Mobile technology interventions for improving medication adherence in patients with mental health disorders

by

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ABSTRACT

Poor medication adherence in the mental health population leads to compromised treatment outcomes and increased health care costs. Traditional interventions for medication adherence, while effective if addressing multiple determinants of medication-taking behavior, are expensive and resource-intense when applied to clinical practice. As a result, novel approaches to medication adherence interventions, such as those supported by mobile technology, must be considered. In the first study of this thesis, a systematic review examined the effect of text message-based interventions on medication adherence in the mental health population. The second study sought to better understand medication-taking behaviors among individuals with mental health disorders to determine how technology-based interventions could improve medication adherence.

The systematic review was completed by searching four electronic databases from January 1999 to October 2015. Of the seven studies which met our inclusion criteria, six were randomized controlled trials and one was a prospective pilot study. Three studies evaluated text messaging in patients with diagnosis of schizophrenia or schizoaffective disorder, two studies evaluated text messaging in patients with chronic alcohol dependence, and two studies evaluated text messaging in patients with mood disorders. Five studies examined medication adherence as an outcome, while all seven measured changes in psychiatric or social functioning scores using a variety of validated scales. One study reported significant improvement in medication adherence, while five studies reported significant improvements in the symptom measurement scales used. Overall, text messaging interventions for medication adherence in the mental health population appears promising in improving medication adherence and behavioral symptoms; however,

methodological limitations of the included studies minimize our ability to determine the extent of the impact.

In our second study, 15 individuals with histories of mental illness and housing instability were interviewed regarding their attitudes toward medications, current medication-taking practices, and perspectives on mobile technology-supported adherence interventions. All patients enrolled in this study were clients of the Pathways to Housing Program - an outreach program providing access to community-based apartments for individuals with history of chronic homelessness and concomitant mental illness. Medication-taking behavior was measured using the Medication Adherence Rating Scale (MARS), with all participants except one scoring in the "good adherence" range (result of 6 or greater on the scale). The mean MARS score was 7.3 out of 10 (SD = 1.5). A number of patient factors such as insight, coping strategies, and attitudes toward medications supported medication-taking in this sample. External factors, such as family support and the therapeutic alliance were also identified as important in enabling medication adherence. Regarding the use of mobile phones to support adherence, some patients were conceptually supportive of the idea; however, none were currently utilizing mobile phones for this purpose. Common barriers to regular mobile phone access included high acquisition and subscription costs, theft, and unfamiliarity with newer device technology.

PREFACE

This thesis is an original work by Tyler Watson. Chapter 3 of this research project received research ethics approval from the University of Alberta Research Ethics Board, Pro00061551 "Text messaging for supporting medication adherence and healthy behaviors," May 18, 2016. Chapter 2 of this thesis has been published as T Watson, S Simpson, C Hughes, "Text messaging interventions for individuals with mental health disorders including substance use: a systematic review," Psychiatry Research, September 2016, vol. 243, 255-262. I was responsible for data collection and analysis, as well as the manuscript composition. S Simpson contributed to the methodology and manuscript edits. C Hughes was the supervisory author and assisted with concept formation, data collection and analysis, and manuscript composition.

DEDICATION

I would like to dedicate this Thesis to my loving wife *Claire McCurdy-Watson* and our energetic son *Cole Watson*, both of whose immense support and encouragement made this work possible.

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Chapter 1. INTRODUCTION

1.1 Introduction

Medication adherence is commonly defined as the degree to which a patient takes their medication as prescribed by their healthcare provider.(1,2) Research suggests that medication adherence for chronic diseases is between 50% and 75%.(3,4) Within the field of psychiatry, medication adherence rates are typically lower when compared to other chronic diseases, with estimates closer to 50%.(5-10) While medication-taking is a complex and multifactorial behavior, significant factors that impact adherence for those with mental health disorders include access to care, self-efficacy, and concomitant disorders such as substance use.(11-15)

Poor medication adherence contributes to increased health care costs. In the United States alone, between $100 and $300 billion of avoidable health care costs have been attributed to medication non-adherence.(16,17) This amount comprises between 3% and 10% of the overall health care budget, and includes direct health care costs such as emergency room visits or hospital admissions, as well as indirect costs such as reduced productivity.(16,17) When examined by disease state, it becomes readily apparent that non-adherence to medications is more costly for some chronic conditions. According to the World Health Organization (WHO), chronic diseases such as chronic obstructive pulmonary disease, diabetes, cardiovascular disease, and mental health disorders along with human immunodeficiency virus and tuberculosis will comprise over 65% of the health care burden worldwide. These conditions carry a significant burden due to their relatively high prevalence as well as costs associated with treatment.(4) The poor are disproportionately represented within this number as they face challenges accessing affordable health care, in addition to food security and stable housing.(4)

In the field of psychiatry, research has demonstrated the benefit of medication adherence on

treatment outcomes as well as reducing health care costs. Gianfrancesco *et al.* examined medical and pharmacy claims data over a 5 year period from a large integrated database of commercial insurers in the United States to understand the link between antipsychotic medication adherence and mental health care utilization for patients with bipolar disorder.(18) In this study, medication adherence was measured by the medication possession ratio (MPR), which is calculated by dividing the number of days' supply of medication a patient has received by the total number of days the patient should have been taking the medication based on the prescription.(19) The resulting value is usually a number between 0 and 1, with a number closer to 1 indicating stronger medication adherence. Gianfrancesco *et al.* found a 1 point increase in MPR, representing a change in adherence from 0 to 100% adherence, was associated with decreased health care expenditures in patients with predominantly manic/mixed symptoms with progressively larger reductions in later treatment stages. As an example, a 1 point increase in MPR in months 1 to 3 was associated with a $123 reduction in total mental expenditures in months 4-6, whereas a 1 unit increase in months 10-12 was associated with $439 reduction in total mental health expenditures in months 13-15. Of note, the data analyzed included patients receiving depot antipsychotics; however as it was a relatively small proportion (0.2%), it is unlikely adherence among these individuals would have impacted the study findings. Hong *et al.* evaluated clinical and economic consequences of non-adherence in patients with a manic/mixed episode of bipolar disorder over a 21 month follow-up period.(20) Nonadherence was significantly associated with decreased likelihood of remission, increased risk of relapse and recurrence, as well as hospitalization and suicide attempts; total costs incurred by non-adherent patients were also significantly higher (£101231 vs £7379, $p<0.05$). A systematic review examining the effect of non-adherence to antidepressants on clinical outcomes and health care

costs also found non-adherence was associated with increased relapse and recurrence, increased emergency room visits and hospitalization rates, as well as increased severity of depression symptoms.(21) Peng *et al.* completed an analysis of a large United States commercial claims database for patients initiated on depot antipsychotics for schizophrenia.(22) These researchers found that switching patients to depot antipsychotics resulted in improved medication adherence (37% to 60% based on MPR), significant reductions in psychiatric hospitalizations as well as duration of hospital admissions, and annual reduction in health care costs of over $3000 per patient.(22) This is consistent with results from a systematic review which found that nonadherence to antipsychotic medication is associated with increased hospitalization rates, resource utilization, and increased direct health care costs in patients with schizophrenia.(23)

1.2 Medication adherence interventions

Given the importance of medication adherence on health outcomes, the WHO stated that improving medication adherence interventions could be more impactful on the health of the world population than any single medical treatment.(4) Interventions to improve medication adherence in psychiatry are designed to impact determinants of medication-taking behavior.(11,12,24) These determinants can be classified as modifiable or non-modifiable, and proximal or distal in terms of the relationship to the end behavior of medication-taking.(11,12,24) Factors such as demographics (age, gender, and race), environmental conditions (family and social supports, previous experiences with system) and illness-specific factors (diagnoses and comorbidities, previous experiences with medication) are generally considered non-modifiable. Modifiable determinants of medication taking include health system factors (therapeutic alliance and access to care), treatment-specific factors (medication regimen, efficacy and adverse effects of therapy) as well as patient perceptions of medications

(knowledge, attitudes, motivations, and self-efficacy). Proximal determinants are considered more directly related to adherence and are usually modifiable; distal determinants are considered to indirectly influence adherence and are rarely modifiable. Medication adherence interventions tend to focus on those determinants that are proximal and modifiable.(4,24)

While historically the focus of medication adherence interventions has been unidimensional (on a single determinant of medication taking behavior), multifactorial interventions addressing multiple determinants of medication adherence are more likely to be efficacious.(4,25,26) Collaborative care and case management have been effective at improving adherence to antidepressants, and this improvement has generally resulted in enhanced patient satisfaction with their therapies as well as symptom control.(21,25) Collaborative care refers to a comprehensive set of individualized strategies and interventions which can include: patient education about conditions and medications, assessment of patient beliefs and expectations of treatment, and the use of adaptable treatment regimens.(27) Also included among these strategies is regular, frequent contact with healthcare providers either in-person or via communication device. In bipolar disorder, studies have also found that coordinated multi-level interventions such as cognitive behavioral therapy (CBT) with group education sessions, peer discussion, and more frequent provider contact with participants were most effective for adherence.(11) These interventions produced better medication adherence, improved and stable drug levels, and fewer hospitalizations. Cognitive behavioral therapy approaches, in concert with environmental cues and supports (checklists, adherence packaging, and directive labels), have proved efficacious in improving medication adherence and reducing relapse rates for patients with schizophrenia.(28) Other strategies that have evidence for success when used concertedly include: interventions with longer periods of follow up, those that focus on the importance of the therapeutic alliance,

and simplified medication regimens.(28,29)

Though comprehensive and multifaceted strategies including CBT, group therapy, and motivational counselling seem to be effective, these interventions are very costly and labor intensive, and are often difficult to sustain long-term.(11,12,30) Because of this, many of these strategies are challenging to implement routinely in clinical practice, and a need exists for comprehensive, yet concise interventions for medication adherence. A potential solution for the above problems is technology-based or technology-supported interventions.(31)

1.3 Technology-based medication adherence interventions

Technology-based medication adherence interventions have the potential to provide cost-effective, convenient, and user-friendly solutions for practitioners and patients alike.(31) Examples of technology-based platforms include email or computer-based services, telephone (including mobile phone) utilization or applications, and other automated reminder systems. Among the plethora of technology-based options, text messaging interventions (also known as short messaging services or SMS) have been targeted as an ideal solution given the prevalence of mobile phone ownership.(32) Ownership or access to mobile phones has increased to 90% worldwide; however within the mental health population ownership is slightly lower (75%).(33) Research has also determined that mobile phones are the most common devices used as a "health tool" while in general, text messaging has become the preferred and most commonly used feature.(33,34) Studies that have examined the impact of text message interventions on medication adherence have found positive results in some patient populations. As an example, Arora *et al.* evaluated the impact of a text message intervention (daily text message to patients including a variety of themes from medication reminders to educational tools) in a sample (n=128) of inner city individuals with poorly controlled diabetes.(35) Medication adherence

scores in the intervention group improved from 4.5 to 5.4 (as measured using the Morisky Medication Adherence Scale), while hemoglobin A1C values decreased by 1.05%.(35) Utilization of emergency services trended lower in the intervention group (35.9% versus 51.6% in control group) and over 90% of participants were satisfied with the service.

The positive effect of text messaging interventions on supporting healthy behaviors has also been noted previously. Suffoletto *et al.* administered weekly intervention and assessment text messages to 105 young adults identified as heavy drinkers through extensive Emergency Department resource use.(36) The intervention, which required participants to respond to the messages, resulted in reductions in the average number of drinking days (3.4 fewer drinking days in last month, p-value = 0.04), as well as the total number of drinks consumed per day (2.1 fewer drinks consumed in last month, p-value = 0.0002). The majority of participants reported satisfaction with the intervention; however 23% of participants did not complete the full study.

In summary, successful medication adherence interventions have the potential to improve patient outcomes and significantly reduce the overall burden on the health care system. However, resource requirements and associated costs with many comprehensive interventions limit their practicality in the clinical setting. Often presented as a solution to this problem, technology-based interventions have the potential of reaching patients in more convenient ways, on a more frequent basis, at a relatively lower cost. Considering the widespread uptake of mobile devices, and existing receptiveness from patients for using these devices to communicate about their health, an opportunity exists to implement flexible medication adherence interventions. Within the mental health population, where greater challenges exist in terms of accessing care and maintaining contact with health supports, mobile interventions may be even more impactful. However, while some evidence is available from other disease states, little is known about the

impact of technology-based interventions on medication adherence within this population. In order to understand how mobile technology can be used in the mental health population, further research is required to assess the nature and impact of such interventions, as well as how patients perceive using mobile devices in this regard.

1.4 Objective

The purpose of this thesis is to evaluate the use of mobile phone-based interventions in supporting medication adherence and other healthy behaviors in people with mental health disorders. Two projects were conducted to determine how text message-based interventions could be used to support medication adherence:

The first project focused on assessing the evidence for text message-based interventions in the mental health population. This project was a systematic review of the literature aimed at synthesizing available information on the impact of text message interventions on medication adherence and mental health related outcomes such as depression or schizophrenia symptoms.

The second project was a qualitative study to better understand medication adherence and attitudes toward medications in patients with mental health disorders and recent homelessness. We also sought to understand what medication adherence supports are effective in this population, and whether mobile technology can assist in the delivery of such supports. This study involved the use of a medication adherence assessment tool to provide an objective estimate of adherence, as well as a short semi-structured interview to understand patient's perspectives on adherence and feasibility of mobile interventions in this population.

1.5 References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. Patient Relat Outcome Meas 2014;5:43-62.

(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med 2005;353(5):487-497.

(3) Dimatteo RM, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40(9):794-811.

(4) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).

(5) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv 2007;58(6):855-863.

(6) DiBonaventura M, Gabriel S, Dupclay L, Gupta S, Kim E. A patient perspective of the impact of medication side effects on adherence: Results of a cross-sectional nationwide survey of patients with schizophrenia. BMC Psychiatry 2012;12.

(7) Adelufosi AO, Adebowale TO, Abayomi O, Mosanya JT. Medication adherence and quality of life among Nigerian outpatients with schizophrenia. Gen Hosp Psychiatry 2012;34(1):72-79.

(8) Dassa D, Boyer L, Benoit M, Bourcet S, Raymondet P, Bottai T. Factors associated with medication non-adherence in patients suffering from schizophrenia: A cross-sectional study in a universal coverage health-care system. Aust New Zealand J Psychiatry 2010;44(10):921-928.

(9) Waterreus A, Morgan VA, Castle D, Galletly C, Jablensky A, Di Prinzio P, et al. Medication for psychosis - Consumption and consequences: The second Australian national survey of psychosis. Aust New Zealand J Psychiatry 2012;46(8):762-773.

(10) Bulloch AGM, Patten SB. Non-adherence with psychotropic medications in the general population. Soc Psychiatry Psychiatr Epidemiol 2010;45(1):47-56.

(11) Berk L, Hallam KT, Colom F, Vieta E, Hasty M, Macneil C, et al. Enhancing medication adherence in patients with bipolar disorder. Hum Psychopharmacol 2010;25(1):1-16.

(12) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry 2013;12(3):216-226.

(13) Weiss RD. Adherence to pharmacotherapy in patients with alcohol and opioid dependence. Addiction 2004;99(11):1382-1392.

(14) Sowers W, Golden S. Psychotropic medication management in persons with co-occurring psychiatric and substance use disorders. J Psychoactive Drugs 1999;31(1):59-70.

(15) Magura S, Laudet AB, Mahmood D, Rosenblum A, Knight E. Adherence to medication regimens and participation in dual-focus self-help groups. Psychiatr Serv 2002;53(3):310-316.
(16) Iuga AO, McGuire MJ. Adherence and health care costs. Risk Manag Healthc Policy 2014;7:35-44.
(17) IMS Institute for Health Care. Avoidable Costs in U.S. Health Care. Available at: http://www.imshealth.com:90/en/thought-leadership/quintilesims-institute/reports/avoidable-costs (accessed April 1, 2017).
(18) Gianfrancesco FD, Sajatovic M, Rajagopalan K, Wang R. Antipsychotic treatment adherence and associated mental health care use among individuals with bipolar disorder. Clin Ther 2008;30(7):1358-1374.
(19) Watanabe JH, Bounthavong M, Chen T. Revisiting the medication possession ratio threshold for adherence in lipid management. Curr Med Res Opin 2013;29(3):175-180.
(20) Hong J, Reed C, Novick D, Haro JM, Aguado J. Clinical and economic consequences of medication non-adherence in the treatment of patients with a manic/mixed episode of bipolar disorder: Results from the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) Study. Psychiatry Res 2011;190(1):110-114.
(21) Ho SC, Chong HY, Chaiyakunapruk N, Tangiisuran B, Jacob SA. Clinical and economic impact of non-adherence to antidepressants in major depressive disorder: a systematic review. J Affective Disord 2016;193:1-10.
(22) Peng X, Ascher-Svanum H, Faries D, Conley RR, Schuh KJ. Decline in hospitalization risk and health care cost after initiation of depot antipsychotics in the treatment of schizophrenia. Clin Outcomes Res 2011;3(1):9-14.
(23) Dilla T, Ciudad A, Álvarez M. Systematic review of the economic aspects of nonadherence to antipsychotic medication in patients with schizophrenia. Patient Prefer Adherence 2013;7:275-284.
(24) Pasma A, Hazes JMW, Luime JJ, Busschbach JJV, van 't Spijker A. How to study determinants related to medication adherence in newly diagnosed polyarthritis patients for the development of a prediction instrument. Patient Prefer Adherence 2014;8:1437-1447.
(25) Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock S, Wines RC, et al. Closing the quality gap: revisiting the state of the science (vol. 4: medication adherence interventions: comparative effectiveness). Evid Rep Technol Assess (Full Rep) 2012(208 .4):1-685.
(26) Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of interventions to improve patient compliance: a meta-analysis. Med Care 1998;36(8):1138-1161.
(27) Bogner HR, de Vries HF. Integrating type 2 diabetes mellitus and depression treatment among African Americans: A randomized controlled pilot trial. Diabetes Educ 2010;36(2):284-292.

