Antihypertensive Deprescribing in Long-Term Care

By

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

Master of Science

in

Clinical Epidemiology

School of Public Health

University of Alberta

Abstract

Antihypertensives are prevalent in long-term care (LTC) populations, however the ratio of benefit to harm of antihypertensive treatment is unclear. There has not yet been a randomized controlled trial to examine the impact of deprescribing all classes of antihypertensive medication in the frail older adult population with a primary outcome of mortality. This thesis is focused on designing a study protocol to address this. This thesis has two parts: (1) a scoping review of cluster randomized trials in LTC and (2) a protocol for a randomized controlled antihypertensive deprescribing trial in LTC.

Study 1. The scoping review was done to help plan the randomized controlled trial. It followed PRISMA guidelines. Studies were included if the design was cluster randomized and residents were from LTC facilities. 195 studies met the inclusion criteria; they were published between 1976 and 2017, with 53% of studies published after 2009. Six percent of studies (n=14) had an Intervention target related to medications, and none of these were on antihypertensive medication. In addition the majority of studies did obtain consent from residents and/or their proxy.

Study 2. The protocol is for a randomized, two parallel group, open-label, event driven trial. It will include 515 LTC residents with a diagnosis of hypertension, on ≥ one antihypertensive medication, and a systolic blood pressure ≤135 mmHg, and follow them for 3 years. The data steward, Alberta Health Services' Research Data Services, will identify and randomize residents, and analyze the results. The facility pharmacist will deprescribe antihypertensives in the intervention group using the algorithm developed by the study authors. The primary outcome is time to all-cause mortality, and secondary outcomes include safety, qualify of life and process measures.

In conclusion, the study designed will help provide clarity to the question of antihypertensive deprescribing in LTC. It is anticipated the results will guide practitioners, and be used in setting hypertension guidelines for the frail older adult population.

Preface

This thesis is an original work by Roni Kraut.

There are two linked projects in this thesis: (1) a scoping review of cluster randomized trials in LTC and (2) a protocol for a study on deprescribing antihypertensive medication in LTC. A version of the former study has been published in Current Gerontology and Geriatrics Research,[1] and the latter will be submitted to BMJ Open.

[1.] Kraut RY, Katz LS, Babenko O et al. A scoping review on the attributes of cluster randomized controlled trials in long-term care facilities. Curr Gerontol Res 2020: 6085368.

Acknowledgements

I wish to thank my supervisors, Dr. Dean Eurich and Dr. Scott Garrison, I am grateful for their assistance and guidance through this work.

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List of Abbreviations

LTC: Long-term care

BP: Blood pressure

AHS: Alberta Health Services

RAI-MDS 2.0: Resident Assessment Instrument Minimum Data Set 2.0

Dx: Diagnosis

QoL-AD: Quality of Life-Alzheimer's Disease

Chapter 1: Introduction

1.1 LTC environment

LTC is defined as a facility-based living environment for individuals that require 24 hour nursing assistance.[1] In Canada there were 236,000 LTC beds in 2016, and the Conference Board of Canada expects this number to double by 2035.[2] Individuals admitted to LTC are increasingly medically complex with a rising proportion having functional limitations and cognitive impairment.[3] In Ontario in 2015, 42% of admitted residents had moderate to severe dementia, and 51% had extensive limitations to their activities of daily living.[3] Individuals are most often admitted into long term care at the end of their life, at a time when they are frail and most susceptible to adverse health consequences from small triggers. In 2017, the annual mortality rate of residents in LTC homes in Canada ranged from 27 – 53%.[4] The vulnerability of LTC residents is particularly felt during COVID-19; there were more than 840 outbreaks in LTC facilities, and LTC residents made up 80% of COVID-19 deaths in Canada.[5] This vulnerability of LTC residents, paired with their complex and multiple medical conditions, creates the perfect storm for polypharmacy.

1.2 Polypharmacy in LTC

Polypharmacy is when an individual is on multiple drugs. The number of drugs needed to be considered polypharmacy is variable, ranging from 2 to upwards of 9.[6] For LTC residents, polypharmacy has been associated with increased mortality and morbidity, and has been associated with worsening qualify of life, including function, cognition, falls and urinary inconinence.[7-8] However polypharmacy is still prevalent in LTC in Canada; in 2016 LTC residents were prescribed an average of 10 different medication classes.[9]

1.3 Antihypertensive medication in LTC

Antihypertensives can add to the burden of polypharmacy in LTC with upwards of 35% of LTC residents on antihypertensives.[10] They encompass 6 different medication classes, including alpha blockers, central alpha agonists, renin angiotensin inhibitors, beta-blockers, diuretics, and calcium channel blockers. Antihypertensive medications are not simply benign medication that lower BP; these drugs have been associated with a myriad of adverse events in frail older adults including falls,[11] cognitive impairment,[12] lower urinary tract symptoms,[13] and depression.[14] Further, the best available evidence, from multiple cohort studies, associates systolic BP lower than 140 mmHg in frail older adults to increased mortality.[15-21]

Antihypertensive medications are often not the focus of deprescribing initiatives in frail older adults and in LTC. [23-24] This may be partly due to the scarcity of evidence around antihypertensive deprescribing. A recent Cochrane review on deprescribing antihypertensives in older people found few studies on this topic and was unable to make a definitive recommendation. The authors indicated it would be advantageous to focus future deprescribing antihypertensive research on the frail older adult population.[25]

1.4 Summary

Current evidence raises the possibility of an unfavourable risk benefit ratio for antihypertensives in the LTC population. However, as yet, randomized controlled trials have not adequately addressed this question. These trials are especially needed to inform clinicians and guidelines committees. This thesis centers on developing a protocol for a well-designed randomized controlled trial that could effectively address this question within the province of Alberta.

1.5 Objectives

There were two objectives for this research project:

1. Characterize published cluster randomized controlled trials in LTC settings to help inform our trial design.

2. Develop, in partnership with Alberta co-investigators able to facilitate this work, a protocol for a randomized controlled trial examining the effect of deprescribing antihypertensive medication on mortality and morbidity, in a LTC population.

For the first objective, we completed a scoping review of cluster randomized trials in LTC. We identified 195 cluster randomized trials in LTC and extracted key characteristics including journal, location, year published, author discipline, funding, methodology, number of participants, and intervention target.

The second objective was accomplished by developing a protocol for a randomized controlled trial. We originally intended to develop a protocol for a cluster randomized trial. However, with the scoping review we gained an appreciation of the additional complexity and power requirements of a cluster randomized trial, and discussions with the AHS Research Data Services led us to believe that a trial with individual level randomization was feasible. Hence, we decided a trial randomized at the participant level would be more appropriate for our purposes. The development of the protocol included multiple steps and collaborating with many individuals including (1) review of current guidelines on hypertension, (2) working with the AHS Research Data Services to delineate variables to include in the study, and to discuss the opportunity for them to identify and randomize patients on behalf of the study, (3) designing a deprescribing algorithm with collaboration from the Cochrane Hypertension Working Group, (4) discussions with geriatric researchers to determine the assessment tool that will best assess frailty in the study, and (5) working with pharmacists and an academic physician to develop a survey to assess facilitators and barriers associated with pharmacists deprescribing antihypertensives.

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Chapter 2: A scoping review on the attributes of cluster randomized controlled trials in long-term care facilities

2.1 Introduction

LTC facilities fulfill an important need in society. Across Europe and North America over 3 million people resided in LTC in 2016, comprising on average 3% of adults over 65 years old.[1] Research is increasingly being conducted in this segment of the population in an effort to optimize care.[2] Cluster randomized trial is a type of randomized controlled trial, where the unit of randomization is the LTC ward or facility instead of the individual, and is often employed in LTC research. This design is especially well suited for evaluating group interventions in LTC, for instance, staff education interventions or new protocols.

Knowledge of the attributes of published cluster randomized trials is advantageous for the design of future research studies. To date, there have been three systematic reviews of randomized controlled trials in LTC, one performed by Gordon and colleagues in 2011[2] and two performed by Diaz-Ordez and colleagues in 2013[3,4]. These systematic reviews focused on the type and target of interventions, consent process, and study quality.[2-4] The present review builds on the previous reviews, with further characterization of cluster randomized trials. The objective of this scoping review was to determine key attributes of cluster randomized trials in LTC.

2.2 Methods

The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines were used.[5] In addition, the methods followed in this review were similar to the methods in Kraut et al. 2017 systematic review.[6]

Study strategy

A medical librarian (S.C.) completed the database search. Databases were searched from their inception to April 1, 2017, using subject headings and text words to retrieve articles related to

the concepts: “long-term care” or “nursing home” and “cluster randomization”. No limits were applied.

The search strategies were adjusted appropriately for each database. The databases in the search were: PROSPERO, Ovid MEDLINE, OVID EMBASE, Ovid Psycinfo, OVID all EBM Review databases, including the Cochrane Database of Systematic Reviews, Proquest Dissertations & Theses, and EBSCO CINAHL. Search strategies are provided in Figure 1. Search results were exported to RefWorks bibliographic software and duplicates were removed.

Papers that were published in languages other than English were translated using Google translate. The references of the three systematic reviews,[2-4] references of the included studies from the literature search, and references of the included studies from the first reference review were checked. Authors were not contacted for additional information.

Study selection

Two criteria were used to determine eligible studies – 1) studies had to be cluster randomized, and 2) studies had to be conducted in a LTC facility. In instances where the type of facility was unclear, the following international definition of a nursing home was used: a facility that provides 24-hour functional support for people who require assistance with their activities of daily living (e.g., dressing, bathing, and eating).[7] In instances of more than one study pertaining to the same research project only the original study was selected.

Study selection was performed by two independent reviewers (R.K., F.C., D.C., or R.A.). Any differences between reviewers were resolved through consensus, and the percentage of agreement between the reviewers was calculated.

Data extraction

The following data were extracted from all included studies: (1) year published, (2) journal title, (3) study location (in cases when the study did not provide the location, the location of the

authors was used as the study location), (4) names of the first and the last authors (the first and the last authors were selected as these authors typically contribute most substantially to a study), (5) highest education level of the first and the last authors (PhD, Master's, MD, undergraduate); if an author had two degrees, the higher degree was selected (for instance, for authors with both a PhD and MD, PhD was selected), (6) discipline of each author (dentistry, epidemiology, medicine, nursing, nutrition, occupational therapy, pharmacy, psychology, physiotherapy, social work, statistics, other, or unknown), (7) funder (government, foundation/charity, medical industry, or other), (8) methodology: stratified randomization, special design (stepped wedge, cross-over, factorial, or > 2 groups), number of residents in a study (originally allocated after randomization), and number of clusters, (9) consent (resident and/or their proxy, only health care worker, only administration and/or indicated resident consent not required, or not stated), (10) target of intervention (behavior/physical restraint, depression, falls/fracture, infection, global function, nutrition, oral health, pain management, physical function/activities of daily living (ADL), prescribing, quality of life, quality of care, skin health, and other). When a study had fewer than four intervention targets, each target was captured. When a study had four or more intervention targets, the target was considered global function.

Author's highest education level and discipline were obtained through information in the study and Google search. Journal impact factor was obtained from the 2017 impact factor listed on the journal website. The 2017 impact factor for all the studies in this review was used due to the inflation of impact factors over time.[8]

Data extraction was completed by two independent reviewers (R.K., L.K., or F.C) and differences between reviewers were resolved through consensus. The percent agreement between the reviewers was calculated.

