Integration of Smart Multidose Blister Packaging for Medication Management

by

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Author's Declaration

I hereby declare that this thesis consists of material all of which I authored or co-authored. Please see Statement of Contributions included in the thesis.

This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Statement of Contribution

Sadaf Faisal was the sole author for Chapters 1, 2, and 9 which were written under the supervision of Dr. Tejal Patel and were not written for publication.

This thesis also consists in part of six manuscripts written for publication. Exceptions to sole authorship of material are as follows:

Research presented in Chapter 3:

The research was conducted at the University of Waterloo by Sadaf Faisal under the supervision of Dr. Tejal Patel. Sadaf Faisal completed the searches and data analysis with assistance from Dr. Tejal Patel. Caitlin Carter assisted in the searches. Jessica Ivo and Catherine Lee assisted in data analysis. Sadaf Faisal drafted the manuscript and each author provided intellectual input on manuscript drafts.

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As lead author of these six chapters, I was responsible for contributing to conceptualizing study design, carrying out data collection and analysis, and drafting and submitting manuscripts. My coauthors provided guidance during each step of the research and provided feedback on draft manuscripts.

Abstract

Medication non-adherence can lead to non-optimal management of chronic diseases and poor health outcomes. Numerous innovative dispensing products offering real-time medication intake monitoring are being developed and marketed to address medication non-adherence and support the in-home medication management process. The integration of emerging medication dispensing devices with real-time medication intake monitoring by patients with chronic diseases for in-home medication administration and within the workflow of community pharmacies is unknown. The overall goal of this thesis was to investigate the medication-taking behaviour and in-home medication management processes of patients with chronic diseases (including storage, organization and administration of medications), examine the integration (described as usability, acceptability, and functionality) of a prototype smart technology-based smart multidose blister package (SMBP) in patients' homes and explore the feasibility of implementation of a real-time adherence monitoring, multidose dispensing system in community pharmacies.

This thesis is comprised of five studies and one reflexivity activity. The first two studies identified and analyzed relevant literature on the integration of smart oral multidose dispensing systems into the daily use of patients and the features and characteristics of smart medication adherence products for in-home patient use respectively. These two literature reviews identified various smart adherence products with variable features, however there was limited evidence related to in-home integration of such products.

The third study aimed to understand the meanings associated with in-home medication management processes and storage practices of older adults with chronic diseases. This study was a qualitative study that utilized a modified ethnographic approach via digital photography walkabouts, observation protocols, and field notes to document in-home medication organization and storage locations. Data consisting of digital photos and observation protocols were analyzed thematically. Ten older adults with an average age of 76 years, of which 80% were female, participated in the study. On average, participants reported five medical conditions, while the average number of medications was 11.1. The thematic analysis of 30 photographs, 10 observation protocols, and field notes resulted in three themes and five sub-themes for the in-home medication management study. Themes included choice of storage location, knowledge regarding appropriate medication storage conditions, and systems to manage in-home medication intake.

The fourth study was a mixed-method study in which study participants who were recruited for the first study, used the SMBP to manage their medications for eight weeks. To examine the integration of SMBP, data was collected using qualitative methods such as in-home observations, photo-elicitation, field notes, and semi-structured interviews along with quantitative methods, including System Usability Scale (SUS) and Net Promoter Score (NPS). The interview guide was developed with constructs from the Technology Acceptance Model (TAM), Theory of Planned Behaviour (TPB), and Capability, Opportunity, Motivation, Behaviour (COM-B) Model. Interview data were analyzed using the Qualitative Analysis Guide of Leuven (QUAGOL) framework to generate themes and subthemes, which were mapped back to TAM, TPB, and COM-

B Model. The qualitative analysis identified three themes and 17 sub-themes including factors influencing medication intake behaviour, facilitators to the product use, and barriers to the product use. The average SUS score was 75.50 and the overall NPS score was 0.

The fifth study was conducted at the respective community pharmacies of patients. Pharmacists and pharmacy assistants packaged and dispensed medications in SMBPs and monitored real-time medication intake via the web portal. This was a mixed-method study, where pharmacy staff participated in semi-structured interviews, and completed the SUS to assess usability. The interview guide was developed with constructs from the TAM, TPB, and COM-B Model. Interview transcripts were analyzed thematically utilizing Braun & Clark's thematic analysis framework, and findings were mapped back to the TAM, TPB, and COM-B Model. Three pharmacists and one pharmacy assistant with a mean of 19 years of practice were interviewed. Three themes and 12 subthemes were generated. Themes included: pharmacy workflow factors, integration factors, and pharmacist perceived patient factors. The mean SUS was found to be 80.63.

The sixth and the last chapter of this thesis was comprised of a reflexivity activity conducted by the pharmacist-researcher during the ethnographic fieldwork. This study provided reflection of a practicing pharmacist and the benefit of reflexivity practice to identify a clinician-researcher's assumptions and beliefs and their impact on the research.

The findings from this thesis indicated that in-home medication management reflects older adults' perspectives regarding privacy, medication-taking routine, knowledge about safe and effective storage, and organization systems. The SMBP was found to be easy to use and acceptable by older adults. However, clinicians should assess an older adult's medication intake behavior and barriers and facilitators to product use before recommending a technology-based adherence product for managing medications. Future research should be designed to understand the impact and effectiveness of these products on health outcomes and examine the sustainability of product induced behaviour change in patients managing complex therapies on regular basis. This research project identified that although pharmacists valued products with real-time adherence monitoring capabilities, it is imperative to carefully assess the infrastructure, including pharmacy workload, workforce, and financial resources, for the successful implementation of such interventions in a community pharmacy setting. Future research should focus on developing frameworks for full-scale implementation of such products in the community pharmacy settings.

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Dedication

To my late father Sardar Ali who believed in girls' education and dreamt about his girls being highly educated and my husband Faisal Firoz who supported me to fulfil that dream.

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List of Abbreviations

ART	Antiretroviral Treatment
CBS	Caregiver Burden Scale
COM-B	Capability Opportunity, Motivation and Behaviour
COVID	Corona Virus Disease
GSM	Global System for Mobile
HADS	Hospital Anxiety and Depression Scale
HCP	Health care Providers
HDL	High Density Lipoprotein
HIV	Human Immunodeficiency Virus
IADL	Instrumental Activities of Daily Living
IoT	Internet of Things
LDL	Low Density Lipoprotein
LTE	Long Term Evolution
MAP	Medication Adherence Product
MEMS	Medication Event Monitoring System
MCI	Mild Cognitive Impairment
MLHFQ	Minnesota Living with Heart Failure Questionnaire
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
NFC	Near Field Communication
NHP	Natural Health Product
NPS	Net Promoter Score
ODB	Ontario Drug Benefit
OTC	Over-the-counter
PIN	Personal Identification Number
QoL	Quality of Life
QUAGOL	Qualitative Analysis Guide of Leuven

RFID	Radio Frequency Identification
SIM	Subscriber Identification Module
SOMDS	Smart Oral Multidose Dispensing Systems
SMBP	Smart Multidose Blister Package
SMS	Short Message Service
STEM	Science Technology Engineering Mathematics
SUS	System Usability Scale
TAM	Technology Acceptance Model
TI	Treatment Interruption
TPB	Theory of Planned Behaviour
USA	United States of America
WHO	World Health Organization
Wi-Fi	Wireless Fidelity
WOT	Wirelessly Observed Therapy

CHAPTER 1

Medication Adherence

1.1. Introduction

According to World Health Organization (WHO), approximately 50% of people with chronic diseases do not take their medication as recommended.[1] Chronic disease are *"diseases of long duration and generally slow progression."*[2] A significant population in developed countries is living with chronic conditions, especially among older adults. For example, approximately 73% of Canadians aged 65 years and older have reported at least one chronic condition.[3] Similarly, in the United States (US), about 80% of older adults reported having at least one chronic disease, and 77% reported having at least two chronic diseases.[4] Chronic diseases such as heart disease, hypertension, diabetes, and cancer, among others, are typically managed with medications. The usage of medications increases with the number of chronic diseases a person has. A Canadian study found that the prevalence of use five or more medications was 31.9% overall, and it increased from 17.8% in patients with two or fewer chronic conditions to 63.8% in patients who had three or more medical conditions.[5] Another US study revealed that 86.1% of patients diagnosed with more than two chronic medical conditions were prescribed five or more medications by their family physician at one office visit.[6]

Chronic diseases generally require long-term use of numerous medication therapies.[7] However, as the WHO determined, non-adherence to therapies is very common among patients with chronic diseases as evidenced by a plethora of studies.[8–14] For example, a recent study based on 2015

prescription claim data reported that approximately 16.3 million Americans were non-adherent to their antihypertensive medications making the overall national non-adherence rate 31.0%.[15] Another systematic review and meta-analysis, which included 36 studies from Europe, North America, and South America, reported the pooled prevalence of medication non-adherence among patients diagnosed with resistant hypertension to be 35% [CI= 95%, 25 - 46%].[16] A 2019 Canadian report released by Express Scripts Canada – a prescription drug plan provider, identified that 70% of plan members were non-adherent to asthma and chronic obstructive pulmonary disorder therapies, 45% to antidiabetic medications, and 37% to antidepressants therapies.[17]

1.2. Impact of Medication Non-adherence

Poor medication adherence can result in non-optimal treatment of chronic diseases, leading to increased emergency room visits, frequent re-hospitalization, poor disease outcomes, death, and high costs to the healthcare system.[7,18] A US-based study has reported that improving adherence to antihypertensive medications in patients with chronic diseases could result in 117,594 fewer emergency room visits, over 7 million fewer inpatient hospital stays, and $4.5 billion in healthcare costs savings annually.[19] Furthermore, this study reported that adherence to antidiabetic and antihypertensive therapies could lead to a healthcare cost saving of $5 billion and $14 billion per year, respectively.[19] Another study examining the impact of adherence in chronic diseases (e.g., diabetes, hyperlipidemia, asthma/chronic pulmonary disease) reported that medication adherence was associated with 8% to 26% fewer hospitalizations, 3% to 12% fewer emergency room visits, and 15% less outpatient clinic visits.[20] Another cohort study of 38,520 patients in the US demonstrated that poor medication adherence to antihypertensive medications was associated with a higher incidence of stroke [aRR=1.27, 95% CI=1.17 - 1.38].[21]

Apart from worsening healthcare outcomes and associated increased cost to health care systems, non-optimal management of chronic diseases due to medication non-adherence may reduce the quality of life for patients. A cross-sectional study exploring the relationship between medication adherence and quality of life (QoL) of patients with diabetes and hypertension reported that adherent patients had significantly higher mean overall perception of QoL (77.9 points vs. 60.5 points, p= 0.001) and health score (79.4 points vs. 59.8 points, p= 0.001) as compared to non-adherent patients.[22] Another study investigating the correlation between medication adherence and QoL of heart failure patients has found a small but positive co-relation between medication adherence and QoL. This study used a validated tool, the Minnesota Living with Heart Failure Questionnaire (MLHFQ), to assess the QoL. Patients with low medication adherence reported a high score on the MLHFQ ($r = 0.177$; $p = 0.018$) indicating lower QoL.[23]

It is also crucial to note that medications are not devoid of harmful effects and may lead to an adverse drug reaction. In some cases, medication-related adverse reactions can result in unintended effects including an increase in morbidity- which can increase hospitalization and mortality.[24] As such, better adherence to some medications may increase the risk of hospitalization and worsen health outcomes. For example, certain medication classes such as antipsychotics, antiretrovirals and steroids can cause drug-induced hyperglycemia which can eventually lead to diabetes.[25] A recent population-based study reported that 8.4% [95% CI = 6.5 – 10.3] of hospital admissions were due to an adverse drug reaction.[26] The study further reported old age, polypharmacy, and comorbidities as main risk factors associated with drug-related hospitalizations. A meta-analysis of 19 studies evaluating the relationship between medication adherence and mortality reported that good adherence (described as adherence > 75%) to drug therapy was associated with low mortality

[OR = 0.56, 95% CI = 0.50 - 0.63] compared to poor adherence. However, the study also reported that mortality risk was doubled [OR = 2.90, 95% CI = 1.04 - 8.11] in patients who had good adherence to antiarrhythmics.[27] Another randomized controlled trial exploring the impact of home medication reviews in older adults and the rate of hospitalization reported a 30% greater rate of readmission in the intervention group [RR = 1.30, 95% CI = 1.07 -1.58; p= 0.009).[28] Authors hypothesized that the improved adherence may have led to some disease-induced illnesses leading to greater hospitalization rates. Therefore, one should not assume that medication adherence can always reduce hospitalization or mortality.

Given that medication adherence and non-adherence impacts health outcomes, it is necessary to accurately assess adherence and determine the effects of adherence both good and bad. However, current strategies by which we measure adherence remain inadequate and do not accurately provide clinicians with information about medication intake behaviours at home.

1.3. Terminologies and Concepts of Adherence

The WHO has defined adherence as "*the degree to which the person's behavior (medication taking, diet, and lifestyle changes) corresponds with the agreed recommendations from a health care provider."*[1] Adherence to the therapy is considered to be a complex, multi-process phenomenon and comprised of three phases.[29,30]

- ***Initiation of the therapy***: When the patient takes the first dose
- ***Implementation of the therapy***: How well the patient is following the actual dosing regimen as prescribed by the health care provider

- ***Discontinuation of the therapy***: When the patient stops taking the medication with or without the health care provider's recommendation

Non-adherence to medication can occur at any of the phases mentioned above. For example, a patient may decide not to fill a new prescription. This type of non-adherence is known as ***primary non-adherence.***[29] On the other hand, a patient may choose not to use the medication once he receives the medication or use the medication less or more frequently than advised by the physician. The patient may administer the drug at another time than the physician's prescribed time or decide to discontinue the therapy without consultation from a health care provider. This type of non-adherence is known as ***secondary non-adherence.***[29]

Medication non-adherence can also be described as intentional or unintentional based on the patient's intent.[30] ***Intentional or active non-adherence*** is a deliberate act, which happens when a patient purposefully decides not to take medication due to their personal beliefs, concerns about the medication, or potential side effects. On the other hand, the patient may consider taking the drug but not according to their health care provider's recommendations.[31] A recent study of people diagnosed with psoriasis using a self-administered therapy identified that 10.9% of patients reported intentional non-adherence due to their beliefs about the disease and the therapy; patients stopped using their medication due to concerns about potential side effects or were overusing medications due to the fear of experiencing a flare-up.[32] ***Unintentional or passive non-adherence*** occurs when the patient wants to take their medications but is unable to follow the regimen due to factors that are out of the patient's control.[30,31] These may include factors such as physical and cognitive limitations, complex treatment regimens, or the inability to access medications due to financial or accessibility reasons. There are multiple studies that have identified forgetfulness as a

significant barrier to adherence among various patient populations.[33–36] Similarly, patients with physical limitations due to age or certain medical conditions such as Parkinson's Disease or arthritis face challenges with medication administration leading to non-adherence.[37] A study exploring the medication packaging issues experienced by older adults identified that one in four older adults had difficulty with opening medication packaging, which could lead to non-adherence.[38]

The concept of adherence is defined or explained by using more than one term in the medical literature. The terms medication adherence and medication compliance have been used interchangeably in health care research and practice as they both attempt to explain medication-intake behaviors.[30] However, the term **adherence** assumes the extent to which a patient actively and mutually agrees with a health care provider's recommendations whereas, **compliance** implies the patient's obedience to the health care provider.[29,30,39] Concordance and persistence are two other terms that have been used in literature to refer to medication adherence. **Concordance** refers to the shared agreement regarding a treatment plan between a patient and health care provider; it does not refer to the medication taking behaviour, rather it describes the interaction among the patient and their provider.[40,41] The term **persistence** describes to "the act of continuing the treatment for the prescribed duration."[42] Although these terms have been used interchangeably, none comprehensively illustrate the degree of complexity and factors that can impact a person's decision to initiate or continue the therapy as recommended by their health care provider.

The term medication adherence is the most general and prevalent term in the literature as it is very widely accepted.[30,39] Medication adherence generally refers to taking the correct dose of

medication, at the right time, with the correct frequency and correct duration of therapy properly discussed and agreed between a patient and a health care provider. Medication management is another broad term that has been discussed in the literature variably. Maidment et al. described medication management as a process with five functional stages including; "(1) identifying a problem, (2) getting diagnosis/medications, (3) starting, changing or stopping medications, (4) continuing to take medications, and (5) reviewing medications."[43] Medication management has also been defined as "ability to self-administer a medication regimen that has been prescribed."[44] Both of these definitions explain the complexity of medication taking as it involves numerous steps, process(s), and patient behaviours. Therefore, it is not erroneous to say that medication adherence depends on appropriate medication management which can be affected by multiple factors.

1.4. Factors Associated with Medication Non-adherence

Taking medications on a regular basis is not a simple task but rather a complex behavioural process. It not only includes administrating the medication but also comprises of accessing medications, preparing the dosage, managing the side effects, and communicating with health care providers.[45,46] Many factors can drive medication taking in patients with chronic diseases.[47,48] The WHO has categorized these factors into the following five groups.[1]

1.4.1. Social and Economic Factors

Factors such as low socioeconomic status, illiteracy, unemployment, and lack of social network can negatively impact an individual's medication intake behaviour.[49,50] A United Kingdom-based study exploring the relationship between socioeconomic status and treatment outcomes for patients

on antiretroviral treatment (ART) reported that 32% of patients receiving ART were non-adherent. The lower socioeconomic status (measured through financial hardship, non-employment, unstable housing status, and non-university education) was strongly associated with non-adherence to ART and virological non-suppression, thus resulted in poor treatment outcomes.[51] Another study investigating the association of financial hardship (assessed by asking a single question about their ability to pay their monthly bills) and non-adherence (determined by using a short 7-item version of Adherence to Refills and Medication Scale) in patients diagnosed with cardiovascular disease described that financial strain was associated with less adherence to medications (Spearman's $\rho = -.24$, $p < .001$).[52]

1.4.2. Healthcare Team and System-related Factors

A good patient-provider relationship allowing for shared decision-making between the patient and health care provider, access to treatment resources, and community support are health system-related factors that can improve medication adherence.[1] Research has reported that having an established relationship with a provider can positively impact adherence among patients diagnosed with chronic diseases.[53,54] A qualitative study exploring views of different stakeholders using mental health services (older adults, community dwelling adults and people working at forensic services) on the impact of trust on safe medication usage identified that a patient's trust in their healthcare provider is vital for appropriate medication taking. The study further elaborated that the lack of trust due to poor communication may cause forcible medication administration or coercion and can adversely affect adherence.[55] Alternatively, a health care provider's lack of education regarding chronic medical conditions and treatments can impact a patient's disease management and adherence.[1] A qualitative study exploring the barriers to prescribe pre-exposure prophylaxis

of Human Immunodeficiency Virus (HIV) infection among primary care and HIV specialist reported a lack of knowledge of medications and skills required to monitor and support adherence as a few of the barriers for health care providers to offer these therapies to their high-risk patients.[56]

1.4.3. Condition-related Factors

Factors such as the disease characteristics, severity of symptoms, and level of disability due to illness are few condition-related factors that can impact the way patients perceive risks associated with their disease.[1] A recent systematic review of factors impacting medication adherence in hypertension treatment identified that patients' understanding of their disease severity and possible complication can motivate them to adhere to their therapies.[36]

1.4.4. Therapy-related Factors

Numerous therapy-related factors, such as but not limited to the complexity of regimen, medication access, medication side effects, and previous treatment failure, have been identified as essential determinants of non-adherence.[1,50,57] Complex therapy regimens often involve multiple medications with variable dosing schedules and different dosage forms.[58] A systematic review identified 28 studies reporting that patients with complex medication regimens are less likely to take their medications as prescribed, and seven studies reported a direct correlation between non-adherence and complexity of regimens.[59] Similarly, undesirable medication side effects are associated with poor adherence. A cross-sectional survey-based study of community dwelling patients with schizophrenia identified that only 42.5% adhered to their medications, 86.2% of patients experienced at least one medication side effect. The study reported that metabolic-related

and agitation/extrapyramidal-related side effects were significantly associated with lower rates of adherence .[60]

1.4.5. Patient-related Factors

A patient's knowledge, attitude, beliefs and expectations, memory, and ability to manage disease symptoms and treatments are all patient-related factors that play an essential role in influencing therapy adherence.[1] For example, a survey-based study reported that, among patients with chronic illnesses with low medication adherence, negative beliefs about their medications' necessity and side effects influenced their adherence.[61] Forgetfulness is another important patient-related factor to consider when exploring non-adherence. In a recent study comprised of patients with coronary artery disease, 84.9% of participants reported forgetfulness as a barrier to medication intake.[34]

Since medication adherence is influenced by multiple factors, it is imperative to carefully and holistically identify what type of non-adherence a patient is experiencing (intentional or unintentional) and assess factors linked to their non-adherence, prior to offering medication adherence interventions to help improve adherence.

1.5. Measurement of Medication Adherence

Measuring and monitoring medication adherence accurately is crucial as non-accurate estimation can lead to various issues such as misjudgment of treatment outcomes, ordering expensive diagnostic procedures, and inappropriate dose intensification.[29] There are multiple ways to assess medication adherence; however, each method has limitations, and none are considered gold standards.[7,29,62] The WHO has classified adherence measurement methods into the following two categories: objective methods and subjective methods.[1,63] **Objective methods** include assessing

adherence by conducting pill counts, reviewing pharmacy dispensing records, measuring clinical outcomes, and monitoring medication intake electronically. **Subjective methods** include asking patients about their medication intake by using questionnaires or utilizing self-report through medication diaries or calendars. Medication adherence measurement methods are further divided into two types.

1.5.1. Direct Methods

Direct methods include measuring a drug or drug metabolite in the biological fluid (blood or urine) of a patient, determining the presence of biomarkers, wirelessly observing therapy (WOT) through ingestible sensors, and directly observing a patient while they are administering medications.[29,63] Direct methods of measuring medication intake are invasive, expensive, and labor-intensive. Although considered to be accurate, these methods have some limitations. For example, it is not possible to monitor the drug assays for all medications or their metabolites. Similarly, individual pharmacokinetic variations, drug metabolism, and drug-drug or drug-food interactions can impact the accuracy of measuring drug levels and should be considered while interpreting the results.[63] In addition, the direct observation of a patient administering their medication by a health care provider may not guarantee that the patient has swallowed their medication completely, as the patient may pretend to swallow the pill at the moment and can discard it afterward. Furthermore, direct patient observation can be costly and may also not be feasible or practical in non-institutionalized settings.

1.5.2. Indirect Methods

Indirect methods of measuring medication intake include patient self-reports (e.g., interviews, patient-kept medication diaries, medication adherence questionnaires, and scales), pill counts,

pharmacy refill record assessments, and electronic medication monitoring (e.g. electronic pill containers, electronic medication blisters, and inhalers).[29,62,64] These methods are commonly used in clinical practice, provide a reasonable estimation of adherence, and are generally inexpensive and non-invasive. However, similar to direct methods, indirect methods have disadvantages. Let us take the example of the pill count method. The pill count refers to the ratio of the number of pills that a patient has administered between two scheduled appointments with the total number of pills that should have taken during that period.[63] The pill count method is the most popular, easy, and economical way to estimate adherence.[63] However, there are several limitations of this method. For example, the pill count method may not be appropriate for estimating medications that patients take on an as-needed basis or in situations where a patient may decide to discard the unused medications prior to the clinic visit or may switch medications between the bottles which can lead to inaccurate adherence assessments.[29,35] Additionally, this method does not validate the medication-taking pattern as removing the medications from the prescription vial does not inform clinicians if the patient has correctly followed the dosing regimen or not.[29] Similarly, the pharmacy refill assessment method, where compliance is assessed by determining the periods between the refills, become less reliable if a patient refills their medication before it is due.[29,63]

Patient self-reporting of adherence by using questionnaires, self-reported diaries, and calendars are other standard methods used to estimate adherence; however, these methods often lead to an overestimation of adherence due to poor memory/ recall bias, personal bias, or not wanting to admit to non-adherence.[29,63] Finally, electronic monitoring of medications is another indirect method used to measure adherence.[29,63] This method records the dosage event with the date and time the patient retrieved their medication from a container.[65] This method, however, does not

guarantee that the patient has ingested the medication.[29,63] Since there is no ideal method to measure medication adherence, multiple assessment methods and a patient-specific approach are recommended to achieve the best possible assessment.[29]

1.6. Interventions to Address Medication Non-adherence

Numerous interventions have been identified to address and improve medication adherence.[66–69] These interventions range from simple strategies such as simplifying the dosage regimen to using technology-based approaches, including patient reminders and electronic medication adherence products. These interventions can be grouped into the following four categories.