(28) Velligan DI, Diamond PM, Mintz J, Maples N, Li X, Zeber J, et al. The use of individually tailored environmental supports to improve medication adherence and outcomes in schizophrenia. Schizophr Bull 2008;34(3):483-493.
(29) Goff DC, Hill M, Freudenreich O. Strategies for improving treatment adherence in schizophrenia and schizoaffective disorder. J Clin Psychiatry 2010;71(SUPPL. 2):20-26.
(30) Farooq S, Naeem F. Tackling nonadherence in psychiatric disorders: Current opinion. Neuropsychiatr Dis Treat 2014;10:1069-1077.
(31) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.
(32) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemed J E Health 2009;15(3):231-240.
(33) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Compu 2015; 19(2):367-378.
(34) International Telecommunications Union. 2012 World Telecommunication Indicators Database. Statistical highlights. Available at: https://www.itu.int/ITU-D/ict/statistics/material/pdf/2011%20Statistical%20highlights_June_2012.pdf (accessed April 1, 2017).
(35) Arora S, Peters AL, Burner E, Lam CN, Menchine M. Trial to examine text message-based mHealth in emergency department patients with diabetes (TExT-MED): a randomized controlled trial. Ann Emerg Med 2014 Jun;63(6):745-54.e6.
(36) Suffoletto B, Callaway C, Kristan J, Kraemer K, Clark DB. Text-message-based drinking assessments and brief interventions for young adults discharged from the emergency department. Alcohol Clin Exp Res 2012 Mar;36(3):552-560.

Chapter 2. SYSTEMATIC REVIEW

Text messaging interventions for individuals with mental health disorders including substance use: a systematic review

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Abstract

Objectives: To characterize the impact of text messaging interventions on medication adherence or health outcomes in people with mental health disorders including substance use.

Methods: A systematic review of the literature was conducted from January 1999 to October 1, 2015 using Medline, Embase, Pyschinfo, and the Cochrane Systematic review databases. Controlled clinical trials or observational studies were included if they used text messaging as the intervention, enrolled adults with a chronic mental health diagnosis or substance abuse, and pre-specified outcomes included adherence or a mental health related outcome.

Results: Seven studies met our inclusion criteria: three studies evaluated text messaging in patients with schizophrenia or schizoaffective disorder diagnosis, two studies evaluated text messaging in patients with chronic alcohol dependence, and two studies reviewed text messaging in patients with mood disorders. Six studies were randomized controlled trials and one study was a prospective pilot study with pre-post intervention design. Text messaging frequency ranged from once weekly to twelve per day. The effect of text messaging on medication adherence was measured in five studies, with one study reporting significant improvement in the text messaging intervention group. Five studies showed significant improvement in a variety of psychiatric and social functioning assessments for the text messaging intervention.

Conclusion: These studies suggest text messaging may be a promising tool to support management of patients with mental illness. Further research examining theory-based text messaging interventions in larger samples of patients is required.

2.1 Introduction

Medication adherence is defined as the extent to which a patient's medication-taking behavior matches that agreed upon with the prescriber.(1,2) Poor medication adherence contributes to increased health care costs and suboptimal therapeutic outcomes.(3-5) Research suggests about one-quarter to one-half of individuals taking medications for chronic conditions are non-adherent.(5,6) The rates of medication non-adherence in patients with mental health disorders are even higher, leading to significant consequences in terms of emergency room visits and hospitalizations.(7-10) . While reasons for medication non-adherence can be multifactorial, active substance use is considered one of the key causes in the field of psychiatry.(11-13) Interventions to enhance medication adherence in psychiatric patients can be classified as psycho-social or pharmacologic in nature.(14) Psycho-social interventions, such as cognitive-behavioral therapy or motivational interviewing, are designed to improve treatment adherence by promoting behavior change. Pharmacologic therapies, the effect of which depends on strong provider-patient relationships, attempt to encourage medication adherence through simplified and adaptable treatment regimens. Assessing the impact of these interventions has been complicated by numerous factors including: difficulties in defining and measuring adherence, stigma associated with psychotropic treatment, and clinician inattention to monitoring medication adherence in practice.(15) What evidence does exist suggests that comprehensive, multi-faceted interventions are most effective in improving medication adherence in this population.(14-16)

Although many existing strategies to improve adherence are expensive and impractical for regular clinical practice, an emerging approach is to use technology-based interventions.(17) Among the many technological (or mobile) interventions available, text messaging or short

messaging services has been identified as a particularly cost-effective and convenient method for promoting medication adherence and improving health outcomes.(18) Cellular phone ownership has become nearly ubiquitous, with an estimated 90% of individuals having access to devices worldwide.(19) Within the mental health population, this percentage may be closer to 75%.(20) Cellular phones are now the most common form of mobile health tool available for use, and within these devices, text messaging is becoming the preferred form of communication.(19,20) Acceptance for using cell phones as a means of communicating about health has been demonstrated in the general population as well as in the mental health population.(20-22) To date, several studies have evaluated the impact of text messaging interventions in people with mental health disorders. The purpose of this systematic review is to synthesize the information generated from studies that have evaluated the impact of text messaging interventions on medication adherence or health outcomes in people with mental health disorders including substance use.

2.2 Methods

2.2.1 Search strategy and eligibility criteria

With assistance from a professional librarian, we conducted a search of the English language literature from January 1999 to October 1, 2015 using Medline, Embase, Psychinfo, and the Cochrane Systematic review databases. References from articles and reviews of interventions to improve medication adherence were also searched to identify additional articles. Key words and subject headings used in the search were: (*text message* or *text messaging* or *short message service* or *texting)* and (*mental disorders* or *mental illness* or *substance-related disorders* or *addiction* or *drug abuse*). Table 2.1 describes the Medline search strategy used.

Studies were included if they met the following inclusion criteria: controlled clinical trial or

observational study, used text messaging as the intervention, enrolled adults (18 years of age and older) with a chronic mental health diagnosis or substance abuse, and either adherence or a mental health-related outcome was a pre-specified outcome.

2.2.2 Study selection

After duplicates were removed, two authors (TW and CH) independently screened titles and abstracts to identify potentially relevant citations. A citation was retained for further review if either investigator selected it. Once the full article for each potentially relevant citation was obtained, two investigators independently reviewed it to determine if it met the inclusion criteria. Discrepancies regarding study inclusion were resolved through discussion between the investigators.

2.2.3 Data abstraction and synthesis

Two investigators (TW and CH) used a standard template to extract the following information: location and practice setting of study, study design (including blinding or investigator involvement in the intervention), sample size, research personnel involved, characteristics of the study participants, details of the intervention and control (if applicable), study duration including follow up, outcome of interest and measurement method, and results reported. Assessment of methodological quality was completed using the tool developed by Downs and Black.(23) This tool assesses reporting quality, external validity, internal validity, and power; it was selected since we anticipated including both randomized controlled trials and observational studies. The investigators were not blinded to authors or journal type.

2.3 Results

2.3.1 Study selection and characteristics

Our literature search identified 694 unique citations, of which fourteen were identified as

potentially relevant. (Figure 2.1) After a review of the full article, seven studies met the inclusion criteria.(24-30) Information on the study design and patient characteristics are summarized in Table 2.2. Study sample sizes ranged from 30 to 254 patients. All studies reported including both men and women with the exception of the study by Granholm *et al.*(26) The most common disease state in which text messaging interventions were trialed was schizophrenia or schizoaffective disorder.(25-27) Two of these studies (25,27) used the definition of schizophrenia as outlined in the fourth edition of the Diagnostic and Statistical Manual (DSM-IV); the other study (26) did not describe the diagnosis or definition used. Two studies examined text messaging interventions in individuals with chronic alcohol use disorder or dependence (24,29) and one of these studies included comorbid depression as defined by the DSM-IV criteria.(24) One study tested their text messaging intervention in a sample of individuals diagnosed with anxiety or depression, however the criteria used for diagnosis were not described.(30) The last study included patients with co-occurring bipolar disorder (as defined by the Composite International Diagnostic Interview) and HIV infection.(28) Four studies provided information about the participant's medication regimens.(25-28) Four studies recruited patients attending outpatient mental health centers (25-27) or hospital-affiliated programs (28), while two recruited patients discharged from an inpatient psychiatric program.(24,30) One study recruited patients directly from the community through advertisements.(29)

2.3.2 Quality assessment

Table 2.3 summarizes criteria used to assess the risk of bias in the studies. All of the studies included clearly described study objectives and main outcomes, however as noted above, two studies (26,30) did not adequately describe diagnostic criteria used for patients included.

Interventions were clearly described for all studies with the exception of van den Berg *et al*. (24-30) All studies included were randomized controlled trials with the exception of Granholm *et al.* (24,25,27-30) However, only four studies clearly reported their randomization methods. (24,25,27,29) Of the randomized controlled trials, three studies were single blinded (24,28,29) and one of these studies reported contamination and loss of blinding.(24) Statistical methods were detailed in the studies, and all studies used valid and reliable measurements for outcomes of interest. Only one of the included studies was considered to have sufficient power to detect a clinically important effect (27); lack of power may account for some of the non-significant differences between groups. The highest attrition rate was seen in the Granholm *et al.* study where approximately 25% of participants dropped out prior to study completion.(26) Over 85% retention of patients was seen in the other studies included.

2.3.3. Text-messaging intervention

Specifics regarding the text messaging intervention and study results are summarized in Table 2.4. Three studies provided subjects with a phone and training on text messaging (26,28,29) while two made use of participant's personal phones.(24,27) Van den Berg *et al.* provided a mobile phone to individuals unable to use their own device, and Beebe *et al.* did not provide information on the source of the phone.(25,30) Three studies described providing participants with incentives for responding to text messages and completing follow up.(25,26,28)

The frequency of text messaging delivery was highly variable across studies, ranging from more complex routines of 12 messages per day (26) to simpler once or twice daily text message interactions. (24,25,27-29) One of the studies included involved once weekly text messaging.(30) Timing of text messaging delivery was either randomized during the course of the study (25), fixed at a specific time of day (24), or was subject to participant preference.(26-

28) Details regarding timing of the text messaging intervention were not provided in two studies.(29,30) The message was either automatically generated by computer (24,26-29) or manually sent by the primary investigator or a trained assistant.(25,30) The content of the text messaging intervention was also highly variable. Agyapong *et al.* created 180 unique messages that were delivered to participants over the course of the study such that no individual received the same message twice.(24) Conversely, the same text messaging content was repeated daily or weekly in the five other studies.(25-29) All studies sent text message reminders about medication-taking except the study by van den Berg *et al.*(24-26,28,29); one study addressed this item exclusively.(27) Two studies included combined text message and telephone interventions in their study designs.(25,30) In addition to medication reminders, four studies included components to assess current symptoms and socialization.(25,26,28,29) Beebe *et al.* also incorporated two-way interaction between the investigator and participant to address and problem-solve on identified issues.(25) Assessment of cravings for, or actual substance abuse itself, was included in three text messaging constructs.(24,25,29)

In three studies, text messaging content was developed by the researchers in cooperation with addictions counsellors or nursing staff to follow up on strategies introduced during formal care in outpatient or inpatient settings.(24,25,30) Most studies did not describe the process or rationale behind the content of their intervention, however Granholm *et al.* and Moore *et al.* described using focus groups with mental health patients and behavioral change theory in their development.(26,28)

2.3.4 Outcomes

Five studies included medication adherence as a primary outcome of interest; however, the methods used to measure adherence varied.(25-29) Two studies used electronic medication

tracking devices (Medication Event Monitoring System – MEMS) to assess medication adherence.(28-29) Montes *et al.* used the Morisky-Green Adherence Questionnaire (MAQ) to evaluate effect of the text messaging intervention between baseline and at 3 months.(27) Beebe *et al.* collected medication adherence data via pill count monthly for 3 months after implementing the text messaging intervention.(25) Granholm *et al.* assessed changes in medication adherence through hierarchical generalized linear modeling (HGLM) of responses to the respective daily assessment questions.(26) No baseline adherence data were obtained in three of the five studies.(25,26,29) Agyapong *et al.* did not measure medication adherence changes despite including text messaging content to address this issue.(24) Of the five studies examining the effect of text messaging interventions on medication adherence, only one reported significant improvement in this outcome.(27) One study identified, through subgroup analysis, significant improvement in medication adherence in patients living independently as opposed to those receiving assisted consistent care.(26) Moore *et al.* found while their text messaging intervention did not significantly improve medication adherence, it did so with dose timing of HIV medications.(28)

All studies measured a variety of behavioral outcomes, including symptom assessment, attitudes toward medications, quality of life, and cognitive assessment. The tools used to evaluate these outcomes are listed in Table 2.4. Five studies reported significant improvements in behavioral change or outcome measures as a result of text messaging interventions.(24-27,30) Agyapong *et al.* reported significant improvement in depression inventory measures at 3 months in the intervention group compared with control.(24) Although Beebe *et al.* did not find a significant improvement with text messaging alone, the combination of text messaging and telephone contact significantly improved mental-health outcome scores as measured by the Brief

Psychiatric Rating Scale (BPRS).(25) The combination of text messaging and telephone intervention was also found to significantly improved Brief Symptom Inventory (BSI) scores in the study by van den Berg *et al.* Montes *et al.* reported improvements in scores measuring quality of life (using the EuroQol Scale for Health-Related Quality of Life) in the text messaging group versus control.(27,30)

2.4 Discussion

Our review synthesized information from studies assessing the impact of text messaging interventions on medication adherence and health outcomes (clinical symptoms, functionality, quality of life) in individuals with mental health disorders including substance use. Seven studies met our inclusion criteria, and collectively suggest that text messaging interventions may be effective in improving medication adherence and/or health outcomes. However, there was substantial variation in key elements of these studies, including the disease states examined (schizophrenia, bipolar disorder, depression), characteristics of the text messaging intervention (content, timing, frequency), and study methodology (randomization, blinding, control group). Despite the positive findings, it is important to recognize methodological limitations in the studies reviewed. Firstly, the relatively small numbers of participants included in each study, as well as the short intervention periods, make it difficult to gauge the true effect of the text messaging interventions. As noted, most studies were not sufficiently powered to measure an effect. Secondly, while six of the included studies randomized participants to treatment or control, only half blinded investigators as to assignment. In one of these three studies, investigators acknowledged instances where rater blinding was lost due to participant disclosure.(24) Thirdly, each study implemented different types of text messaging interventions, both from a frequency of contact and content perspective. Only two studies described their

process and the background theory in developing the text messaging intervention.(26,28) Two other studies (24,25) provided rationale for the content included in their text messaging intervention that was largely distinct to their research interests; the final three studies did not provide a basis for their text messaging construct.(27,29,30) Finally, measures used to interpret results were also highly varied. With respect to medication adherence, two studies directly measured this factor using the MEMS device (28,29), while one other used a validated tool to measure this outcome.(27) The remaining two studies used either patient self-report (26) or pill counts (25) to ascertain changes in this endpoint. Based on these limitations, the overall quality of the evidence reported from these studies is quite low, making it challenging to draw conclusions and generalize the results.

Although there were numerous design differences among the included studies, certain themes were evident particularly with respect to medication adherence. Granholm *et al.* identified that the text messaging intervention significantly improved adherence for individuals not receiving explicit assistance with medications.(26) Montes *et al.* specifically targeted their text messaging intervention towards those with pre-identified suboptimal medication adherence, finding a significant improvement at 3 months.(27) These results suggest text messaging interventions may be more effective in those with underlying difficulties taking their medications at baseline, or those without social supports. Additionally, both studies that used focus groups and aspects of behavioral theory to develop their text messaging constructs found these interventions improved aspects of medication adherence – taking doses at correct times or in individuals with lack of medication supports.(26,28) Two studies did not include details on medication regimens for their participants, and while they reported improved validated scores for mood and symptoms, it cannot be conclusively determined this improvement was related to the text messaging

intervention alone.(24,30)

The effect of the text messaging intervention on medication adherence did not seem contingent on the nature of the interaction. Beebe *et al.* implemented an involved text messaging strategy that permitted bidirectional information sharing between the investigators and participants, while Montes *et al.* tested a simple, unidirectional text messaging (generated automatically and sent to participants).(25,27) Both of these studies reported significant improvement in outcomes related to medication adherence despite the differences in the construct of the intervention. Further, telephone plus text messaging interventions were superior to either intervention alone in two studies, suggesting the importance of comprehensive strategies in improving medication adherence in this population.(25,30) However, caution must be exercised when interpreting conclusions of the Beebe *et al.* study since the primary investigator was directly involved in delivering the text messaging interventions.(25) Also, since communication was bidirectional, specific aspects of support provided during the intervention may not have been reported, opening up more potential for subjectivity and bias. Finally, perhaps exemplifying the potential of overwhelming and exhausting patients, the Granholm *et al.* study (12 text messages sent daily) experienced the highest level of participant drop out (~25%).(26)

Of importance, the provision of incentives to participants for fulfilling required tasks in studies did not seem to influence results. Of the three studies which provided gift cards or money to participants in their studies, only the study by Granholm *et al.* resulted in significant improvement in medication adherence (in an analyzed subgroup).(26) None of the studies included in this review addressed issues of privacy and confidentiality related to the sharing of health information through text messaging.

Some studies were excluded from this review despite utilizing text messaging interventions in

mental health populations. Furber *et al.* implemented a text messaging intervention in patients presenting to the emergency department in a situational or emotional crisis.(31) However, as those participants recruited did not have a chronic mental health diagnosis, the study did not meet our inclusion criteria. In another study, text messaging was used as the delivery mechanism for a questionnaire assessing schizophrenia symptoms.(32) However, since this study did not use text messaging to deliver a subsequent intervention based on the information collected, it was excluded from this review.

Our review is not without limitations. We used very select search terms and inclusion criteria as our population of interest was specific. As a result, we may have missed studies in our search results, though this is unlikely. A second limitation is the inclusion of a pilot study with pre-post intervention design in our review that challenges our ability to make valid conclusions about the true effect of text messaging interventions. However, due to the relative lack of high quality, randomized and controlled data available, we felt it was important to include these studies to identify key themes for future exploration.(33)

Text messaging-based interventions have the unique ability to reach patients in a convenient, cost-effective, and efficient manner. The results of this review, while encouraging, indicate a need for further research to better understand how to implement such interventions in patients with mental health disorders. Additional studies are required to identify the appropriate content and frequency of text messaging interventions, as well as the most appropriate populations within which the intervention can be implemented. Further work should incorporate defined behavioral change theory into text messaging-based interventions to help validate and generalize results. Additional research into the needs, desires and expectations of the mental health population with respect to technology-based interventions will also assist in the development of

appropriate interventions. Such studies should better examine different situations and scenarios in which text messaging interventions are considered acceptable to the studied population, as well as identifying those situations where other forms of interaction are preferred. This foundational research would then allow for the development of larger, randomized trials with sufficient sample size to make valid conclusions about the role of text messaging in the delivery of care to this population.

