Digital Innovations to Support the Health and Wellbeing of Individuals with Problematic Substance Use and Substance Use Disorder

by

Jasmine Marie Brown

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Department of Psychiatry

University of Alberta

Abstract

This dissertation explores the questions "*What technology-based interventions are of most benefit in supporting the health and/or rehabilitation of individuals with substance use disorders? Where and how can they be most effectively embedded in the health system*?"

Chapter 1 begins with an introduction, presenting the need for change associated with the approach and management of substance use disorders (SUDs), and describes the role that digital technology can play in bridging gaps and enhancing care.

Chapter 2 presents a brief historical synopsis of the social and clinical recognition of SUDs to provide a contextual introduction of the field of addiction, and to elucidate the need for change associated with the approach and management to these disorders, for which digital innovations hold promise. This chapter then describes the neurobiological foundations of addiction, followed by an overview of evidence supporting the theoretical and neurobiological mechanisms of treatment and intervention. This information provides a high-level evidentiary basis on which the chapters that follow are built.

Chapter 3 is a review of digital technological addiction and mental health interventions, with an emphasis on interventions targeting SUDs. Evaluations on effectiveness are included where possible. This chapter concludes with a discussion addressing both the opportunities as well as possible negative implications of new innovations.

Chapter 4 is divided into three sections: (1) a historical review of the social and clinical recognition of Fetal Alcohol Spectrum Disorder (FASD), which frames the landscape and context for the study that follows; (2) an original study examining the use of a specialized breathalyzer device, added as an additional service to the regular care for women who are pregnant and have a history of problematic alcohol use and/or are diagnosed with alcohol use disorder, with diagnosis of Fetal Alcohol Syndrome (FAS–the most severe form of FASD) as the

primary outcome measure; and (3) a review that complements the discussion section of the study that precedes it, and explores issues posed for researchers, clinicians, and public policy leaders alike caused by the lack of standardization of diagnostic criteria for FASD.[i]

Chapter 5 provides an evaluation of the Text4Support program–a text messaging intervention using the principles of cognitive behavioural therapy–as a complementary service for individuals seeking addiction and mental health supports.

Chapter 6, reflecting on the work that precedes it, explores the final query of this thesis ("*where can technology-based interventions be most effectively embedded in the health system*?"), and includes a discussion of public policy implications and considerations for further research.

[i] FASD as a clinical disorder is not in question.

Preface

This thesis is an original work by Jasmine Marie Brown. All research projects, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board.

The project identified and described in Chapter 4 was approved under project title: "Prevention of Fetal Alcohol Spectrum Disorder (FASD) by the Use of Technology," No. Pro00055644, 12/17/2015.

The project identified and described in Chapter 5 was approved under project title: "Mobile Based Programming (Text4Support) to Support Individuals Accessing Addictions and Mental Health Services," No. Pro 00086163, 8/28/2019.

Chapter 3 of this thesis includes reference to a publication that was part of a collaboration between multiple faculties at the University of Alberta, and was published as Caulfield, T., Marcon, A., Murdoch, B., **Brown, J.**, Perrault, S., Jarry, J., Snyder, J., Anthony, S., Brooks, S., Master, Z., Rachul, C., Ogbogu, U., Greenberg, J., Zarzeczny, A. & Hyde-Lay, R., "Health Misinformation and the Power of Narrative Messaging in the Public Sphere," Canadian Journal of Bioethics, 2019, vol. 2, issue 2, 51-60. I was responsible for concept development and analysis, as well as manuscript composition and editing. T. Caulfield was the supervisory author and was involved in concept formation and manuscript development and editing. All other authors contributed by providing concept development, analysis, manuscript composition, and editing to varying degrees.

Also included in Chapters 1, 3, and 6 is reference to a multinational collaborative report, APEC Digital Hub for Mental Health (2019). A New Horizon for Occupational Health: APEC White Paper on Workplace Mental Health and Safety. Vancouver, Canada: APEC Digital Hub for Mental Health, endorsed by the 21-member economic forum, the Asia-Pacific Economic Cooperative (APEC). I was responsible for research and information gathering and synthesis, the majority of the manuscript composition and drafting efforts, and editing. I was the sole research assistant providing support for this paper. Other authors included The APEC Digital Hub for Mental Health Workplace and Resilience Work Group (23 members from 12 countries), led by Co-Chairs S. Mahajan and H. Ito, as well as the Digital Hub Executive Team, R.W. Lam, A.J. Greenshaw, P. Upshall, E.E. Michalak, C.H. Ng, J.K. Murphy, and A. Ravindran. These

authors provided country-specific information, and supported manuscript framing and editing. S. Mahajan and H. Ito, as well as the Digital Hub Executive Team, were supervisory authors.

Chapter 4 of this thesis is comprised of multiple publications:

1) **J.M. Brown**, R. Bland, E. Jonsson, and A.J. Greenshaw, (2019) "A Brief History of Awareness of the Link Between Alcohol and Fetal Alcohol Spectrum Disorder," The Canadian Journal of Psychiatry, 64(3), 164–168.
2) **J.M Brown**, E. Jonsson, N. Riley, and A.J. Greenshaw, "Prevention of fetal alcohol spectrum disorder (FASD) by the use of technology," Edmonton (AB): Institute of Health Economics (IHE); 2019, submitted to funders Alberta Innovates July 2019.[ii]
3) **J.M. Brown**, R. Bland, E. Jonsson, and A.J. Greenshaw, (2019), "The Standardization of Diagnostic Criteria for Fetal Alcohol Spectrum Disorder (FASD): Implications for Research, Clinical Practice and Population Health. The Canadian Journal of Psychiatry, 64(3), 169–176.

For all three publications, I was responsible for the methodology development, data collection and analysis, and manuscript composition. Nicole Riley assisted with participant enrolment, data collection, and manuscript edits. E. Jonsson and A.J. Greenshaw were the supervisory authors and were involved with concept formation, methodology development, manuscript composition, and edits. Please see the acknowledgments section for additional notes of thanks to stakeholders involved in the development of the IHE Report, "Prevention of fetal alcohol spectrum disorder (FASD) by the use of technology."

Chapter 5 is comprised of an evaluation of a text messaging program called Text4Support, which seeks to analyze the experience of individuals who were enrolled in the program starting on July 17, 2019, who completed the program at the time of the last data pull–May 15, 2020. Although there was not enough data to reach statistical significance at the time of submission for this dissertation, this study remains ongoing and I intend to draft manuscripts based on a larger data set later in 2020. This chapter then seeks to provide some preliminary analysis, along with foreshadowing of additional analysis intended once more time has elapsed and larger number of participants have completed the full study period.

[ii] The report has not yet been posted publicly, as authors are in process of developing peer-review publications from findings).

Dedication

This dissertation is dedicated to my family. To my husband Paul, my biggest cheerleader and who I love with all my heart and soul, for your unwavering support, encouragement and love, for never letting me think quitting was an option, for dusting me off when I was down, and for giving me the strength to push forward, even despite being 7 months pregnant. To my fur baby Mowgli, for your constant love, devotion, cuddles, and snorts. To my soon to be born child, you provided me with the motivation to not only get this thing done, but also reminded me why I was doing it in the first place. I'm so excited to meet you.

To my parents Ruby and Terry, and siblings Luke and Jotie, who have stuck by me through thick and thin, never letting me beat myself up when I fall down, always being there to answer my call regardless of the hour, and bringing me groceries and lip chap while I was pregnant during a global pandemic. Mom and Dad, you gave me with the best possible childhood, and made sure that any hope or dream I had was within reach. You are my heroes. Luker, you taught me how to code on our computer when I was basically toddler. You are the reason I love science. You remain my role model, and I am so grateful to have you as my brother. I hope I have done you all proud.

This dissertation is also dedicated to my mentors. To Dr. Andy Greenshaw, for your willingness to take me on as a student, for his wise and patient mentorship, and his unwavering confidence and support in my ability to take on the many challenges of a PhD student. I am so grateful for the opportunities you have provided me as a student and can only hope to do you proud as I proceed into this next chapter. To Dr. Egon Jonsson, for truly listening to and caring about the hopes and dreams of your staff and students, and then supporting them and mentoring them in achieving those aspirations. Your contributions to academia and devotion to uplifting others has changed the lives of so many, myself included, and for that I am eternally grateful. To Dr. Peter Silverstone, for your time, support, and commitment to helping me progress and develop as an academic. Our meetings have helped identify and bridge gaps in my knowledge, and have helped me excel. To Dr. Christopher McCabe, you gave me the space, opportunity and support to pursue and complete this PhD, and have provided me with guidance and actively supported my career development. To Janet Davidson, for your mentorship since I was a teenager, and for your support of my PhD application. Janet, I wouldn't be here without you. I am so grateful to have you in my life. Lastly to Dr. Roger Bland, who spent countless hours mentoring me during his time as an emeritus professor. His sharp wit and compassionate heart are missed, and his

contribution to the field of psychiatry can never be matched. I can only hope he is somewhere watching, giving me a thumbs up for not only finishing this dissertation, but also for my absolute insistence on taking my prenatal vitamins on time.

Acknowledgments

The following acknowledgements are linked to the two original studies referenced in chapters 4 and 5 of this dissertation.

The *Prevention of FASD by the use of technology* study was conducted and the report written by Jasmine Brown, Dr. Egon Jonsson, Nicole Riley, and Dr. Andrew J. Greenshaw. Further review of this report was supported by Dr. Christopher McCabe. The authors would like to thank Dr. Amy Salmon for having led the successful development of the Partnership for Research and Innovation in the Health System (PRIHS) grant application, which made this study possible.

The authors are also grateful to Dr. Yukiko Washio, Dr. Tom McClelland, Dr. Vincent Agyapong, Allan Aubry, Mark Snaterse, Cindy King, and Riina Eggins for their time and valuable insight with regard to deliberations around study design and implementation.

The authors would also like to thank our two industry stakeholders, Soberlink, who donated the breathalyzer devices and access to Sober Sky for use in this study, and TELUS, for providing smartphones and cellphone service at a reduced price.

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The Text4Support study was conducted and written in an expedited manner, after the author of this dissertation discovered she was pregnant. The author of this dissertation would like to sincerely thank all members of the study team for their consideration and efforts in the gathering of data and efficient review of materials (which remains ongoing). This includes Principal Investigators V. Agyapong, and A.J. Greenshaw, as well as Text4Support research team members W. Vuong and S. Surood. It also includes C. Kabatoff, Research Ethics Board Consultant, for her patience and direction in the ethics consideration and approvals for this and the aforementioned PRIHS study. Thanks must also be given to S. Poudel, S. Dhannewar, and S. Babbar, who assisted in the gathering of health utilization data.

Table of Contents

List of Tables

List of Figures or Illustrations

Chapter 4: Supporting maternal health through use of technology study

Chapter 5: Mobile-based programming (Text4Support) to support individuals accessing addictions and mental health services

Abbreviations

All abbreviations that have been used in this report are listed here unless the abbreviation is well known, has been used only once, or has been used only in figures or tables, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

AHS	Alberta Health Services
AI	Artificial Intelligence
APEC	Asia-Pacific Economic Cooperative
BAC	Blood Alcohol Concentration
CBT	Cognitive Behavioural Therapy
CNS	Central Nervous System
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
DIMR	Data Integration and Management Repository
DSM	Diagnostic and Statistical Manual of Mental Disorders
EMR	Electronic Medical Records
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorder
FDA	Food and Drug Administration
ICD-9/ICD-10	International Classification of Disease, 9th and 10th Revisions
IVR	Interactive Voice Response
MDI	Material Deprivation Index
ML	Machine Learning
NAc	Nucleus Accumbens
PRIHS	Partnership for Research and Innovation in the Health System
RCMP	Royal Canadian Mounted Police
RCT	Randomized Clinical Trial

RiskSLIM	Risk calibrated Supersparse Linear Integer Models
RPE	Reward Prediction Error
SLIM	Supersparse Linear Integer Models
SUD	Substance Use Disorder
VTA	Ventral Tegmental Area
WHO	World Health Organization

Glossary of Terms

Please note that most of the following definitions are cited directly from the referenced sources indicated.

Addiction: a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems. [1]

Affect regulation: Refers to the mechanism by which our emotions, moods, feelings, and their expressions are modulated in pursuit of an affective equilibrium or homeostasis. [2]

Allostasis: The process by which a state of internal, physiological equilibrium is maintained by an organism in response to actual or perceived environmental and psychological stressors. [3]

Artificial intelligence: An area of computer science that emphasizes the simulation of human intelligence processes by machines that work and react like human beings. [4]

Big data: The emerging use of rapidly collected, complex data in such unprecedented quantities that terabytes, petabytes or even zettabytes of storage may be required. [5, 4]

Blockchain: A digital database containing information (such as records of financial transactions) that can be simultaneously used and shared within a large decentralized, publicly accessible network. [4]

Blood alcohol concentration: A measure of alcohol intoxication for medical and/or legal purposes.

Cognitive behavioural therapy: A type of psychotherapy in which negative patterns of thought about the self and the world are challenged in order to alter unwanted behavior patterns or treat mood disorders such as depression. [6]

Cognitive inhibition: The ability to suppress unwanted or inappropriate actions and impulses. [7]

Digital health: The field of knowledge and practice associated with the development and use of digital technologies to improve health. The term is inclusive of "eHealth," as well as "mHealth." Digital health expands the concept of eHealth to include digital consumers, with a wider range of smart-devices and connected equipment. It also encompasses other

uses of digital technologies for health such as the Internet of things, artificial intelligence, big data and robotics. [4, 8]

eHealth: The use of information and communications technology in support of health and health-related fields. [8]

Health data: The record in electronic or other formats describing or illustrating the physical or mental health, reproductive outcome, quality of life, provision of health services, causes of death of an individual or population. [4]

Health technology: The application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives. [9]

Incentive salience: Posits that addiction is caused primarily by drug-induced sensitization in the brain mesocorticolimbic systems that attribute incentive salience to reward-associated stimuli. If rendered hypersensitive, these systems cause pathological incentive motivation ('wanting') for drugs. [10]

Internet of things: A system of interrelated computing devices, mechanical and digital machines, objects, or people that are provided with unique identifiers and the ability to transfer data over a network without requiring human-to-human or human-to computer interaction. [4]

Machine learning: A branch of computer science aimed at enabling computers to learn new behavior based on empirical data. The goal is to design algorithms that allow the computer to display behavior learned from past experience, rather than human instruction. Machine learning is essential to the development of artificial intelligence, but it is also applicable to many everyday computing tasks. [11]

Mindfulness training: The awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment. It can be practiced formally, through meditation, and informally, by consciously bringing awareness to each moment of each day. [12]

Mobile health (mHealth): A subset of eHealth, defined as "the use of mobile wireless technologies for health." [8]

Neurofeedback training: Neurofeedback means providing feedback for neuronal responses or EEG signals to a person in order to train them in terms of controlling electrical activity of the brain. Neurofeedback is also considered as a training process in which the brain learns to self-regulate itself. During this training process, the brain activity is controlled at both conscious and unconsciousness levels. In this regard, conscious learning occurs when a person finds the relationship between their mental status and applied feedback. [13]

Problematic substance use: Happens when an individual uses drugs or alcohol in a harmful way that has negative effects on their health and life. [14] It does not necessarily denote that they meet the diagnostic criteria for substance use disorder.

Reward deficiency: The RDS concept arose from the findings that dysfunction in the dopaminergic system are implicated in reward mechanisms in the brain and lead to substance seeking behavior and non-substance addictive behaviors. [15]

Risk-calibrated supersparse linear integer models: Machine learning algorithm that solve mixed-integer and nonlinear programs. Produces risk scores directly from data. [16]

Substance use disorder: A cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems. [1]. See page 9 for more information on the diagnostic criteria for SUD (specifically Alcohol Use Disorder).

Supersparse linear integer models: Machine learning algorithm that solve mixed-integer and nonlinear programs. Produces scoring systems optimized for particular true positive/false positive trade-offs. [16]

Telemedicine: The delivery of health-care services, where distance is a critical factor, by all health-care professionals using information and communications technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and the continuing education of health-care workers, with the aim of advancing the health of individuals and communities. [4, 17]

Chapter 1: Introduction

1.1 Overview

It is our duty as researchers, clinicians, and policy makers in the field of addiction and mental health to promote the maintenance of the health and wellbeing of others. Should health falter, it is our responsibility to identify and explore solutions. Should those solutions not be enough, or our health system slow to act, it is our moral obligation to innovate and disrupt in the best interest of those who depend on us.

Digital health technology presents the potential for a range of care solutions and necessitates careful acknowledgement and appreciation, as well as evaluation and/or adoption where appropriate. The world is moving forward with the development of new health technology and innovation in exponential leaps and bounds. Technology proliferates quickly, with most Canadians now armed with various forms of mobile technology and connected instantaneously to online networks and platforms. Yet our health system is still hesitant to adopt simple technologies such as the use of telehealth or email to communicate with patients (albeit now changing in different jurisdictions in response to the recent global COVID-19 pandemic). Canada has long been at a point where existing service provision is grossly underwhelming the expectations and needs of Canadians, and we now have an opportunity to propel our systems into the 21st century through the greater adoption of evidence-supported digital technology to complement and enrich care.

This dissertation ultimately explores the questions "*What technology-based interventions are of most benefit in supporting the health and/or rehabilitation of individuals with substance use disorders? Where and how can they be most effectively embedded in the health system*?" Of the substances of abuse, emphasis is given in analysis to alcohol. However, before exploring this further in the form of reviews of existing evidence as well as the synthesis of new evidence, it is important to explain the need for change associated with the approach and management of substance use disorders (SUDs), as well as describe the role that digital technology can play in bridging gaps and enhancing care.

1.2 Statement of need

SUDs are prolific, costly, and populations in need are being underserved. Approximately one in five of Canadians will have an SUD in their lifetime [18]. Of the substances of abuse, alcohol is

attributed for causing the greatest overall individual and social harm [19]. According to the World Health Organization (WHO), alcohol accounts for 5.1% of the global burden of disease,[iii] is believed to attribute to approximately 13.5% of deaths among individuals aged 20 to 39, and causally linked to over 200 other diseases and injuries [20]. Additionally, it is estimated that 76.3 million individuals worldwide meet the diagnostic criteria for alcohol use disorder [21]. In Canada, the lifetime prevalence rate of alcohol abuse or dependence in Canada is 18.1%, surpassing mood disorders (12.6%) and general anxiety disorder (8.7%) [18].

Mental health costs Canada $51B CAD annually (2003 data; approx. $68B CAD after being adjusted for inflation to 2020), inclusive of factors such as lost productivity, health care costs, and decreased quality of life [22]. Narrowing the focus to SUDs, the cost is estimated to be $38.4B CAD annually, with the largest proportion of those costs attributed to alcohol use in 9 of 12 provinces and territories [23].

To make matters worse, these populations are underserved. It is estimated that a third of Canadians over the age of 15 years do not feel their mental health needs are being adequately met [24], and only half of those experiencing a major depressive episode feel they have received adequate care [25]. Reducing the scope to SUDs and problematic substance use[iv], less than 10% of individual are believed to be successfully linked to treatment services [26]. Additionally, for individuals with problematic alcohol use, only 15-25% of individuals are believed to *seek* treatment [27]. Barriers are believed to include social stigma, denial, concerns over privacy, and/or difficulty connecting effectively with a care provider [27, 28, 29, 30]. With 3.3 million deaths attributed globally annually to harmful alcohol use alone [31], there is urgency to identify effective and timely intervention and treatment options that reduce and eliminate barriers, and investigate innovations where technology may present effective novel solutions.

1.3 Mental wellness during a global pandemic

In late 2019, an outbreak occurred of a disease called COVID-19 (virus name: SARS-CoV-2). Four months later, it was declared a global pandemic by WHO [32].

As of May 5, 2020, COVID-19 has spread across the borders of 187 countries [33], with 3,517,345 known cases, and 243,401 deaths [34]. In anticipation of a high volume of serious

[iii] The WHO's global burden of disease is inclusive of multiple alcohol linked outcomes including death as a result of alcohol attributed traffic injuries, self-harm and interpersonal violence, digestive disorders, cardiovascular diseases, cancers, infectious diseases, as well as other mental disorders and health conditions.
[iv] For definitions of "substance use disorder" and "problematic substance use" please see the Glossary of Terms.

hospitalizations with technical respiratory needs, Canadians have been asked to self-quarantine and/or practice social distancing in an effort to reduce the burden to health systems [35].

In reflection of previous epidemics and pandemics, it is anticipated that individuals will be exposed to numerous factors that may increase risk for developing an addiction and mental health issue that may persist beyond the current health crisis [36] [37, 38], including negative emotions such as stress, sadness, or loneliness [39], as well as problematic drug and alcohol use [40]. Stressors identified in the analysis of previous quarantines have included, concerns over the duration of the quarantine, fears of infection, frustration and boredom, inadequate basic supplies, inadequate information [38]. Stressors post-quarantine including finances (financial loss - socioeconomic distress), and stigmatization over individuals who have gotten sick [38].

The COVID-19 pandemic is also estimated to impact the financial wellbeing and employment status of many Canadians. As of March 2020, 44% of Canadian households reported that they had "lost work" or have experienced layoffs due to COVID-19 [41]. From an economic standpoint, the world economy is forecasted to contract by 3% [42], and Canada by 6.2 % in 2020 [43]. Unemployment in Canada rose to 13% in April 2020 (albeit many jobs are projected to return following the pandemic), with job loss to date experienced more rapidly for lower paid or less stable positions such as those in the accommodation and food services, and wholesale and retail trade [44].

The need to increase access to addiction and mental health services for individuals who are in self- or state-required-isolation and quarantine has never been more significant. During this unprecedented time, digital health innovations provide potential solutions to connect with individuals in their homes.

1.4 The digital revolution and the opportunity it presents

We are in the midst of a digital revolution, where what began with the emergence of the internet has evolved from comparatively simple digitization to the complex, globally-integrated networks and systems we observe today. These systems are restructuring and disrupting governance and economics frameworks, and are so exponentially transformative they are forcing us to reconsider our basic conceptualization of what it means to be a human [45].

Digital innovations including, but not limited to, the internet, smartphones and tablets, wireless wearable devices, and machine learning (ML) and artificial intelligence (AI), present novel mechanisms to increase access to care generally, as well as present new, potentially impactful

and efficacious ways to reach individuals in need in a personalized and timely manner. These innovations can cut through both social stigma and over-bureaucratized brick and mortar health systems, and meets individuals where they are, and when they most need services.

In 2018, 91% of Canadians were estimated to be actively using the internet, up from 83% in 2012 [46]. Mobile technology is also already popular, with 85% of Canadians owning a cellphone and 67% of Canadians owning a smartphone [47]. This trend is not restricted to Canada. There are an estimated 4.1 billion internet users internationally [48]. Ninety-five percent of countries are now estimated to have mobile phone capabilities/infrastructure with 8.3 billion mobile subscriptions worldwide, allowing millions of individuals in lower income countries to "leap frog" the historic necessity of fixed-line phones [49, 50, 51, 48] [52]. Sub-Saharan Africa is considered the fastest growing region in terms of mobile phone subscriptions in the world, with approximately 456 million unique mobile subscribers in 2018, and an estimated increase to approximately 600 million users by 2025 [53].

Unfortunately, most substance use and mental health programming does not use mobile technology or even the internet [54]. Additionally, rural areas in Canada have a lack of addiction and mental health services, with a frequent need for patients to travel long distances to access care, further reducing the likelihood that these individuals will seek care [54].

Digital technology presents exciting opportunities to enhance access to services beyond geographic and/or social barriers. As this disruptive new era continues to evolve it is met with both acceptance and resistance, praise and caution, and adoption and evasion. Nevertheless, the changes we see are exponential and impossible to ignore. It is up to us as academic, political and intellectual leaders to ensure that with these pivotal shifts and novel system transformations, we aim to use technological advancements and opportunities to ultimately improve the human experience in medicine and treatment, use digital advancements to make health services both more accessible and efficient, and ensure their provision enriches rather than diminishes human interaction.

1.5 Thesis statement and overview of dissertation

As noted, this dissertation ultimately explores the questions "*What technology-based interventions are of most benefit in supporting the health and/or rehabilitation of individuals with substance use disorders? Where and how can they be most effectively embedded in the health system*?"

It begins with a literature review of technological interventions that are currently being piloted or used to support the health of individuals with substance use and mental illnesses, with particular emphasis on alcohol use disorders where possible.

This dissertation then describes two studies that seek to use digital technology to support the health of two separate but related population groups. The first study presents findings from research that uses a specialized breathalyzer device, paired to a smartphone, to support the maternal health of pregnant women with a history of problematic alcohol use, and who have sought formal support in the management of their substance use within the city of Edmonton, Alberta. The second study presents analysis of a text messaging support program (Text4Support) based on the principles of cognitive behavioural therapy (CBT) that seeks to bridge care for individuals seeking support for self-identified problematic substance use, within two addiction and mental health service centers also within the city of Edmonton, Alberta. This dissertation then presents analysis reflecting on the findings from the preceding five chapters, with a discussion of public policy implications and considerations for further research.

The research presented in this dissertation is novel and seeks to contribute to the academic body of knowledge around this subject matter in several ways, as well as bridge a gap in dissemination of knowledge between academia and policy. First, many digital innovations are being released without having been evaluated by an independent reviewer or without being evaluated at all, leading to a spread of unfounded and unchallenged claims of efficacy[v]. This dissertation presents evaluation and analysis for two distinct technological interventions being piloted by a Canadian provincial health system.

Second, participants for one of the two intervention evaluations are comprised entirely of pregnant women actively seeking support to manage current or historical problematic alcohol use. This vulnerable group is often avoided by researchers due to the complicated ethics approval process required, and in reflection of anticipated low enrolment rates, due in-part to shame and stigma associated with substance use related problems during or prior to pregnancy[vi]. Therefore, this dissertation presents new research involving an often missed, vulnerable population.

Finally, while the discovery, development, and proliferation of new digital technologies continues at an exponential rate, in keeping with historical trends health systems have been

[v] For more information on "unfounded claims", see Chapter 3.
[vi] See Chapter 4, for a discussion on enrolment challenges with this population group.

slow in their uptake and adoption. Chapter 6 of this dissertation aggregates lessons learned from research and reports from other and/or comparable jurisdictions to support the update of evidence-based technological interventions into practice and real-world application.

Chapter 2: Setting the Stage–A historical brief and the theoretical and neurobiological mechanisms and correlates of addiction

2.1 Overview

Although substance use disorders (SUDs) are both prolific and recognized by the academic and medical community as clinical disorders with genetic and neurological bases, they remain stigmatized. Despite their clinical underpinnings and the emergence of scientific evidence, their social and medical recognition has lagged behind that of other mental illnesses [55]. This historical and ongoing stigma has resulted in a smaller percentage of individuals who need treatment coming forward to seek it [56, 57, 58, 59]. Digital technologies present an opportunity to cut across stigmatic barriers to care, and to bring novel personalized addiction and mental health solutions to individuals wherever they are, whenever they need them.

This chapter begins by providing a brief historical synopsis of the social and clinical recognition of SUDs to provide both a contextual introduction of the field of addiction and to elucidate the need for change associated with the current approach and management of to these disorders, for which digital innovations hold promise. It then describes the neurobiological foundations of addiction, followed by an overview of evidence supporting the theoretical and neurobiological mechanisms of treatment and intervention. This information seeks to provide a high-level evidentiary basis upon which the chapters that follow are built.

2.2 A historical brief

The history of the recognition of mental disorders *generally* as conditions with underlying neurobiological circuitry is not without contention. However, with discovery of psychiatric benefits of imipramine and iproniazid as antidepressants came a pivotal shift in clinical and social paradigms coined the "revolution" [60] or the "golden decade" [61] of psychopharmacology [62, 63]. With this advancement, the social and medical conceptualization of depression shifted to recognize its neurochemical and biological nature [64, 65, 66, 67], redefining it as, "an illness of the brain" instead of an "illness of the mind" [65, 64]. Previous to this shift, a leading school of thought hypothesized that mental disorders were, at root, a "symptomatological manifestation of certain internal personality conflicts" [64].

Recognition of the biological underpinnings of *substance use disorders*, however, have historically taken longer to be socially and medically accepted, despite the emergence of scientific evidence. Several sources chronicle changes between iterations of the Diagnostic and

Statistical Manual of Mental Disorders (DSM) as evidence of this struggle in conceptualization [55], one that has been argued to have been influenced by predominant social movements, including temperance and prohibition as well as the industrial revolution [55]. For example, up until the 3rd iteration of the DSM in the 1980s, SUDs were categorized as being manifestations of other underlying primary psychopathologies [55]. Additionally, criteria for SUDs included reference to "legal problems" up until its 5th iteration, "reflecting an entrenched association of addiction and crime" [55]. This entrenched social stigma has bled into today, and remains a significant barrier for individuals to access and navigate timely and effective services.

2.3 Neurobiological mechanisms of addiction and treatment

In order to outline the clinical rationale for the use digital technological interventions as a potential form of treatment for individuals diagnosed with SUDs, it is first important to describe the neurobiological underpinnings of addiction generally, followed by a discussion of the neurobiological targets or mechanisms of interventions. In reflection of the population groups analyzed in Chapters 4 and 5 (individuals diagnosed with alcohol use disorder, and/or with a history of problematic alcohol use), this section narrows focuses where possible on the neurology of alcohol use disorder.

2.3.1 The neurobiological components of addiction

Although SUDs are defined as, "a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems" [1], their diagnostic criteria necessitates observation or documentation of a constellation of behavioural and physical manifestations, as no biomarker currently exists to definitively test for and diagnose these conditions.

The DSM-5[vii] identifies the following as diagnostic criteria, using behavioural and physical symptoms, for alcohol use disorder:

> *A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:*
>
> 1. *Alcohol is often taken in larger amounts or over a longer period than was intended.*
> 2. *There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.*

[vii] Note that the DSM diagnostic criteria for SUD and alcohol use disorder has changed over several editions. Where appropriate, this paper will distinguish between DSM-editions.

3. *A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.*
4. *Craving, or a strong desire or urge to use alcohol.*
5. *Recurrent alcohol use resulting in a failure to fulfill major role obligations at works, school, or home.*
6. *Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.*
7. *Important social, occupational, or recreational activities are given up or reduced because of alcohol use.*
8. *Recurrent alcohol use in situations in which it is physically hazardous.*
9. *Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.*
10. *Tolerance, as defined by either the following:*
    a. *A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.*
    b. *A markedly diminished effect with continued use of the same amount of alcohol.*
11. *Withdrawal, as manifested by either the following:*
    a. *The characteristic withdrawal syndrome for alcohol.*
    b. *Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.*

Specified based on severity:

- *Mild: Presence of 2-3 symptoms*
- *Moderate: Presence of 4-5 symptoms*
- *Severe: Presence of 6 or more symptoms*

There are fundamental underlying neurobiological changes and genetic influences that are theorized as foundational to these behavioural expressions, which may persist following detoxification and may increase an individual's likelihood to relapse into a SUD following exposure to triggering drug-associated stimulus. These are further expounded below.