1.6.1. Educational Interventions

Educational interventions include providing patients and caregivers with education on the importance of the disease, treatment, and potential adverse effects of treatments.[35] These interventions can be provided through pharmacist counselling, the combination of written and verbal instructions, and asking patient to demonstrate the process of medication administration (e.g. inhalers).[70] There are numerous studies describing the impact of educational interventions on medication adherence, however there is mixed evidence regarding the effectiveness of such interventions. For example, a review based on interventions designed to improve adherence identified nine studies that assessed the impact of patient education on adherence, out of which four studies reported no difference and five studies reported improvement in adherence.[69] This review reported various methods of adherence intervention such as individual education sessions and telephone or face-to-face counselling services offered by health care providers and patient education on the importance of adherence, disease knowledge, and medication goals and plans.[69]

The review further identified that educational interventions that are personalized and offered during the initial diagnosis are found to be modestly effective. Another systematic review published recently, reported minimal effectiveness of various educational interventions provided by health care providers including nurses and pharmacist compared to the control group with no educational interventions[d = 0.18 (95% CI = 0.01- 0.34, $p < 0.04$)].[71]

1.6.2. Behavioral Interventions

Behavioural interventions are strategies that focus on changing the daily medication-taking behaviour of a patient.[66] These interventions include self-management strategies, one-to-one counselling based on motivational interviewing, and planned behaviour education.[69,70,72] A meta-analysis review assessing the use of cognitive-based behaviour change strategies and their impact on adherence reported that these interventions are effective [effect size = 0.34 (0.23 - 0.46), CI = 95%, $p < 0.001$] in improving adherence.[72] Another randomized controlled study in adults over the age of 60 with chronic diseases reported improved medication adherence using behavioural interventions such as systematic education, patient-kept diaries, and telephone reminders compared to usual standard care with no behavioural interventions.[73] In this study, adherence, measured using pill counts, was significantly different between the usual care and intervention groups at three months (78.2% vs. 91.9%, $p = 0.007$) and six months (68.6 % vs. 83.1%, $p = 0.003$).[73]

1.6.3. Medication Dosing and Management Interventions

Medication dosing and management interventions include simplifying dosing regimens, using fixed-dose combinations, medication calendars, medication adherence aids such as weekly

pillboxes or dossettes filled by patients or caregivers, and using multidose blister packaging prepared by pharmacies.[70,74,75] A meta-analysis review exploring the impact of packaging interventions on medication adherence and health outcomes reported an adherence rate of 71% for patients who used pharmacy packaged blister packs or pillboxes compared to 63% for those individuals who did not use such adherence aids.[76] The study also reported that these interventions were more effective when delivered by pharmacies directly to the patient and were less effective in patients experiencing cognitive impairment.[76] Another meta-analysis reported a mean difference of medication adherence by 14.9% [95% CI = 7.4% - 22.5%] in patients who administered the fixed-dose combination of antihypertensive medications as compared to those who were taking the individual medications separately.[77]

1.6.4. Technology-based Interventions

The use of automated reminders or coaching programs via telephone, short message service (SMS) reminders, mobile applications, web-based E-learning, electronic medication packaging devices such as Medication Event Monitoring System (MEMS) caps, and adherence products with real-time medication intake monitoring are a few adherence interventions that can be classified as technology-based interventions.[70,78] In a systematic review, Tran et al. assessing the impact on adherence of a patient reminder system including mobile phone text messaging, telephone calls, and audiovisual reminder function for asthma patients reported that adherence was improved in the intervention group using the reminder system compared to control group which did not receive any reminders.[79] Another systematic review examining the effectiveness of electronic reminders such as SMS reminders and pager messages reported a significant effect on patient adherence and reported improved adherence in 12 out of 13 studies.[80] Heuckelum et al. exploring the impact on

adherence from electronic adherence devices including MEMS, electronic blisters, and electronic inhalers, to name a few, reported positive results on adherence.[67] Although research shows that technology-based interventions can improve adherence, there are inconclusive results on the impact of these interventions on clinical outcomes.

To summarize, there is abundant literature exploring the impact of various adherence interventions stated above and reporting variable effectiveness in medication adherence and clinical outcomes in patients with chronic diseases. A systemic review of randomized controlled trials has shown that simple interventions can effectively increase adherence and improve clinical outcomes for short-term therapies; however, medication adherence to long-term therapies is a complex process and requires a combination approach.[81] A recent network meta-analysis exploring more than 200 studies on medication adherence interventions reported that using multiple interventions is more effective than a single intervention.[82] It is often advisable to use multiple interventions in combination as not one single intervention has been proven to be effective on its own.[70]

1.7. Smart Medication Dispensing Systems

To address, monitor, and improve medication adherence, numerous innovative technologies are being developed.[62,64,78,83] The use of real-time medication intake monitoring devices, otherwise known as "smart products", has grown in the past two decades. Smart products are "objects, or software platforms, that are embedded with processors, sensors, software, and/or connectivity that allow data to be exchanged between the product and its environment, manufacturer, user, and other products/systems."[84,85]

Smart adherence products are the adherence products that can dispense and track real-time medication intake events remotely, via Bluetooth®, Long Term Evolution (LTE), Wireless Fidelity (Wi-Fi®), wired or other means of connectivity, thus making instant real-time electronic adherence feedback a significant component of these type of products.[62] These systems can send reminders and notifications to patients when a dose is due. This feature can be utilized to implement behaviour change in patients experiencing non-adherence due to forgetfulness. Moreover, these products record the date, time, or both when patients access their medication through the product. Although the access of medication through the product serves as a proxy measure of medication ingestion, the adherence captured through these products can provide a time and date stamped adherence measure.

The data gets transmitted to a secure web-based service and can be downloaded, analyzed, or viewed through a web-based platform to provide remote access to health care providers, caregivers, or the patient themselves. The remote monitoring of adherence along with time and date stamp can provide healthcare providers with insight into their patients' medication intake patterns in real-time and may offer an opportunity to intervene in between clinic visits. This is more than what is available through pill counts, mean possession ratios and other methods of adherence assessment. These products also can notify the patient, caregiver, and health care provider immediately if a dose has not been taken in the defined therapeutic window via email, phone call, or text message, promoting intervention to occur promptly. Moreover, real-time medication intake data provides an opportunity for patients to have insight into their medication taking.

1.8. Community Pharmacist's Role in Improving Medication Management

As discussed previously, when it comes to medication management, health care providers offer numerous interventions to their patients ranging from providing education to simplifying their medication regimens. Among these health care providers, community pharmacists are uniquely positioned to identify non-adherent patients and support patients in managing their medications by offering numerous interventions such as patient education, simplifying medication regimens, sending reminder notifications, and preparing blister packages.[86–88] Moreover, community pharmacists interact with their patients on frequently, making them easily accessible to support conversations related to medication management and reinforce adherence strategies.

Research has indicated that pharmacist-led interventions have positively impacted the adherence and improved patients' medication management process. For example, a recent systematic review and meta-analysis reported that pharmacist-led interventions including patient education about disease, medication, adherence, lifestyle and self-management significantly improved the HbA1c level, blood pressure, and lipid levels.[88] Another study reported that pharmacist-led adherence management intervention based on behaviour change framework improved medication adherence (51.8 % in intervention group v/s 22.2% in the control group) and clinical outcome in patients diagnosed with asthma, chronic obstructive pulmonary disease, and hypertension.[89] Another study examining the impact of community pharmacist-led adherence interventions (initial counselling based on motivational interview, follow up counselling, and pick up and refill reminders) on adherence, healthcare utilization, and costs reported that the intervention group reported 3% higher medication adherence, 1.8% fewer hospital admissions, and 2.7% fewer emergency room visits than the control group.[90]

Community pharmacists have played an essential role in their patient's medication management process by providing patient education and adherence solutions such as packaging medications in blister packs and monitoring the adherence via pharmacy refill records. As stated previously, monitoring adherence is a vital step in identifying non-adherence and supporting patients to manage their medications. Innovative technology-based adherence products are becoming popular and are being used to address medication management issues.[62,78,91] Some of these products require pharmacies to package and dispense medications.[91] Furthermore, these products offer the option for health care providers to monitor their patients remotely via a web-based or cloud-based portal and offer a proactive approach to tackle medication non-adherence. Community pharmacists may be ideally situated to utilize this feature to monitor their patients remotely and proactively tackle medication non-adherence.

1.9. Statement of Problem

Medication intake is a complex behaviour, especially if a patient is managing complex therapy regimens on a daily basis. Many patients with chronic diseases manage multiple medications with variable doses and dosing schedules and perform numerous behaviours to accomplish this task. These behaviours may include preparing and administering medication doses, communicating with health care providers about medication side effects, acquiring prescriptions, and accessing pharmacies.[92] These behaviours may be affected by various factors. For example, patients may not have the means to access medications due to financial concerns or get timely refills from the pharmacies. Similarly, they may not have anyone to assist them with organizing and administering their medications, may face limitations in their cognitive capacity to remember to take their medications appropriately, may not have the physical ability to open their medication vials, or the

visual acuity to read administration instructions correctly. In some situations, patients' own beliefs about their medication and disease can impact their medication-taking behaviour as they may be afraid of the side effects or do not understand the importance of proper medication intake to manage their chronic illnesses. In order to provide the best intervention to address medication non-adherence, it is imperative to understand what goes on in a patient's home related to their medication management processes, what people do or do not practice related to their medication intake behaviour, and what factors influence one's ability to administer their medications appropriately.

In the last two decades, there has been an increased interest in developing and utilizing technologies to address non-adherence and support patients in managing their complex regimens. These products range from mobile phone applications, electronic reminders via mobile phone text messages or emails, and smart medication dispensing products that offer real-time medication intake monitoring via web or cloud-based portals.[62,70,78,93] The abundance of emerging innovative smart adherence products calls for research to explore and understand the integration of these products among its users. These products may have the potential to improve adherence for patients and provide clinicians an opportunity to intervene on time. Therefore, it is necessary to explore how these products can be integrated into a patient's home and identify the facilitators and barriers to use these products. In order to integrate a product effectively into daily medication management routines, a user must be able to learn to use the product and be willing to use the product regularly. Similarly, the features of a product and how they work together to provide the desired outcome may also influence a user's ability to adapt a product into their daily routine. Furthermore, many

personal or environmental factors may impact a user's ability to use a product adequately and should be identified before selecting a product for use.

As stated previously, some of these smart products require pharmacies to package and dispense medications, while other products require that the caregivers or patients fill the device independently.[91] Through these products, pharmacists, can also have the opportunity to monitor the real-time medication intake of their patients remotely via a web-based or cloud-based portal and address non-adherence in a timely manner. Therefore, it is imperative to assess the impact of packaging and dispensing medications in these products within the community pharmacy workflow and determine the community pharmacist's involvement in monitoring and responding to real-time medication intake data.

1.10. Thesis Objectives

The overarching intent of this thesis is to understand and explore the integration of a prototype smart multidose blister packaging among patients with chronic diseases, understand their medication intake behaviour, and investigate the feasibility of implementing real-time medication-intake technologies in community pharmacies. To achieve this goal, this research addresses the following key objectives.

1. To identify the existing literature related to the integration of smart multidose oral dispensing products, their impact on medication adherence and identify the smart medication adherence products available for patients to purchase

2. To explore medication intake behaviour and investigate in-home medication intake, administration, and organization process(s) used by older adults managing complex therapy regimens and living independently
3. To examine the integration of a prototype smart multidose blister package for in-home patient use to manage complex therapy regimens
4. To assess the usability of a prototype smart multidose blister package and understand the factors that may impact community pharmacies to offer such a product to their patients

1.11. Thesis Outline

To address the overarching goal of this project, this thesis is comprised of nine chapters in total. Chapter 1 provides an overview of background information about medication adherence, and Chapter 2 describes the research methodology used in chapters 3 to 7. Chapters 3 to 7 are published manuscripts and findings which were integrated to answer the aforementioned research question. Chapter 8, a published manuscript, discusses the experience of a practicing pharmacist conducting ethnography-informed field work. Chapter 9 concludes the findings from Chapters 3 to 7 and discusses the research implications and future directions. The following section provides a brief outline of what each chapter is comprised.

Chapter 1: A brief introduction of medication adherence, types of non-adherence, factors impacting adherence, medication adherence measurement, and interventions to address and improve adherence.

Chapter 2: An overview of theoretical frameworks and methods used in this project.

Chapter 3: A scoping review to identify existing literature about the integration of smart oral multidose dispensing systems (SOMDS) for medication adherence.

"The usability, acceptability, and functionality of smart oral multidose dispensing systems for medication adherence: A scoping review"

Chapter 4: A literature review to compare the features of smart medication adherence products (MAPs), which can inform decisions about which smart MAPs may be best suited for patients based on need, expectation, and capacity.

"A review of features and characteristics of smart medication adherence products"

Chapter 5: A qualitative analysis of photographs and patients' narratives of medication storage, organization, and intake to understand what goes on in patients' homes who manage complex therapy regimens on a regular basis.

"In-home medication management by older adults: A modified ethnography study using digital photography walkabouts"

Chapter 6: A qualitative analysis of patients' interviews to understand the integration of a prototype smart adherence product, their medication intake behaviour, and quantitative assessment of the product's usability by older adults.

"Integration of a smart multidose blister package for medication intake: A mixed-method ethnographic informed study of older adults with chronic diseases"

Chapter 7: A qualitative analysis of interviews of pharmacists and pharmacy assistants to understand factors affecting the implementation of a prototype smart medication adherence product in community pharmacies and quantitative assessment of product usability.

"Implementation of a real-time medication intake monitoring technology intervention in community pharmacy settings: A mixed-method pilot study"

Chapter 8: A commentary about the reflexivity of a practicing pharmacist visiting patients in their homes and conducting ethnography research.

"Lessons in reflexivity of a pharmacist conducting ethnographic research"

Chapter 9: A summary of the findings from the manuscripts in chapters 3-8, research implications, and future direction.

CHAPTER 2

Research Methodology

2.1. Introduction

Medication adherence is one of the biggest healthcare challenges globally. Medication adherence not only involves the correct administering of the medication at the right time, but it also involves numerous process and behaviours, including preparing, storing and administering medications, communicating with health care providers, and accessing medications and healthcare services.

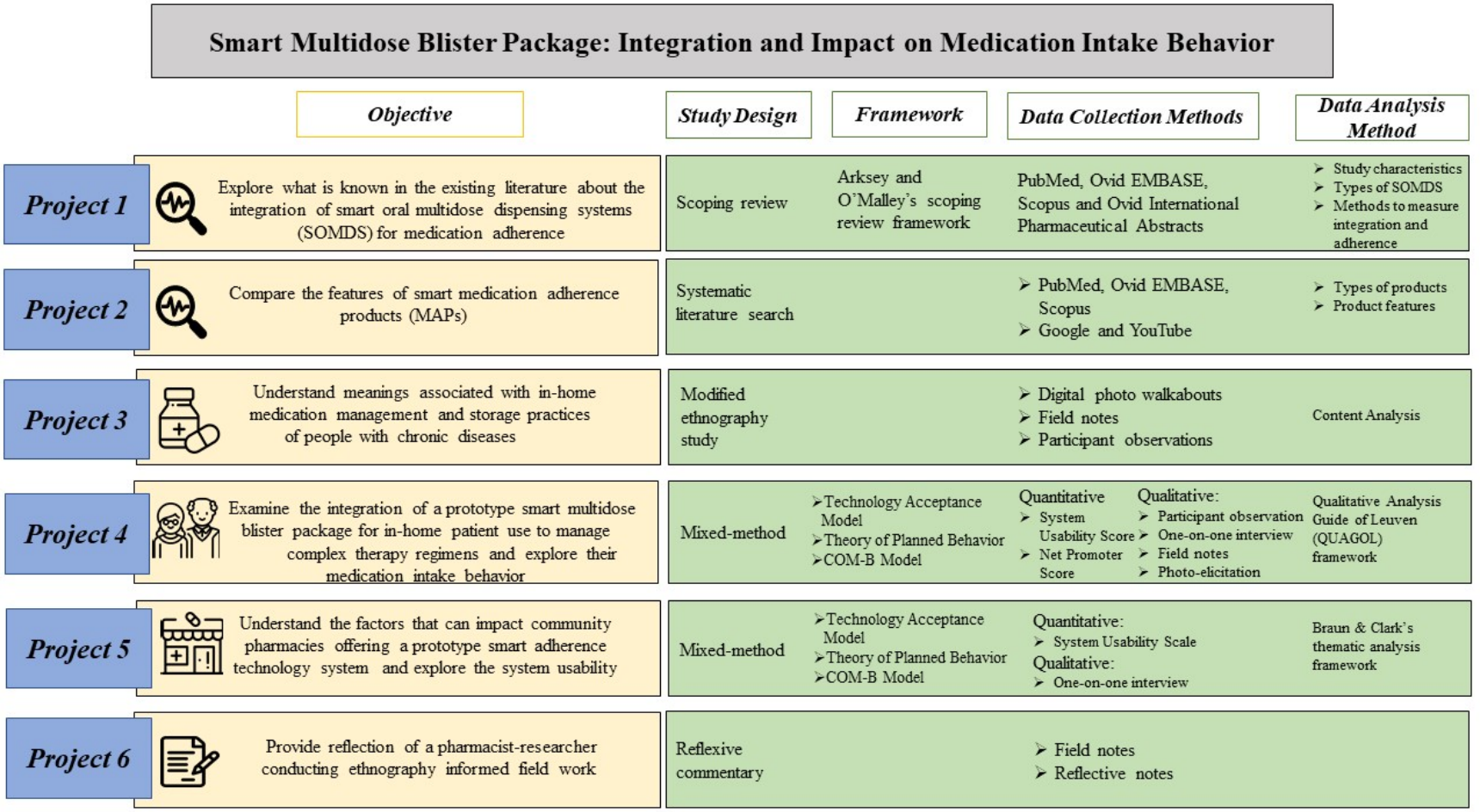
As discussed in Chapter 1, numerous technology-based interventions are being developed and marketed to support complex medication regimens and improve medication intake behaviour. In addition to reminding patients to take their medication on time, some products record real-time medication intake remotely. These products may have a great potential to help patients administer their complex regimens appropriately and allow health care providers to monitor adherence remotely and intervene on time. The potential benefit of these products cannot be realized if end-users are not able to use them effectively. A recent study investigating the usability of electronic medication adherence products reported significant variability in usability and workload of 21 products.[94] Moreover, due to a patient's limitations and wide variety of features these products offer, some products may not be usable by all patient populations. As such, no matter how effective the product is, if an end-user is not able to integrate the product into their daily medication taking process, it is highly unlikely for them to adopt the product. Therefore, it is imperative to explore the integration of these products into daily medication intake routine and investigate their

usability and acceptance. Furthermore, it is essential to clearly understand what kinds of processes and activities people engage in their homes related to medication management and their medication intake behavior before integrating a technology-based product into their daily medication intake routine.

Furthermore, some of the technology-based adherence aids require community pharmacies to package and dispense medications and allow pharmacists to monitor real-time medication intake data via web-based cloud portals. Therefore, it is essential to explore how community pharmacies can offer these technology-based products to their patients and how pharmacists perceive the use of these products for monitoring their patients' real-time medication intake.

Due to the complex nature of medication management, medication intake behaviour and technology integration, we used multiple methods to address this issue. The projects described in this thesis aim to understand (a) the medication-taking behavior and in-home medication management processes of patients with chronic diseases, including storage, organization, and administration of medications, (b) integration of a prototype technology-based smart multidose blister package (SMBP) in patient's homes, and (3) integration of such technologies in community pharmacies. The objective of each research project determined the research methodology used in each of the studies. Figure 2-1 provides an overview of the goals, study design, frameworks used, data collection methods, and data analysis frameworks of all six projects included in this thesis.

FIGURE 2-1: Overview of Objectives, Study design, Frameworks used, Data collection methods, and Data analysis frameworks of the thesis project



The scoping review described in Chapter 3 utilized Arksey and O'Malley's framework to identify and analyze relevant literature on the integration of smart oral multidose dispensing systems into the daily use of patients. For the complete details of the study methodology, refer to Chapter 3. Chapter 4 details a systematic approach to conduct a comprehensive literature search on smart medication adherence products for in-home patient use in both published and grey literature; details of this methodology are provided in Chapter 4.

The project described in Chapter 5 utilized a modified ethnography approach to collect data of in-home medication management processes and storage places. This project used various methods, including in-home digital photography walkabouts, participant observations, and field notes, and utilized qualitative content analysis methodology to determine themes and sub-themes.

Chapter 6 comprised of a mixed-method ethnographic-informed study related to the integration of SMBP. Data was collected qualitatively and quantitatively using in-home observations, field notes, semi-structured interviews with photo-elicitation, System Usability Scale (SUS), and Net Promoter Score (NPS). The interview guide was developed based on the constructs of three frameworks; the Technology Acceptance Model (TAM), Theory of Planned Behaviour (TPB), and Capability Opportunity, Motivation and Behaviour (COM-B) Model. Data were analyzed using the Qualitative Analysis Guide of Leuven (QUAGOL) framework to generate themes and sub-themes.

Chapter 7 used a similar mixed method approach as outlined in chapter 6. Community pharmacists and pharmacy assistants who packaged and dispensed medications in SMBP and monitored real-time medication intake through web-portal were recruited to provide their feedback about the

SMBP and the web-based portal through semi-structured interviews. The interview guide was developed based on TAM, TPB, and COM-B Model; interview transcripts were analyzed thematically. Furthermore, SUS was used to assess the usability of the SMBP and web-based portal.

Chapter 8 describes the reflection of a practicing pharmacist conducting ethnographic fieldwork and the benefit of reflexivity practice to identify a clinician-researcher's assumptions and beliefs and their impact on the research.

2.2. Theoretical Frameworks

For studies described in Chapters 6 and 7 the following three theoretical frameworks were used to collect and analyze data; (a) Technology Acceptance Model (TAM), (b) Theory of Planned Behaviour (TPB), and (c) Capability Opportunity, Motivation, and Behaviour (COM-B) Model.

