3.4.2.1 Strengths of PDA

Overall, women were positive about the tool and the information presented. Almost, all women thought the tool offered comprehensive and valuable information. Women used terms, such as "up-to-date", "evidence-based", "reliable", "relevant", "factual", "useful" and "concise" to express their appreciation for the content. Nearly, all participants thought the tool provided a balanced presentation of options.

> *"I think that it points out the pros and cons and gives you a summary without a judgment"* (interview 5)

There were features that women specifically liked about the tool and thought were most impactful, such as explicit values clarification, infographics for risk presentation and tracking forms.

"What adds value is the infographics and … because if nothing else that's … that portion is an easy read, right, you know, visuals" (Interview 3)

Women mutually believed that the layout of the tool was clear and consistent. They liked how it was broken down into steps. A few thought that putting it in steps may help users follow a logical thinking process and ease some of the stress and confusion typically associated with making decisions about HT.

> *"I think you need lots of information to be able to make an informed decision but it has to be organized and it has to – you have to find a way to go through it all and not have it confusing and this book does that, it helps you go through it without it being confusing"* (Interview 12)

Initially, many were overwhelmed by the number of pages of the booklet especially when presented as an electronic PDF, however almost all women indicated it was easy to read and navigate.

Most women preferred the print version of the booklet. They shared positive comments about its size, logo and colors. Nearly, all shared that the font size was appropriate. One woman specifically commented on the tool's reasonable reading level.

7.3.4.2.1.1 Value of the tool

In many instances, women explained that this tool would have been extremely helpful at the time of their surgeries, when they were actively looking for information and options to manage their symptoms.

Some felt that their access to care was fragmented and searching for valid information was a challenge. Others perceived the lack of reliable information about HT at the time they were searching for relevant information, as a contributing factor to hesitancy and fear of use. As such,

many women ascribed the usefulness of the tool to being an all-in-one resource presenting valid and credible information to help women make informed therapy decisions.

Some women appreciated the usefulness of the tool in targeting values and helping women make treatment choices relevant to those values. Some thought the tool was valuable as it helps woman organize their thoughts and discuss the decision with others who matter most to them. One woman viewed the tool as an opportunity to be more proactive and engaged in one's health care decisions. She described her view as follows:

> *"And it gives you the opportunity to decide yourself and we need to make - be a little more proactive in how we accept our own treatment I think"* (Interview 5)

7.3.4.2.1.2 Context of use and dissemination

Participants generally felt the tool would be most useful to women before undergoing BO surgery.

> *"If those doctors that specialize in this type of surgery, like the hysterectomies, if they had a resource like this to be able to provide to the patient before, you know, to help them make the decision, I think that would be fabulous"* (Interview 3)

As women shared strong beliefs about the value of the tool and the context in which the tool is regarded most useful, some were concerned that the tool may not be as useful if physicians lacked the knowledge and skills to support women using such tool in pursuit of a therapy decision.

In that context, some women voiced the need to educate physicians about the tool and involve them in distributing it to women in need of decision support.

> *"I hope more education gets out once this gets out there, because I find physicians too, that they're very still scared to prescribe" (Interview 10)*

Since prior to surgery was suggested by many of the participants as the ideal time to discuss options, a few women expressed the need to involve surgeons in future PDA dissemination plans.

7.3.4.2.2 Suggestion for improvement

Women shared varied thoughts about ways to help improve the PDA. Their comments were primarily for content, specifically for sections about symptoms of surgical menopause and HT.

7.3.4.2.2.1 Symptoms of surgical menopause

A few women indicated the need to elaborate more on mood changes and its physical, emotional, and social impact. To better capture the range and depth of the symptom as it impacts women's life, one woman suggested the following:

> *"So to me the – calling it mood changes seems to lessen the severity of what it could be. I would call it psychological challenges, so then you can say in there, 'could be depression, could be lack of connection or empathy or whatever'* (Interview 11)

More emphasis on long-term risks, such as cardiovascular disease and early death was expressed by some. A contrary thought however, mentioned that the tool should focus primarily on relaying the impact of symptoms affecting the quality of life, particularly among younger women, such as sexual function, brain function, and mood.

7.3.4.2.2.2 Hormone therapy

Several women suggested using the tool as an avenue to present more information about HT and clear some of the existing confusion. For example, a couple of woman suggested elaborating more on the general role of estrogen and progesterone so women can appreciate what it means to lack these hormones.

A couple of woman felt the need to educate women about standard doses of HT for surgical menopause and possibly how these doses compare to normal levels of hormones and doses of birth control pills.

> *"The other thing I wanted to talk about was dosages. You don't have any dosages of anything in here, like what compares of an oral dose to a patch to a – so that you have some idea of kind of where you should be"* (Interview 10)

A few women suggested adding more information about duration of therapy, and the potential benefits and risks of being on HT past age 50 years. Additionally, one woman proposed, toning the language down when discussing age recommendations for discontinuing HT, while emphasizing the importance of individualizing the decision to symptom burden and women's preference.

While all women understood that the tool was developed for helping women determine if HT was appropriate for managing their surgical menopause, a few advised on presenting women with other treatment options, especially in circumstances where HT is deemed inappropriate.

> *"It just lays out the facts but it's from a medical standpoint, right? So it's not going to talk about other - I guess it did mention in there that there are other options but it doesn't say what they are."* (Interview 6)

7.3.4.2.2.3 Other areas

Many women shared positive insights about patient stories and infographics, proposed suggestions for improving these areas were to present outcome-focused patient stories and include a common referent group across comparisons presented in the infographics.

7.3.4.2.3 Other expectations of support

Even though several women recognized the tool as a step in the right direction towards supporting women who go through early surgical menopause, some participants felt there is more that can be done to address surgical menopausal women support needs.

Women consistently spoke about the value of support groups for women who have experienced surgical menopause and the need for these women to interact and engage with women of similar concerns to normalize fear and improve coping.

> *"I just think that there needs to be support groups out there for ladies and to know that they are there for you to use"* (Interview 6)

7.3.5 Quality assessment against IPDAS criteria

Results of the quality assessment of the PDA are summarized in Table 7.4. Overall, 39 quality items were satisfied. The tool met all 22 "content" quality criteria. Out of the 24 "development" quality criteria evaluated, seven were not met. These were items pertaining to field testing and use of plain language. The tool is yet to be field tested with patient and practitioners who were not involved in the development phase (criteria 1.4, 1.5, 1.6/1.7, 9.3, and 10.6). Despite our efforts in editing the tool professionally for plain language, the SMOG readability score was 10, suggesting the PDA was written at a grade 10 reading level as opposed to the grade 8 level recommended by IPDAS (criterion 10.4). Revising the tool for readability is an important consideration as subsequent phases of development are strategized. Last, we did not implement multiple ways to help patients understand the information presented (criterion 10.5). However, this quality criterion will be considered as we plan for alternative methods for administering the PDA in practice including a web or smart phone application.

7.4 Discussion

This paper describes the systematic development and alpha testing of the SheEmpowers PDA, developed to offer decisional support for women with early surgical menopause as they make HT decisions. The PDA offers support in the form of providing information about HT and other options; clarifying values; and guiding deliberations about given options. Additionally, the PDA provides personal worksheets and tracking forms to help women when discussing treatment preferences with HCPs. Participants in the evaluation phase, perceived the tool as acceptable and offered useful suggestions for targeted modifications. The tool met 39 of the 46 IPDAS quality criteria for content and development. The development of the PDA is still pending field testing and effectiveness assessment.

Besides being evidence based, our tool had quality attributes that were lacking in PDAs for surgical menopause identified in the grey literature.[27, 28] Our PDA included an assessment of the decisional needs of the target population, as well provided outcome probabilities using up-to-date, quality-rated scientific evidence. Identifying the decisional needs of women helped establish core elements of the tool's content and presentation. Presentation of outcome probabilities and certainty assessments was equally important so the information provided causes no harm from decisional bias to end users.[33]

7.4.1 Implemented modifications

One change suggested to improve the PDA was the need to emphasize the impact of surgical menopause on mood, cognition and quality of life. Women with early surgical menopause can struggle significantly with menopausal symptoms related to mood and cognition.[20] As well, quality of life can be greatly compromised. These women primarily consider such factors as they make treatment decisions.[20] Due to the potential role these outcomes can play in driving

women treatment decisions, describing them in ways that help women imagine their impact and clarify associated values is vital for informed decision-making. [38] These outcomes were revisited and further modification were made to aspects of surgical menopause pertaining to mood, cognition and quality of life.

Participants recommended more information on HT in the PDA, including roles of estrogen and progesterone, and duration of HT use. The PDA was updated with this information. Another concern expressed was the lack of consistency among the referent group in the infographics on long term risk. As the referents were women who kept their ovaries and used or did not use HT, to reduce this confusion, the PDA was revised to include a common referent group for comparisons, namely women who kept their ovaries and did not use HT.

7.4.2 Challenge of incorporating other suggestions

Other proposed suggestions that were more challenging to incorporate in the aid included adding information on non-hormonal treatment alternatives and HT dosing, as well as revising patient stories. HT is the most effective option for early surgical menopause. While non-hormonal alternatives have some evidence for improving vasomotor symptoms, these agents are not as effective as estrogen therapy.[58] therefore we decided to focus the PDA on HT decision making. Another reason for choosing to focus on HT is because in this decision context, the complexity in decision-making is associated with HT as opposed to other treatment alternatives. PDAs are valuable in complex, value-sensitive therapy decisions.[59] The request for expanding content to include alternatives to HT is understandable, particularly for women who cannot use HT. However, broadening the focus of the aid will also increase the length of the PDA considerably which may challenge the feasibility of the aid among end users. A more appropriate approach would be to discuss non-hormonal alternatives as a separate supplement or refer end

users to an available resource that can provide more information about non-hormonal alternatives. This is currently being considered by our research team.

A couple of participants suggested including experiences of women post treatment decisions. However, due to the potential influence that outcome-based stories may have on patient's decisions we were unable to accommodate this suggestion.[59] "Patient stories" was an important domain of the SheEmpowers PDA as several focus groups' participants shared a need to learn about how other women approached treatment decisions.[20] In presenting these stories, we were keen to highlight the process that women followed to make therapy decision as a strategy for decision support rather than highlighting the decision that was made. We also were cognizant about including a spectrum of decision-making experiences to avoid potential biases to women decisions.

A few women from the interviews indicated the need to include specific recommendations on HT dosing for women who have had a surgical menopause. However, this would be challenging to include in the PDA as HT doses are often individualized to the patient.

7.4.3 Strengths and limitations

In the development of the SheEmpowers PDA we followed a systematic development model driven by a multidisciplinary group of researchers, clinicians and patient experts. The decisional needs of the target population were gathered from focus groups and a literature review. A spectrum of experiences and decision support needs were identified and were used to draft the initial prototype. The evaluation phase helped us in revising the tool further. However, there are limitations to note. First, we were unable to include certain health outcomes with the use of HT in surgical menopause, such as quality of life as there was a lack of quality studies capturing this data. For some outcomes, probabilities were gathered from high quality studies in natural

menopause and the quality of evidence was downgraded for indirectness. Second, women participating in the evaluation phase were all white, mostly on HT and recruited from two menopause clinics in Edmonton. Their views on the tool may have been affected by their preconceived notions regarding HT prior to assessing the PDA and may not represent other women of different demographics and treatment experiences. Yet, these women offered valuable feedback and suggestions for improvement which could have only stemmed from their own experiences. In addition, clinicians' feedback from our steering committee, may have captured the needs of women with early surgical menopause not represented in our sample. Furthermore, our understanding of women experiences with surgical menopause and HT as well as their opinions about the PDA might have also been affected by our unconscious bias pertinent to social cognitions, such as attitudes and stereotypes we subconsciously harbor that unintentionally affect our interpretations and understandings of study participants and their relevant experiences. The readability score of the PDA suggests that it is written at a level that is slightly higher than the guideline recommendations (grade 8 level or less). Health literacy is an important domain however it is rarely addressed in the PDA literature.[58] Evidence has shown that only 5% of PDAs report reading level as grade 8 or below.[60] As well, patient educational materials are usually written above the 8th grade level.[61] Despite the positive feedback received from the interviews regarding the readability of the PDA, these views may not represent women who are well-educated, as our participants had completed at least their 12th grade education. Revising the tool to a reading level that allows a wide range of women to use the PDA effectively is an important consideration for the following phases of development and evaluation. Last, the PDA mainly addresses modifiable decision support needs, particular to patients, barriers related to

clinicians and health care system were beyond the initial phase of development but will be considered as we move forward with implementation and dissemination.

7.5 Conclusion

We adopted a systematic, evidence-based approach to develop the SheEmpowers PDA. The PDA intended to guide and support women in making HT decisions about managing early surgical menopause, had promising views on acceptability. By reinforcing a sense of control over menopausal health and engagement in therapy decisions, the PDA precisely aims to help women overcome deterrents to decision-making related to lack of knowledge, decision-making skills and involvement in therapy decisions, for an ultimate goal of attaining infomred and value-based decisions. The effectiveness of the tool in terms of achieving those outcomes is yet to be assessed.

7.6 Practice implications

Data from alpha testing showed good acceptability views of the SheEmpowers PDA among patients and clinicians. The next evaluation phase encompasses testing the acceptability and feasibility of the tool on a sample of women and clinicians who were not involved in earlier phases of development under real life setting. This phase represents the beta testing phase of the PDA. Feedback from this phase will guide further revisions of the tool as well as the design of a trial to assess the PDA's effectiveness in improving the "quality of decision" and "decision-making process".

7.7 References

[1] M.S. Hunter, Long-term impacts of early and surgical menopause, Menopause 19(3) (2012) 253-4.

[2] B. Thompson, S.A. Hart, D. Durno, Menopausal age and symptomatology in a general practice, J Biosoc Sci 5(1) (1973) 71-82.

[3] A. Benshushan, N. Rojansky, M. Chaviv, S. Arbel-Alon, A. Benmeir, T. Imbar, A. Brzezinski, Climacteric symptoms in women undergoing risk-reducing bilateral salpingo-oophorectomy, Climacteric 12(5) (2009) 404-9.

[4] H.H. Riedel, E. Lehmann-Willenbrock, K. Semm, Ovarian failure phenomena after hysterectomy, J Reprod Med 31(7) (1986) 597-600.

[5] A. Finch, G. Evans, S.A. Narod, BRCA carriers, prophylactic salpingo-oophorectomy and menopause: clinical management considerations and recommendations, Womens Health (Lond Engl) 8(5) (2012) 543-55.

[6] G.A. Colditz, W.C. Willett, M.J. Stampfer, B. Rosner, F.E. Speizer, C.H. Hennekens, Menopause and the risk of coronary heart disease in women, N Engl J Med 316(18) (1987) 1105-10.

[7] W.A. Rocca, J.H. Bower, D.M. Maraganore, J.E. Ahlskog, B.R. Grossardt, M. de Andrade, L.J. Melton, 3rd, Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause, Neurology 69(11) (2007) 1074-83.

[8] W.A. Rocca, B.R. Grossardt, M. de Andrade, G.D. Malkasian, L.J. Melton, 3rd, Survival patterns after oophorectomy in premenopausal women: a population-based cohort study, Lancet Oncol 7(10) (2006) 821-8.

[9] R. Reid, B.L. Abramson, J. Blake, S. Desindes, S. Dodin, S. Johnston, T. Rowe, N. Sodhi, P. Wilks, W. Wolfman, M. Fortier, L. Graves, B. Guthrie, A. Khan, Managing menopause, J Obstet Gynaecol Can 36(9) (2014) 830-8.

[10] T.J. de Villiers, M.L. Gass, C.J. Haines, J.E. Hall, R.A. Lobo, D.D. Pierroz, M. Rees, Global Consensus Statement on menopausal hormone therapy, Maturitas 74(4) (2013) 391-2.

[11] A. Chubaty, M.T. Shandro, N. Schuurmans, N. Yuksel, Practice patterns with hormone therapy after surgical menopause, Maturitas 69(1) (2011) 69-73.

[12] R.J. Chen, T.C. Chang, S.N. Chow, Perceptions of and attitudes toward estrogen therapy among surgically menopausal women in Taiwan, Menopause 15(3) (2008) 517-23.

[13] L. Lindh-Astrand, M. Hoffmann, L. Jarvstrat, M. Fredriksson, M. Hammar, A.C. Spetz Holm, Hormone therapy might be underutilized in women with early menopause, Hum Reprod 30(4) (2015) 848-52.

[14] F. Chew, X. Wu, Sources of information influencing the state-of-the-science gap in hormone replacement therapy usage, PLoS One 12(2) (2017) e0171189.

[15] J.S. Carpenter, M.M. Byrne, J.L. Studts, Factors related to menopausal symptom management decisions, Maturitas 70(1) (2011) 10-5.

[16] M.A. Gerend, L.S. Aiken, M.J. Erchull, A. Lapin, Women's use of hormone therapy before and after the Women's Health Initiative: a psychosocial model of stability and change, Prev Med 43(3) (2006) 158-64.

[17] A.M. O'Connor, M.J. Jacobsen, D. Stacey, An evidence-based approach to managing women's decisional conflict, J Obstet Gynecol Neonatal Nurs 31(5) (2002) 570-81.

[18] S.L. Hendrix, Bilateral oophorectomy and premature menopause, Am J Med 118 Suppl 12B (2005) 131-5.

[19] T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause 25(7) (2018) 795-802.

[20] R.H. Kenen, P.J. Shapiro, S. Friedman, J.C. Coyne, Peer-support in coping with medical uncertainty: discussion of oophorectomy and hormone replacement therapy on a web-based message board, Psychooncology 16(8) (2007) 763-71.

[21] D. Kuh, R. Hardy, M. Wadsworth, Social and behavioural influences on the uptake of hormone replacement therapy among younger women, BJOG 107(6) (2000) 731-9.

[22] International Patient Decision Aid Standards (IPDAS) Collaboration. What are patient decision aids?, 2003. http://www.ipdas.ohri.ca/what.html. (Accessed August 26, 2016.

[23] D. Stacey, F. Legare, K. Lewis, M.J. Barry, C.L. Bennett, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev 4 (2017) CD001431.

[24] T. Siyam, H. Sultani, S. Ross, T. Chatterley, N. Yuksel, Evaluating the content and development of decision aid tools for the management of menopause: A scoping review, Maturitas 106 (2017) 80-86.

[25] J.S. Carpenter, J.L. Studts, M.M. Byrne, A systematic review of menopausal symptom management decision aid trials, Maturitas 69(1) (2011) 11-21.

[26] J.E. Manson, J.M. Ames, M. Shapiro, M.L. Gass, J.L. Shifren, C.A. Stuenkel, J.V. Pinkerton, A.M. Kaunitz, D.T. Pace, R. Kagan, P.F. Schnatz, S.A. Kingsberg, J.H. Liu, H. Joffe, G. Richard-Davis, S.R. Goldstein, I. Schiff, W.H. Utian, Algorithm and mobile app for menopausal symptom management and hormonal/non-hormonal therapy decision making: a clinical decision-support tool from The North American Menopause Society, Menopause 22(3) (2015) 247-53.

[27] V. Teplin, E. Vittinghoff, F. Lin, L.A. Learman, H.E. Richter, M. Kuppermann, Oophorectomy in premenopausal women: health-related quality of life and sexual functioning, Obstet Gynecol 109(2 Pt 1) (2007) 347-54.

[28] A.M. O'Connor, P. Tugwell, G.A. Wells, T. Elmslie, E. Jolly, G. Hollingworth, R. McPherson, H. Bunn, I. Graham, E. Drake, A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation, Patient Educ Couns 33(3) (1998) 267-79.

[29] A.M. O'Connor, E.R. Drake, V. Fiset, I.D. Graham, A. Laupacis, P. Tugwell, The Ottawa patient decision aids, Eff Clin Pract 2(4) (1999) 163-70.

[30] A. Coulter, D. Stilwell, J. Kryworuchko, P.D. Mullen, C.J. Ng, T. van der Weijden, A systematic development process for patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S2.

[31] G. Elwyn, A. O'Connor, D. Stacey, R. Volk, A. Edwards, A. Coulter, R. Thomson, A. Barratt, M. Barry, S. Bernstein, P. Butow, A. Clarke, V. Entwistle, D. Feldman-Stewart, M. Holmes-Rovner, H. Llewellyn-Thomas, N. Moumjid, A. Mulley, C. Ruland, K. Sepucha, A. Sykes, T. Whelan, Developing a quality criteria framework for patient decision aids: online international Delphi consensus process, Bmj 333(7565) (2006) 417.

[32] N. Joseph-Williams, R. Newcombe, M. Politi, M.A. Durand, S. Sivell, D. Stacey, A. O'Connor, R.J. Volk, A. Edwards, C. Bennett, M. Pignone, R. Thomson, G. Elwyn, Toward Minimum Standards for Certifying Patient Decision Aids: A Modified Delphi Consensus Process, Med Decis Making 34(6) (2014) 699-710.

[33] D. Feldman-Stewart, M.A. O'Brien, M.L. Clayman, B.J. Davison, M. Jimbo, M. Labrecque, R.W. Martin, H. Shepherd, Providing information about options in patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S4.

[34] V.M. Montori, A. LeBlanc, A. Buchholz, D.L. Stilwell, A. Tsapas, Basing information on comprehensive, critically appraised, and up-to-date syntheses of the scientific evidence: a quality dimension of the International Patient Decision Aid Standards, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S5.

[35] L.J. Trevena, B.J. Zikmund-Fisher, A. Edwards, W. Gaissmaier, M. Galesic, P.K. Han, J. King, M.L. Lawson, S.K. Linder, I. Lipkus, E. Ozanne, E. Peters, D. Timmermans, S. Woloshin, Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers, BMC medical informatics and decision making 13 Suppl 2 (2013) S7.

[36] H.O. Witteman, L.D. Scherer, T. Gavaruzzi, A.H. Pieterse, A. Fuhrel-Forbis, S. Chipenda Dansokho, N. Exe, V.C. Kahn, D. Feldman-Stewart, N.F. Col, A.F. Turgeon, A. Fagerlin, Design Features of Explicit Values Clarification Methods: A Systematic Review, Med Decis Making 36(4) (2016) 453-71.

[37] A. Fagerlin, M. Pignone, P. Abhyankar, N. Col, D. Feldman-Stewart, T. Gavaruzzi, J. Kryworuchko, C.A. Levin, A.H. Pieterse, V. Reyna, A. Stiggelbout, L.D. Scherer, C. Wills, H.O. Witteman, Clarifying values: an updated review, BMC medical informatics and decision making 13 Suppl 2 (2013) S8.

[38] D. Stacey, J. Kryworuchko, J. Belkora, B.J. Davison, M.A. Durand, K.B. Eden, A.S. Hoffman, M. Koerner, F. Legare, M.C. Loiselle, R.L. Street, Jr., Coaching and guidance with

patient decision aids: A review of theoretical and empirical evidence, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S11.

[39] D.Stacey, A O'Connor, Ottawa Personal Decision Guide, 2000. https://decisionaid.ohri.ca/docs/das/OPDG.pdf.

[40] A.M. O'Connor, D. Stacey, V. Entwistle, H. Llewellyn-Thomas, D. Rovner, M. Holmes-Rovner, V. Tait, J. Tetroe, V. Fiset, M. Barry, J. Jones, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev (2) (2003) CD001431.

[41] L. Webber, M. Davies, R. Anderson, J. Bartlett, D. Braat, B. Cartwright, R. Cifkova, S. de Muinck Keizer-Schrama, E. Hogervorst, F. Janse, L. Liao, V. Vlaisavljevic, C. Zillikens, N. Vermeulen, ESHRE Guideline: management of women with premature ovarian insufficiency, Hum Reprod 31(5) (2016) 926-37.

[42] The 2017 hormone therapy position statement of The North American Menopause Society, Menopause 24(7) (2017) 728-753.

[43] G. Sarri, M. Davies, M.A. Lumsden, Diagnosis and management of menopause: summary of NICE guidance, BMJ 351 (2015) h5746.

[44] L. Faulkner, Beyond the five-user assumption: benefits of increased sample sizes in usability testing, Behav Res Methods Instrum Comput 35(3) (2003) 379-83.

[45] A. Cranney, O'Connor AM, Ottawa acceptability questionnaire, 2000. http://decisionaid.ohri.ca/eval_accept.html. (Accessed May 31, 2018.

[46] 2006 International Patient Decision Aid Standards (IPDAS) Checklist for Judging the Quality of Patient Decision Aids, 2006.

[47] R. Reid, B.L. Abramson, J. Blake, S. Desindes, S. Dodin, S. Johnston, T. Rowe, N. Sodhi, P. Wilks, W. Wolfman, Managing menopause, Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 36(9) (2014) 830-833.

[48] M.A. Lumsden, The NICE Guideline - Menopause: diagnosis and management, Climacteric : the journal of the International Menopause Society 19(5) (2016) 426-9.

[49] N.F. Goodman, R.H. Cobin, S.B. Ginzburg, I.A. Katz, D.E. Woode, American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of menopause: executive summary of recommendations, Endocr Pract 17(6) (2011) 949-54.

[50] ACOG Practice Bulletin No. 141: management of menopausal symptoms, Obstetrics and gynecology 123(1) (2014) 202-16.

[51] M.H. Moen, M. Rees, M. Brincat, T. Erel, M. Gambacciani, I. Lambrinoudaki, K. Schenck-Gustafsson, F. Tremollieres, S. Vujovic, S. Rozenberg, EMAS position statement: Managing the menopause in women with a past history of endometriosis, Maturitas 67(1) (2010) 94-7.

[52] C.A. Stuenkel, S.R. Davis, A. Gompel, M.A. Lumsden, M.H. Murad, J.V. Pinkerton, R.J. Santen, Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline, J Clin Endocrinol Metab 100(11) (2015) 3975-4011.

[53] W.H. Parker, D. Feskanich, M.S. Broder, E. Chang, D. Shoupe, C.M. Farquhar, J.S. Berek, J.E. Manson, Long-term mortality associated with oophorectomy compared with ovarian conservation in the nurses' health study, Obstet Gynecol 121(4) (2013) 709-16.

[54] C.M. Rivera, B.R. Grossardt, D.J. Rhodes, R.D. Brown, Jr., V.L. Roger, L.J. Melton, 3rd, W.A. Rocca, Increased cardiovascular mortality after early bilateral oophorectomy, Menopause 16(1) (2009) 15-23.

[55] H.M. Boardman, L. Hartley, A. Eisinga, C. Main, M. Roque i Figuls, X. Bonfill Cosp, R. Gabriel Sanchez, B. Knight, Hormone therapy for preventing cardiovascular disease in post-menopausal women, The Cochrane database of systematic reviews (3) (2015) CD002229.

[56] J. Marjoribanks, C. Farquhar, H. Roberts, A. Lethaby, J. Lee, Long-term hormone therapy for perimenopausal and postmenopausal women, The Cochrane database of systematic reviews 1 (2017) CD004143.

[57] Nonhormonal management of menopause-associated vasomotor symptoms: 2015 position statement of The North American Menopause Society, Menopause 22(11) (2015) 1155-72; quiz 1173-4.

[58] M.J. Barry, Shared decision making: informing and involving patients to do the right thing in health care, J Ambul Care Manage 35(2) (2012) 90-8.

[59] V.A. Shaffer, B.J. Zikmund-Fisher, All stories are not alike: a purpose-, content-, and valence-based taxonomy of patient narratives in decision aids, Med Decis Making 33(1) (2013) 4-13.

[60] K.J. McCaffery, M. Holmes-Rovner, S.K. Smith, D. Rovner, D. Nutbeam, M.L. Clayman, K. Kelly-Blake, M.S. Wolf, S.L. Sheridan, Addressing health literacy in patient decision aids, BMC medical informatics and decision making 13 Suppl 2 (2013) S10.

[61] L.M. Stossel, N. Segar, P. Gliatto, R. Fallar, R. Karani, Readability of patient education materials available at the point of care, J Gen Intern Med 27(9) (2012) 1165-70.

Figure 7.1. Flow Chart of the Development model of the SheEmpowers PDA

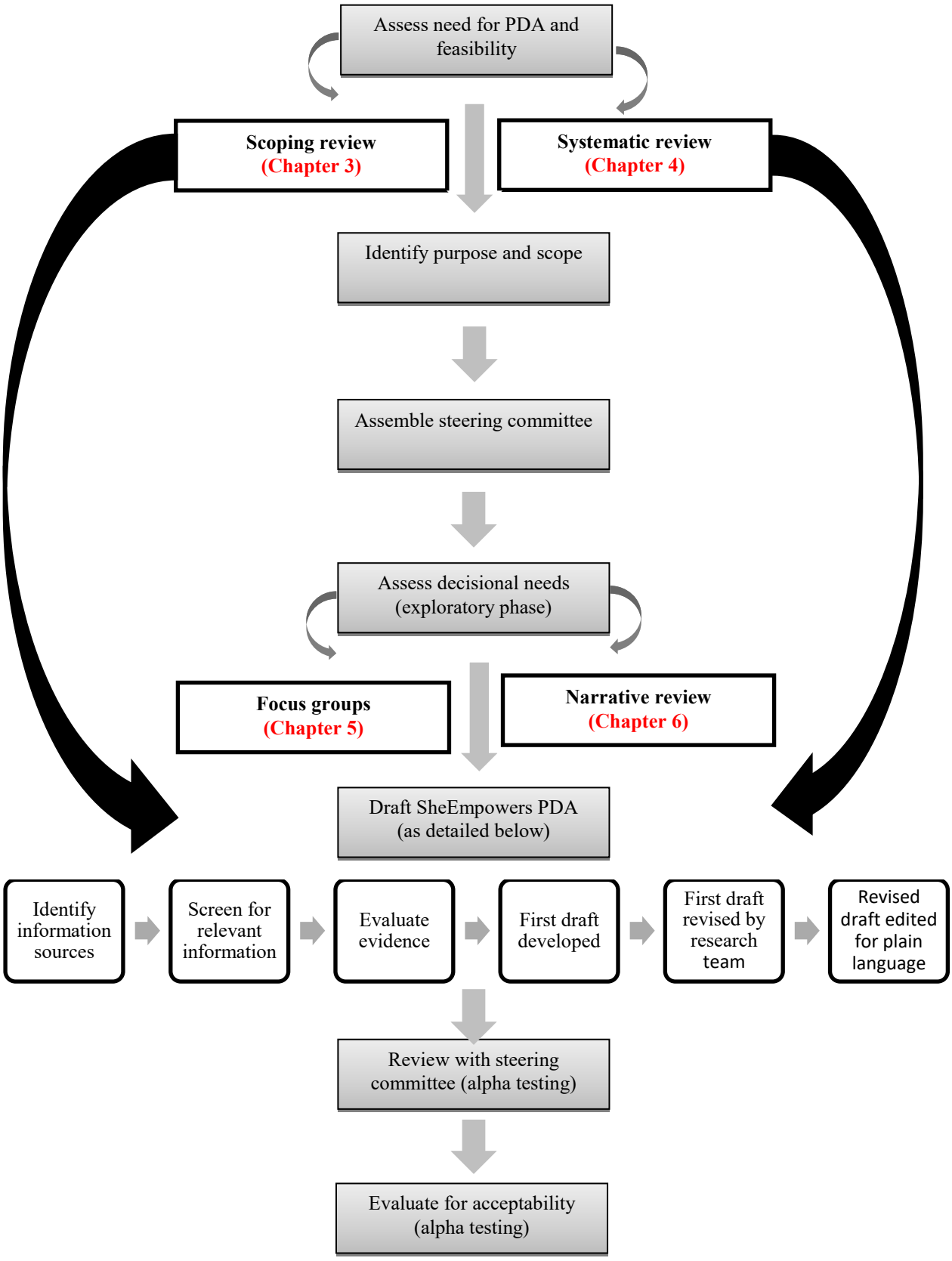


Figure 7.2. Flow chart of patients' recruitment

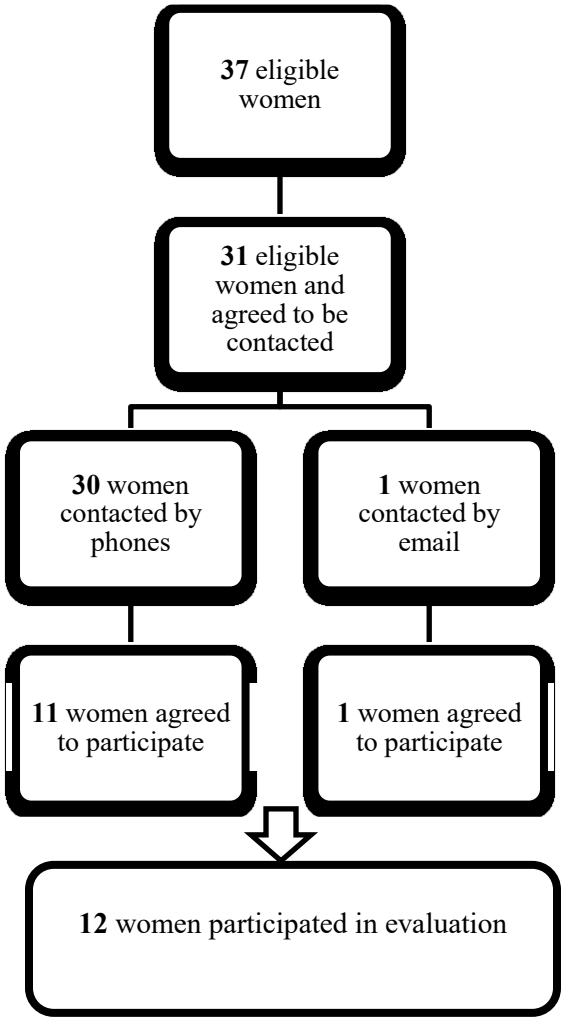


Table 7.1. Participants characteristics

Characteristic	**N(%)** **(N = 12)**
Race	
White	12(100%)
Age	
40-49 years	6(50%)
50-59 years	3(25%)
60 years over	3(25%)
Highest degree completed	
Completion of grade 12	4(33.3%)
Non-university degree	6(50%)
University (undergraduate degree)	2(16.7%)
Current employment	
Yes	10(83.3%)
No	2(16.7%)
Employment status	
Working full-time	9(75%)
On-leave but still employed	1(8.3%)
Retired	1(8.3%)
Other	1(8.3%)