Several prominent discussions on the neurobiological basis of addiction based on clinical neurocircuit and neurobiological observations exist. Although this chapter, and paper generally, focus on Alcohol Use Disorder where possible and applicable, the neuro-molecular basis of addiction will be discussed in the context of SUDs generally, as all drugs of abuse affect the reward circuitry of the brain similarly, despite their initial mechanisms of action and distinct neurobiological targets.

There are multiple models used to describe the neural basis of SUDs, including incentive salience [68], allostasis [69, 70], and reward deficiency [71].

Nestler and Luscher (2019) attempt to summarize these theories of addiction by describing two scenarios contributing to the "remodeling of the brain" in addiction [72]:

1) “Excessive dopamine signaling during drug use may modulate gene expression, altering synaptic function and circuit activity and leading over time to maladaptive behaviors in vulnerable individuals.

2) “Life experience can shape the epigenetic landscape in brain and thereby may contribute to an individual’s vulnerability by amplifying drug-induced changes in gene expression that drive the transition to addiction.”

An overview aggregating these theories is presented below.

The restructuring of the brain’s reward and control systems

All drugs of abuse appear to activate dopamine neurons of the midbrain ventral tegmental area (VTA) that project to the medial nucleus accumbens (NAc) via an increase in extracellular dopamine [73]. The chronic dopaminergic signalling between the VTA and the NAc can then lead to the development of a strong reinforcement loop or reward prediction error (RPE) signal, believed to underly the maladaptive behaviour and the pathological consumption of addictive substances (transition from recreational to compulsive use) through associative learning [74, 72, 75, 76]. These neural alterations then may lead to inhibitory control issues and impaired motivational drive when an individual is faced with drug-related cues [77].

Underlying the RPE may be caused by epigenetic alterations. The repeated use of drugs of abuse can cause downstream signalling cascades, either via specific molecular targets or through increased signaling of dopaminergic neurons, depending on the substance of abuse, which may lead to long-lasting changes in epigenetic expression, in-turn altering brain regulation and function [72]. More is included on epigenetic expression and individual susceptibility to addiction below.

Individual vulnerability to addiction

Only approximately 10-20% of individuals who recreationally use substances of abuse develop a substance use disorder. [78, 79, 80]. Both genetic and environmental factors are believed to contribute to an individual’s susceptibility to addiction. Twin studies support that addiction is heritable [81, 82], with complex genetic mechanisms increasing or decreasing an individual’s vulnerability linked to sequence variations between hundreds of genetic loci [72]. Environmental factors also believed to play are role in individual vulnerability, including with stochastic individually, and may include adverse childhood experiences, trauma, stress, and

pressure from peers, which in turn is believed to potentially induce epigenetic modifications, or "chromatin scars," that increase an individual's vulnerability to addiction [72, 83, 84].

2.3.2 The neurobiological mechanisms of treatment and intervention

The chapters that follow describe numerous forms of digital technological interventions, while providing information on effectiveness where it exists. As most of the interventions discussed are non-pharmaceutical in nature, much of this evaluative work relies on external observations using non-intrusive evaluative methods such as self-reporting and/or behavioural observations, to determine effectiveness. Additionally, the scope of this analysis is often widely applied to the device or innovation itself, without isolating for (or in some circumstances identifying) what is or could be underlying neurobiological mechanisms for which the intervention is (or theorized to be) acting upon to permit change such as the alleviation of craving, decrease in substance use, or reduction in relapse, despite evidence to support that neuronal activity as a possible predictor of relapse [85, 86, 87, 88, 89].

This section will aggregate and summarize research that has examined the possible neural mechanisms underlying common treatment and intervention modalities. This includes many digital interventions for SUD, in recognition that existing evidence (albeit limited) can provide insight into the neurobiological rationale for why the interventions described in the sections that follow may be effective in supporting behavioural change. Acknowledging that treatments have variable effectiveness on any given individual, it is also important to ensure that research builds on the existing neuroscience knowledge base and continues to refine an understanding of the underlying mechanisms that drive this individual variability and that enable the "personalization" of medicine in this field. Similarly, to advance clinical research, it is essential that this enhanced understanding of the underlying neurology informs forthcoming interventions [90].

<u>Phases of treatment: Overview</u>

Treatment can be described in three broad phases: detoxification, initial recovery, and relapse prevention [91]. Some phases may be paired with pharmaceutical intervention, such as agonist treatments like methadone or benzodiazepines to support successful detoxification from substances such as heroin and alcohol respectively, or naltrexone to reduce reward/relief sensations realized in opioid and alcohol use and to support successful maintenance of recovery. All phases require sustained motivation to counter external (places, people, and objects/actions associated with drug use) and internal (emotional and/or hedonic factors such as relapsed drug

use, or anxiety and depressed mood) triggers, for example the toleration of withdrawal symptoms during detoxification, or impulse control/resisting of cravings post-recovery/treatment.

Pharmaceutical interventions are broadly theorized to target the striatal reward pathways ("bottom-up"), while cognitive or behavioural interventions are posited to focus on executive control functions mediated predominantly by the prefrontal cortex ("top-down") [91].

Neuroimaging studies, which are further described below, reinforce the aforementioned bottom-up/top-down statements while maintaining that, regardless of the intervention type, both reward and impulse control (and associative learning) regions of the brain are ultimately stimulated [90].

Neurobiological targets of treatment

Neuroimaging studies provide a possible neurobiological explanation for observed behavioural changes after cognitive interventions have been applied. In a 2013 review of the neurobiological changes resulting from both cognitive and pharmaceutical treatment of SUDs through analysis of neuroimaging, authors found that both forms of treatment affected brain reward regions, as well as those involved in goal-directed behaviour (i.e., the VTA and NAc, as well as regions of the frontal gyrus and orbitofrontal cortex), regardless of substance of abuse for which the individual was dependent. This finding was consistent when controlling for method of neuroimaging [90]. Brain regions involved in executive control functions, specifically the anterior cingulate cortex, middle frontal gyrus, and precuneus were more likely to be activated by cognitive-based treatment methods, reinforcing the "top-down" theoretical model described above [90].

Delving deeper into specific cognitive-based treatment modalities, Zilverstand and colleagues (2016) analyzed and aggregated the results of neuroimaging studies conducted on cognitive behavioural therapy (CBT), cognitive inhibition, motivational interventions, affect regulation, mindfulness training, and neurofeedback training in the treatment of various forms of SUDs [92]. Their analysis concluded the following:

- Reward sensitivity linked to drug-related cues was reduced through use to CBT,
- Cognitive inhibition, motivational interventions and affect regulation increased activation of the inhibitory control network,
- Neurofeedback remained inconclusive, and
- Mindfulness training reduced activation of craving-related networks.

These findings align with effectiveness evaluations, which suggest that interventions tied to theory are more effective than those that are not [93, 94, 95, 49]. It is important to note, however, that the majority of studies included in the Zilverstand et al. (2016) review analyzed interventions for nicotine addiction specifically, and therefore cannot be confidently generalized to all drugs of abuse without further research.

Chapter 3: Supporting Addiction and Mental Health Care Through Use of Technology–A review

3.1 Overview

This chapter provides an overview of select existing digital technological interventions seeking to support the health and wellbeing of individuals suffering from mental health disorders, with particular emphasis on substance use disorders (SUDs) where available.

3.2 Introduction

In our current era, the exploration, development and implementation of technological innovations in health possess a perhaps-unmatched potential for human impact, disruption and advancement.

The diversity of technological innovations continues to proliferate and to differentiate sub-categorically, and includes both interventions using familiar and enduring technologies, such as radio and television for widespread public awareness campaigns, as well as novel and at times contentious, leading edge innovations, such as using emerging technologies like psychotropic medications embedded with tracking mechanisms to record a patient's adherence to medication [96], or the use of machine learning (ML) for the "digital phenotyping" of patients [97, 98].

While the term "health technology" encompasses an ever expanding scope, the line between technology types is blurring, leading some to describe this era as the "digital revolution" and fourth industrial age [99, 100, 101]. Nowhere is this more apparent than with the introduction and application of artificial intelligence (AI) [102, 101].

Digital technology has presented, and continues to present, significant benefit and opportunity for psychiatric care improvement [103], including: overall improved patient care, experience [104, 105] and safety [106], clinical decision support and patient monitoring [107, 108, 109, 110, 111], and collaborative decision making both between service providers, as well as between providers and patients [112, 113]. Digital technologies also support the proliferation and dissemination of learnings for use in the advancement of medical research [114, 115]. Specifically, the impact of technology within the field of addiction and mental health is further amplified given the potential lack of a need for a physician or specialist to be physically located in proximity to a patient for diagnosis and intervention, which contrasts care requirements for many other general health categories [116]. This is particularly helpful for the expansion of

service provision to rural or remote communities, where gaps in service access are particularly marked [117].

The following chapter will summarize reviews of digital technological addiction and mental health interventions, with emphasis on interventions targeting SUDs. Evaluations on effectiveness will be included where possible. This chapter will then conclude with a discussion addressing the opportunities and possible negative implications of new innovations, among other considerations.

3.3 Methods

According to the World Health Organization (WHO), health technology can be defined as "the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives" [9]. For the purpose of this paper, preference will be given to technological interventions involving electronic/digital media (e.g., television, internet, smartphone, computers).

Furthermore, technology can be categorized in many ways: (1) by function (e.g., information sharing, communication, clinical decision support, 'digital therapies', patient and/or population monitoring and control, bio-informatics and personalised medicine [118]); (2) by user (e.g., clients/service users/patients; service providers; health system management; and data management services [119]); or (3) by delivery mechanism (e.g., television, mobile phone, stationary and laptop computer). In recognition that we are in the midst of a "digital revolution" characterized by "a fusion of technologies that is blurring the lines between the physical, digital, and biological spheres" [45], the following review will categorize innovation by function, with the acknowledgement that categorization is becoming increasingly challenging as innovations tend to incorporate multiple users, functions, and delivery mechanisms.

A search of biomedical electronic databases was conducted to identify primary studies, systematic reviews, and evidence-supported government reports, that analyzed interventions to support the health of individuals suffering from an addiction and/or mental health illness, with emphasis on interventions specific to SUD. References were largely limited to full-text publications in English.

The search included subject headings and keyword terms for the following:

- digital health technology
- emerging health technology

- mHealth
- mobile interventions psychiatry/mental health/addictions
- machine learning/artificial intelligence psychiatry/mental health/addictions

This chapter provides a summary of reviews, as well as highlights select models and examples of interest. It is not meant to serve as a comprehensive inventory of all existing digital interventions. Additionally, there is no standardized approach to piloting and evaluating digital technology. As such there is substantial heterogeneity in reviews and case studies presented, in terms of methodology, intervention type, frequency of application, follow-up periods, and diagnosis of interest on which they were applied. More consideration is given to the implications of this variability in the "limitations" section of this chapter.

3.4 Results

3.4.1 Function: Information sharing, public communication, and community building

Digital technologies have become important avenues for information sharing, public communication, and community building. Traditionally, television and radio were common delivery mechanisms for information sharing or public communication interventions, including within the field of addiction and mental health. With the introduction and proliferation of the internet, and its ability to integrate onto multiple platforms and devices, the line between television and computer-interface blurred. This trend has accelerated with the introduction of smart televisions with internet connectivity, cross-platform integration (mobile phone, tablet, etc.), and voice command capabilities among others features. Gradually, devices that once only provided the one-way transmission of information became interactive and responsive online platforms, connecting individuals with other humans or to responsive technologies providing human-like interactions. Today, it is estimated globally 4.1 billion people have access to the internet, and that there are 7.8 billion mobile phone subscriptions [48].[viii]

With these platforms, the sharing of information and experiences has become both engaging and instantaneous. As such, they have become significant sources of health information, and have supported the proliferation of social and health awareness campaigns, as well as facilitated community building amongst individuals with shared histories and/or experiences [120, 121, 122, 123, 124]. This is particularly marked on social media platforms, where social referencing is

[viii] For a discussion on smartphone applications developed for digital therapy and bioinformatics, please see page 24.

suggested to potentially support the de-shaming of mental health, as well as connect individuals to others with similar experiences, which might support a reduction in an individual's perception of loneliness or isolation [125].

Social media platforms including WeChat, Facebook, Twitter, Instagram, YouTube, Reddit, have been widely adopted in Canada, with 25.3 million estimated social network users in 2018, and 27.1 million projected by 2023 [126]. Membership is not restricted to younger demographics, but instead utilized generally by all age groups [127, 128, 124]. Cross-generationally, individuals have been found to utilize platforms to identify cohorts of others with similar conditions for support and information, yet younger generations have been found to generally be more willing to share *personal* health information than older generations [129] [124]. In reflection that 70% of health and mental disorders typically begin in childhood and adolescence [130], and peak alcohol consumption rates are observed between the ages of 18 and 35 years [131], the potential openness of this cohort to engage with and provide health information, in addition to their familiarity with new technology as "digital natives" [132], presents a window of opportunity for prevention, early screening and intervention.

Social media platforms are evolving in function to incorporate various psychosocial supports, including information sharing and community building, as well as prevention, early screening and intervention. WeChat is the largest standalone social smartphone application in the world [133] with over 1 billion monthly active users. Functions of the app include social media and messaging, and it continues to evolve to include new features including add-on applications (apps) that support mental health and wellbeing. Of note are WeChat apps *Know Yourself* and *Jian Dan Xin Li,* both of which provide psychosocial supports. *Know Yourself* offers access to online resources, as well as offline workshops and speakers [134]. *Jian Dan Xin Li* offers online as well as in-person psychotherapy [135, 136, 137]. No evaluations were immediately available in English on the effectiveness of these applications, however this social platform has been highlighted due to the international prominence of the WeChat platform.

Facebook and Twitter, both American social media and networking platforms, have incorporated additional features that support individuals believed to be in crisis, as well as provide syndromic toxicosurveillance. For further information on these features, please see page 23.

Online platforms can be effective tools in community building, providing "socially supportive communication that reinforces self-management, self-esteem, and assistance linking with

treatment [138]" [26]. This includes social media and chat rooms, as well as peer-to-peer platforms such as patientslikeme. Patientslikeme is a community building platform where individuals with similar health conditions can log onto in order to share their experiences and support each other, "which in turn can help them cope with depression and overcome social stigma" [122, 129, 139, 124].

Another example is USP Kenya, a national Kenyan organization, that uses "WhatsApp," a cross-platform social messaging platform owned by social media platform Facebook, to offer peer-to-peer support services, external to the Kenyan health system [116, 140]. The effectiveness of this intervention has not been evaluated.

ML is being explored to assist individuals in connecting with the most appropriate peer-to-peer support groups based on personal need [141], as well as in comment moderation on support group discussion boards such as those supporting individuals who might be contemplating suicide [142, 143]. The effectiveness of these interventions on participant outcomes have yet to be assessed [143].

Online platforms do not come without contention or warning. Social media has been criticized for enabling the spread of misinformation, including unvalidated claims of intervention efficacies or harmful health messaging [124]. Examples include antivaccine rhetoric [144, 145] and misinformation about COVID-19, Zika [146], and Ebola viruses [147], as well as Lyme disease [148]. In a 10-year longitudinal analysis of approximately 126,000 stories and 4.5 million Twitter interactions, authors concluded that falsehoods on the platform spread "further, faster, deeper and more broadly," than the truth [149]. This is only further exacerbated and reinforced through the development of communities that become polarized "echo chambers," which can continue to reiterate and reinforce falsehoods [150]. With the addition of misinformation spreading chat bots [151, 152] and misguided public influencers and celebrities [153, 154], these issues become even more pronounced. Additionally, there are considerable ethical and privacy concerns with the use of 'big data' mined from these platforms, as consent for data access is often not explicitly sought. Ethical and privacy concerns around data are discussed in greater detail in the discussion section of this chapter that follows.

The question then can be posed as to whether this circulation of information translates into behavioural change. Evaluations of awareness campaign interventions using more traditional technological media such as television and radio commonly found that, although these efforts were effective in increasing general public knowledge around a particular issue, there was

limited evidence to support that this knowledge translated into actual behavioural change [155] [156] [157].

However, with the modern-day introduction of interactive, engaging online platforms for information circulation and community building, behavioural change becomes apparent and even pronounced within certain sub-population groups, such as individuals opposed to vaccinations, or individuals at risk of death by suicide.

The resurgence of vaccine-preventable diseases, such as measles, mumps, and pertussis, suggest misinformation around immunizations have successfully led to detrimental behavioural change, i.e., through the avoidance of childhood vaccinations by parents. For example, Clark County in Washington declared a state of emergency after experiencing a measles outbreak in January 2019 of 71 people, 93% of which were children or adolescents and were confirmed not to have been immunized [158, 159]. This proliferation is believe to be linked to anti-vaccination messaging spread largely on social media following a now-retracted article in the Lancet attributing a rise in childhood autism to the measles, mumps and rubella vaccine [160].

Another example is related to "the suicide contagion," where a spike in death by suicide can be observed following public announcements of the suicides of others, as seen with the death of celebrity Robin Williams [161], or following the release of a fictional Netflix series "13 Reasons Why", where a young girl's death by suicide was graphically portrayed [162].

Although multiple online platforms exist to support individuals with SUDs, such as 12-step online sites, Women for Sobriety, etc., the clinical efficacy of these platforms in causing behavioural change "remains unclear" [163]. Further analysis is therefore required to understand the impact of information campaigns on the general public or specifically for individuals with problematic substance use and SUDs.

3.4.2 Function: Digital therapies and treatment

What began as online platforms isolated to traditional desktop and laptop interfaces, transitioned to being accessible via other digital interfaces such as smartphones, and tablets. Following this came the propagation of mobile applications (apps), computer programs designed to be used on smartphone and tablet interfaces. As they evolved to permit greater functionality, so too proliferated the digital therapeutic possibilities.

In 2017 it was estimated that 318,000 health-related apps existed, with 490 apps specifically directed towards addiction and mental health [164]. The most common themes within mental

health apps were related to symptom alleviation and general education [165]. A recent systematic review that analyzed the pooled effects of 17 publications describing 19 randomized clinical trials (RCTs) of online health apps found small effect sizes for depression and smoking RCTs, but no significant pooled effects were found for anxiety, alcohol use, or self-injurious thoughts and behaviours [166]. Authors reflect that these findings do not align with systematic reviews on internet-based digital interventions for mental health, and hypothesize that this might be due to several factors including differing methods of participation (e.g., apps were largely self-guided in nature, and did not include professional guidance or support, whereas internet-based interventions might have included more guided support). Nevertheless, authors suggest that direct translation of the accumulated evidence supporting internet-based interventions to standalone mobile digital interventions "as an effective mean to treat mental health disorders," is not supported given their findings [166].

Unfortunately, although mental health apps show "some face validity," the majority of apps do not provide evidence of effectiveness or safety [167, 165, 166]. Additionally, there is a lack of regulation and validation around claims of intervention efficacy. Equally, applications do not need to show evidence of efficacy or safety prior to their commercial availability. This ultimately confuses consumers, and "dampens" rigorous academic efforts within the field [168]. Although the US Food and Drug Administration (FDA) has tightened regulations and approvals around mobile medical applications, apps that claim effectiveness in alleviating vague symptoms untied to a medical diagnosis, such as general stress management and improved concentration, are not applicable [26, 169].

Text-messaging interventions, which utilize basic infrastructure already embedded on most mobile phones, have been rigorously evaluated and show considerable promise. 98% of cellphones have text messaging capabilities and 85% of Canadians are in possession of a cell phone [51, 170, 47]. Text messaging has been found to be cost-effective [26, 171], increase appointment, pharmaceutical, and treatment adherence [172, 49, 173, 26, 174, 175, 176], reduce substance use, promote abstinence and relapse prevention [26, 174, 177], as well as serve as a connecting mechanism to an individual's support network [26, 178]. In a 2010 review analyzing text-message interventions as tools for behavioural change, "eight out of nine sufficiently powered studies found evidence to support the effectiveness of text messaging as a tool for behavior change in disease prevention [179, 180, 181] and management [182, 183, 184, 185] [186]" [49], specifically for the prevention and management of weight loss, smoking cessation, and diabetes management. Of note, three of the aforementioned studies did not isolate the effect

of the text messaging technology in their analysis [182] [181] [186]. Effects were consistent however, even when controlling for age and ethnicity [49]. A 2017 systematic review of 11 articles examining text-messaging for illicit drug and alcohol found high rates of intervention acceptability (theorized by the author of being improved with personalization), as well as increased pharmaceutical and appointment adherence and improved clinical outcomes (i.e., reduced alcohol, methamphetamine, and opioid use) [174]. Although anticipated for publication in 2020, a meta-analysis analyzing text-messaging interventions addressing problematic alcohol use has not yet been completed [187].

As noted in Chapter 2, evidence supports that intervention programs tied to theory are more effective than those that are not [93, 94, 95, 49]. In reflection of its use without necessity for an in-person professional counselor, the use of cognitive behavioural therapy (CBT) has been explored via text-messaging as an intervention tool, with interest in elevating an individual's mood [188, 189, 190, 191, 192, 193]. Although the theory of planned behaviour and health belief models are other theoretical models that have also been explored in the literature [194], this section will narrow scope to CBT-specific interventions in reflection of the Text4Support study presented in Chapter 4 of this dissertation.

Text4Mood, of which the Text4Support study in Chapter 4 draws heavily upon, is an example of a text messaging intervention using principles of cognitive behavioural therapy, whereby participants received daily supportive text messages for the period of six-months [188]. The intervention sought to influence the mood of participants with depression and/or other mental health problems. In follow-up surveys, participants largely noted that the messages "made them hopeful about managing issues in their lives, feel in charge of managing depression and anxiety, and feel connected to a support system", and generally improved their mental wellbeing. Additionally, over half of participants indicated they would be in favour of text message supports for follow-up care, and for managing medical appointments [188].

Another study titled Text4Baby, which sought to support women through pregnancy through use of supportive and informative text messages, found that participants indicated they associated the receipt of messages with an increased belief that they were more prepared to take on a role of being a new mother than the control group [193].

Similar findings have been experienced in other jurisdictions including, of note, a text intervention directed to impoverished women in Bangalore, and an interactive voice response system for individuals in India screened for mental health issues generally, where the majority

of individuals in both intervention groups indicated that they felt support and reassurance from the messages received by the interventions [190, 192, 191].

CBT has also been deployed via computer-interface. "CBT4CBT" is a community-based outpatient treatment program using a CBT-based computer intervention for individuals diagnosed with alcohol, opioid, or marijuana dependence. This intervention, evaluated via a randomized-control trial, found that although retention rates between groups were comparable, individuals in the experimental group provided evidence of abstinence more frequently and for longer durations than for the control group [195].

Missed or misdiagnosis is a critical clinical error that can potentially be addressed through advancements in digital technologies. AI and ML are being explored for use in clinical decision making [143, 196]. For example, supersparse linear integer models (SLIM) and risk-calibrated supersparse linear integer models (RiskSLIM) are publicly transparent machine-learning algorithms that have been used in both medicine and criminal justice settings to support medical screening, and predict clinical episodes such as seizures or justice-related events such as recidivism. Within the field of addiction and mental health specifically, RiskSLIM has been used to support the screening of ADHD [197]. The algorithm analyzes a patient's responses to a six-question questionnaire and provides the physician with a risk-calibrated diagnosis. The tool was found to have high specificity and positive predictive value, and is considered appropriate for use in speciality settings [198].

3.4.3 Function: Health system navigation, connecting systems of care

Negative features of health and social systems, such as fragmented or episodic care, as well as lack of support for health system navigation and/or connecting with an appropriate provider, are cited as barriers in the accessing of services for individuals experiencing addiction and/or mental health issues [27, 28, 29, 30, 199, 24].

Stigma is in part blamed for these barriers, and can occur on structural (e.g., limited resources), relational (e.g., biased provider-patient interactions) and intra-individual levels (e.g., self-stigma) [200, 201] [202]. Additionally, there is a gap in service care to individuals who are at risk of developing an alcohol use disorder, but are reluctant to seek external support from either the system or community-based groups. Commonly cited rationale given for why individuals accessed online services include 24-hour accessibility, ease of accessibility despite geographic location, anonymity and privacy [203, 204, 205, 206]. Digital technologies provide an opportunity to potentially bridge service gaps and permit greater system integration, which

could improve health and social system coordination, efficiency, patient navigation, satisfaction and overall health outcomes [207].

In addition to benefits described in the previous section, text messaging presents an opportunity for policy makers to bridge health system service gaps. As noted, text-message appointment reminders increases the likelihood that an individual will connect with their next appointment [172, 49, 173, 26, 174, 175, 176]. For example, a study examining a text message reminder service in Nigeria for patients suffering from psychosis found that patients were twice as likely to follow-through on their next appointment than controls [208]. Similarly, a study in India that provided SMS appointment reminders to patients seeking support at a community mental health center found a 63% appointment adherence versus 45.37% from the control group [209].

Another approach that has been explored is automated phone calls, both pre-recorded (one-way) and interactive voice response (IVR), that simply remind a patient of an upcoming appointment or prompt the recipient for voice or keypad responses. This has been presented as an alternative to text-messaging, where written or technological literacy or visual disabilities may prove a barrier [26]. Interestingly, although IVR has had success in supporting chronic disease management [210], to date there is limited evidence of its effectiveness for individual with SUDs to date [211, 212, 213].

A more intricate smart-phone intervention is that of the Alcohol-Comprehensive Health Enhancement Support System (A-CHESS),", which serves a similar role to a 24-hour, personalized health system navigator, offering information, self-assessment tools and personalized goal setting, counseling, and group discussion support, as well as GPS tracking option which alerts an individual when they are entering an area which is deemed high-risk to trigger a relapse. An evaluation of A-CHESS found that individuals in the experimental group experienced greater success in sustaining abstinence, and had less risky drinking days than controls [26, 214].

Digital tools are being used in an increasing number of settings, including in the waiting room. "Common Ground" is a computer-based program offered in some psychiatric clinics to support shared-decision making between providers and patients [215, 216]. Patients arrive at a clinic 30 minutes prior to meeting with a physician, and are assisted by peer staff in completing a one-page report on a web-based computer program that will then be used between practitioner and client in shared-decision making. In addition to the shared decision-making benefit, engagement with the peer staff increases the amount of facetime the client receives. Barriers to

implementation include lack of computer literacy amongst staff and clients, in addition to budgetary constraints on the purchase of new technology and to train staff in its use. Analysis of early adoption demonstrates promising uptake of the program, however no evaluative work on the clinician or client satisfaction with the program was immediately available [215, 216].

ML is being applied on Twitter, to perform a method of syndromic toxicosurveillance. Chary and colleagues (2017), using natural language processing and classification, analyzed the tweets of over a million Twitter users to analyze whether the geographic location of twitter users tweeting about misuse of prescription opioids correlated with US government estimates of the misuse of prescription opioids based on the 2013-2015 National Surveys on Drug Usage and Health [217]. Authors found that there was highly significant correlation, strongest between Twitter users between the ages of 18 and 25 years [217]. This sort of analysis could be used by health care administrators in anticipating health system needs, thus improving where and when services are provided, better connecting programs to patients.

Additionally, ML can potentially support "just-in-time" interventions, connecting an individual to care using the analysis of real-time data, bringing the health system to the patient when they need it, with 24-hour service provision that can be applied wherever they are at a time of need. For example, a study using the AWARE app, an app that helps facilitate meditation, collected 56 indicators including time, movement, and communication data (including psychomotor impairment in indicators such as keystroke speed), paired with self-reported alcohol consumption from non-treatment seeking college students with history of hazardous drinking. ML was then applied to the data set. Authors found ML successfully developed accurate models to detect high-risk drinking episodes in participants [218]. Other examples where ML has been applied in a similarly successful manner include with depression [219], and gambling addictions [220].

Another example involves social media platform Facebook. Facebook has expanded its embedded platform features to include "wellness checks," which uses AI algorithms and pattern recognition software to flag whether an individual is at risk of attempting suicide. In response to identifying a high-risk individual, the platform will encourage peer-responses, and may even alert authorities with granular level detail down to the actual location of the individual in distress. Although it is estimated that the platform has worked with first responders on over 1,000 cases, no evaluative work has been released publicly to date on the effectiveness of the platform's detection and alert service [221, 222].

3.4.4 Function: Bioinformatics and personalized medicine

Devices that read, log, and monitor biomarkers have proliferated significantly within the field of health. They monitor a wide number of indicators and behaviours and can come in various mediums and forms, including, for example, wearable devices paired to smartphone technologies (e.g., Fitbit, Apple watch, WrisTAS), hand-held mobile biomarker monitoring devices with advanced features such as facial recognition technology (e.g., Soberlink breathalyzer), trans-dermal sensors (e.g., SCRAM), or ingested inert radiofrequency emitters (e.g., Abilify MyCite). This section will provide overviews of select examples of these types of digital innovations that seek to support the health of individuals with substance use and mental health issues.

Wrist worn biomarker devices offer continuous physiologic monitoring of indicators such as electrodermal activity, heart rate, movement, and trans-dermal chemical emission, to evaluate the physical and mental wellbeing of an individual. They have been suggested to be a more accurate alternative to self-reporting measures, which are subject to recall biases amongst other factors [223]. "WrisTAS" is an example of a wrist worn biomarker monitoring device seeking to support abstinence and sobriety management specifically. The device takes minute-to-minute readings of trans-dermal electrochemical oxidation of ethanol vapors released during perspiration via a patented electrochemical sensor. An evaluation of this device found that the device demonstrated high sensitivity and specificity [223]. An ankle bracelet version (BI-TAD) also exists [223].

Paired with AI and ML, possibilities for intervention touch points, as well as intervention types, increase exponentially. For example, Boyer and colleagues (2012) suggest that the data extracted from these wearable devices, paired with data from an individual's cellphone and processed by artificial intelligence, may allow for the detection of craving through analysis of aforementioned physiological biomarkers [224]. iHeal is software paired with a wrist biomarker monitoring device, that uses AI used to detect drug cravings and drug use. It measures several physical indicators including electrodermal activity, body motion, skin temperature, and heart rate to provide a reading of an individual sympathetic nervous system, and links readings to self-reported levels of stress and drug craving. The resulting data is processed through a ML algorithm to predict craving in real-time, and offer interventions during periods of particular vulnerability. Although assessment of treatment accessibility was performed through use of a focus group, an RTC to assess effectiveness of this device has yet to be published [224].

iMStrong is another example of a ML algorithm paired to a biomarker monitoring device (Q sensor, Affectiva) used to detect cocaine use [225], using similar sympathetic system physiologic markers to iHeal. The device was validated using urine drug screens and patient self-reports to verify drug use events. Participant acceptability of the device and compliance in a natural setting was deemed high by authors based on participant interviews. Additionally, authors claim biometric readings and assessment of cocaine use was identified when self-report or drug screening "failed." Caution should be taken in interpreting results as sample size was low (n=15) [225].