(a) Technology Acceptance Model

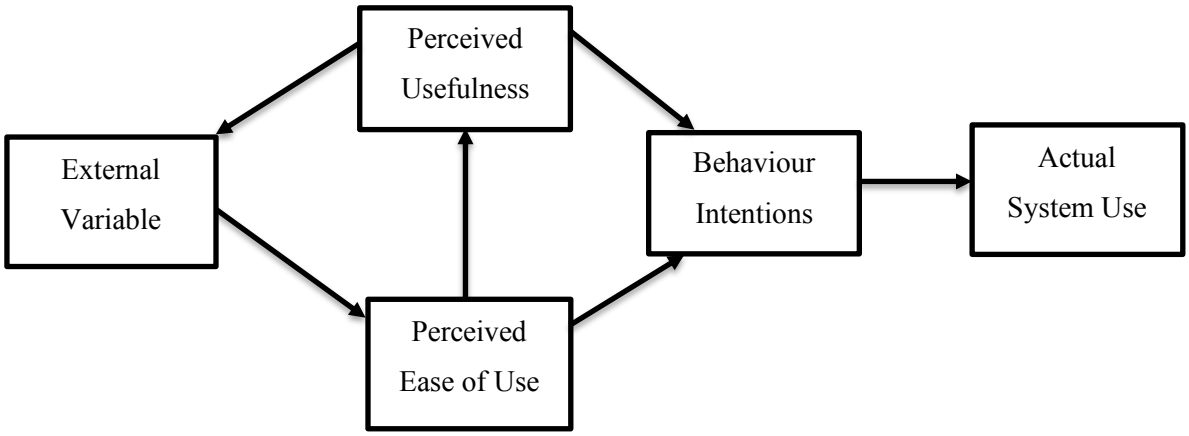
The TAM is the most well-known and used framework to explore and understand technology acceptance, initially developed by Fred Davis in 1986.[95] Since then, it has been used to assess a user's acceptance of numerous technologies, including computers, mobile health technologies, electronic health records and many more.[95] The TAM emphasizes that a user's acceptance of information technologies can be influenced by multiple factors, generally classified into the following three specific attributes;[96]

- **Perceived usefulness** describes "the *potential user's subjective likelihood that the use of a certain system will improve his/her action."*

- **Perceived ease of use** defines "*the degree to which the potential user expects the target system to be effortless."*
- **Behavioral intention** refers to *"a person's intention to use technology."*

The TAM provides a framework to understand a person's intention to use technology versus their actual use. It describes that perceived usefulness and ease of use significantly influence the user's behavioral intention, leading to the actual use of technology. Actual system use occurs when a person incorporates the technology into their daily routine. Some external factors can also influence a person's beliefs toward the system and can include system characteristics, user training, and implementation process.[95,96]

FIGURE 2-2: The Technology Acceptance Model. Adapted from *"Overview of the Technology Acceptance Model: Origins, Development and Future Direction" by Chuttur, M.Y., (2009) Sprouts: Working Papers on Information Systems,9(37). p.10*

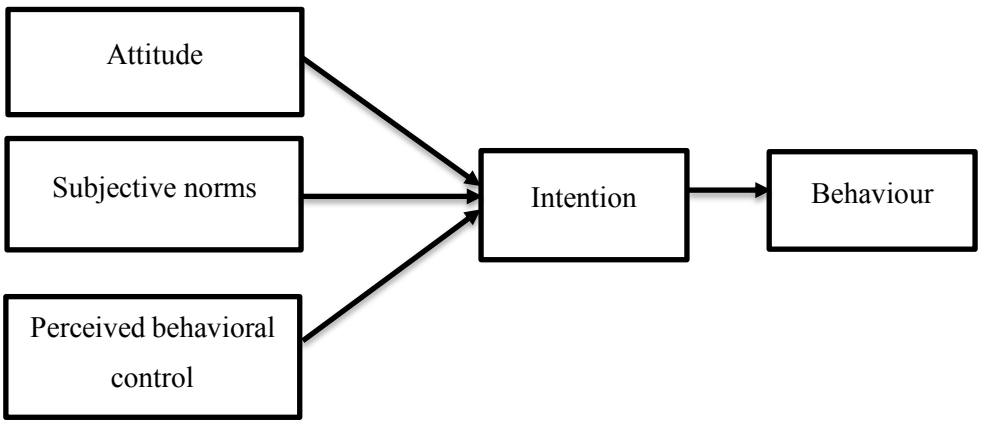


(b) Theory of Planned Behaviour

The TPB provides a theoretical framework to understand variables that can affect behaviour change.[97,98] This theory explains that a person's action or behavior is influenced by their intention to perform the behaviour.[99,100] **Intention** can be defined as "*an individual's motivation toward engaging in a behaviour in the future*" and is driven by the following three factors:[99,100]

- **Attitudes** refer to the *"beliefs about the outcome of the behavior and evaluation of the outcomes*" or an individual's positive or negative estimations about engaging in a particular behaviour and outcome.
- **Subjective norms** are normative beliefs which are the "*beliefs of an individual about the extent to which the significant people in his [or her] life will approve or disapprove of the particular behaviour he is involved in."*
- **Perceived behavioral control** refers to *"factors that can enable or inhibit a person from performing the behavio*ur" or also known as beliefs about the resources available or skills needed to perform the behaviour.

FIGURE 2-3: Theory of Planned Behaviour Model. Adapted from *"A review of health behaviour theories: how useful are these for developing interventions to promote long-term medication adherence for TB and HIV/AIDS?" by Munro et al. BMC Public Health 2007, 7:104*[98]



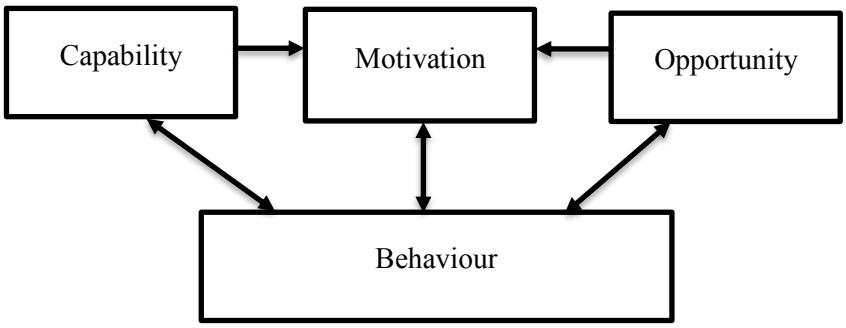
For individuals to engage in a behavior-in this case, taking their medications on time-the following must be considered; (a) their positive or negative beliefs about taking medications, e.g., feeling of well-being, and/or side effects of therapy, (b) how important it is for the people around them to know that they take their medications on time; and (c) the physical and cognitive skills, and resources required to take medications regularly.

(c) Capability Opportunity, Motivation and Behaviour (COM-B) Model

The COM-B Model is a comprehensive behavior system that provides structure to assess different factors affecting successful behavior change.[98] The model comprises of following constructs;[98,101,102]

- **Capability** refers to "*an individual's physical and psychological capacity to engage in a behaviour."*
- **Opportunity** describes the *"factors that lie outside the individual that make the behaviour possible or prompt it."*
- **Motivation** represents *"all the brain processes that energize and direct the behaviour."*

FIGURE 2-4: COM-B Model. Adapted from "Applying COM-B to medication adherence: A suggested framework for research and interventions" by Jackson et.al. The European Health Psych 2014, 7-17



This model explains that for an individual to be motivated for a behaviour such as medication intake, they must have sufficient capability and opportunity.[103] The physical factors such as vision and dexterity, and cognitive functions (e.g., knowledge, memory, and comprehension required to understand the medication regimens or to use a medication management aid can very well impact the capability of a person to administer their medications.[98,101,102] Additionally, social and environmental factors (e.g., lack of healthcare resources, access to the medications, cost, and

available social support for medication management) also influence the opportunity to continue the medication intake process.[98,101,102]

To understand and identify determinants that can affect integration and use of a technology-based adherence product into the daily lives of patients with chronic diseases, we incorporated TAM. TAM framework has been tested in older adult population frequently to assess the technology adoption.[104–106] However, TAM has been criticized due to its limitation of not capturing the impact of social influence and behavioural intention on technology adaption.[107] Therefore, we chose to incorporate two health behaviour theories TPB and COM-B Model to compliment TAM. This integrated approach helped us understand the factors that can impact one's in-home medication intake, medication taking behaviour and barriers and facilitators impacting adoption of a technology-based adherence product. A similar approach was used to understand the technology adoption by community pharmacy staff where we utilized TAM framework to understand the factors that can impact the integration a technology-based adherence product into the community pharmacies. Moreover, we used TPB and COM-B Model to understand and predict the behaviour of pharmacy staff related to technology integration and adoption.

2.3. Project Overview

2.3.1. Ethics Clearance

The research projects described in Chapter 5, 6, 7 and 8 received ethics clearance from the University of Waterloo, Office of Research Ethics (ORE# 41015). All participants provided signed informed consent before in-home visits and interviews (see Appendix D, E and F for the approved information letter and consent form for both participant groups: patients and pharmacy staff).

2.3.2. Recruitment and Sampling Strategy

The research projects described in Chapter 5, 6, 7 and 8 were conducted from November 2019 to June 2020 in two major cities (Burlington and London) in Ontario, Canada. A purposive sampling strategy was used to recruit participants. This sampling method is a non-probability method that involves selecting certain individuals the researcher hopes to include in the study, and participants are selected based on specific characteristics of interest.[108] This sampling approach has been used frequently in qualitative studies as it provides participants that offer rich data in line with the aim of the study. The target population in this study were: (1) people with chronic medical conditions who were on a complex medication regimen; and (2) their health care providers, including pharmacists and pharmacy assistants who packaged and dispensed medications in SMBPs and monitored real-time medication intake via a web portal. The participants were recruited through various avenues such as local pharmacies, researchers' professional networks, community environments, social media, and by approaching previous study participants who had indicated a willingness to participate in future studies. The researcher used an eligibility checklist to screen patient participants (see Appendix C for the approved eligibility checklist).

A sample size determination was made for our quantitative methods, specifically examining the product's usability under investigation. Five to 15 participants can establish the usability of a product; five participants will permit the identification of 80% of usability issues, while up to 15 may be required to identify 100% of usability issues.[109] We aimed to recruit 10 participants to help us identify 80 – 100% of the usability issues. The qualitative studies do not require a sample size calculation. Whether one has reached an adequate sample size is usually determined by data saturation, e.g., the point at which qualitative data analysis does not elucidate any new information.[108]

2.3.3. Study Design

The research project described in Chapter 5 utilized a qualitative study design based on modified ethnography approach. The projects described in Chapter 6 and 7 consists of a mixed-method approach. Both qualitative and quantitative methods were utilized to gather data. Below is a detailed description of the methods used for data collection and analysis.

2.3.4. Qualitative Methods

Qualitative research focuses on people's observed experiences, views, attitudes, and actions in a real-world context or setting.[108,110] Incorporating a qualitative design in this study indicated that the study was conducted in a natural setting to interpret life experiences into meaningful phenomena. This type of study design provides rich and comprehensive insight in order to understand a situation holistically. Overall, this research method can be used to investigate research questions based on 'why', and 'how'.[110]

A modified ethnographic approach was used to collect qualitative data for the projects described in Chapters 5 and 6. Ethnography is one of five qualitative research methods and has a long and rich history in social science research. Ethnography's use in health sciences has been growing rapidly.[111,112] Ethnographies build accounts of culture by utilizing observational methods to study how participants make sense of their world.[111] Culture refers to a "set of guidelines which individuals inherit as members of a particular society."[113] While conducting an ethnography-informed study, language, race, cuisine, or customs can be viewed as one's culture.[114] When it comes to healthcare research, this cultural-based approach can be applied to patients who share a common characteristic, such as a disease condition or a particular aspect of their health.[112,113] People with chronic diseases are often on multiple medications and have a complex medication regimen to follow, which can be considered a culture-sharing aspect. Medication adherence is a

multifactorial process and a significant challenge in this particular population. The use of ethnography-informed methods provided an opportunity to observe this particular culture-sharing group in their natural environment. Moreover, in-depth interviews provided an opportunity to understand, interpret and describe the experiences, processes, activities, and behaviours of integrating a SMBP into their medication intake routine.

(a) Qualitative Data Collection Methods

Patient Study:

The chapters 5, 6 and 8 of this thesis describe the projects that involved patient participants who utilized the SMBP for their daily medication administration. A total of three in-home visits were conducted with patient participants. Background information (see Appendix G) and complete medication history (see Appendix I) were gathered during the first visit. The following methods were used to collect quantitative data (see Figure 2-1 for project specific data collection methods).

In-home Participant Observations are the process in which the investigator is actively observing, listening, and documenting the phenomenon of interest.[115] The particular phenomenon in this study was the medication-taking behaviour and process of integrating a SMBP in the home. During in-home visits, observations were made to explore different patterns (e.g., behaviours, routines, and uniformity) of the group related to their medication-taking behaviour, use of SMBP, reaction to reminders, and overall medication intake process. An observational protocol was used for recording the descriptive and reflective notes made during this process (see Appendix J and K for the observation protocol).

Digital Photography Walkabout is a process of capturing photographs while walking around the place of interest. Photographic research methods are becoming popular in healthcare research.

Numerous studies have utilized photographs to collect data.[116–118] The photography walkabouts allow the researcher to capture visual aspects of the study data, in addition to the narrative stories shared by participants.[118] During the first home visit, photographs of areas where participants store, organize and administer their medications daily were captured to understand what occurs in patients' homes related to their medication management process(s).

Field notes are the notes written by the researchers while conducting fieldwork to record the events, activities, and behaviours of participants.[119] Field notes help the researcher understand the cultural context and social situations during participant interactions. During this research project, field notes were written after each home visit. Additionally, reflective notes were written to record the researcher's own thoughts, concerns, and observations during the fieldwork.

In-depth interview is a process of asking participants open-ended questions and recording their responses. Each participant partook in a one-on-one interview. The interview guide consisted of questions regarding the patient's medication management process, experience integrating the SMBP, and feedback on product use. The three components: usability, functionality, and acceptability, were incorporated into the interview guide to explore the concept of integration.

a. Usability refers to how specified users can use a product to achieve defined goals.[120] This was assessed by asking participants if they were able to remove the tablet from the SMBP.
b. Functionality was defined as "the ability of the product to do what it is intended to do"[121] assessed by inquiring questions related to alarm functioning and tablet retrieval issues from the SMBP.
c. Acceptability was defined as "acceptance of the product by the end-user"[96] determined by inquiring participants about their intention to use the SMBP in the future.

Additionally, constructs from three frameworks, TAM, TPB, and COM-B Model, were used to develop an interview guide (see Appendix N for the interview guide). The first six interviews were conducted at the participant's homes; however, due to limitations placed by the emergence of the Corona Virus Disease (COVID-19) pandemic, the remaining four interviews were conducted over the telephone. All interviews were conducted with two researchers and were audio-recorded and transcribed verbatim.

Photo-elicitation is the process of utilizing visual methods such as photographs or videos during a participant's interview.[122] The visual images guide and enhance the depth of interviews with participants and allow for reflective communication.[123] During the first visit, the researchers took a series of photographs while each participant interacted with the SMBP. The images were compiled into a photo book (see Appendix Q), where each image had a clear description of each step involved in medication retrieval from the SMBP. The participant kept the photobook as a reference during the study period. During the interview process, researchers used these images to initiate a discussion regarding product integration.

Pharmacist and Pharmacy Staff Study

Chapter 7 discusses the study conducted at the community pharmacies. Researchers visited participating community pharmacies twice during the study period to gather background information (see Appendix H) and provide training on how to package medications in the SMBP, and interact with the web portal to monitor real-time medication intake. Community pharmacists and pharmacy assistants who dispensed and packaged participants' medications into the SMBP and remotely monitored their patients' real-time medication intake participated in one-on-one interviews. The interview guide was developed with constructs from three frameworks; TAM, TPB, and COM-B Model (see Appendix O for the interview guide). Due to the COVID-19

pandemic declaration, all interviews were conducted virtually. All interviews were conducted with two researchers and were audio-recorded and transcribed verbatim.

(b) **Qualitative Data Analysis**

Data analysis is a crucial step of qualitative studies. For the project described in Chapter 5, two researchers performed the data analysis. For the projects described in Chapters 6 and 7, the data analysis team comprised four researchers with different backgrounds, including pharmacy, health informatics, and systems design engineering. These researchers perceived the research question from a distinctive lens based on their profession, skills, knowledge, and lived experiences, which allows them to complement each other, inform new approaches, and reduce biases. This research does not provide the sole interpretations from one person's perspective; instead, it provides a detailed and comprehensive view from different disciplines. This type of approach in qualitative studies increases the depth and breadth of the data collection and analysis and reduces individual bias during the research process.[124,125] The data analysis team met every week to discuss the findings for approximately four months. The data from each study was analyzed using a different framework, as discussed below.

Content Analysis

The photograph data collected during the first home visit was analyzed using the content analysis approach, as described in Chapter 5. Content analysis has been used in healthcare research since the 18th century.[126] Hsieh & Shannon (2005) defined content analysis as "a research method for the subjective interpretation of the content of text data through the systematic classification process of coding and identifying themes or patterns."[126] The photographs, observation protocol documents, and field notes were analyzed using the conventional inductive approach (e.g., where

codes were derived from the data and were defined during the data analysis process). The following steps were taken to analyze the data.[127]

1. Data familiarization: The visual data including digital photographs, observation protocols containing older adults' narrative about their medication intake and management and field notes were reviewed by two researchers independently to gain an understanding of the content.
2. Code formulation: Data was coded by utilizing an inductive coding approach. Two researchers independently coded the data to identify the different concepts and patterns.
3. Category development: Codes were examined and grouped into categories based on their content and context. A code book was created containing the photographs, associated codes, categories and their description.
4. Theme development: Themes and sub-themes were developed by grouping categories.
5. Themes review: The research team reviewed the themes and sub-themes and defined the relationship among them.

Qualitative Analysis Guide of Leuven Framework:

The Qualitative Analysis Guide of Leuven (QUAGOL) framework was used to analyze one-on-one interviews of patient participants, discussed in Chapter 6. The QUAGOL framework was developed to analyze qualitative data based on the Grounded Theory Approach by Corbin and Strauss.[117] The data analysis process is comprised of a total of 10 stages divided into the following two broad phases: (a) Preparation of coding process and (b) Actual coding process.

Phase 1: Preparation of Coding Process:

This phase is comprised of 5 stages:

1. Reading and re-reading of interview transcripts: Four team members read and re-read the interview transcripts multiple times to gain a sense of the interview as a whole. The team members underlined key phrases and associated paragraphs and created a short report about each participant's contextual characteristics.
2. Writing narrative interview report: Each team member documented the essential characteristics of each participants' stories related to the research project. A one-page narrative report was created for each participant.
3. Developing a conceptual scheme for each interview: A conceptual interview scheme was developed from the interview's relevant concepts and provided rich insight into the research topic.
4. Assessing the appropriateness of conceptual interview schemes: Next, the research team re-read the interviews with the conceptual interview scheme in mind to examine the appropriateness of the conceptual scheme. The conceptual interview scheme was edited, revised, and refined during this step through detailed team discussions.
5. Constant comparison process: In this stage, the concepts of the interview schemes were compared to each other and further refined.

Phase 2: Actual Coding Process

The actual coding process was composed of the following five steps:

6. Drawing up a list of concepts: A list of concepts was prepared based on the conceptual interview schemes, without any hierarchy. The research team discussed and refined the concepts. The concept list was entered into NVivo Software (version:12.6.1) as preliminary codes.

7. Coding process: The actual coding was performed in this step. Each team member read the interview again with the list of concepts and linked the specific passage of the interview to one or more of those concepts. If new codes were found, they were noted down and verified with the interview data.
8. Analysis and description of concepts: Each code was carefully analyzed by reading the linking passage along with contextual or circumstantial aspects of the interview. The research team came together and discussed each code individually and defined it in their own words.
9. Extraction of essential structure: A list of concepts and their meanings was created and grouped into themes and sub-themes.
10. Description of results: In this stage, the essential findings in response to the research question were systematically and carefully described. The four team members used the constant comparison method to check, discuss, and further refine the findings continually. All four team members re-read the interviews for a final evaluation of the accuracy and comprehensiveness of the results.

Braun and Clarke's Thematic Analysis Framework

Braun and Clarke's thematic analysis framework was used to analyze the interviews of pharmacists and pharmacy assistants, as reported in Chapter 7. Thematic analysis is one of the most commonly used methods to analyze qualitative data. It is a method of identifying, analyzing, describing, and reporting patterns or themes.[128] An inductive approach-where codes and themes emerged within the raw data[129] was used following the 6-stepped approach outlined by Braun and Clark (2006). The framework consisted of following six steps.

1. Familiarizing with the data: All interview transcripts were read word by word to get familiarized with the data.
2. Generating initial codes: Coding is a process of assigning names to a portion of text or phrases.[129] A codebook was created to finalize the list of codes and contained the code name, code description and quotes from the data.
3. Generating initial themes*:* Codes were examined and similar codes were combined together to generate themes.
4. Reviewing themes: Themes were reviewed by the research team to make sure that they made sense. Data associated with the theme was read to verify that it supported the identified theme. Sub-themes were identified within the themes and grouped into different themes.
5. Defining themes: Themes and sub-themes were defined according to content and scope of data and proper titles were given to them.
6. Writing narrative analysis: Detailed analysis was written for each theme to describe the study findings.

2.3.5. Rigor in Qualitative Research

Qualitative research is often criticized for its small sample size, the potential for bias, lack of rigor, and quality. The criteria of rigor in qualitative studies are different from quantitative studies because the qualitative data describes peoples' experiences rather than summarizes data as numbers in quantitative findings.[130] Since the 1980s, qualitative researchers have described the quality and rigor of qualitative studies by using different terminologies such as internal validity, external validity, reliability, and trustworthiness.[108]

There is an ongoing debate whether quantitative terms such as reliability and validity should be applied to qualitative research as they represent the quantitative paradigm of research.[131,132] Validity refers to the "integrity of the methods undertaken and the precision in which the findings accurately reflect the data."[95] The term reliability describes "the consistency of the measures".[108,131] There are many different ways to demonstrate validity and reliability in qualitative studies, such as using multiple coders for interview coding, calculating inter-coder reliability, writing detailed reflective notes, utilizing member check process, and describing the thick description of the study, to name a few.[108]

For this research project, we utilized the alternative criteria offered by Lincoln and Gaba to determine the rigor of qualitative research termed as "trustworthiness."[108] This concept is one of the most popular methods to establish validity and reliability and ensure the rigor of the qualitative studies by applying four sub-criteria of trustworthiness.[124,133] These criteria include (a) credibility, (b) transferability, (c) dependability, and (d) conformability. The following section describes the different strategies that were utilized during this research project to achieve rigor.

a) Credibility

Credibility refers to "the confidence that can be placed in the truth of the research finding."[134] The credibility of the qualitative research corresponds to the internal validity criteria used in the quantitative paradigm.[124] Credibility can be established by using various activities such as member checking, prolonged engagement, and triangulation. To ensure credibility of this research project, various procedures including triangulation and member checking were utilized. Triangulation is a "process of using different data sources, investigators or methods to collect data to enhance the process of qualitative research."[134] To achieve method triangulation, we used more than one method to collect data (e.g., field notes, participant observations, and interviews). The research

team was comprised of researchers from different professional backgrounds, including pharmacy, health informatics, social work, and systems design engineers. Through these diverse professional backgrounds, we reduced individual biasness, explored different theoretical perspectives, and interpreted the study findings in a rich, comprehensive, and credible way. By utilizing a multi-disciplinary research team approach, we were able to achieve investigator triangulation in our study. In addition, we visited our participants multiple times during the study period, at different times of the day, to achieve data triangulation. Moreover, three different frameworks were applied to this research project, which provided further rigor to this study.