2.3 Results

Study selection

The search results and the selection process are shown in Figure 2. There were 7,679 identified studies, and of these 195 met the selection criteria. The term cluster randomized was in the title in 60% (n=85) of studies from the original search and in 2% (n=2) of studies from the reference review (Figure 3). The mean initial agreement among the two reviewers was 87%.

Data extraction

The mean initial agreement for data extraction between the two reviewers was 83%. Table 1 provides some of the characteristics of the included studies.

The studies were conducted worldwide with 52% (n=102) in Europe, 29% (n=57) in North America, 11% (n=22) in Australia/New Zealand, and 7% (n=14) in Asia. The publication date of the selected studies ranged from 1976 to 2017, with 53% of the studies published after 2009 (Figure 4). The countries with over 10% of studies were the United States (23%, n=45) and the United Kingdom (18%, n=36).

The studies were published in 76 unique journals. The most frequent journals were the Journal of the American Geriatrics Society (12%, n=28), International Journal of Geriatric Psychiatry (6%, n=13), Journal of the American Medical Director's Association (5%, n=12), and Age and Ageing (4%, n=10). The median impact factor of the journals was 3.67 (interquartile range (IQR) = 2.78-5.06); 12% (n=24) of studies were published in journals with an impact factor > 10, including BMJ (n=8), JAMA (n=6), Lancet (n=5), Archives of Internal Medicine (n=2), New England Journal

of Medicine (n=1), Annals of Internal Medicine (n=1), and the American Journal of Psychiatry (n=1).

The highest education level of the first and the last authors was a PhD (55%, n=215), followed by MD (16%, n=61), Master's (16%, n=61), undergraduate (2%, n=8), other degree (3%, n=12), and unknown (8%, n=32). With respect to the discipline, 34% (n=134) of the first and the last authors were in medicine and 17% (n=65) of the authors were in nursing. Seventeen percent (n=23) of physician authors and 65% (n=42) of nurse authors had a PhD.

Fifty-five percent of studies (n=107) had one funder, 19% (n=36) had two funders, 10% (n=20) had three funders, 8% (n=16) had more than three funders, and in 8% (n=16) of studies this information was not available. The 195 studies had in total 346 funders, of these 49% (n=169) was government agency funding, 20% (n=70) was foundation or charity funding, 11% (n=40) was medical industry funding, 5% (n=16) was other or unknown types of funding, and 15% of the studies (n=52) did not disclose this information. The studies with industry funding were predominately focused on infection, falls, and oral health.

Eighty-two percent of studies (n=159) had a standard design in which clusters were randomized into a control group and an intervention group and were followed over time. Ten percent of studies (n=20) had more than two groups in their design, the majority of these studies had two intervention groups and one control group. Close to 3% (n=5) had a stepped wedge design, 3% of studies (n=6) had a factorial design, and close to 3% of studies (n=5) had a cross-over design. Fifty-two percent of studies (n=102) used stratified randomization. In studies with fewer than 10 clusters, 27% (n=13) used stratified randomization, while in studies with 10 or more clusters, 62% (n=87) used stratified randomization. The median number of participants (i.e., residents)

per study was 334 (IQR=140–742) and the median number of clusters was 15 (IQR=9–30). The median number of clusters by number of study participants is shown in Table 2.

Seventy-two percent of studies (n=141) obtained consent from the resident and/or their proxies, 2% (n=3) obtained partial consent from the resident and/or their proxies, 3% (n=6) obtained consent only from health care workers, 8% (n=16) obtained consent only from administration and/or the study indicated resident consent was not required, and 15% (n=29) did not provide information on consent. In studies with fewer than 1000 residents, 85% obtained consent from the resident and/or their proxy, whereas in studies with 1000 or more residents, 31% obtained consent from the resident and/or their proxy (Table 2).

Thirteen percent of studies (n=29) focused on infection, 13% (n=28) focused on falls/fractures, and 13% (n=28) were on behavior/physical restraint. Other intervention targets with more than 6 studies were: physical function/activities of daily living (8%, n=17), depression (8%, n=17), prescribing (6%, n=14), global function (5%, n=11), nutrition (5%, n=11), oral health (5%, n=10), quality of life (4%, n=9), quality of care (4%, n=9), pain management (4%, n=9), and skin health (4%, n=9). The focus of studies changed over time, with the numbers of studies focusing on falls decreasing and studies focusing on pain increasing (Figure 5).

2.4 Discussion

Our scoping review provides a detailed characterization of published cluster randomized controlled studies in LTC. The location of the studies in this review is consistent with the geographic distribution of medical research publications overall, with approximately a third of the studies conducted in the US and a third in Europe.[9] In contrast, the predominant funder of the studies and the discipline of authors in this review are different from those in medical research overall: [9] only a minority of the studies in the present review were funded by medical industry and nursing was the second most frequent discipline of the authors.

The majority of studies obtained consent from the resident and/or their proxy. This is notable as consent is more challenging and resource intensive in LTC than in the general population due to lack of competency of many LTC residents.[10]

The majority of the cluster randomized studies focused on geriatric syndromes (i.e., conditions in older people caused by a multitude of risk factors but result in the same outcome[11]) and covered a wide range of these syndromes. Falls/fracture, infection and behavior/restraints were studied more frequently than other syndromes, perhaps because these concerns are more pressing in LTC facilities.

The main limitation of this study is that we may have missed some published cluster randomized trials in LTC. We only reviewed the references of the first and second set of studies included in this review. Further our literature search terms were "long-term care" and "nursing home", which may have missed studies in other types of LTC facilities, for instance, geriatric hospitals. However, our search is the most rigorous of the three published systematic reviews. Diaz-Ordaz and colleagues' literature search up to early 2010 yielded 84 studies, while Gordon and colleagues' literature search up to mid 2009 yielded 77 studies[2-4]. In contrast, our literature search up to the end of 2009 found 92 studies. Further, given the large number of studies in the present review, it is unlikely the missed cluster randomized trials, if any, would have a significant impact on the results.

2.5 Conclusions

Cluster randomized controlled trials in LTC are central for advancing quality of care and translating the findings into practice. They have a very unique set of characteristics, including funding, author discipline, research design, and focus. This review provides the most comprehensive review of study characteristics to further research endeavors in this field.

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Table 1. Characteristics of includes studies

ID	Location	Stratified	Participant/proxy consent	Intervention Target	Number of residents
Avorn 1992[1]	United States	Yes	Not given	Prescribing - psychoactive use	823
Baldwin 2010[2]	Northern Ireland	Yes	Yes	Infection - MRSA	793
Ballard 2016[3]	England	Yes	Yes	Prescribing - psychoactive use, behaviour & depression	277
Barrick 2010[4]	United States	No	Yes	Behaviour	66
Beck 2016[5]	Denmark	No	Yes	Global function	246
Becker 2003[6]	Germany	No	Yes	Falls - incidence	981
Beer 2011[7]	Australia	No	Yes	Quality of life	351
Bellini 2015[8]	Switzerland	No	Yes	Infection - MRSA	4750
Bentzen 2008[9]	Norway	Yes	Partial	Falls - hip protector use	1236
Boorsma 2011[10]	Netherlands	Yes	Yes	Quality of care	462
Booy 2012[11]	Australia	Yes	Yes	Infection - Influenza	393
Bouwen 2008[12]	Belgium	No	Yes	Falls - incidence	379
BrÃne 1989[13]	Sweden	No	Yes	Global function	46
Bravo 2005[14]	Canada	Yes	Yes	Quality of care	122
Brittle 2009[15]	England	No	Yes	Physical function & depression	56
Budtz-Jorgensen 2000[16]	Switzerland	Yes	Yes	Oral health	237
Camerson 2011[17]	Australia	No	Yes	Falls - hip protector use	235
Carman 2000[18]	England	Yes	Yes	Infection - Influenza	1437
Carville 2014[19]	Australia	Yes	Yes	Skin health - skin tears	984
Chami 2012[20]	France	Yes	No	Infection - rates	4345
Chen 2010[21]	China (Hong Kong)	Yes	Not given	Infection - Influenza	Not given
Chen 2015[22]	Taiwan	No	Not given	Physical function	127
Chen 2016[23]	Taiwan	No	Yes	Pain management	195
Cheng 2014[24]	China (Hong Kong)	No	Yes	Cognition	117
Chenoweth 2009[25]	Australia	Yes	Yes	Behaviour	289
Chenoweth 2014[26]	Australia	Yes	Yes	Global function	601
Clare 2013[27]	England	Yes	Yes	Quality of life	65
Colon-Emeric 2007[28]	United States	No	Not given	Fractures	606
Colon-Emeric 2013[29]	United States	Yes	No (health care	Falls - incidence	601
Connolly 2015[30]	New Zealand	Yes	No	Hospitalizations	1998
Corcoran 2017[31]	United States	No	Yes	Physical function & nutrition	121
Cox 2008[32]	England	Yes	Not given	Fractures	6231
Crotty 2004[33]	Australia	No	Yes	Prescribing - appropriate	158
Davison 2007[34]	Australia	No	Yes	Behaviour	113
Davison 2013[35]	Australia	Yes	Yes	Depression	216
De Visschere 2011[36]	Belgium	Yes	Yes	Oral health	1393
De Visschere 2012[37]	Belgium	Yes	Yes	Oral health	373
Drager 2016[38]	Germany	No	Yes	Pain management	747

Drinka, 1998[39]	United States	Yes	Yes	Infection - Influenza	381
Dyer 2004[40]	England	No	Yes	Falls - incidence	196
Edberg 1999[41]	Sweden	No	Not given	Behaviour & depression	22
Eisses 2005[42]	Netherlands	Yes	Yes	Depression	426
Ersek 2016[43]	United States	Yes	Yes	Pain management	485
Evans 1997[44]	United States	No	Yes	Physical restraint	463
Field 2009[45]	Canada	Yes	Not given	Prescribing - appropriate	833
Finnema 2005[46]	Netherlands	Yes	Yes	Behaviour & depression	194
Fleet 2014[47]	England	Yes	Yes	Infection - antibiotic prescribing	1610
Fossey 2006[48]	England	Yes	Yes	Prescribing - psychoactive use	349
Frenkel 2001[49]	England	No	Yes	Oral health	378
Fritsch 2009[50]	United States	Yes	Yes	Quality of care	Not given
Galik 2014[51]	United states	Yes	Yes	Global function	96
Gaskill 2009[52]	Australia	No	Yes	Nutrition	279
Gillis 2016[53]	Belgium	No	Yes	Skin health - bathing	163
Gopal Rao 2009[54]	England	Yes	Not given	Infection - control	565
Gudex 2010[55]	Denmark	Yes	Yes	Global function	348
Gurwitz 2008[56]	Canada and US	Yes	Not given	Prescribing - adverse events	1118
Hanson 2005[57]	United states	No	No	End of life	458
Hanson 2011[58]	United States	Yes	Yes	Nutrition	256
Hanson 2017[59]	United States	Yes	Yes	End of life	302
Hickman 2007[60]	United States	No	Yes	Depression	66
Ho 2012[61]	China (Hong Kong)	No	No	Infection - rates	2407
Hoeffer 2006[62]	United States	No	Yes	Skin health - bathing	69
Houser 2014[63]	United States	No	Yes	Depression & behaviour	20
Hsu 2015[64]	England	Yes	Yes	Global function	17
Huizing 2006[65]	Netherlands	No	Yes	Physical restraint	145
Huizing 2009[66]	Netherlands	No	Yes	Physical restraint	371
Husebo 2011[67]	Norway	No	Yes	Behaviour	352
Jensen 2002[68]	Sweden	Yes	Yes	Falls - incidence	402
Jeon 2015[69]	Australia	Yes	No (health care	Staff - working environment	1730
Jordan 2015[70]	England	No	Yes	Prescribing - adverse events	43
Joranson 2015[71]	Norway	No	Yes	Behaviour	60
Juola 2014[72]	Finland	Yes	Yes	Prescribing - appropriate	227
Juthani-Mehta 2015[73]	United States	Yes	Yes	Infection - pneumonia	834
Kalinowski 2015[74]	Germany	Yes	Yes	Pain management	737
Kennedy 2015[75]	Canada	Yes	No	Prescribing - Osteoporosis	5478
Kerse 2004[76]	New Zealand	Yes	Yes	Falls - incidence	553
Kerse 2008[77]	New Zealand	No	Yes	Physical function, quality of life & falls	682
Kiel 2007[78]	United States	No	Yes	Fractures	1042
Kinley 2014[79]	England	Yes	No	End of life	2444
Kinney 2003[80]	United States	Yes	Not given	Activities of daily living & satisfaction with care	2222
Koczy 2011[81]	Germany	No	No	Physical restraint	430