"Digital phenotyping" is when ML is applied to an individual's smartphone data, inclusive of communications data (texting, calling, etc.), internet and app behaviour, and well as location data, to create objective parameters that are theorized to correlate with clinical diagnosis, and predict behaviour [226, 227]. There is limited evidence to date however, to validate claims around the accuracy of digital phenotyping [116].

Soberlink breathalyzers, advanced breathalyzer devices using facial recognition software and paired to a smartphone and the cloud, seek to serve as daily self-monitoring devices for individuals seeking additional support for problematic alcohol use. An individual receives text message reminders on their phone to provide breath samples (measuring blood alcohol concentration levels) at multiple times a day, at times that can be personalized. This intervention could be administered and monitored remotely by a provider, or an individual could self-administer this intervention and monitor their progress themselves. The device has been validated [228]. Chapter 4 of this dissertation evaluates the use of this device with a particular subset population, specifically, pregnant women seeking support in the management of problematic alcohol use. For more information, please see Chapter 4.

The Secure Continuous Remote Alcohol Monitoring (SCRAM) device serves as an example of transdermal biomarker sensor, specifically tailored to monitor transdermal alcohol concentration in an individual every 15, 30, or 60 minutes. Readings can then be transmitted to a server wirelessly. The device is typically secured on an individual's ankle and locked to ensure that it cannot be removed. Evaluations of this device suggest that device accuracy increased when blood alcohol concentrations (BAC) were higher (e.g., 57% accuracy for drinking episodes BAC <0.08 g/dL versus 88% accuracy for drinking episodes for BAC >0.08 g/dL) [223, 229, 230].

Although both the Soberlink breathalyzer and the SCRAM devices have been more frequently used in criminal justice proceedings to monitor individual adherence to particular judgements around sobriety, they are also being explored for use in general addiction management and treatment [231, 232, 233, 234].

Within the context of pharmaceutical related interventions for SUDs, innovations exist that seek to monitor patient adherence to medication. Wisepill is a pill holding device that transmits a message to a cloud-based server when the case is opened, ultimately seeking to monitor pharmaceutical adherence rates. It has been found to increase adherence for individuals with problematic alcohol use and/or methamphetamine use who are prescribed naltrexone, as well as for patients diagnosed with HIV who are undergoing antiretroviral therapy [235, 236].

Another example is an ingestible digital pill that releases an inert radiofrequency emission when exposed to stomach acid. The pill ultimately communicates with a trans-dermal skin patch linked to cloud-based server. This device is currently being used for 'the treatment of schizophrenia, acute treatment of manic and mixed episodes associated with bipolar I disorder and for use as an add-on treatment for depression in adults' [237, 238, 239]. An evaluation of this device was not immediately available.

ML presents an opportunity for neurodiagnostics using neuroimaging and biomedical informatics. A systematic review by Shatte and colleagues (2018) identified two popular uses of ML to support clinicians in determining diagnosis using AI and neuroimaging data primarily from magnetic resonance imaging, electroencephalography, and positron emission tomography. Most studies in the review sought to assist clinicians in predicting diagnosis of new patients using historical neuroimaging data and prior diagnoses, or for diagnostic differentiation. Findings show promising results using ML for diagnostic support for conditions such as schizophrenia, and Alzheimer's disease, and in the differentiation between autism spectrum disorder and epilepsy, however caution should be applied as authors noted a "lack of consistency in accuracy of techniques and datasets used" [143]. Emphasis should be made on the function of ML and AI as a support, as a systematic review by Nagandra and colleagues (2020), which reviewed findings of several deep learning studies using medical imaging, concluded that there was no evidence to support the conclusion that AI outperforms physicians [240].

3.5 Discussion

Presented in this chapter were novel and promising innovations in digital health technology, with an emphasis where possible on those interventions seeking to support the health and

wellbeing of individuals diagnosed with SUD and/or with a history of problematic substance use. This section will now provide an overview of considerations and cautions, followed by a description of review limitations, concluded by a discussion of future analysis.

3.5.1 Considerations and Cautions

Although it is recognized by many health system stakeholders that digital innovations present opportunities for quality and efficiency improvements in care [241], there are considerations and cautions that should be noted. Considerations noted in this chapter are limited to a focused subset of potential topics (i.e., monitoring for and addressing unvalidated claims and unequal access to digital technology). A broader discussion of limitations and cautions around the use of digital technology is included in Chapter 6, which incorporates learnings and reflections from studies discussed in Chapters 4 and 5.

Enrolment and engagement issues

Evidence suggests that digital health technology interventions are more effective the longer the treatment period and/or the longer the participant adheres to treatment [242]. Additionally, data collection is enriched with larger enrollment and when high participation rates are maintained for longer periods of time. Unfortunately, retention and engagement issues present a fundamental challenge in the application of substance use and mental health related technology interventions [166, 243, 244, 245]. In fact, disengagement from health research studies is generally high, with typically only 10-25% retention of participants by the study's close [246, 247, 248]. This rate mirrors the experience within other industries. For example, an analysis of app engagement from all industries suggest that within a 90-day period, 71% of app users will disengage [249].

There are several design elements that are believed to increase intervention adherence length and engagement, including: reminders, prompts and data completion alerts [166, 245, 243], partner participation [250], ease of use of technology [251], appropriate matching of functional abilities of the participants to task requirements [251], reduced participant burden (including lower rates of frequency where data is requested, reduced complexity of data requested, and passive data collection) [251, 252, 245], awareness of monitoring (e.g., data monitoring) [251], having an accessible study contact and support [251], real-time data monitoring, additional activities that promote engagement with "others" including research team or other members of their community (e.g., additional opportunities to provide feedback to study team, opportunities

to interact with other participants) [245], active chasing [245], and the perception of social benefit from study involvement [253].

Unvalidated claims

There is general agreement among ethicists, legal professionals and researchers that domestic and global legal and regulatory bodies have not been able to keep up with the proliferation of novel innovations, and as a result existing legal and regulatory infrastructure are grossly inadequate [116, 254, 255, 256]. This lack of adequate legal and regulatory protection exposes consumers to risks from digital products including unvalidated claims, which is particularly concerning as it may divert individuals from accessing effective treatment for serious health conditions. Caulfield and colleagues (2019) caution of the detrimental effects of "science hype" and "scienceploitation" [124]. Included within these phenomena are the exaggeration of scientific developments, the use of language that confers scientific legitimacy, and unvalidated "findings" tied to registered clinical trials and predatory journals [257]. Allowing the commercialization of digital technologies in this way may facilitate, "the premature implementation of technologies and the marketing of unproven therapies" [258, 259].

Barriers to entry

Although new digital technologies hold potential for reaching remote areas or communities, it should also be recognized access to technology is not equal, and this inequality must be addressed for benefits of innovations to be realized. For example, although 4.1 billion individuals have access to the internet, it's important to recognize that over 3 billion still do not [48]. In the 2018 review of the role of technological interventions for SUDs in primary care, Togighi and colleagues colleague (2018) caution that barriers imposed on individuals seeking support for addiction and mental health related issues, such as socioeconomic status, level of education, and systemic racism [260, 261], reflect the same barriers imposed on an individual's ability to access new digital technologies [262, 263, 264]. Racial and ethnic minorities have more limited access to, and use of, health technology [265, 266, 267, 268, 269], and older racial minorities are less likely to use digital health technologies, including answering or making phone calls, health related websites, and/or search engines to find health information [269]. However, there is limited variability between ethnic groups in the use of e-mails, text messaging, and mobile apps in the context of health services, which, "highlights the importance of understanding the patterns of health-related technology use across racially and ethnically

diverse populations to appropriately tailor interventions aimed at improving minority health and eliminating health disparities" [269].

This disparity might be explained by diffusion of innovation theory, where early adopters of innovations are typically more affluent members of society, and later adopters tend to be of lower socioeconomic status [270]. Mental health providers and decision makers must level the playing field to ensure the most vulnerable groups have equal access to promising new health interventions. These considerations include what the current iteration of WHO's Global Strategy on Digital Health 2020-2035 terms the "digital determinants of health," and emphasizes their importance in national strategic planning as digital technology development continues to proliferate at an exponential level [4].

3.5.2 Review limitations and future directions

There were several limitations to this review that should be noted.

First, broad search terms were used, and non-peer reviewed literature was largely excluded in order to balance breadth and depth of analysis with the specific scope of the chapters that precede it. This restriction may have resulted in relevant articles being missed.

Additionally, exponential innovation means we need to move exponentially as researchers in this field. It is acknowledged that by the time the first draft of this chapter was completed, a significant number of new relevant studies will have been published, increasing the number of relevant articles missed. Standardized rapid review strategies should be considered to increase the number of systematic reviews that can be produced, in anticipation of an ongoing proliferation of academic articles resulting from advancements at the digital frontier [143]. This effort might be complemented or supported by ML algorithms; this potential use of AI to keep pace with AI-driven developments is a likely harbinger of the emerging technological landscape.

Second, there was substantial heterogeneity in reviews and case studies presented, in terms of methodology, intervention type, length and frequency, uptake and completion rates, and condition on which they were applied, impeding the ability to generalize findings. Furthermore, a common critique presented in systematic reviews on various digital interventions was that research is often "fragmented and requires greater methodological rigor" [271].

Lastly, as alluded to in Chapter 2, where technologies were evaluated for effectiveness and impact, that analysis has been based largely on a combination of surveys and/or passive/active data collection from the new technologies or paired devices. This assessment has not

incorporated an analysis of impact/effectiveness via neurobiological mechanisms, through testing mediums such as magnetic resonance imaging, electroencephalography, and positron emission tomography. This is likely due to the fact that incorporating neuroimaging can be costly, time intensive, and intrusive (which may, in turn, lower enrolment and participation rates).

Based on current evidence (see Chapter 2), it is broadly hypothesized that effective interventions may be those that can successfully target and normalize addiction-related deficits in brain regions related to reward and impulse control [90]. Better understanding and clarity around the neurobiological mechanisms or targets of various forms of interventions, via assessing their impact and effectiveness down to a molecular level, could help elucidate the rationale as to why existing pharmacological and psychosocial treatments may work for some individuals but not for all [90]. Further exploration is required in this regard.

3.5.3 Conclusion

This chapter presented the historical, theoretical, and neurobiological foundations of addiction, as well as methods of action of cognitive interventions generally. This chapter subsequently provided an overview of digital health interventions, followed by a summary of some cautions and considerations in the uptake of new innovations, as well as areas to improve or expand future research in this area.

To conclude, digital health interventions have momentous potential to benefit the health and wellbeing of many. Yet significant issues are limiting this potential, including outdated legal and regulatory frameworks, inequal access to innovations (including the "digital determinants of health"), and shortfalls in study methodology (including lack of rigor and significant heterogeneity in design, lack of analysis of neurological impacts of interventions, and/or lack of effectiveness and impact assessments of new innovations altogether). These issues must be addressed immediately, and continually monitored for the future.

Chapter 4: Supporting Maternal Health Through Use of Technology

4.1 Overview

The following chapter is divided into three sections. It begins with a prologue that describes the history of recognition of Fetal Alcohol Spectrum Disorder (FASD). This prologue is was published in the Canadian Journal of Psychiatry on March 1, 2019. The prologue presents a historical synopsis that frame the overall landscape and context, within which the subsequent study is then administered. Following this prologue, this chapter presents the findings and analysis of a study that investigated the effectiveness of incorporating a specialized breathalyzer device (Soberlink Cellular) into usual care for pregnant women with an elevated risk of having a child with FASD (i.e., with a history of alcohol use disorder, or self- or clinically-identified problematic alcohol use). This study was published as a report by the Institute of Health Economics to Alberta Innovates Health Solutions, in August 2019. The study hypothesized that, with the support of this new technology, participants would be more likely to remain in a treatment program and reduce or abstain from alcohol use during pregnancy, with the primary outcome measure being the diagnosis of FAS for participants' offspring delivered during the study period, determined through review of the electronic medical records (EMRs). An exit interview was also administered following successful completion of the intervention. This analysis concludes with a discussion of the results, along with an epilogue, also published in the Canadian Journal of Psychiatry on March 1, 2019, that describes some further considerations around issues pertaining to the standardization of diagnosis of FASD and its implications on research and public policy. As noted in the preface of this dissertation, I was the lead author for all three publications.

4.2 Prologue review: A brief history of awareness of the link between alcohol and Fetal Alcohol Spectrum Disorder (FASD)

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A Brief History of Awareness of the Link Between Alcohol and Fetal Alcohol Spectrum Disorder

Un bref historique de la decouverte du lien entre l'alcool et le trouble du spectre de l'alcoolisation fœtale

Jasmine M. Brown, Bed, MPP[ix], Roger Bland, CM, MB, ChB, FRCPC, FRCPsych[1], Egon Jonsson, PhD[1], and Andrew J. Greenshaw, PhD, FRSA[1]

4.2.1 Abstract

Objective: Fetal alcohol spectrum disorder (FASD) is a medical term used to describe a range of mental and physical disabilities caused by maternal alcohol consumption. The role of alcohol as a teratogen and its effects on the cellular growth of the embryo and the fetus were not determined on scientific grounds until the late 1960s. However, the link between alcohol use during pregnancy and its harms to offspring might have been observed frequently over the many thousands of years during which alcohol has been available and used for social and other reasons.

Methods and Results: Using sources ranging from the biblical Book of Judges (pre-1700) up until the first public health bulletin (1977), we seek to provide an overview of the academic debate around early historical accounts ostensibly attributed to the awareness of alcohol as a

[ix] Department of Psychiatry, University of Alberta, Edmonton, Alberta

Corresponding Author:
Jasmine M. Brown, BEd, MPP, Department of Psychiatry, University of Alberta and Institute of Health Economics, 1E1 Walter Mackenzie Health Sciences Centre, 8440 112 St. NW, Edmonton, AB T6G 2B7, Canada. Email: JMBrown1@ualberta.ca

prenatal teratogen as well as to describe the social and political influences that sculpted developments leading to the public recognition of FASD.

Conclusions: Our analysis provides a brief overview of the discourse regarding historical awareness of the detrimental effects of prenatal alcohol exposure on fetal development leading to the formal recognition of FASD as a distinct clinical entity. Further research will be required to fully appreciate the scientific, medical, and societal ills associated with prenatal alcohol exposure.

4.2.2 Keywords

fetal alcohol spectrum disorder, fetal alcohol syndrome, history, maternal alcoholism, alcohol, pregnancy, placental barrier

Maternal consumption of alcohol can negatively affect fetal development, resulting in a range of mental and physical disabilities clinically termed fetal alcohol spectrum disorder (FASD). Deficiencies in fetal growth and development of the brain and central nervous system occur and are manifest after birth as cognitive and emotional deficiencies, including problems with memory, learning, attention, and social communication [272, 273]. Impairments may also include growth retardation and malformations of the face. Fetal alcohol syndrome (FAS) is the most severe and visually apparent subtype of FASD and is considered a leading cause of preventable mental disability in Canada and the United States [274]. Although the official recognition of FASD as a clinical disorder is relatively recent [275, 276], details pertaining to the first documented cases suggesting social awareness have been debated. This paper reviews the discourse on the history of this preventable disorder, from the biblical Book of Judges (pre-1700) to the first public health bulletin (1977).

4.2.3 Methods

A search of biomedical electronic databases was conducted to identify primary studies and systematic reviews that analyzed, evaluated, and/or compared and contrasted historical accounts of prenatal alcohol exposure (PAE) and/or FASD recognition. Reference lists obtained from reviews and retrieved articles were used. Non-English-language studies were largely excluded.

4.2.4 Ancient history (pre-1700)

Evidence of historical knowledge of the negative effects of drinking during pregnancy can be dated back hundreds of years [276, 277, 278, 279, 280]. The first proposed acknowledgement of

the teratogenic effects of PAE is attributed to the biblical Book of Judges 13:3-4, from the Old Testament, which conveys to the mother of prominent biblical character Samson, "Thou shalt conceive, and bear a son. Now therefore, beware, I pray thee, and drink not wine nor strong drink, and eat not any unclean thing: For, lo, thou shalt conceive, and bear a son; and no razor shall come on his head; for the child shall be a Nazarite unto God from the womb." Multiple academic references attribute this statement as recognition that drinking alcohol during pregnancy will affect the well-being of the child [277, 279].

Another quotation referenced intermittently in descriptions of FASD-related awareness is from Aristotle's Problemata: "foolish, drunken, or haire-brain women most often bring forth children like unto themselves, morose and languid [280, 281]." As Problemata was assembled from a variety of sources over several eras and translated several times, sources that use or refer to this quote have drawn from Robert Burton's 1621 book The Anatomy of Melancholy [280] as a "primary" source and attribute the quote as indicative of Aristotle's awareness of prenatal alcohol effects [278].

A third historical reference, identified by Jones and Smith [276] in 1973, entails the Carthaginian injunction prohibiting the consumption of alcohol on the eve of a couple's wedding night "in order that defective children might not be conceived." In 1999, Abel [282] attributed this order in part to Plato's Laws [283], which states that couples trying to conceive should not do so while intoxicated: "it is not right that procreation should be the work of bodies dissolved by excess of wine, but rather that the embryo should be compacted firmly, steadily and quietly in the womb." Although there are several different interpretations supporting and contending the historical recognition of FASD [282, 284, 285], these historical references likely represent, at minimum, observations between maternal alcohol consumption and birth defects deriving from prenatal insult. Other researchers have made similar arguments and reflections on the history of FASD [280].

4.2.5 Select artistic and literary references in the 18th and 19th centuries

In the first half of the 18th century, England lifted distilling restrictions, which in turn flooded the market with gin, leading to what was later called the "gin epidemic." The artist William Hogarth's (1697-1764) two paintings of interest during this time are "Gin Lane" and "Beer Street." Both pieces were designed to be viewed alongside each other and are believed to depict the evils of consuming gin in comparison with the virtues of drinking beer [285, 286]. Gin Lane has been suggested to reflect the known social ills of exuberant drinking, with special attention

given to the mother dropping a baby with facial malformations suspiciously resembling those observed in FAS [278]. An anthropologic study analyzing the gin epidemic and Hogarth's paintings concluded that the struggle conveyed is that of social and economic control between classes. Gin Lane symbolized urban decay: "gin was not simply about drunkenness; it was about the new drunkenness of the lower classes [286]."

Regardless of Hogarth's motives for creating Gin Lane, the gin epidemic itself led to what Warren [287] described as the first clear "writings identifying negative outcomes of alcohol consumption on progeny." These writings came from the College of Physicians in London, which, in a presentation to the House of Commons, blamed gin as a culprit for "weak, feeble and distempered" children (Minutes of the College of Physicians in London, 1725; referenced in Hoyme et al. [288]). But as Warren [287] noted, "It is not clear whether these early social commentators viewed the harm befalling offspring as rising from the consumption of the beverage by females or by males, or both; as a consequence of drinking prior to or during pregnancy; or as a consequence of drinking after pregnancy through breast milk; or the feeding of gin in place of, or in addition to breast milk."

The literary world provides evidence that the general public may have had some awareness that drinking during pregnancy may be detrimental to a baby's health. For example, Charles Dickens [289] wrote in his 1836 novel, The Posthumous Papers of the Pickwick Club, "Betsy Martin, widow, one child, and one eye, …but knows her mother drank bottled stout, and shouldn't wonder if that caused it. …Thinks it not impossible that if she had always abstained from spirits, she might have had two eyes by this time." Aldous Huxley's 1932 novel Brave New World [290] refers several times to the perceived ills of adding alcohol to an incubating embryo: "They say somebody made a mistake when he was still in the bottle—thought he was a Gamma and put alcohol into his blood-surrogate. That's why he's so stunted."

4.2.6 Temperance movement, Prohibition, eugenics, and clinical practice

The temperance movement produced significant medical research linking PAE to adverse birth outcomes. Additionally, with the introduction of Charles Darwin's "On the Origin of Species" in the mid-19th century, researchers sought to distinguish between alcohol's hereditary effects on offspring (generational degradation caused by alcoholism of a parent) and the direct prenatal insult of alcohol on a developing fetus (nonhereditary) [278]. In a significant study published in 1899, Sullivan [291] observed a higher mortality rate among the newborns of alcoholic women compared with others in the mother's family and/or incarcerated mothers who had limited or

no access to alcohol. In 1900, Nicloux [292] discovered that the placenta did not serve as a barrier to stop the transfer of alcohol from the mother to the embryo or fetus. In 1904, Ballantyne [293] attributed alcohol to an increased risk of adverse birth outcomes including structural dysmorphia, spontaneous abortion, and premature labor. These initial studies, along with momentum from the temperance movement, led to a modest spur in research from 1909 to 1914 (e.g., Laitinen [294] and Stoddard [295]) [287]. Several animal studies were conducted between 1903 and 1922 that demonstrated physical defects in offspring of alcohol-exposed mothers [278, 296].

When the temperance movement resulted in Prohibition, there was a major shift in public attitudes on alcohol and pregnancy, which allegedly caused some in academia to reverse the conclusions of earlier research due to the now controversial nature of the topic. For example, Warren [287] states that Charles Stockard, a Cornell University academic, conducted a study on PAE in guinea pigs, first aligning his discussion of results with the temperance movement in 1914 and then reinterpreting his findings 18 years later to suggest that alcohol served to "strengthen the stock by eliminating weak fetuses." Other researchers stepped away from the focus altogether, which resulted in a scarcity of published articles from 1930 to 1950. Warren [287] attributes the gap to "the rejection of earlier evidence pertaining to alcohol and pregnancy following the repeal of Prohibition in the United States, Canada, and several European countries; and misinterpretation of earlier research findings in a eugenic rather than toxicological context." Saunders [285] and Warner and Rosett [278] suggest that this lull was the result of alcohol being considered a "moot" or "dead" issue following prohibition and that pre-Prohibition era research was mostly disregarded due to "its moralistic and 'unscientific' language [278]." Randall [296] adds that there was pushback from the medical community, as "most physicians continued to believe that the placenta acted as a barrier to all agents and protected the unborn child." This dismissal of evidence may have occurred in part because obstetricians frequently used alcohol for mothers at risk of premature labor, in addition to the fact that alcohol was one of the few accessible anesthetics at the time for pregnancy [278]. "As a result, obstetrical writers took an ambiguous position toward alcohol [278]." In contrast, Martin and Holloway [297] argue that although "it would take the next few decades" for physicians and researchers to fully acknowledge that presence and harm were synonymous in the maternal consumption of teratogens, the scientific and medical communities were aware that the placental barrier did not in fact protect the fetus from insult, referencing multiple obstetrics textbooks from 1938 to 1951 [297, 298, 299, 300, 301]

that explicitly acknowledge this fact. Martin and Holloway suggest that the aforementioned references, along with a proliferation of prescriptions given to pregnant women during this time, suggest that "fetal harm from maternal ingestion of drugs was simply not a concern of the average physician." Greene and Podolsky attribute the potential oversight by physicians as follows: "The rapid escalation of innovation and promotion in the pharmaceutical industry at mid-century provoked a broader crisis of overflow in medical education in which modern physicians were trapped between commercial and professional sources in an attempt to keep modern by incorporating the glut of emerging technologies, therapeutics, and related information into their practices [297, 302]." Furthermore, as early as the mid-1800s, pro-life advocates emphasized the organic distinction of mother and fetus by placental barrier as evidence of intrauterine autonomy of the child, further politicizing and stigmatizing research and discourse around women's reproductive health [297, 303].

In the 1950s to 1960s, researchers began observing physical malformations in children exposed to radiation from the atomic explosions in Hiroshima and Nagasaki and from the maternal ingestion of thalidomide, which increased the scientific community's interest in the field of teratology. Thalidomide specifically is attributed to having "opened the gates for more researchers, more funding, and more institutional infrastructure in the areas of placentology, teratology and reproductive science [297]." Research on the maternal consumption of alcohol, however, remained unpopular until 1973, when Jones and Smith [276] produced convincing evidence that PAE caused a pattern of fetal malformations [304].

4.2.7 Recognition

Although an unpublished 1957 thesis was allegedly developed by Jacqueline Rouquette that observes patterns of "facies" of children born to alcoholics and attributes responsibility to the mother in the contribution of these malformations [305], the first acknowledgement of a pattern of symptoms for FASD is largely attributed to Lemoine in 1964 and again in 1968 [275]. Lemoine claims he received little recognition for his findings, stating that "my French colleagues did not believe me then and they do not believe me to this day" (letter from Lemoine to Jones and Streissguth [305]). Additionally, as Lemoine's publication was available only in French [296] and did not present specific diagnostic criteria or result in FASD recognition or diagnosis in France [288], Hoyme and colleagues [288] argue that the true recognition of FASD was made in 1973 by Americans Jones and Smith. Jones and Smith[5] specifically coined the term fetal alcohol syndrome, provided diagnostic criteria for the disorder, and "described in detail the

consistent pattern of malformations among children of the mothers with significant prenatal alcohol intake [288]." Of important note is that this 1973 publication was followed by additional supportive research to provide clarity in areas of possible contention regarding the teratogenic effects of PAE [304], as "the existing prevalent view that alcohol was safe in pregnancy led to much skepticism of the proposed teratogenicity of alcohol and whether or not the agent underlying this newly named syndrome was indeed alcohol [287]." In 1974, Jones et al. [306] published a study that adjusted for confounding factors, to clarify that the patterns observed in the 1973 study were due to socioeconomic factors. A proliferation of animal [307, 308] and human studies [309, 310, 311, 312] then followed, seeking to confirm or refute the existence of FAS [287]. Findings from these studies not only supported Jones and Smith's 1973 conclusions but also defined alcohol as a classic teratogen that could affect behavior in the absence of obvious physical deformations.

The first public awareness warning was delivered via the U.S. Food and Drug Administration Drug Bulletin on June 1, 1977, and subsequently by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the Centers for Disease Control and Prevention (CDC) Mortality and Morbidity Weekly Report [287]. "This first advisory recommended a 2 drink per day limit for pregnant women and defined a clear risk at a level equivalent to 6 drinks per day [287]." Following this public service announcement, the advisory was endorsed by the American Academy of Pediatrics, March of Dimes, American Medical Association, and American Society of Addiction Medicine; eventually the American Congress of Obstetricians and Gynecologists formally acknowledged the advisory. The CDC has since updated its policy, emphasizing that "there is no known safe amount of alcohol use during pregnancy or while trying to get pregnant [313]."

4.2.8 Conclusion

We have provided a brief historical review of social, academic, and clinical recognition of the effects of PAE on fetal development and formal acceptance of FASD. The historical literary references clearly recognized that excessive alcohol intake may be harmful to both mother and infant, but publications did not make a clear link to fetal deformities until quite recently. Further work is needed to understand the extent to which social knowledge about the ills of drinking during pregnancy may have existed and the delay in clinical and academic acknowledgement. An additional layer of interest involves the extent to which pro- and anti-

abortion activism, through discourse around intrauterine autonomy, threaded into the proliferation and/or obstruction of research.

4.2.9 Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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IHE Report

Prevention of fetal alcohol spectrum disorder (FASD) by the use of technology

Prepared by:

Jasmine Brown

Dr. Egon Jonsson

Nicole Riley

Dr. Andrew J. Greenshaw

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4.3.1 Executive summary

Fetal alcohol spectrum disorder (FASD) refers to a range of physical, cognitive, and behavioural impairments caused by prenatal exposure to alcohol. Advances in technology now make it possible for individuals, including pregnant women seeking help for alcohol dependence or problematic alcohol use, to self-monitor their drinking through use of a specialized breathalyzer device paired with a smartphone. The information, produced in total privacy and presented as feedback to each individual directly, could potentially change an individual's attitudes and behaviours around consuming alcohol and/or enhance incentive to seek support through various forms of intervention to manage their problematic alcohol use. This study aimed to assess the effectiveness of incorporating a specialized breathalyzer device into usual care for pregnant women with a history of, and actively seeking support for, problematic alcohol use (including alcohol use disorder), and thus at risk of having a child with FASD.

The study was designed as a randomized controlled trial to recruit a sample of 110 pregnant women over a three-year period. The recruits were randomized between a control group and an experimental group on a one-to-one basis. The participants were recruited by health and social support workers in addiction and mental health in collaboration with the study coordinators, as well as by word-of-mouth recommendations from participants enrolled in the study.

The intervention provided to the experimental group consisted of a specialized breathalyzer device with facial recognition technology, along with a smartphone (with subsidized text, phone, and data plans) to receive samples and monitor daily blood alcohol concentration results and reporting. Participants were asked to provide three breath samples daily: upon waking, during a trigger time of their choice during the day, and before going to sleep at night. Considering the varying wake and sleep cycles between individuals, participants in the study set these three daily sample times with the study coordinator when they joined the study, and could request amendments throughout the study should their daily routine change. The primary outcome measure of this study was the diagnosis of fetal alcohol syndrome (FAS), the most severe form of FASD, for participants' offspring delivered during the study period, determined through review of the electronic medical records (EMRs). This study also sought to review the diagnostic elements of FAS in order to track the presence or absence of possible FAS-related indicators (also through EMRs).

This study was not without its challenges. Due to relatively low enrolment, the study design was adjusted to more effectively recruit participants. The study became a single-arm intervention

(down from a two-arm study, with both an experimental and control group), with a companion qualitative study implemented through an exit interview upon delivery. Significant effort was made to inform all possible addiction and mental health-related facilities and clinics with programming focused on supporting pregnant women in Edmonton and Grande Prairie about the study. There were also unanticipated delays in gaining ethics approval due to the sensitive nature of the study, which caused delays in enrolment. The study recruited 18 individuals (19 cases) over the course of a 14-month period. Although it was anticipated that enrolment would increase over the remaining study period, a request for extension was not approved due to the slower than anticipated enrolment (as judged by the grant provider), and the study wrapped up at its natural end date.

In total, 18 women were recruited to participate in the study, with one participating twice due to two pregnancies during the study period (once as a control and once as an experimental participant), resulting in 19 cases (15 experimental and 4 control). For the experimental group, participation lasted on average 98 days, with participants receiving approximately 283 prompts. An average of 188 breath samples were received from participants, for an average compliance rate of 44%, although variability was considerable between participants. Due to low sample size, no conclusive statistical analyses could be made with regard to health data received on participants and their newborns.

This study observed that mobile interventions such as a specialized breathalyzer device paired with a smartphone may help promote a sense of independence and empowerment for pregnant women seeking help for problematic alcohol use. Participants indicated during enrolment and reiterated in their exit interviews that the device was of help to them since it allowed them to document and record their sobriety, to show objective, third-party evidence of actual behavioural change as to their alcohol use during pregnancy, for friends and relatives who may not otherwise believe in such a change. The research team also learned from participants at enrolment and exit interviews that the smartphone, provided to participants to complement the functionality of the specialized breathalyzer, also served as a supportive tool; it enabled the bridging of pathways to care, allowing participants to connect with their support networks and healthcare professionals. These results, however, are hypothesis-generating only, and should be further tested.