Furthermore, we utilized the member checking process to ensure the credibility of our study findings. Member checking or participant validation is when the researchers return the interview data to their participants to confirm the accuracy of the results.[135] This process has been used frequently to validate the rigor of the qualitative studies utilizing interviews to collect data.[136] We sent a document summarizing the themes, sub-themes, and associated quotations to our interview participants and asked them to review and indicate if they agreed or disagreed with our interpretations.

b) Transferability

Transferability in qualitative research can be described as "the degree to which the results of qualitative research can be generalized or transferred to other contexts or settings."[121] The transferability in qualitative research is equivalent to the external validity in quantitative research.[124,134] Qualitative studies are not typically generalizable due to their small sample size and unique phenomenon being studied.[133] However, transferability in qualitative studies can be achieved by a "thick description" of the phenomena.[124] This can be accomplished by incorporating the detailed and accurate description of the study setting, sampling strategy, participants

characteristics, data collection, and analytic process.[133] Moreover, reflexivity is another tool that can provide the context of the study settings and the researcher's own assumptions that can impact data collection, analysis, and result interpretation.[124] For each of our projects, we have provided a "thick description" of study settings, participants' demographic characteristics, study methodology, and interpretation of results to achieve transferability.

c) Dependability

Dependability refers to "the degree to which research procedures are documented, allowing someone outside the research team to follow and critique the research process."[133] This can be achieved by providing a detailed description of the methodology, documenting all activities, decisions, and processes during the research, data collection and analysis methodology details, and practicing reflexivity.[124,133,137] The concept of dependability corresponds to the criteria of reliability in quantitative research. We determined and reported the inter-coder agreement among coders where only two coders were coding the data. A few other approaches that were used to ensure the reliability included: using one system to code data (e.g., paper-based method for initial coding and NVivo Software for final coding was used), developing the initial codebook among coders, comparing coding across multiple researchers, further revising and finalizing the codebook, and using the member checking process. Furthermore, we provided a thick description of study methodology, settings, and participants.

d) Confirmability

Confirmability can be described as "the degree to which another researcher could confirm the research study's findings."[134] The confirmability of qualitative research can be achieved by keeping a record of all the activities and decisions during the research process and providing a reflection of the researcher's own beliefs and assumptions via reflexivity practice.

To ensure the dependability and confirmability of our research, we used the following strategies: (a) we kept a record of the data collection process, (2) multiple team members reviewed the transcripts to ensure accuracy, (3) four team members coded the interviews, (4) the coding system was discussed and verified multiple times by the research team, (5) the codebook was revised and updated, (6) all transcripts files were stored in NVivo database, and (7) the codebook was saved on Microsoft Excel (version 16.16.27) on more than one research computer. We also utilized the Consolidated Criteria for Reporting Qualitative Studies (COREQ) checklist to ensure appropriate and thorough reporting for all three studies of this project.[138] Reflexivity is another vital tool that addresses all four sub-criteria of trustworthiness.[124] Chapter 8 of this thesis project discusses the researcher's reflexivity during this research project and provides detailed context of the study, the researcher's own beliefs, and assumptions during the fieldwork, and the researchers' perceived impact study findings. Table 1 outlines the different methods used to ensure the rigor of this research project.

TABLE 2-1: Concepts, Definition, and Activities used to achieve Rigor

Concept	Definition	Activities
Credibility	*"Confidence that can be placed in the truth of the research finding"*[134]	Member checking Data triangulation Method triangulation Investigator triangulation Reflexivity
Transferability	*"Degree to which the results of qualitative research can be generalized or transferred to other contexts or settings"*[134]	Thick description Reflexivity
Dependability	*"Degree to which research procedures are documented, allowing someone outside the research team to follow and critique the research process"*[134]	Thick description Audit trail of data collection and analysis process Reflexivity
Confirmability	*"Degree to which the findings of the research study could be confirmed by another researcher"*[134]	Audit trail of data collection and analysis process COREQ checklist Determining inter-coder agreement Data triangulation Reflexivity

2.3.6 Quantitative Methods

Quantitative research methods focus on the objective measurement and numerical analysis of data, usually collected by questionnaires or surveys.[108] For the successful adoption of a product, it is crucial to determine its usability. The usability of a product helps identify how easy or difficult the product is for users, as this can very much impact a user's intention to integrate the product into their daily routine.[120] Numerous methods have been identified to evaluate the usability of technology-based products, such as questionnaires, interviews, logs, and the think-aloud method, to name a few.[109] Therefore, in addition to conducting one-on-one interviews about the integration of SMBP, the System Usability Scale (SUS) was used to assess the usability of SMBP. Additionally, to provide an opportunity to the product manufacturer to improve the quality of the SMBP and enhance user satisfaction, the Net Promoter Score (NPS) was also utilized.

a. System Usability Scale

Brooke developed the SUS in 1996 to assess the usability of different products and services subjectively.[139] It is a validated, easy-to-use, and quick tool that has been used frequently to test the usability of websites, cell phones, appliances, software products, and most recently, mobile health applications, electronic medical records, and adherence products.[140–144]

The SUS is composed of 10 statements, each with a five-point Likert scale ranging from “Strongly Disagree” to “Strongly Agree” (see Appendix L). The SUS has a score of 0 to 100. A SUS score of 70 or above indicates that the product is acceptable to its users.[145] The study participants, including patients and pharmacy staff, completed the SUS questionnaire after using the SMBP.

b. Net Promoter Score

The Net Promoter Score (NPS) is a simple and easy tool to assess a patient's experience.[146] The NPS was developed by Fred Reichheld in 2003 for management research.[147] Recently, this tool is gaining popularity to assess treatment outcomes and patient satisfaction about programs and services in healthcare research.[148–150]

The NPS is comprised of a single question: *"How likely is it that you would recommend this product/service/company to a friend or colleague?"* Participants answer this question using a scale ranging from 0 to 10 (0= "*Not at all likely"* and 10= *"Extremely likely"*).[146] The score of 9 or 10 represent participants who like the product or service and would recommend others to use it, known as *"Promoters."* Participants whose score is from 0 to 6 are called *"Detractors"* as they are the ones who are not satisfied with the product and would not recommend others use the product. Finally, participants who score 7 or 8 are called *"Passives"* as they are neither happy nor dissatisfied with the product.[146] The overall NPS score is calculated by subtracting the percentage of promoters from detractors. Passives do not impact the NPS score. In this study, all patient participants completed the NPS question at the end of the study (see Appendix M).

Chapter 3

The Usability, Acceptability, and Functionality of Smart Oral Multidose Dispensing Systems for Medication Adherence: A Scoping Review

This chapter is published as follows:

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3.1. Overview

Background: Medication non-adherence is a leading cause of non-optimal disease management, resulting in poor health outcomes, poor quality of life, and increased healthcare costs. Smart oral multidose dispensing systems (SOMDS) are being developed to address non-adherence; however, little is known about their integration into daily use by patients.

Methods: Using Arksey and O'Malley's scoping review framework, relevant literature was searched for in electronic databases (PubMed, EMBASE, International Pharmaceutical Abstracts, and Scopus). Observational and interventional studies reporting the integration and impact on adherence from SOMDS in adults ≥18 years and published after 1960 were included.

Results: Thirteen articles including one case study, 8 cohort studies, and 4 randomized trials were eligible. SOMDS included smart blister packaging, automated dispensers, and electronic medication trays. The number of medications dispensed per SOMDS was one (n = 3), >1 (n = 2), placebo (n = 1) and not reported (n = 7). Reported outcomes included impact on medication adherence (n = 3), integration (n = 2) and both parameters (n = 8).

Conclusion: Although most studies reported that SOMDS appear usable, there was significant variability in the SOMDS types, patient populations, medication adherence definitions, and measurements; impacting the interpretation of results. Future studies should be designed to address effectiveness of SOMDS on medication adherence in patients with multi-drug therapy and the utilization of real-time adherence data for informing clinical decision making.

Keywords

medication adherence, smart technology, multi-dose packaging, integration, real-time drug intake monitoring

3.2. Introduction

Medication adherence is one of the largest challenges of healthcare systems globally. According to the World Health Organization (WHO), approximately 50% of people with chronic diseases do not take their medication as recommended in developed countries.[1] In Canada, medication non-adherence has been reported to be approximately 52% and accounts for 5% of hospital admissions and 5% of physician visits, resulting in an additional $4 billion in healthcare costs annually.[151] Poor medication adherence can result in non-optimal treatment of chronic diseases, leading to increased emergency room visits, frequent re-hospitalization, poor disease outcomes, poor quality of life and significant costs to the healthcare system.[7,18]

Medication adherence is defined by the WHO as "*the degree to which the person's behavior corresponds with the agreed recommendations from a health care provider*."[1] Adherence to therapy is highly important for ensuring the effectiveness of medications and optimal clinical outcomes. Medication adherence generally refers to taking the right dose, at the right time, with the correct frequency and duration of therapy as prescribed by the health care provider. Adherence to the therapy is considered to be a complex, multi-process phenomenon and is generally comprised of three phases: initiation of the therapy, implementation of the therapy, and discontinuation of the therapy.[29] Non-adherence to medication can occur at any of the aforementioned phases. For example, a patient may decide not to fill the prescription, use more or less of the medication, administer it at a time that was not prescribed by the physician, or decide to discontinue the therapy without the health care provider's recommendation. Medication non-adherence can result from a patient's intentional decision not to take medication due to his or her personal beliefs, concerns, or side effects, or from intentionally changing the dose or time of medication intake.[29,30,39] Unintentional non-adherence occurs when the is unable to follow the

regimen due to physical and cognitive limitations, complex treatment regimens, or due to financial or accessibility limitations.[29,30,39]

Accurate monitoring of medication adherence is of significant importance. Inaccurate measurement of medication adherence can lead to various issues such as misjudgment of treatment, ordering of expensive diagnostic procedures, and the false need of dose intensification.[29] There are multiple ways to assess medication adherence; however, each of these methods has their own advantages and disadvantages and none are considered to be a gold standard.[7,29,62] Studies have shown that the rate of adherence may vary depending on the method of assessment.[7] Direct methods are the most accurate measures of adherence, but are considered to be invasive, expensive and labor intensive.[7,62,64] These methods include direct observation of medication intake, biological fluid (blood or urine) assay for drug and its metabolite detection and presence of biomarkers. Indirect methods are generally inexpensive and non-invasive. Some of these methods include patient self-report (interviews, patient medication diaries, and medication adherence scales or questionnaires), pill counts, pharmacy refill record assessments, and measurement of physiological markers.[29,62,64] Since there is no ideal method to assess medication adherence, multiple methods with a patient-specific approach is generally recommended to achieve the best possible assessment.[29] Unfortunately, indirect methods to measure adherence do not permit a health care provider to address medication non-adherence in between clinical visits. Furthermore, limitations of indirect measures of adherence include inaccurate reporting and overestimation of adherence by patients, and inability to discern actual pattern of medication intake from pharmacy refill records, pill counts and medication adherence scales or questionnaires.[152] Therefore, in order to address, monitor and improve medication adherence, numerous innovative technologies are being developed to monitor adherence on a more frequent or continuous basis. These technology-

based interventions range from electronic adherence monitoring via mobile phones, standard electronic adherence devices (electronic pill bottles, reminders, electronic medications organizers, etc.), to ingestible electronic sensors and real-time electronic medication adherence dispensers.[78,153] The use of real-time medication adherence devices, otherwise known as "smart products," has grown rapidly in the past two decades.

Smart products are objects, devices or software platforms that are embedded with processors, sensors, software or connectivity that allow data to be exchanged between the product and its environment, manufacturer, user and other products/systems.[84] For the purposes of this research endeavor, we have defined smart products as those which have two particular features: connectivity (the ability for collected data to exist outside of the physical device) and automaticity (the ability for data to be analyzed/ processed automatically in order to inform decision making, e.g. automatic data transfer to an online server allowing for real-time medication monitoring).[85] These products have been used primarily in clinical trials and research settings to provide real-time adherence data; however recently, there has been an increased interest in the development and use of real-time monitoring for medication adherence in non-research settings. These products are equipped to transmit data wirelessly to internet servers via a cellular network or web-based service. They also have the ability to send audio or visual reminders and notifications to patients when their dose is due. The availability of real-time drug intake data provides an opportunity for clinicians to identify non-adherence and develop data-informed interventions in a timely manner. Additionally, real-time drug intake data can be used to inform patients of their medication-intake behavior, which can motivate patients to modify their behavior.[78,153]

A recently published systematic review indicates that electronic monitoring is effective in improving adherence.[67] However, of the 10 studies included in the review, 7 investigated devices that are capable of only dispensing single drugs. Most of the studies utilized the Medication Event Monitoring System (MEMS®) SmartCap, which uses opening of the vial as a surrogate marker of medication intake. Only 2 studies included in this systematic review investigated the use of a multi-dose dispenser. While the tracking of medication intake in a multi-dose dispensing device would be similar to single drug dispensers, the use of the 2 devices would differ significantly. For example, the MEMS® SmartCap device mimics the functionality of a regular pill bottle, while multi-dose dispensers are available in different packaging styles such as blister packages, medication trays and pill boxes. Another systematic review indicates the existence of multiple types of multi-dose dispensing systems including the Helping Hand and Intelligent Drug Administration System.[65] However, in this review, the studies conducted with these devices were not considered smart because they did not include real-time monitoring for adherence. As such, the integration and impact on adherence of smart oral multidose dispensing systems (SOMDS) is unclear. Furthermore, how real-time monitoring of adherence impacts the integration of SOMDS in the home also remains to be examined. For these reasons, a scoping review was conducted to identify current literature in this area, summarize research findings and identify gaps in current knowledge in the integration and impact adherence related to SOMDS.

Objectives

The research question was "*What is known in the existing literature about the integration of* SOMDS *for medication adherence?*". For the purpose of this study, integration was defined as usability, functionality, and acceptability of SOMDS.

The objectives of this scoping review were to: identify types of SOMDS, outline methods used to assess the integration of SOMDS, report medication adherence definitions and methods used to measure it, evaluate outcomes in terms of integration and adherence, and inform future research on SOMDS.

3.3. Methods

The scoping review was conducted according to the 5-stage framework by Arksey and O'Malley[154] and reported using the PRISMA Extension for Scoping Reviews (PRISMA – ScR).[155] The scoping review included the following five steps: (1) identifying the research question, (2) identifying the relevant studies, (3) selecting the studies for inclusion, (4) charting the data, and (5) collating, summarizing and reporting the results.

Step 1: Identifying the research question

As detailed earlier, the review aimed to identify the different types of SOMDS available, examine the integration of these devices into the home of a patient, and evaluate the impact on adherence to identify gaps in current research and inform future research.

Step 2: Identifying the relevant studies

A comprehensive search was conducted in January 2019 for relevant literature in PubMed (MEDLINE), Ovid EMBASE, Ovid International Pharmaceutical Abstracts, and Scopus. The search strategy was developed in collaboration with a librarian. Search terms related to medication adherence and pharmaceutical technology were utilized, including medication non-adherence, medication compliance, medication persistence, medication non-compliance, medication reminder, smart technology, electronic monitoring, smart blister, e-blister, and dispensing system.

The Boolean operators AND/OR were used to combine search terms, and where possible, subject headings were combined with keywords in order to build an all-encompassing literature search. Advanced search options, such as subject heading explosion, truncation, and the adjacency feature were used in the search strategy construction, if the database included these functionalities. The database specific search strategies can be found in Appendix 1. Search results were exported into ProQuest® Refworks, where duplicate removal occurred.

Step 3: Study selection

Two reviewers independently screened the first 150 articles, after which inter-rater reliability between the 2 researchers was calculated (the Kappa coefficient was found to be 0.85). Due to strong inter-rater reliability, the remaining titles and abstracts of articles were screened by an independent reviewer. Bibliographies of relevant articles were also reviewed for additional citations. The studies were included in this review if: (1) they were published after 1960, (2) reported outcomes included a measure of integration (acceptability, functionality, and usability) and/or adherence, (3) the product used in the study was smart based on our definition, (4) the age of the participants was ≥18 years, and (6) they were written in English. Studies were excluded if they were referred to only in the grey literature, or available only as dissertations, letters, editorials and commentaries. We also excluded studies that reported the use of SOMDS solely for the purpose of monitoring adherence in phase 2 & 3 clinical trials testing the safety and effectiveness of drugs.

Step 4: Charting the data

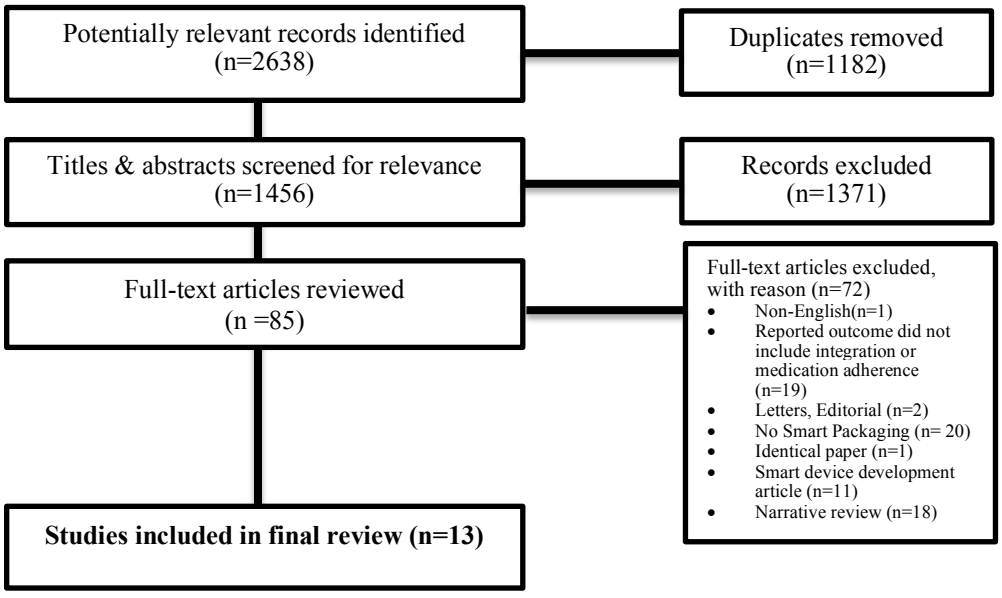
A data charting form on Microsoft® Office Excel for Mac 2011, Version 14.7.7, was developed by 2 reviewers to determine which variables to extract. The form captured relevant information on

key study characteristics and detailed information on the metrics used to describe integration of SOMDS. One reviewer independently charted data from each eligible article. Data charting was performed to capture the following study characteristics: (1) author(s), year of publication, study location, (2) intervention type and comparator (if any), (3) duration of the intervention, (4) study populations, (5) methodology, (6) outcome measures, and (7) results.

Step 5: Collating, summarizing and reporting the results

Abstracted data was collated and summarized into the following categories: demographic characteristics of the participants, general characteristics of the studies (e.g. type of study design, year, country of origin), the SOMDS used and methods to measure integration and medication adherence utilizing both quantitative data and narrative text format. Results were categorized and summarized on the basis of types of SOMDS, reported outcomes in terms of integration and medication adherence, as specified in Step 1 of the framework.[154]

FIGURE 3-1: PRISMA Flow Diagram for Scoping Review



3.4. Results

The initial search yielded 2638 citations, of which 1182 were duplicates. The remaining 1456 citations were screened by title and abstract. Of 1456 articles, 1371 were ineligible after the title and abstract screen, leaving 85 articles for full-text review. Full-text articles were reviewed according to the inclusion and exclusion criteria outlined in Step 3. See Figure 3-1 for a PRISMA Flow diagram of this process.

3.4.1. Characteristics of Included Studies

Of the 13 studies included, 61.5% (n = 8) were cohort studies, 30.8% (n = 4) were randomized control trials and 7.7% (n = 1) were case studies (see Table 3-1). Of the studies included, 23.1% (n = 3) were conducted in Europe, 38.5% (n = 5) in North America, 23.1% (n = 3) in Africa and 15.4% (n = 2) in Asia. All studies were published within the last decade. Of the 13 studies, 23.1% (n = 3) studies assessed medication adherence alone,[156–158] 15.4% (n = 2) of studies assessed integration of smart devices alone[143,159] and 61.5% (n = 8) of studies assessed both medication adherence and integration.[160–167] One study measured integration, but did not report integration as an outcome.[166] Approximately 61.5% (n = 8) of studies reported additional parameters such as blood pressure, Montreal Cognitive Assessment (MoCA) scores, Caregiver Burden Scale (CBS), Hospital Anxiety and Depression Scale (HADS) scores and laboratory data (see Table 3-2).[143,156,157,159,162,164–166]

TABLE 3-1: List of Studies included in Scoping Review

Study	Year	Country	Study Design	SOMDS
Haberer et al.[165]	2010	Uganda	Cohort Study	Wisepill
Van Onzenoort et al.[167]	2012	Netherland	Cohort Study	Blister Pack
Arnet et al.[156]	2013	Switzerland	Case Study	Blister Pack
Brath et al.[162]	2013	Austria	RCT	Blister Pack
Hayakawa et al.[161]	2013	Japan	Cohort Study	Smartphone-based Medication Self-management System
McGillicuddy et al.[164]	2013	USA	RCT	mHealth System
Ligons et al.[143]	2014	USA	Cohort Study	Electronic Medication Management System
Orrell et al.[166]	2015	South Africa	RCT	Wisepill
Lines et al.[158]	2016	USA	Cohort Study	Philips Medication Dispenser
Hoffmann et al.[157]	2017	USA	Cohort Study	Automated Home Medication Dispenser
Siu et al.[160]	2017	Canada	Cohort Study	eDosette
Musiimenta et al.[159]	2018	Uganda	RCT	Wisepill
Shtrichman et al.[163]	2018	Israel	Cohort Study	ReX

Abbreviation: RCT = Randomized controlled trial

TABLE 3-2: Characteristics of Scoping Review Studies

Type of studies	RCT = 4 Cohort studies = 8 Case studies = 1
Total number of participants	N = 922 RCT = 833 Cohort studies = 547 Case studies = 1
Types of participants	Patients = 856 Caregivers = 21 Social supporters = 45
Sex	Total number of patients reported sex = 651 Male = 292 (44.9%) Female = 359 (55.1%) Not reported = 2 studies
Age	Range = 18-92 yrs Age>65 = 7 studies* Age<65 = 5 studies* Not reported = 2 studies
Average number of medications taken by patients	Range = 7 - 14.9 per day
Type of SOMDS	Smart blister packs = 3 studies Automated dispensers = 4 studies Electronic medication trays = 6 studies
Number of medications in SOMDS	Multi-drug medication packaging = 2 studies Single-drug medication packaging = 3 studies Placebo = 1 study Not reported = 7 studies
Duration of study	Range = 4 days- 16 months Not reported = 2 studies
Comorbid conditions	CVD, hypertension, diabetes, hypercholesterolemia = 4 study* Renal transplant = 1 study HIV = 3 studies Memory disorder = 1 study* Healthy volunteer = 1 study Not reported = 4 studies

Abbreviations: CVD= Cardiovascular disease, HIV= Human immunodeficiency virus,
RCT= Randomized controlled trial, SOMDS = Smart oral multidose dispensing systems
* In these cases, some studies reported > 1 group

3.4.2. Types of SOMDS

The scoping review identified three types of SOMDS. Of the 13 studies, 23.1% (n = 3) of studies used smart blister packs, 30.8 % (n = 4) used automated medication dispensers, and 46.1 % (n = 6) used electronic medication trays. See Table 3-3 for a description of the SOMDS identified.