Figure 2.1: PRISMA Citation Flow Diagram. (33)

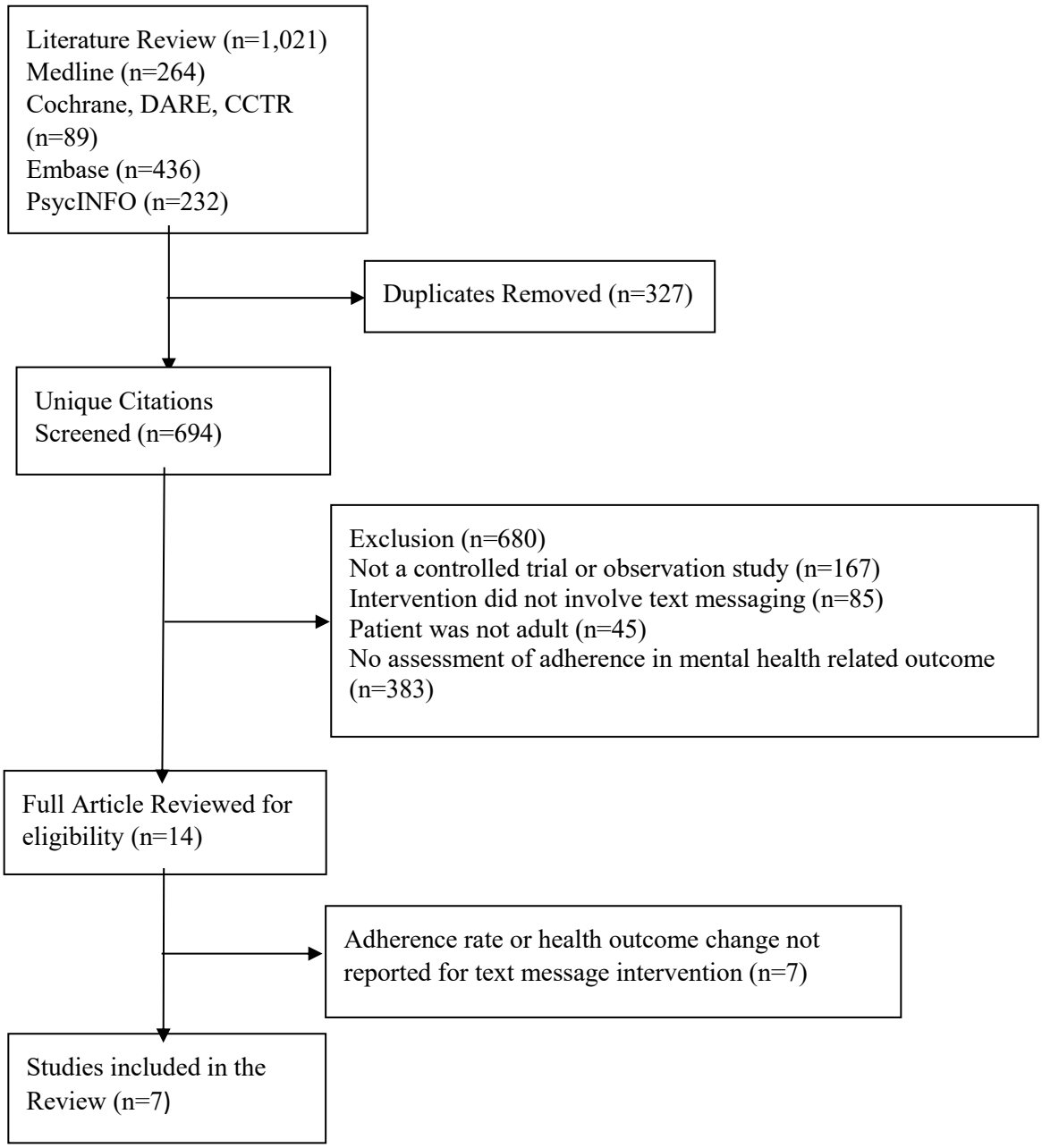

Table 2.1 Medline Search Strategy

1. Text Messaging/
2. (text messag* or short messag* service* or texting).mp.
3. 1 or 2
4. mental disorders/ or exp mood disorders/ or exp personality disorders/ or exp "schizophrenia and disorders with psychotic features"/ or exp substance-related disorders/
5. depression/
6. (drug use* or addict* or drug abuse* or alcohol use* or alcohol abuse* or substance abuse* or substance use*).mp.
7. (schizophrenia or depressi* or personality disorder* or bipolar or mental disorder* or mental* ill*).mp.
8. 4 or 5 or 6 or 7
9. 3 and 8

Table 2.2 Summary of Study Characteristics

First author, year of publication	Total number of participants (N)	Population of Interest	Design	Duration
Agyapong et al. (24)	54	Adults with comorbid major depression and alcohol dependence	Single-blind randomized controlled trial	3 months
Beebe et al. (25)	30	Community-dwelling adults (ages 21-65) with schizophrenia or schizoaffective disorder	Randomized, open label controlled trial	3 months
Granholm et al. (26)	55*	Community-dwelling adults (age >18) with schizophrenia or schizoaffective disorder	Prospective pilot study (pre-post intervention design)	12 weeks
Montes et al. (27)	254	Clinically stable adults (18-65 years old) with diagnosis of schizophrenia	Randomized, open label controlled Trial	3 months
Moore et al. (28)	50	Adults (age>18) with comorbid HIV infection and Bipolar Disorder (Type I or II)	Single-blind randomized controlled trial	30 days

Stoner et al. (29)	76	Adults (ages 21-55) with current alcohol use disorder (alcohol abuse or dependence)	Single-blind randomized controlled trial	8 weeks
van den Berg et al. (30)	113	Individuals discharged from hospital with a diagnosis of depression, anxiety disorder, adjustment disorder or somatoform disorder	Randomized, open label controlled trial	6 months

*42 patients completed the study

Table 2.3 Quality Assessment of Studies

Author last name	Patients included – characteristics reported	Study subjects representative	Blinding of participants and personnel	Validity and reliability of outcome measures	Randomization of study subjects (including method)	Losses of patients to follow up taken into account	Power sufficient
Agyapong et al. (24)	+	-	+/- (single blind)	+	+	+	-
Beebe et al. (25)	+	-	-	+	+	-	-
Granholm et al. (26)	+/-	-	-	+	-	-	-
Montes et al. (27)	+	+	-	+	+	+	+

Moore et al. (28)	+	-	+/- (single blind)	+	-	+	-
Stoner et al. (29)	+	-	+/- (single blind)	+	+	+	-
van den Berg et al. (30)	+/-	-	-	+	-	+	-

"+" = yes, "-" = no, "+/-" = partially

Table 2.4 Text Message Intervention and Outcome Data

Author last name, year of publication	Intervention Frequency	Intervention Content	Measurement	Outcome
Agyapong et al. (24)	Twice daily at 1000 and 1900 post-discharge.	180 unique messages, focusing on material reviewed during inpatient stay (mood, medication adherence, alcohol abstinence)	Primary: BDI score and CAD (using TLFB) measured as number of days abstinent from discharge to study endpoint. Secondary: OCDS, AASES, GAF scores	1. Statistically significant change in BDI Scores within intervention group and with comparison: (8.5 (SD=8.0) vs. 16.7 (SD=10.3); p=0.003. 2. Non-significant trend in CAD scores in favor of intervention: 88.3 (SD=6.2) vs. 79.3 (SD=24.1); p=0.08.

Beebe et al. (25)	Telephone: Weekly telephone call; Text Message: Daily text message; Combined Arm: Weekly phone call and Daily Text Message	Telephone and Text message interventions assessed med adherence, symptoms, socialization, and substance use or cravings	Medication adherence measured by pill count; disease symptoms and clinical presentation by BPRS scale	1. Non-significant differences in medication adherence 2. Significantly lower BPRS scores in telephone plus text group: ($F(4,26) = 4.2$, $p = 0.005$); 3. No differences detected within arms or in any other comparison
Granholm et al. (26)	Three sets of 4 text messages were sent to each participant daily from Monday-Saturday	Each set of TM addressed a specific domain (medication adherence, social function, hallucinations or other symptoms)	Measured through HGLM analysis of changes in responses to daily ambulatory monitoring queries, Changes in battery of scales (PANSS, BDI-II, ILSS, ANART) from baseline to completion	Statistically significant increase in self-reported adherence for independent participants only, not those in assisted living, while number of reported hallucinations decreased; increased odds of having 4 or more social interactions relative to 1; no difference in battery-scales assessed.

Montes et al. (27)	Daily text message delivered at either 11am or 2pm (patient choice)	Addressed medication-taking only	Primary: Medication adherence as measured by the MAQ. Secondary: MAQ at 6 months, Clinical severity scores via CGI-SCH, DAI-10, SUMD, and EQ-5D	The mean change in MAQ at 3 months was -1.0 (CI: -1.02, -0.98) and -0.7 (CI: -0.72, -0.68), respectively (P=0.02) favoring intervention over control.
Moore et al. (28)	Once or twice daily, depending on the treatment regimen	Both Groups: daily SMS assessing mood Treatment Group received additional SMS to remind them to take their medications at pre-specified times (for HIV and Bipolar medications)	Primary: medication adherence and medication dose timing for both HIV and bipolar medications measured by MEMS compared with patient self-report using VAS. Secondary: mood scores as measured by BDI-II and YMRS	Primary: Non-significant differences in medication adherence for overall medications as well as individual medications for HIV or Bipolar disorder Significant difference in participants taking HIV medications closer to the correct dosing time 65.7 (SD=76.5) minutes vs 120.8 (SD=145) minutes P=0.02. Non-significant differences for this factor for bipolar medications. Secondary: Non-

				significant differences in mood scores between groups.
Stoner et al. (29)	Daily assessment of side effects, alcohol use, and cravings; variable frequency reminders for medication adherence based on participant reported adherence	Both Groups: daily SMS assessing side effects, alcohol use, and craving Treatment Group: daily to biweekly reminders to take medication (frequency decreased with improved adherence)	Primary: medication adherence as measured by MEMS Secondary: alcohol use, avoidance, craving changes as measured by variety of scales: AUDIT, ADS, PACS, TLFB	Non-significant differences reported for both primary and secondary outcomes
van den Berg et al. (30)	Control group: standard care and follow up Intervention Group 1: Weekly telephone follow up for one month, then monthly telephone follow up for 5 months Intervention Group 2: Weekly text message (in addition to telephone follow	Intervention Group 1: Standardized questions assessing mood, symptoms, health status and health care system utilization; individualized questions about participants' activities and therapy goals. Intervention Group 2: Content as above plus weekly text	Primary: BSI-18 for symptom and mood assessment; standardized questionnaires for health status Secondary: secondary questionnaires assessing health system utilization	Primary: Significant improvement in BSI-18 anxiety scores in Intervention Group 2 versus control (-2.04, 95%CI -3.99 to -0.076, p=0.042); non-significant differences in BSI-18 depression scores as compared to control. Secondary: No data reported on

	up as in Group 1)	messages tailored to each individual(e.g. therapy goals more general)		health system use

BDI II = Beck's Depression Inventory
ANART = American National Adult Reading Test
BPRS = Brief Psychiatric Rating Scale
CAD = Cumulative Abstinence Duration
ILSS = Independent Living Skills Survey
PANSS = Positive and Negative Syndrome Scale
OCDS = Obsessive Compulsive Drinking Scale
MAQ = Morisky Green Adherence Questionnaire
CGI-SCH = Clinical Global Impression Schizophrenia Scale
AASES = Alcohol Abstinence Self Efficacy Scale
TLFB = Time Line Follow Back
DAI-10 = Drug Attitude Inventory
GAF = Global Assessment of Function
EQ-5D = EuroQol Scale for Health-Related Quality of Life
SUMD = Scale to Assess Unawareness of Mental Disorder
MEMS = Medication Event Monitoring System
ADS = Alcohol Dependence Scale
PACS = Penn Alcohol Craving Scale
TLFB = Time Line Follow Back
VAS = Visual Analogue Scale
YMRS = Young Mania Rating Scale
BSI-18 = Brief SBSI-18 = Brief Symptom Inventory
AUDIT = Alcohol Use Disorders Identification Test

2.5 References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: Challenges and management strategies. Patient Relat Outcome Meas 2014;5:43-62.

(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med 2005;353(5):487-497.

(3) Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007;167(6):540-550.

(4) Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43(6):521-530.

(5) Dimatteo RM, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40(9):794-811.

(6) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).

(7) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49(2):196-201.

(8) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv 2007;58(6):855-863.

(9) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry 2013;12(3):216-226.

(10) Julius RJ, Novitsky MA, Dubin WR. Medication adherence: A review of the literature and implications for clinical practice. J Psychiatr Pract 2009;15(1):34-44.

(11) Sowers W, Golden S. Psychotropic medication management in persons with co-occurring psychiatric and substance use disorders. J Psychoactive Drugs 1999;31(1):59-70.

(12) Weiss RD. Adherence to pharmacotherapy in patients with alcohol and opioid dependence. Addiction 2004;99(11):1382-1392.

(13) Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: A comprehensive review of recent literature. J Clin Psychiatry 2002;63(10):892-909.

(14) Farooq S, Naeem F. Tackling nonadherence in psychiatric disorders: Current opinion. Neuropsychiatr Dis Treat 2014;10:1069-1077.

(15) Berk L, Hallam KT, Colom F, et al. Enhancing medication adherence in patients with bipolar disorder. Hum Psychopharmacol. 2010;25(1):1-16.

(16) Chong WW, Aslani P, Chen TF. Effectiveness of interventions to improve antidepressant medication adherence: a systematic review. Int J Clin Pract 2011;65(9):954-975.

(17) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.

(18) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: a systematic review. Telemed J E Health 2009;15(3):231-240.

(19) International Telecommunications Union, 2012. ITUWorldTelecommunication/ICT Indicators Database. Statistical highlights. Available at: ⟨http://www.itu.int/ITU- D/ict/⟩ (accessed April 2, 2015).
(20) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Comput 2014;19:367-78.
(21) U.S.Department of Health and Human Services, May 2014. Using Health Text Messages to Improve Consumer Health Knowledge, Behaviors, and Outcomes: an Environmental Scan. Available at: ⟨http://www.hrsa.gov/healthit/txt4tots/ environmentalscan.pdf⟩ (accessed April 2, 2015).
(22) Schnall R, Okoniewski A, Tiase V, Low A, Rodriguez M, Kaplan S. Using text messaging to assess adolescents' health information needs: an ecological momentary assessment. J Med Internet Res 2013;15(3). Accessed 21 March 2015.
(23) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998; 52:377–384.
(24) Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. J Affect Disord 2012;141(2-3):168-176.
(25) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs 2014;35:323-329.
(26) Granholm E, Ben-Zeev D, Link PC, Bradshaw KR, Holden JL. Mobile assessment and treatment for schizophrenia (MATS): A pilot trial of an interactive text-messaging intervention for medication adherence, socialization, and auditory hallucinations. Schizophr Bull 2012;38(3):414-425.
(27) Montes JM, Medina E, Gomez-Beneyto M, Maurino J. A short message service (SMS)-based strategy for enhancing adherence to antipsychotic medication in schizophrenia. Psychiatry Res 2012;200(2-3):89-95.
(28) Moore DJ, Poquette A, Casaletto KB, et al. Individualized texting for adherence building (iTAB): Improving antiretroviral dose timing among HIV-infected persons with co-occurring bipolar disorder. AIDS Behav 2015;19(3):459-471.
(29) Stoner SA, Arenella PB, Hendershot CS. Randomized controlled trial of a mobile phone intervention for improving adherence to naltrexone for alcohol use disorders. PLoS ONE 2015;10(4).
(30) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone- and text message-based telemedicine concept for patients with mental health disorders: results of a randomized controlled trial. Psychother Psychosom 2015;84(2):82-89.
(31) Furber G, Jones GM, Healey D, Bidargaddi N. A comparison between phone-based psychotherapy with and without text messaging support in between sessions for crisis patients. J Med Internet Res 2014;16:43-54.
(32) Španiel F, Hrdlicka J, Novák T, et al. Effectiveness of the information technology-aided program of relapse prevention in schizophrenia (ITAREPS): a randomized, controlled, double-blind study. J Psychiatr Pract 2012;18(4):269-280.
(33) Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoSMed 2009;6:e1000097.

Chapter 3. Qualitative Study

Perceptions of patients with mental health disorders on the role of mobile technology for supporting medication adherence

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6, 881 (Text)

Figures: 0

Tables: 4

Abstract

Objectives: To better understand medication-taking behaviors and adherence supports in recently homeless individuals with mental illness to determine whether mobile technology can enable medication adherence.

Methods: This study was completed over a three month period from August to November, 2016 at the Pathways to Housing Program in Edmonton, Alberta, Canada. Individuals were eligible to participate if taking medications regularly; individuals were excluded if acutely ill, unable to speak English, or were otherwise unable to consent. We administered a questionnaire including demographic information and the Medication Adherence Rating Scale (MARS) to determine adherence and attitudes toward medications. Semi-structured interviews were then completed to elicit information about medication-taking strategies and supports, as well as perceptions on using mobile technology for health. Questionnaire data were analyzed using summary descriptive statistics, while interview data were subject to qualitative content analysis.

Results: 15 participants completed the study, most of whom (93%) had permanent housing and were enrolled in the Pathways to Housing Program for over two years. Attitudes toward medications, and estimates of medication adherence, were generally good as measured by the MARS. Participants described a number of patient factors (insight, coping strategies) and external factors (therapeutic alliance, family support) that enabled medication adherence. There was moderate interest in incorporating mobile technology into regular health management with barriers of cost and technology literacy identified as barriers.

Conclusion: Wide-ranging external supports, as well as individual medication-management strategies support good adherence within this population. Mobile technology may be an effective tool to complement existing supports, but significant barriers to implementation exist.