Koike 2009[82]	Japan	No	Yes	Falls - incidence	672
Konner 2015[83]	Germany	Yes	Yes	Pain management	747
Koo 2016[84]	United States	No	Not given	Infection - control	not given
Kopke 2012[85]	Germany	Yes	No	Physical restraint	3771
Kovacs 2007[86]	Spain	No	Yes	Pain management	673
Kuck 2014[87]	Germany	No	Yes	Sleep	107
Kuske 2009[88]	Germany	No	Yes	Quality of care	321
Langer 1976[89]	United States	No	Not given	Depression, behaviour & perceived control	91
Lapane 2011[90]	United States	Yes	No	Prescribing - adverse events	3261
Law 2006[91]	England	No	Yes	Falls - incidence	3717
Lawton 1998[92]	United States	No	Not given	Global function	97
Lee 2002[93]	China (hong kong)	Yes	Yes	COPD	89
Lemaitre 2009[94]	France	Yes	Not given	Infection - Influenza	3400
Leontjevas 2013[95]	Netherlands	No	Yes	Depression	547
Leslie 2013[96]	England	Yes	Yes	Nutrition	41
Lin 2010[97]	Taiwan	No	Yes	Nutrition	85
Linn 1989[98]	United States	Yes	Yes	End of life	306
Liu 2017[99]	China (Hong Kong)	No	Yes	Pain management	128
Loeb 2005[100]	Canada and US	No	Not given	Infection - antibiotic prescribing	4217
Loeb 2006[101]	Canada	Yes	Yes	Infection - pneumonia	680
Looijmans-van den Akker 2010[102]	Netherlands	Yes	Not given	Infection - Influenza	5595
Lord 2003[103]	Australia	Yes	Yes	Physical function, falls - incidence	551
Low 2013[104]	Australia	Yes	Yes	Depression	398
MacEntee 2007[105]	Canada	Yes	Yes	Oral health	152
MacRae 1996[106]	United States	No	Yes	Physical function & quality of life	37
Madigan 2014[107]	Northern Ireland	Yes	No (health care	Nutrition	Not given
Makris 2000[108]	United States	Yes	Not given	Infection - rates	890
Mamhidir 2017[109]	Sweden	Yes	Yes	Pain management	213
McMurdo 1994[110]	Scotland	No	Yes	Physical function	65
McMurdo 2000[111]	Scotland	No	Not given	Falls - incidence	133
McSweeney 2012[112]	Australia	No	Not given	Depression	44
Meeks 2015[113]	United States	Yes	Yes	Depression	82
Meyer 2003[114]	Germany	No	No	Fractures	942
Meyer 2009[115]	Germany	No	Not given	Falls - incidence	1125
Mody 2015[116]	United States	Yes	Yes	Infection - indwelling devices	418
Mohide 1988[117]	Canada	Yes	Not given	Quality of care	1525
Mojon 1998[118]	Switzerland	Yes	Yes	Oral health	116
Molloy 2000[119]	Canada	Yes	Yes	End of life	1292
Monette 2007[120]	Canada	Yes	No (health care	Infection - antibiotic prescribing	2168
Moore 2011[121]	Ireland	No	Yes	Skin health - pressure ulcer	213
Mozley 2007[122]	England	No	Yes	Depression	143
Nagayama 2016[123]	Japan	No	Yes	Quality of life & activities of daily living	54

Naughton 2001[124]	United States	No	Not given	Infection - pneumonia	Not given
Neyens 2009[125]	Netherlands	Yes	Yes	Falls - incidence	518
Nijs 2006[126]	Netherlands	Yes	Yes	Quality of life, physical function & nutrition	178
O'halloran 2004[127]	Northern Ireland	Yes	Yes	Fractures	4117
O'Shea 2014[128]	Ireland	Yes	Yes	Quality of life	304
Olsen 2016[129]	Norway	No	Yes	Depression, behaviour & quality of life	58
Orrel 2007[130]	England	No	Yes	Quality of life/unmet need	238
Patterson 2010[131]	Northern Ireland	Yes	Yes	Prescribing - psychoactive use	334
Pellfolk 2010[132]	Sweden	No	Not given	Physical restraint	355
Peterson 2016[133]	United States	No	Partial	Infection - MRSA	Not given
Pettersson 2011[134]	Sweden	Yes	No (health care	Infection - antibiotic prescribing	2537
Pieper 2016[135]	Netherlands	No	Yes	Behaviour	288
Pitkala 2007[136]	Finland	Yes	Yes	Constipation	209
Potter 1997[137]	Scotland	Yes	Partial	Infection - Influenza	1059
Proctor 1999[138]	England	Yes	Yes	Quality of care	120
Rantz 2001[139]	United States	No	Not given	Global function	7385
Rapp 2013[140]	Germany	No	Yes	Behaviour	304
Rasmussen 2015[141]	Denmark	No	No (health care	Staff - back pain	Not given
Ray 1997[142]	United States	Yes	Yes	Falls - incidence	499
Ray 2005[143]	United States	Yes	Not given	Falls - injuries	10558
Resnick 2009[144]	United States	Yes	Yes	Global function	487
Roberts 2001[145]	Australia	Yes	No	Prescribing - appropriate	3230
Rokstad 2013[146]	Norway	Yes	Yes	Behaviour	624
Rosendahl 2006[147]	Sweden	Yes	Yes	Physical function	191
Roth 2014[148]	Germany	No	Not given	Quality of care	624
Rothan-Tondeur 2010[149]	France	No	No	Infection - Influenza	Not given
Sackley 2006[150]	England	Yes	Yes	Activities of daily living	118
Sackley 2008[151]	England	No	Yes	Urinary continence	34
Sackley 2009[152]	England	No	Yes	Physical function & activities of daily living	243
Sackley 2015[153]	England	Yes	Yes	Activities of daily living	1042
Salva 2016[154]	Spain	No	Yes	Falls - incidence	441
Sambrook 2012[155]	Australia	No	Yes	Nutrition, falls - incidence	602
Schnelle 1999[156]	United States	No	Yes	Sleep	184
Schoonhoven 2015[157]	Netherlands	Yes	Yes	Skin health - bathing	500
Schora 2014[158]	United States	No	Yes	Infection - MRSA	5828
Schou 1989[159]	Scotland	No	Yes	Oral health	187
Schrijnemaekers 2002[160]	Netherlands	Yes	Yes	Behaviour	151
Siddiqi 2016[161]	England	Yes	Yes	Delirium	215
Simmons 2008[162]	United states	No	Yes	Nutrition	124
Simons 2001[163]	England	Yes	Yes	Oral health	164
Sinclair 2012[164]	England	No	Yes	Diabetes	102
Sloane 2004[165]	United States	No	Yes	Skin health - bathing	73
Snyder 2013[166]	United States	Yes	Yes	Nutrition	256

Soon 2002[167]	Canada	Yes	Yes	Depression	103
Splett 2003[168]	United States	No	Yes	Nutrition	394
Stein 2001[169]	United States	Yes	Yes	Prescribing - NSAID use	158
Stern 2014[170]	Canada	No	Yes	Skin health - pressure ulcer	137
Teresi 2013[171]	United States	No	Yes	Resident to resident mistreatment	1405
Testad 2005[172]	Norway	Yes	Not given	Physical restraint	151
Testad 2010[173]	Norway	Yes	No	Behaviour	211
Testad 2015[174]	Norway	No	Yes	Physical restraint	274
Tjia 2015[175]	United States	Yes	No	Prescribing - psychoactive use	5488
Toots 2016[176]	Sweden	Yes	Yes	Physical function & activities of daily living	186
Trick 2004[177]	United States	No	Yes	Infection - MRSA, VRE	283
Tse 2012[178]	China (Hong Kong)	No	Yes	Pain management	535
Tse 2016[179]	China (Hong Kong)	No	Not given	Global function	115
Underwood 2013[180]	England	Yes	Yes	Depression	891
Van de Ven 2013[181]	Netherlands	Yes	Yes	Behaviour	268
Van der Maaden 2016[182]	Netherlands	Yes	Yes	Infection - pneumonia	210
Van der Putten 2013[183]	Netherlands	No	Yes	Oral health	343
Van Gaal 2011[184]	Netherlands	Yes	Yes	Skin health - pressure ulcer, infection – UTI &	392
Van Malderen 2017[185]	Belgium	No	Yes	Quality of life	88
Vigild 1990[186]	Denmark	No	Yes	Oral health	203
Visser 2008[187]	Australia	No	Yes	Behaviour	76
Walker 2016[188]	England	No	Yes	Falls - incidence	52
Ward 2010[189]	Australia	Yes	No	Fractures	5391
Wenborn 2013[190]	England	Yes	Yes	Quality of life	210
Williams 1987[191]	Australia	No	Not given	Global function	20
Williams 2017[192]	United States	Yes	Yes	Behaviour	83
Yeung 2011[193]	China (Hong Kong)	Yes	Yes	Infection - rates	675
Yokoi 2015[194]	Japan	No	Yes	Falls - incidence	105
Zwijsen 2014[195]	Netherlands	No	No	Behaviour	393

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Table 2 Number of clusters and consent by study size

Number of participants	Number of studies	Median number of clusters (IQR)	% of studies reporting participant and/or their proxy consent
<150	49	6 (3-12)	84%
150 - 350	48	15 (8-21)	96%
351 - 999	54	14(12-21)	78%
≥1000	36	38 (20-58)	31%