Table 7.2. Views on acceptability of sections of the PDA

Section (N = 12)	**Poor N(%)**	**Fair N(%)**	**Good N(%)**	**Excellent N(%)**
Definition of early surgical menopause	-	-	4(33.3%)	8(66.7%)
Symptoms of early surgical menopause	-	1(8.3%)	4(33.3%)	7(58.3%)
Long-term effects of early surgical menopause	-	1(8.3%)	4(33.3%)	7(58.3%)
Emotional impact of early surgical menopause	-	-	4(33.3%)	8(66.7%)
Hormone therapy	2(16.7%)	-	7(58.3%)	3(25%)
Benefits of hormone therapy	-	-	6(50%)	6(50%)
Risk of developing long-term risks of early surgical	-	1(8.3%)	5(41.7%)	6(50%)
Risks of Hormone Therapy	-	-	3(25%)	9(75%)
Risk information on hormone therapy	-	-	2(16.7%)	10(83.3%)
Risk factors of breast cancer	-	-	3(25%)	9(75%)
Steps to maintain health and reduce risks	-	1(8.3%)	5(41.7%)	6(50%)
Other factors to consider when deciding on a therapy	-	1(8.3%)	6(50%)	5(41.7%)
Stories about others	-	1(8.3%)	8(66.7%)	3(25%)
Values clarification	-	2(16.7%)	1(8.3%)	9(75%)
Identify what else you need to make a decision	-	1(8.3%)	5(41.7%)	6(50%)
Plan the next steps	-	1(8.3%)	3(25%)	8(66.7%)
Tracking form	-	-	2(16.7%)	10(83.3%)
Available resources	-	-	6(50%)	6(50%)

Table 7.3. Acceptability views on other aspects of the PDA

Other aspect	**N(%)** **(N = 12)**
The length of the presentation was:	
Just right	11(91.7%)
Too short	-
Just long	1(8.3%)
The amount of information was:	
Just right	10(83.3%)
Too little	2(16.7%)
Too much	-
I found the presentation:	
Balanced	10(83.3%)
Slanted towards other option(s)	1(8.3%)
Slanted towards HT	1(8.3%)
Would you have found this decision aid useful when you are making decision about HT?	
Yes	11(91.7%)
No	1(8.3%)
What did you think of the infographics that show risks of early surgical menopause with and without HT?	
Easy to understand and interpret	10(83.3%)
Difficult to understand and interpret	2(16.7%)
What did you think of the infographics that show risks of hormone therapy?	
Easy to understand and interpret	10(83.3%)
Difficult to understand and interpret	2(16.7%)

What did you think of the rest of the sections in the decision aid?	
Easy to understand	12(100%)
Difficult to understand	-
Do you think we included enough information to help women decide on HT for managing symptoms and long-term risks of early surgical menopause?	
Yes	9(75%)
No	3(25%)

Table 7.4. Evaluation of content and development of the SheEmpowers PDA against the IPDAS quality framework

Content Quality Criterion	Criterion number	Met
Provide Information about options in sufficient detail for decision making		
▪ Describes the condition	2.1	☑
▪ Lists the treatment options	2.2	☑
▪ Lists the option of doing nothing	2.3	☑
▪ Describes the natural course without options	2.4	☑
▪ Describes procedures	2.5	☑
▪ Describe positive features	2.6	☑
▪ Describe negative features	2.7	☑
▪ Include chances of positive & negative outcomes	2.8	☑
Present possibilities of outcomes in an unbiased & understandable way		
▪ Use event rates specifying the population & time period	3.1	☑
▪ Compare outcome probability using the same denominator & time period	3.2, 3.3, 3.6	☑
▪ Describe uncertainty around probabilities	3.4	☑
▪ Use visual diagrams	3.5	☑
▪ Use multiple methods to view probabilities	3.7	☑
▪ Allow a patient to view probabilities based on their own situation	3.9	☑
▪ Place probabilities in context of other events	3.10	☑
▪ Use both positive and negative frames	3.13	☑
Include methods for clarifying & expressing values		
▪ Describe the procedures & outcomes to help patients imagine what it is like to experience their physical, emotional & social effects	4.1	☑

▪ Ask patient to consider which positive or negative features matter most	4.2	☑
▪ Suggest ways for patients to share what matters most with others	4.3	☑
Include structured guidance in deliberation & communication		
▪ Provide steps to make a decision (explicitly states decision making process)	6.1	☑
▪ Suggest ways to talk about the decision with a health professional	6.2	☑
▪ Include tools [worksheet, question list] to discuss options with others	6.3	☑
Development Quality Criterion	**Criterion number**	**Met**
Present information in a balanced manner		
▪ Able to compare positive or negative features of options	9.1	☑
▪ Shows negative/positive features with equal detail [fonts, order, display of statistics]	9.2	☑
Have a systematic development process		
▪ Include developers' credentials or qualifications	1.1	☑
▪ Finds out what users need to discuss options (assessment of decisional needs)	1.2, 1.3	☑
▪ Peer reviewed by patients and experts in the field	1.8a, 1.8b	☑
▪ Field tested with patients facing decisions	1.4	☒
▪ Field tested with practitioners presenting options	1.5	☒
▪ The field test with users show the patient decision aid is acceptable	1.6, 1.7	☒
▪ The field test with users show the patient decision aid is balanced	9.3	☒
▪ The field test with users show the patient decision aid is understood by those with limited reading skills	10.6	☒

Use up to date scientific evidence that is cited in a reference section or technical document		
▪ Provides references to evidence used	11.1	☑
▪ Report steps to find, appraise, summarize evidence	11.2	☑
▪ Report date of last update	11.3	☑
▪ Report how often patient decision aid is updated	11.4	☑
▪ Describe the quality of scientific evidence	11.5a, 11.5b	☑
▪ Uses evidence from studies of patients similar to those of target audience	11.6	☑
Disclose conflicts of interest		
▪ Reports source of funding to develop and distribute the patient decision aid	7.1, 7.2	☑
▪ Report whether authors of decision aid stand to gain or lose by choices made by patients using decision aid tool	7.3, 7.4	☑
Use plain language		
▪ Written at a level that can be understood by majority of patients	10.3	☑
▪ Written at grade 8 equivalent or less according to readability score	10.4	☒
▪ Provide ways to help patients understand information other than reading (audio, video, in-person discussion)	10.5	☒
Meets additional criterial if stories are used in the patient decision aid		
▪ Use stories that represent a range of positive and negative experiences	5.2	☑
▪ Reports if there was a financial or other reason why patients decided to share their story	7.5	☑
▪ State in an accessible document that the patient gave informed consent to use their stories	5.5	☑

Appendix 7.1. Clinician stakeholders' invitation letter

UNIVERSITY OF ALBERTA
FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES
3-171 Edmonton Clinic Health Academy
11405 – 87 Ave
Edmonton, Alberta, Canada T6G 1C9
Tel: 780.492.3362
Fax: 780.492.1217
www.pharmacy.ualberta.ca

Developing and evaluating a patient decision aid for managing surgical menopause

Background:

- Women who have their ovaries removed before menopause (also called surgical menopause) may suffer from menopausal symptoms that occur soon after the surgery. These women usually have a hard time making menopausal treatment decisions because of the controversy surrounding menopausal treatments (e.g. hormone therapy). Patient decision aids (PDAs) are powerful tools to help guide women when making a complex treatment decision.
- We recently developed the "**SheEmpowers**" PDA to help women who have surgical menopause make informed and value-based treatment decisions. Currently, we are looking at revising the PDA by a group of women and clinicians who have experience with surgical menopause.
- Engaging women with surgical menopause and their clinicians in the revision process is paramount because it will help us develop a PDA that is relevant to this women population and that focuses on their decision-support needs.

Invitation:

- On behalf of our project team, we would like to invite you to participate as a clinician partner on a steering committee for a project that aims to revise and evaluate the "**SheEmpowers**" PDA. Revising and evaluating the "**SheEmpowers**" PDA will be guided by a steering committee consisting of researchers, clinicians and patients' partners.

Clinicians' requirements, time commitments, expectations and roles:

- The role of clinicians will involve reviewing the PDA and providing feedback and views on how to improve the tool to prioritize the needs of women who have had surgical menopause.
- Clinicians are committed to participate in **one** face-to-face meeting with a research team member between **Apr 25 to May 18, 2018.**
- We require Clinicians to have access to the Internet and have an active email address to be able to receive a soft copy of the SheEmpowers PDA for reviewing.
- We will reimburse you for out-of-pocket expenses related to the committee's meetings (i.e., parking, travel to in-person meetings, etc.).
- To compensate you for your time, effort and valuable feedback we will provide you with a $20 gift card and a thank you card.
- Any private information you bring to the meeting will be kept secure, and if you no longer wish to participate on the Steering committee you are free to withdraw at any time.
- If you are interested to learn more about or take part in future knowledge translation activities relevant to our project, the project team will be more than happy to notify you regularly about knowledge translation updates and opportunities for participation.

Research team member(s) contact information:

- If you are interested in participating and want to learn more about this project please contact Tasneem Siyam at tsiyam@ualberta.ca or at (780)240-5933.

Appendix 7.2. Patient stakeholders' invitation letter

UNIVERSITY OF ALBERTA
FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES
3-171 Edmonton Clinic Health Academy
11405 – 87 Ave
Edmonton, Alberta, Canada T6G 1C9
Tel: 780.492.3362
Fax: 780.492.1217
www.pharmacy.ualberta.ca

Developing and evaluating a patient decision aid for managing surgical menopause

Background:

- Women who have their ovaries removed before menopause (also called surgical menopause) may suffer from menopausal symptoms that occur soon after the surgery. These women usually have a hard time making menopausal treatment decisions because of the controversy surrounding menopausal treatments (e.g. hormone therapy). Patient decision aids (PDAs) are powerful tools to help guide women when making a complex treatment decision.
- We recently developed the "**SheEmpowers**" PDA to help women who have surgical menopause make informed and value-based treatment decisions. Currently, we are looking at revising the PDA by a group of women and clinicians who have experience with surgical menopause.
- Engaging women with surgical menopause in the revision process is paramount because it will help us develop a PDA that is relevant to this women population and that focuses on their decision-support needs.

Invitation:

- On behalf of our project team, we would like to invite you to participate as a patient partner on a steering committee for a project that aims to revise and evaluate the "**SheEmpowers**" PDA. Revising and evaluating the "**SheEmpowers**" PDA will be guided by a steering committee consisting of researchers, clinicians and patients' representatives.

Patient requirements, time commitments, expectations and roles:

- We are looking for women who have had a surgical menopause (removed ovaries before age 45 years) and were involved in decision-making about menopausal treatments. Caregivers and family members of women with surgical menopause are also welcome to participate. NO prior research experience is required.
- The role of patients will involve reviewing the PDA and providing feedback and views on how to improve the tool to prioritize the needs of women who have had surgical menopause.
- Patients are committed to participate in **one** face-to-face meeting with a research team member between **Apr 25 to May 18, 2018.**
- We require patients to have access to the Internet and have an active email address to be able to receive a soft copy of the SheEmpowers PDA for reviewing.
- We will reimburse you for out-of-pocket expenses related to the committee's meetings (i.e., parking, travel to in-person meetings, etc.).
- To compensate you for your time, effort and valuable feedback we will provide you with a $20 gift card and a thank you card.
- Any private information you bring to the discussion table will be kept secure, and if you no longer wish to participate on the Steering committee you are free to withdraw at any time.
- If you are interested to learn more about or take part in future knowledge translation activities relevant to our project, the project team will be more than happy to notify you regularly about knowledge translation updates and opportunities for participation.

Research team member(s) contact information:

- If you are interested in participating and want to learn more about this project please contact Tasneem Siyam at tsiyam@ualberta.ca or at (780)240-5933.

Appendix 7.3. The methods followed to identify, screen and evaluate scientific evidence informing the content of the SheEmpowers PDA

Information sources

We searched Medline, TRIP, Dynamed plus and the Cochrane database of systematic reviews for clinical practice guidelines discussing the topic of surgical menopause, outcomes and treatments; systematic reviews addressing the risks and benefits of HT in surgical/natural menopause; and long term primary studies evaluating the effect of HT in surgical menopause (when no systematic reviews were identified). We also searched Medline plus for patient health information targeting the area of surgical menopause and HT. Search terms were searched as MeSH headings or keywords and were derived from two main concepts "surgical menopause" and/or "hormone therapy". We limited our search to English language.

Screening for relevant information

Search results from relevant sources were exported to one RefWorks account and close duplicates were removed. To check for eligibility, titles and abstracts were initially screened, followed by full-text review to confirm eligibility. Eligible records were then exported to N vivo for data management and extraction.

Information extraction

Data extraction was completed in N vivo by creating nodes. Data extracted included: data on surgical menopause (definition, symptoms and long term outcomes); HT (definition, doses, formulations, duration of therapy, risks, benefits, outcome probabilities, and relative and absolute contraindications); other treatment options (non-hormonal therapies, herbal and complimentary approaches and other management protocols); and resources for menopausal support. To evaluate outcome probabilities, we extracted the following from systematic reviews and primary studies evaluating HT in menopause: number of studies addressing a specific outcome, study design, number of cases in treatment group, number of cases in placebo or comparator, and measure(s) of association. Also, when reported data on the risk of bias, inconsistency, imprecision, indirectness, and publication bias were extracted.

Evaluating the evidence on outcome probabilities

To evaluate evidence on outcome probabilities we used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[11] We chose this approach because it's recommended by IPDAS and offers guidance and tools that aid in certainty assessments. Outcome probabilities were assessed for certainty based on pre-established rating criteria guided by GRADE recommendations for 5 elements of bias (Appendix 7.4): (1) risk of methodological bias, (2) inconsistency across studies, (3) imprecision in effect estimates, (4) indirectness to target population, and (5) risk of publication bias. Biases were rated as "not serious", "serious, or "very serious" and accordingly certainty in outcome probabilities were assessed as "very low", "low", "moderate" or "high". The assessments were completed independently by two reviewers (TS and SR) and discrepancies were resolved by consensus. All certainty assessments were performed on the GRADEpro software.

Appendix 7.4. Criteria for rating evidence of risk estimates reported in SheEmpowers PDA based on the GRADE approach for rating quality of evidence and formulating recommendations

Factor	**Not serious**		**Serious**	**Very serious**
Risk of bias	RCTs: Based on **Cochrane criteria/tool for rating risk of bias** (randomization, allocation concealment, blinding, intention to treat analysis, lost to f/u, selective reporting of outcome, and others) – **when all or most studies have low risk of bias, therefore no limitations and confidence in effect not affected**	Observational studies. Rated using **NCOS** for cohort or case control studies (cut off ≥7 for high quality) – **when all or most studies had a score of 7 and higher (low risk of bias), therefore no limitations and confidence in effect not affected**	Most studies have unknown or low risk of bias; however, **limitations or biases are likely to lower confidence in effect (downgrade 1 level of evidence)**	Most studies have high risk of bias and therefore **limitations or biases are very likely to lower confidence in effect (downgrade by 2 levels of evidence)**
Inconsistency (only applies to collective evidence)	To evaluate if estimates of effects from different studies are not widely differing (signifies unexplained heterogeneity), the following criteria needs to be met: - **Estimates of effects are on the same side** - **Confidence intervals overlap** - **Test of heterogeneity is non-significant (>0.05)** - **I2 statistic is <50%**		If one of the measures of heterogeneity is not met and sensitivity or subgroup analysis failed to explain heterogeneity, then **consider downgrading quality by 1 level**	If more than one measure of heterogeneity is not met and sensitivity or subgroup analysis failed to explain heterogeneity, then **consider downgrading quality by 1 or 2 levels**
Indirectness (rated on GradePro software	If there are sufficient similarities between population of interest and the studies from where		**Use online judgement criteria to determine**	**Use online judgement criteria to determine**

itself)	estimates of effects were extracted, based on: **population, intervention, comparator, direct comparison and outcome)**	**seriousness of indirectness in downgrading quality of evidence by 1 level**	**seriousness of indirectness in downgrading quality of evidence by 2 levels**
Imprecision	**If confidence interval doesn't include null** **or** **If total number of events across both treatment groups >300 (and therefore optimal information size is likely to be met) then imprecision did not seem to affect confidence in effect**	If none of these criteria were met, then we considered downgrading evidence by 1 to 2 levels depending on the seriousness of imprecision. **If CI includes null and number of events are less than 300 then we downgrade by 1 level**	If none of these criteria were met, then we considered downgrading evidence by 1 to 2 levels depending on the seriousness of imprecision.
Publication bias (only applies to meta-analysis and/or systematic reviews)	**Undetected if funnel plot is symmetrical in the relevant meta-analysis or as concluded by authors in the systematic review based on other criteria.** If **only one study** included, then **we considered as undetected.** If studies were pooled outside the context of a systematic review and they **were less than 5 studies** (that is, we cannot develop a funnel plot) **also we considered as undetected**	If **funnel plot is asymmetrical** and/or if **authors of corresponding systematic review concluded that publication bias is likely** then we downgrade the evidence by 1 to 2 levels	If **funnel plot is asymmetrical** and/or **if authors of corresponding systematic review concluded that publication bias is likely** then we downgrade the evidence by 1 to 2 levels
Others (when to consider upgrading evidence)			
Large effect (observational studies)	When relative risk reduction is **≥ 50%, evidence is upgraded by 1 level (RR~2) anything over 1.5 and significant I considered large effect** When relative risk reduction is **≥ 80%, evidence is upgraded by 2 levels (RR = 5 to 10)**	**Level of evidence remains the same if large effect is not found**	**Level of evidence remains the same if large effect is not found**

Plausible confounding (observational studies)	Upgrade level of evidence by 1 point if plausible confounding (factors not controlled for) would have strengthened the observed association or changed it from no effect to an effect. Check discussion section of found studies	Level of evidence remains the same if such scenario doesn't exist	Level of evidence remains the same if such scenario doesn't exist
Dose gradient (observational studies)	Upgrade level of evidence by 1 point if a dose response relationship is observed. Check discussion section of found studies	Level of evidence remains the same if dose response relationship is not observed	Level of evidence remains the same if dose response relationship is not observed

Appendix 7.5. Interview guide

- Greet patient
- Make patient feel comfortable and at ease (e.g. use ice breakers)
- Ask if patient had a chance to sign consent form and if they brought it with them (if forgot to bring - provide a blank copy and ask patient to fill out and sign)
- Ask if patient has any questions or concerns about the study - reassure patient that information we collect from them will be kept confidential.
- Briefly summarize the outline of the interview and what's involved (e.g. fill out a couple of questionnaires to capture acceptability of the tool and demographics and then will be asked a few questions to capture views on tool)
- Ask if patient had the chance to go over tool:
    a. If yes, ask patient to spend a few minutes to review the hard copy so they are able to provide feedback on format/presentation.
    b. If no, ask patient to spend 10 to 15 minutes to review the hard copy so they are able to provide feedback on both content and format.
- After reviewing tool, ask patient to fill out acceptability questionnaire first and then demographics questionnaire.
- Collect questionnaires from patient when done and prepare audio-recorder for recording semi-structured interview.
- Start interview by asking patient open ended questions about the tool (refer to interview questions). Make sure to capture their views on:
    a. Content
        i. Amount of information
        ii. Comprehensibility
        iii. Clarity of information
        iv. Biasness
        v. Relevancy
        vi. Value
    b. Format
        i. Layout
        ii. Clarity of presentation
        iii. Length of presentation
        iv. Clarity of infographics and figures
    c. Risk information section (clear and understandable?)
    d. What do they like about the tool?
    e. What do they dislike about the tool?
    f. How can we make the tool better?
    g. Any further thoughts about the tool that they would like to share?
    h. Summarize in brief points what patient shared about the tool throughout the interview and ask if we accurately captured their views.
- Semi-structured interview should last approximately 20 to 30 minutes. After that, thank patient for their feedback and contribution. And stop recording.
- Thank patient for participating in the evaluation process.
- Hand patient gift card.
- Ask if patient had to pay for parking and collect parking receipt from them (if interview is in ECHA or college plaza)
- Collect their email address or verify if we already have.
- Let patient know that one of the study team members will reimburse them via email interac.

Appendix 7.6. Acceptability questionnaire

My thoughts on the SheEmpowers Patient Decision Aid

We would like to know what you think about the SheEmpowers Patient Decision Aid you just received

1. Please rate each section, by checking off "poor", "fair", "good", or "excellent" to show what you think about the way the information was presented on:

Section	**Poor**	**Fair**	**Good**	**Excellent**
Definition of early surgical menopause	☐	☐	☐	☐
Symptoms of early surgical menopause	☐	☐	☐	☐
Long-term effects of early surgical menopause	☐	☐	☐	☐
Emotional impact of early surgical menopause	☐	☐	☐	☐
Hormone therapy	☐	☐	☐	☐
Benefits of hormone therapy	☐	☐	☐	☐
Risk of developing long-term risks of early surgical menopause with or without hormone therapy (infographics and figures)	☐	☐	☐	☐
Risks of Hormone Therapy	☐	☐	☐	☐
Risk information on hormone therapy (infographics and figures)	☐	☐	☐	☐
Risk factors of breast cancer (figure)	☐	☐	☐	☐
Steps to maintain health and reduce risks of surgical menopause and hormone therapy	☐	☐	☐	☐
Other factors to consider when deciding on a therapy	☐	☐	☐	☐
Stories about others	☐	☐	☐	☐
Values clarification	☐	☐	☐	☐
Identify what else you need to make a decision	☐	☐	☐	☐
Plan the next steps	☐	☐	☐	☐
Tracking form	☐	☐	☐	☐

Available resources	☐	☐	☐	☐

2. The length of the presentation was (check one)
   ☐ Too long
   ☐ Too short
   ☐ Just right

3. The amount of information was (check one)
   ☐ Too much information
   ☐ Too little information
   ☐ Just right

4. I found the presentation (check one)
   ☐ Slanted towards taking self-care or life-style options
   ☐ Slanted towards taking medical therapies
   ☐ Balanced

5. Would you have found this decision aid useful when you are making your decision about hormone therapy for managing early surgical menopause (check one)
   ☐ Yes
   ☐ No
   Comments:

6. What did you think of the infographics and figures that show risks of early surgical menopause with and without treatment? Was it:
   ☐ Easy to understand and interpret
   ☐ Difficult to understand and interpret
   Comments:

7. What did you think of the infographics and figures that show risks of hormone therapy? Was it:
   ☐ Easy to understand and interpret
   ☐ Difficult to understand and interpret
   Comments:

8. What did you think of the rest of the sections in the decision aid?
   ☐ Easy
   ☐ Difficult
   Comments:

9. Do you think we included enough information to help women decide on therapy for managing symptoms and long term risks of early surgical menopause?
   ☐ Yes
   ☐ No
   Comments:

Appendix 7.7. Qualitative Analysis – Reviewer 1 (AS)[h]

THEME	CATEGORY	SUPPORT	INT
CONTENT	Like	"I liked very much about it that it covered so much of the explanations before surgery, after surgery, what the surgery is for and all the availability of the risks and benefits of… the treatments that follow the surgery"	1
		"I don't think they had anything there that shouldn't be there, for sure"	1
		"I think it was pretty balanced, I would say"	1
		"This is basically what they have when you go to the menopause clinic that you – and they keep track of it for you basically, so yeah, that's a good idea."	2
		"I like the name"	2
		"[Values section] I think it's a very good idea, yeah. Because it's exactly right, you don't know because you don't know the long term effects and how can you evaluate that? So that is a good idea to put it at the beginning and then after you read it."	
		"Well I liked that it targets your values, like, what's important to you, I do like that."	
		"I really like the graphs, because you can read it and you can read all the numbers you want but then when you see the graphs it's really clear as to, okay, this is what the results of those studies are showing. …I think that that really helps as the infographics and graphics themselves and reference to the quality of the study and that kind of thing"	3
		"To begin with it seems a little bit overwhelming, but honestly, I think you have to have that much information in there to really provide all of the facts and studies that are out there. So overall, I think it's really good, you know, the amount of information that's here"	3
		"No, I didn't see it as biased, especially the way the surveys, or studies, sorry, were laid out and that information"	3
		"The clarity is good and, really, what adds value is the infographics"	3
		"I also really like this tracking, like, afterwards, you know, that's a really good resource too because after surgery, all of a sudden, all of these things start. You know know, you know, am I making it a bigger deal than it really is. And if you've got something where you can track everything then it's right there in front of you and then when you're talking with your doctor, you know, you've got it all there, so I think that's a really good idea"	3
		"I think that it points out the pros and cons and gives you a summary without a judgment"	5
		"I think the risks are well pointed out. And yet it doesn't add fear, you know, like it's there but it's just a fact. And it gives you the opportunity to decide yourself"	5
		"I think putting it in steps is very good so that, you know, this is what I need to do so find out what it is that I can do and then figure out what the values are and make a decision"	5
		"Instead of just sitting down [with a] piece of paper pro and con here it's got some of your pros and cons and how do they apply to you? What could be better?"	9
		"I thought they [the infographics] were really easy to follow. I liked how you had this grading system here about the quality of the research.. I guess it makes you feel more at ease when you look at [the risk] – oh, that's you know, it's actually very small"	10
		"Yeah I think it's [values clarification] a very good idea. Because as I said before, I think that study gave hormone therapy a really bad name and so people were just like very closed to that option. And then once you read more about it, this is very informative… and when you see the graphs and everything else too, it doesn't look	

[h] Alisha Shivji (Pharm D Candidate)

		so bad”	
	Dislike/ suggestions	“Are they called hot flashes or hot flushes? This one says flushes but I thought I read flashes somewhere”	2
		“But yeah I kind of had it in my head that it was for women planning to have [a hysterectomy], although I do find it useful for myself too, like some of the information in here”	2
		“It included the emotional decision and physical effects, emotional effects. You know, so it kind of covered a broad spectrum”	2
		“I kind of found that it was leaning towards having hormone therapy, I think. Like I mean just maybe just that’s because based on the information it sort of made senses to me that that would be the best route so maybe I was looking at it from a biased point of view without kind of realizing it. The way it talked about benefits, you know, all the improvements you could have if you take hormone therapy. It could help with slowing bone – to me it sounded like there were more positives than negatives for taking hormone therapy”	2
		“I think for me as far as choices for women who can’t go on the hormone therapy route, to me that was lacking a bit, right? There is reference in there that.. you know, see another [supplemental] section… and I didn’t see that information there”	3
		“Well for me when I read “the symptoms of surgical menopause often include,” although it’s all there, I just feel like saying you have no idea. Like, is there a way to emphasize that they can be very severe, you know?.. And it may even be just to say that the symptoms can be moderate to very severe, like, it might be something as simple as that”	3
		“But myself, being a very young woman and a mother of two young girls with a husband and a job and a very active lifestyle within the limitations of my physical health, because I do have other issues, the biggest part for me wasn’t worrying about dying; it was having to live. And this feeling really focuses on the health risk and, you know, dying – what could kill you, and if this was going to be.. to me, it wasn’t about what’s going to kill me whenever; it’s about how I’m going to be able to live my life now, be happy and enjoy my life and be reasonable. So it was that whole emotional piece”	4
		“And to have that complete disconnection with my brain and to function on what I just did and the work that I just put in, I really didn’t think that this focused enough on that, because some women aren’t concerned. There’s a big course of women who are not just concerned about the cancer, the stroke, and the heart; they’re concerned about living their life and enjoying their life and being happy. And that part is really missing in this.	4
		“They don’t understand that their brain is no longer functioning. And it’s mentioned in there about the brain, but it really doesn’t describe that symptom.. that whole cognition piece is probably the bigger issue, because if you are not healthy in your head – you don’t care if you have a sex life, it doesn’t occur to you that you have vaginal dryness and it is that bad, because you’re just trying to cope wit the fact that you’re living in a fog”	4
		“As far as the long term ones, the symptoms of early surgical menopause, they could also be the long term ones, right? Because if you’re not treated properly those can become long term, especially the mood and the difficulty sleeping. So those could also be in the long term, not just the short term”	6
		“So what happened to her – she wasn’t allowed to do the hormone therapy so what did she do to manage her symptoms? Because I bet there’s women in her situation that would like to know what she did.	
		“It did mention in there that there are other options but it doesn’t say what they are.. I think women need to know that only – this isn’t the only option, right? There are different hormone therapy treatments for sure”	6
		“The only other thing is – was the estrogen and the progesterone.. maybe	8

		somewhere in there.. examples. Like estrogen does this and the progesterone does this.. this is what happens if you have too much of the estrogen"	
		[Steps to maintain health and reduce risk] "It's good but I didn't feel you have to have it. Everyone knows you should eat healthy and stay active"	9
		"I didn't see anything about it's okay with your doctor's knowledge to still be on them, it was slanted more towards you should get off them.. you're really promoting a person shouldn't be on them.. maybe add in there somewhere a story if you're a person that needs to remain on them with your doctor's care that's fine too"	9
		"You've got the mood changes in here, but I know, like for me, I had a lot of anxiety after. So I'd just add just maybe more about the emotional impact of anxiety"	10
		"I always though if you keep your uterus you need the combination therapy. See, it says here estrogen only therapy for women who keep their uterus/ But estrogen is only – estrogen only is you have not kept your uterus because you need the progesterone or you put yourself at risk for cancer, right?"	10
		"When it says uterine cancer – they called what I had endometrial hyperplasia with atypia a pre-cancer, right? So, then I don't know if they want to mention anything about it because everybody has different reasons for getting a hysterectomy, right? SO I'm not sure if that's something that needs to be mentioned or not"	10
		"You don't have any dosages of anything in here, like what compares of an oral dose to a patch to as – so that you have some idea of kind of where you should be… like just typical or what you average person, maybe with surgical menopause is on…. Because it just looked like a big sea of where you start and what you should be on. Am I on too much? Am I on too little?"	10
		"Maybe [add] like a little area to journal, like this is the dose and these were the side-effects I was feeling today. You know what I mean? Like a little journaling section…. So it can maybe help you to see where you need to adjust your dosage"	10
		"Here it says 'mood changes,' so that seems really minor when you see t like this, but for me seven years after the surgery I was emotionally numb. I did not cry at sad movies, I did not get mad, I didn't get angry, I didn't – was never extremely happy, I was numb. I had no ups or downs or anything, it was just all the time time and that was a huge thing that I noticed without the hormones, which yeah sure you can call that a mood change but if you, you know, to read it as such is emotionally numb, you don't have emotions, that's a big difference between that and mood changes. It's a lot more severe and has a bigger impact on everything… I would call it psychological challenges, so then you can say in there 'could be depression, could be lack of connection or empathy or whatever'"	11
		"I don't know where in this book would be a good place for it, but I think that's a really good point to make, that the hormones that you go on for therapy are lower than the birth control pill… and they don't [realize] because one has been socially acceptable for women to take all the time and the other one has these bells of cancer ringing on people's ears… I think that would be a beautiful chart actually saying this is the dosage of what people are on when they're on birth control. This is what we're talking about you being on, and this is what your normal levels are"	11
		"It seems to me like this is step two or three or something in a give step process and I don't know that anyone's addressing step one. Step one is should I have the surgery"	11
		"To me these stories would be more impactful if I actually knew how they ended"	11
		"I have no idea if the hormones affect cervical cancer or ovarian cancer because it's talked about breast cancer and heart disease but it's left those two things out which seems like they would be related somehow"	11
		"A link in the resources that talks about the actual procedure, the actual surgery right would be useful too"	11
		"Just added that there are substantially more symptoms it's not just these five or	12

		seven that you have on there, that there's more that's affected by – which I didn't know when I had my hysterectomy, I found out after"	
		"At one point it does say 'refer to our supplemental attachment for alternative hormone therapy suggestions' and you don't have one"	12
		"I am more concerned of cardiovascular information and you do have a little bit about that but not as much as you do with the breast cancer"	12
		"Can you put in there that genotyping [for BRCA gene] is possible, speak to your doctor"	12
FORMAT	Like	"I think you did start out the right direction and keep going and the steps were good.. yeah, I don't think you have to go to one page and go back and, you know, say, well, do they cover this or not"	1
		"It's a cute little book. It's much nicer than reading online"	2
		"I prefer books. I like the size of it and it's not that you're just reading a whole sheet going down kind of, you know, like a whole PDF kind of document. This is kind of broken up a bit."	
		"I like it. I like the size of it. I like that you know, so you can pick it up and read, you know, short little chapters and get a little bullet of information and go back and read the next subject and the next sort of topic. So I thought it was good, I like how it was split up like that"	2
		"I like little pictures in between too, it sort of breaks it all up"	2
		"I liked the visual [infographics], I didn't think it was hard to understand at all"	2
		"I like how it's split up so there's not too much to read all at once if you didn't want to. I mean I'm fine with it but if people wanted to read just a little bit on something"	2
		"And I've never seen anything that has really laid it out like that [infographics], especially for hormone therapy because it's so controversial right?"	3
		"And really, what adds value is the infographics because if nothing else that's.. that portion is an easy read, right, you know, visuals"	3
		"I like the size of the book because it doesn't feel overwhelming"	3
		"I like this format, the way this is laid out, this is very nice. And it's probably more inviting than sitting and reading it on a computer screen. This is more appealing to me."	
		"You know, if I was to have this with me, or you know, if I was new, then I wouldn't feel embarrassed to have it.. I could easily carry this around with me"	8
		"In this format, this little booklet, this is so much easier and just more engaging because [online] I thought 75 pages oh my gosh"	9
		"I just love the colours you've chosen, hyow they contrast, it's not all continuous reading like it appears when you get the print. It's broken up well with colours and pictures and, you know, the contrasting"	9
		"I like the way everything – it's very simple. Like it's the way it's, I guess, outlined on the pages and stuff. It's not a whole bunch on one page. Do you know what I'm saying? It's easier to read. It's not overwhelming"	10
		"It followed, actually, a well thinking process through it. Like you said, you did the survey first and then you got informed about your decision and then you look back on it, so you have time to reflect on that stuff and that's very good"	10
		"After those first weeks after you've had the surgery, to even go to follow that link, it just looks like a bunch of words on a page. But I think if you had a book in front of, you know what I mean, that was clear and concise"	10
		"I think the book is much better than a PDF"	11
		"This doesn't look nearly as scary as opening up the website and seeing 75 pages of writing"	12
	Dislike/ suggestions	"Just a small peek [of] what's available in your tool and how they could get it… yes, just like small pamphlet[s]. Yeah, the small pamphlets that you see in doctor's offices or in clinics, public health offices about what are the symptoms of	1

		meningitis or what are the symptoms of flu…"	
		"I don't think it's [the font] too small. Although yeah, that could be a problem for some people if their eyesight is not great or something."	
		"No, I think it's good unless people like those little tabs to have sections. You know, especially if you like looking through and where's that information about the resources, you know?	
		"Yeah I think that [tabs] would be really beneficial, because there might be just a certain area that's really important to a person too and then, you know, that's the area that they're flipping back to"	3
		"It's [the infographic] just too busy for me"	5
		"It just seemed like an awful lot reading it on the computer"	5
		"Cause like at first when you were like sending this to me, I was just like, 'Oh my God. I can't do this'"	8
		"In black and white on a computer screen they [the infographics] were just too busy and I couldn't tell anything"	9
		"I think I would make it a whole booklet size"	10
		"I do like that it's [symptoms] broken down and explained what each of those things but there's something quite powerful seeing it as a [bulleted] list of possible things that people go through…. Just seeing a list, for me it was a lot more impactful than reading all the details"	11
USEFULNESS	Value	"I'm so glad that this is available"	1
		"This should have been around before I – because you have so many questions, you don't know. It's like going into the unknown. I had no idea so this would have been really helpful for sure.	
		"So yeah, I went to my family doctor, you know… he didn't suggest anything, you know. Well, eventually I did go on something through him, it was Premarin, which I didn't like. And then so the one I'm on now was through this clinic, which was a lot nicer. Their support is much more for sure, yeah. So this could have been really helpful to know."	
		"See we didn't have anything like that, nothing to sort of help us decide"	2
		"Available resources would have been really useful for me too"	2
		"This is really good. I'm just saying there was much more information in here than was available to me when I was going through surgical menopause"	2
		"I think it's useful, I think it's great. And yeah, it covers information that I didn't know then that I know now"	2
		"I think it's well done, it's useful and it should have been done a long time ago. Women need this so good on you"	2
		"I think both prior to surgery and then even after in the whole decision about hormone therapy and that type of thing, absolutely, I think it would help"	3
		"Yeah, because that's the thing is when you're trying to do the research yourself you don't know if.. you know, do you trust that information, especially everything's on the internet, right? And so that really helped to qualify, yeah, the studies and that kind of thing, so that was good.	3
		"Actually this would be really interesting for somebody who's even thinking of having a hysterectomy.. maybe everyone that's having a hysterectomy should have this"	5
		"It encourages you to research, which I think more people need to do rather than just go to my doctor and I want a pill"	5
		"Before I went in there really was no information for me. So I think it is really good for women to have and to know this is what's coming down the pipe for you and to know that there are choices you can make that are going to make it better for you. So I do think it's really something good because it's something that has never been before, right, so it's definitely a step in the right direction"	6
		"Back then I didn't know enough about hormone therapy, and I knew what outweighed the risks of keeping everything, right? So I mean, I was kind of thrown	8

		into it and not really aware of what the next 20 or 30 years of my life were going to look like. You know, and I think that – nobody kind of explained it to me"	
		"Oh absolutely I would love it and I wish – and if it wasn't me with my firm I've got to do this, yes I love the pros and the cons and making an informed decision. A lot of women do want to make an informed decision and I know people that have chosen not to go on hormone, they think oh it's horrible doing this to my body. I don't want to take these chemicals. This is an excellent resource"	9
		"The best thing about this is you have something to discuss with people that you want to talk with it about whereas before it was just kind of like random ideas in kind of grey areas, whereas it's something more concrete"	10
		"This is really good because you can read so much garbage on the Internet, so this is really good that these are printed"	10
		"I found that my care was very fragmented because everybody had a different opinion and whereas this was evidence based – and it's got your facts altogether there"	10
		"I would have [found this useful] because I had to go through and get a lot of information from a lot of different places to make the decision that I did make and I ultimately feel that it was the wrong decision for me"	12
		"Overall I think it is a very helpful tol. Deciding to begin hormone therapy or not is a difficult decision to make and this book takes some of the confusion out of deciding by breaking it down and looking at each section individually, making choices along the way, and coming to a conclusion in the end"	12
	Dissemination	"There is always room for improvement, as to making it more available to many more areas of the medical profession"	1
		"I think that if you can make it more available if your resources would allow you to sort of have a spot or a place in every medical imaging office, medical, family physician's offices, public health offices in the outlying areas, especially to people that just a small peek [of] what's available in your tool and how they could get it"	1
		"If those doctors that specialize in this type of surgery, like the hysterectomies, if they had a resource like this to be able to provide to the patient before, you know, to help them make the decision I think that would be fabulous"	3
		"I'd sure like to see this in our doctor's offices"	5
		"Well even like the Menopause Clinic or, you know, like they should know what is going to happen to you and how bad it can get, right? Or even the surgeons that are taking your uterus and the ovaries, like they should have a good idea of what's going to happen to you afterwards"	6
		"I know you're going to get this published first it's for the menopause clinic specifically, but if this could even be in the physician's offices. You know what I mean? So, it could help those women before they got to that really bad point where they needed to be in urgent referral to those clinics, right?"	10
SUPPORT GAP		"Then with that group that we did before all of the women seemed to have the same thing, right? So that was really helpful."	2
		"Or even support groups, I mean we didn't even know – I didn't know there were [resources available]. I think quite a few of us at the study didn't know that at all"	2
		"I do believe that support groups would be vitally important if there's an opportunity for that"	5
		"And I do think support groups are really – that's what we found last year was everyone just able to talk to somebody else about it. You don't always have that opportunity.. sometimes you think you're standing there alone"	5
		"And you know, there's support groups for everything else, like everything and there really isn't for this"	6
		"Like I would have come to those once a month even if I had to drive two hours I would have come. It was so good to talk to other women that have had that done and to know that you're not.. crazy and you're making stuff up because that's literally how you feel, right? Because your husband doesn't understand it, he's a	6

	good support but he doesn't understand what you're going through, right? So, I think the support groups are huge. I think it would be a fantastic thing to have"	
	"It feels like it's so hush hush and you feel like you're the only one going through this. So it was really good to talk to other ladies"	6
	"I just think that there needs to be support groups out there for ladies and to know that they are there for you to use... the menopause clinic should offer support groups of some sort, even if it's just you get together and you talk"	6
	"Emotionally, mentally, spiritually, having a place to go with all that stuff.. if you don't have support during this, then it's really difficult"	7
	"I thought what would've helped me, I think more groups, like a continuing support group. I have – there's all these groups on Facebook, but you never know.. who's organizing these groups right?"	8