TABLE 3-3: Description of SOMDS

Device Name	Description
Smart Blister Packs	Pre-formed plastic packaging where medications are stored in multiple plastic cavities or pockets and is sealed to an adhesive coated paper.
Unit dose Blister Pack	Prototype self-adhesive labels printed with electronic circuitry affixed to an existing standard medication blister card. The wireless data transfers to a web-based service through either a mobile phone-based gateway (touching the patient-specific blister card based to RFID technology)[162] or via a storage chip containing RFID technology using NFC interface.[167]
Multidose Blister Pack	Prototype device, clear, self-adhesive polymer film, with printed loops of conductive wires affixed to regular multidrug punch cards with 7 x 4 cavities. A small communication device was attached to the blister pack that transmits data wirelessly to a cloud-based system.[156]
Automated Medication Dispensers	Computerized storage units that provide secure dispensing of medications at specified time intervals.
Electronic Medication Management System	Commercially available device which dispenses medications from single-dose blister cards inserted via tray, according to schedules programmed by a pharmacy. The device can provide a 30-day supply of 10 different blister cards. Remote control functionality is available via a secure online web connection that communicates data from EMMA® through an embedded cellular modem or LAN connection.[143]
Philips Medication Dispenser	Commercially available device which can dispense up to 60 cups of medications and up to six doses per day. The medication doses are prepared by pharmacies in machine-dispensed cups with lids. The cups are loaded into the machine by a trained caregiver, family member, or PMD supplier. The machine can alert a caregiver or family member of a missed dose and also track adherence rates.[158]
Automated Home Medication Dispenser	Prototype automated dispenser that can dispense medications based on programmed schedules for up to 90-day of 16 medications. It was equipped with audio and visual reminders to alert patients of dispensed doses. Each dispensed dose was uploaded to an online portal for continuous adherence monitoring. Caregivers received notifications of late or missed doses.[157]

ReX	Prototype hand-held mobile device that consists of a reusable drug dispensing unit, a disposable cassette, a cellphone app, and a Dose-E Analytics cloud system. The disposable cassette contains a storage unit comprised of 16 separate pill compartments pre-packaged by the pharmacy. Additionally, equipped with a mouth piece for direct pill ingestion. In order to administer the drug, the cassette has to be inserted into the DDU. The device records all pill intake events. This information is transmitted through the cellphone app to the Dose-E Analytics cloud. Therapy data can be relayed in real time to a preferred contact person.[163]
Electronic Medication Trays	Multi-compartment medication organizers, also referred to as dosettes, pill organizers, or pillboxes that are *equipped with a smart component by utilizing internet, Bluetooth or GSM technology.*
Smartphone-based Medication Self-management System	Prototype system comprised of a pill box with 21 compartments (can supply up to 3 doses for 7 days) and a mechanical and electronic module; composed of a microcontroller unit, a Bluetooth device, and a switch sensor to sense whether the pillbox is open or closed. Data is stored in a smartphone using a relational database engine synchronized with a database server.[161]
eDosette	Prototype device comprised of a digital image sensor operated by a computer. The device has a specified compartment to store blister packs or dosettes. A series of pictures are taken of the blister pack or dosette by the device hourly. The image data is transmitted to a web-application server continuously, and transformed into a patient-specific MAR.[160]
mHealth System	Prototype system comprised of a wireless GSM electronic medication tray (MedMinder), a wireless Bluetooth enabled blood pressure monitor and a smart phone. The medication tray contains 28 separate compartments to administer up to 4 doses for 7 days. The device sends audiovisual reminders to the patients and text or emails messages to the provider if the compartments were not accessed in a timely manner by the patient. The system also sends weekly medication adherence reports to health care providers.[164]
Wisepill	Commercially available, the device can either store up to a week of medication in a 7-compartment pill box[166] or can hold up to 30 large or 60 small pills in a medication container.[159,165] When the patient opens the device to take pills, the device records a date-and-time stamp. An internal modem and subscriber identity module card enable the device to send a real-time mobile signal to a secure web server.

Abbreviations: DDU = Drug dispensing unit, EMMA® = Electronic Medication Management System GSM = Global system for mobile communications, LAN = Local area network, MAR = Medication administration record, NFC = Near field communication, PMD = Philips Medication Dispenser, RFID = Radio frequency identification

3.4.3. Integration of SOMDS

Ten studies (76.9%) measured the integration of SOMDS by users;[143,159–167] however, one study did not report acceptability, even though it was measured as an outcome.[166] Common methods to measure integration included interviews, questionnaires and device generated reports (see Table 3-4).

TABLE 3-4: Integration of SOMDS (N = 9)

Study (SOMDS)	Methods to Measure Integration				Reported outcomes
	DGR	I	Q	Other	
Acceptability					
Brath et al.[162] *(Blister pack)*			✓		74% of patients thought product worked well 56% of patients were glad physicians knew if and when they took their medications 25% of patients asked for more automated communication with physician
Haberer et al.[165] *(Wisepill)*			✓		All participants found the device: - easy or very easy, or convenient or very convenient to use - attracted attention, but it did not bother the participants Participants liked having their medication adherence monitored regularly
Functionality					
Van Onzenoort et al.[167] *(Blister Pack)*	✓				100% device functionality as assessed by patient ID, date and time of retrieval of tablets 17% of total instances when participant removed multiple tablets from device were inappropriate; 70% of these events was due to a device error
Usability					
Ligons et al.[143] *(Electronic Medication Management System)*		✓		SUS, Video recording & coding	Significant correlation (p=0.0429) found between SUS and task completion Significant correlation (p<0.0001) found between IADLS and task success

				Difficulties found: "Manual Drop" & "Load blister card or new prescription pills", "Need tech support to use system"
Acceptability and Functionality				
Hayakawa et al.[161] *(Smartphone-based Medication Self-management System)*			Not specified	70% of patients intended to use device in future 80% of patients were satisfied with the device
McGillicuddy et al.[164] *(mHealth System)*		✓		75% of patients accepted to participate in study Average satisfaction = 4.8/5 Easy to learn = 4.7/5 Easy to use = 4.3/5
Musiimenta et al.[159] *(Wisepill)*	✓	✓		Device opening data was transmitted: - 89% of the time after a 0-5-minute delay - 9% of the time after a ≥ 60-minute delay - Remaining 2% was not reported Qualitative interview analysis found the following themes: usefulness of device, usefulness of monitoring, appearance of device, battery life of device, social norms, disclosure of medical status and stigma
Acceptability, Functionality and Usability				
Siu et al.[160] *(eDosette)*	✓	✓	✓	Mean ratings were calculated by coding responses as strongly agree= -2, disagree =-1, neutral = 0, agree =1 and strongly agree= 2 Mean ratings reported: - Ease of use = 1.20 - Overall satisfaction = 0.50 - Impact of confidence in taking their medications correctly = 0.60 5% of data was missing due to a device error
Shtrichman et al.[163] *(ReX)*		✓		81% of the patients found the device easy to use initially 87% of the patients found it easy to use in-home 90% of the patients found it comfortable to use in-home Usability not influenced by education level but was influenced by age;

	- Age > 80 = 71% of patients found it easy to use - Age 40-80 = 81% of patients found it easy to use - Age 18-40 = 94% of patients found it easy to use

Abbreviations: DGR = Device generated report, I = Interview, IADL = Instrumental activities of daily living, Q = Questionnaire, SOMDS = Smart oral multidose dispensing system, SUS = System usability scale

3.4.4. Medication Adherence Assessment

Medication adherence was measured and reported variably in 11 studies.[156–158,160–167] Out of the 11 studies that measured medication adherence, three studies did not define adherence (see Table 3-5).[158,161,165] Two studies used standardized medication adherence scales to measure adherence. However, medication adherence was defined differently in the two studies.[160,164] A self-rated questionnaire based on Morisky's scale was used in one study.[160] The second study used a modified Russell et.al score (modified for dosing schedule other than twice daily).[164] Multiple methods were used to measure and report medication adherence using SOMDS (See table 3-6). A total of 5 studies reported an improvement in medication adherence[156,157,162–164] and 2 studies reported a decline in medication adherence after using the SOMDS.[165,166]

TABLE 3-5: Definition of Medication Adherence

Study	Definition of Medication Adherence
Arnet et al.[156]	1) Percentage of overall taking adherence 2) Percentage of correct dosing days calculated over the duration of the observational period 3) Percentage of correct dosing intervals (correct dosing interval: doses were administered within 25% of the prescribed interval)
Brath et al.[162]	Timing and number of pills taken
Hoffmann et al.[157]	Actual pill count divided by expected usage based on prescribing instructions Complete dispensing = if all medications were available in the device and the patient accessed the dispensed medications within the dispensing time window Incomplete dispensing = if one or more medications were not available in the device or if the patient did not access the dispensed medications within the dispensing time window
McGillicuddy et al.[164]	Medications had to be taken within a 3-hour window centered on the prescribed dosing time Score ranged from 0 - 1 (missed dose = 0, dose taken outside the 3-hour window but within a 6-hour window = 0.5, dose taken within the 3-hour window = 1
Orrell et al.[166]	Number of days the container was opened over the number of days of the study
Shtrichman et al.[163]	Percentage of dose taken before and after reminder function
Van Onzenoort et al.[167]	1) Intake Adherence: total number of pills pushed through the pack divided by total number of pill use 2) Timing adherence: total number of pills pushed through the blister pack in specified time frame 3) Days of correct dosing: number of pills pushed through the pack in 24 hours divided by total number of pills
Siu et al.[160]	Percentage of doses actually administered within a 2-hour time window of the average dose administration time

TABLE 3-6: Medication Adherence (N=11)

Study (SOMDS)	Medication Used in SOMDS	Intervention Group	Methods to Measure Adherence				Adherence Measure Frequency	Reported Outcomes
			DGR	PC	SR	Other		
Case Study								
Arnet et al.[156] *(Blister pack)*	Levothyroxine, Rosuvastatin, Aspirin, Paroxetine, Vitamin B complex, and Levetiracetam	None	✓				NR	Time of morning intake: PRE-I = 2:00PM; POST-I = 5:29AM Interval between morning & evening doses: PRE-I = 6.57h; POST-I = 11.28h Compliance: PRE-I = 100%; POST-I = 102.5%* Correct dosing days: PRE-I = 100%; POST-I: 100% Correct dosing interval (levetiracetam): PRE-I = 0%; POST-I = 42.3%
Cohort Study								
Haberer et al.[165] *(Wisepill)l*	Three fixed drug combinations: (Zidovudine OR Stavudine), AND, Lamivudine and Nevirapine, Two fixed drug combinations: (Zidovudine OR	None	✓	✓	✓	30-day VAS	Monthly	Adherence rate determined by the device was 93% Adherence rate determined by self -report & unannounced pill count was 100%

	Lamivudine) and Efavirenz						
Hayakawa et al.[161] *(*Smartphone-based Medication Self-management System*)*	NR	None	✓			NR	36.2 % patients administer their medication with reminder system and 80% found the reminder was effective
Hoffmann et al.[157] *(Automated Home Medication Dispenser)*	NR	None	✓	✓		NR	Baseline adherence = 49% 6-month adherence = 96.8%
Lines et al.[158] *(PMD)*	NR	1. PMD 2. SBP			✓	NR	Patients rarely missed a dose; 75% for PMD and 66% for SBP Due to low response rate and small population size, results were statistically non-significant
Shtrichman et al.[163] *(ReX)*	Placebo (Tic-Tacs®)	1. ReX device 2. Standard pill packaging	✓	✓	✓	NR	Adherence rate: 97.6% for ReX device and 76.3% for standard pill packaging ($p< 0.001$)
Siu et al.[160] *(eDosette)*	NR	None	✓		✓	NR	Adherence rate was between 64-100%
Van Onzenoort et al.[167]	Valsartan	None	✓			NR	Overall Intake adherence = 97.6% Timing adherence= 86.9%

(Blister pack)							Correct dosing = 94.3%
Randomized Control Trial							
Brath et al.[162] *(Blister pack)*	Metformin, Simvastatin, Ramipril and Rosuvastatin	1. Electronic blister 2. SBP	✓	✓+	Medication diary	NR	Timing adherence was 95.59% for all 4 medications Significant improvement in adherence seen in intervention group for metformin only, when compared with control (p=0.04). No significant difference between groups was found with the other medications.
McGillicuddy et al.[164] *(mHealth System)*	NR	1. mHealth System 2. Electronic medication tray	✓			Monthly	Adherence rate= Significantly higher rates compared to the control group (electronic medication tray) over 3 months (P < 0.05)
Orrell et al.[166] *(Wisepill)*	Tenofovir, Lamivudine and Efavirenz	1. Reminder text messages for missed medications using Wisepill 2. Standard care (Wisepill without reminders)	✓	✓		16 and 48 weeks	Median adherence: 100% for self-report/pill return for both groups, 82.1% for intervention measured by Wisepill, and 80.4% for control measured by Wisepill Timing adherence: NR for self-report/pill return for both groups, 47.6% for intervention measured by Wisepill, and 44.8% for control measured by Wisepill

*Due to anticipated consumption of extra doses, resulted in dose change by the physician

+Assessed in control group only

Abbreviations: DGR = Device generated report, NR = Not reported, PC = Pill count, PMD = Philips Medication Dispenser, PRE-I = Pre-intervention, POST-I = Post-intervention, SBP = Standard Blister Packaging, SOMDS = Smart oral multidose dispensing system, SR = Self-report, VAS = Visual analogue scale,

3.4.5. Other Parameters

Eight studies assessed and reported additional parameters such as laboratory tests, blood pressure, cognitive tests, and caregiver burden scores along with medication adherence and integration of SOMDS.[143,156,157,159,162,164–166]

Brath et al. reported fasting blood glucose concentration, Hemoglobin A1C (HbA1C), blood cholesterol concentrations, body weight and blood pressure as additional parameters in a randomized control trial comparing a smart blister pack with a standard blister pack over 13 months.[162] All laboratory parameters and vitals were assessed at baseline, during follow-up appointments and at the end of the study. This study showed significant improvement in systolic and diastolic blood pressures (decrease of 5mmHg/5mmHg; p=0.02/0.003, respectively), total cholesterol (decrease of 10 mg/dL; p=0.02) and LDL cholesterol (decrease of 7mg/dL; p=0.06) in the arm that received a smart blister pack in comparison to the control. Non-significant improvement in HbA1C, fasting plasma glucose, high density lipoprotein (HDL) and body weight was also noted in the arm that received a smart blister pack. McGillicuddy et al. measured systolic and diastolic blood pressure monthly in 19 participants over 3 months, and reported significant improvement in systolic blood pressures in the group using SOMDS at months 1 and 3.[164]

Ligons et al. assessed participants' education status, cognitive function using Mini Mental State Exam (MMSE) and functional capacity using Instrumental Activities of Daily Living (IADLS) in a non-intervention usability study.[143] This study reported that participants who had scored ≥24 on MMSE had better task completion rates (MMSE <24, task completion 37% versus MMSE ≥24, task completion 63%; p=0.04). There was no significant relationship found among participants'

education status and task success, in terms of completion rates.[143] Task completion rates refer to the participant's ability to complete a set of tasks required to use the SOMDS. Another study investigated the use of SOMDS with 21 patient-caregiver dyads to investigate the impact on adherence and caregiver burden.[157] This study found that participants who had scores indicative of mild cognitive impairment (MCI) or dementia according to the Montreal Cognitive Assessment (MoCA), tool that screens for cognitive impairment, were able to use the device. Since caregivers were responsible for filling and refilling the device during the study period, the baseline Caregiver Burden Scale (CBS, a tool to evaluate perceived caregiver burden) was compared to the end of intervention at 6 months. This study reported that use and maintenance of the device in a patient's home did not result in additional caregiver burden.[157]

Orrell et al. compared Wisepill with and without a text messaging reminder in a randomized control trial in patients with HIV. Parameters measured included HIV RNA, treatment interruption (TI) and retention in care at baseline, 16 and 48 weeks in both arms. The study reported that the use of SOMDS significantly reduced the frequency of TI of over 72-hour intervals in patients randomized to Wisepill with text messaging as compared to the control arm ($p=0.003$) although rates of reduction in the control arm were not provided. Additionally, the study noted that there was no difference at 48 weeks between the arms in overall retention in care or virological outcome.[166] Virological load was also reported by another study using the same SOMDS in a similar population of participants with HIV. This study was designed as a prospective cohort and compared adherence at six months between a standard pill bottle and SOMDS. However, due to a small sample size, researchers were unable to find a correlation between non-adherence and virological load.[165]

3.5. Discussion

This scoping review provides a summary of the literature on the integration of SOMDS and their impact on medication adherence. The review identified several studies that have investigated the use of a variety of SOMDS in various populations. Overall, there is significant variability in the methods that are being used to measure adherence. Few studies used a standardized medication adherence scale to measure and report adherence. Some studies only reported the timing and/or numbers of pills taken, while others provided a broader definition including number of pills, correct dosing interval and correct number of days. Therefore, a standardized method to assess medication adherence is needed to better understand the utilization of SOMDS in the future. There was also considerable variability found in methods used to report outcome measures for both adherence and integration. Therefore, the cross-study comparison among the studies in regards to integration of these products and effectiveness on medication adherence was not possible. However, common trends were seen in terms of product acceptability and satisfaction among end users.

Overall, all the studies indicated that SOMDS were easy to learn and participants were satisfied with their use; however, usability issues were reported. These included challenges with hearing the SOMDS,[161] and inserting the blister card into the SOMDS.[143] Technical knowledge was required to operate SOMDS, which was recognized as a significant limitation in an elderly population.[143] Although interface or screen displays were user-friendly and data transfer to the cloud system was convenient and easy, technical improvement was required for some of the SOMDS. For instance, some blister cards had an issue due to breakage of the neighboring blister's conductive track and needed further improvement.[167] The acceptability of all the devices was high

but there were a few instances in which participants expressed a concern about use of SOMDS. For example, some patients felt uncomfortable that their medications were being monitored,[160] although others were happy that their physicians or healthcare team were aware of their real-time medication intake.[162] Moreover, larger devices were felt to limit portability in comparison to smaller device.[159,160] Studies that took place in under-developed countries illustrated concerns regarding the impact of the technology on confidentiality due to social stigma about the disease condition, limited pill capacity of the device, battery change, fear of losing or damaging the device while travelling, shared phone ownership, usability skills and availability of electricity as possible challenges with the integration of SOMDS.[159,165]

SOMDS are available for use by both young and older adults. However, since the number of medications, types of medication formulations being administered and daily doses taken increases with aging due to the increasing number of chronic conditions,[13] multi-dose dispensing systems are frequently being used to address the increasing complexity of medication regimens and resulting non-adherence in older adults.[160] However, before these devices can be used in this population, usability should be considered. Aging may produce a decline in visual and sensory perceptions as well as strength and dexterity which will impact the usability of a product and has the potential to negatively impact adherence to medications.[168] For example, Hayakawa et al. reported that the audio-reminder was inaudible if the device was placed beyond a certain distance.[161] This product would be ineffective for older adults with hearing impairment. Unfortunately, of the seven studies which recruited older adults, only one study reported the influence of age on usability.[163] Among the different age groups (18 – 40 years; 41 – 60 years; 61 – 80 years; 81 – 90 years), there was a decrease in the usability of SOMDS in the participants >80

years.[163] Another study reported that 73% of elderly patients interviewed could use a mobile phone as a user device in a system for medication management.[161] However, this study did not examine the relationship between the participant age and usability of the SOMDS. Furthermore, user-friendliness of one SOMDS in one study cannot be interpreted to represent usability of different SOMDS due to differences in features of these devices. The dearth of data addressing the usability of these devices in this population highlights an important gap that needs to be addressed with future research. Knowing which features impact usability and functionality among older adults can assist clinicians in recommending appropriate devices which improve adherence and not, inadvertently, worsen it.

Caregivers and care providers play an important role in medication management. As the population ages, caregivers (both formal and informal) are increasingly taking on the responsibility for managing medications, especially for older adults with cognitive and physical impairments. A recent qualitative study assessing family caregiver involvement in managing care recipients' medications found that approximately 54% of family caregivers help with the medication management process.[169] However, only 7.7% (n = 1) of studies in our scoping review recruited caregivers to determine if there was a change in caregiver burden through use of SOMDS.[157] Caregivers are an important stakeholder in a patient's adoption of medication adherence products. Therefore, it is imperative to consider caregiver impact and involvement while investigating the integration of SOMDS into daily use.

Another population where the use of SOMDS has been investigated broadly is HIV patients, where long-term adherence has significant implications on mortality among younger patients. Studies

taking place in Africa primarily included patients who were diagnosed with HIV, as it remains one of the biggest health problems in developing countries.[159] Real-time data monitoring of antiretroviral combination medication intake in this population has identified treatment interruptions and allowed timely intervention by the health care providers to improve medication management.[165,166] For example, there was a significant reduction in treatment interruptions in the use of Wisepill with text-messaging.[166]

Although SOMDS have the capability of dispensing multiple medications with more than once daily dosing intervals, only one study utilized SOMDS in this way.[156] Two studies utilized SOMDS for either multiple medications administered as a once daily schedule[166] or one medication administered as a multiple daily dosing schedule.[165] Since people with chronic diseases are on complex therapy and take multiple medications various times during the day, using SOMDS in this population may be beneficial and future studies should address the use of SOMDS in patients on multiple medications with variable dosing schedules.

Real-time medication adherence data can help clinicians identify non-adherence patterns and intervene in a timely manner to improve therapy outcomes. As illustrated by Arnet et al. in their case study, real-time drug intake monitoring notified researchers that the patient was administering more than the prescribed dosage of the sleeping pills.[156] This helped the physician identify and discuss the issue with the patient and resulted in an intervention to address the issue. In the same case study, the pharmacist interpreted real-time medication intake data to identify that the patient was not administering his seizure medication at appropriate intervals. This was resolved with patient education. Both of these examples demonstrate the benefit of real-time medication intake

monitoring as it provides information on non-adherence not only related to dosing, but also dosing intervals. In a randomized control trial conducted by McGillicuddy et al., more therapy changes were made for patients where real-time medication intake data was available in comparison to the control group.[164] Hence, using real-time medication intake data patterns can be used as a valuable resource to personalize adherence intervention, educate patients to avoid or minimize possible adverse effects due to inappropriate dosing intervals and optimize therapy outcomes in a timely manner. The usability of medication monitoring platforms by health care providers, especially pharmacists, is a necessary consideration as many are involved in assisting and helping patients with their medication regimens. Misinterpretation of adherence data being presented is possible if the platform has not considered how to present this data in a user-friendly manner. Furthermore, the workload required to access real-time monitoring adherence information should be considered as this may impact how and whether care providers and clinicians opt to use this information in their decision-making process. Therefore, future studies should consider investigating the utilization of real-time medication adherence data by clinicians to address medication intake behaviors.

Identified Gaps

There were multiple gaps identified through this scoping review. Due to the marked variability in defining, measuring and reporting medication adherence, a cross-study analysis was unable to be performed during this scoping review. We recommend addressing this gap by developing or utilizing a standardized medication adherence definition in future studies in order to enable realistic comparison of current and future research studies on SOMDS.

Another identified gap was the lack of consideration of caregiver impact and involvement while investigating the integration of SOMDS into daily use. Caregivers are an important stakeholder in a patient's adoption of medication adherence products, and as such, should be considered when researching the impact of SOMDS. Furthermore, health care providers and clinicians play an important role in the utilization and monitoring of patients through the use or real-time monitoring data collected by SOMDS. It is important to gain the input of caregivers, health care providers and any other stakeholders who will be interacting with the product regularly should it be released and sold commercially.

The final gap identified through this research endeavor was the use of SOMDS for daily use of multiple medications with variable dosing intervals versus once daily administration. Since people with chronic diseases are on complex therapy and take multiple medications at various times during the day, using SOMDS in this population may be beneficial and future studies should address the use of SOMDS in this particular population.

Other common limitations found across all studies were small sample sizes and short study durations. Small sample sizes in studies impact the generalizability of findings, and adherence reported in short-duration studies should not be interpreted to indicate long-term adherence, especially among patients on multiple medications for chronic conditions.

Strengths and Limitations

The major strength of this scoping review is the vigorous and comprehensive search strategy that was used to capture the breadth of studies published worldwide. Though not all articles were

screened or reviewed by 2 independent researchers, high inter-rater reliability was found between the researchers, indicating high agreeability. Despite these strengths, some limitations of this scoping review should be noted. The scoping review may not have identified all of the articles as the search criteria for this review was limited to articles published in English and non-grey literature.

3.6. Conclusion

To the authors' knowledge, this is the first scoping review that has evaluated the integration of SOMDS for medication adherence. This scoping review of SOMDS demonstrates an extensive landscape of the various types of products, interventions and outcomes that have been studied to improve medication adherence in various patient populations. This review highlighted various types of SOMDS, which provide the capability for real-time medication adherence monitoring via Bluetooth, near field communication (NFC) or radio frequency identification (RFID) technology to a cloud-based web portal. Additionally, these systems have the capacity to send automatic reminders via short message service (SMS) texts, or emails, to patients to remind them to take their medication on time. Since complex medication regimens are used to manage chronic diseases, SOMDS have the potential to improve unintentional medication non-adherence due to forgetfulness. Furthermore, real-time monitoring of SOMDS enables clinicians to monitor adherence and address causes of intentional non-adherence, such as side effects.