Figure 1: Literature search

Medline March 22, 2017

1. ((cluster* adj2 (random* or RCT or group* or unit* or trial* or study or studies)) or (group* adj2 randomi*) or randomi?ation unit*).ti,ab.
2. exp Housing for the Elderly/ or exp Homes for the Aged/
3. exp Nursing Homes/ or exp Rehabilitation Centers/ or exp Skilled Nursing Facilities/ or (nursing home* or extended care* or care home*).mp. or ((senior* or continuing care or disabled or old age or geriatric* or elder care* or rehabilitat* or long term care) adj2 (lodge* or facility* or home* or residence* or centre* or center*)).mp.
4. (exp Nursing Homes/ or exp Residential Facilities/ or exp Rehabilitation Centers/ or exp Skilled Nursing Facilities/) and (elders or older person* or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or old age or (seniors not "high school") or older adult* or centenarian* or nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest old").ti,ab.
5. (exp "Aged, 80 and over"/ or exp Geriatrics/ or exp aged/ or Health Services for the Aged/ or Senior Centers/) and (exp Nursing Homes/ or exp Residential Facilities/ or exp Rehabilitation Centers/ or exp Skilled Nursing Facilities/ or (home* or manor or manors or lodge or lodges or facility or facilities or long term care or assisted living or group homes* or "homes of aged" or nursing home* or care home* or nursing home* or extended care*)).ti,ab.
6. ((elders or older person* or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or old age or (seniors not "high school") or older adult* or centenarian* or nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest old") adj3 (home* or manor or manors or lodge or lodges or facility or facilities or long term care or assisted living or group homes* or "homes for aged" or nursing home* or nursing home* or extended care* or care home*)).mp.
7. 2 or 3 or 4 or 5
8. 1 and 7
9. waiv*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
10. 7 and 9
11. 8 or 10
12. remove duplicates from 11

Database: Embase <1974 to 2017 March 28>

Search Strategy:

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1 ((cluster* adj2 (random* or RCT or group* or unit* or trial* or study or studies)) or (group* adj2 randomi*) or
randomi?ation unit*).ti,ab. (33132)
2 senior centre/ or elderly care/ (38307)
3 (exp nursing homes/ or residential home/) and (elders or older person* or "aged, 80 and over" or older people or
golden age* or elderly or geriatric* or old age or (seniors not "high school") or older adult* or centenarian* or
nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest old").ti,ab. (14691)
4 (exp geriatrics/ or exp aged/ or Health Services for the Aged/ or senior center/) and (exp nursing home/ or exp
residential home/ or (home* or manor or manors or lodge or lodges or facility or facilities or long

term care or
assisted living or group homes* or "homes of aged" or nursing home* or care home* or nursing home* or extended
care*)).ti,ab. (106780)
5 ((elders or older person* or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or old
age or (seniors not "high school") or older adult* or centenarian* or nonagenarian* or octogenarian* or septuagenarian*
or sexagenarian* or "oldest old") adj3 (home* or manor or manors or lodge or lodges or facility or facilities or long
term care or assisted living or group homes* or "homes for aged" or nursing home* or extended care* or care home*)).mp.
(9809)
6 2 or 3 or 4 or 5 (140319)
7 1 and 6 (934)
8 waiv*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug
manufacturer, device trade name, keyword, floating subheading] (4975)
9 6 and 8 (148)
10 7 or 9 (1079)
11 remove duplicates from 10 (1017)

Database: PsycINFO <1806 to March Week 3 2017>

Search Strategy:

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1 ((cluster* adj2 (random* or RCT or group* or unit* or trial* or study or studies)) or (group* adj2 randomi*) or
randomi?ation unit*).ti,ab. (5674)
2 (exp Nursing Homes/ or exp Long Term Care/ or exp Residential Care Institutions/) and (elders or older person* or
"aged, 80 and over" or older people or golden age* or elderly or geriatric* or old age or (seniors not "high school") or
older adult* or centenarian* or nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest
old").ti,ab. (6316)
3 exp Geriatrics/ or exp aging/ or exp elder care/ or exp Geriatric Patients/ or exp Gerontology/ (75253)
4 exp Nursing Homes/ or exp Long Term Care/ or (home* or manor or manors or lodge or lodges or facility or
facilities or long term care or assisted living or group homes* or "homes of aged" or nursing home* or care home* or
nursing home* or extended care*).ti,ab. (166979)
5 3 and 4 (10325)
6 ((elders or older person* or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or old
age or (seniors not "high school") or older adult* or centenarian* or nonagenarian* or octogenarian* or septuagenarian*
or sexagenarian* or "oldest old") adj3 (home* or manor or manors or lodge or lodges or facility or facilities or long

term care or assisted living or group homes* or "homes for aged" or nursing home* or nursing home* or extended care* or
care home*)).mp. (4283)
7 2 or 5 or 6 (15170)
8 1 and 7 (89)
9 waiv*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
(1066)
10 7 and 9 (25)
11 8 or 10 (113)
12 remove duplicates from 11 (113)

CINAHL Searched March 29, 2017

Select / deselect all | Search with AND | Search with OR | Delete Searches

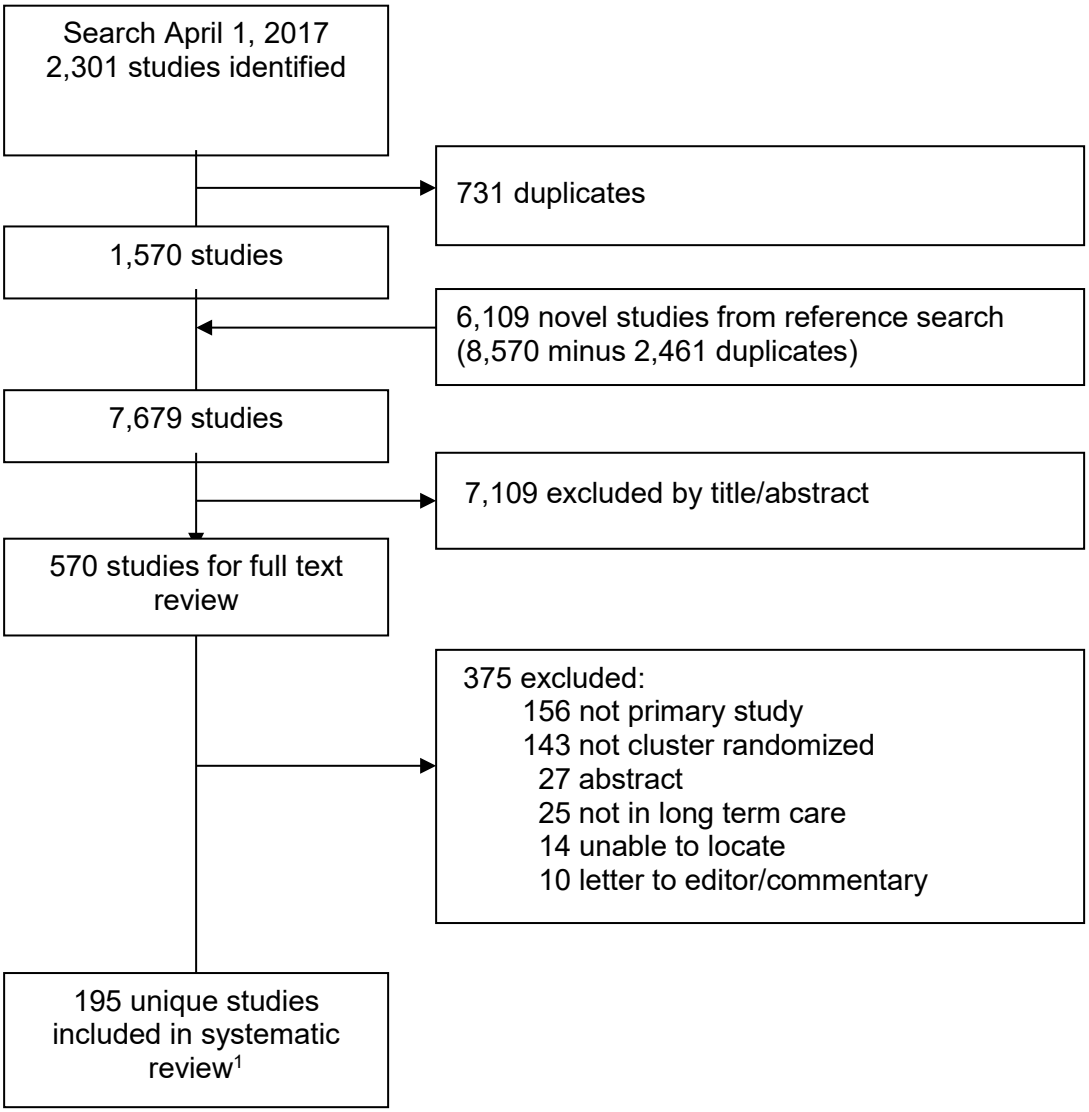
	Search ID#	Search Terms	Search Options	Actions
☐	S15	S1 AND S14	**Search modes** - Find all my search terms	View Results (515)
☐	S14	S2 OR S6 OR S12 OR S13	**Search modes** - Find all my search terms	View Results (60,388)
☐	S13	S9 AND (home* or manor or manors or lodge or lodges or facility or facilities or "long term care" or "assisted living" or "group homes*" or "homes for aged" or "nursing home*" or "extended care*" or "care home*"))	**Search modes** - Find all my search terms	View Results (58,097)
☐	S12	(elders or "older person*" or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or "old age" or (seniors not "high school") or "older adult*" or centenarian* or nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest old") AND (MH "Residential Facilities+")	**Search modes** - Find all my search terms	View Results (10,537)
☐	S11	S9 AND S10	**Search modes** - Find all my search terms	View Results (12,414)
☐	S10	(MH "Residential Facilities+")	**Search modes** - Find all my search terms	View Results (25,722)
☐	S9	S3 OR S7 OR S8	**Search modes** - Find all my search terms	View Results (601,809)
☐	S8	(MH "Geriatrics")	**Search modes** - Find all my search terms	View Results (4,725)
☐	S7	(MH "Aged+") OR (MH "Health Services for the Aged")	**Search modes** - Find all my search terms	View Results (594,276)
☐	S6	S4 OR S5	**Search modes** - Find all my search terms	View Results (2,759)
☐	S5	(MH "Senior Centers")	**Search modes** - Find all my search terms	View Results (1)
☐	S4	(MH "Housing for the Elderly")	**Search modes** - Find all my search terms	View Results (2,758)
☐	S3	(MH "Gerontologic Care")	**Search modes** - Find all my search terms	View Results (16,451)
☐	S2	((elders or "older person*" or "aged, 80 and over" or older people or golden age* or elderly or geriatric* or "old age" or (seniors not "high school") or "older adult*" or centenarian* or nonagenarian* or octogenarian* or septuagenarian* or sexagenarian* or "oldest old") N3 (home* or manor or manors or lodge or lodges or facility or facilities or "long term care" or "assisted living" or "group homes*" or "homes for aged" or "nursing home*" or "extended care*" or "care home*"))	**Limiters** - Full Text **Search modes** - Find all my search terms	View Results (9,732)
☐	S1	((cluster* N3 (random* or RCT or group* or unit* or trial* or study or studies))) OR "randomisation unit*" OR (group N2 randomi* or "randomization unit*")	**Search modes** - Find all my search terms	View Results (12,152)

PROSPERO March 29, 2017

("cluster RCT" OR "cluster randomisation" OR "cluster randomization" OR "cluster trial" OR "cluster randomized" OR "cluster randomised" OR "cluster trials") AND ("seniors center*" OR "nursing home*" OR "elder care" OR "residential facilit*") 41 studies found

Proquest Searched March 29, 1017 Results =21
(noft("nursing home*") OR noft("care home") OR noft("senior* center*") OR noft(residential) OR noft("long term care")) AND (noft("cluster RCT") OR noft("cluster randomisation") OR noft("cluster randomization") OR noft("cluster trial") OR noft("cluster randomized") OR noft("cluster randomised") OR noft("cluster trials")) Results =21
Clinicaltrials.gov Searched March 29, 2017 Results = 29
("nursing home" OR "seniors center" OR residential OR "long term care") AND ("cluster RCT" OR "cluster randomisation" OR "cluster randomization" OR "cluster trial" OR "cluster randomized" OR "cluster randomised" OR "cluster trials") | Older Adult