Appendix 7.8. Qualitative Analysis – Reviewer 2 (TS)[i]

Theme 1	Quotes	Interview
Strengths of PDA		
1. Content	<Files\\180531_0011> - § 4 references coded [5.98% Coverage] Reference 1 - 2.71% Coverage I liked very much about it that it covered so much of the explanations before surgery, after surgery, what the surgery is for and all the availability of the risks and benefits of Reference 2 - 1.11% Coverage I don't think they had anything there that shouldn't be there, for sure. Reference 3 - 0.47% Coverage I think it was pretty balanced Reference 4 - 1.69% Coverage But I think that … yeah, I think you did start out the right direction and keep going and the steps were good.	1
	<Files\\180601_0011> - § 13 references coded [5.43% Coverage] Reference 1 - 0.79% Coverage I just kind of reviewed it when I was reading it and it told the symptoms of surgical menopause. But when I went, they were really clear about telling me, you know, you may not get this, some women get this, some don't but I feel like the majority of us do. Reference 2 - 0.27% Coverage Yeah, no I did read that actually and I thought that was good. Yeah, that was good too. Reference 3 - 0.47% Coverage Yeah, I read this too and I thought that was good. See, we didn't have anything like that, nothing to sort of help us decide. Alright, this is a good idea Reference 4 - 0.48% Coverage This is basically what they have when you go to The Menopause Clinic that you - and they keep track of it for you basically, so. So yeah, that's a good idea. Reference 5 - 0.46% Coverage Yeah. This is really good. I'm just saying there was much more information in here that was available to me when I was going through surgical menopause. Reference 6 - 0.06% Coverage I think it's great. Reference 7 - 0.38% Coverage I do, yeah. I think it's useful, I think it's great. And yeah, it covers information that I didn't know then that I know now. Reference 8 - 0.18% Coverage But I thought it was good information about each section. Reference 9 - 0.58% Coverage No because it's more than I did know. So I feel like, you know it included the emotional decision and physical effects, emotional effects. You know, so it kind of covered a broad spectrum. Reference 10 - 0.19% Coverage I did find it relevant. Yeah, no, I think it's really well done. Reference 11 - 0.72% Coverage Yeah, I think it's a very good idea, yeah. Because it's exactly right, you don't know because you don't know the long term effects and how can you evaluate that? So that is a good idea to put it at the beginning and then after you read it. Reference 12 - 0.52% Coverage I just thought it was really well done like I said before. I think it's well done, it's useful and it should have been done a long time ago. Women need this so good on you. Reference 13 - 0.32% Coverage No, I think that's it. It's really positive I think it's great. I think good job and we need it, so yes.	2
	<Files\\180608_0011> - § 16 references coded [15.09% Coverage] Reference 1 - 0.74% Coverage I was just going to say overall, you know, for the tool and that kind of thing I do … I think it's excellent. I think it's really good information. Reference 2 - 0.45% Coverage	3

[i] Tasneem Siyam (BScPharm, MSc, PhD Candidate)

	Well, I liked that it targets your values, like, what's important to you, I do like that. Reference 3 - 1.69% Coverage So, no, I like that, the values. But I also liked the reference to the studies and then it was very clear as to whether or not this was … how do you frame it in here … like, basically, there would be no more further information whether it's a moderate or high quality, you know, study, that kind of thing. I thought that was really good Reference 4 - 0.72% Coverage Yeah. And I've never seen anything that has really laid it out like that, especially for hormone therapy because it is so controversial, right? Reference 5 - 0.75% Coverage I think that that really helps as the infographics, and graphics themselves and reference to the quality of the study and that kind of thing, so … Reference 6 - 1.09% Coverage Well, like I say, to begin with it seems a little bit overwhelming but, honestly, I think you have to have that much information in there to really provide, you know, all of the facts and studies that are out there. Reference 7 - 1.11% Coverage No, I didn't see it as biased, especially the way the surveys … or studies, sorry, were laid out and that information. So, no, I didn't. I thought it provided clarity but certainly not … didn't lean one way or the other. Reference 8 - 0.66% Coverage I was surprised to see the gallstone reference. I didn't realize that at all but, no, I felt that it was all very relevant and … Reference 9 - 0.95% Coverage I think it's very good. The clarity is good and, really, what adds value is the infographics and … because if nothing else that's … that portion is an easy read, right, you know, visuals. Reference 10 - 0.49% Coverage Absolutely. Because I do think that's what it's all about is personally what's important to you. Reference 11 - 2.27% Coverage I also like this tracking, like, afterwards, you know, that's a really good resource too because after surgery, all of a sudden, all of these things start. You don't know, you know, am I just making it a bigger deal than it really is. And if you've got something where you can track everything then it's right there in front of you and then when you're talking with your doctor, you know, you've got it all there, so I think that's a really good idea. Reference 12 - 1.99% Coverage You know, I think both prior to surgery and then even after in the whole decision about hormone therapy and that type of thing, absolutely, I think it would help. And I like that the information is very concise and touches on all the different factors that you hear about, like, whether it's the risk of blood clots or … well, all of the different symptoms, it's touching on all of them, right? Reference 13 - 0.41% Coverage So, yeah, that's really good, the risk of heart attack, the risk of … you know. Reference 14 - 0.34% Coverage Yeah. No, I do think it would be very valuable, so hats off to you. Reference 15 - 0.96% Coverage Yeah, because that's the thing is when you're trying to do the research yourself you don't know if … you know, do you trust that information, especially everything's on the internet, right? Reference 16 - 0.50% Coverage And so that really helped to qualify, yeah, the studies and that kind of thing, so that was good.	
	<Files\\180609_001> - § 5 references coded [1.86% Coverage] Reference 1 - 0.08% Coverage I think it wasn't overboard, Reference 2 - 0.79% Coverage [Pause] I like that, actually, these are included as well, because I didn't – I get – I didn't get these all in a little bundle until I went to see Dr. [Shandro] at the Grey Nuns. So really, it's only – having this information to be able to rate how you're feeling. Reference 3 - 0.23% Coverage And even the checklist at the end here, from page 60. So 57 – the next steps. Reference 4 - 0.40% Coverage	4

	Yeah. Because if you're really on the fence on what your decision is and you don't know or you don't feel like you have enough facts… Reference 5 - 0.36% Coverage It was a really good tool. And I think that that – when – if I would have had this before, I probably would have changed	
	<Files\\180613_001> - § 24 references coded [14.99% Coverage] Reference 1 - 0.93% Coverage There were a couple of things that I thought were exceptionally good. The risks hormone therapy I thought was good because sometimes we're looking for a cure but we don't really pay attention to what the side-effects might be. Reference 2 - 0.80% Coverage And I thought it was very well explained for the risk factors of breast cancer as well because it seems a lot of people say oh, I'm not going to take hormone therapy that causes breast cancer. Reference 3 - 0.24% Coverage I really like the idea of knowing the facts about menopause Reference 4 - 0.64% Coverage I thought this was really good too, how do I maintain my health and reduce the risk of surgical menopause and hormone therapy. It's pretty much in order. Reference 5 - 0.98% Coverage I think it's good. Like I say I have good for everything, excellent for - good for everything down here and then excellent on the risk hormone therapy, I thought that was very well done. And this one on breast cancer was really excellent. Reference 6 - 0.35% Coverage contraindications, [you should carefully consider.] Yeah, so I mean I would say good. Reference 7 - 0.68% Coverage I think it's good to bring these things to the attention of people because sometimes you don't see what's happening to yourself and this way it sort of brings it up. Reference 8 - 0.98% Coverage Well, I think it does help you to learn the key facts. So I would say this is better than good because it makes you aware of what can or cannot happen and it also doesn't overdo it on everything that can go wrong, it gives you the positive Reference 9 - 0.54% Coverage I'd sure like to see this in our doctor's offices. And I also think it's very objective, not subjective, so that's really important. Reference 10 - 0.20% Coverage Oh, I would put that as excellent because - yeah. Reference 11 - 1.30% Coverage I would have appreciated this. Yes, this would have been really, really good when I had surgery because I had no clue. My doctor then was very, very good and she did a - she did explain a lot of things to me and I didn't feel fearful about anything. I'm just annoyed that it kept coming back [laughs] the symptoms. Reference 12 - 0.16% Coverage And this is excellent too, that's great. Reference 13 - 1.38% Coverage Well, I think in the printed copy it gives you a different thought about it. I mean I work on computers all the time but I hate to go through - like I won't do a long survey. Ask me more than five questions you're done [laughs]. But maybe a bit long but at the same time I can't say there's anything in here that I wouldn't take out. Reference 14 - 0.28% Coverage Yeah, yeah, like every piece of information in there is valuable. Reference 15 - 0.32% Coverage Well, I think it's all important so I don't know how you can remove any of it. Reference 16 - 0.28% Coverage Yeah. I think it's just right for the amount of information for sure. Reference 17 - 0.13% Coverage I thought it was well balanced Reference 18 - 0.58% Coverage And I think it encourages you to research, which I think is more people need to do that rather than just go to my doctor and I want a pill. Reference 19 - 0.37% Coverage	5

	Okay, what did you think of the risks section in the decision aid? They're all easy really Reference 20 - 0.37% Coverage I think that it points out the pros and cons and gives you a summary without a judgment. Reference 21 - 1.19% Coverage it gives you a summary without directing you and gives you lots of area for research. If you're concerned that that isn't enough there's lots of area to go and research it further. But it gives you the highlights and the very actual points of concern for everyone going through menopause Reference 22 - 0.52% Coverage Yeah. But I think the risks are well pointed out. And yet it doesn't add fear, you know, like it's there but it's just a fact. Reference 23 - 0.94% Coverage Yeah. I think putting it in steps is very good so that, you know, this is what I need to do so find out what it is that I can do and then figure out what the values are and, you know, make a decision. I think that's really good. Reference 24 - 0.84% Coverage No, not at all. And I do think the supports groups are really - that's what we found last year was everyone just able to talk to somebody else about it. You don't always have that opportunity and that is -	
	<Files\\180614_001> - § 8 references coded [3.67% Coverage] Reference 1 - 0.36% Coverage Right, yeah. And yeah, that's all great information but when you are not yourself it's really hard to do any of that, right? Reference 2 - 0.36% Coverage It is because I've been through it, right? But before like I said, you think oh, they can't be that, bad, like you have no idea. Reference 3 - 0.25% Coverage Yeah, so these are good but like I said until you've been there you don't know [laughs] Reference 4 - 0.10% Coverage Yeah, this is really good to have. Reference 5 - 0.93% Coverage Yeah because I think it would be better to get on some sort of hormone replacement before you hit the bottom because then you're trying to dig your way out of that hole and make everything better. Whereas if you went on something right away and you were prepared for it, you wouldn't have to dig yourself out of a hole first. Reference 6 - 0.29% Coverage No, but you definitely have to read what it is to see. But I think it's that with any diagram really. Reference 7 - 1.28% Coverage I do like the information that it gives. Like I said before I went in there really was no information for me. So I think it is really good for women to have and to know this is what's coming down the pipe for you and to know that there are choices you can make that are going to make it better for you. So I do think it's really something good because it's something that has never been before, right, so it's definitely a step in the right direction. Reference 8 - 0.10% Coverage No, I think it's pretty good, yeah.	6
	<Files\\180617_001> - § 12 references coded [5.77% Coverage] Reference 1 - 0.30% Coverage No, I printed it off and I read it and I did my little checklist, and all that, and I thought, "Well, that's kind of handy." Reference 2 - 0.10% Coverage But the numbers at the bottom were good. Reference 3 - 0.59% Coverage I did. I did compare it, but I thought, "Oh, I think I'm going more important ones than I did before." 'Cause I thought, "Well, there's things that I probably can control, or you just have to accept that it's also a part of menopause," right? Reference 4 - 0.39% Coverage Yeah, I was overwhelmed by 75 pages, but then I went, "Oh, some of them are going to be like, you know, cover page for this and that," so, it went pretty fast. Reference 5 - 0.48% Coverage And it wasn't heavy reading. And for me, because I've been on it for a while, there was a lot of stuff I	7

	already knew. But, for someone' who's just facing it, I thought it's good information, right? Reference 6 - 0.27% Coverage I think it was. And, of course, you're overwhelmed at first, but you just take little bits at a time and yeah. Reference 7 - 0.41% Coverage But what's to say about not using it? Like, what are you going to put? If you don't, you don't. So, what are you going to say? But if you do, you need that information. Reference 8 - 0.68% Coverage Yeah. And maybe because I use it and I'm pro using it, maybe I . . . think it's heavier that way? I don't know. But, it didn't offend me at all, or think, "Oh brother, this is what they want me to do," because I've already made my mind up, right? And I've seen the benefits of it. Reference 9 - 0.53% Coverage I don't think there was. I thought it was the facts, yeah. What are you going to do if you print stories of women who don't take it? "I couldn't sleep, I got divorced," like, honestly, [unintelligible 00:20:07], right? Reference 10 - 0.45% Coverage Yeah. Yeah, so, they had the information in there about it, and then, also, blood clots and, you know, the different things, which are all things you need to discuss with your doctor. Reference 11 - 0.83% Coverage This is on another note, because I use the patch, it said, risk of blood clots, and the risk may be slightly slower for women who use transdermal formulations. So, when I read those things, the transdermal seems very beneficial, and I thought, "Yes! I'm doing the right thing!" So, it just confirmed in me some things, yeah, which was good. Reference 12 - 0.73% Coverage Well, because I'm on hormone, just reinforced in my case it's been a good thing. I don't know. No, it was informative and helpful. Certainly, for people who are just, you know, looking at going on it, but then for me, who's been on it for a while, it just reinforced, I think, some good things, yeah.	
	<Files\\180625_001> - § 7 references coded [2.96% Coverage] Reference 1 - 0.63% Coverage Right. Yeah, I think that's all good. I mean, I read it. It was kind of like… I guess I never knew that before, so I thought that was good. I mean, I probably did, but not when you guys do the graphs. Like, with the little people and stuff. So I think that was... Reference 2 - 0.40% Coverage It was one thing that I actually went back to. You know, I mean, whatever. Whatever little box you look at, it's… You know. So yeah, I think it was good long-term. Reference 3 - 0.25% Coverage I mean, you know, to take home and, you know… I think they're good. I think it was really good, yeah. Reference 4 - 0.09% Coverage The best part I liked are the graphs. Reference 5 - 0.29% Coverage 'Cause – and it's funny that I like that, 'cause normally, I'm not – yeah, I don't understand them. So no, it was good. Reference 6 - 0.42% Coverage I thought it was, overall, really well done. Like, it's not… You know, if I was to have this with me, or you know, if I was new, then I wouldn't feel embarrassed to have it. Reference 7 - 0.88% Coverage You know, if I'm coming to the doctor's or coming to see, you know, saying like I'm having this or having that or making notes. You know, there's still enough room to, you know… Or if you forget and you tab something, you know, to come see your doctor about the risk of stroke, right? If you may not ask the first or initial or, you know, what are my chances, right?	8
	<Files\\180625_002> - § 10 references coded [9.55% Coverage] Reference 1 - 0.91% Coverage Very clear. Yeah I like how it was set up, it was really good. And talking about the different types was great and how you use them, I think that was in that section. Yeah, that did it and how it goes in the bloodstream and all that, it was good. Reference 2 - 0.74% Coverage Yeah, I thought that was a good tool for people that are thinking of it and don't know anything and just	9

	things for them to consider, I thought that was really good, it's a good tool, very good tool. Reference 3 - 0.41% Coverage It doesn't apply to me but if I'd seen it I think it's great, pros and cons and it's nice to have that tool. Reference 4 - 0.83% Coverage Yeah, I thought that was really great. Really, really good, the pictures and the different colours, well it wasn't so much this way it was light and dark. You know, but having that contrast was nice and having some pictures. Reference 5 - 0.34% Coverage This was better to read. And I thought these were great, great tools, great, great tools. Reference 6 - 0.98% Coverage It was okay. It's nice to know where you can go for the people that want to know or find more research without - I mean people just Google nowadays. So I don't know how many people actually use this but it's nice to have. It's not a bad thing, it's a nice to have. Reference 7 - 1.41% Coverage So that may be too long for those type of people and that's why I said both. But I don't think there's a happy medium so if I had to pick either I would say just right. And the reason I'm picking just right is because [unintelligible [00:19:23] if I could see a little book like this and read about it like this. You know, it's so easy to navigate. I change my mind to just right. Reference 8 - 0.46% Coverage Print. I can honestly say that I love them. See people can say one thing and they see something and it's totally different. Reference 9 - 2.38% Coverage I think that the pros and cons also the back tool for how you were before surgery and after because what my knowledge base tells me is not everybody is the same and it's a fine art to decide on the dosages and if you want to go through the patch or the gel or the pills. And I think that keeping track of your symptoms at these times I think would be a useful tool for the medical profession rather than you remembering or writing down. Well you don't remember to write it down. Here it is and you pick your four choices, what could be better to take into your medical professional. Like I really like that, I think that's really, really good. Reference 10 - 1.09% Coverage And the pros and cons beforehand you can actually - for those type of women who can actually see it visually and think this is a pro and con. Instead of just sitting down on a piece of paper pro and con here it's got some of your pros and cons and how do they apply to you? What could be better?	
	<Files\\180710_001> - § 31 references coded [15.24% Coverage] Reference 1 - 1.52% Coverage I like how you talked about the good support system too. I think that's really important. Yeah, for sure. And actually, the part that I liked in here too – and I remember – is about how you said it'll take time to heal physically and emotionally. And that was something that was really downplayed before my surgery, but the emotional part, it's like, "Oh, you should be fine." I said, "Well, am I going to need any, like, hormones? Am I going to need anything after this?" "No, you should be fine. You might need a mild anti-depressant and that's it," that's what I was told. But that part, yeah, this is definitely better. Reference 2 - 0.68% Coverage so yeah, the emotional healing, I hadn't even thought about it. I didn't think it was going to be a big deal. It was going to be, "No, you'll be fine. We'll look in six to eight weeks. You might need a mild anti-depressant and you'll be fine." So, it didn't even cross my mind. Reference 3 - 0.23% Coverage Oh, this section in here? Yes, very well explained about all the things. Yes, it was very good. Reference 4 - 0.56% Coverage And then again, you don't feel so much like you're dying after because like I – there was lots of times I felt like I had been hit by a truck. But when you look at all this you're like, "Yeah, it's right on target with, you know." Reference 5 - 0.29% Coverage No, I think this is good. It wasn't really explained to me in detail about the heart disease, so this is really good. Reference 6 - 0.66% Coverage	10

Yeah, it doesn't really talk about it. It talks about hormone therapy which I think is good because I think you may as well, in my opinion, you may as well fix what's broken, right, and not try throwing a bunch of different drugs – you know what I mean – at something.

Reference 7 - 0.27% Coverage

Yes. No, this is good. And again, I found that this was really good information and it seems the most up-to-date.

Reference 8 - 1.47% Coverage

Because I found that my care was really fragmented with different physicians between the gynecologist and the family physician to the hematologist that I see because of the clot.

He was like, "Oh yeah, you're good with the patch. You're good. You're good. Don't worry about the patch." And then they had to send all the information to my family physician and to – I've seen people at the menopause clinic too because their like, "I'm not sure if you can be on the patches because of the clot.

So, this is good because it seems to be a consensus on the information and the most up-to-date information.

Reference 9 - 0.06% Coverage

No, no this one is good.

Reference 10 - 0.04% Coverage

This is great.

Reference 11 - 0.35% Coverage

I thought they were really easy to follow. I liked how you had this grading system here about the quality of the research. That was really good.

Reference 12 - 0.17% Coverage

It does. It puts it into perspective. Yeah. And this one I really liked.

Reference 13 - 0.54% Coverage

No, I think it was useful because it talks about the extra vitamin D and extra calcium and not necessarily everybody knows that, right? And it talks about the excess of alcohol consumption as well, so I think that's good.

Reference 14 - 0.29% Coverage

Yeah, I think this other stuff is kind of more general, but I think this part is good. Not everybody knows that, right?

Reference 15 - 0.13% Coverage

The more you read stuff, the more it sinks in, right?

Reference 16 - 0.19% Coverage

I liked that section, yeah. Yeah, I liked that. You want to read more. Yeah.

Reference 17 - 0.86% Coverage

Yes, I do. Yeah. I think it's a very good idea. Because as I said before, I think that study gave hormone therapy a really bad name and so people were just like very closed to that option. And then once you read more about it, this is very informative, then you're like, "Oh." And when you see the graphs and everything else too, it doesn't look so bad.

Reference 18 - 0.77% Coverage

This was good because it – kind of like did you understand what you read, right? So yeah. No, I think this is a good idea. And then you can check your answers. I thought that was kind of cool. Yeah. So, it just clarifies – yeah, did you understand what you read? I think it's good. I would definitely put that in there.

Reference 19 - 0.45% Coverage

I think it's good. I think it just kind of gathers up all your thoughts about, "Do I feel like I have enough facts? Or do I need to look further?" And then the support thing was good.

Reference 20 - 0.27% Coverage

Yeah. And then even talk about like drug coverage and things like that because I mean that can impact, right?

Reference 21 - 0.25% Coverage

Yeah. And focus on the opinion of people who matter most. You know, I think this is really well done.

Reference 22 - 0.56% Coverage

And the best thing about this is you have something to discuss with people that you want to talk with it about whereas before it was just kind of like random ideas in kind of grey areas, whereas it's something more concrete to –

Reference 23 - 0.69% Coverage

Very good, yeah. I like the increments that you use too, like before surgery, right after, and then six weeks after because honestly, I didn't even have my head on to look at too many things. You know what I mean, right after. So, no, I think it's good. And the intervals were good.

	Reference 24 - 0.36% Coverage Okay. Yes. And this is really good because you can read so much garbage on the Internet, so this is really good that these are printed and – yeah. Reference 25 - 0.21% Coverage So, yeah. Yeah. No, I think that's really good, the resources on there are excellent. Reference 26 - 0.13% Coverage No, no. I didn't. No. I thought that was okay. Yeah. Reference 27 - 0.25% Coverage Yeah, for sure. Because, yeah, I think you have your facts and you know what to ask. Yeah, for sure. Reference 28 - 0.51% Coverage Well, it was very factual. I liked that I found that my care was very fragmented because everybody had a different opinion and whereas this has evidence based – and it's got your facts altogether there, I guess. Reference 29 - 1.80% Coverage And then after that, my treatment was delayed a long time just because I guess the research – the research and the information isn't out there that you can still be on the patch if you've had a clot before. Your risk is much lower and it's safe [and it's okay]. So, it took time for that to get, you know, for someone the prescribe the patches and stuff. So, there was a big gap in care there. So, at least that talks about this and it talks about that. It's covered in there. So, yeah. I thought it was just – it was really good, actually, honestly. I had little fragmented pieces from all over the place, just little handouts, like. Some of it was lexicom and different handouts you get from whoever. So, this is good. It was very good. Reference 30 - 0.59% Coverage And it followed, actually, a well thinking process through it. Like you said, you did the survey first and then you got informed about your decision and then you look back on it, so you have time to reflect on that stuff and that's very good. Reference 31 - 0.07% Coverage I think it was well done.	
	<Files\\180719_001> - § 11 references coded [3.27% Coverage] Reference 1 - 0.09% Coverage No I thought it was actually quite thorough. Reference 2 - 0.19% Coverage Yeah absolutely and I would say that it would have been nice to have this information before surgery. Reference 3 - 0.05% Coverage Yeah, I think it was good. Reference 4 - 0.10% Coverage You see I like this, I like how this one's got this- Reference 5 - 0.03% Coverage Yes this was good. Reference 6 - 1.24% Coverage What else can I do to maintain my health and reduce risk of hormone therapy...um...I mean these are just kind of life facts right; we all kind of know that. The specific ones though, you know, quitting smoking, avoid excessive – I mean if these things are specifically – like if any of these things, if you didn't do any of them, increased your risk of issues after menopause differently than a person who's never had the procedure then it's worth saying. If it's the same risk to any human being [laughs] regardless of the procedure then it's kind of like 'well we kind of all know what we shouldn't overeat and we shouldn't overdrink and we shouldn't smoke right. Reference 7 - 0.03% Coverage I love this. Reference 8 - 0.37% Coverage I love this. This would have been really nice so that you could actually see what changed are actually happening. I think again here's a really good example, look at your list if possible symptoms. Reference 9 - 1.15% Coverage Yeah because again the other one looks like four symptoms but it's not it's actually more than that right, but look at how hot flashes, night sweats, incontinence, sleep issues, hair thinning/loss, muscle joints, fatigue, low on energy, loss of interest in sex, weight	11

	would be another one, weight gain/loss...because again I heard people say, "Oh I heard you put on all this weight after surgery", well is that true, is that based on diet, is that based on the fact that you're not energetic, is that actually a symptom that can happen simply from the lack of hormones or whatever right? So this list is – I like it. Reference 10 - 0.01% Coverage No. Reference 11 - 0.02% Coverage Not really	
	<Files\\180719_002> - § 19 references coded [6.16% Coverage] Reference 1 - 0.12% Coverage Nope I put that your definition was excellent. Reference 2 - 0.09% Coverage Those were good or excellent as well. Reference 3 - 0.13% Coverage then the emotional impact is - the description is good Reference 4 - 0.16% Coverage Hormone therapy is – I have good for that one, the hormone therapy Reference 5 - 0.26% Coverage Now where are we, so benefits of hormone therapy I have good; risk of developing long-term risks I have good. Reference 6 - 0.18% Coverage risk of developing long-term; risk of hormone therapy is good, that is good. Reference 7 - 0.24% Coverage Steps to maintain health and reduce risk of surgical menopause and hormone therapy, I have good. Reference 8 - 0.21% Coverage I think that it directly relates to menopause and if it does then it should be in there Reference 9 - 0.14% Coverage Other factors to consider, this one I have good down there Reference 10 - 0.19% Coverage And the stories about others were good and I'm assuming the names and the ages Reference 11 - 1.11% Coverage Because I did find it really interesting to take the survey at the beginning and then even – like I know a fair amount about menopause because I've been dealing with it for a long time, but by the time I got down to the end that maybe things are a little bit different in my mind now because I've gone through this information and so now have my values changed after getting more information or have they stayed the same after getting all that information. Reference 12 - 1.04% Coverage Yeah because there's a lot of information in here and you do ask that. You ask if it's too information and I don't think it is because I think that you can – I think you needs lots of information to be able to make an informed decision but it has to be organized and it has to – you have to find a way to go through it all and not have it confusing and this book does that, it helps you go through it without it being confusing; Reference 13 - 0.48% Coverage Okay identify what else you need to replace decisions...oh so identify what else, so I down there the comparison of the first, so what we just talked about I have there, so...I put good on that one Reference 14 - 0.29% Coverage Plan the next step I have as excellent to help me figure out what to do, and tracking information I have as excellent. Reference 15 - 0.17% Coverage I don't think so. I agree with Sheryl, I don't think you need more- Reference 16 - 0.24% Coverage -because after a year you pretty much know how you're responding. Available resources I have good Reference 17 - 0.37% Coverage No I didn't and I've already been through it all, like been through menopause already so sometimes I felt like I was slanted [laughs] but not you guys. Reference 18 - 0.55% Coverage Number seven what did I think of the infographs and figures showing on the risk of the hormone therapy and I put easy. Easy for that reason, I found them very easy to follow; and what did	12

	I think about the rest of it, very easy. Reference 19 - 0.18% Coverage Well no not really because the information that you have is good information	
2. Format	<Files\\180531_0011> - § 1 reference coded [0.30% Coverage] Reference 1 - 0.30% Coverage I think it followed	1
	<Files\\180601_0011> - § 8 references coded [3.59% Coverage] Reference 1 - 0.18% Coverage It's a cute little book. It's much nicer than reading online. Reference 2 - 0.52% Coverage I like the size of it and it's not that you're just reading a whole sheet going down kind of, you know, like a whole PDF kind of document. This is kind of broken up a bit. Reference 3 - 0.40% Coverage No, I don't think it's too small. Although yeah, that could be a problem for some people if their eyesight is not great or something. Reference 4 - 0.94% Coverage I think it's great. I like it. I like the size of it. I like that you know, so you can pick it up and read, you know, short little chapters and get a little bullet of information and go back and read the next subject and the next sort of topic. So I thought it was good, I like how it was split up like that. Reference 5 - 0.64% Coverage Yeah. And I noticed these, because I'm kind of visual, so I noticed these and then I noticed them being used. Something I noticed oh maybe not, I like little pictures in between too, it sort of breaks it all up. Reference 6 - 0.18% Coverage No, I like the way it was laid out, I thought it was good. Reference 7 - 0.22% Coverage I liked the visual, I didn't think it was hard to understand at all, no. Reference 8 - 0.50% Coverage I thought it was good. Yeah, kind of the same as I said before that it's - I like how it's split up so there's not too much to read all at once if you didn't want to.	2
	<Files\\180608_0011> - § 3 references coded [2.37% Coverage] Reference 1 - 1.08% Coverage And I really like the graphs, because you can read it and you can read all the numbers you want but then when you see the graphs it's really clear as to, okay, this is what the results of those studies are showing. Reference 2 - 0.95% Coverage I think it's very good. The clarity is good and, really, what adds value is the infographics and … because if nothing else that's … that portion is an easy read, right, you know, visuals. Reference 3 - 0.34% Coverage I like the size of the book because it doesn't feel overwhelming.	3
	<Files\\180609_001> - § 2 references coded [0.60% Coverage] Reference 1 - 0.12% Coverage And level of literacy is – it's reasonable Reference 2 - 0.48% Coverage -- most… Well, we have our 40-year-old eyes. Most women, if they're in their thirties and forties, they're not going to have issues with this font size anyway.	4
	<Files\\180613_001> - § 6 references coded [3.83% Coverage] Reference 1 - 0.64% Coverage I thought this was really good too, how do I maintain my health and reduce the risk of surgical menopause and hormone therapy. It's pretty much in order. Reference 2 - 0.61% Coverage I like this format, the way this is laid out, this is very nice. And it's probably more inviting than sitting and reading it on a computer screen. Reference 3 - 0.23% Coverage This is more appealing to me; I'm kind of old school. Reference 4 - 0.94% Coverage	5