Although SOMDS appear to be usable, there is significant variability in: the types of dispensing aids, patient populations and measurement of adherence, which impacts the generalizability of results. Future studies should be designed to address the usability and effectiveness of these

products on medication adherence in patient populations using complex therapy regimens (i.e. multiple medications with variable daily dosing), study larger samples and assess the impact of real-time drug intake data availability on health care providers, particularly pharmacists and physicians.

APPENDIX 3-1: Database specific search strategy

Database	Search Strategy
PubMed	(medication adherence[mesh] OR "medication adherence" OR "medication nonadherence" OR "medication non-adherence" OR "medication compliance" OR "medication persistence" OR "medication non-compliance" OR "medication noncompliance" OR "medication reminder") AND (technology, pharmaceutical[mesh] OR SMART tech* OR "electronic monitoring" OR "smart blister" OR "e-blister" OR "electronic blister" OR "dispensing system" OR automat*)
Scopus	(TITLE-ABS-KEY ("medication adherence" OR "medication nonadherence" OR "medication non-adherence" OR "medication compliance" OR "medication persistence") OR TITLE-ABS-KEY ("medication non-compliance" OR "medication noncompliance" OR " medication reminder") AND TITLE-ABS-KEY ("SMART technology" OR "SMART technologies") OR TITLE-ABS-KEY ("electronic monitoring" OR "smart blister" OR e-blister OR "electronic blister") OR TITLE-ABS-KEY ("dispensing system") OR TITLE-ABS-KEY (automat*))
Embase	1. exp medication compliance 2. (medication adherence or medication adherence or medication nonadherence or medication non-adherence or medication compliance or medication persistence or medication non-compliance or medication noncompliance or medication reminder) 3. (SMART tech* or electronic monitoring or smart blister or e-blister or electronic blister or dispensing system or automat*) 4. (pharm*adj4tech*).mp.[mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, key word, floating subheading word, candidate term word) 5. 1 or 2 6. 3 or 4 7. 5 and 6
IPA	1. (medication adherence or medication adherence or medication nonadherence or medication non-adherence or medication compliance or medication persistence or medication non-compliance or medication noncompliance or medication reminder) 2. (SMART tech* or electronic monitoring or smart blister or e-blister or electronic blister or dispensing system or automat*) 3. (pharm*adj4tech*).mp.[mp=title, abstract, subject heading word, registry word, abstract, trade name/generic name) 4. 2 or 3 5. 1 and 4

Chapter 4

A Review of Features and Characteristics of Smart Medication Adherence Products

This chapter is published as follows:

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4.1. Overview

Background: Smart electronic medication adherence products (smart MAPs) capture and transmit real-time medication intake by using various means of connectivity, allowing for remote monitoring. Numerous such products with different features are available to address medication nonadherence. A comparison of the features of these products is needed for clinical decision-making. Therefore, the objective of this review was to compare smart MAPs available for in-home use.

Methods: We searched grey and published literature and videos to identify smart MAPs. To be considered smart, products required 2 features: connectivity (the ability for collected data to exist outside the physical device) and automaticity (the ability for data to be analyzed or processed automatically). Products were excluded if product descriptions were not available in English, not for in-home use and were unable to dispense medications.

Results: Of the 51 products identified, 38 commercially available and 13 prototypes met the definition. Of these, 75% (n = 38) contained alarms, 24% (n = 12) were unit-dose, 63% (n = 32) were multidose, 43% (n = 22) had locking features, 41% (n = 21) were portable and 88% (n = 45) sent notifications to patients. The cost of marketed products, excluding subscriptions, ranged from $10 to $1500 USD. Some products required a monthly (n = 16) or yearly (n = 1) subscription ranging from $10 to $100 USD.

Discussion: There is a growing market of smart MAPs for in-home patient use with variable features. Clinicians can use these features to identify and recommend products according to the specific needs of their patients to impact medication adherence.

Knowledge into practice

- Numerous Internet-based interventions, such as mobile phone applications and web-based systems, are being developed and used to address medication management with the goal of improving medication adherence.
- This study provides a comparison of features of smart medication adherence products that have been designed to address medication management in patients' homes.
- A comparison of the different features of these products will enable informed decision-making among pharmacists when identifying and recommending a smart medication adherence device based on the patient's needs, expectations and capacity.

4.2. Introduction

Medication adherence is a major health care challenge worldwide. Studies have shown that in developed countries, more than 50% of patients with chronic illnesses do not take their medications as recommended by their health care provider.[1,170] A systematic review designed to determine the prevalence and nature of medication nonadherence reported that 4% of hospital admissions were caused by medication nonadherence in the studies identified.[171] Furthermore, almost all of the hospital admissions identified were considered preventable.[171] Another study aiming to determine impact of nonadherence on emergency room visits, hospitalization and mortality in patients with heart failure found that a 10% increase in adherence caused an 11% decrease in emergency room department visits, a 6% decrease in hospital admissions and a 9% reduction in overall mortality.[172] Two studies have demonstrated a positive correlation among medication adherence and health-related quality of life (HRQoL) in people with chronic illnesses such as diabetes and cardiovascular diseases.[22,173] As such, nonadherence to medications may cause nonoptimal management of disease leading to increased emergency room utilization, hospital readmissions and poor quality of life.[22,171–173]

Numerous Internet-based interventions, such as mobile phone applications providing disease and medication information, electronic reminders via mobile phone text messages or emails, electronic pill boxes and web-based systems for medication monitoring and education, among others, are being developed and used to address medication management, with the goal of improving medication adherence.[70,78,93] In a systematic review of Internet-based interventions for medication adherence, researchers found that these interventions have a promising impact on medication adherence in patients undergoing long-term therapies.[174] Medication adherence monitoring can be

of great value, especially when it promotes discussion between patients and health care providers for successful treatment outcomes.[29,174]

Electronic medication adherence products have the ability to record and store dosing events, have audiovisual reminders or alarms and provide notifications to patients or caregivers if a dose is not taken by the patient, in addition to dispensing medication doses.[65] In 2017, our research group identified 80 electronic medication adherence products with various features.[175] Twenty-one products were randomly selected to assess their usability, workload and user experience.[141,176] We found significant difference in usability and workload of products among a participant population of older adults, caregivers and health care providers.[141] We also concluded that product features such as the ability to store multiple medications, portability, reminder and alarm functions, among others, can be of significant importance for older adults.[176]

Due to the rapid emergence of the Internet of Things (IoT), "a collection of *smart* devices and wearables that collect and communicate data," the adherence data or feedback is now retrievable instantly in some electronic medication adherence products.[62,177] Products with *smart* capabilities are objects, devices or software platforms that are "embedded with processors, sensors, software or connectivity that allow data to be exchanged between the products and its environment, manufacturer, user and other product systems."[84] Smart electronic medication adherence products (smart MAPs) are novel adherence products that have the ability to track real-time medication intake events remotely, via Bluetooth, Long Term Evolution (LTE), Wireless Fidelity (Wi-Fi), wired or other means of connectivity, thus making instant real-time electronic adherence feedback a major component of these type of products.[62] In the past few years, the development and use of

these products has emerged rapidly, and several reviews have been conducted, identifying both smart and electronic products to address medication adherence.[62,65,78,178]

In 2018, a review of medication adherence technologies done by Aldeer et al. described smart technologies for medication adherence, including smart pill containers, ingestible biosensors, wearable sensors, etc. for medication management.[62] Another review about electronic measurement of medication adherence by Park et al. also reported few such products, including smart blisters, smart electronic medication organizers and smart inhalers, along with electronic adherence products.[78] Cheechi et al. conducted a systematic review of electronic medication packaging devices and reported one device with real-time wireless monitoring.[65] Although these 3 reviews referred to smart MAPs generally, they did not report or compare specific features of such products that differentiated them from each other. Another study of electronic monitoring devices exclusively reviewed and described the different features of smart inhalers; however, as extensive as this study was, it did not examine features of devices other than inhalers.[178] Therefore, to the best of our knowledge, there are no studies that have made a detailed comparison of features across different smart medication adherence products.

This area of research is growing and adapting quickly, and products with smart capabilities are being made available for patient use. As a result, it is imperative for clinicians to become familiar with the common features of smart MAPs and to be able to compare them when considering the use of these or recommending them to their patients. Therefore, the primary objective of this research is to compare the features of smart MAPs, which can inform decisions about which smart MAPs may be best suited for patients based on need, expectation and capacity.

4.3. Methods

Study design

This review used a systematic approach to conduct a comprehensive literature search on smart MAPs for in-home patient use. The search was conducted for both published and grey literature to identify as many products as possible and results were summarized by comparing different features of smart MAPs identified.

Search strategy

A comprehensive search was conducted in 3 databases, including PubMed, EMBASE and Scopus until November 30, 2019. Keywords and MeSH terms related to "medication adherence", "smart technology" and "dispensing" were used for the databases search. The Boolean operators AND/OR were used to combine search terms, and where possible, subject headings were combined with keywords in order to build an all-encompassing literature search. See Appendix 1, available online at www.cpjournal.ca, for detailed search strategy used for all databases. All citations were imported to Mendeley Desktop (version 1.19.4) and duplicates were removed. Title and abstracts of the search results were reviewed by 1 researcher (SF) to identify smart medication adherence products. Full text review of potentially relevant citations was completed by a single researcher (SF) to abstract the product information.

To complete the grey literature review, search terms and keywords for Google and YouTube search engines were based on the PubMed MeSH headings. Keywords for the search included medication adherence, smart technology, smart medication dispenser and smart medication devices. One researcher (JI) screened the first 10 pages of Google and first 100 YouTube videos to identify

potentially relevant products. Searches were not restricted to the year of publication or geography, but only articles and product information published in English were included. Two researchers (JI and SF) reviewed the final products that met the inclusion criteria from both published and grey literature to include for data abstraction.

Inclusion and exclusion criteria

Smart MAPs were defined as *any device or product that can be used as a medication management aid and which provides real-time medication intake data using connectivity and automaticity*, where *connectivity* is the ability for collected data to exist outside the physical device, and *automaticity* indicates that the data is analyzed or processed automatically or without direct human control.[85] Products were included if they were for in-home patient use. Both marketed and prototype products were included in this review. Products were excluded if they were stand-alone applications (e.g., mobile applications or software programs), if product descriptions were not available in English or if they were not designed for in-home use.

Data abstraction

Before the process of data abstraction started, 2 researchers developed a list of product features with their definition, based on discussion and previous work with electronic medication adherence products (Table 4-1).

TABLE 4-1 Product Features and their Definitions

Product feature	Definition
Product status	
Marketed	The product is available for purchase.
Prototype	The product is still in development.
Product type	
Automated dispenser	Medication dispensers allow access to medications in one or less human-initiated action. These devices can hold up to a month's worth of medications in small cups, strips or prefilled boxes. Medications are released when the user presses a button.
Dosette or pill boxes	Electronic dosette or pill box with sensors records the time at which the dosette or pill box is opened. Some devices may also record which exact compartment is accessed.
Smart vials or vial caps	Electronic vial or vial cap with sensors on the cap or bottle that record the time at which vial is opened. Data is transmitted to a cloud portal.
Blister packages or blister package holders	Blister package or blister package holder with an electric component with embedded sensors that track when a blister is perforated. Some devices with sensors hold the blister package while others have electronic ink in the foil of the blister package which senses when the foil has been punctured.
Storage boxes	Electronic medication storage box with sensors that record the time at which the box was accessed and transmit this information to a cloud portal.
Inhaler or inhaler devices	Electronic inhaler that digitally records use. Can be the inhaler itself or an electronic device which attaches to an existing inhaler.[78]
Injectors	Electronic injector that digitally records use.
Cost	
Upfront cost	The monetary cost of buying the product or service. This value did not include subscription costs.
Monthly subscription	The monetary cost of monthly subscription use of a product or service. This value includes cost that is mandatory for some products and optional for others.[179]
Yearly subscription	The monetary cost of yearly subscription to use ~~of~~ a product or service. This value includes cost that is mandatory for some products and optional for others.[179]
Storage capacity	
Unit-dose	The ability to store only one dose of one medication.

Multi-dose	The ability to store multiple doses of one or more medications.
Locking feature	A feature that restricts access to medications without the use of a specific procedure such as using a key, entering a Personal Identification Number (PIN) or passcode, or which incorporates facial recognition software.
Portability	Any device that can be easily taken on-the-go and fits inside a purse or small bag.
Alarms	Audio or visual alarms produced by or sent from the product to the user.
Notifications	Alerts including text messages, phone calls or emails sent by the device to a user, caregiver or health care provider
Mobile phone requirements	Any product which requires a user to download an app or own a mobile phone in order to set up and use the product. non-use of a mobile phone, limits the use of features of the product or completely limits use the product.
Connectivity	The manner by which a device is connected or interconnected (e.g., Wi-Fi, Bluetooth, NFC) in order to allow for real-time monitoring.
Additional features	Features not defined in the list above.

As the data abstraction process continued, the list of product features was updated. Two researchers independently recorded abstracted data from literature, web-based information and YouTube videos using a Microsoft Excel file (version 16.16.14). Any disagreements between researchers were resolved by discussion. The following data were abstracted for each product identified:

a) Product name, status and manufacturer
b) Country where product is available to purchase
c) Type of product
d) Cost of product, including both cost of product and subscription fee, if applicable
e) Product features, including storage capacity, number of compartments, alarm or reminder functions, portability, locking feature and any additional features
f) Product notifications, including type of notification (e.g., telephone call, short messaging service (SMS) notification and/or email), notification recipient (patient, caregiver and/or health care provider)

g) Requirement for a cellular device for optimal product functionality

h) The collection and portrayal of real-time medication intake information

4.4. Results

The database search resulted in 307 citations, of which 19 met the inclusion criteria and were included for full-text review of the product information outlined. The initial Google search yielded 1,050,000 results, of which the first 10 web pages or 100 results were reviewed. The YouTube search did not provide an initial number of search results yielded; therefore, the first 100 results were reviewed. Of the results reviewed from both Google and YouTube, 59 were included for full-page review of the product information. Supplemental information regarding YouTube videos was searched using Google if not enough information was provided in the video. Similarly, if not enough information was provided in the Google web page, supplemental information was sought through YouTube, product websites or other third-party websites. See Appendix 4-2 for the PRISMA flow diagram.

In total, 78 products were identified through database, Google and YouTube searches, of which 14 were duplicates. After the duplicates were removed, 64 products were screened for eligibility, leaving 51 products in the final review (Table 4-2).

Of these products, 38 (74.5%) were commercially available and 13 (25.5%) were prototypes. Of the commercially available products, 9 (23.7%) were available globally, 26 (68.4%) in North America, 2 (5.3%) in Europe, and 1 (2.6%) was available globally except in North America. The key characteristics of the smart MAPs identified are described in Table 4-3.

TABLE 4-2 Smart Medication Adherence Products included in Review (N=51)

Smart medication adherence product	Manufacturer
Airduo digihaler™ [180]	Teva Pharmaceutical
DoPill[181]	Domedic
Dyn-e-pill system[182]	NR
Electronic Medication Dispenser[183]	NR
Elliegrid [184]	Elliegrid
Emma[143,185]	INRange Systems, Inc.
e-pill MedSmart Plus[186]	Cadex Watch
Evondos [187]	Evondos
evriMED1000 [188]	Wisepll Technologies
Findair™[189]	Krakow Tech
GlowCap [190,191]	Vitality Inc/NantHealth
GMS Bluetooth Automatic Pill Dispenser[192]	GMS
Hailie™ [193]	AstraZeneca
Hero [194]	Hero
iLidRx[195]	iRXReminder LLC
inPen [196]	Companion medical
JON [197]	MedMinder
Karie [198]	AceAge Inc.
Livi[199]	PharmRight Corporation
MAYA[200]	MedMinder
MedaCube[201]	PharmAdv
Medicube [202]	NR
MedReady MR-357FL[203]	MedReady
Philips Medication Dispenser[204]	Philips
Pill Connect [205]	Euclid
Pillgo [206]	QuaLife
Pillo[207]	Pillo Health
Pillsy[208]	Pillsy Inc
PillTracker[209]	PillTracker
Popit Sense [210]	Popit
Pria [211]	Black+Decker
ProAir™ digihaler™[212]	Teva Pharmaceutical
Propeller Sensor[213]	Propeller Health
RxPense® [214]	Medipense

Sensemedic blister box[215]	Evalan
Sensemedic pill dispenser[215]	Evalan
Sensemedic pill bottle [215]	Evalan
SimpleMed+ Medication Dispenser[216]	Vacia
Smart blister pack[167]	NR
Smart blister pack[217]	NR
Smart bottle [218]	AdhereTech
Smart Drug dispenser[219]	Balda Health care
Smart medication dispenser[220]	NR
Smart pill box [221]	NR
Smart Pill Box Medicine Management System[222]	Bluestar Seniortech
Smart pillbox [223]	Jeyun Medical Co
SmartMedReminderTM system[224]	Concordance Health Solutions
spencer [225]	Catalyst Health
TabSafe[226]	TabSafe Medical Services Inc
Time4Med[227]	Adherence Innovations
Wisepill RT2000[165]	Wisepll Technologies

TABLE 4-3 Product Features (N=51)

Product feature		N=51
Product status (%, n)	Commercially available	74.5% (38)
	Prototype	25.5% (13)
Product type (%, n)	Automated Dispenser	39.2% (20)
	Dosette/Pill box	17.6% (9)
	Vial/Vial cap	13.7% (7)
	Blister Pack	9.8% (5)
	Inhaler device	9.8% (5)
	Storage box	7.8% (4)
	Injectable	2.0% (1)
Type of subscription for commercially available products (%, n)	Monthly subscription	44.7% (17)
	Yearly subscription	2.6% (1)
	Not reported	7.9% (3)
	No subscription	42.1% (16)
Upfront cost in USD dollars of commercially available products (%, n) *	< $50	11.5% (3)
	$50-$99	15.4% (4)
	$100-$500	23.0% (6)
	>$500	15.4% (4)
	Not reported	26.9% (7)
	No charge	7.7% (2)
Monthly and yearly subscription cost in USD dollars of commercially available products (%, n)	< $50	50.0% (9)
	$50-$99	33.3% (6)
	>$100	5.6% (1)
	Not reported	16.7% (3)
Storage capacity of device (%, n)	Unit-dose	23.5% (12)
	Multi-dose	62.7% (32)
	Not reported	13.7% (7)
Locking feature (%, n)	Yes	43.1% (22)
	No	54.9% (28)
	Not reported	2.0% (1)
Portability (%, n)	Yes	41.2% (21)
	No	41.2% (21)
	Not reported	17.6% (9)
Alarm (%, n)	Yes	74.5% (38)
	No	25.4% (13)

Notification to patient (%, n)	Yes	88.2% (45)
	Visual alarms	71.1% (32)
	Audio alarms	64.4% (29)
	SMS messages	26.7% (12)
	Telephone call	11.1% (5)
	Email	8.9% (4)
	Vibrating alarms	6.7% (3)
	Not specified	4.4% (2)
	No	11.8% (6)
Notification to caregiver (%, n)	Yes	47.1% (24)
	SMS messages	70.8% (17)
	Email	45.8% (11)
	Telephone call	29.2% (7)
	Not specified	4.2% (1)
	No	51.0% (26)
	Not Reported	2.0% (1)
Mobile phone requirement (%, n)	Yes	41.2% (21)
	No	58.9% (30)

*Some products had an upfront cost along with a subscription fee

For a list of smart MAPs, and their respective features, please see Appendix 4-3 and 4-4.

4.4.1. Product types

The literature review identified 5 types of oral and 2 types of non-oral smart medication adherence products. The oral products included automated dispensers (n = 20), dosette or pill boxes (n = 9), smart vials or vial caps (n = 7), blister packages or blister package holders (n = 5), and storage boxes (n = 4). The non-oral smart MAPs included inhaler or inhaler devices (n = 5) and injectable devices (n = 1).

4.4.2. Product features

Storage capacity

Approximately two-thirds of the products assessed had the capacity to store multiple doses of 1 or more medications, and as such, were classified as having a multidose storage capacity. These multi-dose devices had a wide range of compartments allowing for the administration of multiple medications at multiple times during the day. For instance, the Philips Medication Dispenser can hold 60 cups of medications for up to 6 doses per day where as MedaCube can hold up to 16 medications and dispense for up to 90 days.[201,204] These multi-dose smart devices provided different means of holding the medications, some (e.g., Wisepill RT 2000) were storage boxes that allowed the user to store any kind of medications they had, others (e.g., MedaCube) required that contents of vials be transferred to bins in the device, where the device would then pick out the number of medications needed from the bin at the appropriate time.[188,201] Some devices required medications to be loaded individually (e.g., Pria or Pillo), others required blister cards (e.g., Emma or RxPense), pill packs (e.g., spencer or Karie), or cups (Philips) to be inserted into the device.[143,198,204,207,211,214,225] Twenty-three percent (n = 12) of the smart MAPs identified were unit dose devices. These products were smart vials or vial caps, injectors or inhalers. A total of 13.7% (n = 7) of smart MAPs identified did not report the storage capacity of the products.

Locking feature

Of the smart MAPs identified, 43.1% (n = 22) contained a locking feature that allowed for access to medication at the prescribed time, as set up initially by the user, caregiver or health care provider. Some devices such as Hero have an optional locking feature that uses a passcode to restrict who has access to the medications.[194] Pria and Pillo use a similar system, however, rather

than a passcode, facial recognition or Personal Identification Number (PIN) code is used to restrict medication access.[207,211] RxPense contains advanced voice Biometrics, allowing for authentication of medication administration through the user's voice, by asking the user to utter a simple phrase displayed on the screen.[214] Some products like Evondos have locked compartments for missed medication doses and restrict who can fill the device by only allowing those with a key to access its interior in order to remove missed doses and fill the device. This key access is given to a health care provider.[187]

Portability

Approximately 40% of products identified were portable. Some portable products included Wisepill RT2000 which weighs 130 g and is 30 x 60 x 130 mm in size, and Popit Sense, which weighs 12 g and is 31 x 45 x 12 mm.[188,210]

4.4.3. Alarms and notifications

Alarms

An alarm or reminder function was found in 74.5% (n = 38) of the products identified. These alarms ranged from visual alarms such as flashing lights, text displayed through the device, audible sounds, vibration prompts or a combination of these. Alarms were utilized to remind users that it was time to take their medications, and in some instances, would give instructions as to which medication or compartment to take, how to access the medication, and any additional reminders that a user may need when taking the medication, such as to take with food or take with a glass of water. For instance, RxPense provides a series of visual, audible and vibration alerts to the user through the device, which can be adjusted based on the user's preference.[214] MAYA and JON, by MedMinder, contain audio and visual alerts to indicate which compartment should be opened and

at which time.[197,200] The visual alert highlights the correct compartment and the audio alert can be programmed to a custom audio message.[197,200]

Notifications

Notifications were provided by the smart MAPs to users, their caregivers and health care providers. Forty-five products (88%) provided notifications to users, and 26 (51.0%) provided notifications to caregivers and/or health care providers. Of the products that provided notifications to users, these notifications were commonly SMS notifications or phone call reminders following a missed medication dosage. Some products provided notifications through a mobile application. Of the products which provided notifications to caregivers and/or health care providers, these notifications were commonly SMS notifications, emails or phone calls. In some cases, these notifications were also provided through the web-based or mobile-based recording platform, primarily to clinicians and/or health care providers. MAYA and JON reminded the patient through a phone call if they missed a dose, and would notify family members or caregivers by phone, email or text message if there is no response following the initial patient phone call.[197,200] The prototype Smart Drug Dispenser by Balda Health Care provides mobile notifications to patients through their mobile app.[219] Clinicians are notified via SMS or email if a patient misses a dosage.[219]

4.4.4. Mobile phone requirement

Of the smart MAPs identified, 41.2% of products required a mobile phone to allow the product to function to its full capacity. In many cases, a cell phone was required in order to download the product's associated app, to set up and fill the product, to demonstrate the user's adherence rate, and/or to track the user's adherence.