Historically, enrolment for interventions focused on vulnerable groups at this level of sensitivity has been challenging for researchers. However, discussions (unprompted, informal texts and calls, and exit interviews) and feedback with participants and addiction support staff provided

the research team with valuable insight on how to better tailor the development and implementation of future intervention studies to support vulnerable individuals struggling with substance use. For example, the research team began using recruitment posters, displayed in a variety of public health and community settings, in response to feedback received by addiction support staff and participants (including use of posters, tweaks to language, and potential poster locations). Individuals with lived experience as members of the research team or as consultants can provide crucial insight into intervention-related study methodology design and implementation, as well as interpretation of findings, in a way that addresses possible gaps overlooked by researchers lacking real-world experience.

This study provides new information on potential preventive health interventions for women struggling with alcohol or substance use disorders. The object of this report is to share our experiences and facilitate the efforts of other researchers and public health sector teams to be better prepared for potential research barriers (for example, low enrolment due to fears of stigma and general distrust in institutions) as well as successes in the implementation of prevention intervention pilots and programs to support the health of women struggling with substance use (for example, peer engagement in study design and implementation).

4.3.2 Introduction

Definition, prevalence, and implications

Fetal alcohol spectrum disorder (FASD) refers to a range of physical, cognitive, and behavioural impairments caused by prenatal exposure to alcohol. These may include neurological and cognitive deficiencies, such as problems with memory, learning, attention, and social communication [273, 272].

FASD is completely preventable in the absence of alcohol consumption during pregnancy. Nevertheless, it is estimated that the 12-month prevalence rate of alcohol use disorder among women in Canada is 3.6% [314]. Although 10% of women admit to having drank during pregnancy (3% admitting to at least one binge drinking episode) [315], on average women are not aware they are pregnant until four to six weeks after conception [316]. Almost half of women responding to a cross-sectional survey reported drinking in the three months prior to discovering they were pregnant [317], the first trimester of which is a period of particular vulnerability to neuronal insult [318].

The prevalence of FASD has for decades been assumed to be about 1% at the population level [319]; however, findings from recent studies point at significantly higher prevalence. A study of

school children in Ontario shows that the prevalence may be as high as 3% [320], and several studies of school children in the United States indicate that it may be up to 5% [321, 322]. The leading cause of mental disability in Canada and the United States is fetal alcohol syndrome (FAS), the most severe form of FASD [274].

The economic implications of FASD are significant, because, in addition to incremental lifetime cost on the health system, individuals born with FASD are at high risk for acquiring secondary disabilities such as withdrawal from school, family and placement breakdown, homelessness, unemployment, alcohol and drug use, and involvement with the criminal justice system [323]. A recent study of the total cost of FASD to Canadian society estimated it to be $9.4 billion per year (2015 price level) [324]. In Alberta, the total cost of FASD is reported to be $1.2 billion per year (2017) [325], and the estimated lifetime incremental cost per FASD case was calculated in a 2011 study as being approximately $800,000 [326]. All estimates identified above are inclusive of both direct costs (for example, health, social, educational, and correctional services) and indirect costs (for example, productivity losses).

New technology to support maternal health

Mothers with substance use disorders experience barriers in both engaging and completing standard treatment, such as caregiving responsibilities and lack of support from partners and family members [327]. These women may avoid treatment due to fears around stigma and stereotyping, as well as government reprisals including child apprehension [328, 57, 58, 59]. In research settings where measuring maternal alcohol consumption through biomarker testing and/or interviews and surveys is included, this fear might be exacerbated, impacting the feasibility of research and the generalizability of research findings.

Advances in technology now make it possible for individuals diagnosed with alcohol use disorder to receive discrete, real-time monitoring, brief interventions, and connections to supportive care through the use of advanced online applications and medical devices. This study made use of the Soberlink Cellular breathalyzer (Soberlink, Inc., *www.soberlink.com*), paired with a smartphone to enable regular reporting of blood alcohol concentration (BAC) levels. The Soberlink Cellular breathalyzer included software with the following features: facial recognition for photo identification of the user; daily, weekly, and monthly reporting to track changes in alcohol consumption; ability to provide information on the history of alcohol use; and capacity for feedback and reinforcing messages. The technology has been validated for technical measurement of alcohol intake [228], and it offers promise both for increasing responsiveness

to existing services and for reducing alcohol use and improving health outcomes. A specialized breathalyzer may complement standard care for pregnant women with alcohol use disorder, offering a convenient, portable, and discrete way to track alcohol use and to communicate their achievements with their friends, family, counsellors, and social services, if they choose to do so.

Prevention of FASD by the use of technology study

In 2015, the Institute of Health Economics (IHE) was awarded a Partnership for Research and Innovation in the Health System (PRIHS) grant to implement and evaluate the incorporation of the Soberlink Cellular device (and associated Sober Sky cloud-based technology) into the regular care for women actively seeking support to address problematic alcohol use.

4.3.3 Methods

Hypotheses and outcome measure

This study investigated the effectiveness of incorporating the Soberlink specialized breathalyzer device (Soberlink Cellular) into usual care for pregnant women with a history of alcohol use disorder, or self- or clinically-identified problematic alcohol use, and thus at elevated risk of having a child with FASD. Our hypotheses were as follows:

- pregnant women using the specialized breathalyzer device are more likely to remain in a substance use treatment program, and reduce, or achieve abstinence from, alcohol use during pregnancy than those provided with usual care alone; and
- this improved likelihood will impact the final outcome in terms of fewer cases of children born with FASD.

The research study was conducted in Edmonton and surrounding areas in the province of Alberta, Canada.

The primary outcome measure of this study was the diagnosis of FAS for participants' offspring delivered during the study period, determined through review of the electronic medical records (EMRs). This study also sought to review the diagnostic elements of FAS in order to track the presence or absence of possible FAS-related indicators (also through EMRs). The intervention was restricted to women in their first or second trimester of pregnancy (minimum exposure) who were actively seeking support for problematic alcohol substance use. EMRs were accessed via the Alberta Health Services (AHS) Administrative Database, through a data agreement completed with the AHS Administrative Database office. Data was accessed from the Alberta

Perinatal Health Program; Data Integration and Management Repository (DIMR) (for ICD-9/-10 billing codes related to FASD diagnosis and associated indicators); and Case Works PHANTIM Databases. A de-identified Sober Sky data report was extracted on all participants to analyze breath samples.

The research team consulted frequently with staff at addiction support clinics throughout the duration of the study, particularly during enrolment. Consultation included one-on-one meetings, presentations from addiction centre staff, phone calls, and emails. Additionally, participants asked questions and/or provided unsolicited advice on the study verbally in phone and/or text interactions with the enrolment coordinator.

The study used the Pampalon Material Deprivation Index (MDI) to document demographic information on the participants, as provincial administrative databases in Canada do not include patients' socioeconomic information [329]. Using six socioeconomic indicators, this deprivation index categorizes over 47,000 dissemination areas/spatial units into one of five quintiles, quintile 1 representing the most privileged population and quintile 5 representing the least. The deprivation index aims to reflect the material and social deprivation status of 98% of the Canadian population. It is important to note that this index reflects socioeconomic conditions at a neighbourhood level versus an individual level.

A voluntary exit interview was provided to all participants who completed the study (that is, continued to provide breath samples and remained in contact with the research team until they gave birth). A copy of the exit interview questions can be found in *Appendix A*. Interviews were audio recorded and transcribed. Responses were then categorized by the research team into common themes.

Target Population

Eligible participants were women in their first or second trimester of pregnancy seeking treatment for self-identified or clinically recognized problematic alcohol use, without severe learning disabilities. Polydrug users, although originally excluded to reduce confounding variables, were ultimately deemed eligible to participate in the study in response to lower than expected enrolment rates.

This study sought to recruit up to 110 pregnant women over a three-year period, as a randomized clinical trial with two arms, a control group and an experimental group. However, due to issues with enrolment, the methodology was adjusted to recruit participants more effectively and appropriately.

A multi-pronged recruitment strategy consisted of printed media (posters and info-cards) distributed to addiction and mental health service providers at various AHS and community support centre locations. Project recruitment presentations were made to the following service providers:

- CASA South
- CASA FASD Central
- Edmonton Fetal Alcohol Network
- Metis Child & Family Services
- Enoch Cree FASD Workshop, Health Centre, and Wellness Centre
- Health for Two Network Meeting-West (includes Child and Family Services, Alberta Works, Alberta Perinatal Program Nurses, Boyle Street, Bissell, First Steps-Catholic Social Services, Jasper Place Wellness Centre, and Brentwood)

We maintained twice-monthly one-to-one contact with front-line care professionals, including addiction counsellors.

These conventional recruitment activities were supported by a social media awareness campaign using the @FASD_Prev_IHE Twitter account.

Individuals who expressed an interest in participation in the study were provided with the contact details for the enrolment coordinator.

Intervention

Enrolment for this study began 1 March 2016 and ended 15 May 2017.

Participants received a prompt via text messaging to provide a breath sample to gauge their BAC, three times per day. The timing of the prompts was as follows:

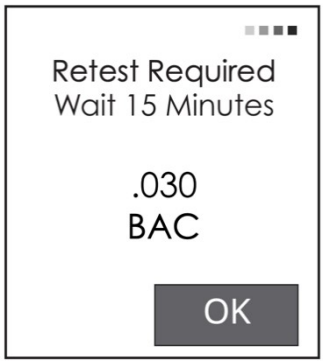
- upon waking;
- during a trigger time of their choice during the day; and
- before going to sleep at night.

These times were set in collaboration with the participants, as wake and sleep cycles were variable depending on the individual's lived environment. The device included facial recognition technology that confirmed the participant's identity while providing the sample and transmitted

the BAC level and identification verification to a password-protected, encrypted, cloud-based network called Sober Sky (also by Soberlink, Inc.).

The breathalyzer provided immediate feedback to the participant with a BAC reading (see example in *Figure 1*). The BAC reading, which was available only to the participant, was generated directly by the specialized breathalyzer device. The research team was able to access the BAC readings in deidentified format, to protect the privacy of the participants.

Figure 1: Example of blood alcohol concentration reading



BAC: blood alcohol concentration

If a participant stopped providing samples three days in a row, the enrolment coordinator would send a text asking if technological assistance was required. If they did not hear back, or if sustained samples were missed, the enrolment coordinator provided two additional warnings with a deadline to comply identified. If the participants continued to miss samples following the identified deadline, the participant was then removed from the study.

Data storage and access

Whenever participants provided self-administered breath samples, the results were stored in the password-protected Sober Sky cloud-based network. Participants were able to access their BAC readings electronically, via daily and monthly reports. Participants could also request that their data be printed by the research team, for their own personal use as a record.

Data protection

All subjects were assigned a unique identification number upon enrolment. All subject data was deidentified by the enrolment coordinator before it was be used by any research staff, thus ensuring participant confidentiality. The research team then accessed this data from the Sober Sky cloud-based network in de-identified form. All electronic records and data are secured and encrypted on secure servers located at the University of Alberta's Faculty of Medicine and

Dentistry. Data will be kept for the mandated five-year requirement and subsequently destroyed by using commercially available methods to ensure complete erasure and destruction. Linking data is contained within a password-protected electronic file on the secure server, which is accessible only by the study and enrolment coordinators. At the end of the study, five years after closing (the time of the study's ethics expiration), the data will be destroyed by the study coordinator. Ownership of data ultimately remains under the control of each participant who donated it; participants are able to request that their data be destroyed at any time. The IHE merely functions as a custodian of the data during this time.

Ethics

Ethics approval was received on 17 December 2015 (Project ID: RES0024199). Any amendments made to the study methodology were first approved by the University of Alberta Health Research Ethics Board – Health Panel, prior to implementation.

Recruitment issues and amended methodology

The study period was from 1 April 2015 to 31 March 2018. Due to delays in ethics approval, enrolment began 1 March 2016 and ended 15 May 2017.

This study is the only FASD prevention intervention study that has utilized the measurement and self-monitoring of biomarkers[i] to promote the reduction of drinking or abstinence in women with a history of problematic alcohol use. Due to the novel nature of this study, as well as the vulnerable predisposition of the population of interest, the research team needed to remain flexible in response to feedback from participants and clinical partners. Accordingly, the design of the study required responsiveness in order to increase enrolment to its full potential during a limited allotment of time. More specifically, in consultation with addiction and mental health service providers, participants, and the AHS Addiction and Mental Health Strategic Clinical Network Assistant Scientific Director, practical changes were made to the study design in response to lower than expected enrolment rates. Changes to the study design were subsequently reviewed and approved by the University of Alberta Health Research Ethics Board – Health Panel, prior to implementation.

[i] A biomarker is a biologically derived, measurable substance that is considered indicative of the presence or severity of a medical state or pathology.

Changes to study design

Changes to the study design included the following:

- reduction of the enrolment target from 110 to 55 individuals;
- expansion of the study from Edmonton's city centre (downtown core) to the City of Edmonton (suburban areas included) and communities surrounding Edmonton, as well as Grande Prairie;
- inclusion of individuals suffering from the problematic use of more than one substance (initially excluded);
- cessation of enrolment into the control group (de-identified health system aggregate data to be used as a comparator group if recruitment was deemed high enough to perform quantitative analysis; and
- inclusion of an exit interview for enhanced qualitative analysis.

Rationale for changes

Sample size and region

After further consultation was conducted at the research sites, the research team discovered that significantly fewer pregnant women were seeking support for substance misuse than anticipated at the time of the study design. In light of that fact, the study zone expanded from the downtown Edmonton core to include the entire City of Edmonton, including suburban areas and surrounding smaller communities, as well as Grande Prairie. There were also unanticipated delays in gaining ethics approval due to the sensitive nature of the study, which caused delays in enrolment. In order to keep to grant timelines, the research team reduced its preliminary sample size goal of 110 to a more reasonable 55.

Inclusion of individuals suffering from the problematic use of more than one substance

The research team originally excluded individuals suffering from the problematic use of more than one substance. This selection aimed to control for comorbidity in substance misuse, considered at the time to be a possible confounding factor, thereby complicating the analysis of birth outcomes. After further engagement with the community, the researchers observed that individuals seeking help for substance misuse often misused multiple drugs, of which alcohol was one [330, 331]. Therefore, isolating only for alcohol misuse was hindering the ability of the research team to enrol participants.

Ceasing the control group

Participants and addiction support staff notified the research team that a major barrier to study recruitment was that the target group of women were reluctant to participate with the existence of a control group. The risk of being randomized to the control group, without intervention while providing the research team with access to their EMRs, was identified as a significant disincentive to enrolment. The decision to remove the control group was made in October 2016, approximately eight months after enrolment began. As crossover of the control patients to the experimental group would have created a systematic variation in the exposure to the intervention within the intervention arm, thereby confounding the effectiveness analysis, the decision was made not to transfer the existing control participants into the experimental group.

4.3.4 Results

Participant enrolment and demographics

The research team was contacted directly or indirectly (that is, through assistance of a healthcare and/or addiction social worker) by 35 women between March 2016 and May 2017. Seven were deemed ineligible based on preliminary screening (for example, more than six months pregnant or without a history of alcohol or substance abuse). Of those that met the eligibility criteria, 28 made an appointment with the project coordinator; nine did not show up as scheduled, and 18 (19 cases, as one participated twice – see below) followed through and met with the coordinator. Reminders were provided the day of the preliminary meeting via text messaging and/or phone call, and all efforts were made to reach out to reschedule any missed appointments.

Of the 18 women, all consented to being in the study, totalling a 100% consent rate. The participant who discovered they were pregnant twice during the enrolment period signed up for the study on two separate occasions. This was permitted, as the first time they signed on to the study they were randomly assigned into the control group, when a control group still existed. The total participant number was therefore 18, for a total of 19 cases. The average age of the participants was 29 years. Six participants completed the study in full, including participation in an exit interview.

Using the Pampalon MDI, postal codes were retrieved for 17 of the 18 individuals who participated in the study (one participant's postal code was unknown and could not be retrieved by AHS data administrators). Of these 17, three fell into quintile 1, one into quintile 2, seven into quintile 3, and seven into quintile 4 (see *Table 1*).

Table 1: General characteristics of the participant population, by Pampalon MDI quintile

MDI quintile	# of participants	Education[a]	Employment[b]	Income[c]	Living status[d]	Marital status[e]	Single parent[f]
1	3	18.1	68.5	$40,148	10.1	12.5	11.6
2	1	27.0	66.0	$29,658	8.3	13.0	13.5
3	7	32.8	63.0	$26,206	8.5	13.5	15.2
4	7	38.7	59.3	$23,215	9.1	14.3	17.3
5	0	48.7	49.0	$18,542	9.6	14.6	21.5

[a] MDI category "SCHOLAR": ratio of individuals aged 15 years and older with no high school diploma to the population aged 15 years and older

[b] MDI category "EMPLOI": ratio of individuals aged 15 years and older who are employed to the population aged 15 years and older [c] MDI category "REVENU": average personal income for the population aged 15 years and older

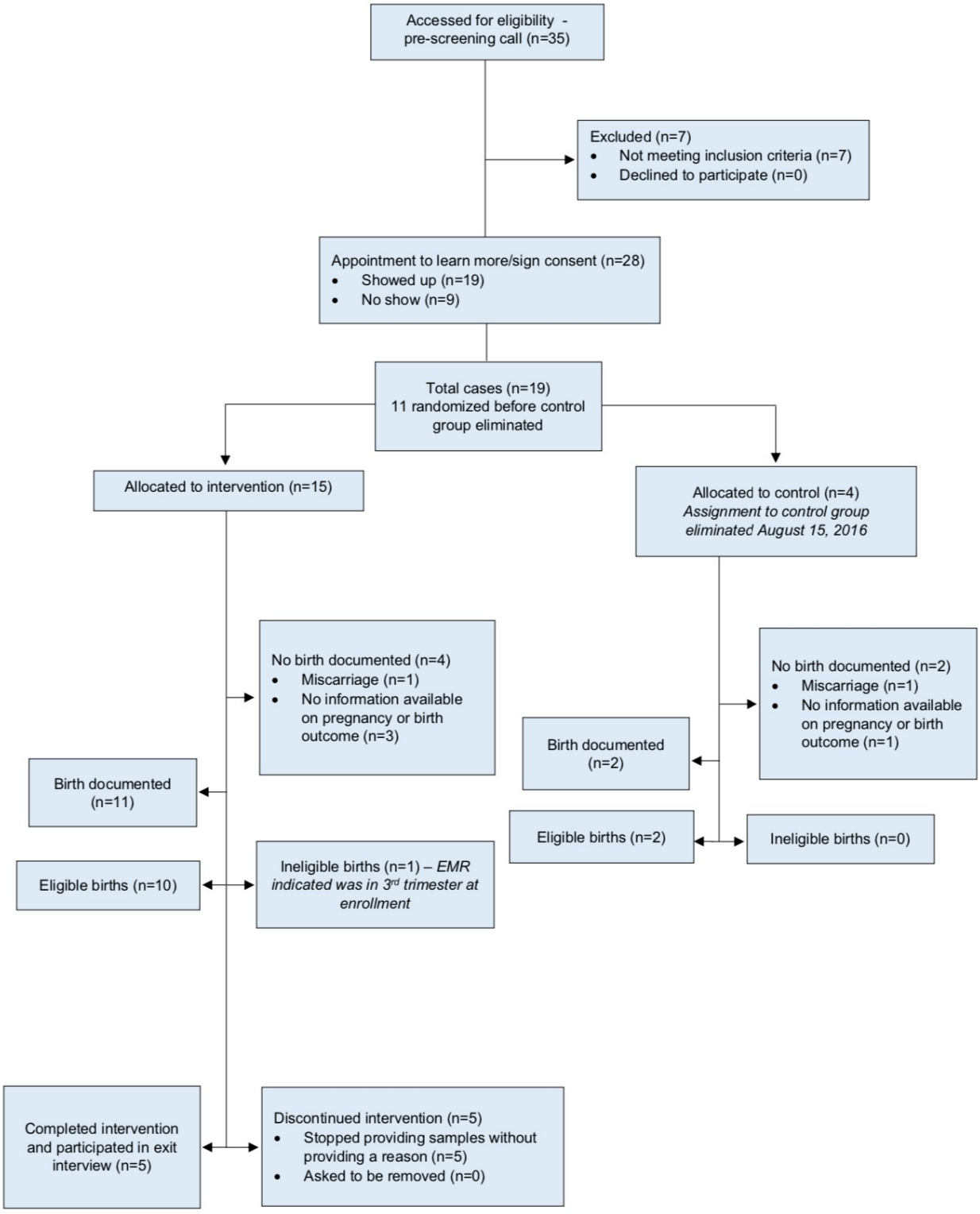
[d] MDI category "SEULES": ratio of individuals aged 15 years and older living alone to the population aged 15 years and older

[e] MDI category "S_D_V": ratio of individuals aged 15 years and older who are separated, divorced, or widowed to the population aged 15 years and older [f] MDI category "F_MONO": ratio of single-parent families to the total number of families MDI: Material Deprivation Index

Summary of results

For a summary of the study enrolment and included participants/cases, see the consort flow diagram in *Figure 2*.

Figure 2: Consort flow diagram



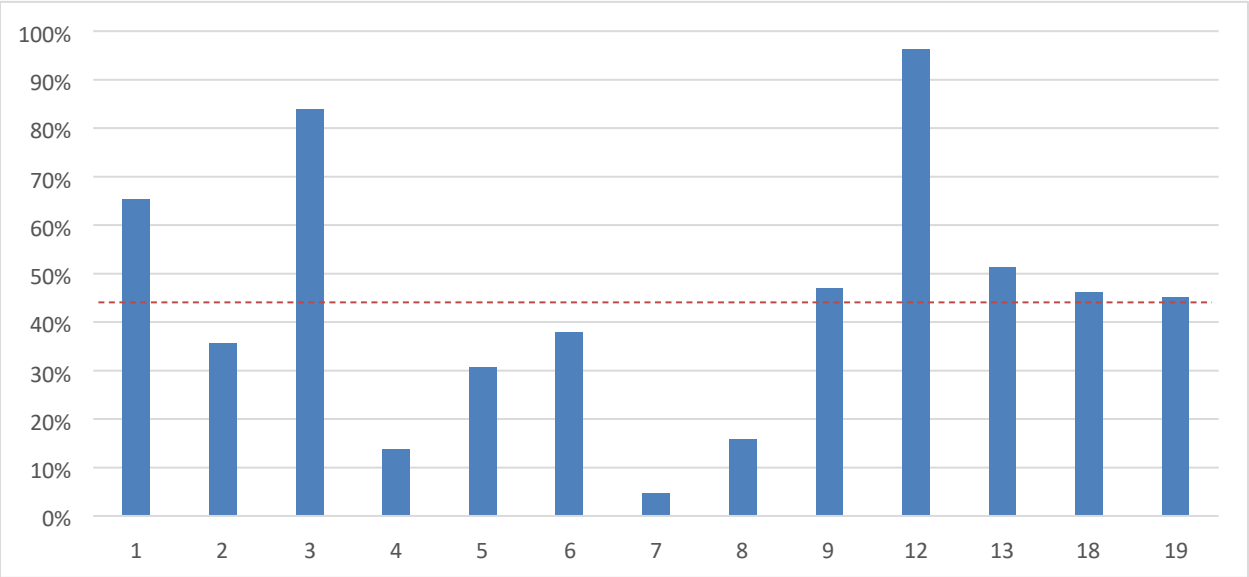
Of the 19 cases followed (18 individuals total), 13 (two control and 11 experimental) had a birth recorded during the study period. Following receipt of the EMRs, we discovered that one control group participant and one experiment group participant suffered miscarriages. We also discovered that one participant was ineligible for the study, as they were enrolled in their third trimester (note that eligibility was outlined clearly at time of enrolment).

Four participants (one control and three experimental) did not have a birth accounted for during the study period. We are not able to conclude from the data whether those who did not have a pregnancy accounted for had an abortion, had an early miscarriage, or were never pregnant. One of these participants continued to provide breath samples until their self-identified delivery date, and subsequently participated in the exit interview. The number of days and compliance rates varied considerably between the three participants in the experimental group without recorded births, from 13 to 120 days, and from 14 to 56% compliant.

Of the 10 eligible experimental participants that carried to term, five remained active in the study (provided regular breath samples) to delivery and participated in the exit interview, and five were removed from the study because they stopped providing breath samples (see *Table 2*). Two of the latter five did not provide any samples following enrolment, and the remaining three were in the study for an average of 48 days (range: 24 to 69), with an average of 70 samples (range: 6 to 117) and a compliance rate of approximately 32%.

For the experimental group as a whole (n=15), participation lasted on average 98 days, with participants receiving approximately 283 prompts. An average of 188 breath samples were received from participants, for an average compliance rate of 44% (standard error for mean compliance rate was 7.3) (see *Figure 3*). However, variability was considerable between participants, with some providing as many as 393 samples (on-time and late) to 469 prompts received over the 157 days enrolled (84% compliance), and others providing as little as four samples (on-time and late) to 29 prompts received over 13 days enrolled (14% compliance).

Figure 3: Compliance rate, by case



Note: The red line indicates the average compliance rate across all cases.

Table 2: Breath sample participation

Case #	Date enrolled	Date completed (child's date of birth) or date removed	Days in study	Total prompts calculated from database	Total prompts missed	Total completed samples on-time/late/ (unscheduled)	Total on-time samples	Total unscheduled samples	Total late samples	# of positive BAC results	With compliant secondary tests	Exit interview	Compliance rate
1	17 Mar 2016	4 Sep 2016; birth verified in EMR	171	512	178	392	245	58	89	0	0	Yes	65%
2	22 Jul 2016	18 Nov 2016; birth verified in EMR	119	354	228	172	118	46	8	26	2	Yes	36%
3	23 Jun 2016	27 Nov 2016; birth verified in EMR	157	469	76	427	313	34	80	2	1	Yes	84%
4	20 Jul 2016	Removed 4 Aug 2016; no birth recorded during study period	13	29	25	5	3	1	1				14%
5	3 Jul 2016	Removed 22 Aug 2016, due to non-compliance; suffered a miscarriage	50	144	100	72	39	28	5	0	0	No	31%
6	6 Jul 2016	Removed 18 Jan 2017; joined in third trimester	196	587	365	326	171	104	51	2	1	No	38%
7	6 Sep 2016	Removed 28 Oct 2016, due to non-compliance; birth verified in EMR	52	107	102	6	3	1	2	0	0	No	5%
8	8 Dec 2016	Removed 18 Jan 2017, due to non-compliance; no birth recorded during study period	41	120	101	53	11	34	8	2	0	No	16%
9	13 Jul 2016	Removed 20 Sep 2016 due to non-compliance; birth verified in EMR	69	202	107	117	72	22	23	1	0	No	47%
10	16 Aug 2016	13 Jan 2017; birth verified in EMR	No sample data. Did not provide samples after enrolment:.										

Case #	Date enrolled	Date completed (child's date of birth) or date removed	Days in study	Total prompts calculated from database	Total prompts missed	Total completed samples on-time/late/unscheduled)	Total on-time samples	Total unscheduled samples	Total late samples	# of positive BAC results	With compliant secondary tests	Exit interview	Compliance rate
11	25 Jan 2017	4 Aug 2017; birth verified in EMR	No sample data. Did not provide samples after enrolment.										
12	11 Jan 2017	31 May 2017; birth verified in EMR	140	423	16	415	366	8	41	0	0	Yes	96%
13	12 Dec 2016	21 Apr 2017; birth verified in EMR	130	354	173	187	155	6	26	0	0	Yes	51%
14	Control – no intervention; suffered a miscarriage												
15	Control – no intervention; no birth recorded during study period												
16	Control – no intervention												
17	Control – no intervention												
18	22 Feb 2017	Anticipated due date given by participant: 6 Jul 2017; no birth recorded during study period	120	321	173	180	109	32	39	17	1	Yes	56%
	1 Feb 2017	Removed 25 Feb 2017 due to non-compliance; birth verified in EMR	24	60	33	87	25	60	2	2	0	No	45%

BAC: blood alcohol concentration; EMR: electronic medical record

Overview of exit interview responses

Six exit interviews were conducted. All six participants consented to the interview, including the development of a transcript of their responses. One of the exit interview participants did not have a pregnancy documented during their participation in the study; however, we included the participant's responses in our analysis because they continued to comply with the study (use of breathalyzer device), had a history of alcohol use, and was of childbearing age (that is, they reflected our at-risk population). A summary of the participants' exit interview responses can be found below in *Table 3*, and copy of the exit interview questions can be found in *Appendix A*.

Table 3: Summary of exit interview responses

	Question (1 = strongly disagree; 5 = strongly agree)	1	2	3	4	5	Notes
1.	The breathalyzer and cellphone helped support me during my pregnancy.				X	XXXXX	
2.	The study helped me monitor my drinking.					XXXXXX	
3.	The study helped me reduce and/or stop my drinking.			X[a]	X[a]	XXXXX	"Stop my drinking, strongly agree. I underlined it here too, stop my drinking.
4.	The study changed the way I thought about drinking during my pregnancy.			X	X	XXXX	
5.	The study was easy to do.		X[b]	X[b]	X	XXXX	"it was hard to always have with me."
6.	I would recommend this study to my friend.					XXXXXX	
7.	The research team answered all my questions and helped me with any technical problems I had throughout the study.		X			XXXXX	One participant was not aware that she could reach out to us for technical support.

[a] One participant provided "3 or 4" as a response to this question.
[b] One participant provided "2 or 3" as a response to this question.

Responses to open-ended questions

The following are paraphrased responses, grouped thematically, to the open-ended questions from the exit interview. A copy of these questions can be found in *Appendix A*:

What did you like about this study?

- Portability of the breathalyzer and having a cellphone.

- Helps support sobriety or slow down drinking (three participants).
- Having a cellphone and coverage of cellphone bill during the study.
- To help with research for other mothers going through the same thing.
- Helped cut down drinking quite a bit.

What did you dislike?

- Discomfort in carrying the devices (two participants).
- Nothing (two participants).
- Having to remember to provide samples.
- Timing for providing samples was not always ideal.

Why did you join the study?

- Counsellor recommended the study.
- Health for Two support worker recommended the study.
- To reduce alcohol intake.
- Referral from a friend and referral from a community support meeting.
- For the cellphone.
- To have a healthy baby.

How was this study useful to you?

- Maintain sobriety; increase responsibility for actions; comfort – reminder for sobriety during stressful moments.
- Helped with sobriety and access to a phone (for contact with doctors and others).
- Helped support sobriety.
- Helped support maternal health (two participants).
- Saved money.
- It was supportive and informative; having free cellphone, cell plan, and breathalyzer was relieving.
- Helped support the baby's health.