Figure 2. PRISMA flow diagram



[1] 195 studies = 142 studies (from original review) + 53 studies (review of citations)

Figure 3. Number of studies with the term cluster randomized in their title from the literature search and the reference review

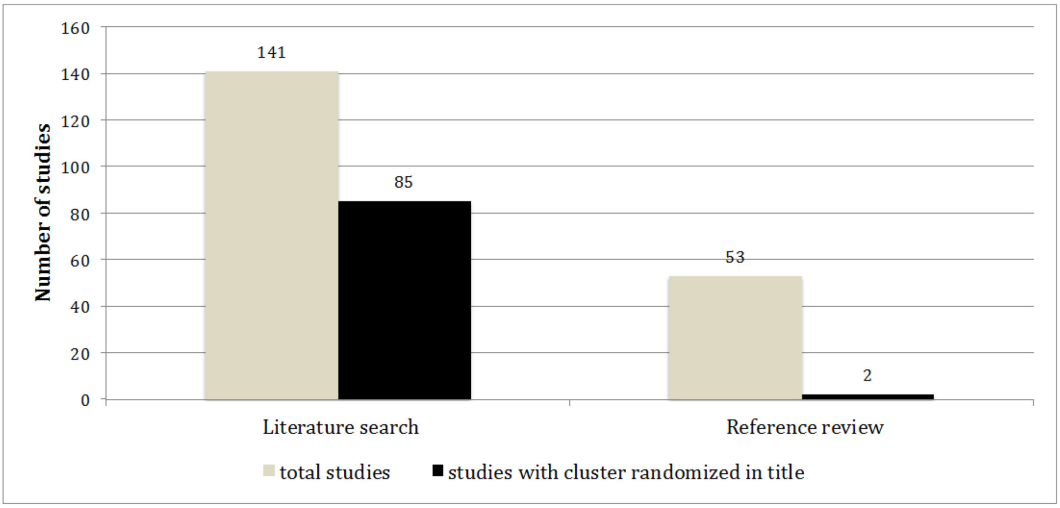


Figure 4. Number of published cluster randomized studies in LTC by year

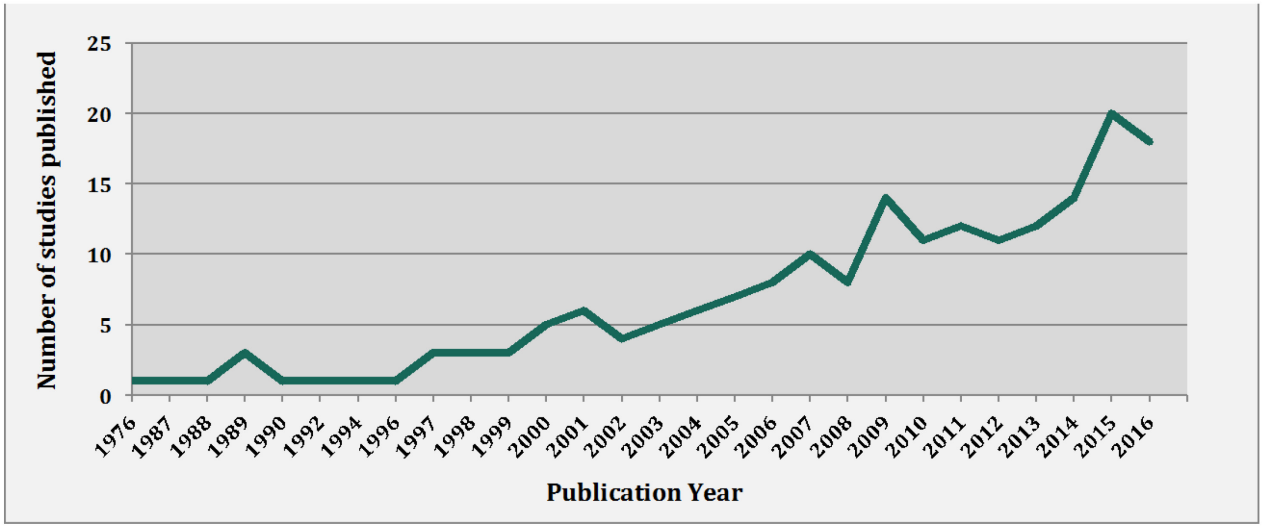
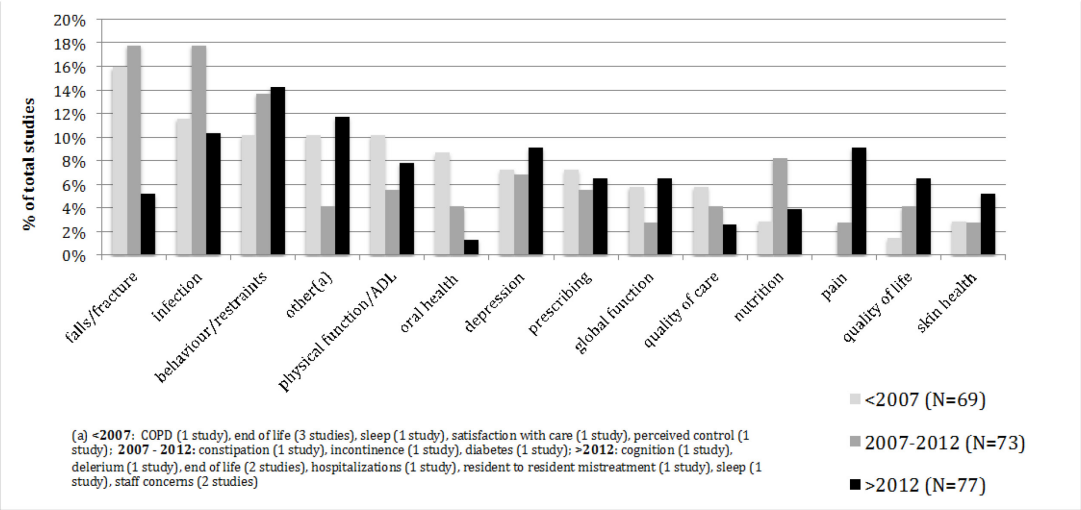


Figure 5. Intervention targets by year of publication



Chapter 3 Antihypertensive deprescribing in long-term care (ADCare): protocol for a randomized controlled trial

3.1 Introduction

Deprescribing is a term first coined in 2003 in Australia to explain a systematic approach to reduce medication in the older adult population.[1] Since then, deprescribing has been found to have a myriad of benefits including reduced mortality,[2] decrease in falls,[2] and reduction in costs.[3] It has become increasingly recognized and accepted in the medical community as an important activity in the ongoing care of frail older adults with multiple co-morbidities.

Most research on deprescribing is centered around higher risk medications, with little attention given to antihypertensive medication.[2] However, antihypertensive medication is important to consider given it is prescribed to upwards of 35% of frail older adults.[4] Further it is associated with decreased quality of life, including falls,[5] cognitive impairment,[6] lower urinary tract symptoms,[7] depression,[8] and polypharmacy,[9] and the best available evidence (cohort studies) has consistently found BP <140/90 is also associated with increased mortality.[10-16]

To date, there have been no randomized controlled trials on deprescribing antihypertensive medication in the frail older adult population with outcomes of cardiovascular events or mortality. There have, however been a few randomized controlled trials that come close to addressing this question. Burr 1977[17](n=141) and Myers 1982[18] (n=77) deprescribed only diuretics in frail older adults and found no impact on cardiovascular events and mortality. Moonen 2015[19] (n=385) deprescribed all classes of antihypertensive, but in older adults that were not frail, and as a secondary outcome found no impact on cardiovascular events and mortality. Further, a cluster randomized trial by Gulla and colleagues 2018[20] (n=295) examined the impact of an educational deprescribing initiative in frail older adults, but the outcome was the number of antihypertensive medication and systolic BP, instead of cardiovascular events and mortality. After 4

months, antihypertensive medication was deprescribed in 32% of residents in the intervention group compared to 10% of residents in the control group, and after 9 months there was no significant difference between the systolic BPs in both groups.

In summary, current evidence provides some support for the safety and effectiveness of deprescribing antihypertensive medication in frail older adults. However, more studies are needed to confirm these findings and help move antihypertensive deprescribing to the standard of care for this population.

3.2 Methods

Aim

The aim of this study is to determine, in frail older adults, whether deprescribing antihypertensive medication to a systolic BP of 140±5 mmHg compared to standard practice will lead to a change in time to all-cause mortality.

Design

This study is a randomized controlled, two parallel groups, open-label, event driven trial. LTC residents will be recruited each month, for a year, and randomized to either an antihypertensive deprescribing group or a usual care control group. This trial will end when 247 events (deaths) are reached, this is estimated to take 3 years post randomization.

Trial participants

The trial will include LTC facilities in Alberta, Canada. A LTC facility is one that provides 24-hour scheduled and unscheduled care to individuals with complex or unpredictable needs.[21] Residents will be included if:

- ≥70 years old;
- have ≥2 dx of hypertension from a community practitioner or ≥1 dx of hypertension from a hospital admission;
- on ≥1 antihypertensive medication; and
- have an average recorded systolic BP over the last 7 months of ≤135 mmHg.

Residents that meet the inclusion criteria detailed above will be excluded if:

- they have ≥2 dx of congestive heart failure from a community physician or ≥1 dx of in-hospital congestive heart failure;
- their physician objects to them participating in the study; or
- they are on antihypertensive medication for symptom relief only, including:
    - ≥2 community dx of benign prostate hypertrophy or ≥1 dx of in hospital benign prostate hypertrophy, and the only antihypertensive prescribed in the last month is an alpha blocker.
    - ≥2 community dx of essential tremor or ≥1 dx of in hospital essential tremor, and the only antihypertensive prescribed in the last month is a beta blocker.
    - ≥2 community dx of migraine or ≥1 dx of in hospital migraine, and the only antihypertensive prescribed in the last month is a beta blocker.
    - ≥2 community dx of tachycardia/atrial fibrillation or ≥1 dx of in hospital tachycardia/atrial fibrillation, and the only antihypertensive prescribed in the last month is a beta blocker or calcium channel blocker.
    - ≥2 community dx of glaucoma or ≥1 dx of in hospital glaucoma, and the only antihypertensive prescribed in the last month is a topical beta blocker.

Once a LTC facility has agreed to the study, AHS Research Data Services (under the direction of co-investigator Dr. Jeff Bakal PhD), will identify eligible residents using linked administrative claims data including diagnoses from outpatient physician billings (2002 - present), diagnoses from hospital separations (2002 – present), recent drugs dispensed according to the Pharmaceutical Information Network (PIN), and clinical outcomes tracked by each LTC facility in the Resident Assessment Instrument Minimum Data Set 2.0 (RAI-MDS 2.0). For the eligibility determination, Dr. Bakal's team will also receive an electronic record of BP recordings directly from the LTC facility.

RAI-MDS 2.0 is a comprehensive international assessment instrument that records resident level information.[22] Residents have a full assessment completed within 14 days of admission and annually, and a partial assessment completed quarterly. RAI-MDS 2.0 includes items pertaining to the health, function, medications, administrative details, and discharge potential of residents. There are numerous RAI-MDS 2.0 scales built using the assessment items.

Randomization

AHS Research Data Services will centrally randomize residents using random number generation, stratified by LTC facility and systolic BP at baseline (systolic <120 mmHg vs. systolic ≥120 mmHg) in blocks of 4. An open-label design will be used, with the pharmacists, the health care team, and the residents not blinded to the intervention.