	Well, I think in the printed copy it gives you a different thought about it. I mean I work on computers all the time but I hate to go through - like I won't do a long survey. Ask me more than five questions you're done [laughs]. Reference 5 - 0.49% Coverage No, I think that the - it just seemed like an awful lot reading it on the computer. It doesn't look so bad on the paper Reference 6 - 0.94% Coverage Yeah. I think putting it in steps is very good so that, you know, this is what I need to do so find out what it is that I can do and then figure out what the values are and, you know, make a decision. I think that's really good.	
	<Files\\180614_001> - § 1 reference coded [0.20% Coverage] Reference 1 - 0.20% Coverage I like the print copy. I'm definitely a paper person, I like the paper.	6
	<Files\\180617_001> - § 7 references coded [1.68% Coverage] Reference 1 - 0.06% Coverage Pictures are always good. Reference 2 - 0.08% Coverage Oh, PDF is fine for me, online. Reference 3 - 0.34% Coverage Just 'cause I could drag it around the house with me a little easier. But, just to know that it's there in the computer, so in the future -- Reference 4 - 0.39% Coverage Yeah, I was overwhelmed by 75 pages, but then I went, "Oh, some of them are going to be like, you know, cover page for this and that," so, it went pretty fast. Reference 5 - 0.28% Coverage No, and I normally need glasses. I think I wouldn't go smaller. Going larger is going to make it more pages again. Reference 6 - 0.12% Coverage No. I could read that without my glasses. Yeah. Reference 7 - 0.40% Coverage I do like the way it is, 'cause each page, although you go 75, you think about that, when you look at each page, you go, oh, I could get through that pretty quick.	7
	<Files\\180625_001> - § 4 references coded [1.47% Coverage] Reference 1 - 0.63% Coverage Right. Yeah, I think that's all good. I mean, I read it. It was kind of like… I guess I never knew that before, so I thought that was good. I mean, I probably did, but not when you guys do the graphs. Like, with the little people and stuff. So I think that was... Reference 2 - 0.66% Coverage Yeah, because I mean, I need glasses, but I thought it was good. There was good colour and the… It was easy reading. I mean, I don't know what the average age is anymore, like for hysterectomies, but whatever. Everybody can get glasses, but I thought it was not too small. Reference 3 - 0.04% Coverage I like the -- Reference 4 - 0.14% Coverage Yeah. So I mean, I could easily carry this around with me.	8
	<Files\\180625_002> - § 12 references coded [8.85% Coverage] Reference 1 - 0.42% Coverage I didn't like the figure people. They were useless and annoying but seeing it in your pamphlet now I like them. Reference 2 - 0.84% Coverage Here they're great because the colours matched these dots and you can see the percentage. On the computer it was just a bunch of these women and it was all very confusing. So let me change my - I'll change it to excellent now. Reference 3 - 0.38% Coverage Yeah. So it's much better in colour, especially these women. I didn't even notice the different colours. Reference 4 - 0.45% Coverage But yeah, it's easy to see, it's easy to understand, the colours and it changes the colours are great, this is	9

	awesome. Reference 5 - 0.31% Coverage Excellent. I like how you have the little pictures; it just broke it up, the reading. Reference 6 - 0.73% Coverage but in this format, this little booklet, this is so much easier and just more engaging because I thought 75 pages oh my gosh. But it went through good but this setup here, this whole book, awesome. Reference 7 - 0.83% Coverage No because I hate small print and I always have to make it bigger or I'm like this and I can read this with no problem. It must be the font type and it's bold. Like this print is bold but this is bolder so it's easy to read. Reference 8 - 0.83% Coverage Yeah, I thought that was really great. Really, really good, the pictures and the different colours, well it wasn't so much this way it was light and dark. You know, but having that contrast was nice and having some pictures. Reference 9 - 1.41% Coverage So that may be too long for those type of people and that's why I said both. But I don't think there's a happy medium so if I had to pick either I would say just right. And the reason I'm picking just right is because [unintelligible [00:19:23] if I could see a little book like this and read about it like this. You know, it's so easy to navigate. I change my mind to just right. Reference 10 - 0.49% Coverage Because it is not overwhelming and big when it's presented like this way. I think it's just right and see my next one is just right. Reference 11 - 1.09% Coverage And the pros and cons beforehand you can actually - for those type of women who can actually see it visually and think this is a pro and con. Instead of just sitting down on a piece of paper pro and con here it's got some of your pros and cons and how do they apply to you? What could be better? Reference 12 - 1.05% Coverage Yes, I love it. I just love the colours you've chosen, how they contrast, it's not all continuous reading like it appears when you get the print. It's broken up well with colours and pictures and, you know, the contrasting. You know, you've got the blue here, you've got the bold, yeah.	
	<Files\\180710_001> - § 6 references coded [2.26% Coverage] Reference 1 - 0.56% Coverage And then, no, I thought his a great visual to show you – like when you think about it, "Oh, no, hormone therapy. Risk of this, risk of that." But when you look at how many people, it gives you that visual out of, you know, really – Reference 2 - 0.26% Coverage I guess it makes you feel more at ease when you look at – oh, that's you know, it's actually very small. Reference 3 - 0.76% Coverage And then find out how comfortable they are about deciding it. No, I think it's good. And I like the way everything – it's very simple. Like it's the way it's, I guess, outlined on the pages and stuff. It's not a whole bunch on one page. Do you know what I'm saying? It's easier to read. It's not overwhelming. Reference 4 - 0.04% Coverage Very organized. Reference 5 - 0.59% Coverage And it followed, actually, a well thinking process through it. Like you said, you did the survey first and then you got informed about your decision and then you look back on it, so you have time to reflect on that stuff and that's very good. Reference 6 - 0.06% Coverage I liked the print copy.	10
	<Files\\180719_001> - § 8 references coded [0.85% Coverage] Reference 1 - 0.26% Coverage Mm-hmm because this book – I actually really like this book, it looks really cute and lots of charts and lots of things that are easy to ready Reference 2 - 0.12% Coverage I think they look really cool and I really like that comparison	11

	Reference 3 - 0.11% Coverage Yeah and I really liked them and they were very powerful. Reference 4 - 0.08% Coverage Again I thought it was fairly impactful. Reference 5 - 0.07% Coverage so I do like how it's been broken out, Reference 6 - 0.01% Coverage No. Reference 7 - 0.15% Coverage Um, I really like this book [laughs]. I think the book is much better than a PDF. Reference 8 - 0.04% Coverage Mm-mm, no it's good.	
	<Files\\180719_002> - § 10 references coded [5.62% Coverage] Reference 1 - 0.01% Coverage I did. Reference 2 - 0.27% Coverage The information on the hormone – on the figures, I thought they were excellent and I found them easy to follow. Reference 3 - 1.04% Coverage Yeah because there's a lot of information in here and you do ask that. You ask if it's too information and I don't think it is because I think that you can – I think you needs lots of information to be able to make an informed decision but it has to be organized and it has to – you have to find a way to go through it all and not have it confusing and this book does that, it helps you go through it without it being confusing; Reference 4 - 0.76% Coverage Okay so the length of presentation...I have just right, I don't think it was too long or too short, and then the amount of information...I had to go too much, too little or just right, and it wasn't – it's not too much or too little but there's other stuff that I think could be added, so I did put too little. Reference 5 - 1.15% Coverage I felt that they were easy to understand and interpret and I thought they were very consistent...and very consistent to me is important because when you have medical issues going on it's really difficult to sometimes think clearly in your head and to have your book laid out very consistently all the way though is easy to follow because then you get to a chart and you go, "Oh yeah now I compare that with this because I - they're both the same", so it's easy to do that. Reference 6 - 0.63% Coverage Deciding to begin hormone therapy or not is a difficult decision to make and this book takes some of the confusion out of deciding my breaking it down and looking at each section individually, making choices along the way, and coming to a conclusion in the end. Reference 7 - 0.07% Coverage Yeah I don't think it is. Reference 8 - 1.23% Coverage But what I liked, like on the website it's all one eight and a half by 11 page written down, so when you start going through it and then you have...of course I'm not going to have any now because I can't find any; and then you have graphs, the graphs are one after the other after the other after the other which is the way it needs to be because that's how it's on the thing; but this is easier to look at and this whole page is just that and this whole page is just that, so I find this is really easy. Reference 9 - 0.10% Coverage at books, yeah I much prefer a book over- Reference 10 - 0.36% Coverage -now I've got to go through 75 pages of writing, but once I started going through it, because you have charts and stuff it goes through really quick,	12

Theme 2	Quotes	Interview
Suggestions for improvement		
1. Suggestions for improving content	<Files\\180601_0011> - § 7 references coded [2.02% Coverage] Reference 1 - 0.28% Coverage This one says flushes but I thought I read flashes somewhere. I mean I'm just being picky. Reference 2 - 0.31% Coverage So here it says that 27, 120, 32, 122 and 76 over here. I feel like almost the 76 should be over here. Reference 3 - 0.19% Coverage Yeah, absolutely. We have to look at that. So pages 24 and 26. Reference 4 - 0.12% Coverage It's geared to people going through it. Reference 5 - 0.43% Coverage Yeah and I do see now that it is for that sort of a more broader category. And available resources would have been really useful for me too. Reference 6 - 0.39% Coverage And then you had also mentioned the hot flashes versus hot flushes, it'd be good to be consistent which is a totally fair comment. Reference 7 - 0.31% Coverage And then also the figures, kind of reviewing those and ensuring that all that information is straight	2
	<Files\\180608_0011> - § 4 references coded [3.61% Coverage] Reference 1 - 1.01% Coverage I read "the symptoms of surgical menopause often include", although it's all there, I just feel like saying you have no idea. Like, is there a way to emphasize that they can be very severe, you know? Reference 2 - 0.58% Coverage So I did feel like … and I'm not sure how you would articulate that but I feel like saying … putting a warning sign Reference 3 - 0.81% Coverage further options for those that can't be looking at the hormone therapy. But, no, other than that … I do like the idea of the tabs though, that's a really good … Reference 4 - 1.22% Coverage And then possibly thinking of a way to incorporate how severe the symptoms are, because I guess the worry with that is you want to … you want them to know that it can be very severe but you also don't want to seem biased or anything like that	3
	<Files\\180609_001> - § 11 references coded [9.89% Coverage] Reference 1 - 1.04% Coverage And one other piece that I was a little bit surprised, that this decision-making tool didn't have, was… Because honestly, I didn't – I made a note when I was reading, when I was doing it – yes, it's important to know the risk and what the risks are for your health, your health – that it comes, your sole risks, your heart attack risks, osteoporosis. Reference 2 - 0.70% Coverage Yeah, and then this is what my note was, was the deaths showed cancer and heart disease. For me, it's brain function. And well… All right my sex life, my memory, and more important to enjoy living, as opposed to worrying about dying. And… Reference 3 - 0.25% Coverage And so that whole cognition part being not in there is part of that informed choice Reference 4 - 0.35% Coverage it's that part of the cognition. It's, you know, it's very important that women know. I didn't know it was a symptom. Reference 5 - 0.82% Coverage And then when people go off on the deep end and they get – emotionally, and they get moody? Well, that's probably why, but they don't understand that their brain is no longer	4

	functioning. And it's mentioned in there about the brain, but it really don't describe that symptom. Reference 6 - 0.19% Coverage But it doesn't describe the symptoms of what that looks like. Reference 7 - 2.89% Coverage So having that very dry of what that looks like… If women pick this up right now and they had surgical menopause last year, and they have not had a HRT – hormone replacement therapy – if they picked it up and read that, it might click in, but because there's not being very descriptive on that… And like I think just the women that I know that are going through natural menopause and who have the surgical menopause, and they're not on hormone replacement therapy, that whole cognition piece is probably the bigger issue, because if you are not healthy in your head or – you don't care if you have a sex life, you don't care – it doesn't occur to you that, yeah, you have vaginal dryness and it is that bad, because you're just trying to cope with the fact that you're living in a fog. And that's the word that I use; it's "living in a fog." So I don't know… It might not be relevant, but I do find that – like, that's as important a piece as stroke risk, heart attack, and… Reference 8 - 0.21% Coverage I think that a description of the symptoms of what that cognition -- Reference 9 - 2.02% Coverage Brain fog. Well, when I tell other people how – what happened to me, it was like – I describe it as – it was like I had a mental disconnect. And that was my brain fog. And because of that, I – and then I worried, and then that started the anxiety. And I was anxious, because one of my… So it snowballed. Like, that whole piece around that cognition actually snowballed and leads into all of those other symptoms that you see in here. But sometimes, that's the biggest symptom, and you don't realise that that's happening. But you notice, "Oh my God. My anxiety's so bad. I had a panic attack today. I took the wrong turn. I had to pull over and freaked out. Blah-blah-blah-blah." Reference 10 - 1.31% Coverage I think that those symptoms, where that cognition piece and how that brain fog looks like to women is probably as important as all of the other pieces that are in here. 'Cause I know lots of women who have had menopause, and they said, "Oh, well, you know, hot flashes, blah-blah-blah-blah. That don't bother me. Blah-blah-blah." But when I talk about the brain fog and all of the things that that brain fog kind of led to, like, oh my God, no. Reference 11 - 0.13% Coverage but the physical symptoms too is the other.	
	<Files\\180613_001> - § 5 references coded [2.43% Coverage] Reference 1 - 0.32% Coverage but I think this could be laid out a little more precisely maybe. I don't know. Reference 2 - 0.23% Coverage It is. I don't know how you could lessen it actually. Reference 3 - 0.37% Coverage Maybe lessen the charts, I don't know. Maybe do small graphs or something, I don't know. Reference 4 - 0.22% Coverage I want to look at a chart that just tells me exactly Reference 5 - 1.29% Coverage Yeah. I think putting it in steps is very good so that, you know, this is what I need to do so find out what it is that I can do and then figure out what the values are and, you know, make a decision. I think that's really good. I can't even think of anything maybe other than a few less charts but that's my thing.	5
	<Files\\180614_001> - § 12 references coded [7.19% Coverage] Reference 1 - 1.07% Coverage Well, I guess it depends, right? If somebody isn't seeing a doctor or physician that is capable of dealing with this, which I have found everywhere, they don't know about how bad like the short - like the immediate, these ones, how bad they can really get, right? So their idea of treating you is to give you antidepressant, right to get you through that. So, yeah I don't know.	6

	Reference 2 - 0.41% Coverage Yes, to read it and if you haven't gone through it you're like oh yeah mood changes whatever it's going to be like PMS. It is so not like that. Reference 3 - 0.37% Coverage So yeah, so as far as the long term ones, the symptoms of early surgical menopause, they could also be the long term ones, right? Reference 4 - 0.58% Coverage So yeah and I just did that after you sent me this and I went online and I was looking at it because I was I want to see what this is about. And then when I saw that I'm like yeah, no, I'm not signing up. Reference 5 - 0.58% Coverage It just lays out the facts but it's from a medical standpoint, right? So it's not going to talk about other - I guess it did mention in there that there are other options but it doesn't say what they are. Reference 6 - 1.46% Coverage I think women need to know that only - this isn't the only option, right? There are different hormone therapy treatments for sure. And when I did ask Dr. Shandro at the Menopause Clinic about that, and she just abruptly told me I don't know anything about that so we're not going there. So you're supposed to be looking after the patients, after the people who come to see you, so you need to be aware of whether that, I don't know, it's not from the drug companies so I find a lot of doctors won't even discuss it. Reference 7 - 0.49% Coverage maybe kind of looking, relooking, at where in the values section we should add mood swings because since it kind of can be a risk or a benefit, so kind of re-evaluating that Reference 8 - 0.17% Coverage And it can be a long term thing also not just a short term. Reference 9 - 0.46% Coverage maybe just going through our resource list one more time and just making sure that they've all been reviewed? So we know that we're getting reliable resources out. Reference 10 - 0.72% Coverage And then one I think really valuable point that you made was in the stories about others elaborating on okay, someone couldn't take hormone therapy so what do we do so that people know where to go or what route to go down if that's not an option for them. Reference 11 - 0.33% Coverage another really valuable point you made I think is we stated that there are other options but what are those options? Reference 12 - 0.54% Coverage Just like the, like I said at the beginning the effects, right, long term and short term effects, they can kind of cross over into each other. But yeah, other than that, no, this is good.	
	<Files\\180617_001> - § 8 references coded [4.95% Coverage] Reference 1 - 0.49% Coverage No, because I think it just gives you an overall, and everybody's situation is individual, so then, you have to go deeper with your own care team, right, to see what is going to be applicable for you. Reference 2 - 0.49% Coverage 'Cause I notice where it says, you know, "Early 50s, people should be coming off their hormone," and . . . and so, and that's kind of what I'm looking at now is like, how much longer should I be on it? Reference 3 - 0.22% Coverage Okay, so, that's actually a very good point, having kind of more forms in the tracking form Reference 4 - 1.36% Coverage Yeah, so, why do they want – see now, that brings up a question of – to me to ask at the clinic, hopefully I get back there, is, the benefits and risks of being on or off in your later 50s and even into 60, right? But then, like you said, it's an individual thing where the older woman tried to come off, but her symptoms were too great. So then, do you just lower the dose? You know, what do you do? It's individual, but, again, but, just because I'm at the older age of maybe thinking about coming off, that's where I thought it needed a bit more information. Reference 5 - 1.07% Coverage	7

	But even if we could maybe make that clearer, that after that, you should decide with your doctor whether to continue hormone therapy. Maybe we can just make it more explicit that it's an individualized thing, and dependent on your symptoms, someone might choose to continue. Just so that people don't feel like, "Oh, I'm at exactly age 51, and now I need to go discuss with my doctor and get off this." So, okay, I think that's a good point. Reference 6 - 0.58% Coverage So, the tracking form, possibly having more space to track your symptoms in future years, which I think is important, 'cause it's not something that's limited to within the first year after surgery. So, I think that's a great suggestion. Reference 7 - 0.45% Coverage And I mean, I can take those forms and just cross out 6 months and put 6 years, or whatever. But, having it there jogs your memory that, "You know what? I've got to revisit this to see." Reference 8 - 0.29% Coverage make it a little more explicit that it's an individualized decision when and whether to come off of the hormone therapy,	
	<Files\\180625_001> - § 10 references coded [9.12% Coverage] Reference 1 - 1.05% Coverage It'll like – you know, you can – everything is on, you know, Google Drive or something like that, something that – another person who's going to be going through this surgery can listen to other women. You know how we did the – and used – you know, once everybody kind of opens up, you know, but have it kind of… So they talk about their symptoms, you know, talk about personal – how – what actually happens, how their body changes, right? Reference 2 - 0.58% Coverage I think when I first started with this, I was like – couldn't… Like, I was only 36, so I wasn't 100 percent sure what did what. So that's the only thing. Maybe somewhere in there… Examples. Like, estrogen does this and… You know what I mean? Reference 3 - 0.89% Coverage The progesterone does this. If you have little of this… This is what happens if you have too much of the estrogen. You know, something like that, because as… I'm thinking back to when I was 36, and I was just like, "Oh my God." You know, I had just had my second baby. You know, I had just been dealing with, you know, hormones and too much estrogen. Maybe that, you know? Reference 4 - 0.46% Coverage Right. Like, this kind of – like, when I read this after, like the early death, like I never thought about early death, 'cause at such a young age, right? I just knew that I needed to prevent… Reference 5 - 2.16% Coverage 'Cause both my friends – well, I guess all three of them probably have had depression and are – will probably stay on something because of how they overall feel, right? So I don't know, 'cause depression's not on here anywhere. And when you have a complete hysterectomy, I mean, you do go into a depression of some sort. I think it's just – I don't know how people avoid it. And you know, my other three friends are like – you know, they're active. They're grandparents. You know, they're young grandparents, right? But they all said the same thing, that they just kind of feel – things never kind of picked up after their surgeries, so I don't know. Maybe if there was something… Because I would never have thought depression. I mean, I think that's maybe why I fought Dr. Shandrow so much – you know, that internally I fought it, because I was just like, "Well, why would I get depression?" You know? Reference 6 - 0.55% Coverage I'm sure you… Like, how you guys have your charts here on the stats of, you know, how many women go into depression, how many people, you know, stay in it throughout, or something like that. I mean, I'm sure you guys, you know… Reference 7 - 0.93% Coverage That's the other thing is like not recognising, but having all these weird feelings and crying and trying to get your body regulated and stuff. So I don't know how many people would recognise it. And being 36, I was – you think you have a happy life. I was married, I had two kids, they're healthy, but your body is going through so	8

	many changes. I mean, I never would have recognised it. Reference 8 - 1.00% Coverage making the depression part a little more explicit, just so people know to watch out for it – so, whether it's talking about there's a spectrum for mood changes to like depression, and maybe adding in some stats on depression, so that women have an idea of how common it is. Possibly considering maybe a bigger print, if that works out. And then you agreed with the tabs idea, that that would be a valuable add to it. Reference 9 - 0.09% Coverage Well, one thing is your family life. Reference 10 - 1.40% Coverage Yeah. Yeah. Something for – I don't know – because it's all about us, but yet it's – when you're married, it's not really all about us; it's about how it impacts our kids and being sick or having mood swings or being, you know, a cow. You know what I mean? It's difficult. So yeah, I think for sure that it should be implemented someplace around… You know, I don't know about – I haven't really talked to my friends about… You know, they have all been married, you know, over 25 years, so it was tough. I think it was tough on our husbands, so… Yeah, I think that's about it. I think…	
	<Files\\180625_002> - § 4 references coded [3.80% Coverage] Reference 1 - 2.02% Coverage There didn't say anything about people staying on them longer. You seem to pick the age of 50 as the stopping point and maybe not mention the age, just say, you know, you know, maybe say usually early 50s or a lot of times, a lot of times when you're in your early 50s wouldn't be so - come off as stark when I read it. Because when you're this age or this woman is this age. If you said usually in your early 50s or most times in the early 50s people come off wouldn't be as abrasive as saying exact age and then that's followed up by that woman. Reference 2 - 0.83% Coverage It's just everyone knows that, you see it other places it's you should be healthy, you should be eating healthy, you should be exercising. You're told that everywhere so putting it in here it's like oh, why is this in here? Reference 3 - 0.81% Coverage you know, like you noted some ways like most times in your early 50s or a lot of times in your early 50s and then also mentioning that many people don't do that or aren't able to come off and that that's okay as well. Reference 4 - 0.14% Coverage Yeah, so toning that down to be softer.	9
	<Files\\180710_001> - § 20 references coded [10.95% Coverage] Reference 1 - 0.41% Coverage you've got the mood changes in here, but I know, like for me, I had a lot of anxiety after. So, I'd just add just maybe more about the emotional impact of the anxiety. Reference 2 - 0.52% Coverage And then the early death. This one I find interesting. Maybe we can expand on this one. Just about the early death. Like what – you just say early death. Like is it – you're saying here it's just overall, right? Reference 3 - 0.28% Coverage Is it more related to heart or is it more – you know what I mean? Like is it more related to stroke or heart or.... Reference 4 - 0.42% Coverage Yeah. Yeah, with that again, maybe just a timeframe that people can kind of expect, you know? And like I said, maybe a range from just mild to full-blown depression, right? Reference 5 - 0.22% Coverage So, I don't know if that's something that could be, I don't know, maybe included in there. Reference 6 - 0.94% Coverage Yeah, Okay, this section, I did this section because – I'm not sure. Maybe I'm wrong, but I always thought if you keep your uterus you need the combination therapy. See, it says here estrogen only therapy for women who keep their uterus. But estrogen is only – estrogen only is you have not kept your uterus because you need the progesterone you put yourself at risk for cancer, right?	10

	Reference 7 - 1.02% Coverage My only other comment about this section was it talks about protect the uterus from cancer of the uterus. So, what I had, endometrial hyperplasia with atypia, which they call, "A pre-cancer," right? So, then you always – in my mind I was thinking, "Oh no, should I be on hormone therapy then?" Because they called it a pre-cancer and had stated in here before – I think it was this section. Maybe it was another one. Reference 8 - 1.11% Coverage Oh, right. A woman who's had breast or uterine cancer should talk to her doctor about whether it's appropriate or not. So, like I said, when it says uterine cancer – they called what I had endometrial hyperplasia with atypia a pre-cancer, right? So, then I don't know if they want to mention anything about it because everybody has different reasons for getting a hysterectomy, right? So, I'm not sure if that's something that needs to be mentioned or not. Reference 9 - 0.19% Coverage I liked that section, yeah. Yeah, I liked that. You want to read more. Yeah. Reference 10 - 0.08% Coverage Yeah, I think that's a good idea. Reference 11 - 0.91% Coverage Yeah. The tabs would be good idea. The other thing I wanted to talk about was dosages. You don't have any dosages of anything in here, like what compares of an oral dose to a patch to a – so that you have some idea of kind of where you should be. Do you know what I – like it's just because of like a big – it's like a big forest out there, but what dose you should be one. Reference 12 - 0.37% Coverage Like just typical or what your average person, maybe with surgical menopause is on in a tablet, a patch, and what's the other from? A ring or whatever. Reference 13 - 0.07% Coverage Yeah, that's a good idea. Reference 14 - 0.70% Coverage Just like I said, looking for like average dosages because it just looked like a big sea of where you start and what you should be on. Am I on too much? Am on too little? You know, like yeah, that would have been nice. And the testimonials, like that's really nice to read more of those. Reference 15 - 0.88% Coverage So, one thing is specifying the mood changes a little bit, talking a little bit about the anxiety and the depression that it can cause and that it can be long-lasting so that people know it's not just transient and mild. And then, also expanding on the point about early death because it is pretty ambiguous. I definitely see where you're coming from on that. Reference 16 - 1.32% Coverage And then for managing symptoms, we talked a lot about hormone therapy, but we didn't really touch on anti-depressants. So, talking about that would be helpful. And then fixing that big typo there that you find about estrogen only when it should be estrogen and progesterone for those who keep their uterus. Possibly seeing if we can incorporate pre-cancer because it's kind of a grey zone so that people know they can discuss this with their doctor. Looking back to the booklet size, because maybe an actual, like, 8½ by 11 size would be good? Reference 17 - 0.21% Coverage And then you agreed with the idea of adding in more tracking forms for beyond one year? Reference 18 - 0.26% Coverage As well as possibly adding tabs in it, talking about what estrogen/progesterone do. And, yeah, so that Reference 19 - 0.85% Coverage Maybe we could also – like maybe you could also include a little section about – like say you start on a hormone therapy, whether it's patch, pills, or whatever, right? Maybe like a little area to journal, like this is this dose and these were the side-effects I was feeling today. You know what I mean? Like a little journaling section. Do you follow? Reference 20 - 0.19% Coverage So, like kind of a tracking form, but for the side-effects of the medication?	
	<Files\\180719_001> - § 35 references coded [23.98% Coverage] Reference 1 - 1.58% Coverage	11

I feel that the list is short because when I went to the menopause clinic and they gave me this page of possible symptoms and I knew of difficulty sleeping, mood changes, I think those were the main ones and maybe the fourth one on the list, I think maybe those three I think I knew about and it seemed like, 'well I can manage all those so I don't need hormones' was kind of my view of it but when I went to the menopause they actually had a list of all of these things, very broken down and very detailed and I looked at that list I checked off so many things I didn't even know were related to it. That to me was quite helpful, I mean that was - when I looked at that list and checked everything off I need to be on hormones, just the moment I looked at that list because I didn't know all those things related, and it was a lot more than this.

Reference 2 - 1.12% Coverage

so for example here it says 'mood changes', so that seems really minor when you see it like this, but for me seven years after the surgery I was emotionally numb. I did not cry at sad movies, I did not get mad, I didn't get angry, I didn't – was never extremely happy, I was numb. I had no ups or downs or anything, it was just all the time and that was a huge thing that I noticed without the hormones, which yeah sure you can call that a mood change but if you, you know, to read it as such is emotionally numb, you don't have emotions, that's a big difference between that and mood changed right?

Reference 3 - 1.37% Coverage

mood changes sounds like PMS right, you go through mood - so that sounds kind of like, well we all have mood changes. It doesn't sound like a condition, it sounds like well everyone goes through mood changes. So to me the – calling it mood changes seems to lessen the severity of what it could be. I would call it psychological challenges, so then you can say in there, 'could be depression, could be lack of connection or empathy or whatever'; and then yes it could be the whole...some people would have that lack of feeling like a hormone or whatever but that's not the only thing. It can be completely unrelated because a lot of my symptoms I said I didn't even know would have been connected. I would have never connected those dots.

Reference 4 - 0.60% Coverage

Yeah almost like the other way around saying, 'Difficulty sleeping due to low oestrogen levels and it could be – it's just one of those – when you see the hot flashes for a lot of times people see the first part and they don't see the rest of it right; so you see that, 'well I don't have hot flashes, it's not a concern'.

Reference 5 - 0.64% Coverage

so you have hot flashes which would cause trouble sleeping, you have insomnia because of – you know those things - to me it was so much more powerful see in a list, not detailed but breaking these bullets, these could all be more bullets right, that loss of interest in sex is one, painful sex would be another one; do you see what I'm saying?

Reference 6 - 0.13% Coverage

I talked about that one. I think you could add depression to this one

Reference 7 - 0.56% Coverage

The moment you have a bunch of different issues like difficulty sleeping, you know, have problems in that area and problems in that area and problems in that area; definitely that would be a long-term effect, it's not something that's going to happen overnight but could absolutely happen to people.

Reference 8 - 0.73% Coverage

I guess I felt like maybe what would be beneficial – maybe it's just a link or something but reading it you don't really understand what some of these thing are, like someone might not understand what a patch is or the fact that you have to wear a patch, to change it twice a week. I mean for me I'm still young so it's twice a week probably for the rest of my life. That's kind of big right?

Reference 9 - 0.20% Coverage

Or the tablet or those different ways, there's ones that you can take orally and then there's other type-

Reference 10 - 0.73% Coverage

Yeah exactly, so I don't necessarily know that it needs to be in here or like even some of these things. If you were wanting to know more about that it would be kind of helpful to have a bit of a link or something or somewhere to point you to where you

could actually get more details, or whatever exactly is a cream, because a cream, well that sounds reasonable, I could just use that right?

Reference 11 - 1.42% Coverage

and at that point actually, and I don't know where in this book would be a good place for it, but I think that's a really good point to make, that the hormones that you go on for therapy are lower than the birth control pill because I know women who are quite and confident, "No I'm on the birth control pill", "What pill?" because I've got osteoporosis but I'm not going to go onto hormones after surgery, like that would be crazy; like "Actually you do realize that the stuff you're on is a lot higher dose", and they don't because one has been socially acceptable for women to take all the time and the other one has these bells of cancer ringing on people's ears and they don't see to – even the doctors - not all the doctors seem to understand that either.

Reference 12 - 0.15% Coverage

And to it's almost a caveat at the beginning of the book, "Hey did you know"?

Reference 13 - 0.66% Coverage

Yeah be brief there, and then if you want to have more detail what that stuff is you could always have a, you know, in the reference section say, 'here's more details of that would be' but take some of those point and break them shorter because I just think it – because of the amount of information and the stuff like that that can be bulleted, bullet it.

Reference 14 - 1.54% Coverage

You need to find the mean because...so what I would do because people are absolutely going to compare these two things, and since this is in the same category it would make much sense is if this is obviously out of a 1,000 women; make it out of 2,000 women and then you could have the same stats on both pages right because it's - so this is out of 1,000 women and this is out of 1,000 and these are different women. Put the groups together now it's out of 2,000 and you could use statistics and you could have percentages...because otherwise it's just confusing [laughs]. I mean if you had three groups you could add them all up and divide them; and you could probably do out of two, you could divide it and add them up to 2,000 and then find out what the average is between them and then just do the average of say 100 women or-

Reference 15 - 0.31% Coverage

-compare; and then having, you know, obviously you need to have one chart that shows for regular women, but I really think they need to have the same information.

Reference 16 - 1.36% Coverage

Yeah, yeah really good. I think there was one thing here that you didn't say that I thought might be valuable to have. I mean it's not exactly directly related to hormone therapy but it's just the fact that if you have – and I don't know if this is the right place to talk about it but I know in here somewhere I don't want to mention it, if you have the hysterectomy to begin with, if it's a full one you know you won't get a ovarian cancer, you won't bet cervical cancer, you won't get – right, that might be something 'by the way did you know if you have this procedure your risk for this is zero [laughs] and if you don't you know-', and it will come up in one of my other questions so I'll wait till we go further one that.

Reference 17 - 0.35% Coverage

And see – so I just feel like there needs to be a bit of a precursor and I don't know if that's a different group who does that or a different study that used to do that and if there's-

Reference 18 - 0.81% Coverage

Because well let's see, does it say it in the surgical menopause part, does it say-? [B-roll] See okay, right here it says surgical menopause is the removal of both ovaries which can lead to a sudden drop in hormone levels so it seems like this book is now dedicated to people who have had both ovaries removed, so if this hormones actually also affect people who haven't had both ovaries removed then that needs to be in there too right.