Will you continue monitoring your drinking through use of a breathalyzer, even after your pregnancy?

- Yes (five participants).
- No.

If you had joined the study at another time in your life, do you think this study would have helped support you more? Less?

- More (six participants).

What other types of support have you tried? Have they been helpful? In what way?

- Gone to "treatment." It helped increase awareness/knowledge of harms of drugs and alcohol on body. Treatment program was "pushy."
- Community supports – "I reach out to everyone I can." Neonatal intensive care unit provides temporary housing, support for transition to new housing, access to social workers, bus tickets, "whatever I need."
- HERR Program. "There are people I talk to when I have cravings."
- Meetings, counselling.
- None (two participants).

Do you see this type of support as different from other supports? How so?

- Yes, because it's voluntary. "It gave me independence."
- Study viewed as 24/7 support; phone allowed contact with support network. Community supports are restricted to certain hours of day.
- Being monitored to be held accountable, developing a record of sobriety.
- Self-monitoring. "You don't have to communicate to other people, you just do it."
- Constant reminder, something (record of sobriety) to look forward to at the end.
- Yes. "AADAC didn't help me," "HERR is more verbal, more 1-on-1 (in comparison to breathalyzer intervention)."

How do you think we can attract more people to participate in the study?

- Share success stories from other participants.

- Post at different hospitals (two participants – one elaborated to say prenatal doctors' offices).
- Focus on potential participants who are strongly motivated to change their behaviour.
- Emphasize the offer of a new phone more prominently in enrolment materials.
- Recommendation to post on Facebook, in women's shelters, and schools.

4.3.5 Discussion

This study failed to meet its target sample size, and initially proposed randomized controlled study design. Due to such limitations, the study was unable to conduct the quantitative analysis of birth outcomes. This study was nonetheless valuably innovative, as it is the only FASD prevention intervention study that has utilized the measurement and self-monitoring of biomarkers to promote the reduction of drinking or abstinence in pregnant women with a history of problematic alcohol use. This study was unsuccessful at recruiting an adequate number of participants for a variety of reasons that reflect similar challenges described in the literature of other intervention studies involving a population group of reflective demographics. Those reasons include hesitancy to participate in research addressing substance use disorders for fear of stigma, stereotyping, and reprisals.

Our analysis below provides additional insight and considerations useful to researchers designing future studies in this space and to policy-makers considering adoption of new technologies in this space.

<u>Independence and empowerment: Self-help and an objective record of sobriety</u>

Self-help support tools have been found to be of interest to individuals suffering from alcohol use disorder [332, 333]. Additionally, integrating technology-based self-help directly into an individual's existing living situation and daily routine may not only be impactful, but may also protect a person's sense of dignity and promote empowerment [334, 335]. In the exit interview, two participants suggested that the independence enabled by this form of prevention intervention was a feature that they liked. Another participant indicated that the "self-monitoring" nature of the study distinguished it from other forms of intervention they had received: "you don't have to communicate to other people, you just do it."

Multiple participants emphasized at intake and during the exit interview that the device was beneficial in documenting their drinking history, as an objective, third-party record of sobriety. One participant highlighted that their record provided them with comfort in "stressful moments," serving as a reminder of their documented history of sobriety, motivating them to abstain from drinking.

> *"…in my stressful moment and when I'm overwhelmed, I blow in it and seeing that…knowing that it comes up and just having that reference of sobriety, it gives me that comfort and, that I'm doing a*
>
> *really good job. I feel good."*
>
> – Study participant

Text messaging as a support tool

Women are more likely than men to be exposed to domestic abuse and violence, and are also more likely than men to isolate themselves when struggling with an addiction [336]. Participants noted that the free smartphone and cellphone plan provided them with access to their support network and healthcare professionals, and that the device provided them with a sense of "after-hours" support[ii] and monitoring. In frequent informal discussions with participants as well as counsellors and other addiction support staff, the research team members were told that there is an inherent gap in pathways of care between visits to mental health support staff and professionals. For example, there is no current capacity for follow-up phone calls by health service staff after a patient leaves a program such as detox or rehabilitation to ensure they connect with their assigned addiction counsellor afterwards.

Additionally, the research team received questions (via text messages and calls) from participants about maneuvering through the mental health system and requests to connect participants to mental health and social welfare services, suggesting another potential gap in services.

According to a 2014 provincial gap analysis, in 2010/11, although mobile technology had been widely adopted in Canada with 85% of Canadians owning a cellphone (67% owning a smartphone, specifically), only 19 to 40% of programs provided screening, assessment, treatment, peer support, and follow-up care by phone [188, 54]. The use of mobile technology (such as cellphones, apps, and wearable devices) to support rehabilitation and existing treatment methods presents an exciting opportunity that could increase the availability,

[ii] Please note, the research team members were clear with participants that their role was to support technology issues and answer questions about the study only, not to provide mental health or addiction counselling or support. Nevertheless, if a participant asked if the research team could help connect them with a health professional, we helped make that connection.

accessibility, and effectiveness of treatments. To build on knowledge from this breathalyzer study, an analysis of the effectiveness of text messaging apps to support substance use-related disorders might be considered. For example, the *text4baby* study by Evans and colleagues (2012), aimed at all pregnant women generally, found that the receipt of supportive and informative text messages was associated with an increased belief among their study participants that they were more prepared to take on a role of being a new mother than the control group. "This may reflect the cumulative effect of multiple messages on a range of topics and the specific focus of those messages on being prepared for the challenges of pregnancy and motherhood and importance of being proactive to maintain good health." There were no other observations of significance, however, found in this study [193].

Similarly, in 2016, Agyapong and colleagues launched the *Text4Mood* program. Text4Mood was a six-month mobile health program that applied cognitive behavioural therapy principles through use of text messaging in order to evaluate whether daily supportive text messages helped to influence mood in participants with depression and other mental health problems. The majority of participants in this study indicated that the program improved their overall mental health well-being, "made them hopeful about managing issues in their lives, feel in charge of managing depression and anxiety, and feel connected to a support system [188]." Of particular interest was that "the majority of respondents were most certainly in favour of text support for follow-up care (52%) and in favour of text messaging for managing medical appointments (57%). Use of technology-based services as part of health care was also identified as most certain in emails for managing medical appointments (49%) and web-based counselling (42%) by plurality of the respondents [188]."

Communities in Northern Alberta experience on average the highest prevalence of mental health problems [54]. Additionally, there is a lack of addiction and mental health services in rural Alberta [54]. Patients often need to travel extensive distances in order to access care, which in turn reduces the likelihood that they will seek care when needed. Technology enhances communication and may present an opportunity to further expand outreach to distant, rural communities for addiction and mental health services.

Enrolment issues: Lessons learned

Enrolment in this study was low, which is common for a study analyzing a vulnerable population group. There are factors that mitigate against enrolment at every stage of the recruitment process, including stigma (systemic and self) around problematic alcohol and drug consumption, as well as gender bias.

Factors that may have contributed to this low rate include: concerns from addiction support staff/counsellors and at-risk women of negative stereotyping [337]; over-identification of marginalized populations [338]; fear of reprisals [338]; and perceived lack of benefit of detection of alcohol consumption and FAS diagnosis [339]. One comparable study was conducted by Zelner and colleagues (2012), where researchers assessed the willingness of at-risk women to participate in a meconium fatty acid ethyl ester screening program to flag children at risk of FASD, for access to targeted resources and treatment. They too found low participation rates. The authors attributed this low rate to possible maternal "embarrassment, guilt, fears of stigmatization and child apprehension (despite assurance otherwise)" [338].

Low enrolment rates are further exacerbated when consideration is given to the prevalence of individuals with problematic alcohol and drug consumption who choose not to seek help from a healthcare professional [340]. There is also a gender bias in the recognition of alcoholism in general medical inpatient settings, where men are recognized for drinking problems more frequently than women, and are therefore flagged for risky alcohol use more frequently, leading to an underrepresentation of this group [341].

To increase the enrolment rate for future studies, researchers should include peer engagement in their research. These individuals can operate as consultants and/or equal members of the research team, from methodology development and implementation, to analysis of findings and report development. Peer engagement is an essential component in developing prevention intervention pilots and programs. Individuals with lived experience can provide crucial insight into how best to reach potential study participants for enrolment, flag confounding factors that might have been otherwise overlooked due to lack of real-world experience of researchers, and provide valuable discernment into the description and interpretation of findings in a way that is sensitive and does not reinforce harmful stereotypes [342, 343].

Additional considerations

Pampalon Material Deprivation Index

The MDI was calculated on the basis of the postal code on file for mothers at the time of delivery. Therefore, caution should be used in the interpretation of MDI, as the postal code provided may not have been accurate. The research team is aware that some participants were homeless (this detail was disclosed to the research team in informal communications with participants). If some participants were living rough (that is, homeless) at the time of the study, this could presumably cause a systematic difference of the baseline risk of alcohol use during

the study, and therefore pose as a systemic confounder of the observed effectiveness of the intervention.

Hospitalization and/or use of rehabilitation/detox services

Participants who were hospitalized or admitted to rehabilitation and/or detox facilities may have experienced disruption in access to their devices. This would have reduced the maximum possible compliance rate to less than 100%. One participant reported that this was in fact the case. Therefore, these compliance data should be interpreted with caution, and future studies should consider ways to capture data on admission to facilities that would impede participant access to the intervention.

4.3.6 Conclusion

According to the World Health Organization, health technology is defined as "the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives [344]." Electronic innovations, including the Internet, cellphones, wearable wireless health trackers, and video games, offer new approaches in health promotion and new avenues for reaching individuals on a wide range of sensitive health topics. In the context of prevention interventions for pregnancy, research has only begun to breach the surface on the opportunities that might lie in new technologies.

This study provides new (albeit limited, due to sample size) information on potential preventive health interventions for women struggling with alcohol or substance use disorders. Mobile interventions can potentially help promote a sense of independence and empowerment for individuals seeking treatment for alcohol use. Our early qualitative insights suggest that, for some participants, the intervention supports their own efforts to stay sober, empowers them, and functions as a tool that bridges gaps in the pathways to care. Devices such as this can additionally document and record their sobriety as potential evidence of behavioural change. These results, however, are hypothesis-generating only and should be further tested in large well-powered studies.

For some participants, we found that adherence to the device and study requirements for regular samples was feasible. The active control group is believed to have lowered the enrolment rate and potential. Consideration for future studies, therefore, should be given to expanding the study to women of childbearing age (regardless of pregnancy status), or further to any individual – male, female, or other – with self-reported or clinician-diagnosed problematic substance use via cluster randomized control trials, and/or stepped wedge trials.

Although no statistically significant conclusions could be made on this intervention, feedback from study participants provided the research team with valuable insight on how to better tailor the development and implementation of future intervention studies to support vulnerable individuals struggling with substance use. Our research experiences outlined in this report will facilitate the efforts of other researchers and public health sector teams to be better prepared for the range of potential

barriers as well as successes in the implementation of prevention intervention pilots and programs to support the health of women struggling with substance use.

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4.3.8 Declared competing interest of authors

Competing interest is considered to be financial interest or non-financial interest, either direct or indirect, that would affect the research contained in this report or create a situation in which a person's judgement could be unduly influenced by a secondary interest, such as personal advancement.

The authors of this publication claim no competing interest.

4.4 Epilogue review: The standardization of diagnostic criteria for Fetal Alcohol Spectrum Disorder (FASD)–Implications for research, clinical practice, and population health

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The Standardization of Diagnostic Criteria for Fetal Alcohol Spectrum Disorder (FASD): Implications for Research, Clinical Practice and Population Health

Jasmine M. Brown, BEd, MPP[x], Roger Bland, CM, MB, ChB, FRCPC, FRCPsych[1], Egon Jonsson, PhD[1], and Andrew J. Greenshaw, PhD, FRSA[1]

4.4.1 Abstract

Objective: Fetal Alcohol Spectrum Disorder (FASD) is a preventable disorder caused by maternal alcohol consumption and marked by a range of physical and mental disabilities. Although recognized by the scientific and medical community as a clinical disorder, no internationally standardized diagnostic tool yet exists for FASD.

Methods and Results: This review seeks to analyse the discrepancies in existing diagnostic tools for FASD, and the repercussions these differences have on research, public health, and government policy.

Conclusions: Disagreement on the adoption of a standardised tool is reflective of existing gaps in research on the conditions and factors that influence fetal vulnerability to damage from exposure. This discordance has led to variability in research findings, inconsistencies in government messaging, and misdiagnoses or missed diagnoses. The objective measurement of

[x] Department of Psychiatry, University of Alberta, Edmonton, AB, Canada

Corresponding Author:
Jasmine M. Brown, BEd, MPP, Department of Psychiatry, University of Alberta and Institute of Health Economics, 1E1 Walter Mackenzie Health Sciences Centre, 8440 112 St NW, Edmonton, AB T6G 2B7, Canada. Email: JMBrown1@ualberta.ca

the timing and level of prenatal alcohol exposure is key to bridging these gaps; however, there is conflicting or limited evidence to support the use of existing measures.

4.4.2 Keywords

fetal alcohol spectrum disorder, fetal alcohol syndrome, diagnostic guidelines, diagnosis phenotypes

4.4.3 Introduction

Fetal alcohol spectrum disorder (FASD) describes a range of physical and mental disabilities caused by alcohol consumption during pregnancy [272, 273]. It is estimated that 630,000 children are born with FASD globally annually [345]. This figure, however, is based solely on published studies. As there is limited information available on the prevalence of FASD in many countries, the global prevalence rate may be significantly higher.

Since the first formal recognitions of FASD [275, 306, 276], numerous diagnostic guidelines, criteria, and recommendations have been proposed [273, 346, 347, 288, 348, 349, 350, 351, 1, 352]. Most are similar for the most severe form of FASD—fetal alcohol syndrome (FAS)—but differ in specificity of recommendations, criteria, clinical cut-offs and nomenclature for less severe forms [346, 347, 351, 1, 353]. This leads to uncertainty around the social and economic cost of this preventable disorder.

We review the development of existing diagnostic tools and examine the potential impact the lack of diagnostic standardization has on clinical practice, research, and population health.

4.4.4 Methodology

A search of the biomedical electronic database PubMed was conducted to identify primary studies and systematic reviews that analyzed, evaluated, and/or compared and contrasted diagnostic tools for FASD. Reference lists from retrieved articles, and grey references were used to identify additional studies. Grey references were obtained by a Google search. Non-English studies were largely excluded.

4.4.5 Overview of diagnostic tools Institute of Medicine (IOM) criteria for FASD diagnosis

In 1996, the United States Congress mandated the Institute of Medicine (IOM) to conduct a study of FAS and related birth defects. In part, the objective was to develop diagnostic guidelines '…which could subsequently be used in epidemiologic, clinical, and basic research [347].' They included 4 subtypes of FASD; in order of severity, these are FAS, partial FAS (pFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD) [347].

FAS is described as presenting '…with growth deficiency, with height or weight below the 10th percentile, facial characteristics (e.g., small eyes, smooth philtrum, and thin upper lip), CNS damage (structural, neurological, and/or functional impairment);' pFAS presents with some but not all of the physiological symptoms of FAS. Patients with ARND do not present with any facial deformities but have symptoms of CNS damage associated with FAS. Patients with ARBD present with physical defects, such as malformations of the heart, bone, kidney, vision, or hearing systems [347].

The IOM was criticized as lacking criteria for diagnostic categories and clinical definitions for ARBD and ARND, and the need for the documentation of family and genetic history [354]. The Canadian guidelines (below) also criticized the definition IOM uses for partial FAS, claiming that 'using the term partial FAS in the absence of measurable brain deficits could be harmful for the individual because the diagnosis of partial FAS implies brain dysfunction [354].'

Hoyme and colleagues (2005 and 2016) provide greater clarification on clinical criteria, claiming to 'operationalize the IOM categories' [288, 348]. The amended criteria provide a more defined demarcation of 'documented' prenatal alcohol exposure (PAE), and better describes the neurobehavioural criteria for the diagnosis of FAS, pFAS, and ARND. Hoyme and colleagues also revised the diagnostic criteria for ARBD, provided an updated research dysmorphology scoring system, and a new lip/philtrum guide incorporating a 45-degree view.

4.4.6 CDC FAS: Guidelines for referral and diagnosis

In 2002, the U.S. Congress mandated the Centers for Disease Control (CDC) to develop guidelines for FAS diagnosis to be incorporated into medical guidelines and curricula, and be recognized by professional organizations and accrediting boards [349]. Guidelines only include criteria for FAS and do not include other subcategories of FASD [355]. The CDC reported that no existing criteria were uniformly accepted, and that the IOM criteria did not provide reliability and accuracy, nor take into consideration ethnic or differential diagnostic considerations.

4.4.7 4-Digit Diagnostic Code

The 4-Digit Diagnostic Code, the 'Washington Criteria', (1997, updated in 1999 and 2004) created a more sensitive diagnostic tool than the IOM, using 4 key common and accepted diagnostic features of FAS (growth deficiency, the FAS facial phenotype, CNS damage or dysfunction, and gestational exposure to alcohol), ranking each on a 4-point Likert Scale [350]. Its purpose was to 'improve the ease, accuracy, and reproducibility of diagnoses across the full spectrum of FASD' [356]. This tool is currently used in clinics in the US and Canada [351].

Although developed to create a single, standardized diagnostic guideline, it was criticized for being impractical in real-world applications and not controlling for differential diagnosis, motivating Hoyme and colleagues to provide updated IOM guidelines in 2005 [288].

4.4.8 Canadian guidelines for diagnosis

In 2005 (and later reviewed in 2015), a subcommittee of the Public Health Agency of Canada's National Advisory Committee on Fetal Alcohol Spectrum Disorder created a comprehensive guideline for the diagnosis of FASD, in conjunction and consultation with the 2002 CDC guidelines. The purpose was to reach agreement on a Canadian standard for diagnosis. IOM Criteria and 4-Digit Diagnostic Code were harmonized: IOM terminology was used, and the 4-Digit approach to describing, assessing, and measuring features indicative of FAS was adopted. The guidelines recommend review by a multidisciplinary team, a neurobehavioural assessment, analysis and documentation of maternal alcohol history, and a differential diagnosis [273]. A significant number of Canadian clinics claim to use the 2005 Canadian guidelines [357].

The 2015 update to this guideline included several amendments: [351]

- The use of fetal alcohol spectrum disorder (FASD) as a diagnostic term.
- The inclusion of special considerations for diagnosing FASD in infants, young children, and adults.
- The deletion of "growth" as a diagnostic criterion.
- The addition of a new "at-risk" category for FASD.
- Revision and refinement of brain domains evaluated in the neurodevelopmental assessment.

4.4.9 Diagnostic and Statistical Manual of Mental Disorders (5th edition) (DSM-5)

The DSM-5 diagnosis 'Neurodevelopmental Disorder Associated with Prenatal Alcohol Exposure" (ND-PAE)' describes the range of neuro-disabilities associated with prenatal alcohol exposure (PAE). ND-PAE can be diagnosed regardless of the presence or absence of the physical effects of PAE [353]. Confirmation of maternal alcohol consumption is required. Although ND-PAE is mentioned under 'other specified neurodevelopmental disorder', no diagnostic criteria or detailed description is provided in the DSM-5 [1]. Further reference is made under 'conditions needing further study'. The proposed criteria for ND-PAE do not include criteria for recognizing facial deformities characteristic of more severe cases, nor do they recognize FASD subtypes.

DSM-5 is believed to have incorporated new terminology and diagnostic criteria to remedy the lack in clarity and consistency across existing diagnostic systems around less severe forms of

FASD [353]. The proposed criteria emphasize psychometric measurements over features that might arguably be attributed to familial genetics (e.g., head circumference, facial dysmorphic features, and body length and weight) [353]. The DSM-5 criteria, although not yet validated, are widely used [353, 346].

4.4.10 ICD-10

According to the American Academy of Pediatrics, the following ICD-10 codes can be used for a primary diagnosis of FASD: [349, 358]

P04.3 - Newborn (suspected to be) affected by maternal use of alcohol (excludes FAS)

Q86.0 - FAS (dysmorphic) *no further description offered for this specific code.

F06.30 - Mood disorder due to known physiological condition, unspecified

P00.4 - Newborn (suspected to be) affected by maternal nutritional disorders

P01.9 - Newborn (suspected to be) affected by maternal complication of pregnancy, unspecified

G93.4 - Encephalopathy, other and unspecified (static)

G96.8 - Other specified disorders of central nervous system

G96.9 - Disorder of central nervous system, unspecified

4.4.11 Alcohol: Teratogenic mechanisms of prenatal alcohol exposures

The recognition of FASD as a clinical disorder is established. There is scientific evidence that CNS damage (structural, neurological, and/or functional impairment) linked to prenatal exposure to alcohol is characteristic of FASD in all subtypes, and recognized in all diagnostic tools [346, 351]. The teratogenic mechanisms of alcohol on brain structure and function at a cellular level, described largely through animal studies, have demonstrated sensitivity of the brain to PAE and have resulted in successfully modelling select behavioural deficits associated with FASD [359, 360, 361, 362]. Basic studies of brain structure and function have shown that alcohol exposure may influence calcium signalling pathways [363], and alter glutamate receptor function [364], resulting in increased oxidative stress and neuronal damage due to hypoxia [359]. In addition to those processes related to apoptotic neurodegeneration [365], there is evidence for genetic changes that may include epigenetic consequences: these include altering DNA methylation patterns [366, 367], inducing histone modification, enrichment of histone acetylation (H3K9 ac) and methylation (H3K27me2,3, and H3K9me2), and increased expression of histone acetyltransferases and methyltransferases [368]. The structural

consequences include impairment of neuronal proliferation and migration [359, 369], including GABAergic inter-neuronal migration [370]. Evidence from these and other preclinical studies indicate clearly that alcohol induced neuronal disruptions can lead to wide-spread structural and functional brain malformations, affecting cognitive performance and behaviour [371, 372, 373, 374, 375, 376, 377, 378, 379].

Longitudinal human studies have provided key evidence for the altered trajectory of brain development in children and adolescents diagnosed with FASD. Abnormalities were observed in cortical volume and thickness, varying depending on brain tissue type and region. Grey matter in healthy development follows an inverse U-shape trajectory, possibly reflecting the natural process of neural plasticity followed by refinement [380, 381]. Greater decreases in grey matter inversely correlated with increased IQ [382, 383, 384]. Individuals with FASD, however, exhibit a more linear downward trajectory, with greater decreases in grey matter correlating with decreased IQ [384, 385, 386]. White matter mean diffusivity increased earlier in childhood in healthy controls than in FASD groups, suggesting delayed neural refinement and axonal myelination in FASD groups [386]. There was a concentration of abnormalities observed in medial brain regions [384, 385, 386, 387]. This may be reflective of prenatal disturbances to the midline tissues of the neural tube, which is particularly vulnerable to the teratogenic effects of alcohol exposure during embryogenesis [388]. Longitudinal studies also provide insight into brain activation differences between healthy controls and FASD groups, observing group differences in both neuronal recruitment patterns and functional MRI signal intensity over time (increased intensity in controls, decreased intensity for FASD groups) [389].

4.4.12 Ambiguity leads to discrepancy

Although there is conclusive evidence that alcohol is teratogenic, human studies have failed to elucidate the dose response relationship between alcohol and FASD [390]. There are 3 significant gaps that promote ambiguity. First, although it is now widely accepted that exposure to moderate to heavy concentrations of alcohol can be detrimental to the health of the developing embryo or foetus, studies examining the effects of low levels of exposure are inconclusive [391, 392, 393, 394, 395, 396, 397, 398]. Second, there are gaps in knowledge about what impedes and/or facilitates the teratogenic vulnerability of a foetus. A foetus' susceptibility to FASD may be modified by genetic susceptibility, maternal health [399, 400], or maternal environment (socioeconomic status, availability of healthy food and vitamins, stress, among others) [401, 402]. Third, FASD can be misdiagnosed or underdiagnosed because children with FASD may not express the 'complete' phenotype or may present subtle physical symptoms (e.g.,

pFAS, ARBD, ARND), and the lack of adequate follow-up, communication, and consideration in diagnostic processes can lead to a failure in identification [347, 288, 350, 403, 404]. A 2015 study of 547 children who underwent a comprehensive diagnostic evaluation found a missed diagnosis rate of over 80% and a misdiagnosis rate of 6.4% [405]. The consequence is that '…the majority of these cases go undetected until secondary disabilities develop and the child has begun their schooling [406].' Early diagnosis facilitates earlier developmental interventions and supports, potentially improving the child's quality of life and social functioning.

Diagnostic discrepancies between diagnostic tools lead to variability in research findings (e.g., prevalence rates), and inconsistencies in government messaging. Objective measurement of the timing and level of PAE is key to bridging these gaps.

4.4.13 Difficulty in measuring PAE

Measurement of PAE may be based on maternal surveys and interviews, clinical observation, medical records, and/or the examination and measurement of known biomarkers in fluids, such as maternal blood, sweat, oral fluid, hair, and placenta, and/or newborn blood, urine, hair, and meconium [406, 407]. There is conflicting or limited evidence to support the use of these tools.

A systematic review found T-ACE and TWEAK questionnaires to have similar sensitivities and specificities, and were concluded to be '…efficient screening tools for identifying alcohol consumption during pregnancy [408, 409].' But tools do not identify all at-risk individual, or provide a detailed account of PAE (e.g., frequency, concentration, and/or developmental stage of exposure). Self-report is not an accurate measure of alcohol consumption in pregnancy, due to factors like underreporting and recall bias [410]. The validity of patient response is influenced by the interview environment, context of the interviews, how questions are posed, among other reasons [411]. Some advocate for a combination of questionnaires and/or self-reporting and biomarker testing [57, 412].

There is insufficient evidence to support the use of existing biomarkers for accurate PAE measurement in practice [407]. They provide minimal information about alcohol consumption, are cumbersome, and require repeated application [407, 58]. Target population groups may avoid disclosing accurate information or participating in research or measuring maternal alcohol consumption through biomarker testing or interviews and surveys due to concerns of negative stereotyping [413], fear of reprisals [414], and a perceived lack of benefit of the detection of alcohol consumption and FAS diagnosis [415]. An assessment of the willingness of women at risk to participate in a meconium fatty acid ethyl ester (FAEE) screening program found low

participation rates, and this was attributed to possible maternal, '…embarrassment, guilt, fears of stigmatization and child apprehension (despite assurance otherwise). [338]'

4.4.14 Discrepancies in diagnostic tools

In the absence of an objective test or biomarker that can reliably identify FASD, disagreement within diagnostic tools arises regarding what diagnostic criteria can definitively and reliably identify a child with FASD. Physical features are an area of contention in diagnostic systems. The 4-Digit diagnostic code, Canadian guidelines, and CDC Guidelines require 3 facial features for FAS diagnosis, and Hoyme requires 2 facial features [288, 349, 351, 416]. Some sources argue that the physical pattern of malformation for FAS, '…remains the only substitute for a specific "biomarker" of exposure [346],' which argues that, 'the pattern of physical features of FAS is today considered specific enough that a diagnosis of FAS can be established in the absence of confirmation of prenatal alcohol exposure,' but acknowledge that physical features may only be found in the most severe subset of patients with FASD (FAS). Alternatively, DSM-5 criteria for ND-PAE emphasize the measurement or observation of neurocognitive impairments and do not consider the presence or absence of dysmorphic physical symptoms [353].

The DSM-5 requires confirmation of maternal alcohol consumption, specifically consumption that is, ' …above "minimal" levels (>13 drinks/month and >2 drinks/occasion)'. This threshold was suggested in reflection of a high base rate of drinking amongst women of child-bearing years, as a minimum level, to avoid 'over-use of diagnosis [353].' Some tools, however, such as IOM/Hoyme [347, 288, 348], do not require confirmation of PAE for FAS diagnosis.

A study examining 5 diagnostic tools (IOM/Hoyme, 4-Digit Diagnosis, Canadian guidelines, CDC guidelines, Emory) used on 1,581 patients applying for multidisciplinary evaluations found, 'there were substantial differences among systems in how physical features were identified and in the definition of neurobehavioural deficits [355].' For example, although the Canadian guidelines and CDC were in almost complete agreement on the physical features, the 4-digit code and IOM/Hoyme diagnostic tools were not. Concordance was greater between systems when the less severe forms of FASD (pFAS, ARND, ARBD) were amalgamated into one category (FASD v. no FASD diagnosis). Growth also showed a high degree of concordance between systems [355]. Disagreement between systems was attributed to differences in disciplines that led to the development of individual tools, with different levels of specificity in the definition of FASD, and through the use of different reference data for 'normal' physical measurement [355]. It has been stated that '…these 5 systems employ a wide variety of measures and thresholds in meeting the neurobehavioral criterion and there is inconsistency among them [355].'

4.4.15 Discordance in research

The lack of standardization of diagnostic criteria weakens accuracy, objectivity, and reproducibility, and limits the ability to compare results between FASD investigations. For example, international FASD prevalence rates vary considerably, from 7.7 per 1,000 population in some studies [345] to 0.2 to 5 per 1,000 population in others [417]. Variation is suggested to stem from, '…differences in FASD case definition and diagnostic methods, as well as geographical and population factors…. [417]'

4.4.16 Inappropriate patient care and inconsistent government messaging

A lack of standardization of diagnostic tools causes clinical ambiguity, which can lead to 'inappropriate patient care, increased risk of secondary disabilities, missed opportunities for prevention and inaccurate estimates for incidence and prevalence [354].' A Canadian study examined multidisciplinary FASD diagnostic teams and found that just over 15% of individuals diagnosed with FASD had discrepancies between their diagnosis and the identified clinical description used to justify the diagnosis [357]. It was acknowledged that there is the occasional need for clinicians to make judgement calls in the process of diagnosis but cautioned that this rate of non-standard cases in their study seemed high. 'This raises the possibility that clinicians misunderstand or misremember the stated diagnostic rules or routinely stretched them to cover borderline cases [357].' To further complicate matters, in the 1980s, the Fetal Alcohol Study Group of the Research Society on Alcoholism proposed the term fetal alcohol effects (FAE) be used to refer to any symptom(s) thought to be a caused by prenatal alcohol consumption. This diagnostic imprecision and oversimplification, '…led clinicians either to disregard alcohol as a contributing factor for any children's problems or to over diagnose the contribution of alcohol to such problems, which hampered efforts to determine the actual magnitude of FASD [288, 418].'

The gap in conclusive evidence of what level of alcohol, if any, is safe to consume during pregnancy led the Government of Canada to recommend that 'the safest option during pregnancy or when planning to become pregnant is to not drink alcohol at all [394].' Regardless, the maternal alcohol consumption rate in Canada is approximately 10%, with 3% of women engaging in at least one binge drinking episode during pregnancy [419]. Additionally, most pregnancies in Canada and the US are unplanned [420], and women, on average, do not know they are pregnant until 4 to 6 weeks after conception [421]. In a cross-sectional survey, 45% of surveyed women reported consuming alcohol in the 3 months before they discovered they were pregnant, 60% of whom did not learn they were pregnant until after the fourth week of gestation [421].