3.1 Introduction

Poor medication adherence is a major contributor to suboptimal therapeutic outcomes as well as increased health care costs.(1,2) Non-adherence to medication poses a significant challenge for chronic disease management across all fields of medicine, including that of chronic mental illness. Medication adherence rates in patients with mental health disorders are often reported to be lower than other chronic diseases, with average adherence rates of approximately 50%.(3,4) Among the factors contributing to poor medication adherence in this population are those related to patient self-efficacy (motivations, attitudes, and beliefs) and system supports (access to care, therapeutic alliance).(4) Active substance use is also a contributor to poorer medication adherence as people with mental illness are twice as likely to have substance use problems.(5,6)

In more recent years, there has been increased interest in the use of text messaging (TM) or short messaging service (SMS) to improve care and support medication adherence in a number of diseases.(7) Estimates suggest that 90% of individuals worldwide have access to a cell phone, and TM is the most commonly used feature.(8,9) In the area of mental health, a number of studies have evaluated TM for appointment or medication reminders, as well as delivering supportive messages and improving self-management of illness.(10) A systematic review examining the impact of TM interventions on medication adherence and mental health outcomes noted mixed findings among seven studies included.(11) One study reported improved medication adherence as a result of the TM intervention (12), while five studies found improvement in mental health as measured by a variety of psychiatric and social functioning scales.(13-17) Quantifying the impact of TM from studies conducted to date is hampered by the relatively small numbers of participants included in each study, as well as the short follow-up

periods.(11) Variation in research methodology, assorted TM intervention constructs, different patient populations included as well as outcome measurements also limit the ability to gauge the true effect of TM or assess which patients may benefit the most from this intervention.(11)

In terms of patient perceptions and acceptability of TM interventions, studies that have evaluated these outcomes have generally reported positive findings.(10,18) However, consideration must be given to the feasibility and acceptability of TM interventions as part of ongoing clinical care in real world settings. Researchers have explored patient perceptions regarding the use of mobile phones and TM for communication about health, including in populations that are considered vulnerable and difficult to reach.(19-22) Patients identified convenience, reduced isolation, enhanced self-monitoring of health conditions, and improved medication adherence as potential benefits of mobile phone use.(19,20) On the contrary, concerns about privacy and complexity of the monitoring program or construct have been cited as potential barriers to implementation.(19,23) Short, positive, and directive text messages with information about medications and disease management were reported to be most beneficial in studies that included homeless persons.(22,23)

In order to determine how TM interventions can best be implemented in vulnerable populations with complex health needs, such as those with mental illness and transiently housed, a better understanding of medication taking behaviors and needs of this population, as well as access to mobile phones is required. The objectives of this study were to investigate attitudes towards medications and current medication-taking behaviors of patients with mental illness and recent homelessness. In addition, we wanted to better understand medication adherence supports in this patient population and attitudes towards mobile technology for supporting medication adherence and other healthy behaviors.

3.2 Methods

3.2.1 Study Design

We used a constructivist approach and qualitative description method to answer our study questions. Constructivism is a philosophical approach that focuses on the development of knowledge about the phenomenon of interest through social interaction with study subjects.(24, 25) This theory allows for the co-creation of knowledge with the participant and is considered most appropriate when there is some knowledge of the phenomenon of interest but further social interaction is required to understand the reality of the phenomenon. Qualitative description is the best method to use when a thorough description of a phenomenon is desired within the reality of the events being described.(26) We approached data collection from a low inference perspective, focusing more on understanding the phenomenon of interest as opposed to explaining or interpreting it.

In order to collect data effectively within this lens, we used semi-structured interviews. Semi-structured interviews are used to obtain descriptions of the phenomenon from the interviewee in a manner that permits flexibility to explore and understand meaning.(27) This form of data collection allows for the agenda to be set by the interviewer but leaves enough room for spontaneous descriptions and narratives from the interviewee.(25)

3.2.2 Setting and Sample

This study was conducted using a sample of patients affiliated with the Boyle McCauley Health Center's (BMHC) Pathways to Housing Program in Edmonton, Alberta, Canada.(28,29) Edmonton is the capital city in the province of Alberta with a population of approximately 900 000 individuals. The BMHC provides comprehensive primary health services to individuals in Edmonton who face numerous barriers to accessing care. These barriers include homelessness,

addictions, and mental illness. The Pathways to Housing Program is an outreach program within the BMHC that incorporates housing-first principles. This program provides immediate access to community-based apartments for individuals with histories of chronic homelessness and concomitant mental illness and/or addictions. Once enrolled in the program, patients receive support from Assertive Community Treatment (ACT) team members with the intent of reintegrating individuals into society and sustaining housing. This support includes a wide array of services from mental and physical health to substance use disorder treatment and employment and educational services. The ACT team consists of a physician, psychiatrist, social workers, registered nurses, addictions counsellors, occupational therapists, and other professionals including a clinical pharmacist. Patients enrolled within the program are typically seen in the community (e.g. patient's residence) or clinic a minimum of once weekly; clinic visits are usually reserved for medical appointments with the physician, psychiatrist, or pharmacist.

All patients enrolled in the Pathways to Housing Program and taking medications to treat chronic mental health disorders were eligible to participate in this study. Individuals who were acutely ill, psychiatrically or otherwise, who did not speak English, or were otherwise unable to provide consent were excluded.

3.2.3 Procedures

Patients were prescreened using our eligibility criteria by the Pathways to Housing Program staff. Patients were approached by the staff during regular home visits (or scheduled clinic visits), provided the information letter, and asked if they were interested in participating in the study. The staff who approached individuals were members of the ACT team and included licensed practical nurses, registered social workers, and occupational therapists who regularly interact with the

patients enrolled in the program. It was clearly emphasized to all potential participants both verbally and in writing that they were in no way obligated to participate in the study, and that refusing to participate would not affect the care they receive.

Patients interested in participating in the study signed a form consenting to be contacted by a study investigator (TW) to schedule a time to review the study, obtain written consent, and if applicable, complete the questionnaire and interview (approximately 45 minutes total). All interviews were conducted in the Pathways to Housing clinic. Participants were offered an incentive ($20 food gift card) as compensation for their time.

Our sample size consisted of patients who met the eligibility criteria and provided written consent to participate. Purposeful sampling was used in this study in an effort to select participants who could contribute most readily to understanding the phenomenon of interest.(24) For example, as consent to be contacted forms were received, the study investigator reviewed each potential participant with the program management and physicians. Based on feedback from these consultations, individuals deemed most likely to provide detailed feedback related to the study objectives were selected for participation. Criteria to identify these participants included historical participation in research initiatives at the program as well as perceived use of technology.

3.2.4 Data Generation

Data were generated over the course of a three month period from August to November, 2016. Prior to conducting the semi-structured interviews, a standardized questionnaire was administered to collect participant demographic and medical information, as well as adherence behavior. The following demographic information was included in the questionnaire: gender, age, housing, employment, education, ethnicity, medication use, and Pathways to Housing

affiliation items. We used a questionnaire for this portion of the study to ensure we collected standard information regarding demographics in an efficient manner. Questionnaires are effective tools to use in data collection for this reason, and also to facilitate quick and accurate data analysis.(30)

To elicit information about adherence and attitudes towards medications, the Medication Adherence Rating Scale (MARS) was included as part of the questionnaire. The MARS scale is a brief 10 item questionnaire (yes/no response) which was developed from two existing scales – the Drug Attitude Inventory and the Medication Adherence Questionnaire –with the overall goal of providing a more reliable and valid tool for patients with psychoses.(31) It is simple to use and has been validated in patients with mental illness as well as those who are homeless with schizophrenia, and was chosen for this study as the vast majority of patients enrolled in the Pathways to Housing program have concomitant mental illnesses.(32,33) The MARS has a 3 factor structure and includes questions related to medication adherence (factor 1 - items 1-4) as well as attitudes toward taking medications (factor 2 - items 5-8) and attitudes toward psychotropic medications and side effects (factor 3 - items 9, 10).(31,34)

Following completion of the questionnaire, the study investigator (TW) interviewed participants using semi-structured questions with question flow largely determined by the participant. Where required, open-ended "reset" questions were used to ensure study objectives were addressed. Interview questions explored attitudes toward medications, medication-taking strategies, and supports for medication adherence. Questions regarding technology use were developed using previous literature on cell phone use within the mental health population.(9,35) These questions addressed: patient access to mobile phones, benefits and barriers to mobile phone access/use, attitudes toward using mobile phones for medical needs, benefits and concerns of

communicating via mobile phones with healthcare team. Questions were intended to encourage conversation and were adapted as the study progressed. (see Table 3.1 for original version). Interviews were approximately 30 minutes in length and were digitally audio-recorded and transcribed verbatim by a professional transcription service. All participants were informed about the audio recording of the session prior to initiating the interview.

3.2.5 Data Analysis

Questionnaire response data was entered into a Microsoft Excel database (Version 14, 2010). Summary, descriptive statistics were used to analyze data and describe the socio-demographic characteristics and medical history of the sample, as well as their medication-taking behaviors and attitudes.

All interview data were subject to qualitative content analysis using nVivo qualitative data analysis software (Version 11). Qualitative content analysis is the process where persistent ideas within the data are identified to allow analysis of underlying themes. The use of qualitative content analysis supports our method of qualitative description, and allowed us to produce a comprehensive summary of our interview data in a systematic fashion.(36) Data analysis of interviews occurred concurrently with data collection to ensure responsiveness to the information gathered.

Codes or categories were not identified prior to the interviews but developed as transcripts were reviewed. To code, interview transcripts were read and reread to highlight pervasive ideas and concepts in the data. Coding was completed by the same study investigator (TW) who completed the interviews. Ideas were highlighted and labelled into similar, individual codes through this process. The individual codes were then reread and grouped into categories which

were summarized descriptively following verification of internal and external homogeneity. In this case, external homogeneity ensures the differences between each category are clear and distinct, while internal homogeneity confirms the codes assigned within each category clearly fit within the grouping based on the descriptive summary.(24) All categories were then analyzed as a group to identify common themes that connected all data.

Field notes were taken by the interviewer during all interviews to inform further probing questions and also supplement transcripts and facilitate coding, categorization, and theme generation. Field notes ensured that contextual information not available at the time of interview analysis remained available for reference. The interviewer also scrutinized his own perspective on the flow, direction, and outcome of each interview to better understand how pre-existing identities impacted data collection and interpretations. This concept, known as reflexivity, in combination with field note use, allowed our semi-structured interview guide and questions to adapt as the study progressed.(24)

Data gathering and analysis ceased when no new or relevant information was obtained during interviews and when the categories were clear and refined.(24,25) Data saturation is reached when conclusions from the data appear robust, and no gaps or unexplained responses exist. In order to ensure saturation was reached, purposeful sampling was used to obtain cohesive and homogenous data from study participants. Finally, negative cases (data contrary to what most participants stated) were all followed up to identify potential gaps in our theory and to ensure all phenomena were explained. Based on our choice of method and data analysis, we anticipated needing to sample between 12 and 20 individuals to understand our phenomena of interest.(24,26)

This research was approved by the Human Research Ethics Board at the University of Alberta.

3.3 Results

3.3.1 Description of Participants

Of the 76 individuals enrolled in the program at the time of the study, 15 were excluded based on our pre-screening criteria. Of the remaining 61 individuals, 40 provided consent to be contacted by the study investigator to discuss the study further, 11 were unable to be reached due to a variety of circumstances (hospitalized, incarcerated), and 10 refused to be contacted. Using purposeful sampling, we contacted 15 of the 40 patients, all of whom provided consent and completed the study.

Table 3.2 summarizes the sociodemographic characteristics and medical history of participants. The median age was 46 years; approximately half of participants were male and most were unemployed and did not have a high school diploma. With respect to housing, 14 participants (93%) had permanent housing while 13 individuals (87%) had resided in the same dwelling for over 6 months. All participants except one were affiliated with the Pathways to Housing Program for greater than two years. Participants most frequently reported mental health diagnoses of schizophrenia (47%), depression (47%), and bipolar disorder (40%); approximately two-thirds reported current substance use (67%). All participants reported receiving home delivery of medications, and all but one received adherence packaging.

3.3.2 *Medication Adherence*

With respect to medication-taking behavior as measured using the MARS, all participants except one scored in the "good adherence" range (result of 6 or greater on the scale). The mean MARS score was 7.3 out of 10 (SD = 1.5) with scores ranging from 5 to 10. When examining specific aspects of the scale, participants scored relatively poorly on items addressing forgetfulness (40% of participants scored adequately on this item) and attitude toward psychotropic medications

including side effects (67% of participants scored adequately on this item). Table 3.3 identifies the adherence response frequencies with accompanying percentages for each MARS item.

3.3.3 Interview Findings Overview

Study findings have been organized into three main areas: (1) Patient factors influencing medication adherence, (2) External factors influencing medication adherence, and (3) Technology use and health. Patient-related factors that influence adherence include learned coping strategies, insight, and attitudes towards medications. External factors describe the impact of family and friends, peers, and health team supports for medication-taking activities. Finally, technology use and health describes current access to communication technology, including mobile devices, and participants' perceptions toward potential use for health-related purposes. Findings related to patient and external factors are summarized in Table 3.4.

3.3.4 Patient Factors

Individual-specific coping strategies, such as establishing regular routines and avoiding risky situations or triggers were important in enabling adherence to medications. When discussing his approach to medication-taking and planning his daily routine, one participant had to account and prepare for any required activities that took place outside his home (P2H1): *"I don't carry because, you know, I don't want to get [robbed] for my meds because, you know, some of them are probably worth money on the street, right."* He went on to describe how caution must be exercised even when people were visiting his home: *"And when I got company I hide [my medications]."*

Participants also linked risk-avoidance to their medication-taking and healthy behavior strategies. In these instances, risk avoidance largely amounted to staying away from areas where exposure to illicit drugs, and subsequent drug use, may occur. As many participants enrolled in

this study were dealing with substance use issues, the ability to maintain stability and sobriety were pivotal in their recovery. As one individual described (P2H14): *"I don't go down to the places anymore. People there are selling - and all down that street - you just walk down that street and everyone's selling something."*

The establishment of medication management routines within the home was also important in enabling consistent medication-taking. Systems and routines described included timing pill-taking with meals, handwriting information on medication packages to serve as a reminder, and placement of medications in consistent areas to queue adherence. This latter scenario is exemplified by the following participant description (P2H14): "*I take my night meds and I put them on my night table. So they're there. So I know at night when I'm ready for bed, I get my drink of water and I take my meds."*

Participants' attitudes towards their medication and side effects also impacted decisions about taking medications. As most participants in the study had tried several medications throughout the course of their illness, negative experiences and the fear of side effects influenced medication taking activities:

"I took them before and I had a real bad reaction because the clozapine is so powerful" said one participant (P2H11). *"It makes you feel tired and like you almost start to slur your words a bit. It makes you really sluggish."*

Despite having experienced side effects of medications, all participants indicated they try taking their medication as regularly as possible. The rationale provided by many participants was their current medication regimens provide them with beneficial symptom control that overcomes the concerns related to side effects. This symptom control, in most cases, was sufficient to allow participants to maintain a semblance of normalcy and stability within their respective

environments. This sentiment is exemplified in the following quote (P2H10):

"Yeah, like I don't know what normal is, right, because I'd never taken bipolar medication. And I've never felt normal before; if this is normal, then I quite like it."

The concept of remaining in control was strongly linked to normalcy and stability, with many participants indicating the importance of medication in helping them manage their unhealthy behaviors. One participant spoke at length about how his medications helped him control unwanted behaviors (P2H15): *"I feel more stable, if you want to put it that way,"* he said. *"My meds definitely levelled me out. I [used to] go out and do stupid things like buy cars and stuff like that. So, I mean, I'm kind of glad I'm kind of stable."*

Other participants expressed similar feelings when reflecting on their approach to medication-taking. However, an interesting dichotomy was seen in some cases whereby participants felt somewhat disillusioned and frustrated with the efficacy of their medications. Certain participants were able to reflect that, while they were certainly coping more effectively on their current medication therapy than in the past, their symptom control was not as quick or to the extent they expected:

"Um, you know I feel better now. But see I don't know if it's the medication or the help I'm getting or I don't know the attention. I mean I don't know what [the meds] are doing. I think they're important. I'd like to say hell yeah they're the greatest things in the world but it doesn't work that way. As much as I might not believe in taking the medication, I don't know, maybe it will work." (P2H4)

3.3.5 External Factors

Participants consistently discussed the importance of feeling supported and enabled when questioned about medication adherence. Support from family and friends were of particular

importance with participants expressing sentiments such as understanding, guidance and acceptance when describing these social connections.

"I phoned my parents and said I have bipolar should I take [my medications]? And they [said] if it helps with your PTSD, definitely." (P2H10)

Peer support was often cited as an important factor in an individual's process of reconciling their symptoms with medical diagnoses and medication therapy. Participants were often able to develop insight into their symptoms through discussions with others who were experiencing similar symptoms or circumstances. Sharing of experiences often occurred informally through discussions with friends or acquaintances as one participant explained: *"But it turns out there's a lot of people out there with the same issues"* (P2H1). He later continued (in reference to seeking out others with similar symptoms): "*Well, once I was diagnosed I started investigating my own shit. I've had conversations with people who've already been [on medications for schizophrenia] and, I've got a few friends around with [those] issues, right."*

Support programs offered through the Pathways to Housing Program were also factors in the exchange of information between peers who were facing similar challenges. Participants were able to connect and discuss a variety of issues related to their health, including medications, addictions, and their recovery progress. As one participant described it, *"I'm just looking for answers in recovery group"* (P2H10), "*I like it because it keeps me busy and it keeps me out of trouble."*

Other system supports included adherence aids provided to participants by their pharmacy. Most individuals indicated that receiving their medications in packaged strips or blister packs was beneficial in establishing a routine for taking their medications. Having medications

delivered to their homes also overcame the barrier of needing transportation to the pharmacy.

"Yeah, the packaging I like. It makes it easier." (P2H2)

"Yeah, [delivery] is [handy]. Because, you know, sometimes, you know, where the pharmacy's located is [kind of] far away." (P2H13)

Other forms of medication supports included direct instruction from Pathways to Housing staff members, as well as the involvement of home care or community mental health workers. This latter group was referenced by 3 individuals as being instrumental in helping them to remember to take their medications, and to take their medication on time:

"[The staff] they dispense. So, you know, they come and remind me if I sleep in." (P2H7)

The Pathways to Housing team, with their outreach and office-based health services, were also frequently identified by participants as essential in their treatment progress. Many participants described feeling hopeless prior to enrolment in the Pathways to Housing program; however their overall outlook within this supportive environment has improved. Participants also extended feelings of gratitude to other, affiliated health care providers whom they feel comfortable speaking with regarding medications and health concerns:

"And without [Pathways staff] I wouldn't be here right now." (P2H15)

"I can talk to [the Pharmacist] if I have questions about something and he'll explain it to me or look it up." (P2H9)

While satisfied with current health services, participant buy-in of treatment plans and subsequent

medication adherence was occasionally affected by past experiences with health care providers and the health system. These experiences were often referenced when individuals discussed the process of reconciling their symptoms with a provided diagnosis, as many wished to understand their illness and the associated treatment: *"The doctor there, we'd only had two conversations maybe five or six minutes long each and he said "schizophrenic". I thought he came to that conclusion way too quickly."* (P2H11)

This individual further described how this experience created reservations in his ongoing engagement with treatment plans due to lack of agreement on diagnosis: "*I feel like I've been labelled and it's something that I'm not really comfortable with… So I was a little frustrated, like maybe he was wrong? And then now that I've been diagnosed and that, I've kind of got the label*." (P2H11)

3.3.6 Technology use and health

The ability to remain connected to various supports, health care or otherwise, was identified as crucial for many participants. Having consistent means of connecting with others in their social circle (family and friends) provided comfort and a sense of security to these individuals. In addition to in-person communication, participants maintained contact with key supports through telephones (mobile or landline), and social media networks. All 15 participants had landlines (or home phones) within their current residence, while 8 had mobile phones as well.