Reference 19 - 0.91% Coverage

It would be wonderful if it was even in the beginning of the book saying, a two page thing saying "So your doctor told you that you should get a hysterectomy, here are some things to consider, do you get your ovaries out, do you have a choice? If the doctor says no you should get your ovaries out do you stop there and go "Okay

	doctor", or do you have a choice to say, "Actually no I want you to take them", or, "Okay refer me to someone else because I think you're not listening to me"." Reference 20 - 1.78% Coverage Yes and the reason it was really cool reading the stories because I was there for that session so I know all the people that told the stories, but what was missing – so if I was reading it as someone who hadn't been there for the whole thing is...okay so are you liking being on the hormones, so are you right now complaining saying this is where I'm at; like this one says I shouldn't be on hormones so my question was 'oh so is that going okay with you, are you having issues with this'. This one says, 'after seven years I haven't been on hormones but now I am', so is this a good thing or bad thing; so what does that mean, is it – I don't know what's the moral of your story? The moral of my story is I'm in a good place now because now I'm doing this, and you know hormones I'm giving a thumbs up or bad experience with hormones can't be on them thumb down, you know. To me these stories would be more impactful if I actually knew how they ended. Reference 21 - 0.71% Coverage I have no idea if the hormones affect cervical cancer or ovarian cancer because it's talked about breast cancer and heart disease but it's left those two things out which seems like they would be related somehow; and again if one of these sections was use hormone therapy right before there it says, keep ovaries or whatever, yeah you have an increased chance of ovarian cancer. Reference 22 - 1.59% Coverage Yeah...yeah I think it's good. Again a link in the resources that talks about, you know, the actual procedure, the actual surgery right would be useful to – because you can go online. I mean I went online and today I was reading how people who don't get their ovaries removed and have endometriosis and that's why they're going to get the surgical menopause or hysterectomy to begin with, if they don't get their ovaries removed there is 65% chance of endometriosis coming back. I feel fairly confidence that's probably accurate because I remember my surgeon saying that, but again I don't know if I'm checking a valid website. It's the internet right, it could be anything out there, it sounds plausible and it sounds like a valid website but under the resources it had 'here are some legitimate resources you can check out for surgical menopause'. Reference 23 - 0.15% Coverage -all I had to add on there was that the pre-surgery resources would be wonderful. Reference 24 - 0.88% Coverage you know what I can think of one more thing that this hasn't discussed anywhere that is actually really important, and it's 'how long are you on hormones?" We're talking about going on hormones here, we're talking about the effects of them, you know, 'oh so you're going to be on it for just six months' oh I have a risk of osteoporosis and all that stuff and bone loss and all sorts of things so I was told I have to be on this for the rest of my life and that's unusual Reference 25 - 0.27% Coverage Does it talk about the hormone levels, like I said compared to the birth control; and I think that would be a beautiful chart to actually saying- Reference 26 - 0.79% Coverage -'this is the dosage of what people are on when they're on birth control. This is what we're talking about you being on', and this is what – and this was the important thing that I did at the menopause clinic, and they said, "This is what your normal levels are", so comparing this is your normal levels, this is the artificial levels and this is what you get when you're on the pill", to have a beautiful chart like that-	
	<Files\\180719_002> - § 13 references coded [6.00% Coverage] Reference 1 - 0.52% Coverage Gosh there's so many, dry eyes is one of them. I have problems with my eyes all the time...there's so many, skin-. Every part of your body is affected by oestrogen, some to higher degrees and some to lower degrees. Reference 2 - 0.35% Coverage You do have - down in the resources you have a little resource there about another place to go but I think it would be nice to have it in here. Reference 3 - 0.93% Coverage	12

	Oh okay, yeah. So it's both ovaries and do not use hormone therapy, both ovaries and use hormone therapy, both ovaries or keep ovaries and not use therapy, and keep ovaries and use therapy is what I'm thinking because it would be interesting to see the difference between that because you don't have information on women our age. You don't have a lot of information on women our age. Reference 4 - 0.69% Coverage That what this is all about right? So that - I would be interested to see how that would be – the difference of these two would compare whether you had both of your ovaries removed and didn't or did use hormone therapy, or kept both your ovaries and did or didn't use hormone therapy. Reference 5 - 0.47% Coverage Okay so basically – okay so what I'm getting is we should make it more clear because here' it's not very clear that this is not hormone therapy and the other one is using hormone therapy, okay. Reference 6 - 0.51% Coverage So you have a whole section of breast cancer stuff, I would be – like I am more concerned of cardiovascular information and you do have a little bit about that but not as much as you do with the breast cancer. Reference 7 - 0.61% Coverage Because there's a few things that are way more serious than others right, breast cancer, heart and strike disease, that's more serious than hot flashes and night sweats and a dry vagina; so I would just like to see more about cardiovascular as well. Reference 8 - 0.72% Coverage I think it would be helpful to have it because this is like a little workbook to put that in here at the end with all, you know, not included in this but either before or after it so that you can kind of look and see where you're at when you're in the final steps of making your decision process. Reference 9 - 0.26% Coverage Because you don't need to put everything down, and the menopause clinic doesn't put everything down either. Reference 10 - 0.24% Coverage including alternatives to hormone therapy like it says that we would include, that would be helpful Reference 11 - 0.32% Coverage like you mentioned we have like a vast amount of information on breast cancer but also focusing on cardiovascular just because- Reference 12 - 0.33% Coverage So can you put that in there that genotyping is possible, speak to your doctor or whatever, whatever you guys say in those fancy words Reference 13 - 0.05% Coverage It should be pages.	
2. Suggestions for improving format	<Files\\180601_0011> - § 3 references coded [1.13% Coverage] Reference 1 - 0.22% Coverage I think it's good unless people like those little tabs to have sections. Reference 2 - 0.42% Coverage You know, especially if you like looking through and where's that information about the resources, you know? So you can have a little - Reference 3 - 0.49% Coverage You mentioned that it would be a good idea to think about putting tabs in there, which I think was a really good comment, to easily find what you need to look for.	2
	<Files\\180608_0011> - § 1 reference coded [0.81% Coverage] Reference 1 - 0.81% Coverage further options for those that can't be looking at the hormone therapy. But, no, other than that … I do like the idea of the tabs though, that's a really good …	3
	<Files\\180613_001> - § 2 references coded [1.88% Coverage] Reference 1 - 0.77% Coverage whatever you can reduce. Like you have kind of put in a graph here, maybe sometimes pictures are better than words though. But maybe the pictures - like to me this doesn't mean anything. Reference 2 - 1.11% Coverage I think a sentence saying use of estrogen therapy may - there's a risk of breast cancer associated with	5

	estrogen [therapy.] It may, I don't know if you could say lessen. Like there's very little difference between not using estrogen therapy and using estrogen therapy.	
	<Files\\180614_001> - § 1 reference coded [0.21% Coverage] Reference 1 - 0.21% Coverage Yeah probably instead of having to flip through to see where you're going.	6
	<Files\\180617_001> - § 1 reference coded [0.41% Coverage] Reference 1 - 0.41% Coverage I mean, 'cause you guys could've condensed it down to smaller print or shoving more on a page. But, and then, what would it be? 50 pages? And then, still, it's, yeah . . .	7
	<Files\\180625_001> - § 1 reference coded [0.23% Coverage] Reference 1 - 0.23% Coverage No. Maybe it could be a little bit bigger. Maybe. Yeah, I bet it could be a little bit bigger.	8
	<Files\\180625_002> - § 1 reference coded [0.37% Coverage] Reference 1 - 0.37% Coverage Yes and that you strongly suggest people read it in colour instead of black and white definitely.	9
	<Files\\180710_001> - § 3 references coded [0.49% Coverage] Reference 1 - 0.19% Coverage You could probably, honestly, I think I would make it a whole booklet size. Reference 2 - 0.24% Coverage Yeah. I think if you made it a booklet size, like how it printed out, I think it's a good idea. Reference 3 - 0.06% Coverage Oh, that's a great idea.	10
	<Files\\180719_001> - § 6 references coded [3.27% Coverage] Reference 1 - 1.12% Coverage Okay so what I think – what I was trying to say was that what you've done nicely here is compare – take is some five or six high-level things and then in here you've explained them all and put them all out, however some of them can stand on their own right, so you have hot flashes which would cause trouble sleeping, you have insomnia because of – you know those things - to me it was so much more powerful see in a list, not detailed but breaking these bullets, these could all be more bullets right, that loss of interest in sex is one, painful sex would be another one; do you see what I'm saying? Reference 2 - 0.31% Coverage I realize that this is a cause of this, like one of these is causes of that, but even maybe let's say these were bullets under the bullets; do you know what I mean? Reference 3 - 0.53% Coverage Okay so this is your topic, this is your main bullet, then you could say like a bullet point that you're, you know, you're thin and fragile, that...you could have discomfort during sex; like you could break things out as bullets rather than not a long explanation, you know what I mean? Reference 4 - 0.17% Coverage Because just seeing a list, for me it was a lot more impactful than reading all the details. Reference 5 - 0.95% Coverage Mm-hmm because this book – I actually really like this book, it looks really cute and lots of charts and lots of things that are easy to ready, but I definitely think – I mean here we got some - a lot of writing or whatever and that's fine but I think the things that you – you know you want to make a point pretty quickly; like this one here you're going to read that. You're going to read what is sort of going on and so you're going to read all of this but symptoms type of thing, a bulleted list makes so- Reference 6 - 0.18% Coverage then the infographic, revisiting that and figuring a way to compare the two pages to each other;	11
	<Files\\180719_002> - § 9 references coded [3.60% Coverage]	12

	Reference 1 - 0.95% Coverage You have one at the beginning, so you go through the information and you check it off according to what you already know before going through this and then you have one at the end; so you go through it after you've got the information but there's no conclusion, there's no place where you can take the two, the charts that you have and put them together to figure out where our charts are. Reference 2 - 0.54% Coverage There's no place in your book, you've got all the little, like these at the end but there's no place to put the two comparisons side by side so you can see where you were before and where you are now to figure out what you- Reference 3 - 0.43% Coverage Like put them on, even on – so you can just copy your answers from the first section onto this page and have your answers from your last section on that page and then you could- Reference 4 - 0.45% Coverage -and I can go back and look at the end and I can compare then myself, but I think it would be easier if you just had them in one spot at the end where you can just put them together. Reference 5 - 0.21% Coverage -pre-book and after the book, and then you could go back just to the same page and- Reference 6 - 0.06% Coverage So on page 40 to say- Reference 7 - 0.13% Coverage Refer back to page 9 for answer sheet', or whatever. Reference 8 - 0.50% Coverage then with the infographics, we've gotten a couple of people with the same comment, that it's not necessarily clear that one group is taking hormone therapy and one is not, so making those labels more clear Reference 9 - 0.34% Coverage having a way to easily compare between the two and maybe just putting them both on the same page like you mentioned, that was a great idea.	

Theme 3	Quotes	Interview
Value of tool		
1. Usefulness	<Files\\180601_0011> - § 2 references coded [1.11% Coverage] Reference 1 - 0.59% Coverage Yeah, this should have been around before I - because you have so many questions, you don't know. It's like going into the unknown. I had no idea so this would have been really helpful for sure. Reference 2 - 0.52% Coverage I just thought it was really well done like I said before. I think it's well done, it's useful and it should have been done a long time ago. Women need this so good on you.	2
	<Files\\180608_0011> - § 3 references coded [2.09% Coverage] Reference 1 - 0.48% Coverage Absolutely. Because I do think that's what it's all about is personally what's important to you. Reference 2 - 0.66% Coverage Because these decisions just aren't black and white, it's not like you can just go to a doctor and say is this the right way to go. Reference 3 - 0.95% Coverage Yeah, because that's the thing is when you're trying to do the research yourself you don't know if … you know, do you trust that information, especially everything's on the internet, right?	3
	<Files\\180609_001> - § 2 references coded [0.85% Coverage] Reference 1 - 0.36% Coverage It was a really good tool. And I think that that – when – if I would have had this before, I probably would have changed Reference 2 - 0.49% Coverage I know it's trying to take something that's really, really large and overlooked, and stick it into one compact little peice that's useable for the general population.	4
	<Files\\180613_001> - § 5 references coded [3.81% Coverage] Reference 1 - 1.29% Coverage I would have appreciated this. Yes, this would have been really, really good when I had surgery because I had no clue. My doctor then was very, very good and she did a - she did explain a lot of things to me and I didn't feel fearful about anything. I'm just annoyed that it kept coming back [laughs] the symptoms. Reference 2 - 0.27% Coverage Yeah, yeah, like every piece of information in there is valuable. Reference 3 - 0.57% Coverage And I think it encourages you to research, which I think is more people need to do that rather than just go to my doctor and I want a pill. Reference 4 - 0.59% Coverage And it gives you the opportunity to decide yourself and we need to make - be a little more proactive in how we accept our own treatment I think. Reference 5 - 1.09% Coverage Yeah and I do get - like that to me is very well done. You know, sometimes we go to the doctor and they just say here, take this. No, I don't want to do that, I want to know why I'm doing that. Some people don't care but I think a lot do, I think a lot	5

	more do now.	
	<Files\\180614_001> - § 1 reference coded [1.28% Coverage] Reference 1 - 1.28% Coverage I do like the information that it gives. Like I said before I went in there really was no information for me. So I think it is really good for women to have and to know this is what's coming down the pipe for you and to know that there are choices you can make that are going to make it better for you. So I do think it's really something good because it's something that has never been before, right, so it's definitely a step in the right direction.	6
	<Files\\180625_001> - § 1 reference coded [0.88% Coverage] Reference 1 - 0.88% Coverage You know, if I'm coming to the doctor's or coming to see, you know, saying like I'm having this or having that or making notes. You know, there's still enough room to, you know… Or if you forget and you tab something, you know, to come see your doctor about the risk of stroke, right? If you may not ask the first or initial or, you know, what are my chances, right?	8
	<Files\\180625_002> - § 1 reference coded [1.52% Coverage] Reference 1 - 1.52% Coverage Oh, I would love it, oh absolutely I would love it and I wish - and if it wasn't me with my firm I've got to do this, yes I love the pros and the cons and making an informed decision. A lot of women do want to make an informed decision and I know people that have chosen not to go on hormone, they think oh it's horrible doing this to my body. I don't want to take these chemicals. This is an excellent resource.	9
	<Files\\180710_001> - § 4 references coded [2.45% Coverage] Reference 1 - 0.55% Coverage And the best thing about this is you have something to discuss with people that you want to talk with it about whereas before it was just kind of like random ideas in kind of grey areas, whereas it's something more concrete to – Reference 2 - 0.79% Coverage Yeah, for sure. I think it's a good idea. Like I got into the menopause clinic on an urgent referral because I was in rough shape. But it would be nice that, I guess, if it was available to more women, then like the list was so long to get in there at that time. So, it would be nice if more women could access that. So, yeah. Reference 3 - 0.51% Coverage Well, it was very factual. I liked that I found that my care was very fragmented because everybody had a different opinion and whereas this has evidence based – and it's got your facts altogether there, I guess. Reference 4 - 0.59% Coverage And it followed, actually, a well thinking process through it. Like you said, you did the survey first and then you got informed about your decision and then you look back on it, so you have time to reflect on that stuff and that's very good.	10
	<Files\\180719_002> - § 2 references coded [1.16% Coverage] Reference 1 - 0.52% Coverage I had to go through and get a lot of information from a lot of different places to make the decision that I did make and I ultimately feel that it was the wrong decision for me, so don't think that this was helpful. Reference 2 - 0.63% Coverage Deciding to begin hormone therapy or not is a difficult decision to make and this book takes some of the confusion out of deciding my breaking it down and looking at each section individually, making choices along the way, and coming to a conclusion in the end.	12
2. Context of use	<Files\\180608_0011> - § 1 reference coded [1.72% Coverage] Reference 1 - 1.72% Coverage So this resource as well … like, I'm thinking of it … but the doctor that I consulted with was Dr. Capstick. If those doctors that specialize in this type of surgery, like the	3

	hysterectomies, if they had a resource like this to be able to provide to the patient before, you know, to help them make the decision I think that would be fabulous.	
	<Files\\180613_001> - § 4 references coded [3.27% Coverage] Reference 1 - 0.43% Coverage Actually this would be really interesting for somebody who's even thinking of having a hysterectomy, eh? Reference 2 - 1.15% Coverage Sometimes you don't have a choice, I mean there - it could be that. But these are all things that would kind of spark you into okay, this is what's happening to me, there's a reason for it and maybe this is how I - like maybe everyone that's having a hysterectomy should have this? Reference 3 - 0.40% Coverage Yeah. I think this would be really valuable for somebody who was having the surgery, this section. Reference 4 - 1.29% Coverage I would have appreciated this. Yes, this would have been really, really good when I had surgery because I had no clue. My doctor then was very, very good and she did a - she did explain a lot of things to me and I didn't feel fearful about anything. I'm just annoyed that it kept coming back [laughs] the symptoms.	5
	<Files\\180614_001> - § 1 reference coded [1.28% Coverage] Reference 1 - 1.28% Coverage I do like the information that it gives. Like I said before I went in there really was no information for me. So I think it is really good for women to have and to know this is what's coming down the pipe for you and to know that there are choices you can make that are going to make it better for you. So I do think it's really something good because it's something that has never been before, right, so it's definitely a step in the right direction.	6
	<Files\\180710_001> - § 4 references coded [0.89% Coverage] Reference 1 - 0.39% Coverage I thought it was good. I thought it was very comprehensive, definitely. I think too, it would have been good to know this before you even chose to have surgery. Reference 2 - 0.12% Coverage But I think also, it should be given to you before. Reference 3 - 0.06% Coverage Before you have surgery. Reference 4 - 0.32% Coverage Oh yeah, I think I would have known more want to expect and you would have felt like you were going crazy. Do you know what I mean?	10
	<Files\\180719_001> - § 1 reference coded [0.19% Coverage] Reference 1 - 0.19% Coverage Yeah absolutely and I would say that it would have been nice to have this information before surgery.	11
3. Supports of physicians (dissemination)	<Files\\180531_0011> - § 5 references coded [12.20% Coverage] Reference 1 - 1.75% Coverage There always is room for improvement, as to making it more available to many more areas of the medical profession. Reference 2 - 2.29% Coverage I think that if you can make it more available, if your resources would allow you to sort of have a spot or a place in every medical imaging office -- Reference 3 - 2.82% Coverage medical, family physician's offices, public health offices in the outlying areas, especially to people that just a small peak is what's available in your tool and how they could get it. Reference 4 - 4.28% Coverage Yes. Yes, just like small pamphlet. Yeah, the small pamphlets that you see in doctor's offices or in clinics, public health offices about what are the symptoms of meningitis or what are the symptoms of flu, certain type of flu or the … where do you get	1

	the vaccines or how do you … Reference 5 - 1.07% Coverage Yes, or a reference to it, you know, that the doctor has access, so …	
	<Files\\180608_0011> - § 1 reference coded [1.72% Coverage] Reference 1 - 1.72% Coverage So this resource as well … like, I'm thinking of it … but the doctor that I consulted with was Dr. Capstick. If those doctors that specialize in this type of surgery, like the hysterectomies, if they had a resource like this to be able to provide to the patient before, you know, to help them make the decision I think that would be fabulous.	3
	<Files\\180609_001> - § 4 references coded [2.15% Coverage] Reference 1 - 0.53% Coverage The other part was being informed is one thing, but having doctors on the same page and who are able to actually assist you for that decision or go through those steps with you. Reference 2 - 0.32% Coverage But then, that would lead you right back to my issue. You don't always have someone to discuss that with, so… Reference 3 - 0.89% Coverage I didn't have anyone to ask information to, doctors weren't able to help me, and as long as there was some study on this out there, and that was to a predominant theme, that was the direction [unintelligible 00:33:21]. "Well, you can look it up." But you know, who really wants to sit down and read -- Reference 4 - 0.41% Coverage Well, and I should go to the research documents. And if we can't get to there, and if we don't understand that language, then you're not…	4
	<Files\\180614_001> - § 2 references coded [1.05% Coverage] Reference 1 - 0.41% Coverage And when you go see the doctor and they tell you I don't know what to do with you, that doesn't help that when you're in that position, so yeah. Reference 2 - 0.64% Coverage I think this is really good, I think it's just a matter of getting physicians to relay it to the patients to say, you know, this is going to happen to you. Not, you know, oh yeah we'll just do this and see how it goes, right?	6
	<Files\\180617_001> - § 3 references coded [1.27% Coverage] Reference 1 - 0.48% Coverage No, because I think it just gives you an overall, and everybody's situation is individual, so then, you have to go deeper with your own care team, right, to see what is going to be applicable for you. Reference 2 - 0.23% Coverage I think so. Yeah. And I always encourage them to discuss with their doctor, because their own -- Reference 3 - 0.56% Coverage So, where is this going as in exposure to women? Because, I didn't know it was out there 'til you contacted me and said, "Would you do this?" So, you guys are just developing this? Is it going to be in doctors' offices and stuff?	7
	<Files\\180710_001> - § 5 references coded [2.91% Coverage] Reference 1 - 0.64% Coverage So, I don't know if that's something that could be, I don't know, maybe included in there. Because I find too that physicians – I hope more education gets out once this gets out there, because I find physicians too, that they're very still scared to prescribe. Reference 2 - 0.43% Coverage I feel like this information isn't out there, especially in maybe physicians that aren't up to date on everything. What they remember is that study – what was it called? The W – Reference 3 - 0.22% Coverage Yeah, that's a good idea. And so, will physicians be trained on this tool and how to use it? Reference 4 - 0.81% Coverage And like maybe having – I know you're going to get this published first it's for the menopause	10

	clinic specifically, but if this could even be in the physician's offices. You know what I mean? So, it could help those women before they got to that really bad point where they needed to be in urgent referral to those clinics, right? Reference 5 - 0.81% Coverage Yeah, I guess you could do a link to it. That would be a good idea. But as I said, after those first weeks after you've had the surgery, to even get to follow that link, it just looks like a bunch of words on a page. But I think if you had a book in front of, you know what I mean, that was clear and concise, you know, like – yeah.	
	<Files\\180719_001> - § 6 references coded [6.29% Coverage] Reference 1 - 0.93% Coverage Yeah I...and you know the other challenges. I mean it says wonderful things like 'you should discuss it with your doctor'. I have an awesome doctor who knew right away, "I don't know what's best for you, I've got to send you to a clinic"; and she sent me to a clinic who then had all these options and the doctor's like, "Okay that's great now I know". But you know most doctors don't actually necessarily know about all these things let alone in which circumstance this person would use this one. Reference 2 - 1.59% Coverage Because you mentioned about having it in the menopause clinic but the thing is there's a very, very small percentage of women actually get to the go the menopause clinic and usually when they get there it's because they have a problem. It's not accessible to the majority of people. I think in my humble opinion the most important place for it is with the surgeons. It would be good for the surgeons to read it, it would be really cool if there was an initial, you know – because there's again very few surgeons who do the surgical menopause or the surgical hysterectomy's, there's very few of them that do it and their clinics are quite small and it would be I think fairly easy just to get a couple books in those clinics because that's when the decision needs to be made because by the time the menopause clinic these charts are no longer relevant. Reference 3 - 1.94% Coverage That's after the fact right, that's a year down, two years, five years, 10 years down the road and you should already be on hormones by them because the thing is, is that you need to have this information before you've been off hormones for long; so they need to be in the surgery. They need to be in that preliminary you've gone to see the surgeon, he's talking to you about menopause and he should be handing you a brochure or something about this, because the thing is the surgeon's know nothing about the hormones and they really don't. I have yet to hear of anyone who talked to their surgeon that knew anything about this because they specialize in cutting and not in that – and you don't see them after. And so I even asked my surgeon, "Well who do I see about this after the fact?" "Your doctor"; my doctor didn't know diddley about it either and he also said, "And if you don't plan on going to hormones you don't need to worry about it" [laughs]. So they're just concerned with that part, the actual surgery, they don't get all this Reference 4 - 0.21% Coverage And heck even if they don't want to read it well they should [laughs], having available for their patients, yeah. Reference 5 - 0.67% Coverage That's really the first place it's got to go because everything else is just after the fact. It would be lovely if also, I mean the menopause clinic would have it but if – that's only really relevant if they have expanded to the point that anyone can go to the menopause clinic. The menopause clinic I don't know if you guys are working with them at all or not- Reference 6 - 0.95% Coverage So this is kind of nice because they do talk about hormones and in fact, you know, for them maybe it's, you know, something that is in line with what they're doing but it's this part that they give us a handout because you go there and it's a classroom lesson for three hours or something and then you go home, but well if you had this to take home with you those are fairly inexpensive photocopies that they could hand out right, and the book itself is something that they could	11

	just reuse in the clinics right.	

Theme 4	Quotes	Interview
Other Expectations		
	<Files\\180601_0011> - § 1 reference coded [0.84% Coverage] Reference 1 - 0.84% Coverage Yeah or even support groups, I mean we didn't even know - I didn't know there were. I think quite a few of us at that study didn't know that at all. In fact I think there were some women that didn't know about The Menopause Clinic. I think I remember telling a lady about it.	2
	<Files\\180609_001> - § 2 references coded [0.69% Coverage] Reference 1 - 0.28% Coverage They should have… You know, like, they have the Alberta Health Link, where you can call in. Reference 2 - 0.41% Coverage Well, and I should go to the research documents. And if we can't get to there, and if we don't understand that language, then you're not…	4
	<Files\\180613_001> - § 2 references coded [1.98% Coverage] Reference 1 - 1.13% Coverage Oh yeah, 38 years old. Yeah, it's interesting because you get such conflicting stories, like if you saw two doctors in the same clinic you'd have a different idea of what goes on. I do believe that support groups would be vitally important if there's an opportunity for that. Reference 2 - 0.85% Coverage No, not at all. And I do think the supports groups are really - that's what we found last year was everyone just able to talk to somebody else about it. You don't always have that opportunity and that is -	
	<Files\\180614_001> - § 5 references coded [2.48% Coverage] Reference 1 - 1.04% Coverage Yeah, so it definitely has not been a positive - I would not recommend anybody to have surgical menopause or go and have - yeah, unless it was absolutely life or death because it has not been good. The knowledge out there to help you through it is not good. And, you know, there's support groups for everything else, like everything and there really isn't for this. Reference 2 - 0.35% Coverage Right, yeah. And yeah, that's all great information but when you are not yourself it's really hard to do any of that, right? Reference 3 - 0.20% Coverage Uh huh or create support groups for women that have gone through this. Reference 4 - 0.42% Coverage Not so much the tool, no. I just think that there needs to be support groups out there for ladies and to know that they are there for you to use, so. Reference 5 - 0.47% Coverage Really good, yeah. And that's what we said like the Menopause Clinic should offer support groups of some sort, even if it's just you get together and you talk, right?	6
	<Files\\180617_001> - § 2 references coded [0.50% Coverage]	

	Reference 2 - 0.36% Coverage I think so too, as a support system around you, and . . . emotionally, mentally, spiritually, having . . . a place to go with all that stuff, right?	
	<Files\\180625_001> - § 3 references coded [2.02% Coverage] Reference 1 - 0.57% Coverage I don't know. I think maybe if – and I mean, I went to – like, you go into that big session they had and whatever. But I just find, maybe, if there's women maybe on a TV, like how they have those, and you sit and watch that one day or… Reference 2 - 1.06% Coverage It'll like – you know, you can – everything is on, you know, Google Drive or something like that, something that – another person who's going to be going through this surgery can listen to other women. You know how we did the – and used – you know, once everybody kind of opens up, you know, but have it kind of… So they talk about their symptoms, you know, talk about personal – how – what actually happens, how their body changes, right? Reference 3 - 0.40% Coverage And so, I don't know as far as helping other people… I don't know. Like, I thought what would have helped me. I think more groups, like a continuing support group.	8
	<Files\\180719_001> - § 8 references coded [8.73% Coverage] Reference 1 - 1.61% Coverage Yeah so...now...um here's the section where I felt like...I don't know for sure if it belongs in this book but it seems to me like this is step two or three or something in a five step process and I don't know that anyone's addressing step one. Step one is should I have the surgery, should I get my ovaries taken out, and I have a good friend of mine who's about to go for a hysterectomy for osteoporosis and she has a surgeon who's told her, "Don't take your ovaries out; if you take your ovaries out you have 100% of cancer." Where's the book on that because my surgeon told me if I had my ovaries out – if I didn't have my ovaries out I have a very high chance of still having endometriosis, it won't solve the problem that I'm going for, and I have – I'm at greater risk for other things and I absolutely should get my ovaries out as far as he's concerned. Reference 2 - 0.56% Coverage so I feel like there needs to be that, you know that first checklist that you have here about, you know, reasons to use hormone therapy, it's reasons should I get m ovaries and if I do here's the options about hormone therapy right, because before you can decide whether or not you need hormone therapy Reference 3 - 0.95% Coverage There's no information for us for that, it is just the surgeon just says, "This is what you need to do"; and so hey I know that if I take my ovaries out this is something I need to know about and I need to consider. If I don't take ovaries out do I need this, does it affect my hormones at all, heck I still don't even know the answer to that, I don't know if I kept my ovaries if I would need hormones still or if they still provide – they're still giving me everything I need. Do you know that answer to that? Reference 4 - 0.35% Coverage And see – so I just feel like there needs to be a bit of a precursor and I don't know if that's a different group who does that or a different study that used to do that and if there's- Reference 5 - 0.77% Coverage my friend's got her surgery coming up at the end of the month and I said, "Well if you leave them you can always go back and take them, if you take them you can never put them back", because you know her surgeon is so against taking them; but then thinking that in this a woman's choice you should give that information firsthand and not but one person and particularly people who have this bias wheel of things. Reference 6 - 1.59% Coverage Because you mentioned about having it in the menopause clinic but the thing is there's a very, very small percentage of women actually get to the go the menopause	11

clinic and usually when they get there it's because they have a problem. It's not accessible to the majority of people. I think in my humble opinion the most important place for it is with the surgeons. It would be good for the surgeons to read it, it would be really cool if there was an initial, you know – because there's again very few surgeons who do the surgical menopause or the surgical hysterectomy's, there's very few of them that do it and their clinics are quite small and it would be I think fairly easy just to get a couple books in those clinics because that's when the decision needs to be made because by the time the menopause clinic these charts are no longer relevant.

Reference 7 - 1.94% Coverage

That's after the fact right, that's a year down, two years, five years, 10 years down the road and you should already be on hormones by them because the thing is, is that you need to have this information before you've been off hormones for long; so they need to be in the surgery. They need to be in that preliminary you've gone to see the surgeon, he's talking to you about menopause and he should be handing you a brochure or something about this, because the thing is the surgeon's know nothing about the hormones and they really don't. I have yet to hear of anyone who talked to their surgeon that knew anything about this because they specialize in cutting and not in that – and you don't see them after. And so I even asked my surgeon, "Well who do I see about this after the fact?" "Your doctor"; my doctor didn't know diddley about it either and he also said, "And if you don't plan on going to hormones you don't need to worry about it" [laughs]. So they're just concerned with that part, the actual surgery, they don't get all this

Reference 8 - 0.96% Coverage

So this is kind of nice because they do talk about hormones and in fact, you know, for them maybe it's, you know, something that is in line with what they're doing but it's this part that they give us a handout because you go there and it's a classroom lesson for three hours or something and then you go home, but well if you had this to take home with you those are fairly inexpensive photocopies that they could hand out right, and the book itself is something that they could just reuse in the clinics right.

Appendix 7.9. Grade evidence table for surgical menopause outcomes with no HT

Setting: Bilateral oophorectomy before age 45-50 years with no HT versus preserved ovaries

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	no HT with bilateral oophorectomy	Preserved ovaries	Relative (95% CI)	Absolute (95% CI)		
CVD-related mortality (Rivera 2009); No HT means estrogen was either not given at all or discontinued before age 45 years. (follow up: median 25 years; assessed with: Death from CVD was assessed using phone interviews and medical records. For each deceased woman, we obtained a copy of the death certificate from either the records-linkage system or the vital statistics offices of individual states.)[51]												
1	observational studies	not serious	not serious	not serious	not serious	strong association	38/262 (14.5%)	104/1417 (7.3%)	**HR 1.84** (1.27 to 2.68)	**57 more per 1,000** (from 19 more to 111 more)	⨁⨁⨁◯ MODERATE	Important
All-cause mortality (Rocca 2006); No HT means estrogen not given to age 50 years (follow up: range 25 years to 29.5 years; assessed with: all women were followed up passively through review of inpatient and outpatient medical records in the records-linkage system of the Rochester Epidemiology Project, which includes records from the Mayo Clinic and all other medical providers in Olmsted County.16 Finally, vital status was assessed from a death certificate database from the State of Minnesota.)[52]												
1	observational studies	not serious	not serious	not serious	not serious	strong association	23/79 (29.1%)	229/1417 (16.2%)	**HR 1.93** (1.25 to 2.96)	**127 more per 1,000** (from 36 more to 245 more)	⨁⨁⨁◯ MODERATE	Important
Cognitive impairment (Rocca 2007); No HT means estrogen not given to age 50 years (follow up: median 25.1 years; assessed with: Telephone Interview for Cognitive Status-modified assessed at direct interviews)[53]												
1	observational studies	not serious	not serious	not serious	not serious	strong association	33/340 (9.7%)	98/1472 (6.7%)	**HR 1.89** (1.27 to 2.83)	**56 more per 1,000** (from 17 more to 111 more)	⨁⨁⨁◯ MODERATE	Important

CI: Confidence interval; **HR:** Hazard Ratio

Bibliography:

[1] C.M. Rivera, B.R. Grossardt, D.J. Rhodes, R.D. Brown, Jr., V.L. Roger, L.J. Melton, 3rd, W.A. Rocca, Increased cardiovascular mortality after early bilateral oophorectomy, Menopause 16(1) (2009) 15-23.

[2] W.A. Rocca, B.R. Grossardt, M. de Andrade, G.D. Malkasian, L.J. Melton, 3rd, Survival patterns after oophorectomy in premenopausal women: a population-based cohort study, Lancet Oncol 7(10) (2006) 821-8.

[3] W.A. Rocca, J.H. Bower, D.M. Maraganore, J.E. Ahlskog, B.R. Grossardt, M. de Andrade, L.J. Melton, 3rd, Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause, Neurology 69(11) (2007) 1074-83.

Appendix 7.10. Grade evidence table for surgical menopause outcomes with HT

Setting: Bilateral oophorectomy before age 45-50 years with HT versus preserved ovaries

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HT with bilateral oophorectomy	Preserved ovaries	Relative (95% CI)	Absolute (95% CI)		
CVD-related mortality (Rivera 2009) (follow up: median 25 years; assessed with: Death from CVD was assessed using phone interviews and medical records. For each deceased woman, we obtained a copy of the death certificate from either the records-linkage system or the vital statistics offices of individual states.)[51]												
1	observational studies	not serious	not serious	not serious	serious [a]	all plausible residual confounding would reduce the demonstrated effect	7/151 (4.6%)	104/1417 (7.3%)	**HR 0.65** (0.30 to 1.41)	**25 fewer per 1,000** (from 29 more to 51 fewer)	⨁⨁◯◯ LOW	Important
All-cause mortality (Rocca 2006) (follow up: range 25 years to 29.5 years; assessed with: all women were followed up passively through review of inpatient and outpatient medical records in the records-linkage system of the Rochester Epidemiology Project, which includes records from the Mayo Clinic and all other medical providers in Olmsted County.16 Finally, vital status was assessed from a death certificate database from the State of Minnesota.)[52]												
1	observational studies	not serious	not serious	not serious	serious [a]	all plausible residual confounding would reduce the demonstrated effect	10/45 (22.2%)	229/1417 (16.2%)	**HR 1.27** (0.67 to 2.39)	**39 more per 1,000** (from 50 fewer to 182 more)	⨁⨁◯◯ LOW	Important
Cognitive impairment (Rocca 2007) (follow up: median 25.1 years; assessed with: Telephone Interview for Cognitive Status-modified assessed at direct interviews)[53]												
1	observational studies	not serious	not serious	not serious	serious [a]	all plausible residual confounding would reduce the demonstrated effect	3/87 (3.4%)	98/1472 (6.7%)	**HR 0.79** (0.25 to 2.54)	**14 fewer per 1,000** (from 49 fewer to 94 more)	⨁⨁◯◯ LOW	Important

CI: Confidence interval; **HR:** Hazard Ratio

Explanations

a. Confidence interval includes null and total number of events are less than 300

Bibliography:

[1] C.M. Rivera, B.R. Grossardt, D.J. Rhodes, R.D. Brown, Jr., V.L. Roger, L.J. Melton, 3rd, W.A. Rocca, Increased cardiovascular mortality after early bilateral oophorectomy, Menopause 16(1) (2009) 15-23.