Intervention group

AHS Research Data Services will provide pharmacists with a list of residents in the intervention group. This will be done a week prior to when the pharmacist completes their every 2-week medication cards. The pharmacist will then deprescribe biweekly, using a set algorithm (see figure 1), until a systolic BP of 140 ±5 mmHg is reached, or the resident is no longer on antihypertensive medication. The study team will host an education session for the pharmacists to discuss the study flow and deprescribing algorithm prior to starting the intervention. In addition, the study team will provide study material to physicians at the participating LTC facilities, along with the lead investigator's contact information should they have any questions.

LTC staff will take residents' BP weekly, until the new dosage regime has been established to the pharmacist satisfaction (estimated to be approximately 2 weeks). Afterwards staff will resume taking BP at their previous frequency (monthly). Staff will take BP in the usual way, namely one reading with the resident sitting at no specific time of day. We decided not to measure BP with serial readings; it will be more time consuming for LTC staff and also less conservative.[23]

RATIONAL FOR BP TARGET: We selected a target systolic BP of 140 ±5 mmHg for our study to be conservative. The 2014 Dalhousie Academic Detailing Service and the Palliative and Therapeutic Harmonization program guidelines recommend even greater deprescribing of antihypertensives, to a seated systolic BP between 140 and 160 mmHg, for adults who are severely frail (a score ≥7 on the Clinical Frailty Scale or the Frailty Assessment for Care-planning Tool).[24] The Criteria to Assess Appropriate Medication use Among Elderly Complex Patients (CRIME) Project, based on literature and expert option, recommended against controlling BP to less than 140/90 mmHg.[25] The STOPP/ START criteria version 2 have recommendations only for starting antihypertensive medication. However, they recommend to start when systolic BP is consistently >160 mmHg or if diabetic when systolic BP is consistently >140 mmHg.[26] This recommendation appears to be based on expert opinion as the 3 studies cited do not pertain to frail older adults.

The key hypertension guidelines, including 2018 European Society of Cardiology guidelines,[27] 2019 draft British NICE guidelines,[28] 2017 American College of Cardiology guidelines,[29] 2014 JNC 8 guideline,[30] and 2018 Canadian hypertension guidelines,[31] do not provide a target systolic BP for frail older adults.

Control group

The residents in the control group will have usual care with the standard pharmacist medication review (every quarter in Alberta). We will use the administrative data to determine if there have been any changes in the antihypertensive medication of the control group during the study.

Baseline characteristics

Baseline characteristics to be collected are detailed in table 1.

There are many measures available to assess frailty. We selected the frailty index as it is calculated using RAI-MDS 2.0 data, it is validated, and can differentiate the frailty level among LTC residents.[32,33] The calculation will be done using upwards of 51 deficit items from RAI-MDS 2.0 (N. Peel personal communication January 15, 2020) and with the cut-off of ≥ 0.25 to indicate frailty.[34] We will also calculate

the Frail-NH measure to ensure both measures define similar populations as frail. The Frail-NH is a screening tool for frailty; it is based on the accumulation of deficit and calculated using 6 deficits from RAI-MDS.[35]

Outcomes

The primary outcome is all-cause mortality.

The secondary outcomes include:

- All-cause hospitalization or emergency room visit.
- Non-vertebral fracture.
- Average per-resident biweekly cost of 1) antihypertensive prescriptions, and 2) total prescriptions, 3 – 6 months post randomization.

The process outcomes include:

- Number of antihypertensive medications, 3 and 6 months post randomization.
- Number (and proportion) of antihypertensive medications, with a ≥ 50% reduction from baseline in the number of milligrams dispensed per week, 3 and 6 months post randomization
- Number of different medications used in the last 7 days, as recorded in the RAI-MDS 2.0 quarterly assessments in the 3 – 6 month window post randomization.
- Average systolic BP and average diastolic BP over the entire study period.

The safety outcomes include:

- A composite of: new dx of stroke, heart attack, congestive heart failure, and atrial fibrillation.
- Each element of this composite outcome.

The exploratory outcomes include:

- Worsening (dichotomous yes/no) in the Cognitive Performance Scale score, as recorded in the RAI-MDS 2.0 quarterly assessment in the 3–6 window post-randomization.

- Worsening (dichotomous yes/no) in the Activities of Daily Living short form scale, as recorded in the RAI-MDS 2.0 quarterly assessment in the 3–6 month window post-randomization.
- Worsening (dichotomous yes/no) in the Depression Rating Scale score, as recorded in the RAI-MDS 2.0 quarterly assessment in the 3–6 month window post-randomization.
- Record of falling (dichotomous yes/no), as recorded in the RAI-MDS 2.0 quarterly assessment in the 3–6 month window post-randomization.

The exploratory outcomes are meant to assess the impact of this intervention on qualify of life. We selected these measures based on the QoL-AD Scale, a validated Alzheimer's qualify of life assessment tool.[36] We included the variables from QoL-AD that were both available in the quarterly RAI-MDS 2.0 report and applicable to LTC. These include memory (RAI-MDS 2.0 Cognitive Performance Scale), mood (RAI-MDS 2.0 Depression Rating Scale), energy, ability to do chores around the house, and ability to do things for fun (RAI-MDS 2.0 Activities of Daily Living Short Form Scale, and RAI-MDS 2.0 record of falling). The variables not included were: physical health, living situation, family, marriage, friends, self as a whole, money, and life as a whole.

The RAI-MDS 2.0 Cognitive Performance Scale is correlated with the Mini Mental Status Exam and has also been validated with clinical assessment.[37,38] A score of 0-1 indicates cognitively intact, a score of 2-3 indicates mild to moderate impairment, and a score of 4-6 indicates severe impairment. The inter-RAI 2.0 Activities of Daily Living Short Form Scale short ranks four categories (hygiene, walking, toilet use, and eating) on a scale of 0 – 4, with higher scores indicating more dependence.[39] The RAI-MDS 2.0 Depression Rating Scale ranks 7 items on a three point scale. There is conflicting data on its effectiveness; however, it is the only scale available on the RAI-MDS 2.0 for measuring mood related concerns.[40]

Data collection

AHS Research Data Services will directly access and analyse the outlined linked Alberta administrative claims databases, RAI-MDS 2.0, and BP data from the LTC facility. For Alberta administrative claims, the

baseline data will be taken at the date of randomization and following will be pulled quarterly. For RAI-MDS 2.0 data, the baseline will be taking from the admission RAI-MDS 2.0 assessment (if admitted to the LTC facility during the study) or the last RAI-MDS 2.0 quarterly assessment prior to randomization (if admitted to the LTC facility prior to randomization). In addition, the outcomes will be taken from the first RAI-MDS 2.0 quarterly assessment that is at least 3 months post randomization, and if applicable, 6 months post randomization. Lastly, the BP at baseline will be the average BP of the last 7 months at the time AHS research Data Services identifies eligible residents. Seven months was selected as this is what is available from Point Click Care BP reports. Following, the BP will be captured over the entire study period. If the facility inputs BP into Point Click Care, the Point Click Care BP report will be provided directly to AHS Research Data Services. If the facility does not, the BPs will be recorded into a spreadsheet by a research assistant, and this spreadsheet will forwarded to AHS Research Data Services.

Antihypertensive deprescribing algorithm

We have developed our own algorithm (figure 2) as there is currently no standard approach for deprescribing antihypertensive medication in this population. The Canadian Deprescribing Network is planning to develop an algorithm; however, it will not be completed until after this study starts (B. Farrell, personal communication, November 19, 2019). Our algorithm has been reviewed by a pharmacist (CS) and two geriatricians (PK, MM), all who have extensive experience in deprescribing. It has also been reviewed and approved by the Cochrane Hypertension Working Group.

Internal feasibility study

We will conduct a staged implementation with a "pilot" of our study in at least one LTC facility to determine whether recruitment is sufficient, and that the algorithm works effectively. If it appears there may be insufficient recruitment, we will look at implementing the following changes: modifying exclusion criteria, recruiting additional facilities, and/or increasing the duration of the study. If, even with these measures, it appears that we will not be able to enrol a sufficient number of residents, we will discuss with co-investigators and funders whether the trial should be discontinued. In addition, if our algorithm

does not appear to work effectively, we will rework the algorithm in collaboration with the facility pharmacist. Further, during this "pilot", AHS Research Data Services will provide the list of eligible residents to the pharmacist for review prior to randomization, to ensure the criteria is effective for selecting eligible residents.

Statistical analysis

We will analyse the primary outcome, all-cause mortality, using time to event survival analysis, to determine if there is a difference in time to all-cause mortality between the intervention and the control groups. We will use the Kaplan-Meier curve to visualize differences between the two groups, and utilize the Cox proportional hazard to determine if there is a significant difference in time to all-cause mortality between the two groups. The proportional hazard assumption will be tested using Schoenfeld residuals. Co-variates for this analysis include frailty index at baseline and end stage disease at baseline (RAI-MDS 2.0 item). Frailty index is included because frailty has been found to be highly predictive of mortality in older adults,[41] and frailty index is a reliable measure of this.[32,42] In addition, end stage disease is included to capture the severity of a resident's medical conditions; it has been found to be significantly associated with LTC mortality in Canada.[43] We will present the non-adjusted results as secondary analysis.

For the secondary outcomes, all-cause hospitalizations or emergency room visit and non-vertebral fracture, we will again use time to event survival analysis, with Cox proportional hazard model, to determine if the intervention results in a significant difference in outcome between the two groups. The co-variates for the former include number of different medications used in the last 7 days at baseline, and number of all-cause hospitalizations or emergency room visits in the year prior to randomization. Both of these factors were found to be associated with an increased risk of hospitalization among residents of assisted living facilities in Alberta.[44] The co-variates for the later include frailty index at baseline and prior fracture dx at baseline. Both lower frailty and prior fracture dx were associated with an increased risk of fractures in frail older adults.[45] The proportional hazard assumption will again be tested using Schoenfeld

residuals and we will present the non-adjusted results as secondary analysis. In addition, we will use the Student's t-test to determine if there is a difference between the groups for the average per-resident biweekly cost of antihypertensive prescriptions and total prescriptions.

For the process outcomes, we will use Student's t-test to determine if there are any significant difference between groups. For the composite safety outcome, we will use time to event survival analysis with Cox proportional hazards model, and include end stage disease at baseline as a co-variate. In addition, each element of the safety composite will be analyzed with a non parametric approach (ex. Chi-squared test for categorical data) given few individual safety events are expected. The exploratory outcomes will be examined with the Chi-squared test.

We will adjust for the stratification variables, LTC facility and systolic BP at baseline (systolic <120 mmHg vs. systolic ≥120 mmHg), in all the analyses.

The median and interquartile range for the systolic and the diastolic BP of the intervention and the control group will be calculated by week, and shown graphically to illustrate the BP trajectory over time.

Sample size calculation

We hypothesize there is a difference in survival time between the two groups of ≤30%, (i.e. 5 months). This is consistent with the power calculation of other randomized controlled trials on antihypertensive prescribing for older non frail adults, including Treatment of Hypertension in Patients 80 Years of Age and Older (HYVET) [46] and Target BP for Treatment of Isolated Systolic Hypertension in the Elderly (VALISH).[47] Setting the type 1 error to 0.05 and the type 2 error to 0.8, we calculated 247 events are needed over the course of the study. Assuming censoring of 40% (residents transfer to another non-participating facility and residents surviving over the study period), weighted average life expectancy of 1.3 years, and weighted average length of time following residents of 2.8 years, 515 residents will be needed for the study.[48] We estimated censoring, weighted average life expectancy, and weighted average length of time

following residents, using resident data from a LTC provider that has expressed interest in participating in the study.