This divergence between government messaging and public behaviours may reflect the contentious history of the recognition of FASD, maintained by the ambiguity around the dose-response relationship between alcohol exposure and FASD. FASD was first recognized in 1973, but it took several supportive studies and 4 additional years before the American FDA released their first public awareness warning via the June 1st, 1977 Drug Bulletin, followed by the NIAAA recommending safe consumption of 2 drinks per day to a maximum of 6 drinks a day for pregnant women [422]. Subsequently, the American Academy of Pediatrics endorsed the advisories, followed by the March of Dimes, American Medical Association and American Society of Addiction Medicine and eventually the American Congress of Obstetricians and Gynecologists [422].

4.4.17 Conclusion

FASD is recognized by the scientific and medical community as a preventable, clinical disorder, and alcohol as teratogenic. Ambiguity around exposure thresholds and the impeding or facilitating factors for teratogenic prenatal vulnerability lead to discrepancies between diagnostic tools and variability in research findings. These, in turn, lead to inconsistencies in government messaging, misdiagnoses or missed diagnoses, increased risk of secondary disabilities, inappropriate patient care, and imprecision around the true social and economic cost of FASD. The objective measurement of the timing and level of PAE is a key to bridging these gaps; however, there is conflicting or limited evidence to support the use of existing tools. The implementation and support of successful prevention interventions, including those to support maternal psychiatric health before, during, and after pregnancy [400] could yield an increase in positive pregnancy outcomes as well as significant public sector financial gain [326]. According to Thanh and colleagues, the lifetime incremental cost per case with FASD is approximately $800,000 [326]. Significant opportunity exists for researchers and policy makers to bridge these remaining gaps, and mould future public discourse, behaviours and perhaps even social culture around alcohol consumption during pregnancy.

4.4.18 Declaration of conflicting interests

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Chapter 5: Mobile-Based Programming (Text4Support) to Support Individuals Accessing Addictions and Mental Health Services

5.1 Outline

The following chapter provides an overview of the Text4Support program and evaluation study. The evaluation study is a limited, initial analysis of the Text4Support program analyzing the experience of individuals who were enrolled in the Text4Support program beginning in July 17th, 2019, who had completed the 6-month program at the time of the last data pull - May 15th, 2020. This data set did not include a large enough sample of participants to reach statistical significance. For example, although enrolment began at n=296, survey participation on the 12-week and 6-month surveys was low, at n=41 and 26 respectively, and therefore only anecdotal inferences can be made.

This chapter also provides additional, supplementary analysis using a larger data set that includes both Text4Support participants who completed the program within the above date range, and those whose participation was still ongoing on May 15th, 2020 at time of last data pull. This larger sample is used to conduct an analysis of baseline survey results, with a focus on participant self-identified barriers to care. This larger data set provides interesting findings on barriers to accessing care that add to considerations raised in other chapters of this dissertation.

An ideal evaluation of the Text4Support program would include a full data set of 12 months of enrolment data to account for factors such a seasonality, with a control group that spans that time period, paired with AHS administrative data on diagnosis and health utilization patterns for both groups. To ensure all participants have completed the program prior to analysis, 18 months of data will be required given the 6-month program duration. Nonetheless, this chapter provides some preliminary analysis, and sets out directions for the future analysis once sufficient time has elapsed to retrieve a larger data set.

5.2 Introduction

Global mobile phone ownership has proliferated exponentially, and presents an unprecedented opportunity to bring substance use and mental health related support services to more individuals in new and innovative ways, regardless of where they or and when they need them. Currently, it is estimated that there are up to 8.3 billion mobile phone subscriptions worldwide (2019) [52]. Nationally, 90% of Canadians are estimated to have a mobile phone (up 1.8% from 2016/17) [423]. Additionally, mobile service coverage is expansive, with 99.4% of the Canadian

population estimated to have mobile coverage, including 98.0% of rural communities and 88.2% of First Nations reserves [423].

Substance use and mental illness are the leading causes of disability in Canada, and supply is not meeting demand for services. A third of Canadians over the age of 15 years indicate that they do not feel their mental health needs are being adequately met [24], and only half of those experiencing a major depressive episode claim to have received adequate care [25]. In Alberta, a similar observation is made, with 49% of Albertans indicating that they did not receive any and/or adequate services to address their mental health needs [54]. The cost of the Canadian mental health burden is too high to ignore, estimated at $51B annually, including lost productivity, health care costs, and decreases in quality of life [22], substance use and mental health issues.

Text messaging using mobile phones and/or smartphones may present a cost-effective avenue [26] to expand the range of individuals who can be reached with mental health services, whether they live in dense urban zones or remote rural regions, bridging systems of care and increasing access to services for those who need it, wherever they are. Text messaging capabilities are considered standard and already embedded on 98% of mobile phones [51, 170, 47], allowing researchers and health care administrators the opportunity to tap into pre-existing infrastructure and networks. Additionally, in consideration of the simplicity of the skill set required, individuals of all ages are generally literate in the sending and receiving of text-messages. Unfortunately, addiction and mental health treatment and programming in Alberta are currently not taking advantage of this potential, with only 10-40% of programs utilizing phones, and 2-7% utilizing the internet [54]. Additionally, communities in more remote areas with less access to resources [54] typically experience higher prevalence rates of substance use and mental illness. As a result, patients often need to travel extensive distances to access care, which in turn reduces the likelihood that they will seek care when needed [54].

Text4Support is a new texting-based service from Alberta Health Services (AHS), launched in late 2018, that mirrors the successful study from Agyapong and colleagues (2016), called Text4Mood [424]. The Text4Support programme allows subscribers to receive daily supportive text messages written by cognitive behavioural therapists and mental health professionals in collaboration with service users. The goal of Text4Support is to provide additional support to individuals who are waiting to access AHS addiction and mental health (AMH) services. This innovation seeks to address a lack of timely access to psychological therapies for patients with addictions and mental health concerns/issues, including long wait times to access services, and

for patients who cannot readily access services due to transportation or geographical barriers. Text4Support is not meant to replace AHS AMH services, but instead to complement existing services. This study analyzes data collected by the Text4Support implementation team for internal monitoring purposes to evaluate the Text4Support program.

The goal of this study was to assess whether the Text4Support program improved the overall mental well-being of participants.

5.3 Methods

Evaluation study design and participants

This study was a retrospective analysis of an existing program called Text4Support, where daily supportive text messages were delivered to participants' mobile phones over the course of a 6-month period, with the option to opt out of the program at any time. Participants were recruited from ACCESS 24/7 and ACCESS Open Minds clinics[xi] starting in July 2019, and enrolment remains ongoing.

As part of the Text4Support program, Alberta Health Services administered follow-up surveys with enrolled participants at 12-week and 6-month marks, to monitor program effectiveness and participant outcomes. With permission from AHS, our study team extracted anonymized data from these surveys for analysis.

Additionally, with the assistance of AHS research data administrators, anonymized data was extracted from Connect Care (CC-CIS (CVO)), eClinician, Discharge Abstract Database (DAD), National Ambulatory Care Reporting System (NACRS), and Enterprise Data Warehouse in order to: (a) develop an aggregate control group of individuals accessing the two sites (ACCESS 24/7 and ACCESS Open Minds), who were not referred into the Text4Support Pilot; (b) develop aggregate groups, to document high-level health system utilization of a list of specific data variables of interest, including addiction and mental health diagnoses, for both experimental and control groups; and (c) gather individual-level, anonymized data for the experimental group only, to compare survey results of individuals within the experimental group with their addiction and mental health related diagnoses given after joining the Text4Support pilot (e.g., for documentation and analysis of comorbidities if an individual identified "anxiety" as their

[xi] ACCESS clinics serve as a one-stop-shop for individuals seeking to access urgent and non-urgent community addiction and mental health related programs and services including navigation support, screening, assessment, referral and consultation services, as well as crisis outreach, intervention and short term stabilization [593].

"theme" or "texting group" for the Text4Support service, but their primary diagnosis when accessing the ACCESS 24/7 or ACCESS Open Minds site was a substance use disorder).

The study protocol was approved by the Research and Ethics Board of the University of Alberta on August 28, 2019.

Study participants met the following inclusion criteria:

1. age 18 years and above;
2. had a mobile phone with text-messaging capabilities;
3. were generally familiar with text messaging technology (could successfully retrieve text messages); and,
4. were able to read English.

Patients who did not have mobile phones or refused to consent were excluded from the study.

Intake

Individuals seeking access to mental health and addiction services ACCESS 24/7 and ACCESS Open Minds Clinic, when meeting with a medical professional at the facility, were asked if they would like to participate in the Text4Support program. If they were interested, their phone number was added to the Text4Support program system, and they were asked to pick a "theme" or "texting group" for their daily text messages. The theme is based on a primary self-identified concern as to why they are accessing services, and could be one of the following:

- Anxiety
- Problematic elevated or irritable mood
- Unusual experiences
- Difficulties managing emotions and relationships
- Depression
- Substance use
- Coping with major life events
- General wellbeing

Within 24 hours of joining the program, they then received a text message with an online link to a consent form, as well as a baseline survey. Following successful completion of the consent form, the participant then began receiving text messages with content based on the theme

chosen. Additionally, participants received a follow-up survey at 12-week and 6-month marks to assess participant satisfaction and impact.

The experimental/intervention arm consisted of participants referred to the Text4Support program by a physician or mental health therapist. These individuals may have been seeking or actively engaged in addiction and mental health services, or seeking one-off support.

As described above, the control group was developed via de-identified, aggregate data linkages from AHS administrative databases: Connect Care (CC-CIS (CVO)); eClinician; Discharge Abstract Database (DAD); National Ambulatory Care Reporting System (NACRS); and, Enterprise Data Warehouse.

Intervention

As noted, the Text4Support program reflects the 2016 Agyapong and colleagues Text4Mood study [188]. Text4Mood was a 6 month long mobile health program that used principles of cognitive behavioural therapy through use of text messaging in order to evaluate whether daily supportive text messages helped to influence mood in participants with depression and other mental health problems.

When individuals signed up for Text4Support, they received one text message every day at noon, for six months. Individuals could choose to opt out of this service at any time. AHS administered Text4Support feedback surveys, sent out at 12-week and 6-month marks during the six months that an individual receives text messages. These surveys asked individuals for feedback on the Text4Support experience and their mental and physical health. This service and its associated surveys were developed for service evaluation and improvement purposes.

Examples of text messages included the following:

- *Take a moment to notice how you feel. Don't judge your emotions or do anything to change them. Just observe them.*
- *Identify something small that makes you anxious. Do it numerous times and see what happens to your anxiety. Does it decrease?*
- *Learning to identify our thoughts is a skill. Today, for several brief situations, ask yourself, "What was going through my mind?"*
- *It can be helpful to test beliefs with behavioural experiments. For example, try smiling and saying "Hi" to people and see what happens.*

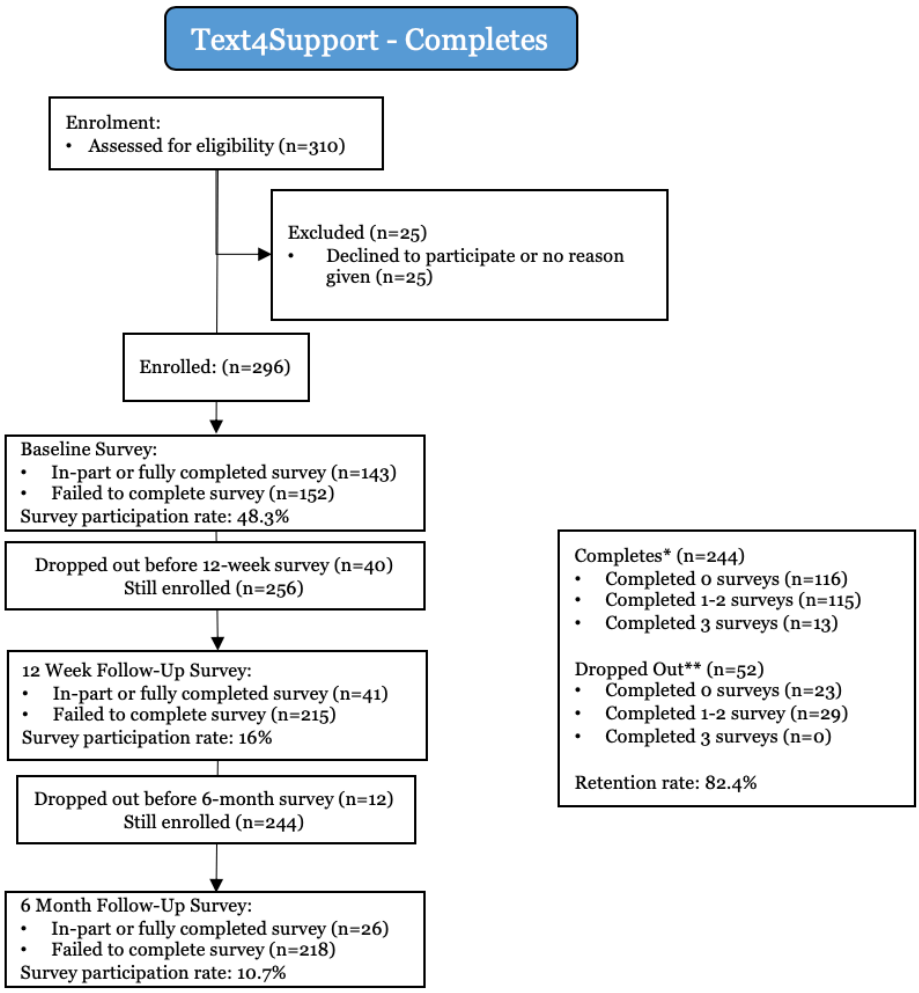
- *Monitor your mood from on scale from 1-10 with 1 being lowest and 10 highest. Make a note of activities that improve your mood.*

This study hypothesized that the Text4Support program would improve the overall mental wellbeing of participants. The primary outcome measure was to explore follow-up surveys provided by participants at 12-week and 6-month marks of the program, to assess self-reported improvement in overall mental wellbeing over the course of the intervention. Secondary outcome measures included analysis of inter-group variation, drop-off/engagement rates, health care utilization patterns, and exploration of possible explanations for why this intervention may or may not have worked for particular groups.

5.4 Consort flow diagram

Between July 17 and November 15, 2019, 310 potential participants were deemed eligible to enter the study. Of those eligible, 296 gave consent to enter the study, and 25 declined, allowing for an enrolment rate of 95.5%. Reasons for declining to participate were not documented by front-line staff (see Figure 4). Of the enrolled participants, 52 asked to stop receiving text messages after enrolment, and 244 remained in the study for the full 6-month period, at a retention rate of 82.4%. Participants who dropped out were in the program for an average of 45.4 days (SD: 51.6).

Figure 4: Consort flow



* Completes: Participants who remained in the Text4Support program for the full 6-month duration.
** Dropped out: Participants who requested to stop receiving text messages after having enrolled in the program.

Statistical analysis

Enrolment reached a total of 296 participants total, which was less that the target sample size of 500 identified in our protocol. This study remains ongoing, and further analysis is anticipated on a larger data set.

Data were analyzed using Excel and SPSS.

5.5 Results

Baseline demographic and clinical characteristics

As shown in Table 4, participants in the Text4Support program who completed the program by May 15, 2020 (n=296) were mostly female and had an average age of 36. 143 participants completed the baseline survey, which included demographic questions, with a survey participation rate of 48.3%. For those who did complete the baseline survey, most were European/Caucasian in ethnicity, attained a high school or post-secondary education, and rented or owned a home. As noted, participants chose a theme for text messages based on primary self-identified concern as to why they were accessing services. Almost half of participants chose the depression texting group, followed by anxiety and substance use.

Table 4: Baseline demographic characteristics of participants

Characteristics of study participants (n=296)	
Characteristic	Value
Gender* (n=296)	n (%)
Female	188 (63.5)
Male	108 (36.5)
Age (years), mean (SD)	36 (13)
Age group (years) (n=296)	n (%)
18-24	71 (24.0)
25-34	96 (32.4)
35-44	55 (18.6)
45-54	39 (13.2)
55-64	26 (8.8)
65+	9 (3.0)
Ethnicity (n=143)	n (%)
African/Caribbean	4 (1.4)
Asian	6 (2.0)
European/Caucasian	98 (33.1)
I do not know	3 (1.0)
Indigenous (i.e., First Nations, Metis, and Inuit)	9 (3.0)
Latin American	1 (0.3)
Middle Eastern	1 (0.3)
Unknown**	172 (58.1)
Prefer not to disclose	2 (0.7)
Education (n=143)	n (%)
8th grade or less	2 (0.7)
High school	40 (13.5)
Unknown**	159 (53.7)

Post-secondary	53 (17.9)
Other	1 (0.3)
Some high school	15 (5.1)
Some post-secondary	22 (7.4)
Technical/trade school	4 (1.4)
Housing (n=143)	n (%)
Couch surfing	1 (0.3)
Live with family or friends	35 (11.8)
Living rent free with partner	1 (0.3)
Low income housing	1 (0.3)
Unknown*	159 (53.7)
Own home	32 (10.8)
Rented accommodation	66 (22.3)
Shelter/street	1 (0.3)
Identified texting group (theme) (n=296)	n (%)
Anxiety	82 (27.7)
Coping with major life events	9 (3.0)
Depression	131 (44.3)
Difficulties managing emotions and relationships	11 (3.7)
General wellbeing	5 (1.7)
Problematic elevated or irritable mood	14 (4.7)
Substance use	36 (12.2)
Unusual experiences	8 (2.7)

*Please note that "gender diverse" and "if gender not listed, please specify:" were additional options provided to participants, however for this data set no one chose those options.

**Unknown is defined as participants who did not complete the baseline survey and/or who chose not to provide any answer to this specific question.

To gauge level of support, participants were given 3 Likert scale questions inquiring into their levels of personal support (i.e. do you feel you have someone… to turn to for support when needed? You can trust and confide in? To go to for help in case of illness or disability?) and asked to rate their level of agreement with said statement, from "not at all" to "most of the time." Of those who completed the baseline survey, 43.9% of respondents scored high, 38.8% moderate, and 15.8% low support.

To measure level of comfort with technology, participants were also given 3 Likert scale questions asking their comfort level with mobile technology (i.e. I use mobile technology often; I am comfortable using mobile technology; I enjoy using mobile technology) and asked to rate their level of agreement with the statement, from strongly agree to strongly disagree. Of those who completed the baseline survey, 86% of respondents scored high, 9% moderate, and 5% low in comfort level with mobile technology.

Self-reported improvement

The primary outcome measure for this study is an analysis of the self-reported improvement in overall mental wellbeing over the course of the intervention. This measure was done via the Clinical Outcomes Routine Evaluation System (CORE-10) – a validated brief 10-item assessment and outcome measurement tool drawn from CORE-OM. The tool assesses "global distress," covering anxiety, depression, trauma, physical problems, functioning and risk to self [425].

As Figure 4 depicts, participation rates for the baseline, 12-week, and 6-month surveys saw a reduction over time, from 48.3% completion rate for the baseline, to 16% survey completion at 12 weeks, and 10.7% completion at 6 months. Table 2 provides figures for aggregate participant CORE scores. Please note that the sample size for 12-week and 6-month surveys is low and lacks statistical significance. Therefore, the results presented below are anecdotal observations, and more research is needed in order to draw any more formal conclusions.

Of those who completed the survey, participant clinical numeric scores generally saw an improvement of 23.5% from baseline to 12-weeks, and deterioration of 13.3% between 12-weeks and 6-months. Overall, however, participants reported an improvement (baseline to 6-months) of 19%. A considerable confounding variable is the impact of the global COVID-19 pandemic, which may have affected the financial, emotional, and physical wellbeing of the general population, including individuals participating in the study, and may have impacted their responses to survey questions.

Table 5: Self-reported wellbeing reported at baseline, 12 weeks, and 6 months

Aggregate participant CORE scores			
	Baseline score (n=143)	12-week score (n=41)	6-month score (n=26)
Mean (SD)	24.2 (6.8)	17.3 (8.8)	19.6 (8.1)
Clinical difference change (B-12W)		Improvement (+23.5%)	
Clinical difference change (12W to 6M)		Deterioration (-13.3%)	
Clinical difference change (B-6M)		Improvement (+19.0%)	

Note: Higher CORE Scores indicate greater level of distress.

Participant satisfaction

Tables 6 a, b, and c provide participant satisfaction data for Text4Support participants from surveys administered at 12-weeks and 6-months. Participants in the Text4Support program mostly agreed that the Text4Support text messages were on topic, to the point, supportive, and positive for both the 12-week and 6-month surveys. A high percentage of participants indicated

that they “always” or “mostly” read the text messages (98%, and 96% for the 12-week and 6-month surveys respectively).

Similarly, a large majority of respondents said the read the messages *and* took action “always,” “mostly,” or “sometimes,” (84% at 12 weeks and 83% at 6 months), suggesting a high level of engagement with the texts which resulted in a behavioural response. For psychological support, most participants reported the service helped improve overall mental well-being, cope with loneliness, and cope with stress at the 12-week survey and 6-month surveys. Participants’ responses were mixed for whether the messages improved overall physical well-being. Interestingly, at 6-months, participants mostly agreed that Text4Support improved their overall quality of life. Overall satisfaction for the program was high, with 60% ranking the program at between 8-10 out of 10 in both 12-week and 6-month surveys. As noted above, sample size for both surveys are insufficient to establish statistical significance, and further analysis on a larger data set is required.

Table–6a: Participant satisfaction with Text4Support - 12-week survey responses

Participant satisfaction with Text4Support - 12-weeks (n=42)						
		Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Text4Support text messages were:	On topic.	14 (35%)	22 (55%)	3 (8%)	1 (3%)	0 (0%)
	Not relevant to my concern.	1 (3%)	5 (13%)	8 (20%)	18 (45%)	8 (20%)
	To the point.	12 (30%)	22 (55%)	4 (10%)	1 (3%)	1 (3%)
	Not helpful.	0 (0%)	1 (3%)	5 (13%)	24 (62%)	9 (23%)
	Supportive.	18 (45%)	19 (48%)	3 (8%)	0 (0%)	0 (0%)
	Not encouraging.	0 (0%)	2 (5%)	4 (10%)	21 (53%)	13 (33%)
	Positive.	17 (43%)	22 (55%)	1 (3%)	0 (0%)	0 (0%)
	Negative.	0 (0%)	2 (5%)	3 (8%)	18 (45%)	17 (43%)
		Always	Mostly	Sometimes	Rarely	Never
How often did you…	Read the text messages?	32 (80%)	7 (18%)	0 (0%)	1 (3%)	0 (0%)
	Read the text messages and take action?	3 (8%)	11 (28%)	19 (48%)	6 (15%)	1 (3%)
		Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Participating in Text4Support has helped me to…	Improve my quality of life?	4 (10%)	14 (35%)	18 (45%)	3 (8%)	1 (3%)
	Improve my overall mental well-being?	6 (15%)	20 (50%)	11 (28%)	2 (5%)	1 (3%)
	Improve my overall physical well-being?	3 (8%)	11 (28%)	16 (41%)	7 (18%)	2 (5%)
	Cope with loneliness?	5 (13%)	17 (43%)	14 (35%)	4 (10%)	0 (0%)
	Cope with stress?	4 (10%)	20 (51%)	11 (28%)	4 (10%)	0 (0%)
		Yes	No			
Are you currently accessing services for a..	Mental health concern(s)?	31 (79%)	8 (21%)			–
	Substance use concern(s)?	3 (9%)	30 (91%)			

Table 6b: Participant satisfaction with Text4Support - 6-month survey responses

Participant satisfaction with Text4Support - 6-months (n=26)						
		Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Text4Support text messages were:	On topic.	10 (42%)	10 (42%)	3 (13%)	0 (0%)	1 (4%)
	Not relevant to my concern.	1 (4%)	2 (8%)	8 (33%)	10 (42%)	3 (13%)
	To the point.	11 (46%)	7 (29%)	5 (21%)	0 (0%)	1 (4%)
	Not helpful.	1 (4%)	0 (0%)	3 (13%)	14 (58%)	6 (25%)
	Supportive.	10 (42%)	12 (50%)	2 (8%)	0 (0%)	0 (0%)
	Not encouraging.	1 (4%)	0 (0%)	4 (17%)	11 (46%)	8 (33%)
	Positive.	13 (54%)	9 (38%)	2 (8%)	0 (0%)	0 (0%)
	Negative.	1 (4%)	0 (0%)	5 (21%)	7 (29%)	11 (46%)
		Always	Mostly	Sometimes	Rarely	Never
How often did you…	Read the text messages?	18 (78%)	7 (18%)	4 (17%)	0 (0%)	0 (0%)
	Read the text messages and take action?	3 (14%)	11 (28%)	9 (41%)	1 (5%)	2 (9%)
		Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Participating in Text4Support has helped me to…	Improve my quality of life?	4 (17%)	10 (42%)	10 (42%)	0 (0%)	0 (0%)
	Improve my overall mental well-being?	5 (21%)	11 (46%)	8 (33%)	0 (0%)	0 (0%)
	Improve my overall physical well-being?	4 (17%)	5 (21%)	13 (54%)	1 (4%)	1 (4%)
	Cope with loneliness?	6 (25%)	7 (29%)	9 (38%)	2 (8%)	0 (0%)
	Cope with stress?	7 (29%)	11 (46%)	5 (21%)	1 (4%)	0 (0%)
		Yes	No			
Are you currently accessing addiction and mental health services for a…	Mental health concern(s)?	18 (75%)	6 (25%)			
	Substance use concern(s)?	3 (14%)	19 (86%)			

Table 6c: Overall participant satisfaction with Text4Support (both 12-week and 6-month surveys)

Overall participant satisfaction			
		12 weeks (n=42)	6 months (n=26)
Using any number from 0 (not at all satisfied) to 10 (very satisfied), how would you rate your overall satisfaction with Text4Support?	Satisfied (8-10)	24 (60%)	15 (60%)
	Neutral (5-7)	13 (33%)	8 (32%)
	Dissatisfied (0-4)	3 (8%)	2 (8%)

Perceived barriers to care

Tables 7 a and b present Text4Support participant perceived barriers of care, categorized by gender, ethnicity, housing, highest education completed, level of support, clinical scores, and texting group. These data are presented as percentages of participants who indicate that a particular item presents a barrier to them. Overall, "costs of services'" is the barrier identified most frequently, with 44% of respondents identifying this as an issue. This is followed by "not knowing how to access services", a barrier for 41% of respondents, and "not knowing what services are available" and "stigma with accessing services," both identified as barriers by 37% of respondents.

Between females and males, women identify cost of services most frequently as a barrier to care, whereas men identify not knowing how to access services. Younger participants report cost more frequently as a barrier, whereas for older participants cost and not knowing how to access services are equally barriers. Amongst participants with high school education or less, not knowing how to access services is the primary barrier to care. Whereas amongst individuals with higher education, cost of services is most frequently identified. When reviewing ethnicity, cost is most frequently identified by the ethnic majority, while not knowing how to access services is most frequently cited barrier amongst non-Indigenous visible minority groups, and Indigenous participants report not knowing what services are available as the largest barrier. Individuals who report higher levels of social supports most frequently report cost as a barrier to care, while those with less support report not knowing how to access services more frequently. The most frequently noted barriers based on texting group was mixed amongst individuals in different categories.

Table 7a: Perceived barriers of care categorized by demographic characteristics of participants

		Gender		*Age*			*Education*			*Ethnicity*				*Housing*		
Barrier	Total	F	M	19-34	35-44	45+	High school or less	Completed or partial post-secondary	Other*	European/ Caucasian	Visible minority**	Indigenous	Unknown/ prefer not to say	Stable ***	Unstable ****	Other
Count	*143*	*98*	*45*	*92*	*25*	*26*	*57*	*75*	*5*	*98*	*12*	*9*	*5*	*133*	*2*	*2*
Access to childcare	7	10	0	9	8	0	11	5	0	6	0	33	0	8	0	0
Cost of services	44	44	44	50	36	31	42	51	20	49	42	22	20	46	50	50
Hour the services are available	18	22	9	20	12	19	23	16	0	22	8	11	0	18	50	50
I did not experience barriers	10	11	7	9	12	12	5	15	0	9	8	0	20	11	0	0
I do not know	9	9	9	9	4	15	12	8	0	4	42	11	20	8	50	50
Location of services	24	27	18	24	24	23	25	25	20	26	17	22	20	26	0	0
Not knowing how to access services	41	39	47	45	40	31	39	45	40	44	50	56	20	42	50	50
Not knowing what services are available	38	40	36	41	40	27	46	35	60	38	42	67	20	38	100	50
Stigma with accessing services	38	38	38	41	44	19	35	43	40	42	33	44	20	38	100	50
Transportation to services	19	19	18	22	12	15	30	11	20	19	17	22	20	20	50	0
Type of services available	17	19	13	17	24	12	25	13	0	22	8	0	20	17	100	0
Wait times to access services	31	33	27	33	36	19	37	29	20	34	33	22	20	31	100	50

** Defined as trades training; realtor certification*
*** Defined as African/Caribbean; Asian; Latin American; Middle Eastern*
**** Defined as rented accommodation; own home; live with family or friends*
***** Defined as couch surfing; shelter/street*

Table 7b: Perceived barriers of care categorized by level of support, clinical support, and texting group identified

		Level of support			*Clinical score*					*Texting group*							
Barrier	Total	High	Moderate	Low	Severe	Moderate-to-severe	Moderate	Mild	Low	Anxiety	Coping with major life events	Depression	Difficulties managing emotions and relationships	General well-being	Problematic elevated or irritable mood	Substance use	Unusual experiences
Count	*143*	*61*	*54*	*22*	*60*	*45*	*22*	*12*	*4*	*41*	*5*	*66*	*6*	*3*	*10*	*9*	*3*
Access to childcare	7	7	9	5	7	4	14	8	0	12	0	8	0	0	0	0	0
Cost of services	44	43	52	41	58	31	45	25	25	41	40	52	33	0	40	33	33
Hour the services are available	18	13	19	36	25	9	23	17	0	17	0	20	33	0	20	22	0
I did not experience barriers	10	20	4	0	0	13	18	17	50	17	0	3	0	33	30	11	0
I do not know	9	5	9	18	12	11	5	0	0	7	0	14	17	0	0	0	0
Location of services	24	16	35	23	30	22	14	17	25	17	40	21	33	0	50	33	33
Not knowing how to access services	41	38	48	45	50	44	23	17	50	44	80	45	33	0	30	11	33
Not knowing what services are available	38	34	48	36	45	42	23	17	50	32	60	44	33	33	40	33	0
Stigma with accessing services	38	39	44	27	50	33	32	8	25	37	80	36	50	33	10	44	67
Transportation to services	19	18	19	27	30	9	9	17	25	24	0	12	17	0	30	44	33
Type of services available	17	18	15	27	22	11	23	17	0	20	20	15	50	33	0	22	0
Wait times to access services	31	26	41	27	40	31	23	8	0	29	40	30	67	0	30	33	0

5.6 Supplementary analysis

5.6.1 Data set

Between July 17, 2019 and May 15, 2020, 734 participants were enrolled into the Text4Support program. Of those enrolled, 393 completed the baseline survey, with a survey participation rate of 54.5%.