4.4.5. Smart Medication Adherence Product connectivity and real-time monitoring

Smart MAPs were connected by a variety of means including cellular network (e.g., 2G/ 3G/ 4G and LTE, via Subscriber Identification Module (SIM) card), Wi-Fi/ Ethernet, Near Field Communication (NFC), Radio Frequency Identification (RFID) or Bluetooth to provide real-time medication monitoring to a user's caregiver or health care provider. Real-time medication monitoring was provided to health care providers and caregivers through a mobile application, or web-based portal hosted through the cloud.

4.4.6. Cost

The upfront cost of marketed smart MAPs ranged from $10 to $1500 US. Some products (n = 7) required a subscription fee along with this upfront cost. Of the products requiring a subscription fee, 42.71% (n = 16) charged a monthly fee ranging from $10 to 100 US and 2.6% (n = 1) charged a yearly fee of $99 US (approximately $8.25 per month). Two products had an optional subscription fee. EllieGrid had an optional fee to obtain report data for approximately $4 per month.[184] Wisepill had an optional fee of $0.50 per month for on-call support.[188] In some products, such as Hailie, ProAir digihaler and Airduo digihaler and inPen, the cost is dependent on co-pay as per a patient's insurance plan or the dispensing pharmacy.[180,193,196,212] In this review, we have reported the cost for these devices, based on the projected price without co-pay. Two products, Propeller Sensor and Smart bottle from AdhereTech, were available for patients free of charge.[213,218]

4.4.7. Additional features

Of the smart MAPs identified, many contained additional features that we did not summarize above. For instance, some devices such as RxPense, spencer and Evondos have voice and video

conferencing directly from the device, allowing for virtual visual visits.[187,214,225] Evondos also has the ability for caregivers and/or health care providers to send messages to the device user through the device screen to allow for the collection of information, such as "How do you feel after receiving your bloodwork today?"[187] Some devices such as Livi, Philips, Karie and Pillgo, also allow for an early-dose function.[198,199,204,206] This feature allows users to request access to their medications prior to their scheduled dose.

4.5. Discussion

This overview summarizes a comprehensive range of features of smart MAPs for medication management. The most prevalent features of these products that were compared in this review include type of product, country or region of availability, cost and product-specific features such as storage capacity, audiovisual alarms, locking ability, portability and feedback via notification process.

We found that smart MAPs differ in their physical characteristics as well as the features they offer. A number of studies have begun to investigate the usability and acceptability of smart MAPs, along with other electronic medication products being released in the market.[94,143,156,157] The need for different features of these products may depend on particular needs, expectations and capacities of the user. For instance, the number of compartments to hold medications will drive the choice of product based on the number of times a user is prescribed to take a medication. Convenience in the number of times a product will need to be refilled will also impact which product is chosen. Therefore, number of compartments in the device is a useful feature to consider when choosing a product for patients, especially those who are on multiple regular drug therapies managing multiple

medications (e.g., individuals with chronic diseases or older adults with multiple comorbidities). Similarly, locking features may be required for patients with memory or cognitive impairments in order to prevent accidental double dosing due to forgetfulness, or for overdosing in individuals prescribed narcotics, or to prevent young children from accessing their parents' or grandparents' medications. Our previous research regarding the user experience of MAPs has shown that portability is a feature that users consider when choosing a product for their medication management needs.[176] Similar results were shown by a qualitative study regarding patients' views about electronic adherence devices. This study reported that patients preferred products that were light weight and smaller in size due to the fact that they were more convenient to carry around.[228] As such, portability is an important feature to consider when recommending or purchasing a product for individuals who are living independently or who have active lifestyles.

Reminders or alarm functions are another important feature of the smart MAPs reviewed. A systematic review on drug reminder packaging has indicated that using devices that have alarms or reminder functions can improve adherence.[65] Smart products with reminder functions that allow audio and/or visual cueing of dosage events may be useful in changing the behaviour associated with medication intake, especially in patients with nonadherence due to forgetfulness. Given increasing risk of declining vision, hearing and sensation as individuals age, options for the type of reminders, whether visual, auditory and vibratory, are important factors for consideration when choosing a product to use.

Smart MAPs have the ability to record, analyze and transmit medication intake data to a web-based portal in real time. When it is time to take the medications or when users do not access the

medication as scheduled via smart products, these products have the ability to analyze that information and send messages to patients. Thus, these products not only act as a reminder to address forgetfulness or unintentional nonadherence but also allow health care providers to remotely access patient's adherence data in a timely manner. Conventional methods of measuring adherence such as pill counts, patient self-reports and pharmacy refill records are often used in practice; however, these methods lack reliability.[167,223] Although real-time medication adherence data cannot guarantee that the patient has actually ingested, injected, inhaled or applied the medication, this data can allow clinicians to act in a timely manner, initiate a conversation about the link between adherence and optimal management of diseases and avoid unnecessary dose increases or additional therapy.[178] The availability of real-time adherence data can help clinicians, not only in clinical decision-making, but also as a tool to motivate patients to modify their medication-intake behaviour or assess why nonadherence is occurring.[78] As such, this data can be valuable in providing integrated care to complex patients. Studies have reported that monitoring real-time medication intake behaviour provides an opportunity for health care providers to achieve positive adherence outcomes in nonadherent patients.[229] Future studies should examine patient preference of these products, product usability, impact on adherence and use in routine clinical care.

Strengths and limitations

To the best of our knowledge, this is the first systematic review that summarizes features of smart medication adherence products. The searches were limited to products available in English, and the first 10 pages of Google, and first 100 YouTube videos. Therefore, this may not be representative of the global market of smart MAPs and some available products may have been

missed. This review only focuses on describing features of the products through the information available online. As such, these products were not purchased or tested by our research team. There may be additional features not described in the product description available online that may impact the results of this review. Additionally, not all products included in this study were tested with patient populations to enable us to report impact on patient adherence through product use. Furthermore, where adherence has been measured, there is significant variability in the definition of adherence utilized in the studies, as well as the tools used to measure adherence. Therefore, a review of adherence for these products would require another systematic review of the studies conducted. However, this review simulates the features by which a clinician could review the products prior to making a recommendation. Neither the usability of these products, nor the impact on adherence, or health outcomes through the use of these products was analyzed; however, this was not the objective of this study.

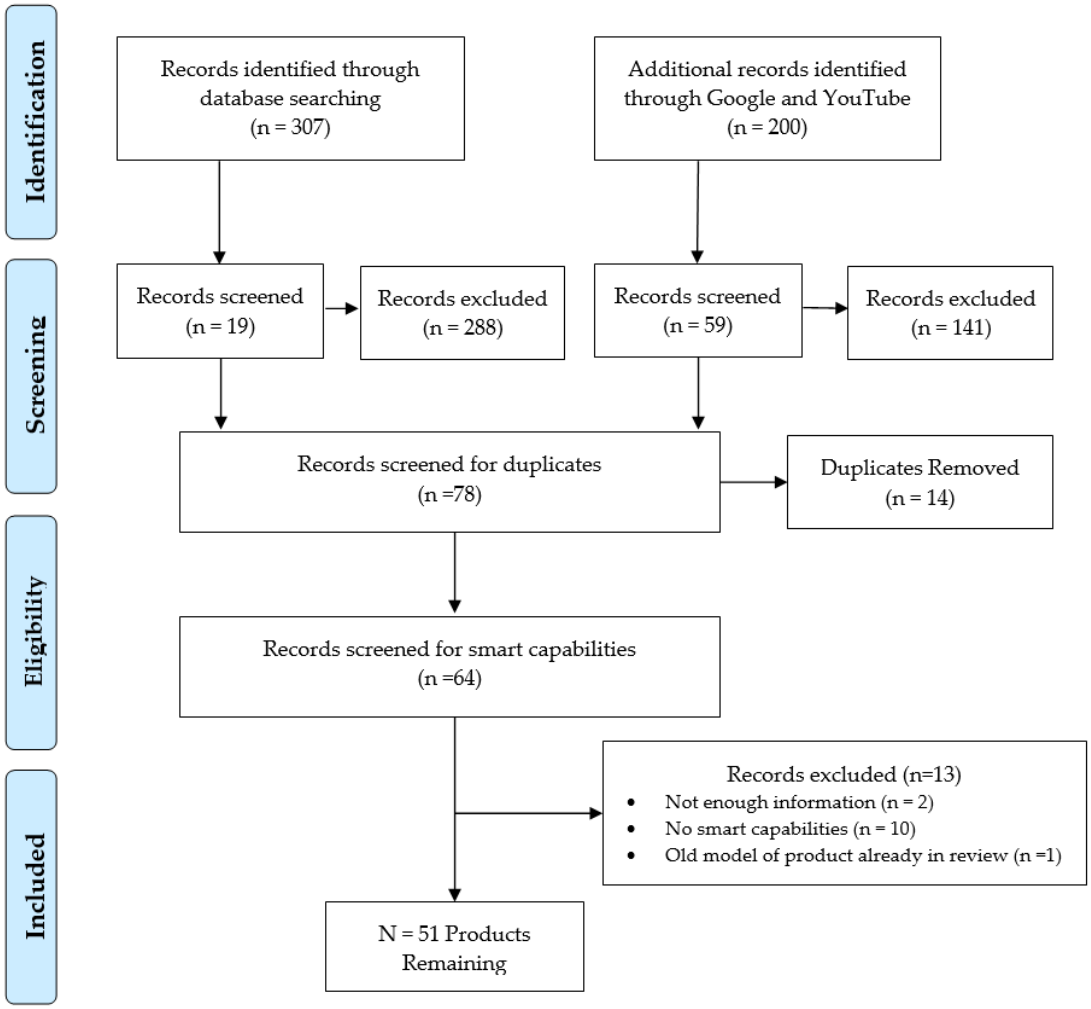
4.6. Conclusion

Smart MAPs are being developed and are available to purchase for patient use. However, due to the variability of their features, it can be challenging for clinicians to search for an appropriate product. Clinicians should be able to identify the products on the basis of their features and match them with their patients' needs. Our study may serve as a resource to inform clinicians about the key features that are currently offered by smart medication adherence products. Clinicians can then use this knowledge to recommend products that best match patient limitations and expectations.

APPENDIX 4-1: Database-specific Search Strategy

Database	Search Strategy
PubMed	(medication adherence[mesh] OR medication adherence[ti] OR medication therapy management[mesh] OR medication therapy management[ti] OR medication management[ti]) OR ((medication*[ti] OR drug*[ti]) AND (adhere*[ti] OR nonadher*[ti] OR compli*[ti] OR comply[ti])) AND (mobile applications[mesh] OR mobile*[ti] OR smart*[ti] OR mhealth[ti] OR technology[mesh] OR technolog*[ti] OR electronics[mesh] OR electronic*[ti] OR computers, handheld[mesh]) AND (dispens*[ti] OR product*[ti] OR device*[ti] OR delivery unit[ti])
Scopus	(TITLE-ABS-KEY (medication AND compliance) OR TITLE-ABS-KEY (medication AND adherence) OR TITLE-ABS-KEY (medication AND non-adherence) OR TITLE-ABS-KEY (medication AND management) AND TITLE-ABS-KEY (smart AND technology) OR TITLE-ABS-KEY (smart AND dispenser) OR TITLE-ABS-KEY (smart AND blister))
Embase	8. (medication adherence or medication management or medication therapy management).ti 9. (dispens* or product* or device* or delivery unot*).ti 10. (smart*or mhealht*or technolog* or electronic* or mobile*).ti 11. ((medication or drug) adj3(adh*or nonadh* or compli* or comly*)).ti 12. 1 or 4 13. 2 and 3 and 5

APPENDIX 4-2: PRISMA Flow diagram for the Review of Smart Medication Adherence Products



APPENDIX 4-3: Commercially Available Oral Smart MAPs

Product Name	Product Manufacturer	Country or Region of Availability	Cost	Subscription Fee	Storage Capacity	Alarm	Locking Feature	Portability	Patient Notifications	Cell Phone Required
Automated Dispensers										
Emma	INRange Systems, Inc.	NA	NR	✓	Multidose	✓	✓		✓	
e-pill MedSmart Plus	Cadex Watch	Global	$$$$		Multidose	✓	✓		✓	
Evendos	Evendos	Europe	NR	✓	Multidose	✓	✓		✓	
GMS Bluetooth Automatic Pill Dispenser	GMS	NA	$$$		Multidose	✓	✓	✓	✓	✓
Hero	Hero	NA	$$$	✓	Multidose	✓	✓		✓	
Karie	AceAge Inc	NA	$$$	✓	Multidose	✓	✓		✓	✓
Livi	PharmRight Corporation	NA	$$	✓	Multidose	✓	✓		✓	
MedaCube	PharmAdv	NA	$$$$		Multidose	✓	✓		✓	
MedReady MR-357FL	MedReady	NA	$$$	✓	Multidose	✓	✓		✓	
Philips Medication Dispenser	Philips	NA	$$	✓	Multidose	✓	✓		✓	
Pillo	Pillo Health	NA	$$$$	✓	Multidose	✓	✓		✓	✓
Pria	Black+Decker	NA	$$$$	✓	Multidose	✓	✓		✓	✓
RxPense®	Medipense	Global	NR		Multidose	✓	✓		✓	
Smart Pill Box Medicine Management System	Bluestar Seniortech	NA	$$	✓	Multidose	✓	✓	NR	✓	✓
Spencer	Catalyst Health	NA	NR	✓	Multidose	✓			✓	
TabSafe	TabSafe Medical Services Inc	NA	$$$	✓	Multidose	✓	✓		✓	
Blister Packages/ Blister Package Holders										
Popit Sense	Popit	Global except NA	$$		Unitdose	✓		✓	✓	✓

SimpleMed+ Medication Dispenser	Vacia	Global	$$	✓	Multidose	✓	✓		✓	✓
Dosette/ Pill Boxes										
Elliegrid	elliegrid	NA	$$$	✓	Multidose	✓			✓	✓
JON	MedMinder	NA	$$	✓	Multidose	✓	✓	NR	✓	
MAYA	MedMinder	NA	$	✓	Multidose	✓		NR	✓	
Pillgo	QuaLife	Global	$$$		Multidose	✓			✓	✓
Wisepill RT2000	Wisepll Technologies	Global	NR		Multidose			✓	✓	✓
Storage Boxes										
evriMED1000	Wisepll Technologies	Global	$	✓	Multidose	✓			✓	
Sensemedic blister box	Evalan	Global	NR		Unitdose			NR	✓	
Sensemedic pill dispenser	Evalan	Global	NR		Unitdose			NR	✓	
Vials/ Vial Caps										
GlowCap	Vitality Inc / NantHealth	NA	$	✓	Unitdose	✓		✓	✓	
ILidRx	iRx Reminder LLC	NA	NR	NR	Unitdose	✓	✓	✓		✓
Pillsy	Pillsy Inc	NA	NR		Unitdose	✓		✓	✓	✓
Sensemedic pill bottle	Evalan	Global	NR		Unitdose			NR	✓	
Smart bottle	AdhereTech	NA (SP)	Free		Multidose			✓	✓	
SmartMedReminderTM system	Concordance Health Solutions	NA (SP)	NR	NR	Multidose	✓		✓	✓	✓

NA = North America, NR = Information was not reported, SP = Specialty Pharmacies

$ is < $50, $$ is between $50 – $99, $$$ is between $100 – $499, $$$$ is > $500

APPENDIX 4-4: Commercially Available Non-Oral Smart MAPs

Product Name	Product Manufacturer	Country or Region of Availability	Cost	Subscription Fee	Alarm	Portability	Patient Notifications	Cell Phone Required
Smart inhalers								
Airduodigihaler™	Teva Pharmaceutical	NA	$$			✓		
Findair™	Krakow Tech	EU	$$			✓	✓	✓
Hailie™	AstraZeneca	NA	$$$			✓	✓	✓
ProAir™ digihaler™	Teva Pharmaceutical	NA	$$			✓		
Propeller Sensor	Propeller Health	NA	Free			✓	✓	✓
Smart injectors								
inPen	Companion medical	NA	$$	✓		✓		✓

EU = Europe, NA = North America, NR = Information was not reported

$ is < $50, $$ is between $50 – $99, $$$ is between $100 – $499, $$$$ is > $500

APPENDIX 4-5: Prototype Smart MAPs

Product Name	Product Manufacturer	Storage Capacity	Alarm	Locking Feature	Portability	Patient Notifications	Cell Phone Required
Automated Dispenser							
Electronic Medication Dispenser	NR	Multidose	✓		NR	✓	
Dyn-e-pill system	NR	Multidose	✓	✓	NR	✓	✓
Smart drug dispenser	Balda Healthcare	Unitdose	✓	✓	✓	✓	✓
Medicube	NR	Multidose	✓	NR	NR	✓	
Blister Pack							
Smart blister pack	NR	Unitdose			✓	✓	✓
PillTracker	PillTracker	Unitdose	✓	✓	✓	✓	
Smart blister pack	NR	Unitdose			✓		
Dossette/Pill boxes							
DoPill	Domedic	Multidose	✓		✓	✓	
Smart medication dispenser	NR	Multidose	✓				
Pillconnect	Euclid	Unitdose	✓	✓	✓	✓	✓
Smart pillbox	Jeyun Medical Co	Multidose	✓			✓	
Smart pill box	NR	Multidose	✓			✓	
Storage Box							
Time4Med	Adherence Innovations	NR			✓		

NR = Information was not reported

Chapter 5

In-home Medication Management by Older Adults: A Modified Ethnography Study using Digital Photography Walkabouts

This chapter is published as follows.

Faisal S, Ivo J, McMillan C, Grindrod K, Patel T. In-home medication management by older adults: a modified ethnography study using digital photography walkabouts. *Age Ageing*. 2022;51(1):afab207. doi:10.1093/ageing/afab207

5.1.Overview

Background: Medication mismanagement can lead to non-optimal management of chronic diseases and poor health outcomes.

Objective: The purpose of this study was to better understand meanings associated with in-home medication management and storage practices of older adults with chronic diseases.

Methods: A modified ethnographic approach using digital photography walkabouts, observation protocols and field notes were used to document in-home medication organization and storage locations. Thematic analysis was used to generate themes and sub-themes.

Results: Data from multiple home visits of 10 participants (mean age = 76 years; 80% females) including 30 photographs, 10 observation protocols and field notes were analyzed. The average number of medications used was reported to be 11.1 (range: 5-20). Themes and sub-themes include: choice of storage location (sub-themes: impact on medication behaviour, visibility of medications, and storage with other items), knowledge regarding appropriate medication storage conditions (sub-themes: impact on safety of patient and impact on stability of medications), and systems to manage in-home medication intake.

Discussion: In-home medication management reflects older adults perspectives regarding privacy, medication taking routine, knowledge about safe and effective storage, and organization systems. The lack of knowledge causing inappropriate medication storage not only impacts the stability of medications, but also increases risk of medication errors and safety, ultimately affecting medication intake behaviours.

Keywords:

Qualitative, older people, photo walkabout, medication safety, chronic disease, in-home medication storage, medication intake

Key Points:

• In-home medication management is dependent on storage location and conditions, and organisation systems.

• The choice of storage location may impact medication intake behaviour based on visibility and co-storage with other items.

• Knowledge about appropriate storage of medications can impact stability and safety of medication use.

5.2. Introduction

The use of medications for the prevention and treatment of diseases is ubiquitous and is higher in older adults due to the increased prevalence of chronic diseases with age. In the USA, approximately 80% of older adults reported having at least one chronic disease and 77% are reported to have at least two.[4] Numerous studies have reported that on average, older adults administer five or more medications on a regular basis.[230–232] Managing multiple medications on a regular basis can be a complex and difficult task to achieve in people with chronic diseases.[1,233] Additionally, factors such as complex dosing regimens, limitations in cognitive and/or functional capabilities to manage such regimens, and drug-related adverse effects can also compromise the ability to manage medications effectively, resulting in suboptimal adherence and furthermore, increased health care utilisation.[1,30] A qualitative study exploring patient perspectives about managing complex medication regimens in individuals with osteoarthritis and coexisting medical conditions demonstrated that a lack of adequate understanding of dosing regimens increased the risk of medication mismanagement and medication errors.[57] A systematic literature review reported that on average, drug related issues such as non-compliance and treatment failure contributed to 15.4% of hospital admissions with an average mortality rate of 2.7%.[234] The term "medication management" refers to a patient's "ability to self-administer a medication regimen that has been prescribed."[44]

Adequate medication management at home not only involves appropriate intake of medications, which includes correct dosing, timing and the appropriate duration of therapy, but it also entails appropriate storage of medications.[235] However, published research indicates that significant problems exist with medication storage and management in the home. A previous study on

medication management practices in patients with chronic illness reported that 70% of patients were inappropriately managing their medications (e.g. duplicated therapy, drug hoarding, not having a drug administration schedule, and presence of expired medications) and 52% were storing their medications inappropriately (e.g. multiple storage areas, no specific location, and more than one medication in one container).[236] Another study reported that only 51.2% of older adults complied with the recommended storage conditions for their medications at home.[237] Though the problem of inadequate medication management and storage appears to be prevalent, much of these findings were determined based on survey methodologies or telephone interviews.[237–242] Studies, where patients were visited in their homes by the researchers, used quantitative study designs,[236,243,244] however, none of these studies provide adequate information or insight about the context of medication management and storage. For example, an in-home study based in Ontario, Canada assessed participant's medication cabinets as a part of their in-home medication review conducted by pharmacists; however, the study did not analyze why patients followed certain medication intake processes or used specific locations to store their medications in their homes.[245] Another study in Canada qualitatively explored in-home medication management issues faced by older adults, family members and caregivers; however, they excluded patients who lived alone and independently managed their medications.[246]

Qualitative study designs provide rich and comprehensive insight to understand a phenomena as a whole rather than measuring it as a number.[110,131] This methodology can help researchers observe participants in their natural settings and understand aspects of 'what', 'why' and 'how'.[131] Moreover, the use of photographic methods has emerged in healthcare research to understand the lived experiences of participants.[116,118,247,248] The use of photographs alongside other data

collection methods, provides an opportunity to, not only describe deep multidimensional data but also provides an understanding of the daily lives of participants.[122] Therefore, in order to gain a holistic insight into medication management practices within patient's homes, we designed a qualitative study using digital photography walkabouts (a process of taking pictures while walking around the place of interest), and observation protocols to explore in-home medication intake and administration, storage, and organization process(s) used by older adults living independently.[118]

5.3.Methods

5.3.1. Objectives

The objective of this study is to elucidate meanings associated with in-home medication management and storage practices of older adults with chronic diseases.

5.3.2. Study Design

A modified ethnographic approach framed this qualitative study by using digital photography walkabouts to explore the meanings older adults associated with in-home medication management and storage practices. This study was a part of a larger ethnography project aimed to understand the medication-intake behaviour of individuals with chronic diseases utilising a prototype smart multi-dose blister packaging system. Participants were recruited through a purposive sampling strategy with the use of recruitment flyers posted in strategic locations (e.g. community pharmacies). Additionally, professional networks, including colleagues of the authors and individuals who work in primary care, were invited to facilitate recruitment. Community pharmacists were provided with a script approved by the ethics board, with which to approach potential participants in their practice. Once the potential participants indicated their interest and

gave consent to share their contact details, community pharmacists forwarded the participants' contact details, to the researchers. One of the research team members contacted the potential participants to determine their eligibility. Participants were eligible to take part in the study if they (1) were 18 years of age or older; (2) had more than one chronic disease; (3) were on complex medication regimens, defined as taking five or more medications per day or if taking less than five medications per day, taking a more than once-daily dosing schedule; (4) were self-managing their medications on regular basis and (5) were able to speak English. If deemed eligible, one of the researchers contacted potential participants via phone or email to explain the study and schedule an in-home visit, if interested.