Assuming a facility on average has 75 residents, and 22 residents are recruited from each facility (15 at the start of the study and 7 in the first year), we will need at least 23 facilities for sufficient power. These LTC facilities will be recruited with the help of Sandra Woodhead Lyons, Executive Director for the Institute of Continuing Care Education and Research (ICCER). There are currently 8 LTC facilities that have expressed interest in participating.

Safety reporting

The independent data safety and monitoring board (IDSMB) will be chaired and staffed by Dr. Jim Wright, a hypertension specialist and coordinating editor of the Cochrane Hypertension Working Group. They will review primary, secondary and safety outcomes received from AHS Research Data Services when half of the outcomes are reached.

Sub-study

To help delineate barriers and facilitators of this initiative, we will survey participating pharmacists pre and post implementation. The survey is designed based on the RE-AIM research translation framework.[49] RE-AIM evaluates 5 dimensions (reach, effectiveness, adoption, implementation, maintenance) to determine whether an initiative is workable in the real world. The questions in the survey will cover the adoption, implementation and maintenance dimensions, as these are the most relevant from the pharmacist perspective. The survey has been reviewed by four pharmacists with front-line experience in LTC setting.

If there is sufficient data, we will do subgroup analysis, including the following variables: years worked as a pharmacist, number of days working in LTC each month, number of residents provide care to, province work in, and number of prescriptions deprescribed in a typical month prior to the intervention.

Ethics

The ethics application is under construction at the time of this thesis is being submitted.

Knowledge translation

We will publish the results of the study in a peer-reviewed journal, and present the findings at conferences. We will also provide the findings to the LTC facilities involved in the study. In addition, the University of Alberta Patients Experience Evidence Research (PEER) group will help disseminate the results though their conference, Tools for Practice, and Best Science in Medicine podcast.

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Table 1. Variables collected and data sources

Variable	Admin data (AHS)	RAI – MDS 2.0	Point Click Care / Facility records
Baseline characteristics:			
Age	✓		
Gender	✓		
Height		✓	
Weight		✓	
Average systolic BP			✓
Average diastolic BP			✓
Length of stay in long-term care	✓		
Non-vertebral fracture ((≥1 dx)	✓		
Heart attack (≥2 dx or ≥1 in-hospital dx)	✓		
Stroke (≥2 dx or ≥1 in hospital dx)	✓		
Chronic kidney disease (≥2 dx or 1≥ in hospital dx)	✓		
Dialysis (≥1 procedure)	✓		
Diabetes (≥2 dx or ≥1 in hospital dx)	✓		
ADL short form scale		✓	
Cognitive performance scale		✓	
Depression rating scale		✓	
Frailty Index		✓	
Frail NH		✓	
Average biweekly cost of antihypertensives per	✓		

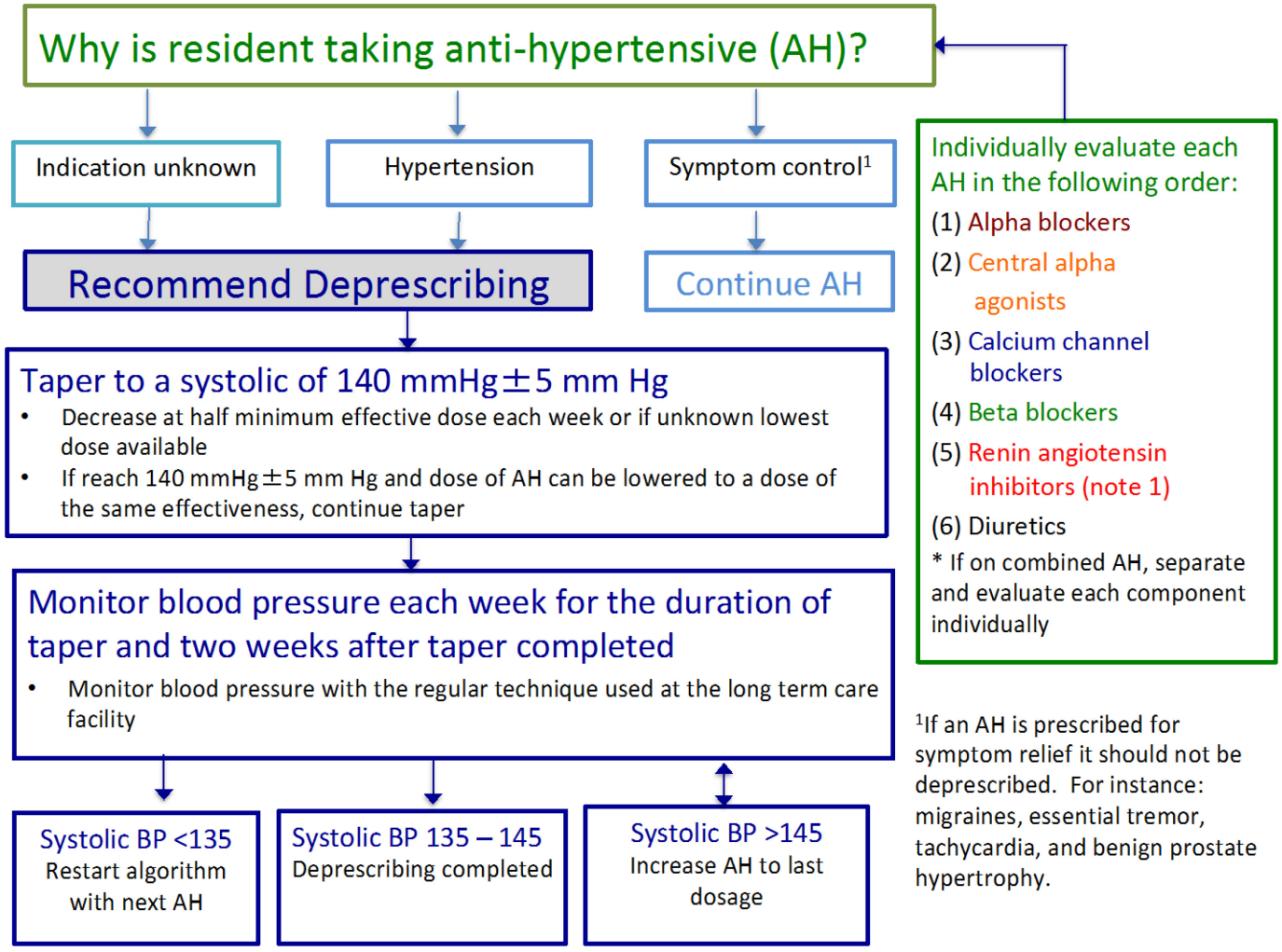
resident			
Average biweekly cost of all prescriptions per resident	✓		
Number and dosage of antihypertensive medication	✓		
Number of different medications used in the last 7 days		✓	
Collected for the purpose of inclusion / exclusion: (≥2 dx or ≥1 in-hospital dx)			
Congestive heart failure	✓		
Hypertension	✓		
Benign prostate hypertrophy	✓		
Essential tremor	✓		
Migraine	✓		
Atrial fibrillation	✓		
Tachycardia	✓		
Glaucoma	✓		
Any once daily antihypertensive	✓		
Primary and secondary outcomes:			
Death	✓		
Hospital/emergency admission	✓		
Non-vertebral fracture ((≥1 dx)	✓		
Average biweekly cost of antihypertensives per resident	✓		
Average biweekly cost of all prescriptions per resident	✓		
Process outcomes:			

Number of antihypertensive medications	✓		
Number and proportion of antihypertensive medications with ≥50% decrease in the number of milligrams dispensed per week[a]	✓		
Average systolic BP			✓
Average diastolic BP			✓
Number of different medications used in the last 7 days		✓	
Number of days between baseline RAI-MDS 2.0 and randomization		✓	
Number of days between randomization and RAI-MDS 2.0 follow up assessment		✓	
Safety outcomes: (≥ 1 dx or ≥1 hospital dx)			
Number of new stroke dx	✓		
Number of new heart attack dx	✓		
Number of new congestive heart failure dx	✓		
Number of new atrial fibrillation dx	✓		
Exploratory outcomes:			
ADL short form scale		✓	
Cognitive performance scale		✓	
Depression rating scale		✓	
Collected for use as covariates in the statistical analysis:			
End stage disease; 6 months of less to live (yes/no)		✓	
Number of emergency visits and hospital admissions in the previous year (if the emergency visit resulted	✓		

in a hospital admission it will only be included once)			

[a] Total weekly dosage of a medication will be calculated by multiplying the number of pills dispensed by the dosage per pill (mg).

Figure 1. Deprescribing algorithm



[1]If an AH is prescribed for symptom relief it should not be deprescribed. For instance: migraines, essential tremor, tachycardia, and benign prostate hypertrophy.

Alpha blockers (peripheral)

Average Systolic BP lowering; 8 mmHG

Name, dosages available	Min effect. dose (Max effect. dose)
Doxazosin(Cardura)[T] 1[a], 2[a], 4[a] mg	4 mg daily (4 – 12 mg daily)
Prazosin (Minipress)[T] 1[a], 2[a], 5[a] mg	10 mg daily (10 – 20 mg daily)
Terazosin (Hytrin)[T] 1, 2, 5, 10 mg	5 mg daily (5 – 20 mg daily)

Central alpha agonists

Average systolic BP lowering: not available

Name, dosages available	Starting dose
Clonidine (Catapres, Dixarit)[T] 0.025, 0.1, 0.2 mg	0.1 mg BID
Methyldopa (Aldomet)[T] 125, 250, 500 mg	250 mg BID@

B_1 adrenergic receptor blockers

Average systolic BP lowering: 10 mmHG

Name, dosages available	Min effect. dose (Max effect. dose)
Atenolol (Tenormin)[T] 25, 50[a], 100[a] mg	25 mg/day (25-100 mg daily)
Bisoprolol (Monocor)[T] 5[a], 10 mg	5 mg daily (5–20 mg daily)
Nebivolol (Bystolic)[T] 2.5, 10, 20 mg	5 mg daily (5 -20 mg daily)
Metoprolol (Lopresor)[T, L] 25[a], 50[a], 100[a] mg SR: 100, 200 mg	25 mg daily (25-200 mg daily)

B_1 and B_2 adrenergic receptor blockers

Average Systolic BP lowering: not available

Name, dosages available	Starting dose
Nadolol (Corgard)[T] 40[a], 80[a], 160[a] mg	40 mg daily
Propranolol 10[a], 20[a], 40[a], 80[a], 120[a] mg[T] LA: 60, 80, 120, 160 mg[c]	10 mg BID
Sotalol (Sotacor)[T,] 80[a], 160[a] mg	40 mg BID
Timolol (Blocadren)[T] 5[a], 10[a], 20[a] mg	5 mg BID

Partial B_1 and B_2 agonists

Average systolic BP lowering: 8 mmHG

Name, dosages available	Min effect. Dose (Max effect. dose)
Acebutolol (Monitan, Sectral)[T] 100[a], 200[a], 400[a] mg	400 mg daily (400 mg daily) 400 mg was the only dose in studies
Pindolol (Visken)[T] 5[a], 10[a], 15[b] mg	10 mg (10 - 30 mg daily)