Participants' views differed with respect to their interest in having a mobile phone. Some indicated their needs were met by their landline, and that having a mobile phone would not provide any obvious advantages from a connectivity perspective (P2H11): "*Just with the house phone I can [stay connected], you know. But to be honest with you [having a mobile phone]*

wouldn't be a whole different for me because I'm just used to the [landline]."

For those individuals with landlines only, some were intentional about keeping just this service, and not obtaining a mobile phone. In one case, the rationale for keeping a landline only was a coping strategy aimed at avoiding potentially risky behaviors. This individual, a male with history of depression and alcohol abuse, spoke about the accessibility of mobile phones, and how this was actually a negative in his view (P2H4): *"I'd like a cell phone but then I wouldn't want one because then some – if I have a cell phone then I can be reached wherever. Whereas if I just have my landline and if I'm not home nobody can reach me. So I've got my privacy in that way."*

In contrast, many participants expressed a desire to obtain a mobile phone in the near future. This desire was especially evident among participants who had previous experience with mobile phone capabilities. Remaining connected with family and friends, being able to access services when not at home, and the convenience of text messaging were described as advantages of mobile phone ownership:

"If I needed to call a cab from somewhere, on the street, or reaching out to somebody saying 'I'm on my way, I'm coming, I'll be 14 minutes late.' Just the ease of access to things. And texting, I got good at texting on the little phone that I had." (P2H3)

However, many barriers were identified by participants in maintaining consistent mobile phone access. The prohibitive costs of owning and maintaining mobile phone subscriptions were one of the major barriers that participants faced. *"I can't afford it. I can't justify an $85 a month cell phone bill, I can't."*(P2H11) Given the chaotic background of many of these individuals, mobile phones were often stolen or lost, resulting in defaulted payments and an inability to re-establish

device ownership (P2H3): *"I owe on two cell phones already. I lost them so I stopped paying the bills. So it's on my credit check [and I've] got to pay it off before I get another phone*."

In some cases, the need for maintaining a mobile device was worth the cost associated with replacing theft or loss of a device. *"[My phone] has been stolen many times. I've [had] at least seven phones stolen,"* stated one female participant when describing the challenges of staying in touch with friends and supports (P2H14). *"But I always manage to get another cell phone".* One male participant has had similar experiences with phone theft, so much so that he is discouraged from purchasing a new device (P2H9). *"[The mobile phone] got stolen. Then I had like three more after that and I they got stolen or broken so I just stopped buying them."*

Another barrier to consistent mobile device access and use is familiarity and comfort with mobile technology. The functionality of many mobile phones has advanced tremendously over the past 10 years which creates challenges for many participants in adapting to newer devices. Given the lack of consistent access to mobile phones, some participants were unfamiliar with mobile phone functions that are now routinely used by others. When discussing his lack of interest in mobile phones and devices, one male participant explicitly identified his lack of comfort with newer devices as a barrier to acquiring a new mobile phone (P2H4):

"*I've just fallen so far back in the electronic age, it's just like 'whoa' it just flew right by me. I'm kind of embarrassed that I don't know I don't speak that language. It's a whole new world."*

Another participant had similar thoughts regarding features of newer mobile phones; however he remained interested in simple devices. These more basic phones would meet his communication needs without being too overwhelming from a functionality perspective: *"I would get a flip*

phone (like an old one) instead of an iPhone. I just want a phone that you can talk on and text. Just simple - keep it simple."(P2H5)

When asked specifically about using mobile phones to enable connectivity with health care supports outside of the home, participants expressed different perspectives. Some individuals provided specific examples where communicating by mobile phones in this manner is or could be beneficial. When discussing cravings and efforts to maintain control over substance use habits, one participant expressed a desire to be able to connect with her mental health supports (P2H14): *"If I'm having a hard time with something or if I'm in a situation and I'm having a hard time coping I could just call somebody and talk to them. Because it gets really confusing and overwhelming sometimes."*

In contrast, when considering text messaging to communicate with healthcare providers, another participant expressed reservations about this and preferred phone conversations. This participant was uncomfortable with the idea of texting in these instances because she felt it violated an aspect of the healthcare provider-patient relationship: *"If they text messaged me, I'd find that odd. I just didn't find the need to do that with them. I don't know, is it unprofessional?"*(P2H10)

While no participants were currently using mobile devices to support medication adherence, conceptually the idea was viewed positively by many participants. One individual with underlying issues in remembering to take medications (scored 0/2 on MARS items related to forgetfulness or carelessness with medications) viewed text message communications and pill reminders very favorably: *"A text message to take my meds? Yes. Please. Sign me up for that."* (P2H12)

Some participants could not see an added benefit of medication adherence reminders via a mobile device. One such participant expressed her opinion on this potential reminder system: *"As it is right now, I think I'm pretty good for medications and keeping track of when my [antipsychotic shot] is due."*(P2H3). This individual reported a consistent routine and support system, including medication reminders from home care staff to rely upon for treatment adherence.

3.4 Discussion

We explored adherence and attitudes towards medications in individuals with a history of homelessness and mental health disorders. Approximately 90% of individuals in our study were classified as adherent, with an average MARS score of 7.3 out of 10. Medication adherence rates within the mental health population vary between studies, but are generally considered sub-optimal with estimates of 50% commonly reported.(4,5,37) Previous studies in patients with mental health disorders such as schizophrenia and bipolar disorder have found mean MARS scores ranging from 5.8 (SD=2.7) to 6.5 (SD=2.8).(38,39) While comparable to previous studies, the higher MARS scores in our study may be due to in part to greater insight and generally positive attitudes toward medications in our sample. Most participants in this study recognized the need to take their medications regularly due to insight into their relatively poor health status when non-adherent to therapy. Previous research has shown that insight can greatly affect medication-taking behavior. Novick *et al*. analyzed the relationship between insight and medication adherence (using MARS to assess adherence) on patient outcomes for those diagnosed with schizophrenia or bipolar disorder.(39) Patients with better insight into their mental health disorder were associated with higher medication adherence scores ($p<0.0001$) regardless of disorder type (schizophrenia or bipolar).(39) Similar findings on the effect of

insight and attitudes toward medications on adherence have been previously described using other measurement scales (40-42) and in patients with other mental health disorders such as depression.(43)

In our study, medication adherence behavior was influenced by patient-related and external factors. Patient factors included insight into one's illness and attitudes towards medications. Further, the concepts of stability, safety, and consistent routines were described by participants as key factors in establishing a "normal" life. Coping strategies such as avoidance of risky behaviors and boundary-setting in relationships were also frequently cited as mechanisms for participants to retain control over their environment. Feeling safe and establishing control often begins with having consistent and stable housing. Medication adherence rates in patients who are homeless or transiently-housed tend to be lower than the general or mental health population.(44-46) In our study, participants all had a history of homelessness which previously impacted their self-control and ability to establish stable routines. However, with stable housing in place, participants had a means to safely store their medications and avoid frequenting potential risky areas where substance use is common. The concepts of stability and control, as well as perceived efficacy of medication have been identified as crucial to maintaining medication adherence in previous studies. Tranulis *et al.* conducted semi-structured interviews in patients with schizophrenia in an effort to better understand the dynamic nature of medication adherence behaviors.(47) Through these interviews, a number of participants emphasized the importance of feeling in control of their lives, and that adherence to medication changed as one's perception of self-control was established.(47) In our study, many participants attributed normalcy and feeling in control to the efficacy of medications themselves, resulting in mostly positive attitudes toward medications and medication-taking. Attitudes toward medications and

their efficacy (or perceived efficacy) have frequently been associated with medication adherence behaviors in other studies. In a qualitative study exploring patient (as well as carers and professionals) perceptions on medication adherence in schizophrenia, Kikkert *et al.* identified that, to patients, medication efficacy was the most important factor influencing adherence.(48) A number of external factors, from health system supports to family and peer reassurance, also played a significant role in adherence behavior within this sample. Participants cited medication delivery, adherence packaging, and medication assistance activities of outreach staff in discussing their ability to adhere to therapy. All participants in this study received delivery of their medications, and all but one had adherence aid packaging (medication strips, blister packaging). Patients who are homeless or recently-housed often face challenges in retrieving their medications from pharmacies due to a lack of transportation and other factors; home delivery overcomes these barriers.(44,45,49) Previous research also noted that accessibility and timeliness of medication receipt influenced adherence.(48) Adherence packages, dosettes, and other medication organizers have been shown to significantly improve medication adherence.(50,51) In a retrospective cohort study of 1007 Medicaid participants, researchers examined the impact of specialized medication packaging synchronized with home delivery of medications and telephone-based monitoring, on medication adherence. In this study, the authors found significant improvement in medication adherence at 12 months; this effect remained significant in a subgroup analysis of patients taking psychiatric medications.(51) The provision of medications in adherence packages facilitates a more structured and organized approach to medication-taking, thereby overcoming barriers of forgetfulness and complicated regimens.(45)

The importance of the therapeutic alliance in supporting adherence behaviors was also identified

in our study. Individuals with mental health diagnoses and history of substance use often experience frequent disruptions in their social as well as health-related relationships.(5,21,23) These patients are further marginalized due to inconsistent follow-up with healthcare providers, which is a contributing factor for poor medication adherence in this population.(5,21,23) Individuals enrolled in the Pathways to Housing program are required to connect with a member of the ACT team on a weekly basis. Consistent access to care and the ability to attend appointments regularly are common barriers to medication adherence for individuals with mental illness and inconsistent or unstable housing. (4,49) The contact provided by the ACT team, which usually occurs within the individual's current residence, overcomes the barrier of regularly accessing care often seen in this population. Our results are consistent with other research describing the importance of the physician-patient relationship in supporting medication adherence for patients with schizophrenia (48), as well as support from family and friends.(47,48)

In terms of perceptions regarding mobile technology, our findings suggest that some individuals are interested in mobile technology-based interventions however this is not universal and significant barriers exist. About half of participants reported having access (owned or shared) to mobile phones. This is somewhat lower than what has been reported in the literature for individuals with mental illness (77%) but is comparable to reports describing mobile phone access for the homeless (44% to 62%).(9,23) Barriers to consistent mobile phone access identified in this study include cost considerations, theft, and technology literacy. The prohibitive costs of obtaining and maintaining mobile phone services for these individuals have previously been identified in the literature.(21-23) In Canada, mobile phone subscription costs are among the highest in the developed world – almost double the cost of subscriptions in

Europe.(52) Cost considerations regarding mobile phone access include acquisition, maintenance, and replacement costs. A potential strategy shown to facilitate regular mobile device access for homeless individuals involves the use of pre-paid phones instead of monthly plans.(53) Pre-paid phone plans allow flexibility in use as money can be added to accounts when available, as compared to monthly contract plans which require money to be available up-front. All participants with mobile phones in this study referenced monthly service plans during their interviews, so perhaps encouraging the use of pre-paid plans would enable further use of this technology. Technology literacy is another common barrier to adopting mobile phones into routine activities among marginalized individuals.(54) Research has suggested that, in those with low income backgrounds, lack of familiarity with mobile phones and other eHealth applications can hamper success of interventions designed in this fashion.(54) In our study we also found some participants felt overwhelmed with the capabilities of newer mobile devices, so offering easier-to-use interfaces may encourage uptake and adoption.

Among those individuals who described having consistent access to mobile devices, there was mixed feedback in terms of utilizing this technology to support their health. Some participants could not identify with the need for such technology-based interventions. This is likely due to the comprehensive supports provided to them from the Pathways to Housing team and others. While no participants were using their mobile devices for any medication adherence interventions, many were using their mobile phone as an important method of communicating with the Pathways to Housing team. Participants who did not see value in the use of mobile phones to support medication-taking typically had consistent reminder systems in place within their homes. This included the use of adherence packaging, assistance from housing program staff, and other reminder systems (e.g. placing medications on the night stand). Additionally,

some participants identified that implementing mobile phone-based reminders for medication-taking may become an annoyance. At least one participant expressed concerns about the privacy and professional aspect of using mobile devices to discuss health information with practitioners. While most participants had no concerns in this regard, privacy and confidentiality remains an important consideration that should be addressed prior to introducing such medication adherence interventions.

While much of the available literature examining mobile-based interventions in the mental health populations (or in those who are homeless or recently housed) report high levels of support and satisfaction with these services (12,13,23,55), our study suggests additional investigation is required to determine which individuals would benefit most from such interventions. Further, these interventions cannot simply be applied to a general population of individuals; rather, they must be targeted (in addition to other medication adherence supports) towards those who have capacity, interest, and defined need for such a service.

Rigor was achieved in this study by following principles of validity, reliability, and objectivity described previously.(56) This resulted in a thorough description of medication taking activities and views on potential for mobile phone supports within our sample. Further, the study investigator (TW) used a reflective approach by maintaining a journal to review and explore his assumptions, expectations, and overall impact on the data gathering process. However, this study is not without limitations. First, the MARS is a self-report scale and as such participants may have overestimated their level of adherence. Second, we intentionally selected individuals considered to be medically stable based on feedback from the Pathways to Housing psychiatrist and general practitioner. The intent in doing so was to ensure our discussion about medication adherence did not introduce stress into the lives of more chaotic individuals. However, it may be

that these individuals with less active and formalized supports for medication adherence would actually benefit the most from these interventions. Third, the participants included in this study were not homogenous in terms of mental health disorders but have common experiences with homelessness and substance use. These individuals were also being actively followed by multiple members of the Pathways to Housing team which makes it very challenging to generalize these results to other populations.

3.5 Conclusion

Our study identified that overall medication adherence was high and participants in our sample had generally positive attitudes toward medications. A number of patient-related and external factors, such as insight and therapeutic alliance, affected medication-taking. We further identified that the perceived need by participants for additional medication adherence interventions using mobile technology is not that high, as these individuals are already receiving wide-ranging housing and health services. Significant barriers to accessing and maintaining mobile devices are major limitations for designing future interventions.

Table 3.1 Interview questions

1. Tell me about your day from the moment you wake up, to the moment you go to bed.
    a. *Prompts – how does taking your medications fit in? What gets in the way of taking your medications*?
2. What helps you to remember to take your medications? What motivates you to take your medication
    a. *Prompts – Pathways team, medication packaging, reminders; family support, feeling well*

       --transition: thank you for sharing that information…I'd like to talk about how you use technology such as mobile phones.--
3. Do you currently own, share, or otherwise have access to a mobile phone? Tell me about how you use the phone.
    a. *Prompts: voice calls, text messaging, email, internet, take pictures, play games*
    b. *Prompts 2: use for health purposes?*
4. If you do <u>not</u> currently have access to a cell phone or mobile device, is there a reason for this?
    a. *Prompts:*
        i. *Too expensive, costly*
        ii. *Broke it, could not get fixed*
        iii. *Lost it, could not get replaced*
        iv. *Stolen, could not get replaced*
        v. *Don't need it*
        vi. *Too difficult to use*
        vii. *Got tired of it, was a hassle*
5. What do you think about using your mobile phone to communicate with your health team (Pathways, others on team)?
    a. *Prompts: What could be some benefits of this means of communication? Med reminders, connectivity/support, logistics*
    b. *Prompts 2: What are some barriers or concerns you can identify (example – is privacy a concern)? Frequency of contact, timeliness of response*

Table 3.2 Demographic characteristics and medical history

Characteristic	Overall (n=15)
Age, years; mean (SD)	44 (9)
Male, n (%)	8 (53)
Ethnicity, n (%)	
White[a]	10 (67)
Black	1 (7)
Aboriginal	3 (20)
Other[a]	2 (13)
Housing Status, n (%)	
Permanent	14 (93)
Temporary	1 (7)
Housing Duration, n (%)	
3 to 6 months	2 (13)
> 6 months	13 (87)
Education, n (%)	
some high school or less[c]	10 (67)

high school diploma[b]	2 (13)
some college[b,c]	3 (20)
college diploma	1 (7)
N/A	1 (7)
Employment, n (%)	
Volunteer	1 (7)
Temporary or Part-Time	1 (7)
Full-Time	1 (7)
Not Employed	12 (80)
Duration with P2H Program, n (%)	
1 to 2 years	1 (7)
>2 years	14 (93)
Mental Health Diagnoses, n (%)	
Schizophrenia	7 (47)
Bipolar Disorder	6 (40)
Depression	7 (47)
Anxiety Disorder	4 (27)

Other[d]	3 (20)
Addictions, n (%)	
Current Substance Use[e]	10 (67)
Past Substance Use[e]	5 (33)
N/A	1 (7)
Medication Supports, n (%)	
Home Delivery	15 (100)
Adherence Packaging	14 (93)
Other[f]	5 (33)

[a]one individual identified themselves as White and Aboriginal

[b]one individual obtained a high school diploma and attended college for a period thereafter

[c]one individual attended high school and college; no diplomas were obtained

[d]three patients reported diagnosis of PTSD

[e]one patient reported past and current substance abuse

[f]five patients reported receiving reminders to take their medications from community-based programs

Table 3.3 Items and frequencies of responses indicating adherence using the Medication Adherence Rating Scale (31)

Item	Response Indicating Adherence	Frequency of responses indicating adherence 'N' (%)
Do you ever forget to take your medicine?	"No"	6 (40.0)
Are you careless at times about taking your medicine	"No"	11 (73.3)
When you feel better, do you sometimes stop taking your medicine?	"No"	13 (86.7)
Sometimes if you feel worse taking meds, do you stop?	"No"	12 (80.0)
I take my medication only when I feel sick	"No"	15 (100)
It is unnatural to be controlled by medicine	"No"	12 (80.0)
My thoughts are clearer on medication	"Yes"	10 (66.7)
Staying on meds prevents me getting sick	"Yes"	11 (73.3)
I feel weird, like a 'zombie' on meds	"No"	10 (66.7)
Meds make me feel tired and sluggish	"No"	10 (66.7)

Table 3.4 Factors influencing medication adherence

Factor Affecting Adherence	Example Quotation
Patient Factors	
Coping and Boundary Setting	"I don't go down to the places anymore. People there are selling - and all down that street - you just walk down that street and everyone's selling something."
Routine	"I mark some of them with a black felt marker so I know which ones to take at bedtime. And the other ones I just take in the morning."
Insight	"I feel more stable, if you want to put it that way. My meds definitely levelled me out."
Attitude toward medications	"Um, you know I feel better now. But see I don't know if it's the medication or the help I'm getting or I don't know the attention. I mean I don't know what [the meds] are doing. I think they're important."
External Factors	
Family support	"I phoned my parents and said I have bipolar should I take [my medications]? And they [said] if it helps with your PTSD, definitely."
Peer support	"But it turns out there's a lot of people out there with the same issues."
Therapeutic support	"You know I can talk to [the pharmacist] if I have questions about something and he'll explain it to me or look it up."
Medication support	"Yeah, the packaging I like. It makes it easier."
Stigma	"The doctor there, I can't remember his name, but, uh, we'd only had two conversations maybe five or six minutes long each, and he said schizophrenic. I thought he came to that conclusion way too quickly."