5.6.2 Results

Tables 8 a and b present Text4Support participant perceived barriers to care, categorized by gender, ethnicity, housing, highest education completed and texting group. These data are presented as column percentages.

Overall, almost half of respondents identified not knowing what services are available (45%), most frequently as a barrier to care. This was followed closely by cost of services at 44%, and "stigma with accessing services," reported by 36% of respondents.

In line with the data set described in Table 7, women identified cost of services most frequently as a barrier to care, whereas men identified not knowing how to access services. This data sample included participants who self-identified as gender diverse, for which 67% of these individuals noted costs of services as a barrier.

Younger and older participants generally report cost and not knowing how to access services most frequently barriers, and access to childcare was reported amongst individuals falling within average childbearing years, and not an issue for respondents over age 44. With regard to education, 33% of individuals who had 8th grade education or less indicate access to childcare as being a barrier to care, which is significantly higher than the average (8%), and generally report more barriers with greater frequency than individuals with higher levels of education. A general trend of reduction of reported barriers is seen as the level of academic achievement increases.

Individuals with less stable housing report higher than average levels of stigma, although sample size was low. For individuals with more stable housing, the most frequently identified barrier is not knowing what services are available (48%), followed by cost of services (46%), and not knowing how to access services (36%).

With regard to ethnicity, cost is most frequently identified by the European/Caucasians, as was the case in the section above. Not knowing how to access services was reported high amongst Asians at 60% (n=10), which was significantly higher than the average of 41%. Indigenous and

Africa/Caribbean individuals both reported stigma and childcare with greater frequency than other groups.

When reviewing barriers based on texting groups, individuals who signed up under "problematic elevated or irritable mood" tend to report more barriers with greater frequency than other texting groups. Substance use texting group members reported with higher than average frequency that transportation to services, as well as types and hours of services available were barriers. Childcare was noted as a barrier amongst 17% of respondents in the general-wellbeing category which was significantly higher than the average at 8%.

Table 8a: Perceived barriers to care categorized by demographic characteristics of participants

		Gender			*Age category*						*Highest education completed*					
Barrier	Total	Male	Female	Gender diverse	18-24	25-34	35-44	45-54	55-64	65+	8th grade or less	Some high school	High school	Some post-secondary	Post-secondary	Other
Count	*370*	*130*	*234*	*6*	*88*	*140*	*78*	*35*	*27*	*3*	*6*	*35*	*103*	*67*	*136*	*7*
Access to childcare	8	1	12	0	5	12	9	0	0	0	33	9	8	7	5	14
Cost of services	44	38	47	67	47	46	46	29	44	33	50	43	44	46	49	43
Hour the services are available	17	12	20	17	16	18	18	11	22	0	17	23	20	18	14	0
I did not experience barriers	12	12	12	17	11	8	15	20	15	33	0	14	11	13	15	0
I do not know	8	8	8	33	9	9	6	9	7	0	17	6	11	10	6	0
Location of services	21	16	23	33	18	19	26	17	30	0	50	26	20	18	23	14
Not knowing how to access services	41	45	39	17	38	47	38	34	41	0	67	29	43	39	46	29
Not knowing what services are available	45	44	46	33	49	47	41	46	33	33	50	46	49	42	48	43
Stigma with accessing services	36	38	36	17	35	39	45	20	30	0	33	31	37	43	37	57
Transportation to services	19	15	21	17	25	17	17	11	26	0	50	31	24	16	13	14
Type of services available	18	16	19	17	20	16	22	11	26	0	17	20	22	16	18	0
Wait times to access services	30	23	35	0	41	29	29	20	15	0	33	34	33	31	29	14

Table 8a: Perceived barriers to care categorized by demographic characteristics of participants (cont'd)

		Housing						*Ethnicity*							
Barrier	Total	Rented accommodation	Own home	Live with family or friends	Couch surfing	Shelter/ street	Other	European/ Caucasian	Indigenous	African/ Caribbean	Asian	Latin American	Middle Eastern	Prefer not to disclose	I do not know
Count	*370*	*153*	*81*	*106*	*4*	*2*	*4*	*252*	*32*	*15*	*10*	*7*	*3*	*8*	*5*
Access to childcare	8	10	9	4	0	50	25	7	19	20	0	0	0	0	0
Cost of services	44	48	46	46	0	50	50	50	28	33	40	29	67	25	40
Hour the services are available	17	23	14	13	0	50	25	18	25	13	20	14	0	25	0
I did not experience barriers	12	6	23	16	0	0	0	13	9	13	10	0	0	13	40
I do not know	8	8	9	7	0	100	25	6	13	20	40	14	0	13	0
Location of services	21	20	21	25	0	0	0	21	28	7	40	29	0	25	0
Not knowing how to access services	41	48	36	38	75	50	50	42	53	40	60	71	100	38	20
Not knowing what services are available	45	50	38	48	50	100	25	46	50	47	40	57	100	50	0
Stigma with accessing services	36	37	40	36	75	50	50	37	41	47	30	14	100	38	0
Transportation to services	19	21	9	24	25	100	25	19	31	20	0	29	33	13	20
Type of services available	18	18	19	22	25	50	0	19	22	13	10	29	0	38	20
Wait times to access services	30	35	20	32	25	100	25	32	38	33	20	29	67	25	0

Table 8b: Perceived barriers to care categorized by texting group theme

		Texting group							
Barrier	Total	Anxiety	Coping with major life events	Depression	Difficulties managing emotions and relationships	General well-being	Problematic elevated or irritable mood	Substance use	Unusual experiences
Count	*373*	*95*	*12*	*171*	*15*	*12*	*20*	*43*	*5*
Access to childcare	8	8	8	9	7	17	5	0	0
Cost of services	44	44	33	45	47	42	50	42	20
Hour the services are available	17	14	17	16	20	17	25	26	0
I did not experience barriers	12	12	8	13	13	8	15	9	0
I do not know	8	6	17	10	7	8	0	7	0
Location of services	21	19	25	17	27	0	45	28	40
Not knowing how to access services	41	40	42	43	27	25	45	44	20
Not knowing what services are available	45	47	42	45	40	33	50	44	20
Stigma with accessing services	36	41	33	34	33	33	25	40	60
Transportation to services	19	18	25	13	20	8	40	30	40
Type of services available	18	21	17	11	33	8	25	35	20
Wait times to access services	30	33	33	26	47	17	40	30	20

5.7 Discussion

There are several interesting observations that can be made in the analysis of this data, although due to low sample size, further research is needed for observations to be substantiated.

Enrolment, engagement, satisfaction, and survey completion

The enrolment and retention rates for the Text4Support program was high at 95.5% and 82.4%, respectively. This may have been due to high user satisfaction as suggested from 12-week and 6-month surveys, where overall satisfaction for the program was ranked as high, with 60% rating the program between 8- 10 out of 10 for both 12-week and 6-month surveys.

This high degree of self-reported user acceptability and retention has been reflected in other text messaging studies. A systematic review examining text messaging to support the health of individuals with problematic drug and alcohol use found high rates of intervention acceptability [174]. In the Text4Mood study, on which the Text4Support program was largely based, participants responding to follow-up surveys generally indicated the messages "made them hopeful about managing issues in their lives, feel in charge of managing depression and anxiety, and feel connected to a support system" and generally improved their mental health well-being [188]. This is consistent with other text messaging interventional studies to support mental wellbeing, including Text4Baby, which sought to support women through pregnancy, and a text intervention directed to impoverished women in Bangalore, where the majority of individuals in both intervention groups indicated they felt support and reassurance from the messages received by the interventions [190, 192, 191] [193].

Of interest is whether the intervention led to behavioural change. As noted, 84% (12-wk) and 83% (6-mth) of respondents indicated that they "always," "mostly," and "sometimes," read the messages AND took action, which suggests that participants experienced a high level of engagement with the texts which resulted in a behavioural response. This is reflected in other studies, where text messaging has been found to increase appointment, pharmaceutical, and treatment adherence [172, 49, 173, 26, 174, 175, 176], reduce substance use, and promote abstinence and relapse prevention [26, 174, 177]. Additionally, this finding has been observed in the management and treatment of other illnesses. A review analyzing text-message interventions as tools for behavioral change, found evidence in eight out of nine sufficiently powered studies that text messaging was found to be an effective tool for behavioral change in disease prevention [179, 180, 181] and management [182, 183, 184, 185] [186] [49], specifically in the management of weight loss, smoking cessation, and diabetes management.

Although enrolment, engagement and satisfaction rates were high, survey participation rates observed a drop from baseline at 48.3% to only 10.7% by the 6-month survey. The response rate for the baseline survey reflects the rates recorded in other studies. For example, a meta-analysis from Burgard and Colleagues (2020), which examined response rates for online psychological surveys focused on adults with depression and/or general anxiety disorder, observed a mean response rate of approximately 43% [426]. Another meta-analysis from 2008 demonstrated lower response rates, of 34% for online surveys, versus 45% for paper surveys [427].

Regardless of the greater adoption of the internet among the general population, response rates for online surveys are observed generally to have remained low [428]. In fact, survey response rates to online surveys are estimated to be 10% lower than surveys offered through other mediums, including paper surveys distributed by mail, and/or telephone surveys [429]. Factors contributing to variability in response rates are believed to include population groups (employees in a company versus the general population), socio-demographic factors (access to and literacy of technology, age, race), and personality types (conscientiousness, agreeability, and openness) [429]. Another factor attributed to low response rates is the potential influence of "over surveying" populations [430].

According to several reviews, the following approaches to survey delivery and design may improve response and engagement rates: researchers should pilot the survey with a sample group of respondents prior to wider dissemination; survey should be administered using different online mediums and techniques when possible (text messaging, emails, phone prompts, etc.); increasing the ease of survey accessibility should be incorporated into design; the survey should be fit to the population of interest and accommodate anticipated respondent comfort level and literacy with technological medium through which the survey is being administered; and, finally, less is more - there is a negative correlation between number of survey items and response rates [429, 426].

Clinical improvement

Data from this study suggests that participants within this intervention may have realized an overall improvement in clinical wellness. However, this program was offered to complement existing services, for which, based on responses on the 12-week and 6-month surveys, 79% (12-week) and 75% (6-month) of respondents indicated that they were currently accessing services for a mental health concern, and 9% (12-week) and 14% (6-month) for a substance use concern. This evaluation did not isolate for types of services and treatments that individuals may have been exposed to at the time of this intervention, for which may have contributed to clinical

scores observed. This limitation equally applies to the deterioration observed in clinical scores between 12-week and 6-month surveys.

Of note is the outbreak of the COVID-19 pandemic, and its potential confounding influence on the clinical scores of individuals during their time in the Text4Support program. As noted in earlier chapters, pandemics may contribute to negative emotions such as stress, sadness, or loneliness [39], as well as problematic drug and alcohol use [40]. Additionally, this particular pandemic has already led to the proliferation of significant stressors amongst the general public including pessimistic national and global financial forecasts [42], as well as job loss [44] [41].

Barriers to care

Due to low sample size, inferences cannot be reliably drawn from Tables 7a and 7b. As such, supplementary analysis has been provided, to permit a more fulsome discussion reflecting on Tables 7a and 7b as well as supplementary Tables 8a and 8b.

The top three most frequently reported perceived barriers to care reported were not knowing what services were available, costs of services, and stigma with accessing services.

Literature providing further analysis on the lack of knowledge around what services are available as a barrier to addiction and mental health care is limited, and therefore deeper reflection on this factor using higher power studies was not possible. However, where noted in the literature, "not knowing what services were available" was grouped in as a barrier of "personal circumstance" versus "feature of the health care system," along with "haven't gotten around to it yet" or "job interfered" potentially suggesting that the onus is on the individual versus the health system to find solutions to said barrier [431, 432]. This is perhaps tied to issues around cost coverage, as not all services and treatments are covered by Canada's Universal health care system (see discussion that follows), and/or reflects systemic stigma, where the expectation is for individuals suffering from mental health issues to be independently motivated enough to identify solutions themselves, instead of health systems proactively reaching out to share service information in a proactive manner.

The impact of the burden of cost was an issue raised by all groups, and is reinforced in the literature as being a barriers to Canadians seeking to accessing services and treatment. Although Canada is known for its universal health care system, health care within Canada does not fully cover certain forms of needed substance use and mental health services such as psychotherapy [433], and does not provide coverage for all pharmaceutical prescriptions [434, 435]. Instead, its focus is to address acute mental health service needs of severe presentations of addiction and mental health [436]. Therefore, individuals who have mild to moderate addiction and/or mental

health issues frequently must pay for services out of pocket [436]. However, it is estimated that the medical coverage for 1 in 5 Canadians do not cover pharmaceuticals, and 1 in 10 cannot afford to pay out of pocket [434].

Although stigma with accessing services was noted frequently as a top barrier across all respondent groups, it was higher than average for individuals with less stable housing, as well as Indigenous and African/Caribbean individuals. Systemic prejudice and racism are reflected in the literature as being a significant barrier to care. For example, there are identified system biases to process someone through intake, including in the physical, linguistic and geographic accessibility of centres and services (e.g. assumptions that transit to a facility would not be a problem, intake forms are written at an appropriate reading level for a wide audience including accommodating newcomers, that individuals are able to record and monitor time with ease, etc.) [436]. "Factors including race, class, socioeconomic status, ability/disability, gender identity, sexual orientation, citizenship status, and mental health diagnosis influence people's experience accessing services which affect their ability to receive support. Experiencing multiple barriers creates an intersectionality that heighten marginalization and creates difficulty accessing services [437]."

Limitations

As noted, this study had several limitations, including low sample size and limited data set. However, this study does provide a high-level anecdotal analysis based on what data could be extracted in time for the development of this chapter. Further research and analysis will be conducted in the coming months, including working with Dr. Agyapong and his team to extract a larger data set. This will include 12 months worth of enrollment data, with all participants having completed the program prior to analysis (18 months total of data). The 12-month window will enable future research to account for factors such a seasonality, with a control group that spans that time period paired with AHS administrative data on diagnosis and health utilization patterns for both groups.

Another limitation of this study is that clinical outcome scores were subject to various confounding variables as highlighted above.

The Text4Support baseline survey included a series of questions seeking to ultimately assess individuals' level of personal support. Unfortunately, that question was not repeated in 12-week and 6-month surveys, likely to reduce respondent burden. Considering that text messaging has been found to serve as a connecting mechanism to an individual's support network [26, 178], it

would have be interesting to examine whether an individual's perceived level of support changed over the course of the intervention.

5.8 Conclusions

This study provided a preliminary analysis of the efficacy of a supportive text messaging intervention seeking to support the mental health and wellbeing of individuals accessing mental health and addiction services at two mental health and addiction clinics. The findings from this study, albeit anecdotal due to low sample size, provide interesting insights that appear to reflect the findings of other higher-powered studies. Taken together, this study suggests that, at minimum, supportive text messaging offers a viable tool to complement existing programs, as well as to increase patient-system contact for patients seeking support for addiction and mental health concerns.

Chapter 6: Discussion and Conclusions

6.1. Overview

This paper explored digital health interventions aimed at supporting the health of individuals with addiction and mental health issues, with particular emphasis on substance use disorders and/or problematic substance use. To this end, it provided a literature review of existing interventions, as well as two studies evaluating the effectiveness of two separate digital health interventions. These findings broadly suggest that digital technology may provide complementary treatment options to improve patient health outcomes, as well as solutions to alleviate existing service gaps and system issues.

Reflecting then on the preceding insights, this section will explore the final query of this thesis "*where and how can technology-based interventions be most effectively embedded in the health system*?"

Acknowledging the breadth of this question, this chapter provides an overview of the 'where', 'why', and 'how', innovations can be implemented. These sub-questions are disciplines unto themselves, and this chapter does not attempt to provide comprehensive analysis of each. Rather, attempting to answer this question broadly, it seeks to provide context for the lessons learned in earlier chapters and suggest potential future directions and considerations for the implementation of technology-based mental health interventions.

6.2 Introduction

As noted in earlier chapters, it is widely recognized by that the further adoption of evidence-supported digital health technologies can enhance health outcomes, as well as improve quality, efficiency, accessibility, and affordability of care [438, 4]. In fact, their potential for health system impact means digital health technologies are being afforded considerable weight on the global stage, with international organizations such as the World Health Organization postulating that, "there is a growing consensus in the global health community that the strategic and innovative use of digital and cutting-edge information and communications technologies will be an essential enabling factor towards ensuring that 1 billion more people benefit from universal health coverage, that 1 billion more people are better protected from health emergencies, and that 1 billion more people enjoy better health and well-being (WHO's triple billion targets included in its Thirteenth General Programme of Work, 2019–2023)." [4]

Where, then, do opportunities exist for digital health innovations to be embedded into the care system, in order to better support the health of individuals with addiction and mental health

issues? This chapter will first provide an overview of select settings where the embedding of certain technologies may enable service enhancement and improvement. It then makes a larger argument for the development and implementation of a *digital health strategy* that is inclusive of *system integration* (including data integration).

6.3 Specific location opportunities

There are significant opportunities presented by digital technologies that may be applied at several touch points throughout an individual's journey through life.

6.3.1 Opportunities in primary care

Primary care settings are ideal for the application of a patient-centered model for services such as prevention and awareness education, early screening and intervention, referrals for psychotherapies and specialty care, and progress monitoring for individuals seeking support for an addiction and/or mental health issue [26, 439, 440] [441, 442]. Additionally, for many, primary care settings are often the first and only point of contact with the health system [441]. It is currently estimated in Canada that a quarter of hospital visits are due to addiction and mental health disorders, and that they account for approximately one third of hospital stays [441]. From a cost-benefit perspective, adequate addiction and mental health services in a primary care setting would improve health outcomes for patients and, at minimum, offset costs for service expansion in these clinical settings by reducing administration and care in acute settings such as emergency rooms and hospitalizations [440, 443, 26].

Additionally, further funding and support for mental health promotion and treatment in primary care settings is jointly supported and recommended by both the Canadian Medical Association and the Canadian Psychiatric Association [441]. Of significant importance, patients are in favour of treatment and management of substance use disorder in primary care settings, with several studies suggesting not only that there is high acceptability and uptake for the treatment and management of substance use disorders in this setting [444, 445] [26], but that the application of technological interventions at this juncture in the continuum of care may produce positive outcomes similar to those seen in specialized treatment settings [446, 49, 214, 447] [26].

By reducing the administrative burden on both patient and clinicians, and by permitting enhanced decision making supports and shared decision making, digital technology innovations can play a significant role in enhancing care in primary care settings. "Common Ground," as

described in Chapter 3, is an example of a computer-based shared program that could be expanded in waiting rooms across Canada to support shared decision making [215, 216].

Additionally, also highlighted in Chapter 3, artificial intelligence and machine learning models such as SLIM and RiskSLIM are being explored to support clinical decision making, which could help missed or misdiagnosis errors and improve clinical care in this setting [197] [143, 196]. Additionally, digital supports for the treatment of other disorders in primary care settings, such as diabetes self-management, smoking cessation, and human immunodeficiency virus, have been explored and demonstrate patient improvement [26, 448, 449, 450]).

Of important benefit, these digital support tools could help alleviate administrative burden on both the doctor and patient, freeing the doctor up for richer engagement with the patient; it is currently estimated that doctors spend on average only between 10-15 mins with any individual patient in a primary care setting [451, 452].

6.3.2 Opportunities in crisis

In moments of individual crisis, the inherently static nature of the health system is evident, and reflects the current mismatch in patient need versus our current model of service provision. For example, the current model is to wait for the patient to seek services once in crisis, rather seeking out or meeting patients immediately where and when they are experiencing crisis. This can be addressed in part with the aid of digital technologies.

Digital technologies can support individuals from crisis management through to treatment and post-treatment health maintenance. As noted in Chapter 3, Facebook "Wellness checks" can flag an at-risk individual via support from artificial intelligence and mobilize the individual's immediate community, as well as health authorities, to respond and provide support.

Additionally, technologies using digital data and biomarker readers, such as machine learning and its application to the AWARE app, wrisTAS, SCRAM, Abilify MyCite, iHeal, and Soberlink, provide opportunities for "just in time interventions", where health and community supports may be mobilized in a time of crisis, even potentially curtailing acute episodes altogether for some individuals who would have otherwise ended up in emergency rooms.

6.3.3 In and between treatment and services

As discussed in Chapters 3, 4 and 5, there are significant opportunities to embed digital interventions in the health system to support treatment, to increase general access points to care, to bridge gaps in a patient's care pathway, and to support navigation of the system generally. With the aim of concision, this chapter will not repeat findings from earlier chapters

and instead discuss any additional considerations in embedding those evidence-supported innovations.

A pronounced area for system improvement noted in earlier chapters is in linking a patient's care pathway. Bridging systems that enable individuals to access health services in a timely, effective and efficient manner are pivotal for addiction and mental health management. Innovations, such as text messaging and IVR, as referenced in Chapters 3 and 5, should be employed by health systems to tighten the connection between the individual in need and the health system, bridge navigation gaps, and increase points of access for a patient. Clients could sign up to receive text messaging and/or IVR services with the assistance of any front-line worker in any setting, or independently using an online platform, and the service itself would ultimately follow the individual client/patient.

Another example of where a gap in services exist, for which digital technologies might serve as a bridge, is in post-treatment recovery or remission maintenance. The rate of relapse following standard 3 to 6-month treatments is high [453, 454]. Maintained contact with the patient post treatment may help extend rates of abstinence or reduced substance use following treatment [455, 456, 457, 458]. Virtual innovations such as online platforms/communities, telehealth, and wearable health monitoring apps, may provide options for extending support services following treatment, where otherwise the patient is often considered graduated from a treatment program or "recovered," and the onus of maintaining their "recovered" status rests solely with the individual. Virtual options in this circumstance have the added benefit of providing discretion for individuals who otherwise avoid more visible supports or in-person group settings due to stigma and shame [459, 460], but generally should be offered to compliment any existing post-treatment services, such as follow-up meetings with addictions counselors (see below).

A question that must be addressed is to what degree these innovations should complement or replace existing services and programs. Unfortunately, there is no easy answer, and more research is needed to first evaluate interventions generally to ensure effectiveness, then to evaluate the innovations in comparison with existing programs and services, as is done in comprehensive health technology assessments. As comparison studies are significantly limited at this time on digital innovations and existing predominant service options, the most appropriate action is to proceed with the administration of evidence-supported innovations where service gaps exist. And, where services are currently available, offer digital solutions to compliment, rather than replace, existing programs unless rigorous analysis emerges, appropriate to context, that might suggest a change. For example, in remote communities,

access to in-person interventions might not exist, and that gap could be supported by virtual supports. Alternatively, someone actively seeking in-person care in an urban setting might choose to incorporate digital tools to amplify service impact [125]. Regardless of situation, it is important to ensure the adoption of technology ultimately enriches care and gives individuals choice, reinforces a patient-centred model, and acknowledges the importance of personalized medicine in effective addiction and mental health care.

6.3.4 Opportunities in community settings

There is a global trend to devolve power of service provision to local-level, community-based organization and interventions, as they are perceived to be, "most familiar with local conditions and create greater accountability for health and well-being of communities as well as individuals" [207]. With the proliferation of internet access, the traditional brick and mortar limitations applied to care settings have given way to new digital communities and gathering spaces, where individuals can access services and supports, at times for free and without limitations on "hours of operation." Examples raised in Chapter 3 included online platforms such as Patientslikeme, or the use of the cross-platform social messaging application "WhatsApp" to offer a free peer-to-peer support service.

Several studies estimate that amongst individuals with severe mental health issues, between 38-78% sought online mental health information [461, 462, 463], and that individuals seeking information do so to read more information about their diagnosis, prescribed medications, and/or possible self-help/coping skills. In fact, some prefer to have the option of connecting virtually to services and networks, with studies suggesting that some individuals actively seek virtual options over in-person support services [464, 465].

The creation of additional digital mental health supports, unbound by traditional limitations of physician versus virtual establishments and outside of the formal health system, speak to a larger discussion around the impact or influence of the "digital revolution" on the traditional perception of the "continuum of care". While health services have historically been provided within the formal system in disjointed silos, the answer to the question, '*where should digital technologies be most effectively embedded in the health system?*' should now be '*wherever the patient is.*'

<u>School and workplaces</u>

Community is inclusive of settings such as schools and workplaces [441]. Schools and workplaces present additional opportunities for digital technological innovations to be applied, for both health and wellness promotion as well as early screening and interventions.

School

Interventions in school settings presents an optimal touch point for health interventions, in reflection that the age of onset for half of all addictions and mental health disorders is in childhood or adolescence [466], and the uptake of digital technologies by these "digital natives" is high.

Provided the appropriate information and tools, schools offer an opportunity for parents and teachers to identify and respond to children and youth during earlier signs of distress, which may effectively reduce or halt the onset of future illness and disorders. Information campaigns, using digital technologies such as the internet, cellphone applications, and social media platforms, may assist in the dissemination of screening tools and educational materials to support awareness promotion and early identification of risk or illness amongst students, parents, and teachers alike, while potentially reducing stigma. Mindfulness training and self-management techniques such as cognitive behavioural therapy could be taught in school, and complemented by mobile apps or online platforms to allow for learnings and practices to follow children throughout their daily lives, where they are, when they need them, including while in transit, leisure time and at home, helping to promote resilience training.

Additionally, in consideration of the ever-expanding use of electronic devices both generally and in classrooms and/or to support learning (e.g. online courses, and programs), machine learning has been applied to student data to flag students who were in distress and could be expanded. [467].

Workplace

Individuals over the age of 18 years spend 60% of their daily lives at work [468, 469], yet $1 trillion USD is estimated to be lost annually globally due to lost productivity as a cause of depression and anxiety [470]. In Canada, mental illness is attributed for the absence of an estimated 500,000 individuals per week [471], and make up 30% of disability claims and 70% of disability costs [472].

An analysis by Chisholm and colleagues (2016) estimated a return on investment of $4 to $1 USD invested in depression and anxiety due to better health and ability to work [473]. A Canadian case study of Bell Canada, a telecommunications company, supported that estimate concluding that investing in mental health and wellness contributed to a return of $4.10M annually, as well as a 20% reduction in short-term disability [474].

The 2020 APEC white paper on workplace mental health and safety, titled "A New Horizon for Occupational Health" highlighted several digital technologies being applied in a workforce setting that serve to support mental health and wellbeing. These include Jian Dan Xin Lin and Know Yourself, both of which are applications of the WeChat platform (highlighted in Chapter 3) offering in-person and online psychotherapy services and educational materials [135]. Other digital technologies highlighted include, "IncludeMe," a Canadian application using evidence-based resources and game play to educate managers and owners on how to promote workplace mental health and wellness, and how to support the health of individuals who identify that they are experiencing distress, and Thailand's Ooca program which offers virtual access to mental health professionals and online employee assistance programs [135].

6.3.5 Opportunities in health system administration and improvement

Digital technologies also have the opportunity to significantly impact health system administration and improvement. One of the significant steps required in system integration, as discussed later in this chapter, is data integration, where the application of digital innovations to system administration and electronic medical record data develops a feedback loop for system monitoring, evaluation and improvement, in-turn improving health outcomes and service provisions to support individuals with addiction and mental health issues.

With the appropriate privacy assurances in place (see privacy discussion presented later in this chapter), this data might also include data extracted from the use of other health innovations such as health applications on mobile phones, and biomarker reading devices. Establishing this feedback loop, and creating optimal baseline infrastructure for real-world evaluation of innovation on health outcomes (and the application of some digital analytics technologies such as machine learning), also requires the adoption and expansion (in both use and in data integration/sharing) of electronic medical records, and other health system administration data.

Traditionally, medical records have been paper based, transmitted or shared via arduous processes such as fax machine and accessed by researchers in person. Although this archaic approach is still in use [475], there is a global trend towards the adoption of electronic medical records, with exclusive use in Canada increasing from 10% in 2007 to 16% in 2010 (28% in the province of Alberta) [476]. Unfortunately, the use of electronic medical records is not applied in all settings and, unlinked to other ministries, reinforces siloes of care. The solution is an expanded adoption of electronic medical records, health administration data, and other appropriate data, and the cross-sectoral sharing of data, otherwise termed "*data integration*," to support system improvement.

Evidence suggests that data integration improves system efficiency and health outcomes while being cost effective, as it facilitates the evaluation of value-for-money to inform health care decision making, elimination the administrative duplication and identifying service gaps, while facilitating more efficient and effective service coordination [477, 478, 479] [477, 480] [481, 482]. It can also stimulate economic growth in the field of research (as costs to perform longitudinal studies are reduced with an integrated real-time data system), which increases the attraction and retention of skilled academics, grant funding opportunities, and the creation of research and data administration employment opportunities [481].

Currently, most health systems rely on need-based data integration and provision (e.g. basic research requests for specific variables from various administrative data sets) [479]. However, with more advanced, continuous data integration linked to digital analytic systems such as machine learning, the applications for system and service improvement are exponential. While continuous data integration is preferable (e.g. multisector data sharing that permits real-time data upload and integration), periodic data integration is currently more common though still the exception. Examples include ConnectCare [483], the Manitoba Population Research Data Repository [484, 482, 485], and CIHI's clinical administrative database [486].

Continuous, real-time data integration is built and based upon digital frameworks, and the application of new innovations such as machine learning or the integration of untraditional data sets, from mobile devices, online platforms, and biomarker reading devices, could allow for significant opportunities for health system and health outcome optimization. For example, integrating data from social media and applying machine learning algorithms could permit health administrators to track syndromic toxiosurveillance at a population level (as was done with Twitter data by Chary and Colleagues (see Chapter 3) on the misuse of prescription opioids [217], or in the real-time monitoring and evaluation of effectiveness of existing or piloted interventions and treatment from both a population perspective, as well as down to an individual level, for real-time decision making instead of retrospective analysis, as is currently the case.

There are several key considerations to data integration, as well as factors that enable its success which will be touched upon later in this chapter.

An example of the use of health data for health system improvement is the PROMIS program through the National Institutes of Health, which gathers patient-reported outcomes directly from the patient via iPad on a variety of validated psychometric scales. That data is then

processed through analytic software and is used to predict patient health service utilization [487, 460].