Non-Selective *B* and *Alpha* blockers

Average systolic BP lowering: 6 mmHG

Name, dosages available	Min effect. dose (Max effect. dose)
Carvedilol (Coreg)[T] 3.125, 6.25, 12.5, 25 mg	12.5 mg daily (12.5-50 mg daily)
Labetalol (Trandate)[T, L] 100[a], 200[a] mg IV: 5 mg/ml	400 mg daily (600-800 mg daily)

Calcium Channel Blockers (Non-Dihydropyridine)

Average systolic BP lowering: not available

Name, dosages available	Starting dose
Diltiazem (Cardizem)@ Regular[T]:30, 60[a] mg XL[C]: 120, 180, 240, 300, 360 mg XL[T]: 120, 180, 240, 300, 360 mg IV 5mg/ml	120 mg daily
Verapamil (Isoptin)[T] Regular 80, 120 mg SR 120, 180[a], 240[a]	80 mg three times daily SR: 120 mg daily

Calcium Channel Blockers (Dihydropyridine)

Average systolic BP lowering: not available

Name, dosages available	Starting dose
Amlodipine (Norvasc)[T] 2.5, 5[a], 10 mg	5 mg daily
Felodipine (Plendil, Renedil)[T] 2.5, 5, 10 mg	5 mg daily
Nifedipine (Adalat)[T] 5, 10, mg[C] XL: 20, 30[a], 60[a] mg	5 mg TID XL: 30 mg XL

- T: tab, L: liquid, C: capsule, a: scored tab, CD: controlled delivery, SR: sustained release, XL: extended release
- Name, dosages and starting dose from Rx file database, except if indicated by @, dosage from uptodate
- Minimum and maximum effective doses are from Cochrane systematic reviews (see note 2 for references). A dose range for the maximum effective dose means there is no statistically significant difference between the doses.

Angiotensin Converting Enzyme Inhibitor

Average systolic BP lowering: 8 mmHG

Name, dosages available	Min effective dose (max effective dose)
Benazepril (Lotensin)[T] 5[a], 10[a], 20[a] mg	20 mg daily (20-80 mg daily)
Captopril (Capoten)[T] 6.25, 12.5, 25[a] , 50[a], 100[a] mg	37.5 mg/day (37.5–200 mg daily)
Cilazapril (Inhibace)[T] 1[a], 2.5[a] , 5[a] mg	2.5 mg daily (2.5–10 mg daily)
Enalopril (Vasotec)[T,⊥] 2.5[a], 5[a] , 10[a], 20[a] mg IV: 1.25 mg/ml	5 mg daily (5-20 mg daily)
Fosinopril (Monopril)[T] 10[a], 20 mg	20 mg daily (20–40 mg daily)
Lisinopril (Zestril, Prinivil)[T] 5[a], 10, 20 mg	10 mg daily (10-80 mg daily)
Perindopril (Coversyl) 2, 4[a], 8 mg	4 mg (4-16 mg daily)
Quinapril (Accupril)[T] 5[a], 10, 20, 40 mg	Insufficient data Insufficient data
Ramipril (Altace)[T, C] 1.25, 2.5, 5, 10, 15 mg	5 mg Insufficient data
Trandolapril (Mavik)[C] 0.5, 1, 2, 4 mg	1 mg daily (1 mg–16 mg daily)

Angiotensin II Receptor Blocker (ARB)

Average systolic BP lowering: 8 mmHG

Name, dosages available	Min effective dose (Max effective dose)
Candesartan (Atacand)[T] 4[a], 8[a], 16[a], 32[a] mg	4 mg daily (4-32 mg daily)
Eprosartan (Teveten)[T] 400, 600 mg	Insufficient data Insufficient data
Irbesartan (Avapro)[T] 75, 150, 300 mg	75 mg daily (75-300 mg daily)
Losartan (Cozaar)[T] 25, 50, 100 mg	50 mg daily (50-150 mg daily)
Telmisartan (Micardis)[T] 40[a], 80[a] mg	20 mg daily (20–160 mg daily)
Valsartan (Diovan)[T] 40[a], 80, 160, 320 mg	20 mg daily (80-320mg daily)

Diuretics – Thiazide like

Average systolic BP lowering: 9 mmHG

Name, dosages available	Min effective dose (Max effective dose)
Chlorthalidone (Hygroton)[T] 50[a] mg	12.5-15 mg daily (12.5-75 mg daily)
Hydrochlorothiazide (Hydrodiuril)[T] 12.5, 25[a], 50[a] mg	3-6.26 mg daily (25-100 mg daily)
Indapamide (Lozide)[T] 1.25, 2.5 mg	1.25 mg daily (1.25-5mg daily)
MetoLazone (Zaroxolyn)[T] 2.5 mg	0.5 mg daily (0.5-2mg daily)

Note 1: Renin angiotensin inhibitors can be deprescribed in patients with chronic kidney disease or/and coronary artery disease as:

- No evidence of kidney benefit of renin angiotensin inhibitors for mild kidney disease (stage 1 -3) (Sharma P, Blackburn RC, Parke CL et al. Cochrane Database of Syst Rev 2011;10:CD007751).
- Evidence renin angiotensin inhibitors worsen kidney function in moderate to severe kidney disease group (stage 3 – 6) (Bhandari S, Ives N, Brettell et al. Nephrol Dial Transplant 2016;31(2):255-261).
- No evidence of reduction of cardiovascular event between people on renin angiotensin inhibitors and active controls (Bangalore S, Fakheri R, Wandel SW et al. BMJ. 2017;356:j4).

Note 2: Cochrane references:

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Figure 2. Survey: Barriers and Facilitators of Antihypertensive Deprescribing

Background information:

1. How do you identify at this time?
    a. Male
    b. Female
    c. Decline to answer
    d. Other

2. How many years have you worked as a pharmacist?
    a. 0 – 4 years
    b. 5 – 9 years
    c. 10 – 14 years
    d. 15 – 19 years
    e. > 20 years

3. On average, how many days a month, do you provide on site clinical care in a long-term care facility? _____

4. On average, how many residents are you responsible for each month? _____

5. What province do you work in?
    a. Alberta
    b. British Columbia

Adoption:

Legislation was passed in Alberta to allow pharmacists to prescribe medication in long-term care facilities as at August 15, 2020. The questions in this section relate to activities since this date.

6. In a typical month, how many orders/prescriptions did you **prescribe** in long-term care**?**
   a. none
   b. 1 - 5 prescriptions
   c. > 5 prescriptions

7. In a typical month, how many prescriptions did you **deprescribe** in long-term care?
   (includes lowering dose and stopping a medication)
   a. none
   b. 1 - 5 prescriptions
   c. > 5 prescriptions

8. How often do you deprescribe the following drug classes in long-term care:

	Never	Sometimes	Often	Always	Please provide your reason
Benzodiazepine receptor agonists					
Proton Pump Inhibitors					
Antipsychotics					
Antihyperglycemics					
Cholinesterase Inhibitors or Memantine					
Antihypertensives					
Other – please describe and rate: _____					

9. How confident are you in your ability to deprescribe antihypertensives?

How confident

0 1 2 3 4 5 6 7 8 9 10

Not at all confident — Extremely confident

10. What systolic blood pressure would trigger you to deprescribe an antihypertensive in frail older adults (>65 years olds) long-term care? _____

11. To what extent do these factors affect your comfort level in deprescribing antihypertensive medication?

	Not at all	Minimally	Neutral	Moderately	Strongly	Please provide your reason
Insufficient evidence						
Unclear clinical practice guidelines						
Concern about a cardiovascular event occurring						
Other – please describe and rate: _____						

12. How supported do you feel in your practice to deprescribe medication in long-term care?

	Not at all	Minimally	Neutral	Moderately	Strongly	Please provide your reason	NA
My pharmacist peers							
Pharmacy manager							
Provincial pharmacy association							
Provincial regulatory body (pharmacy college)							
AHS manager							
Nursing manager at the facility							
Front line nursing staff							
Nurse practitioner							
Attending physicians							
Medical Advisory Committee							
Facility Residents							
The resident's family							
Other - please describe and rate: _____							

Implementation:

13. Do you anticipate pharmacists would need additional time outside their regular allocated time to deprescribe antihypertensive medication in long-term care?
    a. Yes
    b. No
    c. Unsure

    If yes, how much additional time per month per resident? _____

14. Did you have sufficient patient/resident information to deprescribe antihypertensive medication (blood pressures, list of medical conditions, physicians available to consult with, etc.)?
    a. Yes
    b. No
    c. Unsure

    Please provide the reason for your answer.

    _____

15. How helpful were the following aids in deprescribing antihypertensive medication and why.

	Not helpful	Neutral	Somewhat helpful	Very helpful	Please provi your reason
Algorithm					
Pre-education webinar					
Other - please describe and rate: _____					

Maintenance:

16. Please choose the top three issues that should be addressed to support pharmacists deprescribing antihypertensive medication in frail older adults going forward.

Issues:

- Pharmacists lack of confidence in deprescribing
- Pharmacist lack of expertise regarding hypertension management
- Pharmacists lack of evidence for decisions in frail older adults
- Residents and family not supportive of deprescribing
- Nursing staff not supportive of deprescribing
- Physicians not supportive of deprescribing
- Pharmacy manager not supportive of deprescribing
- Community pharmacist not supportive of deprescribing
- Additional pharmacist time required for deprescribing
- Additional workload in dispensary to process prescriptions
- Lack of facility charting regarding blood pressure
- Lack of facility charting regarding health conditions
- Nursing time required to take blood pressure more often
- Physicians not available to discuss patient cases
- Other _____

17. Do you feel deprescribing antihypertensive medication was beneficial in your long-term care facility?

    a. Yes

    b. No

c. Unsure

d. Not applicable

Please provide the reason for your answer.

_____

18. Are there any other comments you would like to provide to the research team?

Chapter 4: Summary

4.1 Summary of research

The scoping review completed for this thesis found a substantial number of cluster randomized trials have been published in long-term care. However, of the 195 cluster randomized trials in the review, only 14 pertained to medication prescribing, and none of these were on deprescribing antihypertensives. It was also interesting to note resident consent was obtained in the majority of studies, and studies that obtained waivers of consent were often the larger studies with greater than 1000 residents. This is likely because waivers of consent facilitate larger enrolment.

The second part of the thesis was the design of a protocol for an antihypertensive deprescribing randomized controlled trial in long-term care. We designed a randomized controlled, two parallel groups, open-label trial in long-term care in partnership with the AHS Research Data Services. The study, once complete, should help alleviate uncertainty around the impact of deprescribing antihypertensives in frail older adults.

4.2 Implications for future research

We set the BP deprescribing target to 140±5 mmHg to be conservative. If we are successful in demonstrating benefit to residents, it would be useful to have follow-up trials on deprescribing to higher systolic BP targets (for instance 150mmHg and 160mHg systolic) to determine whether higher BP targets in the frail older adult population are reasonable. In addition, there have been well designed studies on BP targets for non-frail older adults, and we anticipate the older adults in our study will be at the other end of the spectrum (very frail). Therefore, it would be useful to have similar studies done on older adults that are in-between these two extremes, such as community dwelling frail older adults, to help further guide practitioners and guidelines committees.

We incorporated a quantitative survey to determine the barriers and facilitators pharmacists faced with antihypertensive deprescribing. It would be useful to have a follow up focus group with pharmacists to further expand on these factors to determine how best to implement BP deprescribing in long-term care facilities.

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