3.6 References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: Challenges and management strategies. Patient Relat Outcome Meas. 2014;5:43-62.

(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med. 2005;353(5):487-497.

(3) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatric Services. 2007;58(6):855-863.

(4) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry. 2013;12(3):216-226.

(5) Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: A comprehensive review of recent literature. J Clin Psychiatry. 2002;63(10):892-909.

(6) Rush B, Urbanoski K, Bassani D, et al. Prevalence of co-occurring substance use and other mental disorders in the canadian population. Can J Psychiatry. 2008;53(12):800-809.

(7) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemedicine and e-Health. 2009;15(3):231-240.

(8) International Telecommunications Union. 2012 World Telecommunication Indicators Database. Statistical highlights. Available at: https://www.itu.int/ITU-D/ict/statistics/material/pdf/2011%20Statistical%20highlights_June_2012.pdf (accessed April 1, 2017).

(9) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Personal and Ubiquitous Computing. 2014.

(10) Berrouiguet S, Baca-García E, Brandt S, Walter M, Courtet P. Fundamentals for future mobile-health (mHealth):A systematic review of mobile phone and web-based text messaging in mental health. J Med Internet Res. 2016;18(6).

(11) Watson T, Simpson S, Hughes C. Text messaging interventions for individuals with mental health disorders including substance use: A systematic review. Psychiatry Res. 2016;243:255-262.

(12) Montes JM, Maurino J, Medina E. Short message service to improve treatment adherence and quality of life in patients with schizophrenia in spain: The sms study. European Psychiatry. 2012;27.

(13) Agyapong V, Ahern S, Farren C. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. Alcohol and Alcoholism. 2013;48:i24

(14) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs. 2014;35(5):323-329.

(15) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone-and text message-based telemedicine concept for patients with mental health disorders: Results of a randomized controlled trial. Psychother Psychosom. 2015;84(2):82-89.

(16) Stoner SA, Arenella PB, Hendershot CS. Randomized controlled trial of a mobile phone intervention for improving adherence to naltrexone for alcohol use disorders. PLoS ONE. 2015;10(4):e0124613.

(17) Moore DJ, Poquette A, Casaletto KB, et al. Individualized texting for adherence building (iTAB): Improving antiretroviral dose timing among HIV-infected persons with co-occurring bipolar disorder. AIDS Behav. 2015;19(3):459-471.
(18) Agyapong VI, Milnes J, McLoughlin DM, Farren CK. Perception of patients with alcohol use disorder and comorbid depression about the usefulness of supportive text messages. Technol Health Care. 2013;21(1):31-39.
(19) Proudfoot J, Parker G, Pavlovic DH, Manicavasagar V, Adler E, Whitton A. Community attitudes to the appropriation of mobile phones for monitoring and managing depression, anxiety, and stress. J Med Internet Res. 2010;12(5).
(20) Price M, Williamson D, McCandless R, et al. Hispanic migrant farm workers' attitudes toward mobile phone-based telehealth for management of chronic health conditions. J Med Internet Res. 2013;15(4).
(21) McInnes DK, Li AE, Hogan TP. Opportunities for engaging low-income, vulnerable populations in health care: A systematic review of homeless persons' access to and use of information technologies. Am J Public Health. 2013;103(SUPPL. 2).
(22) Asgary R, Sckell B, Alcabes A, Naderi R, Adongo P, Ogedegbe G. Perceptions, attitudes, and experience regarding mHealth among homeless persons in new york city shelters. J Health Commun. 2015;20(12):1473-1480.
(23) McInnes DK, Fix GM, Solomon JL, Petrakis BA, Sawh L, Smelson DA. Preliminary needs assessment of mobile technology use for healthcare among homeless veterans. Peerj. 2015;3:e1096.
(24) Mayan M. Essentials of Qualitative Inquiry. Walnut Creek, CA: Left Coast Press; 2009.
(25) Given L. The SAGE Encyclopedia of Qualitative Research Methods. Thousand Oaks, CA: SAGE Publications; 2008.
(26) Sandelowski M. Focus on research methods: Whatever happened to qualitative description? Res Nurs Health. 2000;23(4):334-340.
(27) Kvale S, Brinkman S. Interviews: Learning the craft of qualitative research interviewing. Thousand Oaks, CA: SAGE Publications; 2015.
(28) Services & Programs. Boyle McCauley Health Centre website. http://www.bmhc.net/. Accessed April 7, 2017.
(29) Pathways to Housing Program. Boyle McCauley Health Centre website. http://www.bmhc.net/services/pathwaystohousing.html. Accessed April 7, 2017.
(30) Bordens KS, Abbott BB. Research design and methods: A process approach. New York, NY: McGraw-Hill; 2002.
(31) Thomson K, Kulkarni K, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophr Res. 2000:42(3):241-47.
(32) Nguyen T, Caze AL, Cottrell N. What are validated self-report adherence scales really measuring?: A systematic review. Br J Clin Pharmacol. 2014;77(3):427-445.
(33) Zemmour K, Tinland A, Boucekine M, et al. Validation of the medication adherence rating scale in homeless patients with schizophrenia: Results from the french housing first experience. Sci Rep. 2016;6.
(34) Sajatovic M, Valenstein M, Blow F, et al. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv. 2007;58:855-63.

(35) Smith A. Americans and their cell phones. Pew Research Center, Internet and Technology website. http://www.pewinternet.org/2011/08/15/americans-and-their-cell-phones/. Accessed April 7, 2017.

(36) Silverman D. Qualitative Research 3rd Edition. London, UK: Sage Publications; 2011.

(37) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv. 1998;49(2):196-201.

(38) Fialko L, Garety PA, Kuipers E, et al. A large-scale validation study of the medication adherence rating scale (MARS). Schizophr Res. 2008;100(1-3):53-59.

(39) Novick D, Montgomery W, Treuer T, Aguado J, Kraemer S, Haro JM. Relationship of insight with medication adherence and the impact on outcomes in patients with schizophrenia and bipolar disorder: Results from a 1-year European outpatient observational study. BMC Psychiatry. 2015;15(1).

(40) Mohamed S, Rosenheck R, McEvoy J, Swartz M, Stroup S, Lieberman JA. Cross-sectional and longitudinal relationships between insight and attitudes toward medication and clinical outcomes in chronic schizophrenia. Schizophr Bull. 2009;35(2):336-346.

(41) Rosa AR, Marco M, Fachel JMG, Kapczinski F, Stein AT, Barros HMT. Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. Prog Neuro-Psychopharmacol Biol Psychiatry. 2007;31(1):217-224.

(42) Strauss JL, Johnson SL. 2006. Role of treatment alliance in the clinical management of bipolar disorder, stronger alliances prospectively predict fewer manic symptoms. Psychiatry Res 145: 215–223.

(43) Sirey AJ, Bruce ML, Kales HC. Improving antidepressant adherence and depression outcomes in primary care: The treatment initiation and participation (TIP) program. Am J Geriatr Psychiatry. 2010;18(6):554-562.

(44) Milloy M-, Kerr T, Bangsberg DR, et al. Homelessness as a structural barrier to effective antiretroviral therapy among HIV-seropositive illicit drug users in a Canadian setting. AIDS Patient Care STDS. 2012;26(1):60-67.

(45) Coe AB, Moczygemba LR, Gatewood SBS, Osborn RD, Matzke GR, Goode JVR. Medication adherence challenges among patients experiencing homelessness in a behavioral health clinic. Res Soc Adm Pharm. 2015;11(3):e110-e120.

(46) Kidder DP, Wolitski RJ, Campsmith ML, Nakamura GV. Health status, health care use, medication use, and medication adherence among homeless and housed people living with HIV/AIDS. Am J Public Health. 2007;97(12):2238-2245.

(47) Tranulis C, Goff D, Henderson DC, Freudenreich O. Becoming adherent to antipsychotics: A qualitative study of treatment-experienced schizophrenia patients. Psychiatr Serv. 2011;62(8):888-892.

(48) Kikkert MJ, Schene AH, Koeter MWJ, et al. Medication adherence in schizophrenia: Exploring patients', carers' and professionals' views. Schizophr Bull. 2006;32(4):786-794.

(49) Argintaru N, Chambers C, Gogosis E, et al. A cross-sectional observational study of unmet health needs among homeless and vulnerably housed adults in three canadian cities. BMC Public Health. 2013;13(1).

(50) Petersen ML, Wang Y, Van Der Laan MJ, Guzman D, Riley E, Bangsberg DR. Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: A marginal structural model analysis. Clin Infect Dis. 2007;45(7):908-915.

(51) Zillich AJ, Jaynes HAW, Snyder ME, et al. Evaluation of specialized medication packaging combined with medication therapy management: Adherence, outcomes, and costs among medicaid patients. Med Care. 2012;50(6):485-493.
(52) Price Comparisons of Wireline, Wireless and Internet Services in Canada and with Foreign Jurisdictions. Canadian Radio-television and Telecommunications Commission website: http://www.crtc.gc.ca/eng/publications/reports/wall2015/rp150618.htm. Accessed April 7, 2017.
(53) Le Dantec CA, Edwards WK. Designs on dignity: Perceptions of technology among the homeless. Conf Hum Fact Comput Syst Proc. 2008:627-636. Accessed 30 March 2017. doi: 10.1145/1357054.1357155.
(54) Jensen JD, King AJ, Davis LA, Guntzviller LM. Utilization of internet technology by low-income adults: The role of health literacy, health numeracy, and computer assistance. J Aging Health. 2010;22(6):804-826.
(55) Moczygemba LR, Cox LS, Marks SA, Robinson MA, Goode J-R, Jafari N. Homeless patients' perceptions about using cell phones to manage medications and attend appointments. Int J Pharm Pract. 2017; 25(3): 220-30.
(56) Morse JM, Barret M, Mayan M J, Olson K., Spiers,J. Verification strategies for establishing reliability and validity in qualitative research. Int J Qual Methods 2002;*1*(2):13–22.

CHAPTER 4: SUMMARY

4.1 General Discussion

Effective interventions for medication adherence are those that cover a range of determinants and are adapted to the individual's needs and expectations. Interventions that have been most successful, however, are relatively costly and labor-intense to implement.(1,2) Considering the significant health care costs associated with poor medication adherence, and the fact that medication adherence rates remain suboptimal, more efficient and practical solutions must be considered.(3-6) Medication adherence rates, while unsatisfactory in many disease states, are particularly an issue in the mental health population and those who face challenges maintaining stable housing.(7-9) Individuals with concomitant mental health diagnoses and unstable housing tend to be more marginalized as compared to other populations when it comes to establishing and maintaining regular health care. (10) Medication adherence rates and other activities indicative of healthy behavior tend to be impacted as a result. As one of the major barriers to positive health outcomes for these individuals remains regular contact with providers, proposed solutions to overcome this hurdle have included mobile-based technology platforms.(11) However, to understand whether such devices can be incorporated into the delivery of medication adherence interventions, further information regarding patient access to mobile phones and perceptions regarding their use for health care is required. Thus, this thesis addressed two distinct but related questions using different methodologies in an attempt to better understand how technology can support medication adherence in the mental health population. The results from both projects will help inform and direct development of more effective medication adherence interventions in the mental health population, including those that utilize mobile technology platforms.

4.1.1 Text messaging interventions for individuals with mental health disorders including substance use: a systematic review

The first project was a systematic review of the literature to examine the impact of text messaging interventions on medication adherence and health outcomes in individuals with mental health disorders, including substance use.(12) We synthesized the results of six randomized controlled trials and one prospective study that measured changes in medication adherence or health outcomes using validated mental health or general wellness scales. Measurement of adherence in these studies was varied, and included Medication Event Monitoring System (MEMS), pill count and patient self-report. To evaluate the methodology used in each study, we completed the tool developed by Downs and Black which assesses reporting quality, external validity, internal validity, and power.(13) There was significant variation in the nature of the text messaging construct: frequency of text messaging ranged from once weekly to twelve per day, delivery was random or user-controlled, while content was repetitive or unique with each interaction and was unidirectional or bidirectional in nature. Two of the studies used behavioral change theory and patient consultation in the development of the text message construct.

Five studies reported significant improvement in a variety of mental health and social functioning scales as a result of the text messaging intervention.(14-18) Medication adherence was measured in five studies, one of which reported significant improvement in this outcome in patients who were previously identified to have suboptimal adherence.(17) Further, in an analysis of subgroups, one study reported significant improvement in medication adherence among individuals who did not receive formal medication assistance.(16) These findings suggest that text messaging interventions may be most impactful for individuals with poor

underlying adherence and/or not receiving formalized medication supports. Further, studies that included text messaging and telephone interventions, tended to have greater impact on medication adherence or health outcomes when these interventions were combined as compared to either strategy when used alone. Methodological quality was found to be poor using the Downs and Black tool, largely due to small enrollment numbers, short intervention periods, and a lack of consistency in investigator blinding among the controlled trials. Based on these results, we concluded that text messaging interventions may assist in improving medication adherence and subsequent health outcomes within the mental health population. However, the inconsistencies and deficiencies in methodology used, including the variability of the text messaging construct, limit our ability to quantify this impact.

To our knowledge, this was the first systematic review of the literature examining the impact of text messaging on medication adherence in the mental health population. However, our results are similar to Berrouiget *et al.* who completed a systematic review of the applications of mobile phone text messaging in mental health care.(19) That review included randomized and non-randomized studies that examined text message interventions for mental health promotion, prevention, or monitoring. A variety of medical conditions were included in this review, from substance abuse to schizophrenia to eating disorder. Among the randomized studies, results were generally positive in terms of improving treatment adherence and monitoring symptoms. Text messaging was also effective at improving appointment attendance and was well-accepted by patients in all studies except one. The authors of this systematic review concluded that text messaging has promise in supporting management of mental health patients including medication adherence.

The results of our systematic review support the need for further research evaluating text

messaging interventions on medication adherence over a longer period of follow-up within the mental health population, particularly among those who have poor underlying adherence. We feel that text messaging interventions appear to be a promising tool as part of a coordinated comprehensive approach to patient care.

4.1.2 Perceptions of patients with mental health disorders on the role of mobile technology for supporting medication adherence

The intent of the second study was to better understand attitudes and opinions of individuals with mental health illness and history of unstable housing when it comes to medication adherence supports. This included ascertaining access to and attitudes toward mobile devices being used for health communications and medication-taking. We first sought to understand the problem of medication adherence and perspectives on medications and medication-taking among individuals enrolled in the Pathways to Housing Program, an organization that provides health services to individuals with concomitant housing instability and mental illness. We used the Medication Adherence Rating Scale (MARS) to assess adherence and attitudes towards medications.(20) We then completed face-to-face individual interviews with participants to discuss medications and medication supports, including the role of mobile devices and technology in health.

Overall, almost all participants scored in the "good adherence" range as indicated by the MARS (average of 7.3 out of 10). A number of patient factors such as coping mechanisms and insight as well as external factors such as frequent contact with health providers and adherence packaging, influenced medication adherence in this sample. Approximately half of participants had access to mobile phones and the concept of using mobile phones for medication adherence did not resonate with many participants. Those who identified benefits of using their mobile

device for such services tended to have less-structured medication-taking systems within their home, and scored relatively poorly on forgetfulness aspects of the MARS. In general, participants were more supportive of using their mobile devices for communications with their health team, as opposed to as a medication adherence tool, and cited convenience and timely contact as the main advantage in doing so. However, participants also identified a number of barriers to establishing and maintaining mobile phone services which impacted their receptivity to using them for health-related purposes. These barriers include: high cost of acquiring and maintaining mobile phones, theft/loss due to situational instability, and technology familiarity/literacy.

Approximately 50% of participants reported ownership or access to mobile phones in our study which is comparable to other literature.(21,22) Regarding attitudes toward the use of mobile devices for health purposes, participants expressed modest interest in such services or capabilities. Previous studies have shown relatively increased openness from patients when considering further utilization of mobile phones for medication adherence or health services.(22,23) We feel this difference is largely due to the presence of a number of external and patient-related factors, discussed earlier in this thesis. External factors, such as strong therapeutic alliances and home medication delivery with adherence packaging, help overcome many of the barriers to consistent care that comparable patients face, and allow responsive care to unique patient circumstances. This allows for the development of insight, coping strategies, and consistent medication-taking routines (patient factors). Our participants' subsequently had relatively high medication adherence and positive attitudes toward medications compared with similar studies.(7-9)

4.2 Implications and Future Directions

4.2.1 Implications for Clinical Practice

Improving adherence to chronic medications has been identified as one of the most important, if not the most important, direction for clinical practice in terms of improving health outcomes and reducing the burden of disease.(24) However, from the clinician perspective, medication adherence remains a challenging behavior to routinely address in practice due to time and system constraints.(25) For clinicians practicing in mental health who encounter patients facing housing stability challenges, engaging and supporting medication adherence poses an even greater challenge.(23) Medication adherence is an immensely complicated health behavior that is influenced by a variety of patient and system-related factors including knowledge and attitudes, social and therapeutic supports, and illness features such as symptom severity and comorbidities. (25) As such, comprehensive strategies and solutions, individualized to the patient in question, need to be introduced in order to see effective results.

This research suggests that coordinated multi-level interventions, as offered by the Pathways to Housing Program and related care providers (e.g. community pharmacy), are important in supporting medication adherence within the mental health and transitionally-housed population. While text messaging offers the potential to assist patients with mental health disorders in taking their medications regularly, access and affordability of mobile phones may be problematic particularly for individuals residing in the inner-city environment. Adherence interventions in practice should be individualized, taking into account the patient's needs and expectations. Our research suggests a possible role for utilizing mobile devices for regular, convenient communications with patients in practice. However, the impact of such mobile-based

interventions will only be as effective as the comprehensive approach taken by all team members within the therapeutic alliance.