[2] W.A. Rocca, B.R. Grossardt, M. de Andrade, G.D. Malkasian, L.J. Melton, 3rd, Survival patterns after oophorectomy in premenopausal women: a population-based cohort study, Lancet Oncol 7(10) (2006) 821-8.

[3] W.A. Rocca, J.H. Bower, D.M. Maraganore, J.E. Ahlskog, B.R. Grossardt, M. de Andrade, L.J. Melton, 3rd, Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause, Neurology 69(11) (2007) 1074-83.

Appendix 7.11. Grade evidence table for breast cancer outcome with ET

Setting: ET (CEE 0.625mg) compared to no ET (placebo) for women in menopause without an intact uterus

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ET (CEE 0.625mg)	no ET (placebo)	Relative (95% CI)	Absolute (95% CI)		
Breast cancer (Marjoribanks 2017) (follow up: median 13 years)[157]												
1	randomized trials	not serious	not serious	serious [a]	not serious[b]	none	168/5310 (3.2%)	216/5429 (4.0%)	**RR 0.80** (0.65 to 0.97)	**8 fewer per 1,000** (from 1 fewer to 14 fewer)	⊕⊕⊕◯ MODERATE	Important

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Only about 33% of the study sample was 50-59 years of age at baseline (i.e. the age women are most likely to consider HT for vasomotor symptoms); mean participant age was 63 years.

b. Confidence interval includes 1 but doesn't include appreciable values of benefit and harm. Also number of events is ~300

Bibliography:

[1] J. Marjoribanks, C. Farquhar, H. Roberts, A. Lethaby, J. Lee, Long-term hormone therapy for perimenopausal and postmenopausal women, The Cochrane database of systematic reviews 1 (2017) CD004143.

Appendix 7.12. Grade evidence table for breast cancer outcome with EPT

Setting: EPT (CEE 0.625mg and MPA 2.5mg) continuous compared to no EPT (placebo) for women in menopause

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EPT (CEE 0.625mg and MPA 2.5mg) continuous	no EPT (placebo)	Relative (95% CI)	Absolute (95% CI)		
Breast cancer (follow up: median 13.2 years)[157]												
1	randomised trials	not serious	not serious	serious [a]	not serious	none	434/8506 (5.1%)	323/8102 (4.0%)	**RR 1.28** (1.11 to 1.47)	**11 more per 1,000** (from 4 more to 19 more)	⊕⊕⊕◯ MODERATE	Important

Explanations
a. Only about 33% of the study sample was 50-59 years of age at baseline (i.e. the age women are most likely to consider HT for vasomotor symptoms); mean participant age was 63 years.
Bibliography:
[1] J. Marjoribanks, C. Farquhar, H. Roberts, A. Lethaby, J. Lee, Long-term hormone therapy for perimenopausal and postmenopausal women, The Cochrane database of systematic reviews 1 (2017) CD004143.

Appendix 7.13. Grade evidence table for cardiovasucular outcomes

Setting: HT commenced less than 10 years after the menopause compared to no HT (palcebo) for women in menopause and no cardiovascular disease history

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HT commenced less than 10 years after the menopause	no HT (placebo)	Relative (95% CI)	Absolute (95% CI)		
Coronary heart disease (death from cardiovascular causes and non-fatal myocardial infarction) (Boardman 2015)[158]												
4	randomized trials	serious [a]	not serious	serious [b]	not serious	strong association	10/1000 (1.0%)	18/1000 (1.8%)	**RR 0.52** (0.29 to 0.96)	**9 fewer per 1,000** (from 1 fewer to 13 fewer)	⊕⊕⊕◯ MODERATE	Improtant
Stroke (Boardman 2015)[158]												
3	randomized trials	not serious	not serious	serious [b]	not serious	none	13/1000 (1.3%)	9/1000 (0.9%)	**RR 1.37** (0.80 to 2.34)	**3 more per 1,000** (from 2 fewer to 12 more)	⊕⊕⊕◯ MODERATE	Improtant
Venous Thromboembolism (Boardman 2015)[158]												
3	randomized trials	not serious	not serious	serious [b]	not serious	strong association	11/1000 (1.1%)	6/1000 (0.6%)	**RR 1.74** (1.11 to 2.73)	**4 more per 1,000** (from 1 more to 10 more)	⊕⊕⊕⊕ HIGH	Improtant

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Downgraded one level due to risk of bias. The results are significant due to the DOPS 2012 trial, that has high risk of bias. We downgraded our confidence in the results of that meta-analysis because, had the DOPS not been there, the meta-analysis would not be significant.

b. Data is from studies on women with natural post-menopause who commenced HT less than 10 years after menopause and not on women who have had early surgical menopause.

Bibliography:

[1] H.M. Boardman, L. Hartley, A. Eisinga, C. Main, M. Roque i Figuls, X. Bonfill Cosp, R. Gabriel Sanchez, B. Knight, Hormone therapy for preventing cardiovascular disease in post-menopausal women, The Cochrane database of systematic reviews (3) (2015) CD002229.

Appendix 7.14. Qualitative evaluation of PDA by steering committee

Element of review	Date of interview	Clarity of information presented	Way information presented	Amount of information presented	Biasness of information	Length of tool	Usefulness	Relevancy to women	Comprehensibility of tables
Reviewer 1 - Wendy	April 26, 2018	Very clear and comprehensible, simple language	Booklet layout is great, way information presented is very structured and clear	Just about right, not too little or too much	The booklet highlighted the facts and was not biased towards one treatment over the other	No comments about length	Very useful, especially highlighting information on early menopause and the way this ties in with importance of preventative measures and the need to think beyond managing your menopausal symptoms	Very relevant and impactful. This is really what women needs to raise awareness about surgical menopause and the things they need to think about to make a treatment decision	Very clear. Loved infographics. Not the graphs so much. Especially the fact the colors in the graph doesn't match with infographics. Reviewer suggest deleting graphs and just including infographics.
Reviewer 2 - Sue	May 2, 2018	Like size, layout, simple language, found an easy read and user friendly, also likes name as feels that it empowers women with information and resources	Clear and well laid out	Just about right for the question the tool is addressing	The booklet highlighted the facts, although questioned oneself if the tool was supported by a pharmaceutical company or pharmacy program	Good length for the amount of information presented. Women do not have to go over entire book in one session can break out in multiple sessions	Very useful in the sense that it helps women to think about all the different issues that they may encounter after surgery at different stages of their surgical menopause as their reasons for taking or declining therapy may change in that respect.	Relevant to women and addressed important topics that women need to consider when making decisions	Risk information - needed to look at infographic and diagram a couple of times to grasp content. Information in circles was clear, level of evidence in the arrows was clear and clearly laid out in the beginning of this section. Graph may not mean anything to women who cannot read graph or are not seeking more information in that sense.

Reviewer 3 - Tami	May 2, 2018	Information presented is clear however language level may be a bit high, higher than grade 8	liked way information presented in some sections e.g. Walking women through steps of decision-making in the beginning, symptoms section, fact that we mentioned connection between mood and sleep, also that fact that we emphasized that not all women will experience symptoms and only some may experience some of all of symptoms.	Some areas need to be shortened a bit and made into bullet points such as page 14 and 16	Tool has to be biased towards HT because women suffer a lot by not taking HT and not realizing its benefit early on after surgery and it's not only about managing symptoms	Cannot be made appreciably smaller if need to include all relevant information that will address all facts and help women make decisions	Very useful to women, would be nice if it can offer to women in the clinic	Highlighting information on sleep, mood and weight gain and the impact of estrogen in managing these symptoms might make it more relevant to what she sees in the clinic	Risk information section was very clear, she like infographics, circles at the bottom to contrast numbers, color codes. The graphs were okay but did not lie colors suggest changing to the same colors used in infographic.

Reviewer 4 - Shelly	May 4, 2018	Liked a lot of the sections but have several comments to make information more presentable	Booklet is well laid out and easy to navigate	Some sections needed to be framed a little better by providing more introductions and staging up before discussing topic of focus. That is, prepare the women for what is going to be discussed next. See how we can make better column for details.	No comments about biasness were made	Tool is not lengthy. It contains meaningful and important information that is not hard to understand. Tool is easily navigated	Very useful to women. Has more value if able to reach women at an early stage of their surgical menopause, before surgery or soon after before they develop long term effects or when they can realize full benefit of HT in terms of preventing long term effects.	Yes, extremely relevant for these women especially younger women. Menopause clinic mostly see women who are in their late stages of surgical menopause when use of HT might be controversial and if there is a way to make this tool available to younger women that would be the best situation. Tool can facilitate discussion on management of surgical menopause post-surgery between physician and their patients. It's a good way to make it less daunting to open these doors.	Risk information section esp. not very clear without color codes. Only helps if hard copy is provided to patient or if available as an online resource.

Reviewer 5 - Lori	May 9, 2018	Liked clarity of information	Lay out is nice and clear	Just about right. However, also mentions that this really depends on women and their need for information. Some women before surgery they do not want to hear much about risks and side-effects as overwhelmed by what their dealing with at the moment and at other times women want to know everything. So this is very subjective.	No comments about biasness were made	Appropriate	Very useful	Yes, very relevant especially to women before they perform surgery at the preadmission stage as well as after	Risk information section is clear and understandable
Reviewer 6 - Kyla	May 11, 2018	Like clarity of information, finds it easy to understand and read through. A lay person can go over it fairly quickly	Likes sections where we layout different steps of the tool. Clarifying values section finds extremely helpful as it will help women to determine reasons for taking or not taking HT. Adding meaning and value to their decision.	Information presented is just about right in amount	No comments about biasness	Appropriate	Very useful. Tool is very much needed. Patient wished she had this resource when she had to go through surgery.	Very relevant to women's needs. Addresses most of their concerns.	Risk information section is comprehensible in the colored version. Black and white copy makes really hard to understand. Graphs are helpful in the sense that it helps to look at the data differently and allow you to make close comparison between the different groups for the different outcomes. No issues with colors revealed.

Appendix 7.15. Qualitative evaluation of PDA by steering committee – suggestions for improvement

Reviewer	Comments	Content/format	Change	What is the change?	Who will change?	Where will you change?	Wait until after evaluation by women	Do not Change
Wendy	1. Rephrase early death comment when talking about long terms risks of menopause as it may scare some women especially younger women.	Content	-	-	-	-	x	-
Wendy	2. When talking about need for counselling mention need to educate partners and significant others and recommend group counselling.	Content	x	pg. 13 Since your wellbeing can affect the wellbeing of your partner and family. Family and group counselling might be an option you want to consider to maintain a healthy relationship with your spouse and family.	Tasneem	Word document	-	-
Wendy	3. Remove graphs from all risk presentation sections.	Format	x	Change colors but keep graph	Aya	Adobe PDF document	-	-
Wendy	4. Enlarge X 10 section on infographics to highlight that these numbers are based on 1000 women.	Format	x	Make X 10 bigger	Aya	Adobe PDA document	-	-
Wendy	5. In values clarification section, under reasons to decline HT suggest rephrasing the word "avoid" as the statements now seems definitive and may not be helpful for women to clarify their values as the way it's written it makes all women consider these points as very important which may lead to more decisional conflict. Suggest revising to how important is it for you "to reduce your risk" as opposed to avoid.	Format	x	Check tammy's suggestions	Tasneem	Word document	-	-

Wendy	6. Under values clarification section, under reasons to take HT, reconsider point #4 as again this is something we do not have good evidence for and it will bias women decision as it is an important consideration for everyone in general. May need to include point about memory loss instead.	Format	x	Remove point on early death and include other symptoms instead	-	-	x	-
Wendy	7. Add more resources under counselling services (sage and support network), financial support (AISH, prescription costs, EI, CPP), and online websites for patient support such as menopause chicks (Wendy to send links and hard copies for these resources to include in booklet)	Content	-	-	-	-	-	pg. 53 Sage and support network under counselling services; AISH, EI and CPP under financial support; menopause chicks under patient support groups. Include as a separate sheet for Alberta residents. No need to include Alberta specific resources in the guidebook.
Sue	1. Elaborate more on sexual dysfunction and how it can impact relationships.	Content	x	May find sex less pleasurable or lose interest in having sex.	-	-	x	-
Sue	2. Change order of symptoms presentation, include mood prior to sexual dysfunction.	Format	x	Change order of symptoms	Tasneem	Word document	-	-

Sue	3. In emotional impact would be helpful to provide timelines on when person may expect to feel normal again and that it may take up to 16 weeks, so more on post-surgical expectations.	Content	x	pg. 9 Your body will need time to heal after having surgery and get used to the hormonal changes that happen as a result. Physical healing may take 6 weeks or so. Emotional healing may take longer. During this time, you may not feel yourself, and your menopausal symptoms might be worsened by the physical impact of surgery.	Tasneem	Word document	-	-
Sue	4. Highlight difference between physical healing and emotional healing and that emotional healing often takes a longer time.	Content	x	pg. 9 Your body will need time to heal after having surgery and get used to the hormonal changes that happen as a result. Physical healing may take 6 weeks or so. Emotional healing may take longer. During this time, you may not feel yourself, and your menopausal symptoms might be worsened by the physical impact of surgery.	Tasneem	Word document	-	-
Sue	5. Reinforce point on importance of self-care even if busy with kids and work.	Content	x	Include under section of life style	-	-	-	-
Sue	6. More information on use of progesterone as a factor to protect against breast cancer.	Content	-	-	-	-	x	Insufficient evidence
Sue	7. Dose and duration section suggest modifying to bullet points to make more clear and readable esp. for people who have a short attention span.	Format	x	Pg. 16 Just breakdown in bullet points	Tasneem	Word document	-	-

Sue	8. Under benefits>>say something about effect on fat redistributions (central obesity).	Content	x	Found a meta-analysis about impact on increasing lean body mass and managing central obesity (reference: Salpeter SR, Walsh JME, Ormiston TM, Greyber E, Buckley NS, Salpeter EE. Meta-analysis: effect of hormone-replacement therapy on components of the metabolic syndrome in postmenopausal women. Diabetes, Obesity and Metabolism. 2006;8(5):538–554. [PubMed])	-	-	x	-
Sue	9. In risk information section to clearly distinguish between evidence for removing ovaries and taking or not taking HT, write Not HT or HT at the top of the page as a headline to make a clear distinction as now doesn't read very clear.	Format	x	May need to include a sentence about lack of evidence in terms of 2 comparative groups (comparing women who removed ovaries and took HT and those who did not take it)	Aya	Adobe PDF document	-	-
Sue	10. When discussing HT risks would like to include a section on how to mitigate breast cancer and blood clots risks in general as these are critical factors that women consider when making treatment decisions. So need to be discussed in the context of other factors that can modify this risk.	Content	x	Pg. 24 Include under life style section) Many of these risks can be reduced by maintaining a healthy life style, some of these include such as avoiding cigarette smoke, excessive alcohol intake and maintaining regular physical activity and a health body weight. You can reduce your risk of breast cancer by maintaining a healthy body weight, avoiding cigarette smoke and excessive alcohol consumption and engaging in regular physical activity.	Tasneem	Word document	-	-

Sue	11. In the section on side-effects, add a sentence that side-effects can be modified by mode of delivery or type of estrogen formulation used.	Content	x	Pg. 24 Many of these side-effects can be managed by adjusting dose or switching to another HT formulation	Tasneem	Word document	-	-
Sue	12. Impact on migraine may also depend on dose.	Content	-	-	-	-	-	Varies and depends on other things as well. So lets not go into that kind of details.
Sue	13. In values clarification section, timing of answering these questions can impact your answer, hence need to reassess your treatment decision by going over this tool and asking yourself these questions is important q 6 months or so.	Content	x	Bring it out again in the values clarification section. That your values may change with time	-	-	-	x - there is already a comment in the beginning of the tool that it can be used progressively.
Sue	14. Suggest adding a question about quality of life in the section about reasons to take HT.	Content	x	Include as a separate point under reasons to take HT	Tasneem	Word document	-	-
Sue	15. May need to expand on menopausal symptoms for example how important is it for you to manage your hot flashes and night sweats, to improve your sleep, to improve your sexual activity, to maintain or improve your quality of life, etc.	Format	x	Include as separate points under reasons to take HT and remove early death. Put hot flashes and night sweats together	Tasneem	Word document	-	-

Sue	16. Suggest rephrasing questions on reasons to decline HT as the way it's written out now may not help women in clarifying their values as someone may end up rating all these factors as very important and in that sense the section may not be very useful in clarifying values. Suggest revising to "how concerned are you about the risk of strokes, breast cancer, blood clots, etc. with HT.	Format	x	Check Shelly's suggestions	Tasneem	Word document	-	-
Sue	17. Suggest adding a section on impact of lifestyle on health and how many of these risks may be mitigated by being more health cognizant and make smart lifestyle choices, tool may be a great avenue to educate women in that sense.	Content	x - (ways to mitigate risks (after discussing HT risks))	Add a section on life style choices for mitigating HT risks	Tasneem	Word document	-	-
Sue	18. Following values clarification section, as opposed to just including a section to write notes suggest encouraging women to write down pros and cons for HT that apply to themselves (make it more personal) that will help them to think about things more analytically rather than emotionally with their right brain. So suggest putting a plan table where women can list their pros and cons to taking HT to be able to visualize that factors that they are considering to make a decision and when side of the scale weighs in more.	Format	x	Include a table were women can list pros and cons. E.g. now we encourage you to take the time to write down pros and cons of HT that apply to yourself in the following table. As well as a notes section	Aya	Adobe PDA document	-	-

Tami	1. Need to mention that not all women will experience symptoms and that some women may not have any symptoms.	Content	x (already included but double check)	Just bring out more if you can	Tasneem	Word document	-	-
Tami	2. Term used for effect of estrogen on brain function may need to be revised. The term they often use in the clinic is effect on memory and concentration. Do we need to rephrase the term memory loss?	Format	x	Change to effect on memory and concentration	-	-	x	-
Tami	3. Testosterone is not approved for use for sexual dysfunction in women, careful when recommending.	Content	x	In some women who continue to have poor sexual function testosterone and androgen therapy might be a helpful. It's not approved for that use in Canada. Please discuss with your doctor about options for sexual dysfunction.	-	-	x	-
Tami	4. Page 14 and 16 look busy, may need to make more concise and easy to follow through by for example putting into bulled points.	Format	x	Put in points instead	Tasneem	Word document	-	-
Tami	5. Worried that when we talk about different formulations that are available and when we talk about testosterone that women would think that we are referring to BHT and that we are supporting these products hence need to clearly distinguish between the availability of these products commercially. Maybe add a very brief section on BHT?.	Format	x	Mention commercially available products. Do not include a section on BHT.	Tasneem	Word document	-	-

Tami	6. Section on HT risks suggest changing heading of breast cancer to low risk of breast cancer because this is the biggest concern these women have when deciding on HT so we need to show them that the risk is low, however we do not have the evidence to support this claim. However she also suggested putting risk of breast cancer with HT more into perspective by comparing this risk to risk of breast cancer with other factors such as age, smoking, obesity, low physical activity, etc. in the form of infographics (after HT risks section).	Format	x - add infographic that show risk with other risk factors in contrast to risk with ET and EPT.	Change heading to what is the risk of .....? Look at SOGC/NICE guidelines for numbers of cases for risk factors for breast cancer	Aya	Adobe PDF document		
Tami	7. Suggest referring women to patient testimonials section of the tool early on in the booklet (do we need to include table of contents in the beginning of the tool?).	Format	x	Include table of content in beginning for “know facts” sections	Aya	Adobe PDA document	-	-
Tami	8. Stress fact that their response to questions in values clarification section will change before and after surgery and with time.	Content	x	Include in beginning of “values clarification” section	Tasneem	Word document	-	-
Tami	9. Suggest including a values clarification section in the beginning to see how their responses may change after they learn the facts and go over the tool.	Content	x	add values clarification section in beginning of tool	Aya	Adobe PDF document	-	-
Tami	10. Suggest changing "reason to decline HT" to " what would make you think HT is less attractive"	Format	x	Change what would make you think HT is a less attractive option.	Tasneem	Word document	-	-

Tami	11. Suggest instead of including reasons in a question format just to include general sentence at the top of the section (e.g. how concerned are you about the following risks) and then list risks. Same with benefit section (e.g. how important is it for you to) and then list benefits (manage symptoms, restore quality of life, maintain your sleep, avoid bone loss, avoid cardiovascular disease, etc.).	Format	-	Change to: (e.g. how concerned are you about the following risks) and then list risks. Same with benefit section (e.g. how important is it for you to) and then list benefits (manage symptoms, restore quality of life, maintain your sleep, avoid bone loss, avoid cardiovascular disease, etc.).	-	-	x	-
Tami	12. Page 48 make top part bold.	Format	x	See formatting suggestion and change	Aya	Adobe PDF document	-	-
Tami	13. Page 52 move better choice better health at the bottom to the top, right underneath self-management programs and workshops in Alberta.	Format	x	See formatting suggestion and change	Tasneem	Word document	-	-
Shelly	1. Suggest changing name to “MenoPower” as the way it is right now doesn't reflect that the book addresses menopause (has no connection to menopause) but rather a general term reflecting body image and self-acceptance or simply focusing on self-development and acceptance.	Content	-	-	-	-	-	x
Shelly	2. Suggest removing the acronym PDA as could be mean so many things and may not speak clearly to women as to what it means. Suggest removing and just keep decision aid tool.	Content	x	Just expand to patient decision aid for early surgical menopause	Aya	Adobe PDF document	-	-

Shelly	3. In pg. 6 Suggest setting the stage up before we talk about what the tool offers by including a couple of sentences about surgical menopause, what it means and why do women need to go through this. That is, the section needs framing before we go into the detail of what the tool is about.	Content	x - see Shelly's notes	Make changes based on Shelly's notes	Tasneem	Word document	-	-
Shelly	4. Keep the tool focused on "you" rather than "women" so women could feel a connection with the tool and that it directly speaks to them and addresses their concerns. Change terms about women to "you" once you start to discuss different sections of the tool (starting from know the facts until plan for next steps"	Content	x - see Shelly's notes	Make changes based on Shelly's notes	Tasneem	Word document	-	-
Shelly	5. Include reasons for surgical menopause (either here or in pg. 6) along with definition. Also include age range of early surgical menopause as not clear when do we consider surgical menopause early.	Content	x - see Shelly's notes	Make changes based on Shelly's notes	Tasneem	Word document	-	-
Shelly	6. Under symptoms, suggest adding more to hot flashes section (e.g. as most frequent symptom on menopause). Also, switch order between vaginal dryness and loss of interest in sex. That is, put vaginal dryness and urinary incontinence together. Also include a statement on length of time symptoms is expected to last so women can have some expectations	Content	-	-	-	-	x	-

	to work with when deciding on treatments.							
Shelly	7. May want to comment on recovery after surgery and physical healing from after effect of surgery which is very different from surgical menopause and may take up to 6 weeks but eventually will settle down. This often overlaps with menopause and therefore its Important to include just to validate how they feel or may feel after surgery and give them hope that they will eventually get better once the physical body is healed from surgery.	Content	x (where to include?)	Include when talking about symptoms of menopause.	Tasneem	Word document	-	-
Shelly	8. Suggest discussing role of hormonal fluctuations in contributing to menopausal symptoms as well as long term effects. Move section on hormonal fluctuations to before we start to talk about symptoms.	Format	x	Move section on hormonal fluctuations to before we start to talk about symptoms.	Tasneem	Word document	-	-

Shelly	9. Pg. 11. remove term replacement of estrogen. 10. may need to revise section about checking with doctors for a bone scan as the Canadian guidelines do not recommend testing women younger than 50 for BMD as they have low fracture risk. Also, bone scans for these women can only be ordered by specialists,	Content	x	Make suggested change " remove term replacement from pg. 11	Tasneem	Word document	-	-
Shelly	10. Suggest adding ways for women to reduce their risks of fractures such as ca and vitamin d supplements as well strength exercises and need to optimize these along with recommended treatments.	Content	x	To include in the lifestyle section	Tasneem	Word document	-	-
Shelly	11. When talking about emotional support, suggest acknowledging cancer scare of women and how many of them may have resorted to surgery to reduce their cancer risk. And so you may want to invite them to explore and revisit these feelings after surgery so they are able to connect to tool in a non-inflammatory way.	Content	-	-	-	-	x	-
Shelly	12. Before start talking about HT and the recommendations suggest inviting women to other coping strategies such as having a good support system and a healthy life-style and then move to option of HT for helping with symptoms.	Content	x	See Shelly's notes	Tasneem	-	-	-

Shelly	13. When talk about doses and formulations, remove cream as not commercially available unless you are referring to BHT. Also move ring to local therapies for vaginal symptoms relief. Also, include a section on BHT for women who would like to consider this option.	Content	x	Remove cream and move ring to local therapies. Do not include a section on BHT	Tasneem	-	-	-
Shelly	14. pg. 18, to make women feel guided mention that they can follow-up with menopause specialist or others for ongoing support.	Content	x	pg. 18, to make women feel guided mention that they can follow-up with menopause specialist or others for ongoing support	Tasneem	-	-	-
Shelly	15. Risk information, infographics do not speak to me or pop out without colors. Found arrows and graph more comprehensible. Also, suggest including age range of population at top of page of infographics. Same apply to other infographics.	Format	x	Include age range of population at top of page of infographics. Same apply to other infographics.	Aya	Adobe PDF document	-	-
Shelly	16. When talking about breast cancer, highlight that estrogen without progesterone was not associated with a risk increase.	Content	x	Highlight that estrogen without progesterone was not associated with a risk increase.	Tasneem	Word document	-	-
Shelly	17. Under cardiovascular risks define soon (e.g. within 10 years of having surgery).	Content	-	-	-	-	-	We do not know. We do not have the evidence for surgical menopause.
Shelly	18. highlight that risk is dependent on formulation and lower with transdermal formulations. 19. Under side-effects, when we talk about vaginal bleeding need to include that this only occurs in women who left	Content	x	There might be difference in risks based on doses and formulations.	Tasneem	Word document	-	-

	uterus behind.							
Shelly	19. Include comment about what to do when experience side-effects (counsel HCP as doses and formulation may need to be adjusted to better meet your needs).	Content	x	Under side-effects mention: counsel HCP as doses and formulation may need to be adjusted to better meet your needs	Tasneem	Word document	-	-
Shelly	20. pg. 27 change VTE to blood clots and CVD to heart diseases.	Content	x	Make suggested changes	Tasneem	Word document	-	-
Shelly	21.In infographics about breast cancer risks change progestogen to progesterone to make less confusing for patients.	Content	-	-	-	-	-	We will define progestogen in the beginning of the book and keep using the term progestogen all along.
Shelly	22. pg. 15 change estrogen plus progestogen to estrogen combined with progesterone therapy.	Content	x	Leave as is and define progestogen both natural progesterone and synthetic)	Tasneem	Word document	-	-
Shelly	23. Frame infographics by including age-range at top (pg. 33 and 32).	Format	x	Include age range of population at top of page of infographics. Same apply to other infographics.	Aya	Adobe PDF document	-	-
Shelly	24. pg. 34 change terms endometrial to uterine and thrombophilia to blood clotting disorders.	Content	x	Make suggested changes	Tasneem	Word document	-	-
Shelly	25. When talking about BRCA change 1/2 to 1 or 2.	Content	x	Make suggested changes	Tasneem	Word document	-	-
Shelly	26. pg. 35 change "need not" to consider.	Format	x	Make suggested changes	Tasneem	Word document	-	-

Shelly	27. Revise section on endometriosis may need to add more information there to make more clear. As the way its presented not shows that estrogen therapy is not recommended as may worsen endometriosis that is areas external to uterus and hence even if they do not have uterus they may need to take EPT instead of ET.	Format	x	Progesterone in combination with estrogen in some women	Tasneem	Word document	-	-
Shelly	28. Change hypertension to high blood pressure.	Content	x	Make suggested changes	Tasneem	Word document	-	-
Shelly	29. Change term "in surgical menopause" to " women who experience surgical menopause".	Content	x	Make suggested changes	Tasneem	Word document	-	-
Shelly	30 Provide some background before talking about patient testimonials (see Shelly's suggestion in hard copy provided).	Content	x	See Shelly's notes	Tasneem	Word document	-	-
Shelly	31. In patient stories: include age at surgery for each patient to make more relevant to younger women.	Content	x	Include age at surgery for each women	Tasneem	Word document	-	-
Shelly	32. In section about values clarification to truly capture preference which has an emotional component, suggest rating reason to take or decline HT in terms of degree or concern or worry rather than importance. This may help women to better determine their preference and weigh things out more clearly.	Format	x	Same as Tammy's suggestions.	Tasneem	Word document	-	-
Shelly	33. May need to rephrase terms reasons to choose or decline HT. for example HT pros and cons.	Format	-	-	-	-	x	-

Shelly	34. pg. 48 suggest putting benefits before harm.	Format	x	Make suggested change	Tasneem	Word document	-	-
Shelly	35. Check spelling of complimentary.	Content	x	Check complimentary spelling	Tasneem	Word document	-	-
Shelly	36. pg. 41. add HCP after doctor	Content	x	36. pg. 41. add HCP after doctor	Tasneem	Word document	-	-
Lori	1. Likes name. To highlight that the tool is for menopause suggests, adding at the bottom of cover letter that it's a surgical menopause decision aid tool.	Content	x	Change PDA to A Surgical Menopause Patient Decision Aid	Tasneem	Word document	-	
Kyla	1. In section about emotional impact add the need for counselling therapy.	Content	x	Specify need for counselling under emotional support	Tasneem	Word document	-	-
Kyla	2. In the section about risk information, can add at the top that 1 big woman is equal to 10 small women.	Format	x	Either make X 10 bigger or add at the top that 1 big women is = to 10 small women.	Aya	Adobe PDF document	-	-
Kyla	3. Add a section at the end of things women need to discuss with surgeon, family doctor, and when to ask for referral to menopause clinic.	Content	-	-	-	-	x	-
Kyla	4. Add a tracking sheet were women can have the chance to track the changes in their bodies and symptoms throughout menopausal experience over time (before surgery, right after, 6 months down line and then every 1 to 2 years thereafter). This sheet can be used to communicate the changes in their physical and emotional health with their primary care physician.	Content	x	Tracking forms for menopause. Check for examples online	-	-	x	
Kyla	5. Add a section at the end where women can put in the name and contact info of their surgeon and physician in case they had to resort to them for support throughout	Content	x	Add at the end of tool.	Tasneem	-	-	-

	their menopausal experience.							

8 Chapter 8. General Discussion and Recommendations

8.1 General discussion

Considering the perceived uncertainty surrounding HT risks, women with early surgical menopause face decisional conflict when deciding on a treatment for their symptoms. HT is a recommended treatment when no contraindications exist, particularly for women with early menopause who are subject to severe and prolonged health consequences due to early estrogen deprivation.[159] Yet, HT has been perceived negatively by women and clinicians and often times menopausal women are reluctant to use.[18] The negative impressions that women associate with HT began in the late 1990's, when media reports about HT research raised concerns about its long-term risks. However, not until the publication of the initial results of the WHI, was the fear and shift away from HT most evident. The initial WHI findings published in 2002 showed an increased risk of invasive breast cancer, strokes, blood clots and myocardial infarction with EPT.[19] These risks were overstated in the initial media release and misleadingly inferred to all menopausal women irrespective to age and comorbidities which set the tone for a hyped media response and a distorted perception of HT risks.[96] Even though subsequent analyses showed that these risks may not apply to younger menopausal women,[21, 160] the use of HT is still a subject of fear among women of younger age.

Given that, menopausal women have varied perceptions regarding the benefit-risk ratio of HT and a situation of complex decision-making ensues when deciding if HT is a suitable option.[31] In early surgical menopause, however, the complexity of the decision involved is not the only challenge encountered. These women have other barriers to effective decision-making inherent in the health condition involved, such as the abrupt presentation of severe menopausal

symptoms, the long-term health sequelae and the need to make a decision on a short timeline.[13, 161] In addition, the emotional outcomes associated with the health experience can influence a woman's approach in making treatment decisions.[28, 32, 99] In BRCA mutation(s) carriers who undertake risk-reducing oophorectomies to manage their gynecological cancer risk, fear of breast cancer also poses a particular challenge. Essentially, these complexities formed the grounds upon which a PDA in the context of early surgical menopause was considered necessary. The need for measures of decision support in early surgical menopause, such as PDAs was also based on findings from a cross-sectional chart review completed previously by members of our study group.[18] The chart review showed that despite their prevalent and severe menopausal symptoms, women who have undergone surgical menopause are not being adequately treated with HT; less than half were started on HT after a surgical menopause and only one-third had continued taking HT post-surgery.[18]

In the process of developing a PDA for early surgical menopause, the first step was to search the literature to identify the nature and extent of research done in the area of decision aids for surgical menopause.[12] As such, we completed a scoping review that identified and evaluated the development and content of decision aids used for managing menopause in the published and unpublished literature, with a special focus on surgical menopause.[162] The most important finding of the scoping review was the lack of peer-reviewed, evidence-based decision aids for managing early surgical menopause. This reinforced the decision to develop a PDA for this decision context. Another finding was that many of the decision aids identified lacked quality. Identifying these limitations, allowed us to focus our efforts in developing a PDA that met internationally recognized quality standards. Issues identified included the small proportion of decision aids informed by needs assessment, the poor presentation of outcome probabilities and

the lack of reported steps involved in finding, appraising and summarizing scientific content. Furthermore, we highlighted common practices in the field of decision aids for menopause which guided a few aspects of the PDA development, such as the use of explicit values clarification and informing theoretical framework. There are no direct scientific benefits of having an explicit values clarification method as opposed to implicit.[135] We however intended to include an explicit values clarification section in the PDA upon realizing that the majority of decision aids identified from the review explicitly incorporated values clarification. Most of the decision aids were also focused on HT as the most effective treatment modality. Perhaps the explicit inclusion of values clarification is of particular importance to HT decisions due to their value-sensitive nature. In value-sensitive health decisions, patients are encouraged to evaluate their personal importance of treatment outcomes as a means of decision support.[9, 130] Findings from our review also helped us consider ODSF as a potential development framework for the PDA. Half of the decision aids identified in our review were informed by the ODSF, however this was not the main reason for considering this approach.[130] Rather, it is the relevance of ODSF to HT decisions that predominantly guided our choice. Despite informing the development of hundreds of decision aids for a variety of clinical domains and decision contexts,[161, 163] ODSF was found to be particularly relevant to HT decisions and this framework was first evaluated in the context of a decision aid developed for HT decision-making in post-menopausal women.[130] The framework was developed for health decisions, that are stimulated by a new diagnosis or health transition and require careful deliberation about given options, similar to the one involved with deciding on HT for early surgical menopause.[161]

Second, to assess the feasibility of developing a PDA, we needed to determine if recent evidence on risks and benefits of available treatment options exist.[12] Current guidelines on the use of

HT for early menopause and primary ovarian insufficiency including surgical menopause were available.[164] However, the evidence for the use of HT in BRCA mutation carriers who experience early surgical menopause due to RRSO was unclear. These women have a higher baseline risk of breast cancer compared to others and the decision to take HT for their symptoms is controversial. Furthermore, current guidelines for early menopause may not apply to them because it is unclear if HT counteracts the breast cancer risk-reduction benefit of RRSO. Addressing this population in our PDA was necessary because many of these women will experience early surgical menopause as part of the RRSO to manage their cancer risk. For adequate breast and ovarian cancer risk-reduction, current guidelines recommend BRCA mutation carriers to undertake RRSO before age 40 years or after completion of child-bearing. Due to their young age at surgery, these women might be at a particular risk of developing severe menopausal symptoms and long term risks, warranting the need for HT. Therefore, we completed a systematic review and meta-analysis that assessed the effect of HT on quality of life and breast cancer risk in women who have BRCA mutations and who also underwent RRSO.[165] Findings from the systematic review showed that these women had improvements in overall menopause-specific QOL with the use of HT, which was consistent with findings from studies of HT in symptomatic women with natural or surgical menopause. Only four studies evaluated the risk of breast cancer and none showed an increased risk with HT use. However, studies were methodologically flawed. Other outcomes addressed in the review were for vasomotor symptoms and vulvovaginal atrophy and both were shown to improve with HT in the cumulative analysis. The review depicted the benefits of HT in improving quality of life and managing common menopausal symptoms post RRSO, however no firm conclusions were drawn on the safety of HT in terms of breast cancer risk due to the scarcity and methodological

limitations of available evidence. Informed by findings from our systematic review, we include these effects in the PDA under special considerations of using HT. Specifically, the benefits of using HT in the specific population of BRCA carriers in managing common menopausal symptoms and restoring the quality of life were indicated. We also emphasized that evidence on HT safety in reference to breast cancer risk is lacking; in this view, BRCA carriers were advised to carefully consider the HT option with their clinicians (Appendix 8.1).