6.4 System integration and the case for a digital health strategy

This chapter has examined some opportunities where digital technologies and/or interventions might be integrated into specific touchpoints in the care of individuals suffering from addiction and mental illnesses. A larger argument is for the development and implementation of a system-wide *digital health strategy*, which could include testing, evaluating, and integrating multiple forms of technologies and interventions (e.g. Internet of things, artificial intelligence, big data analytics, blockchain) using different interfaces (e.g. cellphones, computers, tablets, etc.), in multiple settings interspersed throughout a patient-centred, continuum of care. This would necessitate cross-sectoral, and cross-ministerial integration, otherwise termed *system integration* (and inclusive of data integration).

6.4.1 System integration - key benefits, drivers, and trends

In the field of addiction and mental health, a client's needs often cross pollinate between institutions (e.g. social services, criminal justice, education, etc.), and service provision frequently spans beyond sectoral boundaries (e.g. public, private, community/voluntary). System integration is increasingly being perceived as a health system goal both locally in Canada and internationally [207, 488], as it has the potential to enable substantial systemic and clinical benefits, while bridging services across historically disparate jurisdictions. System integration can be described as "efforts to increase the coordination of operations within the human and social services system," with the overarching aim to, "improve efficiency and health outcomes [207]." The World Health Organization defines system integration further as:

> "… an approach to strengthen people-centered health systems through the promotion of the comprehensive delivery of quality services across the life-course, designed according to the multidimensional needs of the population and the individual and delivered by a coordinated multidisciplinary team of providers working across settings and levels of care. It should be effectively managed to ensure optimal outcomes and the appropriate use of resources based on the best available evidence, with feedback loops to continuously improve performance and to tackle upstream causes of ill health and to promote well-being through intersectoral and multisectoral actions [489]." [488]

Benefits of integration include improving health system efficiency through the reduction of duplication of activities such as administrative services, which in turn may improve value for

money and thus increase financial and staffing resources that can feed back into the system to improve services [207]. It often includes efforts to integrate data between sectors which, if done successfully, can lead to improved system performance and enhanced strategic planning (i.e. a system improvement "feedback loop") [207]. As health system performance improves, so too is the need for crisis services reduced, as clients experience greater access to responsive health services that have adequate resources provide more personalized and holistic care [207]. Additionally, data integration, is believed to support real-world, evidence-informed decision making [477, 480], improve system efficiency and health outcomes [477, 478, 479], be cost-effective [481, 482], stimulate the research economy [481], and enhance rapport and trust between health system stakeholders [481].

A key "driver" emboldening health systems to adopt systems integration includes general patient familiarity with digital technologies, and their growing expectancy around its use to enhance the provision of care. Patients are accustomed to incorporating new digital technology into their personal and business lives, and transfer those expectations for convenience and personalization to the health system [207, 490]. As such, they are becoming less tolerant of the status quo with the knowledge that there are other feasible options available that can improve their care provision and health outcomes [207, 490]. Patients also have greater expectations around the provision of personalized medicine, including options for service provision that follow along an individual's journey through life or through the continuum of care ("client pathways"), expecting coordinated supports to meet them where they are, when they need them, regardless of bureaucratic and sectoral boundaries [207].

Other key drivers of system integration, such as demographic and economic factors [491], are also creating a space for the further adoption of digital technology. For example, populations are aging, and their needs are becoming more complex. While population growth is slowing in some regions of the world, it is proliferating in others, as migration patterns are not always constrained by laws or blood [207, 490]. Additionally, budgets are constrained and with the introduction of the global health pandemic COVID-19, economic circumstances and labour market outlooks are bleak (see Chapter 2). There is a global trend for health systems to structure funding policies based on demonstration of value for money, while making system decisions that are based on real-time, real-world data analytics [207]. Digital innovations present the opportunity to support health systems in making decisions both nimbly and efficiently.

6.4.2 A digital health strategy to facilitate system integration

Reflective of system integration, public, private, academic, and community/voluntary sectors all play pivotal roles in the conceptualization and widespread implementation of digital technologies in the field of addiction and mental health. However, these cross-jurisdictional, cross-sectoral stakeholders do not always work in collaboration with each other and are often working in disjointed siloes, which reduces the impact of realized benefit of adoption of evidence-supported digital intervention. The World Health Organization for example promotes the notion that "digital health initiatives must be part of the wider health and digital *ecosystem* and guided by a robust strategy that integrates leadership, financial, organizational, human and technological resources," [4] cautioning that evidence suggests "…ill-coordinated or disjoined digital health initiatives lead to vertical or stand-alone information and communications technology solutions that, although well-intended, often result in information fragmentation and, consequently, poor delivery of services." [4]

Multi-system integration efforts, inclusive of both multi-sector (e.g. private, community, academic and public sectors), and across-ministries (e.g. inclusive of social services, employment, housing, education, criminal justice, etc.), can be optimally facilitated through the widespread incorporation and adoption of a system-wide digital health strategy, and vice versa, a system-wide digital health strategy requires systems integration in order to optimize impact.

The World Health Organization has taken efforts to document global digital health strategies [492], however only two documents from Canada Health Infoway, a government of Canada subsidized not-for-profit which seeks to expand digital health technologies, are noted: (1) "Vision 2015 Advancing Canada's Next Generation of Healthcare;" and, (2) the "Pan-Canadian Digital Health Strategic Plan 2013," the latter of which is now already 7 years old. Although the strategic plan outlines enablers and opportunities for action at a high level, it does not provide a prescriptive or detailed plan of action items with identified roles and responsibilities, key performance indicators to evaluate impact or success, and therefore is informative in nature, rather than directive or practical.

In September, 2018, Innovation, Science, and Economic Development Canada (arm of the Government of Canada), released the "Report from Canada's Economic Strategy Tables: Health and Biosciences" which, among several recommendations, identified the need for a national digital health strategy focused on ultimately developing a pan-Canadian interoperable digital health platform, as well as the harmonization of data and privacy frameworks, a single electronic

medical record for each Canadian patient that can be accessed by the patient, and high quality internet access for all Canadians [493].

Impact from COVID: With the global pandemic restricting the movement of individuals, the acceptance of virtual care solutions for use by Canadian physicians has increased [494]. Whether or not this change becomes sustained following the discovery of a vaccine, remains to be seen.

6.5 Considerations in the implementation of health innovations

This section discusses additional considerations with regard to the implementation of digital health innovations, pooling lessons learned from efforts to embed and scale individual evidence-supported innovations through to larger system and data integration efforts.

6.5.1 Regulatory and legal burden

Although protective in intent, national and provincial policies and regulations may also impede innovation testing, procurement or dispersion. A commonly referenced implementation barrier includes issues with the general procurement and reimbursement processes within Canada. Out of 137 countries, Canada is ranked 68th on the Global Competitiveness Index of Government Procurement of Advanced Technology (2017-18) [495]. Canada's process is criticized for favoring innovation that, "requires the least amount of financial and infrastructure investment, [496]" [497] with most short-term gain [498], prioritizing "cost-containment rather than on value generation [499, 500]" [497]. Additionally, Canada's thirteen provinces and territories have differing reimbursement policies, further muddying the waters and regulatory burden, in turn increasing costs to jump individual jurisdictional application hurdles, for those few innovators and developers with volatile bottom lines who were successful in jumping the R&D valley of death [501, 502, 503, 497]. An adjustment to regulatory structures is needed, including consolidation of reimbursement policies and application processes, to reduce the burden for innovators [504, 505].

There are significant opportunities for health system improvement that may be permitted through the application of novel technological interventions to health system data, including but not limited to electronic medical records. Unfortunately, existing federal and provincial legislation that seek to protect the general public's personal information were developed in silos, within differing historical contexts, and are therefore criticized for being complex and challenging to maneuver, even for health system stakeholders such as various government ministries, who are the administrators of this data.

Frequently referenced federal legislation seeking to control the flow of information between ministries and with stakeholders includes the *Privacy Act* [506] and the *Youth and Criminal Justice Act* [507]. With the addition of provincial legislation, complexity becomes compounded further as data protection legislation exists between different ministries, which obscures cross-ministry data sharing in the care for complex needs individuals whose care plan might cross-pollinate between sectors (e.g. education, health, and social services). In Alberta for example, data protection legislation includes but is not limited to the *Health Information Act*, the *Personal Information Protection Act*, the *Health Information Regulation*, the *Alberta Electronic Health Record Regulation*, the *Designation Regulation*, and the Freedom of Information and Protection of Privacy Act, and the *Children First Act*.

6.5.2 Multi-stage decision making in implementation

Digital intervention and other evidence-based practices traditionally have slow uptake into the health care system. It is estimated that only 14% of evidence-based practice actually make it into use, and it takes approximately 17 years to adopt [508]. Significant legal and regulatory factors aside, effective embedding of innovations into regular health service provision requires health system stakeholder buy-in, from senior administrator down to front-line worker. Widespread adoption of innovations may be conceptualized to be "fundamentally a social process" [509], where the decision to adopt at any given link in the implementation chain may be altered or enhanced by several factors, including various "attitudinal facilitators or barriers."

Barriers or impeding factors include:

- A disconnect between health system components (e.g., policy makers making regulatory, process and procurement decisions without input from those involved in the actual delivery of care) [510].
- Researchers and innovators catering to venture capitalists without input from health system stakeholders including policy makers, health system delivery administrators, and clinicians [511, 512, 503, 513, 514, 515, 497] - leading to a mismatch between what is developed and the actual needs of the health system [497].
- Technology being implemented via a "push" versus "pull" model, lowering the likely success rate of its uptake as service providers are not effectively matching service provision to need (e.g., they lack external validation, client appeal, not culturally relevant or appropriate, and/or are perceived as too complex [516, 517, 518, 519, 520, 521, 504].
- Decision-framing employed by individual health system players in the implementation of an innovation, including the "endowment effect," where individuals tend to inflate the

value they ascribe to a particular action when they take ownership in it; perceived risk or loss aversion, where individuals must evaluate the benefit to adoption to outweigh possible losses; and, "reference dependent," where the stakeholder must have enough perceived incentive to disrupt their status quo or daily routines [522].
- Negative perception of intervention (e.g., concern over potential loss of the therapeutic relationship [523]; perceived lower quality, inexpensive replacement of face-to-face services [524]).

In addition to strong leadership [504, 505], addressing communication barriers is key, including factors such as sector or stakeholder differences in definitions and terminology [477], and historical contexts and world views [505].

Solutions may include:

- Enhanced connections and networks by promoting active, close collaboration and communication, between all appropriate stakeholder groups, including individuals with lived/living experience, to facilitate information sharing, and implementation support [525, 526, 527, 528, 504, 529, 505].
- Use of clear and consistent language [504].
- Eliciting perspectives from various stakeholders and chart differences in stakeholder positions. Use this information to strategically introduce an innovation for implementation to various stakeholders that effectively speaks to their potential biases and aversions (effective decision-framing) [522].
- Implementing a "push" versus "pull" model, through the greater inclusion and consultation of patient/clients, to ensure service provision is adequately and appropriately matched to need [527, 530, 504].

Additionally, in consideration of the fee-for-service model employed by many health systems, efforts should be made to ensure reimbursement parity between new innovations if they replace or complement existing services, so as to ensure there is no unintended financial incentive to persist with the status quo.

6.5.3 Lack of skills or capacity of the innovators

Aside from decision-making, other considerations exist. Although an innovator or developer has successfully piloted their innovation, they may lack the skill or capacity to scale-up services for more widespread use - which may impede their ability to effectively champion the embedding of their innovation into the health system. This includes failing to incorporate feedback-loops to

improve quality and address "kinks" quickly while implementation is underway, as well as learning how to effectively advertise a new innovation to health system administrators and decision makers [531, 532, 533, 504]. Furthermore, system stakeholders who would need to incorporate innovations into their routines, as well as their managers, may have insufficient training in the innovations use. A natural solution would be skills training for the developer/innovator in areas of deficit, and workforce training for those who would be expected to oversee and/or actively participate in implementation efforts [504, 505].

Additional capacity issues that emerge may be related to lack of technological support infrastructure for the innovation of interest (e.g., general ability or variation in capacity to collect and analyze data due to differences in operational processes or technology systems; insufficient internet access or speed in rural or impoverished areas that hinders the performance of an innovation) [477] [534]. Solutions to these issues involve investment into the development of infrastructure or bridging/addressal of operational processes where a deficit/issue has been identified.

6.5.4 Prohibitive costs

Although it is estimated that digital technologies are generally cost effective [104, 105] [535, 536, 537], rising expenditure into the expansion of existing technology or investment into new technology makes up a significant percentage of annual health budgets. It is estimated that global health systems invested approximately $125 billion USD on digital health technology products and services in 2015, a cost expected to inflate to $297 billion USD by 2022 [538]. Electronic medical records represents the greatest single product investment of that spending, "at $23·4 billion globally with a compound annual growth rate of 7·1% from 2017–2023. [539]" [241]. Additionally, new digital technologies are generally costly to bring to market and developers inherit significant financial risk in their attempts to do so, creating a barrier for potentially impactful innovations to be adopted by health systems [68].

6.6 Cautions and reflections

Although digital interventions have the potential to enhance and expand service provision significantly, caution is warranted to ensure that any foreseeable unintended policy repercussions are carefully mapped, as well as strategically and proactively addressed in order to mitigate any potential harm to individuals.

6.6.1 Protecting privacy and human rights

It is recognized by many health system stakeholders that digital innovations including automation present opportunities for quality and efficiency improvements in service provision [241]. There is, however, also general agreement among ethicists, legal professionals, and researchers that domestic and global legal and regulatory bodies have not been able to keep up with the propagation of novel innovations, and are therefore existing legal and regulatory infrastructure is grossly inadequate [116, 254, 255, 256].

Comparable to general health data, mental health data sharing and integration between service sectors can support health system integration, thus potentially increasing system efficiency and enabling better health outcomes and experiences for patients. At the same time, personal mental health data is uniquely sensitive, as it can be used against an individual in circumstances such as criminal justice proceedings (e.g., assessment of culpability), and support discrimination from financial and insurance agencies, as well as when seeking or retaining employment. Guta and colleagues (2018) caution that digital mental health technologies may become part of a "larger integrated surveillance apparatus," which could further stigmatize and marginalize vulnerable communities, such as individuals with problematic substance use, or particular psychiatric disorders [540].

A marked example of the misuse of mental health data exists in Canada. The Toronto Police Service released health sensitive data to the Royal Canadian Mounted Police (RCMP) managed Canadian Police Information Centre, which then choose to share this data with the US Department of Homeland Security and, in turn, the US Customs and Board Protection. This data was then used to refuse entry to Canadians with a history of mental health related hospitalizations and/or suicide attempts under the *American Immigration and Nationality Act* [541]. The RCMP were charged by the Office of the Privacy Commissioner of Canada for failing to respect the *Privacy Act* in the sharing of data [541].

In reflection of the former, the use of mental health data in enforcement efforts, especially for those illnesses historically socially stigmatized as being linked to criminality, such as addiction, therefore is certainly a justification for concern and caution in the uptake of certain technologies such as biomarker reading devices, including Soberlink breathalyzer devices (referenced in Chapter 3 and tested in Chapter 4), as well as WrisTAS (referenced in Chapter 3). Health administrators must take extra precaution in ensuring that enforceable protective legislation and policies exist in the adoption of technologies such as this to ensure that the sole purpose of the innovation's use is for health promotion, stabilization, and enhancement of care – to ensure

the rights and privacy of individuals with addictions and mental health issues are protected, and stigma not reinforced.

With these considerations in mind, the further aggregation and integration of health system data, inclusive of electronic medical records, as well as administrative and biomarker data, is crucial for the application of digital analytic technologies seeking to facilitate health system optimization, as well as to enable, optimize, and/or evaluate digital innovations generally, and thus remains a pivotal consideration in the successful embedding of novel innovations into the health system. However, as noted above, privacy concerns often hinder data expansion and liberalization efforts. This issue is further elucidated below.

Privacy concerns over data access and use are shared among members of the general public and can impede health innovation implementation. Concerns are believed to stem primarily from a lack of public knowledge of what information is being collected by system stakeholders and how this information is being used (e.g., whether it could influence their eligibility for benefits and access to programs and services; whether it is being accessed for commercial reasons) [542, 543], as well as whether data is secure from hackers and leaks [477].

In addition to ensuring protective legislation is in place, transparency with the intention of building public awareness and buy-in is a possible solution [504] [544, 543] . This can include:

- The inclusion of the general public in planning, infrastructure development, implementation, and research methodology development and interpretation (for example, patient advocates) [481, 545, 546, 547].
- Clear and transparent communication efforts of research findings [548, 481] and in the provision of public information on data use and security/privacy enforcement efforts [542, 549].

A current example of efforts in transparency and inclusion includes the National Health Service's (NHS) HealthVault platform. In response to concerns on data regulation and use, the NHS is currently exploring use of the HealthVault platform through Microsoft, developed the Healthlocker initiative, [116], which seeks to enable patients to access their health records, add notes, and view how their records are being used [116].

6.6.2 Of doom and denial

The world has always been in a state of natural gradual flux and adaptation, spurred by the progression of science and technology. With advancements in *digital* science, however, change

has become exponential, and what were traditional shifts in landscape by the periodic disruption of new innovation has evolved into what is now a worldwide digital revolution.

The use of technology worldwide has increased significantly, as can be observed via capital markets. While the top five publicly traded companies in 2008 were Exxon, Petro-China, Walmart, China Mobile, and P&G, in just over a decade, the top five publicly traded companies have become dominated by technology companies, with Apple, Amazon, Alphabet, Microsoft, and Facebook (2019) [460, 550]. Additionally, psychotherapy experts predict online therapies, smartphone apps, self-help resources beyond books, virtual realities, and social networking interventions to be the top five trends in therapy provision by 2022 [551].

With attention towards this growth has come polarized arguments around the gravity of a "digital revolution": one of doom, and another of denial.

Of doom

The emergence of artificial intelligence, as well as other new technologies like nanotechnology, wireless wearable tech, virtual reality, and 3D printing, paired with the ongoing interplay between these fields, unveil new possibilities, previously considered science fiction or simply unimaginable [45]. Prominent figures such as Stephen Hawking and Elon Musk have raised alarms with the proliferation of advancements in the AI space generally, with Hawking stating "the development of full AI could spell the end of the human race," and Musk cautioning that "with AI we are summoning the demon." In 2017, a group of 116 AI specialists, including Elon Musk, and Mustafa Suleyman, wrote a joint letter to the United Nations calling for the ban on autonomous weapons, in fear of AI and its possible military and security applications [552, 553]. Reflecting this concern, Izumi Nakamitsu, High Representative for Disarmament Affairs at the United Nations, cautioned in a plenary session at the 2017 "AI for Global Good Summit," that "there are currently no multilateral standards or regulations covering military AI applications," and "there is a very real danger that without prompt action, technological innovation will outpace civilian oversight in this space" [554]. Reflecting on discussions around protecting human rights and privacy above, the lack of multilateral standards or regulations eerily reflects similar debates underway in other fields such as health.

Of denial

Alternatively, other prominent voices in the field of AI have suggested this positioning to be alarmist. Yann LeCun, Chief AI Scientist for Facebook for example has countered that, "there would be no Ex Machina or Terminator scenarios, because robots would not be built with human drives – hunger, power, reproduction, self-preservation [555]." Also, hesitant to

attribute this magnitude of alarm with AI, Andrew Ng, founder of Landing AI, deeplearning.ai, and co-founder of Coursera, has stated "fearing a rise of killer robots is like worrying about overpopulation on Mars before we populate it." However, one must weigh the potential conflict of interest in their words, as it would be arguably be in their interest to keep regulations and legal framework as liberal as possible in their explorations of testing and bringing various innovations to market.

In health

The military use or general use of AI might be one thing, but what then does this mean when translated over to medicine?

While adoption by the health sector might be slow, the private sector is less hesitant to invest in and bring to market new technologies, some of which can be distributed directly to consumer without need for health system interaction. This can be seen with the proliferation of health apps for mobile phones, self-help websites and online platforms, as well as in the sales of unvalidated treatments, as discussed earlier in this paper. The fact that an individual can legally purchase a transcranial direct current stimulation device for self-administration on online shopping platform Amazon.ca, without a prescription or training, off their phone within seconds [556] serves as evidence to support the necessity to not only update our legal and regulatory systems in order to protect individuals of current harms, but to do so proactively as well so as not to continue to act reactively to new, albeit now arguably foreseeable or anticipated risk. Conversely, doctors are still predominantly using archaic technologies such as fax machines in medical communications, which serves as a strong argument to also find balance in legal and regulatory structures, as well as health system culture to ensure that there are no undue barriers exist that restrict humanity's ability to benefit from new innovations and interventions.

Regulatory and legal considerations aside, what other factors remain undiscussed that are reinforcing a culture of stagnation inertia in health systems? There is debate as to whether or not digital technological advancements, including but not limited to AI, will ultimately outperform and replace humans in health sector positions, and therefore resistance might be a cause of fears over job security.

On one hand, although still in its infancy, there is evidence to suggest that digital technologies can outperform humans in some tasks, and cannot yet do so in others.

For example, an AI model, educated on x-rays from almost 30,000 women from the US and UK, was recently documented as having outperformed radiologists in a first/single reading of mammograms, with a reduction in false positives of 5.7% (US data) and 1.2% (UK data), and

false negatives of 9.4% (US data) and 2.7% (UK data). Of note was that the physicians had access to more information than the AI, including patient history and previous mammograms, and were still outperformed [557].

Furthermore, patients may be more comfortable interacting with and disclosing sensitive information to technological devices over humans, likely in reflection of fears of stigma. For example, individuals have been found to be more comfortable providing sensitive health information to a 'virtual human' over an actual physician [558], although further research is needed within the context to mental health [125]. The question must then be posed, does or could this interaction translate into the development of a therapeutic "relationship"?

The therapeutic relationship between an individual and their mental health specialist can impact patient outcome [559]. In several studies analyzing the therapeutic relationship between patients and smartphone apps or mobile phones, it was found that this relationship was established between human and device, where some patients reported missing the technology or app [560], or displaying "sentimental and anthropomorphic views" towards it [561], with one study going so far as to say that the relationship was as strong as in-person relationship [562].

AI and other digital technologies, however, are not a silver bullet, and although advanced in some fields, AI remains in its infancy. Several examples of the current limitations of AI are described below.

AI and other digital technology typically rely on data that was initially gathered by humans, which increases the likelihood that output from these innovations replicates prejudice, gender bias, and racism. In a study titled, "Men also like shopping: reducing gender bias amplification using corpus-level constraints," Zhao and colleagues concluded that for datasets that included bias (e.g., 33% more photos of women cooking in a kitchen than men), image recognition machine learning algorithm models amplified that bias to 68% when asked to label new images, including labelling men as women who were portrayed cooking in a kitchen [563].

A 2016 study comparing the diagnostic accuracy of a computer web and app-based diagnostic tool called Human DX to physicians using clinical vignettes, found 84.3% accuracy for physicians, versus 51.2% for the computer program [564]. This would be less concerning if it were not for the fact that since 2015, it is estimated that the tool had already been used by over 2.5 thousand physicians and trainees in over 40 countries. In another example, was a case study of a machine learning algorithm, which in predicting complication risk in hospitalized pneumonia patients, suggested individuals with asthma were low risk [565].

In consideration of the seriousness of diagnostic error, if automation replaced complete human oversight in patient care and assessment, and a computer virus were to be introduced or a computer "glitch" or inaccuracy caused errors in prescription drugs for one or more conditions like hypertension or diabetes, for example, the result could be catastrophic mortality. These sorts of examples are what led Harry Shum from Microsoft to allegedly conclude that "computers today can perform specific tasks very well, but when it comes to general tasks, AI cannot compete with a human child. [566]"

Fear of becoming obsolete in the face of new innovations, as we have seen in earlier industrial revolutions, is not new. And although this fear is not without merit, it also less likely to be realized in the immediate future for many health positions. As Frey and Osborne note in their 2013 study which examined the probability of computerization of 702 occupations, although 47% of all jobs are at high risk for automation, they are believed to be in areas such as transportation and logistics, and office and administration support positions, whereas positions requiring creativity and/or social skills are lower risk [567]. In fact, authors specified that positions such as mental health and substance abuse social workers were low risk, and even went so far as to state that physicians and surgeons were not computerizable at all. Another more modest estimate comes from the OECD where they estimated that only 14% of existing positions (all fields) globally are currently at risk of automation [568].

Returning to the question as to whether innovations should be used to complement or replace existing services, programs, and/or, in this case, positions, the answer appears that the immediate role of technological innovations should be to complement existing health structures for the foreseeable future. Until innovative technologies mature, and sufficient safeguards are in place to the wellbeing of patients is protected, we should heed the World Health Organization's 2018 recommendation to ensure the ultimate goal of the adoption of technology in health is to enrich human interaction at points of care, rather than replace it [566, 438].

6.7 Conclusions

This chapter sought to answer the question, "where can digital health technologies be best embedded into the care system in order to provide the most significant impact on health outcomes for individuals with addiction and mental health issues?" The answer provided in summary is at multiple points throughout the system, as well as to the system as a whole. Or put more simply, services should be embedded wherever the patient is, for access whenever they need it. This chapter suggests that this can be achieved through system integration inclusive of a digital health strategy with a phased approach to innovation implementation. System

integration will facilitate the best possible quality of care, inclusive of the full continuum of services (from prevention through to remission and recovery), that meets the patient where they are, when they need it, following the patient throughout their journey through life, and truly enabling patient-centred care.

Digital health must become an integral part of strategic health planning. It must drive value, and be accessible, sustainable, and ethical, protecting the privacy and rights of others, and addressing health system barriers to care and digital discrepancies.

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Appendices

Appendix A: Exit interview

Institute of Health Economics Exit Interview Form

**PLEASE NOTE: we would like to audio record and transcribe your answers to this questionnaire. Your responses will be transcribed without any information that could identify you. The audio recording and the transcript will be stored in a password protected file on a secure server. This exit interview is voluntary. You may choose to stop the recording at any time. You may also request that the recording and/or transcript be deleted at any time. The results will be used only for scientific research. As required at the University of Alberta, the records will be kept for 5 years, after which they will be destroyed. Should you agree to proceed, your consent will be verbally requested again at the beginning of the recording as a record of consent.*

We want to learn from you and make our study great!

Please rate the following information on a scale of 1 to 5, with 5 being "strongly agree" and 1 being "strongly disagree":

1) The breathalyzer and cell phone helped support me during my pregnancy.	1	2	3	4	5
2) The study helped me monitor my drinking.	1	2	3	4	5
3) The study helped me reduce and/or stop my drinking.	1	2	3	4	5
4) The study changed the way I thought about drinking during my pregnancy.	1	2	3	4	5
5) The study was easy to do.	1	2	3	4	5
6) I would recommend this study to my friend.	1	2	3	4	5
7) The research team answered all my questions and helped me with any technical problems I had throughout the study.	1	2	3	4	5

Please answer the following questions verbally, in your own words:

8) What did you like about this study?

9) What did you dislike?

10) Why did you join the study?
11) How was this study useful to you?
12) Will you continue monitoring your drinking through use of a breathalyzer, even after your pregnancy?
13) If you had joined the study at another time in your life, do you think this study would have helped support you more? Less?
14) What other types of support have you tried? Have they been helpful? In what way?
15) Do you see this type of support as different from other supports? How so?
16) How do you think we can attract more people to participate on the study?

Any other comments?

Appendix B: Student achievements in PhD program

Graduate Committee Members:

- Dr. Andrew Greenshaw, Professor & Associate Chair, Department of Psychiatry, University of Alberta
- Dr. Egon Jonsson, Department of Psychiatry, University of Alberta
- Dr. Peter Silverstone, Professor, Department of Psychiatry, University of Alberta

Oral Presentations:

- Adult Grand Rounds 2016/17, Graduate program requirement, Edmonton, AB
- Adult Grand Rounds 2017/18, Graduate program requirement, Edmonton, AB
- Adult Grand Rounds 2018/19, Graduate program requirement, Edmonton, AB
- Research Day Presentation 2018; Graduate program requirement, Edmonton, AB
- Mapping the Emerging Issues in the Public Representation of Bioscience & Health Issues; Roundtable workshop;
- Canadian Psychiatric Association Conference 2018, Presenter of publication titled "A Brief History of Awareness of the Link Between Alcohol and Fetal Alcohol Spectrum Disorder", Jasmine was first author, other authors included Dr. Roger Bland, Dr. Egon Jonsson, and Dr. Andrew Greenshaw, Toronto, ON
- Canadian Psychiatric Association Conference 2018, Presenter of publication titled "The Standardization of Diagnostic Criteria for Fetal Alcohol Spectrum Disorder (FASD): Implications for Research, Clinical Practice and Population Health", Jasmine was first author, other authors included Dr. Roger Bland, Dr. Egon Jonsson, and Dr. Andrew Greenshaw, Toronto, ON

Current Publications:

- **J.M. Brown**, R. Bland, E. Jonsson, and A.J. Greenshaw, (2019) "A Brief History of Awareness of the Link Between Alcohol and Fetal Alcohol Spectrum Disorder," The Canadian Journal of Psychiatry, 64(3), 164–168.
- **J.M Brown**, E. Jonsson, N. Riley, and A.J. Greenshaw, "Prevention of fetal alcohol spectrum disorder (FASD) by the use of technology," Edmonton (AB): Institute of Health Economics (IHE); 2019, submitted to funders Alberta Innovates July 2019.[12]

[12] The report has not yet been posted publicly, as authors are in process of developing peer-review publications from findings).

- **J.M. Brown**, R. Bland, E. Jonsson, and A.J. Greenshaw, (2019), "The Standardization of Diagnostic Criteria for Fetal Alcohol Spectrum Disorder (FASD): Implications for Research, Clinical Practice and Population Health. The Canadian Journal of Psychiatry, 64(3), 169–176.
- Caulfield, T., Marcon, A., Murdoch, B., **Brown, J.M.,** Perrault, S., Jarry, J., Snyder, J., Anthony, S., Brooks, S., Master, Z., Rachul, C., Ogbogu, U., Greenberg, J., Zarzeczny, A. & Hyde-Lay, R., "Health Misinformation and the Power of Narrative Messaging in the Public Sphere," Canadian Journal of Bioethics, 2019, vol. 2, issue 2, 51-60.
- APEC Digital Hub for Mental Health (2019). A New Horizon for Occupational Health: APEC White Paper on Workplace Mental Health and Safety. Vancouver, Canada: APEC Digital Hub for Mental Health.

Grades in Required Graduate Course Work:

- PSYCI 515; Grade: A-; Completed Winter 2016
- PSYCI 603; Grade: A+; Completed Fall 2016
- PSYCI 511; Grade B; Completed Winter 2017

Ethics Training Requirements:

- G.E.T course - Completed 2016
- ESI (FoMD Ethics & Scientific Integrity Day) - Completed 2019