4.2.2 Implications for Practice Research

These research projects have identified a number of gaps in the literature regarding the impact of technology-based medication adherence interventions for the mental health population. Firstly, there is an overall scarcity of data examining technology-based medication adherence interventions in individuals with mental health disorders. Prior to the outset of this project, no previous systematic reviews on this topic were identified; therefore we feel our work presents a significant contribution to the emerging field of technology-supported health delivery. Secondly, what data is available regarding such interventions is relatively poor in terms of methodological quality and utilizes innumerable content and construct approaches. Consequently, our ability to quantify and generalize results from these studies remains limited. Larger, randomized controlled trials conducted over a longer period of follow-up should be considered to more effectively understand the impact of technology-based medication adherence interventions. Thirdly, many of the studies examining technology-based medication adherence interventions were conducted as part of a single intervention. Future research is needed to examine the effect of incorporating mobile-based technology into other intervention initiatives (counselling, education, medication packaging) rather than replacing such offerings. This research should also look to include the patient in the development of intervention design to ensure alignment with construct and expectations. Finally, while this research provides patient perspectives on the utility of mobile technology for communicating about health and medications, future research must also consider the health practitioner's attitudes and beliefs regarding the potential of such

interventions.

4.3 Conclusion

This thesis examined the role of mobile phone interventions to support medication adherence in patients with mental health disorders. Our findings suggest that text messaging interventions may be effective in supporting medication adherence, particularly among those individuals with underlying challenges taking medications. However, use of technology-based interventions need to be designed in conjunction with patient needs, and used in combination with complementary strategies addressing multiple determinants of medication-taking.

4.4 References

(1) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.

(2) Furiak NM, Ascher-Svanum H, Klein RW, Smolen LJ, Lawson AH, Montgomery W, et al. Cost-effectiveness of olanzapine long-acting injection in the treatment of patients with schizophrenia in the United States: A micro-simulation economic decision model. Curr Med Res Opin 2011;27(4):713-730.

(3) IMS Institute for Health Care. Avoidable Costs in U.S. Health Care. Available at: http://www.imshealth.com:90/en/thought-leadership/quintilesims-institute/reports/avoidable-costs (accessed April 1, 2017).

(4) Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007;167(6):540-550.

(5) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49(2):196-201.

(6) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).

(7) Milloy M-, Kerr T, Bangsberg DR, et al. Homelessness as a structural barrier to effective antiretroviral therapy among HIV-seropositive illicit drug users in a Canadian setting. AIDS Patient Care STDS. 2012;26(1):60-67.

(8) Coe AB, Moczygemba LR, Gatewood SBS, Osborn RD, Matzke GR, Goode JVR. Medication adherence challenges among patients experiencing homelessness in a behavioral health clinic. Res Soc Adm Pharm. 2015;11(3):e110-e120.

(9) Kidder DP, Wolitski RJ, Campsmith ML, Nakamura GV. Health status, health care use, medication use, and medication adherence among homeless and housed people living with HIV/AIDS. Am J Public Health. 2007;97(12):2238-2245.

(10) Argintaru N, Chambers C, Gogosis E, et al. A cross-sectional observational study of unmet health needs among homeless and vulnerably housed adults in three Canadian cities. BMC Public Health. 2013;13(1).

(11) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemed J E Health 2009;15(3):231-240.

(12) Watson T, Simpson S, Hughes C. Text messaging interventions for individuals with mental health disorders including substance use: A systematic review. Psychiatry Res. 2016;243:255-262.

(13) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998; 52:377–384.

(14) Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. J Affect Disord 2012;141(2-3):168-176.

(15) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs 2014;35(5):323-329.
(16) Granholm E, Ben-Zeev D, Link PC, Bradshaw KR, Holden JL. Mobile assessment and treatment for schizophrenia (MATS): A pilot trial of an interactive text-messaging intervention for medication adherence, socialization, and auditory hallucinations. Schizophr Bull 2012;38(3):414-425.
(17) Montes JM, Medina E, Gomez-Beneyto M, Maurino J. A short message service (SMS)-based strategy for enhancing adherence to antipsychotic medication in schizophrenia. Psychiatry Res 2012;200(2-3):89-95.
(18) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone- and text message-based telemedicine concept for patients with mental health disorders: results of a randomized controlled trial. Psychother Psychosom 2015;84(2):82-89.
(19) Berrouiguet S, Baca-García E, Brandt S, Walter M, Courtet P. Fundamentals for future mobile-health (mHealth):A systematic review of mobile phone and web-based text messaging in mental health. J Med Internet Res. 2016;18(6).
(20) Thomson K, Kulkarni K, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophr Res. 2000:42(3):241-47.
(21) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Compu 2015; 19(2):367-378.
(22) McInnes DK, Fix GM, Solomon JL, Petrakis BA, Sawh L, Smelson DA. Preliminary needs assessment of mobile technology use for healthcare among homeless veterans. Peerj. 2015;3:e1096.
(23) Moczygemba LR, Cox LS, Marks SA, Robinson MA, Goode J-R, Jafari N. Homeless patients' perceptions about using cell phones to manage medications and attend appointments. Int J Pharm Pract. 2017; 25(3): 220-30.
(24) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).
(25) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry. 2013;12(3):216-226.

BIBLIOGRAPHY

Chapter 1: Introduction Chapter References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. Patient Relat Outcome Meas 2014;5:43-62.
(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med 2005;353(5):487-497.
(3) Dimatteo RM, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40(9):794-811.
(4) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).
(5) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv 2007;58(6):855-863.
(6) DiBonaventura M, Gabriel S, Dupclay L, Gupta S, Kim E. A patient perspective of the impact of medication side effects on adherence: Results of a cross-sectional nationwide survey of patients with schizophrenia. BMC Psychiatry 2012;12.
(7) Adelufosi AO, Adebowale TO, Abayomi O, Mosanya JT. Medication adherence and quality of life among Nigerian outpatients with schizophrenia. Gen Hosp Psychiatry 2012;34(1):72-79.
(8) Dassa D, Boyer L, Benoit M, Bourcet S, Raymondet P, Bottai T. Factors associated with medication non-adherence in patients suffering from schizophrenia: A cross-sectional study in a universal coverage health-care system. Aust New Zealand J Psychiatry 2010;44(10):921-928.
(9) Waterreus A, Morgan VA, Castle D, Galletly C, Jablensky A, Di Prinzio P, et al. Medication for psychosis - Consumption and consequences: The second Australian national survey of psychosis. Aust New Zealand J Psychiatry 2012;46(8):762-773.
(10) Bulloch AGM, Patten SB. Non-adherence with psychotropic medications in the general population. Soc Psychiatry Psychiatr Epidemiol 2010;45(1):47-56.
(11) Berk L, Hallam KT, Colom F, Vieta E, Hasty M, Macneil C, et al. Enhancing medication adherence in patients with bipolar disorder. Hum Psychopharmacol 2010;25(1):1-16.
(12) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry 2013;12(3):216-226.
(13) Weiss RD. Adherence to pharmacotherapy in patients with alcohol and opioid dependence. Addiction 2004;99(11):1382-1392
(14) Sowers W, Golden S. Psychotropic medication management in persons with co-occurring psychiatric and substance use disorders. J Psychoactive Drugs 1999;31(1):59-70.
(15) Magura S, Laudet AB, Mahmood D, Rosenblum A, Knight E. Adherence to medication regimens and participation in dual-focus self-help groups. Psychiatr Serv 2002;53(3):310-316.
(16) Iuga AO, McGuire MJ. Adherence and health care costs. Risk Manag Healthc Policy 2014;7:35-44.
(17) IMS Institute for Health Care. Avoidable Costs in U.S. Health Care. Available at: http://www.imshealth.com:90/en/thought-leadership/quintilesims-institute/reports/avoidable-costs (accessed April 1, 2017).

(18) Gianfrancesco FD, Sajatovic M, Rajagopalan K, Wang R-. Antipsychotic treatment adherence and associated mental health care use among individuals with bipolar disorder. Clin Ther 2008;30(7):1358-1374.
(19) Watanabe JH, Bounthavong M, Chen T. Revisiting the medication possession ratio threshold for adherence in lipid management. Curr Med Res Opin 2013;29(3):175-180.
(20) Hong J, Reed C, Novick D, Haro JM, Aguado J. Clinical and economic consequences of medication non-adherence in the treatment of patients with a manic/mixed episode of bipolar disorder: Results from the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) Study. Psychiatry Res 2011;190(1):110-114.
(21) Ho SC, Chong HY, Chaiyakunapruk N, Tangiisuran B, Jacob SA. Clinical and economic impact of non-adherence to antidepressants in major depressive disorder: a systematic review. J Affective Disord 2016;193:1-10.
(22) Peng X, Ascher-Svanum H, Faries D, Conley RR, Schuh KJ. Decline in hospitalization risk and health care cost after initiation of depot antipsychotics in the treatment of schizophrenia. Clin Outcomes Res 2011;3(1):9-14.
(23) Dilla T, Ciudad A, Álvarez M. Systematic review of the economic aspects of nonadherence to antipsychotic medication in patients with schizophrenia. Patient Prefer Adherence 2013;7:275-284.
(24) Pasma A, Hazes JMW, Luime JJ, Busschbach JJV, van 't Spijker A. How to study determinants related to medication adherence in newly diagnosed polyarthritis patients for the development of a prediction instrument. Patient Prefer Adherence 2014;8:1437-1447.
(25) Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock S, Wines RC, et al. Closing the quality gap: revisiting the state of the science (vol. 4: medication adherence interventions: comparative effectiveness). Evid Rep Technol Assess (Full Rep) 2012(208 .4):1-685.
(26) Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B. Effectiveness of Interventions to Improve Patient Compliance a Meta-Analysis. Med Care 1998;36(8):1138-1161.
(27) Bogner HR, de Vries HF. Integrating type 2 diabetes mellitus and depression treatment among African Americans: A randomized controlled pilot trial. Diabetes Educ 2010;36(2):284-292.
(28) Velligan DI, Diamond PM, Mintz J, Maples N, Li X, Zeber J, et al. The use of individually tailored environmental supports to improve medication adherence and outcomes in schizophrenia. Schizophr Bull 2008;34(3):483-493.
(29) Goff DC, Hill M, Freudenreich O. Strategies for improving treatment adherence in schizophrenia and schizoaffective disorder. J Clin Psychiatry 2010;71(SUPPL. 2):20-26.
(30) Farooq S, Naeem F. Tackling nonadherence in psychiatric disorders: Current opinion. Neuropsychiatr Dis Treat 2014;10:1069-1077.
(31) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.
(32) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemed J E Health 2009;15(3):231-240.
(33) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Compu 2015; 19(2):367-378.
(34) International Telecommunications Union. 2012 World Telecommunication Indicators Database. Statistical highlights. Available at: https://www.itu.int/ITU-D/ict/statistics/material/pdf/2011%20Statistical%20highlights_June_2012.pdf (accessed April 1, 2017).

(35) Arora S, Peters AL, Burner E, Lam CN, Menchine M. Trial to examine text message-based mHealth in emergency department patients with diabetes (TExT-MED): a randomized controlled trial. Ann Emerg Med 2014 Jun;63(6):745-54.e6.
(36) Suffoletto B, Callaway C, Kristan J, Kraemer K, Clark DB. Text-message-based drinking assessments and brief interventions for young adults discharged from the emergency department. Alcohol Clin Exp Res 2012 Mar;36(3):552-560.

Chapter 2: Systematic Review References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: Challenges and management strategies. Patient Relat Outcome Meas 2014;5:43-62.
(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med 2005;353(5):487-497.
(3) Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007;167(6):540-550.
(4) Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43(6):521-530.
(5) Dimatteo RM, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002;40(9):794-811.
(6) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).
(7) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49(2):196-201.
(8) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv 2007;58(6):855-863.
(9) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry 2013;12(3):216-226.
(10) Julius RJ, Novitsky MA, Dubin WR. Medication adherence: A review of the literature and implications for clinical practice. J Psychiatr Pract 2009;15(1):34-44.
(11) Sowers W, Golden S. Psychotropic medication management in persons with co-occurring psychiatric and substance use disorders. J Psychoactive Drugs 1999;31(1):59-70.
(12) Weiss RD. Adherence to pharmacotherapy in patients with alcohol and opioid dependence. Addiction 2004;99(11):1382-1392.
(13) Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: A comprehensive review of recent literature. J Clin Psychiatry 2002;63(10):892-909.
(14) Farooq S, Naeem F. Tackling nonadherence in psychiatric disorders: Current opinion. Neuropsychiatr Dis Treat 2014;10:1069-1077.
(15) Berk L, Hallam KT, Colom F, et al. Enhancing medication adherence in patients with bipolar disorder. Hum Psychopharmacol. 2010;25(1):1-16.
(16) Chong WW, Aslani P, Chen TF. Effectiveness of interventions to improve antidepressant medication adherence: a systematic review. Int J Clin Pract 2011;65(9):954-975.
(17) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.
(18) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: a systematic review. Telemed J E Health 2009;15(3):231-240.
(19) International Telecommunications Union, 2012. ITUWorldTelecommunication/ICT Indicators Database. Statistical highlights. Available at: ⟨http://www.itu.int/ITU- D/ict/⟩ (accessed April 2, 2015).

(20) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Comput 2014;19:367-78.
(21) U.S.Department of Health and Human Services, May 2014. Using Health Text Messages to Improve Consumer Health Knowledge, Behaviors, and Outcomes: an Environmental Scan. Available at: ⟨http://www.hrsa.gov/healthit/txt4tots/ environmentalscan.pdf⟩ (accessed April 2, 2015).
(22) Schnall R, Okoniewski A, Tiase V, Low A, Rodriguez M, Kaplan S. Using text messaging to assess adolescents' health information needs: an ecological momentary assessment. J Med Internet Res 2013;15(3). Accessed 21 March 2015.
(23) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998; 52:377–384.
(24) Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. J Affect Disord 2012;141(2-3):168-176.
(25) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs 2014;35(5):323-329.
(26) Granholm E, Ben-Zeev D, Link PC, Bradshaw KR, Holden JL. Mobile assessment and treatment for schizophrenia (MATS): A pilot trial of an interactive text-messaging intervention for medication adherence, socialization, and auditory hallucinations. Schizophr Bull 2012;38(3):414-425.
(27) Montes JM, Medina E, Gomez-Beneyto M, Maurino J. A short message service (SMS)-based strategy for enhancing adherence to antipsychotic medication in schizophrenia. Psychiatry Res 2012;200(2-3):89-95.
(28) Moore DJ, Poquette A, Casaletto KB, et al. Individualized texting for adherence building (iTAB): Improving antiretroviral dose timing among HIV-infected persons with co-occurring bipolar disorder. AIDS Behav 2015;19(3):459-471.
(29) Stoner SA, Arenella PB, Hendershot CS. Randomized controlled trial of a mobile phone intervention for improving adherence to naltrexone for alcohol use disorders. PLoS ONE 2015;10(4).
(30) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone-and text message-based telemedicine concept for patients with mental health disorders: results of a randomized controlled trial. Psychother Psychosom 2015;84(2):82-89.
(31) Furber G, Jones GM, Healey D, Bidargaddi N. A comparison between phone-based psychotherapy with and without text messaging support in between sessions for crisis patients. J Med Internet Res 2014;16:43-54.
(32) Španiel F, Hrdlicka J, Novák T, et al. Effectiveness of the information technology-aided program of relapse prevention in schizophrenia (ITAREPS): a randomized, controlled, double-blind study. J Psychiatr Pract 2012;18(4):269-280.
(33) Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoSMed 2009;6:e1000097.

Chapter 3: Qualitative Study References

(1) Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: Challenges and management strategies. Patient Relat Outcome Meas. 2014;5:43-62.
(2) Osterberg L, Blaschke T. Adherence to medication. New Engl J Med. 2005;353(5):487-497.
(3) Sajatovic M, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv. 2007;58(6):855-863.
(4) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry. 2013;12(3):216-226.
(5) Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: A comprehensive review of recent literature. J Clin Psychiatry. 2002;63(10):892-909.
(6) Rush B, Urbanoski K, Bassani D, et al. Prevalence of co-occurring substance use and other mental disorders in the Canadian population. Can J Psychiatry. 2008;53(12):800-809.
(7) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemedicine and e-Health. 2009;15(3):231-240.
(8) International Telecommunications Union. 2012 World Telecommunication Indicators Database. Statistical highlights. Available at: https://www.itu.int/ITU-D/ict/statistics/material/pdf/2011%20Statistical%20highlights_June_2012.pdf (accessed April 1, 2017).
(9) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Personal and Ubiquitous Computing. 2014.
(10) Berrouiguet S, Baca-García E, Brandt S, Walter M, Courtet P. Fundamentals for future mobile-health (mHealth):A systematic review of mobile phone and web-based text messaging in mental health. J Med Internet Res. 2016;18(6).
(11) Watson T, Simpson S, Hughes C. Text messaging interventions for individuals with mental health disorders including substance use: A systematic review. Psychiatry Res. 2016;243:255-262.
(12) Montes JM, Maurino J, Medina E. Short message service to improve treatment adherence and quality of life in patients with schizophrenia in Spain: The sms study. European Psychiatry. 2012;27.
(13) Agyapong V, Ahern S, Farren C. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. Alcohol and Alcoholism. 2013;48:i24
(14) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs. 2014;35(5):323-329.
(15) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone-and text message-based telemedicine concept for patients with mental health disorders: Results of a randomized controlled trial. Psychother Psychosom. 2015;84(2):82-89.
(16) Stoner SA, Arenella PB, Hendershot CS. Randomized controlled trial of a mobile phone intervention for improving adherence to naltrexone for alcohol use disorders. PLoS ONE. 2015;10(4):e0124613.