The second phase of the project served as the stepping stone for developing the PDA. It assessed the decisional needs of the target population gathered from two needs assessments, specifically from five focus groups and a narrative review .[166, 167] The focus groups were exploratory in nature, using a descriptive qualitative research design to explore the process of decision-making about menopausal therapies in a sample of women who have had an early surgical menopause.[166] We refrained from using a needs assessment framework when analyzing the transcripts to get a true sense of the data and avoid any biases to the interpretation of shared accounts. A major theme identified in the focus groups was “being my own advocate” which stressed that women with early surgical menopause seek more control over their menopausal health and treatment decisions. Another important theme was the perception of support received during the menopausal experience. In this theme, women shared several perceptions of inadequate support including the lack of adequate information about surgical menopause and treatments, the lack of guidance and engagement in therapy decision-making and the lack of social support. These were all viewed as modifiable deterrents to effective decision-making. To make an informed decision about treatments, women expressed a need to learn more about the symptoms of surgical menopause, treatment options, resources and avenues for support and stories of similar experiences, preferably before the surgery. From these findings, we developed

an appreciation of the decision support needs of these women, which informed major sections of the decision aid. We also realized that developing a PDA was of value because it empowered women to have a sense of ownership towards their health and healthcare decisions. This, in essence, inspired the name of the "SheEmpowers" PDA. A limitation of the focus groups is that our sites of recruitment were confined to two menopause clinics in Edmonton, Alberta. And so, our sample population may have been too specific to represent the full spectrum of experiences and decisional needs of women with surgical menopause.

The narrative review was completed to get a broader sense of the decisional needs in the general population of women with surgical menopause.[167, 168] The review proposed a model suggesting that surgical menopausal women go through a risk evaluation process where they weigh competing risks to make treatment preferences which in turn guide treatment decisions. This risk evaluation process was guided by emotional/subjective dimensions, such as perceptions of HT risks and benefits, value placed on present versus future health, experiences and inferences made from commonly sought information sources. It was inferred that women draw more upon emotional judgements for developing risk perceptions as they felt that they do not have a clear understanding of HT and involved outcomes. The review underlined the value-sensitive nature of decision-making about HT in surgical menopause, as well as the impact of emotional dimensions on HT decisions. As such, the value PDAs offer in helping women create a fine balance between the integration of emotion and reason for effective decision-making was realized. Similar to focus group findings, lack of knowledge and limited patient involvement in therapy decisions were other modifiable deterrents to decision making identified.

In both needs assessments, the role of health professionals, particularly physicians in affecting women's decisions about HT and menopausal therapies was highlighted. In the focus groups

women particularly commented on the inadequate support received from their physicians and surgeons, before being referred to the menopause clinic, like the perceived lack of interest in menopausal concerns and perceived lack of patient centered care and engagement in decision-making.[166] In the narrative review, physician's recommendation was shown as a main external influencer of HT decisions and in several reports was shown to affect women's risk perceptions and treatment preferences. Directly targeting these physician-related barriers to decision-making was beyond the scope of our PDA. However, the PDA was developed to encourage patient driven SDM conversations by empowering women with the information and skills for participation in decision-making. In that sense, the PDA can support collaboration in therapy decision-making among women and HCPs including physicians.

Drawing on findings from the needs assessments and the earlier scoping and systematic reviews, a PDA that specifically targeted women with early surgical menopause was developed (Appendix 8.1). The PDA focuses primarily on domains considered necessary for therapy decision-making based on women decisional needs, expert's opinion and best practices for decision aid development. These domains were information on surgical menopause and HT, outcomes and resources for menopausal support; patient stories; explicit values clarification; and guidance in deliberation.

An important component of a decision aid is the information section which includes information on the index decision, the condition involved, treatment modalities and outcome probabilities.[138] Most decision aids include an information section but vary in length and formats. The section may be brief and emphasize contrasting treatment options. In our PDA, a detailed information section was felt necessary, as participants in the focus groups identified having adequate knowledge as a key factor in decision-making. Additionally, receiving

conflicting information about HT from various sources was viewed as a modifiable deterrent to effective decision-making.[99, 166, 169] Studies have shown that detailed decision aids are associated with better knowledge improvement and lower decisional conflict.[170, 171] The comprehensive information section in our PDA was revised multiple times for fine tuning and concise presentation. The information section of the tool is broken down into areas that women imminently felt the need to learn about including consequences of surgical menopause, short- and long-term outcomes, emotional impact, details on HT, HT outcomes and patient stories. A section on resources for menopausal support is also included at the end of the tool. Women in the focus groups were interested to learn about all available treatment options and not just HT. Although, an attempt was made to include this information in the initial draft, this increased the length of the PDA posing challenges to the aid's usability.

Balancing the presentation of information is an important consideration for any decision aid.[141] Despite the fact that in early surgical menopause current clinical evidence supports HT uptake,[92] due to the value-sensitive nature of the decision involved, therapy decisions should be guided by women's informed judgement of treatment outcomes. The objective of our aid was to promote informed decision-making about HT rather than informed uptake. In that sense, the focus was to strive for neutrality in the provision of information about given options to enable end users to seek a balanced consideration of the options in a way that will limit biases resulting from preconceived notions, perceived norms, subjective perceptions and inferences from sought information sources and inadequate knowledge.[141] To allow for a balanced content, the aid places an equal weight on discussing HT benefits and risks. Outcome probabilities are also displayed in a balanced format using a side by side presentation of absolute risks and using visual as opposed to textual interpretation of outcome data. Findings from both the qualitative

and quantitative analysis of the evaluation phase showed that the aid provided a balanced and unbiased presentation of information about given options.

The use of patient stories in decision aids is optional and should reflect views of the target population.[148] In the focus groups, women expressed the need to learn from other women about their experiences and how they approached treatment decisions.[166] Patient stories are included in the PDA to highlight the decision making process. In the evaluation phase, women suggested including the outcome of the decisions with the patient stories, however we did not revise the stories to reflect outcomes to avoid any potential bias outcome-based stories may have on women's decisions.[149]

Presenting explicit probabilities to describe the likelihood of treatment outcomes is an integral component of a decision aid.[127, 145] It enables patients to develop realistic views on treatment outcomes before clarifying their values.[130] Decision aids identified for surgical menopause in our scoping review often lacked information on outcome probabilities.[162] In this review, an identified barrier to effective decision-making was relying on subjective perceptions to manage preferences and treatment decisions. It was important to address this limitation in the PDA by providing up-to-date, quality-rated outcome probabilities to help women clarify values and decide on treatment preferences. Probabilities in the PDA are presented in a side by side format to provide a balanced presentation of outcome information and enable patients to process relevant information without bias.[141] Furthermore, we use several methods to display outcome information, such as graphs, pictograms and numbers.[145] Based on patients' feedback from the alpha testing, a common denominator was used across comparisons for the numerical representation of outcome information.

Including methods for values clarification is a recommended practice for decision aids.[135] Findings from our scoping review helped establish the inclusion of an explicit values clarification. This was further supported by the narrative review findings. Women with surgical menopause intuitively negotiate competing risks to make a treatment decision, an approach similar to completing a values clarification exercise in a decision aid but perhaps lacking structure, guidance and rationalism.[168] As a result, explicitly incorporating a structured activity to help women rationally weigh competing expectation based on clarified values was believed to be of particular value to this decision context. The values clarification method was primarily guided by the Ottawa Personal Decision Guide which uses rating scales to capture values.[172] However, the wording in the rating scale was slightly modified based on steering committee feedback. For example, the statement reading "how much each reason matters to you" was changed to "how important is it to you to manage the following symptoms" when discussing benefits and "how concerned are you about the following risks" when discussing risks. The features associated with patient's values were mostly informed by shared insights from the focus groups and experts' suggestions from the steering committee.

Incorporating guidance in deliberation was important not only because it's a quality dimension of decision aids,[127] but also because of the value it offers in terms of guiding patients in decision making and SDM engagement.[7] This was a support need women acknowledged in the focus groups. Guidance in deliberation and decision making is emphasized in several ways in the aid which like the values clarification methods was informed by the Ottawa Personal Decision Guide.[172]

A symptom-tracking forms for guidance in decision making, was a unique feature of our aid suggested by a patient expert in the steering committee. This form was incorporated in the aid to help women track and communicate their symptoms to their health professionals.

8.2 Future recommendations for the decision aid

This thesis outlined the development and alpha testing of a PDA for HT decision-making in early surgical menopause. Building on the work completed as part of this thesis, envisioned future projects include evaluating the tool for acceptability, feasibility and effectiveness in clinical settings, as well considering dissemination and implementation strategies for wider adoption among women of the target population and their health professionals.

8.2.1 Beta testing

The next step in the evaluation of the SheEmpowers PDA is to assess the acceptability and feasibility from women and clinicians who were not involved in the initial phases of development. Eligible participants will include women at the point of decision making about managing early surgical menopause and clinicians assisting them with this decision. This represents the beta testing phase and should be undertaken under real life settings.[128] Our alpha testing phase included women who were very similar in terms of demographics and treatment behaviors. In the beta testing phase, it would be beneficial to recruit participants from multiple sites and clinical settings for a more diverse and representative sample, in hopes of capturing a wider outcome perspective. Another sampling consideration for the beta testing phase, is to evaluate the decision aid in women with lower health literacy. The acceptability of the aid among patient with low health literacy is a development quality criterion that needs to be considered.[155] Several designs can be used for this testing phase including a post-test only mixed method study design, similar to the one implemented for our alpha testing phase; the focus

here will be mainly on assessing acceptability and feasibility views, especially with respect to suitability, ease of use, and practicality.[12] Another approach to beta testing is using a before/after study design which allows for assessing acceptability views as well as other decisional measures pertaining to knowledge, expectations, values clarification and decisional conflict as a pilot for the succeeding trial on effectiveness.[12] Generally, in beta testing, offering clinicians the chance to comment about the tool and elaborate on barriers and facilitators to adopting the decision aid in practice, will help identify wider implementation needs as well as create opportunities for future collaboration in evaluation and/or dissemination activities.[128] Feedback from this phase will guide further revisions of the PDA as well as the design of a trial to assess its effectiveness.

8.2.2 Evaluation of effectiveness

Assessing the effectiveness of the SheEmpowers PDA is necessary for implementation and dissemination. Assessing effectiveness involves determining if the application of the PDA is superior to other information guides and standards of care, in terms of improving decisional outcomes, such as with the quality of decision and decision-making process.[136] This evidence is ideally gathered from large-scaled RCTs. An ideal RCT for testing the SheEmpowers effectiveness would involve multiple recruitment sites including primary, specialized and community care settings. Eligible participants would include women who have had or about to have an early surgical menopause (≤45 years), are at the point of deciding about HT, can read and write English, and are willing to give an informed consent for participation. Additionally, to facilitate the identification and recruitment of eligible participants it is necessary to involve HCPs as research partners. Participants will be blinded to the intervention to reduce information bias. The control group would receive a standard information brochure on surgical menopause

and relative treatments available from a professional health organization like the North American Menopause Society (NAMS). Recruited women will then be randomized to intervention or control and in a sealed envelope the decision aid or brochure will be mailed to them for self-review. Women will be advised to return to their health professional at 4 weeks for a consultation. At the end of the consultation, women and their health professionals will be instructed to self-administer a follow-up questionnaire for assessing outcomes of interest. Patient demographics, medical, surgical and social history will be captured at baseline along with other measures of decisional outcomes. Primary decisional outcomes would include knowledge, expectations, clarity of values, decisional conflict and decision consistency with values which are primarily rooted in the objectives of the SheEmpowers PDA. Secondary outcomes can potentially include other decisional outcomes of relevance such as skill in decision-making and satisfaction with decision-making, as well as other outcomes related to health and menopause related quality of life.

8.2.3 Implementation and dissemination

Careful planning of the implementation and dissemination process is important for successful application and wide-scaled adoption of the decision aid. A key limitation of studies reporting the development or evaluation of decision aids identified for menopause was that none of their reports discussed dissemination and implementation plans. However, this seems to be a general issue with PDAs development and not limited to the area of menopause.[128] Decision aids have significant benefits to patients, clinicians and health care systems, but poor clinical implementation is a common issue.[173] Many challenges surround the implementation of decision aids. These are often related to health professionals lack of trust and acceptability of SDM interventions like decision aids.[110] Additional implementation challenges include time

constraints, the lack of financial compensations, and organizational cultures that are not supportive of decision aid use.[6, 110, 174] Reflecting on these challenges and on suggestions for implementation offered by participants in the alpha testing phase, we strategized implementation and dissemination methods to facilitate wider adoption and clinical utility of the SheEmpowers tool. The feasibility of these methods should be evaluated in the beta testing phase and accordingly targeted revisions should be made.

8.2.3.1 Implementation plans

Feedback from the evaluation phase underlined the need for the SheEmpowers tool to support therapy decision-making, particularly before the surgery. There was a general consensus among women that the PDA should be provided before surgery, to prepare women for the experience and to consider the need for support. For example, support in the form of referrals to menopause specialists and informed discussions with clinicians for personalized information on available options.

Yet, the various stages of surgical menopause experience hold different physical and emotional manifestations and challenges.[13, 166] Since treatment decisions are bound by these progressive changes in the health experience, we anticipate the "SheEmpowers" PDA to target a broader population of surgical menopausal women, at various stages of their experience. This primarily includes women who are contemplating an oophorectomy (pre-surgically) and carefully considering the decision of removing their ovaries in light of available treatment options for managing induced menopause. Providing the aid prior to the surgery can inform women on surgical menopause and available treatments; and help them plan ahead for support. In women who receive the aid pre-surgery, the use of the aid can also be reinforced post-surgery at the 6-week visit with the surgeon. Alternatively, the aid can also be first administered post-

surgery. For example, at the 6-week follow up appointment with the surgeon, a time when women typically present with symptoms and are actively searching for treatments and management approaches. The tool can also be used in women past the 6-week follow-up period, a few months or even years past their surgeries in various settings, such as primary care clinics or GP offices, OB-GYN or in specialized menopause clinics. Since needs and values that define therapy decisions may change throughout a woman's health experience, the tool can be used progressively every time a woman needs to reconsider her therapy decision.

Another implementation plan to consider is making the aid directly accessible to women within or outside the context of the health care system, without relying on clinicians to initiate access to PDA. This is important because the PDA was specifically developed to empower women with the information, resources and skills in decision-making and help them overcome perceived barriers to SDM, including barriers related to HCPs. Within the health care system this would look like an automated delivery system that identifies eligible patients to support the use of the PDA ahead of a relevant clinical encounter.[175] This method was the most often cited facilitator of decision aids implementation in the literature.[173] Among others, methods targeting women outside the context of the health care system include promoting the tool in women advocacy groups and on the internet using social media platforms. Assessing the feasibility and effectiveness of these plans in future implementation trials would be necessary to identify best strategies for supporting routine integration into practice.

8.2.3.2 Dissemination plans

Finding from the alpha testing phase showed that women were passionate about the SheEmpowers PDA and felt the need to make it more widely available. These women shared useful tips for dissemination, which mostly involved educating HCPs, especially physicians and

surgeons about the tool and involving them in distribution and dissemination activities. There is a clear need to include targeted information to prepare clinicians for discussions on managing early surgical menopause driven by patients' use of the PDA. However, to expand the adoption of the PDA other dissemination strategies should be explored. Going forward, our dissemination plan would need to include interventions involving clinicians including physicians as well as other HCPs; and methods targeting women.

To promote the aid among clinicians and create opportunities for collaboration and dissemination a reasonable plan would be to offer a shorter version. As such, the clinical utility of the PDA and its suitability among clinicians can be reinforced. Evidence shows that health professionals are more likely to recommend a decision aid that they agree with its content and value.[176] The shorter version can also serve as an encounter tool to facilitate SDM between women and clinicians without causing delays to the work flow.

Another plausible plan includes, establishing partnerships with professional organizations, such as the Canadian Menopause Society (SIGMA), the Society of Obstetricians and Gynecologist in Canada (SOGC), NAMS and the International Menopause Society (IMS) to promote the tool among their health professional members through websites, newsletters or other means of targeted communications. Strategies raising awareness of the aid among menopause specialists, such as in OB/GYN offices and specialty menopause clinics should be considered. These strategies may involve presenting the PDA at medical conferences, clinical rounds and educational seminars targeting specialists. Adoption at organizational settings such as primary care and public health clinics as well as outpatient and community pharmacies is also important. Making a pamphlet version of the aid available in such settings can assist with wider distribution. The pamphlet will ideally include information on ordering printed copies of the aid and a link to

access an online version. Other dissemination strategies to consider is to publish the development and evaluation findings in peer-reviewed journals and present the PDA at national and international scientific conferences.

Discussed dissemination strategies thus far may only be sufficient to raise awareness and interest in PDA which is initially required for attaining more progressive implementation levels. Other strategies to reinforce positive attitudes towards the PDA within organizational settings and actual adoption and integration within routine practice will need to be identified. Successful measures in the literature include identifying and collaborating with clinical champions or leaders within the respective organizations to establish implementation and encourage other HCPs to adopt the PDA.[176, 177] As well, providing academic detailing or outreach visits to: offer education using audit and performance feedback, identify barriers to implementation and develop potential solutions.[178, 179]

Dissemination strategies directed at women involve first, promoting the tool in advocacy or support groups targeted at women with early menopause. Second, the tool can be made readily available online through submitting to the Ottawa Health Research Institute Decision aid library inventory (DALI). The inventory is readily available for the general public. Third, our tool was developed to be used as a print booklet, however, to facilitate accessibility and wider dissemination among women, discussion about setting up an online version of the tool, such as a smart phone application, are applicable. Nevertheless, this would be contingent on funding opportunities for disseminating the aid as there are major costs involved with setting-up and maintaining online applications. A suitable approach though might involve finding an organization that can host an online version of the decision aid and provide the funds for maintaining and updating the online tool.

8.3 Other future recommendations

Reflecting on findings and key limitations of the different projects involved in developing the SheEmpowers PDA, a few opportunities for future research or recommendations were identified.

8.3.1 Guidance for PDA developers

An important limitation identified from the scoping review was the inadequate reporting of development procedures of decision aids.[162] Identified studies were mostly evaluation trials with only a few development descriptions.[43, 130, 180] Granting that many of these decision aids were developed before the IPDAS and therefore were not necessarily informed by development frameworks, overall the practice of disclosing PDAs development is still poorly acknowledged.[128, 139] Despite the rapidly evolving field of PDA, there are several areas that are yet to be informed by evidence. This may continue to be the case if proper reporting and development recommendations are not followed. PDA developers can play a major role in contributing effectively to the growing practice of PDA by following development recommendations and transparently reporting steps involved in developing their tools. Even though current guidelines for PDA stress the importance of transparent reporting, recommendations to assist developers in meeting these criteria are advisable. Perhaps something like criteria by peer-reviewed journals advising authors to submit PDA development and effectiveness reports appraised against the IPDAS quality checklist, similar to the practice involved with submitting Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE) checklists for systematic reviews. Such mandates may allow developers to consider inconsistencies in their reporting and an opportunity to improve on their current or future reporting strategies.

8.3.2 More research in surgical menopause

Another key limitation identified from searching for evidence on surgical menopause and respective treatments, was the limited published research regarding the risks and benefits of HT specific to surgical menopause to guide us. In early surgical menopause, limitations in available research have led to current treatment guidelines being mostly informed by large, long-term prospective cohorts which despite their good quality, may not have firm conclusions. Furthermore, the lack of published studies available has also resulted in some outcomes not being addressed, such as HT effect on general or menopause-specific quality of life, depression, sexual function and others. To shed more light on these areas and increase younger women trust in HT, the need for quality evidence gathered from well-planned, large-scaled RCTs and/or long-term prospective cohorts is necessary. As evidence from these studies accrues, viable modifications to the aid will be implemented.

8.3.3 Unmet support needs

An interesting finding from the focus groups was the expressed need for social support.[166] Surgical menopause can be a severe health experience and adjusting to its manifestations requires a good support system for coping and reassurance. A decision aid is useful but only addresses some of the support needs that women with surgical menopause commonly report. The need for social support is an unmet support need that women from the focus groups felt can best be fulfilled through support groups. The support they felt while participating in the focus groups, motivated them to express the need for an ongoing support group for surgical menopause. Women stressed on the importance of having the support groups organized by a credible organization for maintenance.

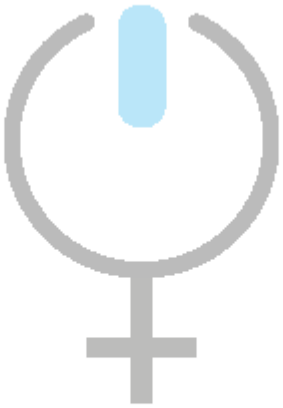
The “SheEmpowers” PDA is a step in the right direction in supporting women with early surgical menopause. However, other support gaps for this population still need to be addressed. The psychological implications of surgical menopause can render many women feeling isolated and emotionally labile. In this context, support groups are extremely helpful. They offer a platform through which women of similar experiences can interact for emotional, social and intellectual support.[99] They also help women who have been faced with an emotionally overwhelming health experience to normalize their fear and learn to cope with the encountered challenges.[181, 182] The value of positive social interactions and emotional support is mainly seen in women as opposed to men populations and has been linked to improvements in psychological distress.[183] Supporting women with early surgical menopause and helping them cope with triggered psychological challenges through providing social support in the form of organized support groups held by a credible organization is an important future consideration.

8.4 Conclusion

Surgical menopause can be a severe health experience with major compromises to physiological and psychological health as well as long term complications. One area that women need support in is the area of decision-making about HT. In light of perceived uncertainty about HT, therapy decision-making in early surgical menopause can be complex. Women with early surgical menopause can benefit from a decision support intervention to help ease the decisional complexity and conflict as they engage in treatment decisions. PDA are useful decision support interventions in the context of complex health care decisions.[120] Through following a systematic, evidence-based approach, driven by a multidisciplinary group of researchers, clinicians and patient experts, and primarily informed by women decision support needs, the SheEmpowers PDA was developed. The PDA intended to guide and support women in making

HT decisions about managing early surgical menopause. Positive impressions on acceptability were gathered from women and clinicians involved in the development phase. However, further evidence on acceptability, feasibility and effectiveness are yet to be assessed. As the "SheEmpowers" PDA was recognized as a step in the right direction in supporting women with early surgical menopause, moving forward, efforts will focus on revising the tool for effectiveness and wide-scaled implementation for an ultimate goal of offering decisional support to surgical menopausal women.

Appendix 8.1. PDF version of the SheEmpowers PDA



SheEmpowers

A PATIENT DECISION AID
FOR EARLY SURGICAL MENOPAUSE

References

[1] G. Elwyn, D. Frosch, R. Thomson, N. Joseph-Williams, A. Lloyd, P. Kinnersley, E. Cording, D. Tomson, C. Dodd, S. Rollnick, A. Edwards, M. Barry, Shared decision making: a model for clinical practice, J Gen Intern Med 27(10) (2012) 1361-7.

[2] G. Makoul, M.L. Clayman, An integrative model of shared decision making in medical encounters, Patient Educ Couns 60(3) (2006) 301-12.

[3] G. Elwyn, M.A. Durand, J. Song, J. Aarts, P.J. Barr, Z. Berger, N. Cochran, D. Frosch, D. Galasinski, P. Gulbrandsen, P.K.J. Han, M. Harter, P. Kinnersley, A. Lloyd, M. Mishra, L. Perestelo-Perez, I. Scholl, K. Tomori, L. Trevena, H.O. Witteman, T. Van der Weijden, A three-talk model for shared decision making: multistage consultation process, Bmj 359 (2017) j4891.

[4] A. Towle, W. Godolphin, Framework for teaching and learning informed shared decision making, Bmj 319(7212) (1999) 766-71.

[5] F. Legare, S. Ratte, D. Stacey, J. Kryworuchko, K. Gravel, I.D. Graham, S. Turcotte, Interventions for improving the adoption of shared decision making by healthcare professionals, Cochrane Database Syst Rev (5) (2010) CD006732.

[6] G. Elwyn, I. Scholl, C. Tietbohl, M. Mann, A.G. Edwards, C. Clay, F. Legare, T. van der Weijden, C.L. Lewis, R.M. Wexler, D.L. Frosch, "Many miles to go ...": a systematic review of the implementation of patient decision support interventions into routine clinical practice, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S14.

[7] F. Legare, N. Moumjid-Ferdjaoui, R. Drolet, D. Stacey, M. Harter, H. Bastian, M.D. Beaulieu, F. Borduas, C. Charles, A. Coulter, S. Desroches, G. Friedrich, A. Gafni, I.D. Graham, M. Labrecque, A. LeBlanc, J. Legare, M. Politi, J. Sargeant, R. Thomson, Core competencies for

shared decision making training programs: insights from an international, interdisciplinary working group, J Contin Educ Health Prof 33(4) (2013) 267-73.

[8] N. Joseph-Williams, A. Lloyd, A. Edwards, L. Stobbart, D. Tomson, S. Macphail, C. Dodd, K. Brain, G. Elwyn, R. Thomson, Implementing shared decision making in the NHS: lessons from the MAGIC programme, Bmj 357 (2017) j1744.

[9] M.J. Barry, Shared decision making: informing and involving patients to do the right thing in health care, J Ambul Care Manage 35(2) (2012) 90-8.

[10] A.M. O'Connor, D. Stacey, V. Entwistle, H. Llewellyn-Thomas, D. Rovner, M. Holmes-Rovner, V. Tait, J. Tetroe, V. Fiset, M. Barry, J. Jones, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev (2) (2003) CD001431.

[11] V.M. Montori, A. LeBlanc, A. Buchholz, D.L. Stilwell, A. Tsapas, Basing information on comprehensive, critically appraised, and up-to-date syntheses of the scientific evidence: a quality dimension of the International Patient Decision Aid Standards, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S5.

[12] A. O'Connor, M.J. Jacobsen, Workbook on Developing and Evaluating Patient Decision Aids, 2003. www.ohri.ca/decisionaid. (Accessed August 26 2016).

[13] S.L. Hendrix, Bilateral oophorectomy and premature menopause, Am J Med 118 Suppl 12B (2005) 131-5.

[14] S.S. Faubion, C.L. Kuhle, L.T. Shuster, W.A. Rocca, Long-term health consequences of premature or early menopause and considerations for management, Climacteric 18(4) (2015) 483-91.

[15] R. Reid, B.L. Abramson, J. Blake, S. Desindes, S. Dodin, S. Johnston, T. Rowe, N. Sodhi, P. Wilks, W. Wolfman, M. Fortier, L. Graves, B. Guthrie, A. Khan, Managing menopause, J Obstet Gynaecol Can 36(9) (2014) 830-8.

[16] W.A. Rocca, B.R. Grossardt, V.M. Miller, L.T. Shuster, R.D. Brown, Jr., Premature menopause or early menopause and risk of ischemic stroke, Menopause 19(3) (2012) 272-7.

[17] T.J. de Villiers, M.L. Gass, C.J. Haines, J.E. Hall, R.A. Lobo, D.D. Pierroz, M. Rees, Global Consensus Statement on menopausal hormone therapy, Maturitas 74(4) (2013) 391-2.

[18] A. Chubaty, M.T. Shandro, N. Schuurmans, N. Yuksel, Practice patterns with hormone therapy after surgical menopause, Maturitas 69(1) (2011) 69-73.

[19] J.E. Rossouw, G.L. Anderson, R.L. Prentice, A.Z. LaCroix, C. Kooperberg, M.L. Stefanick, R.D. Jackson, S.A. Beresford, B.V. Howard, K.C. Johnson, J.M. Kotchen, J. Ockene, Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial, JAMA 288(3) (2002) 321-33.

[20] J.J. Hillman, I.H. Zuckerman, E. Lee, The impact of the Women's Health Initiative on hormone replacement therapy in a Medicaid program, J Womens Health (Larchmt) 13(9) (2004) 986-92.

[21] G.L. Anderson, M. Limacher, A.R. Assaf, T. Bassford, S.A. Beresford, H. Black, D. Bonds, R. Brunner, R. Brzyski, B. Caan, R. Chlebowski, D. Curb, M. Gass, J. Hays, G. Heiss, S. Hendrix, B.V. Howard, J. Hsia, A. Hubbell, R. Jackson, K.C. Johnson, H. Judd, J.M. Kotchen, L. Kuller, A.Z. LaCroix, D. Lane, R.D. Langer, N. Lasser, C.E. Lewis, J. Manson, K. Margolis, J. Ockene, M.J. O'Sullivan, L. Phillips, R.L. Prentice, C. Ritenbaugh, J. Robbins, J.E. Rossouw, G. Sarto, M.L. Stefanick, L. Van Horn, J. Wactawski-Wende, R. Wallace, S. Wassertheil-Smoller,

Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial, JAMA 291(14) (2004) 1701-12.
[22] M.L. Stefanick, G.L. Anderson, K.L. Margolis, S.L. Hendrix, R.J. Rodabough, E.D. Paskett, D.S. Lane, F.A. Hubbell, A.R. Assaf, G.E. Sarto, R.S. Schenken, S. Yasmeen, L. Lessin, R.T. Chlebowski, Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy, JAMA 295(14) (2006) 1647-57.
[23] A. Morabia, M.C. Costanza, Recent reversal of trends in hormone therapy use in a European population, Menopause 13(1) (2006) 111-5.
[24] S. Brown, Shock, terror and controversy: how the media reacted to the Women's Health Initiative, Climacteric 15(3) (2012) 275-80.
[25] F. Chew, X. Wu, Sources of information influencing the state-of-the-science gap in hormone replacement therapy usage, PLoS One 12(2) (2017) e0171189.
[26] R.J. Chen, T.C. Chang, S.N. Chow, Perceptions of and attitudes toward estrogen therapy among surgically menopausal women in Taiwan, Menopause 15(3) (2008) 517-23.
[27] F. Pansini, A.B. Bacchi Modena, D. de Aloysio, M. Gambacciani, M. Meschia, F. Parazzini, G. Sciacchitano, R. di Micco, E. Peruzzi, G. Maiocchi, Sociodemographic and clinical factors associated with HRT use in women attending menopause clinics in Italy, Climacteric 3(4) (2000) 241-7.
[28] D. Kuh, R. Hardy, M. Wadsworth, Social and behavioural influences on the uptake of hormone replacement therapy among younger women, BJOG 107(6) (2000) 731-9.
[29] Patterns of use of hormone replacement therapy in one million women in Britain, 1996-2000, BJOG 109(12) (2002) 1319-30.

[30] M.A. Gerend, L.S. Aiken, M.J. Erchull, A. Lapin, Women's use of hormone therapy before and after the Women's Health Initiative: a psychosocial model of stability and change, Prev Med 43(3) (2006) 158-64.

[31] J.S. Carpenter, M.M. Byrne, J.L. Studts, Factors related to menopausal symptom management decisions, Maturitas 70(1) (2011) 10-5.

[32] M. Crowe, B. Burrell, L. Whitehead, Lifestyle risk management--a qualitative analysis of women's descriptions of taking hormone therapy following surgically induced menopause, J Adv Nurs 68(8) (2012) 1814-23.

[33] Maturitas, Editor's Choice. http://www.maturitas.org/content/highlights.

[34] J.S. Carpenter, J.L. Studts, M.M. Byrne, A systematic review of menopausal symptom management decision aid trials, Maturitas 69(1) (2011) 11-21.

[35] W.H. Utian, Semantics, menopause-related terminology, and the STRAW reproductive aging staging system, Menopause 8(6) (2001) 398-401.

[36] W.H. Utian, D.F. Archer, G.A. Bachmann, C. Gallagher, F. Grodstein, J.R. Heiman, V.W. Henderson, H.N. Hodis, R.H. Karas, R.A. Lobo, J.E. Manson, R.L. Reid, P.J. Schmidt, C.A. Stuenkel, Estrogen and progestogen use in postmenopausal women: July 2008 position statement of The North American Menopause Society, Menopause 15(4 Pt 1) (2008) 584-602.

[37] E. Mikhail, J.L. Salemi, M.F. Mogos, S. Hart, H.M. Salihu, A.N. Imudia, National trends of adnexal surgeries at the time of hysterectomy for benign indication, United States, 1998-2011, Am J Obstet Gynecol (2015).

[38] L.T. Shuster, D.J. Rhodes, B.S. Gostout, B.R. Grossardt, W.A. Rocca, Premature menopause or early menopause: long-term health consequences, Maturitas 65(2) (2010) 161-6.

[39] D. Meirow, H. Biederman, R.A. Anderson, W.H. Wallace, Toxicity of chemotherapy and radiation on female reproduction, Clin Obstet Gynecol 53(4) (2010) 727-39.

[40] W.H. Gotlieb, G.B. Baruch, E. Friedman, Prophylactic oophorectomy: clinical considerations, Semin Surg Oncol 19(1) (2000) 20-7.

[41] ACOG Practice Bulletin No. 89. Elective and risk-reducing salpingo-oophorectomy, Obstet Gynecol 111(1) (2008) 231-41.

[42] The North American Menopause Society. Menopause Practice: A Clinician's Guide, The North American Menopause Society, Mayfield Heights, Ohio, 2014.