(17) Moore DJ, Poquette A, Casaletto KB, et al. Individualized texting for adherence building (iTAB): Improving antiretroviral dose timing among HIV-infected persons with co-occurring bipolar disorder. AIDS Behav. 2015;19(3):459-471.
(18) Agyapong VI, Milnes J, McLoughlin DM, Farren CK. Perception of patients with alcohol use disorder and comorbid depression about the usefulness of supportive text messages. Technol Health Care. 2013;21(1):31-39.
(19) Proudfoot J, Parker G, Pavlovic DH, Manicavasagar V, Adler E, Whitton A. Community attitudes to the appropriation of mobile phones for monitoring and managing depression, anxiety, and stress. J Med Internet Res. 2010;12(5).
(20) Price M, Williamson D, McCandless R, et al. Hispanic migrant farm workers' attitudes toward mobile phone-based telehealth for management of chronic health conditions. J Med Internet Res. 2013;15(4).
(21) McInnes DK, Li AE, Hogan TP. Opportunities for engaging low-income, vulnerable populations in health care: A systematic review of homeless persons' access to and use of information technologies. Am J Public Health. 2013;103(SUPPL. 2).
(22) Asgary R, Sckell B, Alcabes A, Naderi R, Adongo P, Ogedegbe G. Perceptions, attitudes, and experience regarding mHealth among homeless persons in new york city shelters. J Health Commun. 2015;20(12):1473-1480.
(23) McInnes DK, Fix GM, Solomon JL, Petrakis BA, Sawh L, Smelson DA. Preliminary needs assessment of mobile technology use for healthcare among homeless veterans. Peerj. 2015;3:e1096.
(24) Mayan M. Essentials of Qualitative Inquiry. Walnut Creek, CA: Left Coast Press; 2009.
(25) Given L. The SAGE Encyclopedia of Qualitative Research Methods. Thousand Oaks, CA: SAGE Publications; 2008.
(26) Sandelowski M. Focus on research methods: Whatever happened to qualitative description? Res Nurs Health. 2000;23(4):334-340.
(27) Kvale S, Brinkman S. Interviews: Learning the craft of qualitative research interviewing. Thousand Oaks, CA: SAGE Publications; 2015.
(28) Services & Programs. Boyle McCauley Health Centre website. http://www.bmhc.net/. Accessed April 7, 2017.
(29) Pathways to Housing Program. Boyle McCauley Health Centre website. http://www.bmhc.net/services/pathwaystohousing.html. Accessed April 7, 2017.
(30) Bordens KS, Abbott BB. Research design and methods: A process approach. New York, NY: McGraw-Hill; 2002.
(31) Thomson K, Kulkarni K, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophr Res. 2000:42(3):241-47.
(32) Nguyen T, Caze AL, Cottrell N. What are validated self-report adherence scales really measuring?: A systematic review. Br J Clin Pharmacol. 2014;77(3):427-445.
(33) Zemmour K, Tinland A, Boucekine M, et al. Validation of the medication adherence rating scale in homeless patients with schizophrenia: Results from the french housing first experience. Sci Rep. 2016;6.
(34) Sajatovic M, Valenstein M, Blow F, et al. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. Psychiatr Serv. 2007;58:855-63.

(35) Smith A. Americans and their cell phones. Pew Research Center, Internet and Technology website. http://www.pewinternet.org/2011/08/15/americans-and-their-cell-phones/. Accessed April 7, 2017.

(36) Silverman D. Qualitative Research 3rd Edition. London, UK: Sage Publications; 2011.

(37) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv. 1998;49(2):196-201.

(38) Fialko L, Garety PA, Kuipers E, et al. A large-scale validation study of the medication adherence rating scale (MARS). Schizophr Res. 2008;100(1-3):53-59.

(39) Novick D, Montgomery W, Treuer T, Aguado J, Kraemer S, Haro JM. Relationship of insight with medication adherence and the impact on outcomes in patients with schizophrenia and bipolar disorder: Results from a 1-year european outpatient observational study. BMC Psychiatry. 2015;15(1).

(40) Mohamed S, Rosenheck R, McEvoy J, Swartz M, Stroup S, Lieberman JA. Cross-sectional and longitudinal relationships between insight and attitudes toward medication and clinical outcomes in chronic schizophrenia. Schizophr Bull. 2009;35(2):336-346.

(41) Rosa AR, Marco M, Fachel JMG, Kapczinski F, Stein AT, Barros HMT. Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. Prog Neuro-Psychopharmacol Biol Psychiatry. 2007;31(1):217-224.

(42) Strauss JL, Johnson SL. 2006. Role of treatment alliance in the clinical management of bipolar disorder, stronger alliances prospectively predict fewer manic symptoms. Psychiatry Res 145: 215–223.

(43) Sirey AJ, Bruce ML, Kales HC. Improving antidepressant adherence and depression outcomes in primary care: The treatment initiation and participation (TIP) program. Am J Geriatr Psychiatry. 2010;18(6):554-562.

(44) Milloy M-, Kerr T, Bangsberg DR, et al. Homelessness as a structural barrier to effective antiretroviral therapy among HIV-seropositive illicit drug users in a Canadian setting. AIDS Patient Care STDS. 2012;26(1):60-67.

(45) Coe AB, Moczygemba LR, Gatewood SBS, Osborn RD, Matzke GR, Goode JVR. Medication adherence challenges among patients experiencing homelessness in a behavioral health clinic. Res Soc Adm Pharm. 2015;11(3):e110-e120.

(46) Kidder DP, Wolitski RJ, Campsmith ML, Nakamura GV. Health status, health care use, medication use, and medication adherence among homeless and housed people living with HIV/AIDS. Am J Public Health. 2007;97(12):2238-2245.

(47) Tranulis C, Goff D, Henderson DC, Freudenreich O. Becoming adherent to antipsychotics: A qualitative study of treatment-experienced schizophrenia patients. Psychiatr Serv. 2011;62(8):888-892.

(48) Kikkert MJ, Schene AH, Koeter MWJ, et al. Medication adherence in schizophrenia: Exploring patients', carers' and professionals' views. Schizophr Bull. 2006;32(4):786-794.

(49) Argintaru N, Chambers C, Gogosis E, et al. A cross-sectional observational study of unmet health needs among homeless and vulnerably housed adults in three Canadian cities. BMC Public Health. 2013;13(1).

(50) Petersen ML, Wang Y, Van Der Laan MJ, Guzman D, Riley E, Bangsberg DR. Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: A marginal structural model analysis. Clin Infect Dis. 2007;45(7):908-915.

(51) Zillich AJ, Jaynes HAW, Snyder ME, et al. Evaluation of specialized medication packaging combined with medication therapy management: Adherence, outcomes, and costs among medicaid patients. Med Care. 2012;50(6):485-493.
(52) Price Comparisons of Wireline, Wireless and Internet Services in Canada and with Foreign Jurisdictions. Canadian Radio-television and Telecommunications Commission website: http://www.crtc.gc.ca/eng/publications/reports/wall2015/rp150618.htm. Accessed April 7, 2017.
(53) Le Dantec CA, Edwards WK. Designs on dignity: Perceptions of technology among the homeless. Conf Hum Fact Comput Syst Proc. 2008:627-636. Accessed 30 March 2017. doi: 10.1145/1357054.1357155.
(54) Jensen JD, King AJ, Davis LA, Guntzviller LM. Utilization of internet technology by low-income adults: The role of health literacy, health numeracy, and computer assistance. J Aging Health. 2010;22(6):804-826.
(55) Moczygemba LR, Cox LS, Marks SA, Robinson MA, Goode J-R, Jafari N. Homeless patients' perceptions about using cell phones to manage medications and attend appointments. Int J Pharm Pract. 2017; 25(3): 220-30.
(56) Morse JM, Barret M, Mayan M J, Olson K., Spiers,J. Verification strategies for establishing reliability and validity in qualitative research. Int J Qual Methods 2002;*1*(2):13–22.

Chapter 4: Discussion References

(1) Granger BB, Bosworth HB. Medication adherence: Emerging use of technology. Curr Opin Cardiol 2011;26(4):279-287.

(2) Furiak NM, Ascher-Svanum H, Klein RW, Smolen LJ, Lawson AH, Montgomery W, et al. Cost-effectiveness of olanzapine long-acting injection in the treatment of patients with schizophrenia in the United States: A micro-simulation economic decision model. Curr Med Res Opin 2011;27(4):713-730.

(3) IMS Institute for Health Care. Avoidable Costs in U.S. Health Care. Available at: http://www.imshealth.com:90/en/thought-leadership/quintilesims-institute/reports/avoidable-costs (accessed April 1, 2017).

(4) Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. Arch Intern Med 2007;167(6):540-550.

(5) Cramer JA, Rosenheck R. Compliance with medication regimens for mental and physical disorders. Psychiatr Serv 1998;49(2):196-201.

(6) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).

(7) Milloy M-, Kerr T, Bangsberg DR, et al. Homelessness as a structural barrier to effective antiretroviral therapy among HIV-seropositive illicit drug users in a Canadian setting. AIDS Patient Care STDS. 2012;26(1):60-67.

(8) Coe AB, Moczygemba LR, Gatewood SBS, Osborn RD, Matzke GR, Goode JVR. Medication adherence challenges among patients experiencing homelessness in a behavioral health clinic. Res Soc Adm Pharm. 2015;11(3):e110-e120.

(9) Kidder DP, Wolitski RJ, Campsmith ML, Nakamura GV. Health status, health care use, medication use, and medication adherence among homeless and housed people living with HIV/AIDS. Am J Public Health. 2007;97(12):2238-2245.

(10) Argintaru N, Chambers C, Gogosis E, et al. A cross-sectional observational study of unmet health needs among homeless and vulnerably housed adults in three Canadian cities. BMC Public Health. 2013;13(1).

(11) Krishna S, Boren SA, Balas EA. Healthcare via cell phones: A systematic review. Telemed J E Health 2009;15(3):231-240.

(12) Watson T, Simpson S, Hughes C. Text messaging interventions for individuals with mental health disorders including substance use: A systematic review. Psychiatry Res. 2016;243:255-262.

(13) Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998; 52:377–384.

(14) Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: Single-blind randomised trial. J Affect Disord 2012;141(2-3):168-176.

(15) Beebe L, Smith KD, Phillips C. A comparison of telephone and texting interventions for persons with schizophrenia spectrum disorders. Issues Ment Health Nurs 2014;35(5):323-329.
(16) Granholm E, Ben-Zeev D, Link PC, Bradshaw KR, Holden JL. Mobile assessment and treatment for schizophrenia (MATS): A pilot trial of an interactive text-messaging intervention for medication adherence, socialization, and auditory hallucinations. Schizophr Bull 2012;38(3):414-425.
(17) Montes JM, Medina E, Gomez-Beneyto M, Maurino J. A short message service (SMS)-based strategy for enhancing adherence to antipsychotic medication in schizophrenia. Psychiatry Res 2012;200(2-3):89-95.
(18) Van Den Berg N, Grabe H-, Baumeister SE, Freyberger HJ, Hoffmann W. A telephone- and text message-based telemedicine concept for patients with mental health disorders: results of a randomized controlled trial. Psychother Psychosom 2015;84(2):82-89.
(19) Berrouiguet S, Baca-García E, Brandt S, Walter M, Courtet P. Fundamentals for future mobile-health (mHealth):A systematic review of mobile phone and web-based text messaging in mental health. J Med Internet Res. 2016;18(6).
(20) Thomson K, Kulkarni K, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizophr res. 2000:42(3):241-47.
(21) Campbell B, Caine K, Connelly K, Doub T, Bragg A. Cell phone ownership and use among mental health outpatients in the USA. Pers Ubiquitous Compu 2015; 19(2):367-378.
(22) McInnes DK, Fix GM, Solomon JL, Petrakis BA, Sawh L, Smelson DA. Preliminary needs assessment of mobile technology use for healthcare among homeless veterans. Peerj. 2015;3:e1096
(23) Moczygemba LR, Cox LS, Marks SA, Robinson MA, Goode J-R, Jafari N. Homeless patients' perceptions about using cell phones to manage medications and attend appointments. Int J Pharm Pract. 2017; 25(3): 220-30.
(24) World Health Organization. Adherence to Long-term therapies: Evidence for Action. Available at: http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf (accessed April 1, 2017).
(25) Kane JM, Kishimoto T, Correll CU. Non-adherence to medication in patients with psychotic disorders: Epidemiology, contributing factors and management strategies. World Psychiatry. 2013;12(3):216-226.

Appendix A: University of Alberta Ethics Approval

Date:	May 18, 2016
Study ID:	Pro00061551
Principal Investigator:	Christine Hughes
Study Title:	**Perceptions of patients with mental health diseases on the role of text messaging for supporting medication adherence**
Approval Expiry Date:	Wednesday, May 17, 2017
Approved Consent Form:	Approval Date Approved Document 5/18/2016 Patient Information Letter and Consent.docx 5/18/2016 Consent for Release of Contact Information
Sponsor/Funding Agency:	University of Alberta

Thank you for submitting the above study to the Health Research Ethics Board - Health Panel . Your application, including the following, has been reviewed and approved on behalf of the committee;

Interview Guide (3/8/2016)
Participant Survey Final (5/10/2016)
Research Proposal (5/10/2016)

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. Subject consent for access to identifiable health information is required for the research described in the ethics application, and appropriate procedures for such consent have been approved by the HREB Health Panel. In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (Wednesday, May 17, 2017), you will have to re-submit an ethics application.
Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approval should be directed to (780) 407-6041. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,
Anthony S. Joyce, Ph.D.
Chair, Health Research Ethics Board - Health Panel
Note: This correspondence includes an electronic signature (validation and approval via an online system

Appendix B: Consent for Release of Contact Information Form

UNIVERSITY OF ALBERTA

FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

3-171 Edmonton Clinic Health Academy
11405 – 87 Ave
Edmonton, Alberta, Canada T6G 1C9
Tel: 780.492.3362
Fax: 780.492.1217
www.pharmacy.ualberta.ca

Consent for Release of Contact Information

Study Title: Perceptions of patients with mental health diseases on the role of text messaging for supporting medication adherence

Investigators:

Dr. Christine Hughes, Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta

Mr. Tyler Watson, MSc Pharmacy Student, Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta

This form is for you to provide consent for a member of the study team to contact you to tell you more about the research study and see if you might be interested in taking part.

Study Summary:

There are a number of reasons why people do not take their medications, and a number of ways to help people take their medicines. We are interested in better understanding how people with mental illness take their medications, as well as what they think about their medicines. We also want to understand how technology, such as mobile phone text-messaging, can help people take their medicines. This study will involve a short survey that you will be asked to complete and a one-on-one interview. The survey has questions about how you take your medicine and your thoughts about your medicine. The interview has questions about your access to mobile phones and your thoughts on using a mobile phone to communicate with your health care providers

Completing this form does not provide consent to participate in the study. You do not need to provide your contact information at all.

CONSENT:

By signing this consent, I give permission to the study team to contact me in order to give me more information about this study and to be asked to participate in the study.

Patient Name: _____

Phone number: _____

Patient Signature: _____ Date: _____

Person obtaining consent:

Name: _____ Signature: _____ Date: _____

Appendix C: Patient Information Sheet and Consent Form

UNIVERSITY OF ALBERTA

FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

3-171 Edmonton Clinic Health Academy
11405 – 87 Ave
Edmonton, Alberta, Canada T6G 1C9
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www.pharmacy.ualberta.ca

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Perceptions of patients with mental health diseases on the role of text messaging for supporting medication adherence

Principle Investigator:
Dr. Christine Hughes, Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta

Co-investigator:
Mr. Tyler Watson, MSc Pharmacy Student, Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta

Introduction:
You are being asked to take part in a study to understand how text messaging may be used to help you take your medications. If there is anything you do not understand, please ask a Pathways staff member. Once you understand the study and if you decide to take part, you will be asked to sign a consent form. You will get a copy of the information sheet. You are free to skip any questions you do not wish to answer. You may choose not to take part or stop the study at any time. This will not affect the care you get

Purpose of the study:
Taking medicines for mental health conditions on a regular basis improves patient outcomes. There are a number of ways to help people take their medicines. We want to know how you are taking your medicines and what you think about your medicines. We also want to understand how technology, such as mobile phone text-messaging, can help people take their medicines. You are being asked to take part in a pilot study to understand how you are taking your medicines, what you think about these medicines, and how text-messaging may support you.

What is involved?
If you agree to take part, you will be asked to fill in a short survey and take part in an interview. The written survey should take about 15 minutes. The one on one interview will take about 30 minutes. We value your time. You will be given a $20 food gift card to complete the survey and interview. The survey has questions about your personal and health background such as your age, gender, and medical diagnoses. The survey also has questions about how you take your medicines and your thoughts about medications. The interview has questions about your current access to mobile phones, and how you

currently use a mobile phone. There are also questions asking about using a mobile phone for health-related means such as communication by text-message with your health care providers. Your answers to both the survey and interview will be confidential. Even the health care providers looking after you will not know your answers. Your answers will not change your care in clinic in any way.

Possible benefits
There will be no direct benefits to you. This study will help us understand how you are currently taking your medications. This study will help develop new strategies to help patients to take their medications including mobile phone text messaging.

Possible risks
There is little risk to you by taking part in this study. It will take about 45 minutes of your timein total. This will not change the care from your doctor or health care team.

Confidentiality
Data from the survey and interview will not identify you by name, only by a study number. During the data collection and after, the information will be kept in a secure area (locked office) of one of the investigators for a minimum of 7 years. Your name or health information will not be talked about outside the clinic. We will not publish any information which could identify you in any way.

Withdrawal
You can stop taking part in this study at any time. You do not have to provide a reason for stopping. Your medical care will not be changed in any way. If you decide to withdraw part way through the study you will still receive the $20 gift card.

Contact Names and Telephone Numbers:
If you have concerns about your rights in the study, you may contact the Health Research Ethics Board (HREB) at the University of Alberta at 780-492-0302. This office has no link with the study investigators.

Thank you for taking part in this study. We would be happy to answer your questions at any time, now or at any time in the future.

Please contact any of people below if you have any questions or concerns:

Phone: 780-492-5903 Dr. Christine Hughes, Associate Professor, Faculty of Pharmacy & Pharmaceutical Sciences

Phone: 780-293-4051 Mr. Tyler Watson, MSc Pharmacy Student, Faculty of Pharmacy & Pharmaceutical Sciences, University of Alberta

CONSENT

Title of Project: **Perceptions of patients with mental health diseases on the role of text messaging for supporting medication adherence**

Investigators: Dr. C. Hughes (780-492-5903), Mr. T. Watson (780-293-4051)

	Yes	No
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to withdraw from the study at any time, without having to give a reason and without affecting your future medical care?	☐	☐
Has the issue of confidentiality been explained to you?	☐	☐
Do you understand who will have access to your records, including personally identifiable health information?	☐	☐
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, give his/her name _____	☐	☐

Who explained this study to you? _____

I agree to take part in this study.

_____ _____ _____

Signature of Research Participant Date Witness

_____ _____

Printed Name Printed Name

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate._____ _____

Signature of Investigator or Designee Date