[43] F. Legare, D. Stacey, S. Dodin, A. O'Connor, M. Richer, F. Griffiths, A. LeBlanc, J.L. Rousseau, S. Tapp, Women's decision making about the use of natural health products at menopause: a needs assessment and patient decision aid, J Altern Complement Med 13(7) (2007) 741-49.

[44] L.J. Orozco, M. Tristan, M.M. Vreugdenhil, A. Salazar, Hysterectomy versus hysterectomy plus oophorectomy for premenopausal women, Cochrane Database Syst Rev (7) (2014) CD005638.

[45] H.K. Perera, C.V. Ananth, C.A. Richards, A.I. Neugut, S.N. Lewin, Y.S. Lu, T.J. Herzog, D.L. Hershman, J.D. Wright, Variation in ovarian conservation in women undergoing hysterectomy for benign indications, Obstet Gynecol 121(4) (2013) 717-26.

[46] M. Geary, A. Geoghegan, M. Foley, Prevention of ovarian cancer: a survey of the practice of prophylactic oophorectomy by consultant gynaecologists in Ireland, Ir Med J 90(5) (1997) 186-7.

[47] Canadin Institute of Health Information. Inpatient Hospitalizations, Surgeries and Newborn Indicators, 2014–2015, 2015.

[48] G.A. Colditz, W.C. Willett, M.J. Stampfer, B. Rosner, F.E. Speizer, C.H. Hennekens, Menopause and the risk of coronary heart disease in women, N Engl J Med 316(18) (1987) 1105-10.

[49] W.H. Parker, M.S. Broder, Z. Liu, D. Shoupe, C. Farquhar, J.S. Berek, Ovarian conservation at the time of hysterectomy for benign disease, Obstet Gynecol 106(2) (2005) 219-26.

[50] W.H. Parker, V. Jacoby, D. Shoupe, W. Rocca, Effect of bilateral oophorectomy on women's long-term health, Womens Health (Lond Engl) 5(5) (2009) 565-76.

[51] C.M. Rivera, B.R. Grossardt, D.J. Rhodes, R.D. Brown, Jr., V.L. Roger, L.J. Melton, 3rd, W.A. Rocca, Increased cardiovascular mortality after early bilateral oophorectomy, Menopause 16(1) (2009) 15-23.

[52] W.A. Rocca, B.R. Grossardt, M. de Andrade, G.D. Malkasian, L.J. Melton, 3rd, Survival patterns after oophorectomy in premenopausal women: a population-based cohort study, Lancet Oncol 7(10) (2006) 821-8.

[53] W.A. Rocca, J.H. Bower, D.M. Maraganore, J.E. Ahlskog, B.R. Grossardt, M. de Andrade, L.J. Melton, 3rd, Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause, Neurology 69(11) (2007) 1074-83.

[54] W.A. Rocca, B.R. Grossardt, L.T. Shuster, Oophorectomy, menopause, estrogen, and cognitive aging: the timing hypothesis, Neurodegener Dis 7(1-3) (2010) 163-6.

[55] T.R. Rebbeck, N.D. Kauff, S.M. Domchek, Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers, J Natl Cancer Inst 101(2) (2009) 80-7.

[56] M.S. Hunter, Long-term impacts of early and surgical menopause, Menopause 19(3) (2012) 253-4.

[57] M. Rodriguez, D. Shoupe, Surgical Menopause, Endocrinol Metab Clin North Am 44(3) (2015) 531-42.

[58] S.M. Bhattacharya, A. Jha, A comparison of health-related quality of life (HRQOL) after natural and surgical menopause, Maturitas 66(4) (2010) 431-4.

[59] S.L. Davison, S.R. Davis, Androgens in women, J Steroid Biochem Mol Biol 85(2-5) (2003) 363-6.

[60] L. Dennerstein, J. Randolph, J. Taffe, E. Dudley, H. Burger, Hormones, mood, sexuality, and the menopausal transition, Fertil Steril 77 Suppl 4 (2002) S42-8.

[61] P.M. Sarrel, Sexuality and menopause, Obstet Gynecol 75(4 Suppl) (1990) 26S-30S; discussion 31S-35S.

[62] S.B. Bellerose, Y.M. Binik, Body image and sexuality in oophorectomized women, Arch Sex Behav 22(5) (1993) 435-59.

[63] V. Teplin, E. Vittinghoff, F. Lin, L.A. Learman, H.E. Richter, M. Kuppermann, Oophorectomy in premenopausal women: health-related quality of life and sexual functioning, Obstet Gynecol 109(2 Pt 1) (2007) 347-54.

[64] P.E. Tucker, M.K. Bulsara, S.G. Salfinger, J.J. Tan, H. Green, P.A. Cohen, The effects of pre-operative menopausal status and hormone replacement therapy (HRT) on sexuality and quality of life after risk-reducing salpingo-oophorectomy, Maturitas 85 (2016) 42-8.

[65] J.B. Madalinska, J. Hollenstein, E. Bleiker, M. van Beurden, H.B. Valdimarsdottir, L.F. Massuger, K.N. Gaarenstroom, M.J. Mourits, R.H. Verheijen, E.B. van Dorst, H. van der Putten, K. van der Velden, H. Boonstra, N.K. Aaronson, Quality-of-life effects of prophylactic salpingo-

oophorectomy versus gynecologic screening among women at increased risk of hereditary ovarian cancer, J Clin Oncol 23(28) (2005) 6890-8.

[66] A. Graziottin, Menopause and sexuality: key issues in premature menopause and beyond, Ann N Y Acad Sci 1205 (2010) 254-61.

[67] J. Challberg, L. Ashcroft, F. Lalloo, B. Eckersley, R. Clayton, P. Hopwood, P. Selby, A. Howell, D.G. Evans, Menopausal symptoms and bone health in women undertaking risk reducing bilateral salpingo-oophorectomy: significant bone health issues in those not taking HRT, Br J Cancer 105(1) (2011) 22-7.

[68] J.B. Madalinska, M. van Beurden, E.M. Bleiker, H.B. Valdimarsdottir, J. Hollenstein, L.F. Massuger, K.N. Gaarenstroom, M.J. Mourits, R.H. Verheijen, E.B. van Dorst, H. van der Putten, K. van der Velden, H. Boonstra, N.K. Aaronson, The impact of hormone replacement therapy on menopausal symptoms in younger high-risk women after prophylactic salpingo-oophorectomy, J Clin Oncol 24(22) (2006) 3576-82.

[69] N. Johansen, A.H. Liavaag, T.G. Tanbo, A.A. Dahl, A.H. Pripp, T.M. Michelsen, Sexual activity and functioning after risk-reducing salpingo-oophorectomy: Impact of hormone replacement therapy, Gynecol Oncol 140(1) (2016) 101-6.

[70] A. Finch, K.A. Metcalfe, J.K. Chiang, L. Elit, J. McLaughlin, C. Springate, R. Demsky, J. Murphy, B. Rosen, S.A. Narod, The impact of prophylactic salpingo-oophorectomy on menopausal symptoms and sexual function in women who carry a BRCA mutation, Gynecol Oncol 121(1) (2011) 163-8.

[71] A. Finch, G. Evans, S.A. Narod, BRCA carriers, prophylactic salpingo-oophorectomy and menopause: clinical management considerations and recommendations, Womens Health (Lond Engl) 8(5) (2012) 543-55.

[72] J.C. Gallagher, Effect of early menopause on bone mineral density and fractures, Menopause 14(3 Pt 2) (2007) 567-71.

[73] T. Yoshida, K. Takahashi, H. Yamatani, K. Takata, H. Kurachi, Impact of surgical menopause on lipid and bone metabolism, Climacteric 14(4) (2011) 445-52.

[74] D.J. Hadjidakis, E.P. Kokkinakis, M.E. Sfakianakis, S.A. Raptis, Bone density patterns after normal and premature menopause, Maturitas 44(4) (2003) 279-86.

[75] L.J. Melton, 3rd, C.S. Crowson, G.D. Malkasian, W.M. O'Fallon, Fracture risk following bilateral oophorectomy, J Clin Epidemiol 49(10) (1996) 1111-5.

[76] K.K. Vesco, L.M. Marshall, H.D. Nelson, L. Humphrey, J. Rizzo, K.L. Pedula, J.A. Cauley, K.E. Ensrud, M.C. Hochberg, D. Antoniucci, T.A. Hillier, Surgical menopause and nonvertebral fracture risk among older US women, Menopause 19(5) (2012) 510-6.

[77] E. Lokkegaard, Z. Jovanovic, B.L. Heitmann, N. Keiding, B. Ottesen, A.T. Pedersen, The association between early menopause and risk of ischaemic heart disease: influence of Hormone Therapy, Maturitas 53(2) (2006) 226-33.

[78] W.H. Parker, M.S. Broder, E. Chang, D. Feskanich, C. Farquhar, Z. Liu, D. Shoupe, J.S. Berek, S. Hankinson, J.E. Manson, Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study, Obstet Gynecol 113(5) (2009) 1027-37.

[79] B.K. Jacobsen, I. Heuch, G. Kvale, Age at natural menopause and all-cause mortality: a 37-year follow-up of 19,731 Norwegian women, Am J Epidemiol 157(10) (2003) 923-9.

[80] B.K. Jacobsen, S.F. Knutsen, G.E. Fraser, Age at natural menopause and total mortality and mortality from ischemic heart disease: the Adventist Health Study, J Clin Epidemiol 52(4) (1999) 303-7.

[81] F. Atsma, M.L. Bartelink, D.E. Grobbee, Y.T. van der Schouw, Postmenopausal status and early menopause as independent risk factors for cardiovascular disease: a meta-analysis, Menopause 13(2) (2006) 265-79.

[82] E. Maichuk, I.V. Voevodina, T.V. Mitrokhina, I.A. Makarova, S.V. Iureneva, [The risk of atherosclerosis and osteoporosis development in post-ovariectomy syndrome women during hormone replacement therapy], Ter Arkh 86(8) (2014) 75-9.

[83] A.M. McCarthy, A. Menke, K. Visvanathan, Association of bilateral oophorectomy and body fatness in a representative sample of US women, Gynecol Oncol 129(3) (2013) 559-64.

[84] S. Kilic, N. Yilmaz, G. Erdogan, M. Aydin, N. Tasdemir, M. Doganay, S. Batioglu, Effect of non-oral estrogen on risk markers for metabolic syndrome in early surgically menopausal women, Climacteric 13(1) (2010) 55-62.

[85] M. Farahmand, F. Ramezani Tehrani, M. Bahri Khomami, M. Noroozzadeh, F. Azizi, Surgical menopause versus natural menopause and cardio-metabolic disturbances: A 12-year population-based cohort study, J Endocrinol Invest 38(7) (2015) 761-7.

[86] W.H. Parker, D. Feskanich, M.S. Broder, E. Chang, D. Shoupe, C.M. Farquhar, J.S. Berek, J.E. Manson, Long-term mortality associated with oophorectomy compared with ovarian conservation in the nurses' health study, Obstet Gynecol 121(4) (2013) 709-16.

[87] T.K. Phung, B.L. Waltoft, T.M. Laursen, A. Settnes, L.V. Kessing, P.B. Mortensen, G. Waldemar, Hysterectomy, oophorectomy and risk of dementia: a nationwide historical cohort study, Dement Geriatr Cogn Disord 30(1) (2010) 43-50.

[88] R. Bove, E. Secor, L.B. Chibnik, L.L. Barnes, J.A. Schneider, D.A. Bennett, P.L. De Jager, Age at surgical menopause influences cognitive decline and Alzheimer pathology in older women, Neurology 82(3) (2014) 222-9.

[89] J. Mytton, F. Evison, P.J. Chilton, R.J. Lilford, Removal of all ovarian tissue versus conserving ovarian tissue at time of hysterectomy in premenopausal patients with benign disease: study using routine data and data linkage, Bmj 356 (2017) j372.

[90] M. van der Klift, C.E. de Laet, E.V. McCloskey, O. Johnell, J.A. Kanis, A. Hofman, H.A. Pols, Risk factors for incident vertebral fractures in men and women: the Rotterdam Study, J Bone Miner Res 19(7) (2004) 1172-80.

[91] W.A. Rocca, B.R. Grossardt, L.T. Shuster, Oophorectomy, estrogen, and dementia: a 2014 update, Mol Cell Endocrinol 389(1-2) (2014) 7-12.

[92] The 2017 hormone therapy position statement of The North American Menopause Society, Menopause 24(7) (2017) 728-753.

[93] S. Ghazal, L. Pal, Perspective on hormone therapy 10 years after the WHI, Maturitas 76(3) (2013) 208-12.

[94] L. Lindh-Astrand, M. Hoffmann, L. Jarvstrat, M. Fredriksson, M. Hammar, A.C. Spetz Holm, Hormone therapy might be underutilized in women with early menopause, Hum Reprod 30(4) (2015) 848-52.

[95] J.S. Haas, B. Geller, D.L. Miglioretti, D.S. Buist, D.E. Nelson, K. Kerlikowske, P.A. Carney, E.S. Breslau, S. Dash, M.K. Canales, R. Ballard-Barbash, Changes in newspaper coverage about hormone therapy with the release of new medical evidence, J Gen Intern Med 21(4) (2006) 304-9.

[96] W.H. Utian, A decade post WHI, menopausal hormone therapy comes full circle--need for independent commission, Climacteric 15(4) (2012) 320-5.

[97] D. Feldman-Stewart, C. Tong, R. Siemens, S. Alibhai, T. Pickles, J. Robinson, M.D. Brundage, The impact of explicit values clarification exercises in a patient decision aid emerges

after the decision is actually made: evidence from a randomized controlled trial, Med Decis Making 32(4) (2012) 616-26.

[98] W. Utian, Managing menopause after HERS II and WHI: coping with the aftermath, Menopause Management, 2002.

[99] R.H. Kenen, P.J. Shapiro, S. Friedman, J.C. Coyne, Peer-support in coping with medical uncertainty: discussion of oophorectomy and hormone replacement therapy on a web-based message board, Psychooncology 16(8) (2007) 763-71.

[100] G.D. Constantine, S. Graham, C. Clerinx, B.A. Bernick, M. Krassan, S. Mirkin, H. Currie, Behaviours and attitudes influencing treatment decisions for menopausal symptoms in five European countries, Post Reprod Health 22(3) (2016) 112-22.

[101] M. Gibson-Helm, H. Teede, A. Vincent, Symptoms, health behavior and understanding of menopause therapy in women with premature menopause, Climacteric 17(6) (2014) 666-73.

[102] E.E. Simpson, Predictors of intentions to use hormone replacement therapy in clinical postmenopausal women, Climacteric 15(2) (2012) 173-80.

[103] D.R. Lauver, L. Settersten, S. Marten, J. Halls, Explaining women's intentions and use of hormones with menopause, Res Nurs Health 22(4) (1999) 309-20.

[104] C.B. Johannes, S.L. Crawford, J.G. Posner, S.M. McKinlay, Longitudinal patterns and correlates of hormone replacement therapy use in middle-aged women, Am J Epidemiol 140(5) (1994) 439-52.

[105] T. Strinic, D. Bukovic, D. Karelovic, A. Despot, N. Bukovic, E. Giudici, H. Silovski, Socio-demographic characteristics of postmenopausal estrogen users, Coll Antropol 26(1) (2002) 245-9.

[106] K.D. Huston SA, Shimp LA, Use, intentions, and beliefs about hormone replacement therapy in women with and without diabetes., Maturitas. 1 (2006) 58-68.

[107] F. Legare, G. Godin, E. Guilbert, L. Laperriere, S. Dodin, Determinants of the intention to adopt hormone replacement therapy among premenopausal women, Maturitas 34(3) (2000) 211-8.

[108] F. Legare, G. Godin, V. Ringa, S. Dodin, L. Turcot, J. Norton, Variation in the psychosocial determinants of the intention to prescribe hormone therapy prior to the release of the Women's Health Initiative trial: a survey of general practitioners and gynaecologists in France and Quebec, BMC Med Inform Decis Mak 5 (2005) 31.

[109] E. Oshima Lee, E.J. Emanuel, Shared decision making to improve care and reduce costs, N Engl J Med 368(1) (2013) 6-8.

[110] F. Legare, S. Ratte, K. Gravel, I.D. Graham, Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions, Patient Educ Couns 73(3) (2008) 526-35.

[111] G. Elwyn, D. Frosch, R. Thomson, N. Joseph-Williams, A. Lloyd, P. Kinnersley, E. Cording, D. Tomson, C. Dodd, S. Rollnick, A. Edwards, M. Barry, Shared decision making: a model for clinical practice, J Gen Intern Med 27(10) (2012) 1361-7.

[112] D. Stacey, F. Legare, K. Lewis, M.J. Barry, C.L. Bennett, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev 4 (2017) CD001431.

[113] M. Fujimori, Y. Shirai, M. Asai, N. Akizuki, N. Katsumata, K. Kubota, Y. Uchitomi, Development and preliminary evaluation of communication skills training program for

oncologists based on patient preferences for communicating bad news, Palliat Support Care 12(5) (2014) 379-86.

[114] K.L. Lim, P. Jacobs, A. Ohinmaa, D. Schopflocher, C.S. Dewa, A new population-based measure of the economic burden of mental illness in Canada, Chronic Dis Can 28(3) (2008) 92-8.

[115] M.A. Rubin, The Collaborative Autonomy Model of Medical Decision-Making, Neurocrit Care 20(2) (2014) 311-318.

[116] M. Younas, E. Bradley, N. Holmes, D. Sud, I.D. Maidment, Mental health pharmacists views on shared decision-making for antipsychotics in serious mental illness, Int J Clin Pharm (2016).

[117] A.M. O'Connor, H.A. Llewellyn-Thomas, A.B. Flood, Modifying unwarranted variations in health care: shared decision making using patient decision aids, Health Aff (Millwood) Suppl Variation (2004) VAR63-72.

[118] D. Stacey, F. Legare, N.F. Col, C.L. Bennett, M.J. Barry, K.B. Eden, M. Holmes-Rovner, H. Llewellyn-Thomas, A. Lyddiatt, R. Thomson, L. Trevena, J.H. Wu, Decision aids for people facing health treatment or screening decisions, Cochrane Database Syst Rev 1 (2014) CD001431.

[119] International Patient Decision Aid Standards (IPDAS) Collaboration. What are patient decision aids?, 2003. http://www.ipdas.ohri.ca/what.html. (Accessed August 26, 2016.

[120] D. Stacey, F. Legare, K.B. Lewis, Patient Decision Aids to Engage Adults in Treatment or Screening Decisions, JAMA 318(7) (2017) 657-658.

[121] G. Gresham, Informed Decision Making for Patients With Advanced Pancreatic Cancer Considering Chemotherapy: Development and Evaluation of a Clinical Decision Aid for Patients, Epidemiology and Community Medicine, University of Ottawa, Ottawa, 2013, p. 170.

[122] J.E. Manson, J.M. Ames, M. Shapiro, M.L. Gass, J.L. Shifren, C.A. Stuenkel, J.V. Pinkerton, A.M. Kaunitz, D.T. Pace, R. Kagan, P.F. Schnatz, S.A. Kingsberg, J.H. Liu, H. Joffe, G. Richard-Davis, S.R. Goldstein, I. Schiff, W.H. Utian, Algorithm and mobile app for menopausal symptom management and hormonal/non-hormonal therapy decision making: a clinical decision-support tool from The North American Menopause Society, Menopause 22(3) (2015) 247-53.

[123] V.R. Stalmeier P, Abhyankar P, Blumenthal-Barby J, Bravo P, Buchholz A, Col N, Ozanne E, Vidal DC., Balancing the presentation of information and options., in: I.V.R.L.-T. H (Ed.) 2012 Update of the International Patient Decision Aid Standards (IPDAS) Collaboration's Background Document. Chapter I, 2012.

[124] M. Noruzinia, I. Coupier, P. Pujol, Is BRCA1/BRCA2-related breast carcinogenesis estrogen dependent?, Cancer 104(8) (2005) 1567-74.

[125] D. Feldman-Stewart, M.A. O'Brien, M.L. Clayman, B.J. Davison, M. Jimbo, M. Labrecque, R.W. Martin, H. Shepherd, Providing information about options in patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S4.

[126] B. Burrell, V. Valledor, M. Crowe, L. Whitehead, Negotiating competing discourses: the decision to take menopausal hormone therapy following surgical menopause, Women Health 50(6) (2010) 527-43.

[127] G. Elwyn, A. O'Connor, D. Stacey, R. Volk, A. Edwards, A. Coulter, R. Thomson, A. Barratt, M. Barry, S. Bernstein, P. Butow, A. Clarke, V. Entwistle, D. Feldman-Stewart, M. Holmes-Rovner, H. Llewellyn-Thomas, N. Moumjid, A. Mulley, C. Ruland, K. Sepucha, A. Sykes, T. Whelan, Developing a quality criteria framework for patient decision aids: online international Delphi consensus process, Bmj 333(7565) (2006) 417.

[128] A. Coulter, D. Stilwell, J. Kryworuchko, P.D. Mullen, C.J. Ng, T. van der Weijden, A systematic development process for patient decision aids, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S2.

[129] M.A. Durand, M. Stiel, J. Boivin, G. Elwyn, Where is the theory? Evaluating the theoretical frameworks described in decision support technologies, Patient Educ Couns 71(1) (2008) 125-35.

[130] A.M. O'Connor, P. Tugwell, G.A. Wells, T. Elmslie, E. Jolly, G. Hollingworth, R. McPherson, H. Bunn, I. Graham, E. Drake, A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation, Patient Educ Couns 33(3) (1998) 267-79.

[131] C.J. Raats, H. van Veenendaal, M.M. Versluijs, J.S. Burgers, A generic tool for development of decision aids based on clinical practice guidelines, Patient Educ Couns 73(3) (2008) 413-7.

[132] G. Elwyn, I. Kreuwel, M.A. Durand, S. Sivell, N. Joseph-Williams, R. Evans, A. Edwards, How to develop web-based decision support interventions for patients: a process map, Patient Educ Couns 82(2) (2011) 260-5.

[133] I.M.D. Foundation, Informed Medical Decisions Foundation. Healthwise for every health decision, 2018. http://www.informedmedicaldecisions.org. (Accessed August 5, 2018 2018).

[134] V.M. Montori, M. Breslin, M. Maleska, A.J. Weymiller, Creating a conversation: insights from the development of a decision aid, PLoS Med 4(8) (2007) e233.

[135] A. Fagerlin, M. Pignone, P. Abhyankar, N. Col, D. Feldman-Stewart, T. Gavaruzzi, J. Kryworuchko, C.A. Levin, A.H. Pieterse, V. Reyna, A. Stiggelbout, L.D. Scherer, C. Wills, H.O.

Witteman, Clarifying values: an updated review, BMC medical informatics and decision making 13 Suppl 2 (2013) S8.

[136] K.R. Sepucha, C.M. Borkhoff, J. Lally, C.A. Levin, D.D. Matlock, C.J. Ng, M.E. Ropka, D. Stacey, N. Joseph-Williams, C.E. Wills, R. Thomson, Establishing the effectiveness of patient decision aids: key constructs and measurement instruments, BMC medical informatics and decision making 13 Suppl 2 (2013) S12.

[137] G. Elwyn, M. Stiel, M.A. Durand, J. Boivin, The design of patient decision support interventions: addressing the theory-practice gap, J Eval Clin Pract 17(4) (2011) 565-74.

[138] N. Joseph-Williams, R. Newcombe, M. Politi, M.A. Durand, S. Sivell, D. Stacey, A. O'Connor, R.J. Volk, A. Edwards, C. Bennett, M. Pignone, R. Thomson, G. Elwyn, Toward Minimum Standards for Certifying Patient Decision Aids: A Modified Delphi Consensus Process, Med Decis Making 34(6) (2014) 699-710.

[139] H.O. Witteman, L.D. Scherer, T. Gavaruzzi, A.H. Pieterse, A. Fuhrel-Forbis, S. Chipenda Dansokho, N. Exe, V.C. Kahn, D. Feldman-Stewart, N.F. Col, A.F. Turgeon, A. Fagerlin, Design Features of Explicit Values Clarification Methods: A Systematic Review, Med Decis Making 36(4) (2016) 453-71.

[140] D. Stacey, J. Kryworuchko, J. Belkora, B.J. Davison, M.A. Durand, K.B. Eden, A.S. Hoffman, M. Koerner, F. Legare, M.C. Loiselle, R.L. Street, Jr., Coaching and guidance with patient decision aids: A review of theoretical and empirical evidence, BMC medical informatics and decision making 13 Suppl 2 (2013) S11.

[141] P. Abhyankar, R.J. Volk, J. Blumenthal-Barby, P. Bravo, A. Buchholz, E. Ozanne, D.C. Vidal, N. Col, P. Stalmeier, Balancing the presentation of information and options in patient

decision aids: an updated review, BMC medical informatics and decision making 13 Suppl 2 (2013) S6.

[142] V.M. Montori, A. LeBlanc, A. Buchholz, D.L. Stilwell, A. Tsapas, Basing information on comprehensive, critically appraised, and up-to-date syntheses of the scientific evidence: a quality dimension of the International Patient Decision Aid Standards, BMC medical informatics and decision making 13 Suppl 2 (2013) S5.

[143] D. Feldman-Stewart, M.A. O'Brien, M.L. Clayman, B.J. Davison, M. Jimbo, M. Labrecque, R.W. Martin, H. Shepherd, Providing information about options in patient decision aids, BMC medical informatics and decision making 13 Suppl 2 (2013) S4.

[144] D.D. Matlock, E.S. Spatz, Design and testing of tools for shared decision making, Circ Cardiovasc Qual Outcomes 7(3) (2014) 487-92.

[145] L.J. Trevena, B.J. Zikmund-Fisher, A. Edwards, W. Gaissmaier, M. Galesic, P.K. Han, J. King, M.L. Lawson, S.K. Linder, I. Lipkus, E. Ozanne, E. Peters, D. Timmermans, S. Woloshin, Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers, BMC medical informatics and decision making 13 Suppl 2 (2013) S7.

[146] R. Garcia-Retamero, M. Galesic, Who profits from visual aids: overcoming challenges in people's understanding of risks [corrected], Soc Sci Med 70(7) (2010) 1019-25.

[147] G.H. Guyatt, A.D. Oxman, G.E. Vist, R. Kunz, Y. Falck-Ytter, P. Alonso-Coello, H.J. Schunemann, GRADE: an emerging consensus on rating quality of evidence and strength of recommendations, Bmj 336(7650) (2008) 924-6.

[148] H.L. Bekker, A.E. Winterbottom, P. Butow, A.J. Dillard, D. Feldman-Stewart, F.J. Fowler, M.L. Jibaja-Weiss, V.A. Shaffer, R.J. Volk, Do personal stories make patient decision aids more

effective? A critical review of theory and evidence, BMC medical informatics and decision making 13 Suppl 2 (2013) S9.

[149] V.A. Shaffer, B.J. Zikmund-Fisher, All stories are not alike: a purpose-, content-, and valence-based taxonomy of patient narratives in decision aids, Med Decis Making 33(1) (2013) 4-13.

[150] M.M. Garvelink, M.M. ter Kuile, A.M. Stiggelbout, M. de Vries, Values clarification in a decision aid about fertility preservation: does it add to information provision?, BMC medical informatics and decision making 14 (2014) 68.

[151] S.L. Sheridan, J.M. Griffith, L. Behrend, Z. Gizlice, C. Jianwen, M.P. Pignone, Effect of adding a values clarification exercise to a decision aid on heart disease prevention: a randomized trial, Med Decis Making 30(4) (2010) E28-39.

[152] A.M. O'Connor, P. Tugwell, G.A. Wells, T. Elmslie, E. Jolly, G. Hollingworth, R. McPherson, H. Bunn, I. Graham, E. Drake, A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation, Patient Educ Couns 33(3) (1998) 267-79.

[153] M.J. Barry, E. Chan, B. Moulton, S. Sah, M.B. Simmons, C. Braddock, Disclosing conflicts of interest in patient decision aids, BMC medical informatics and decision making 13 Suppl 2 (2013) S3.

[154] A. Rostom, A. O'Connor, P. Tugwell, G. Wells, A randomized trial of a computerized versus an audio-booklet decision aid for women considering post-menopausal hormone replacement therapy, Patient Educ Couns 46(1) (2002) 67-74.

[155] K.J. McCaffery, M. Holmes-Rovner, S.K. Smith, D. Rovner, D. Nutbeam, M.L. Clayman, K. Kelly-Blake, M.S. Wolf, S.L. Sheridan, Addressing health literacy in patient decision aids, BMC medical informatics and decision making 13 Suppl 2 (2013) S10.

[156] M.J. Grant, A. Booth, A typology of reviews: an analysis of 14 review types and associated methodologies, Health Info Libr J 26(2) (2009) 91-108.

[157] J. Marjoribanks, C. Farquhar, H. Roberts, A. Lethaby, J. Lee, Long-term hormone therapy for perimenopausal and postmenopausal women, The Cochrane database of systematic reviews 1 (2017) CD004143.

[158] H.M. Boardman, L. Hartley, A. Eisinga, C. Main, M. Roque i Figuls, X. Bonfill Cosp, R. Gabriel Sanchez, B. Knight, Hormone therapy for preventing cardiovascular disease in post-menopausal women, The Cochrane database of systematic reviews (3) (2015) CD002229.

[159] H. Hamoda, The British Menopause Society and Women's Health Concern recommendations on the management of women with premature ovarian insufficiency, Post Reprod Health 23(1) (2017) 22-35.

[160] J.E. Rossouw, R.L. Prentice, J.E. Manson, L. Wu, D. Barad, V.M. Barnabei, M. Ko, A.Z. LaCroix, K.L. Margolis, M.L. Stefanick, Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause, JAMA 297(13) (2007) 1465-77.

[161] A.M. O'Connor, M.J. Jacobsen, D. Stacey, An evidence-based approach to managing women's decisional conflict, J Obstet Gynecol Neonatal Nurs 31(5) (2002) 570-81.

[162] T. Siyam, H. Sultani, S. Ross, T. Chatterley, N. Yuksel, Evaluating the content and development of decision aid tools for the management of menopause: A scoping review, Maturitas 106 (2017) 80-86.

[163] Ottawa Hospital Health Research Institute. Patient Decision Aids. Ottawa Decision Support Framework (ODSF), 2017. https://decisionaid.ohri.ca/odsf.html. (Accessed Sep 19 2018).

[164] L. Webber, M. Davies, R. Anderson, J. Bartlett, D. Braat, B. Cartwright, R. Cifkova, S. de Muinck Keizer-Schrama, E. Hogervorst, F. Janse, L. Liao, V. Vlaisavljevic, C. Zillikens, N. Vermeulen, ESHRE Guideline: management of women with premature ovarian insufficiency, Hum Reprod 31(5) (2016) 926-37.

[165] T. Siyam, S. Ross, S. Campbell, D.T. Eurich, N. Yuksel, The effect of hormone therapy on quality of life and breast cancer risk after risk-reducing salpingo-oophorectomy: a systematic review, BMC Womens Health 17(1) (2017) 22.

[166] T. Siyam, S. Ross, T. Shandro, S. Hagen, L. Battochio, N. Yuksel, Perspectives and decision-making about menopausal therapies in women who had bilateral oophorectomy, Menopause 25(7) (2018) 795-802.

[167] N. Yuksel, T. Siyam, J. Carbon, Determinants of Hormone Therapy Uptake and Decision Making in Surgically Menopausal Women, International Menopause Society (IMS) Annual Meeting, Climacteric, Prague, Czech Republic, 2016.

[168] T. Siyam, J. Carbon, S. Ross, N. Yuksel, Determinants of Hormone Therapy Uptake and Decision-Making in Bilateral Oophorectomy (BO): A Narrative Review, University of Alberta, Edmonton, 2018, p. 22.

[169] N. Hallowell, A qualitative study of the information needs of high-risk women undergoing prophylactic oophorectomy, Psychooncology 9(6) (2000) 486-95.

[170] S. Leatherman, L. Warrick, Effectiveness of decision aids: a review of the evidence, Med Care Res Rev 65(6 Suppl) (2008) 79S-116S.

[171] B. Speller, Development and Alpha Testing of a Fertility Decision Aid for Young Canadians Diagnosed with Breast Cancer at Risk of Infertility Following Cancer Treatment, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, 2017, p. 193.

[172] A. O'Connor, D. Stacey, Ottawa Personal Decision Guide, 2000. https://decisionaid.ohri.ca/docs/das/OPDG.pdf.

[173] G. Elwyn, I. Scholl, C. Tietbohl, M. Mann, A.G. Edwards, C. Clay, F. Legare, T. van der Weijden, C.L. Lewis, R.M. Wexler, D.L. Frosch, "Many miles to go ...": a systematic review of the implementation of patient decision support interventions into routine clinical practice, BMC Med Inform Decis Mak 13 Suppl 2 (2013) S14.

[174] F. Legare, D. Stacey, P.G. Forest, M.F. Coutu, P. Archambault, L. Boland, H.O. Witteman, A. LeBlanc, K.B. Lewis, A.M.C. Giguere, Milestones, barriers and beacons: Shared decision making in Canada inches ahead, Z Evid Fortbild Qual Gesundhwes 123-124 (2017) 23-27.

[175] C. Brackett, S. Kearing, N. Cochran, A.N. Tosteson, W. Blair Brooks, Strategies for distributing cancer screening decision aids in primary care, Patient Educ Couns 78(2) (2010) 166-8.

[176] K.A. Silvia, K.R. Sepucha, Decision aids in routine practice: lessons from the breast cancer initiative, Health Expect 9(3) (2006) 255-64.

[177] V. Uy, S.G. May, C. Tietbohl, D.L. Frosch, Barriers and facilitators to routine distribution of patient decision support interventions: a preliminary study in community-based primary care settings, Health Expect 17(3) (2014) 353-64.

[178] D. Stacey, M.P. Pomey, A.M. O'Connor, I.D. Graham, Adoption and sustainability of decision support for patients facing health decisions: an implementation case study in nursing, Implement Sci 1 (2006) 17.

[179] M. Holmes-Rovner, K. Kelly-Blake, F. Dwamena, K. Dontje, R.C. Henry, A. Olomu, D.R. Rovner, M.L. Rothert, Shared Decision Making Guidance Reminders in Practice (SDM-GRIP), Patient Educ Couns 85(2) (2011) 219-24.

[180] M.M. Schapira, M.A. Gilligan, T.L. McAuliffe, A.B. Nattinger, Menopausal hormone therapy decisions: insights from a multi-attribute model, Patient Educ Couns 52(1) (2004) 89-95.

[181] J. Wade, P.K. Pletsch, S.W. Morgan, S.A. Menting, Hysterectomy: what do women need and want to know?, J Obstet Gynecol Neonatal Nurs 29(1) (2000) 33-42.

[182] M.T. Hoybye, C. Johansen, T. Tjornhoj-Thomsen, Online interaction. Effects of storytelling in an internet breast cancer support group, Psychooncology 14(3) (2005) 211-20.

[183] Canadian Institute for Health Information . The Role of Social Support in Reducing Psychological Distress Canadian Institute for Health Information, 2012, p. 5.