During this home visit, prior to obtaining written consent, researchers provided an information letter to participants. The information letter outlined the study details including what is involved in the participation of the study, number of home visits, data collection methods, description of the smart blister package as well as collecting of photographs. The information letter also described the benefits and risks of participating in the study, and how personal information will be captured and deidentified. Participants were invited to indicate which section of data collection they were comfortable with having collected. Once participants decided to take part in the study, a written consent was obtained prior to any data collection. Participants were asked to utilise a smart multi-dose blister packaging system to administer their medications for 8 weeks and take part in three in-home visits. Data collected from the first in-home visit will be reported in this study. For the purpose of this study, we defined in-home medication management as *'how patients organize, store and administer/take their medications in their homes'*. Digital photography walkabouts

included taking photographs of the places in participants homes, where they were storing and organizing their medications.

Ethical Approval

Ethics approval was obtained from the Office of Research Ethics, University of Waterloo prior to recruitment. All participants provided written informed consent prior to the start of the study.

5.3.3. Data Collection

Data was collected in two cities in Canada from November 2019 to February 2020 by three researchers with backgrounds in pharmacy, system design engineering and health informatics. The researchers visited participants in their homes as pairs. Ethnographic informed field notes, observation protocols, and digital photography walkabouts were used to observe and gather data during home visits while collecting older adults' narratives related to their medication management and storage practices. Demographic data including age, gender, living situations, self-reported medical conditions, current use of medication adherence aids, and any involvement of a caregiver in managing medications was collected. A complete list of prescription and non-prescription medications was obtained.

During the in-home visits, an observation protocol was used to capture participant's narratives and researcher's observation of in-home medication storage and management. The observation protocol included the following information: the physical location of medication storage in the home, the location where the participant administers their medications, the methods of administering different medications including scheduled, as needed, and non-prescription

medications [e.g. over the counter (OTC), vitamin supplements, and natural health products], the use of any cues or reminders for medication administration, and processes of organizing medications (e.g. use of pill vials or administration aids such as pharmacy prepared blister package, pill boxes, or dossettes, etc.), and a walkthrough of participant's medication administration process. Additionally, field notes were written to document researcher's reflection of participant's narratives about reasons for choosing a specific storage location or process. During the home visit, participants were asked to show the researchers places where they store their medications. With participants' permission, multiple photographs of the medication storage places were taken with an iPhone camera (iPhone 6S, version 13.3.1). While one researcher was taking photographs, the other researcher recorded field notes and observation protocols. The photographs were downloaded on a computer and all confidential information was digitally deidentified. Data from field notes and observation protocols was transcribed on Microsoft Word (Microsoft® for Mac version 16.16.13).

5.3.4. Data Analysis

Data obtained from photographs, observation protocols, and field notes were qualitatively analyzed using conventional content analysis.[126] The following steps were used to analyze the data:

1) Familiarizing with the data: Two researchers (JI and SF) examined visual data from photographs independently and recorded the content of photographs (e.g. objects seen in the photograph, location of the contents of the photograph in the home). The researchers also reviewed observation protocols and field notes to gain familiarity with the data as a whole.

2) Coding the data: Two researchers (JI and SF) independently reviewed the data and coded the photographs, along with narrative provided by older adults via observation protocol and field notes by using an inductive approach to identify the different concepts and patterns.[249] To ensure consistency in the coding process, inter-rater reliability was calculated using percent agreement.[250] A percent agreement of 77% was found among two researchers (JI and SF). Disagreement arose due to differences in backgrounds of the researchers, where one researcher (SF) was informed by their pharmacy background and the other (JI), by their research background. Any differences were resolved through discussion.
3) Creating categories: Codes were examined by two researchers (JI and SF) and grouped into categories. A code book was created using Microsoft® Word (Microsoft® for Mac version 16.16.13). The initial code book contained photographs, name of codes, categories and descriptions. Categories were further refined by discussion between researchers (JI and SF) to ensure clarity, comprehensiveness and context.
4) Developing themes: Categories were grouped into themes and sub-themes.
5) Reviewing themes: Themes and sub-themes were reviewed, defined and the relationship among them was determined by discussion and consensus among researchers (JI, SF and TP).

5.4.Results

5.4.1. Demographic Characteristics

A total of ten older adults participated in this study, where the average age was 76 years (range: 57-88 years) and all participants reported more than three medical conditions (see Table 5-1).

Table 5-1: Demographic Characteristics of Study Participants

Variable	(N=10)
Gender (n, %)	
Female	8 (80.00%)
Male	2 (20.00%)
Age (years)	
Mean ± SD	75 ± 6.7
Range	57 - 88
Current Living Arrangements	
Lives alone	2 (20.00%)
With Spouse	7 (70.00%)
Others	1 (10.00%)
Education	
College/University	4 (40.00%)
College/University no degree	2 (20.00%)
High School	1 (10.00%)
< High School	3 (30.00%)
Number of Medications per day taken by participant	
Mean ± SD	11.1 ± 5.1
Range	5 – 20
Prescription medication	
Mean ± SD	7.4± 4.7
Range	4-16
Non-prescriptions (Over the Counter, Natural Health Product/Vitamin)	
Mean ± SD	3.7± 1.8
Range	0-6
Caregiver involve in medication management	
Yes	2 (20.00%)
No	8 (80.00%)
Medication aids used (n, %)	
Yes	9 (90.00%)
Pharmacy prepared blister pack	5 (55.55%)
Patient prepared dossette	4 (44.44%)
Reminder or alarm	0 (0.00%)
No	1 (10.00%)

Locations for medication storage	
Multiple locations	3 (30.00%)
Kitchen + Other*	2 (66.67%)
Bathroom + Other*	1 (33.33%)
Single location	7 (70.00%)
Kitchen	4 (57.14%)
Other*	3 (42.86%)

*= Dining room, living room, bedroom, linen closet

A total of 48 photographs were taken during the in-home visits, of which 18 duplicates were removed. Observation protocols, field notes and 30 photographs from 10 participants were analyzed and resulted in 3 themes and 5 sub-themes.

5.4.2. Themes and Sub-themes

Content analysis of the study data resulted in three overarching themes related to in-home medication management: (1) choice of storage location (subthemes: impact on medication behaviour, visibility of medications and storage with other items or in multiple locations), (2) knowledge regarding appropriate medication storage conditions (sub-themes: impact on patient safety and impact on medication stability) and (3) systems to manage in-home medication intake.

Theme 1- Choice of Storage Location

Photograph analysis and discussion with participants indicated various reasons to choose specific locations to store their medications. The choice of storage location was driven by three sub-themes: impact on medication intake behaviour, visibility of the medications and storage with other items or in multiple locations.

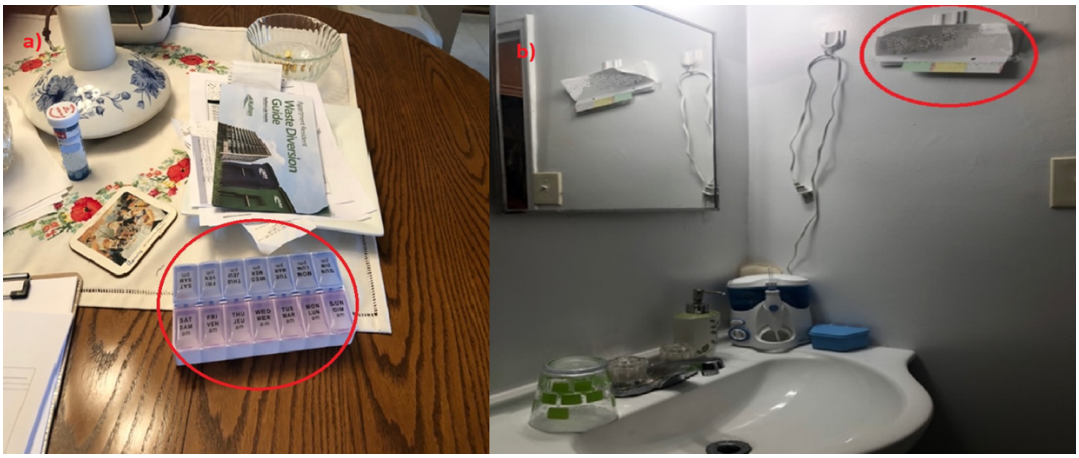
Sub-theme 1.1: Impact on medication behaviour

Participants chose specific locations to store their medications due to a variety of reasons that affected their daily medication intake behaviour. Some of these locations provided participants with an opportunity for easy access to their medications and served as reminders or cues to administer their medications on time. Some participants chose locations based on where they spent most of their day. As seen in Figure 5-1a, one participant was storing their medications on the

living room coffee table because most of their time was spent in the living room. Having the medications visible on the coffee table and close-by served as a reminder to take them on time.

Another study participant hung their scheduled medications (packaged in a blister pack by their pharmacy) on a hook adjacent to their bathroom sink (see Figure 5-1b). The participant explained their choice for this location of storage as a 'reminder or cue for medication administration' in the morning (009-PT). This participant further explained that they take their morning medications after brushing their teeth, after that they strip off one of the pockets of the blister pack and keep it in their shirt's pocket to take before lunch (009-PT).

Figure 5-1 (a): Medication dossette box stored on the coffee table (b): Medication blister package stored in the bathroom as a reminder for daily morning intake



Sub-theme 1.2: Visibility of medications

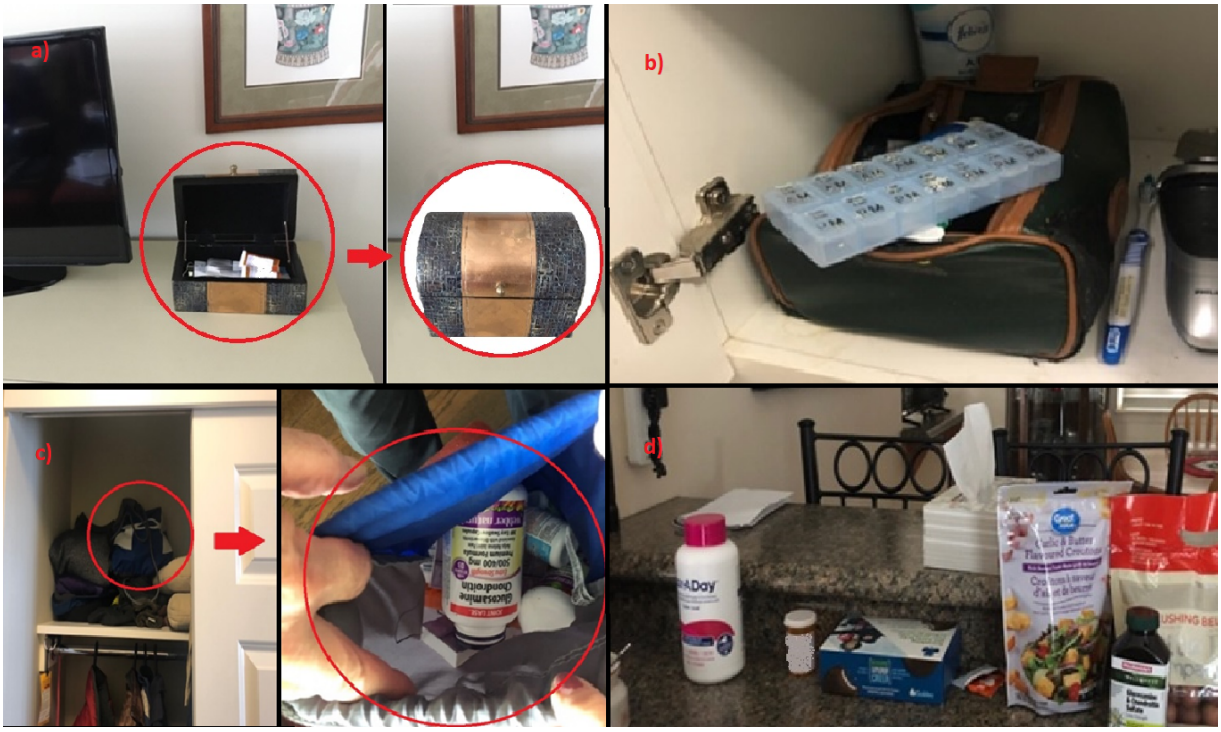
Some participants stored their medications in specific locations for the explicit purpose of ensuring privacy. For example, participants purposely stored their medications in boxes or bags that did not look like traditional medication containers or did not store them in designated, traditional locations such as medicine cabinets. Some participants stored their medications in hidden locations

such as under the sink or in closed cabinets where they were not visible to visitors in the home. This was highlighted as one of our sub-themes.

One study participant kept a dossette box in between books on a coffee table. The participant explained that they are a very private person and they do not want anyone to see what and how many medications they are taking. The same participant was also taking one medication separately from the dossette box. The participant stored that medication vial in an ornate box right beside the television in the living room. The box looked like a decorative piece and not a medication container. One would not expect to find medications in that box unless you open it (see Figure 5-2a), again serving to provide privacy to the participant. Another participant kept their daily use dossette box in the bathroom cabinet with everyday use toiletries (see Figure 5- 2b); however, all of their remaining medications was kept in a gym bag in a coat closet in the hallway (see Figure 5- 2c). Both of these places were not outwardly visible to others.

In contrast, one participant kept their medications on the kitchen counter out in the open as shown in Figure 5-2d. This participant was suffering from multiple comorbidities and had limited mobility due to chronic back pain. The participant had also moved their bed into their living room to accommodate their limited mobility. Since their daily lifestyle had been impacted by limitations due to their disease condition, the participant was not concerned with hiding their medications.

Figure 5-2 (a): Medications stored in a box that does not look like traditional medication container (b): Daily use dossette box stored in the bathroom with other daily use toiletries (c): Medications stored in gym bag in a hallway coat closet (d): Medications stored on the kitchen counter



Sub-theme 1.3: Storage with other items or store in multiple locations

In this study, some participants used more than one location to store their medications. Medications that were packaged in blister packs or dossette boxes were stored in a separate location from medications that were administered out of the prescription vials, as well as OTC medications, medications dosed on an 'as needed' basis and herbal products. Participants stored some of their medications along with other objects such as food, household items, and toiletries. As shown in Figure 5-3, one participant stored their daily use blister pack in the kitchen cabinet along with glassware separately from OTC medications, which were stored on the kitchen counter along with food items.

Figure 5-3: Medications stored with other household items

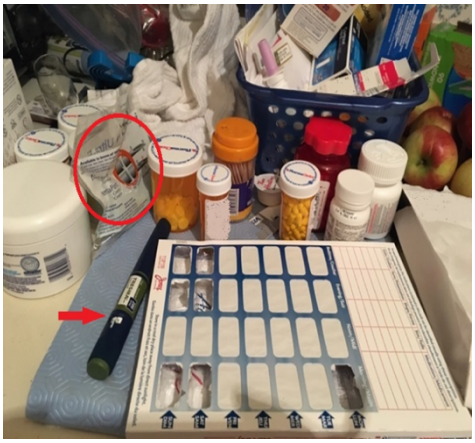
Theme 2- Knowledge regarding appropriate medication storage conditions

The second theme that surfaced during our data analysis was the knowledge participants had about appropriate medication storage conditions. This theme comprised of two sub-themes: impact on patient safety and impact on medication stability.

Sub-theme 2.1: Impact on patient safety

The continued storage of outdated and discontinued medications was an aspect identified during home visits. Most of our study participants were storing their expired and discontinued medications alongside current medications. During one home visit, we also found used needles, a hazardous item, being stored in an open container rather than a Sharps container for proper needle disposal. As shown in Figure 5-4, the participant was keeping used insulin needles stored outside of a Sharps container, in the same place as their other medications, highlighting a safety risk not only to the patient, but to other household members. To ensure the safety of the participant, the researchers advised the participant to contact the pharmacy and request a Sharps container for the safe disposal of used needles.

Figure 5-4: Insulin pen needles stored outside of sharps container



Sub-theme 2.2: Impact on medication stability

In this study we found that 68% of participants stored their medications in the kitchen (e.g. on the kitchen stove, under the kitchen sink and kitchen cabinet beside the stove), and 20% in the bathroom. The particular locations of medication storage can impact the stability of the medications due to elevated temperatures, increased humidity, or moisture; the effectiveness of the medication may therefore be compromised.

Theme 3: Systems in-place to manage in-home medication intake

All of our participants had developed some kind of routine or system for the administration of their daily medications, which emerged as our third theme. These different systems to manage medications include the use of adherence aids (e.g. pharmacy prepared blister packages, or patient prepared dossette boxes) or following a routine to administer their medications on a regular basis. One study participant who was on a twice daily regimen had three large-sized plastic containers (one for her morning medications, one for evening medications and one for vitamins/supplements/discontinued medications). The participant described their medication administration routine as follows:

For my AM (morning) medications I take them out [of the vial] and put them on the lid of the plastic container at my kitchen sink, fill a glass of water and take both [lid and glass of water] to my bedroom, where I take them while watching TV. For my PM (evening) meds I take them right at my kitchen sink while standing (001-PT)

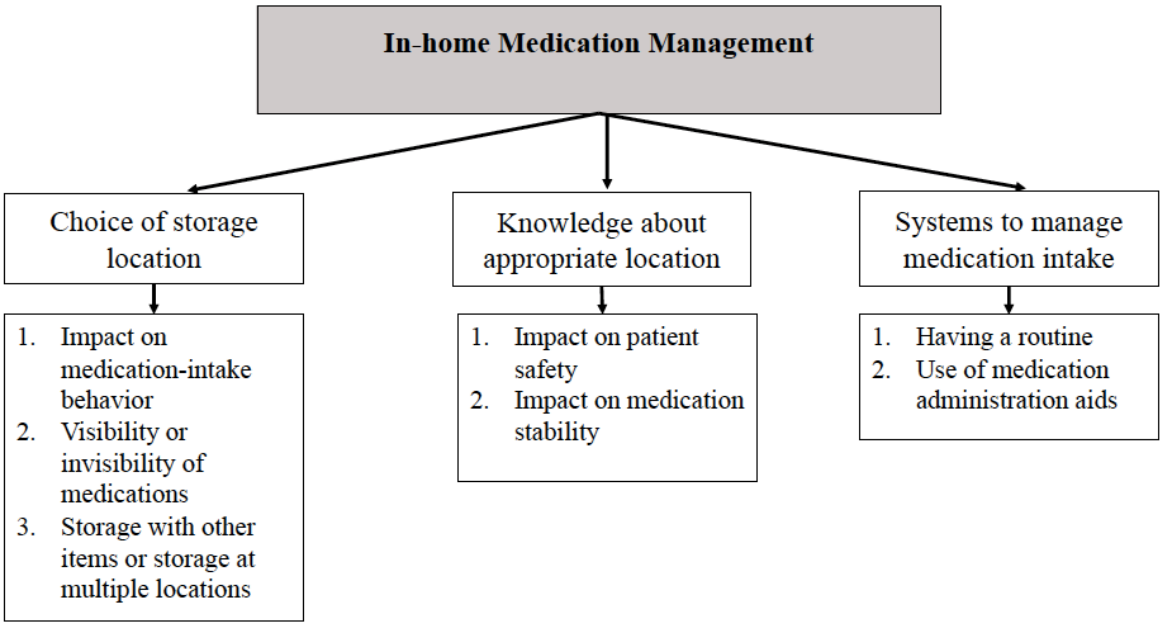
Another participant described their medication administration routine as follows:

I take a half glass of water and half cup of coffee [in the morning]. My medications are stored in bathroom cabinet in a dossette box. I empty them out in my hand and come to the kitchen sink and administer them over there. I follow the same routine at night (015-PT)

One participant kept their empty pharmacy vial on the kitchen counter as a reminder to call the pharmacy for refill. The participant described that this is their system of obtaining the refills from the pharmacy. Another participant mentioned that their pharmacy delivers their blister pack every Friday. They mark their calendar to check non-blister pack medications, insulin, and needle supply to be sure that if they need any additional items, they can all be delivered at once. Few participants stored all health-related documents such as pharmacy records and doctor appointment cards in the same location as their medications to keep organised.

We summarized our findings through an informational diagram (see Figure 5-5). This diagram outlines the different aspects of in-home medication storage and management based on the themes and sub-themes which emerged from this study.

Figure 5-5: Informational diagram representing in-home medication management



5.5.Discussion

Digital photography walkabouts along with observation protocols and field notes enabled us to gather detailed and in-depth knowledge about how older adults take, organise, and store their medications. This study extends existing literature about in-home medication management practices by elaborating on the reasons for using such storage locations and the meanings older adults attach to these locations relating to privacy, medication stability and safety, and medication taking routines.

Studies on in-home drug storage have reported that the rationale to store medications in specific areas or locations depends on the frequency of administration, visual reminders, and patient's daily routines.[239,251] Our study reported similar findings as all participants were using locations pertaining to their suitability. Patients may use multiple locations to store their medications which

can have both positive and negative impacts on their in-home medication management process. Our study found that many participants used different locations to store their regular and as-needed medications. When talking to participants about why they kept locations separate, they expressed that the separation helped decrease confusion by keeping, for instance, morning medications separate from nighttime medications. Patients may also find some places easier to access and prefer to store their medications there. Additionally, this study revealed that some patients store their medications with non-medicinal items such as kitchenware and bathroom products. Sorensen *et al*. reported that along with other factors (e.g. increase number of medications taken, the severity of illness and number of medications present at home, etc.), the use of multiple storage locations is considered to be a factor associated with poor health outcomes.[235,252] However, in our study, we found that participants were storing their medications separately and in more visible locations to serve as reminders for their daily medication intake. In this respect, the storage of medications in separate locations may impede adherence for certain patients, while serving as a useful reminder to improve adherence in other cases. The impact of storage on adherence likely is dependent on patient routines, characteristics and medication intake behaviours. It is imperative that reasons for storage locations be examined before patients are advised to change the locations or collate the storage locations into one space.

Another important concept that was highlighted during this study was the variation related to the visibility of medications among older adults and how they attach certain meanings to storing their medications in a specific way. For example, some patients preferred to hide their medications in places where no one would expect to look for them, while others were not as concerned with hiding or keeping their medications private. Some older adults' in-home medication management is

intertwined greatly with their lives due to significantly impactful chronic illness, making them not as concerned about the visibility of their medications. A previous study exploring the in-home medication management in elderly patients reported similar findings.[248] The study reported that some older adults were not concerned about displaying their medications out in the open in their homes, while some considered medications a private matter and hid them in places such as piano benches, where no one would expect to find them.[248] Therefore, the choice of location of medication storage can very well depend on the privacy needs of a particular individual. While the need for privacy has to be respected, the storage of medications out of sight may impact an individual's ability to adhere to a medication regimen, thereby impacting health outcomes. The visibility of medication vials or containers may serve to remind individuals with impaired memory. In this case, it is necessary for healthcare professionals to devise strategies to improve medication taking in individuals who are identified as forgetful but who also prefer privacy.

Our study also reported that patients may experience medication related safety issues due to their in-home medication management systems. These safety issues can arise due to inappropriate storage conditions, the presence of expired or outdated medications, and retention of discontinued medications alongside current therapy regimens. Multiple studies have indicated that the most common places for in-home medication storage are bathrooms and kitchens.[118,239,240] Inappropriate medication storage conditions in these locations can lead to reduced stability of medicinal ingredients and may lead to a reduction in effectiveness and increased toxicity of the medications.[253] Elevated temperatures due to food preparation and hot appliances in kitchens can lead to chemical degradation and instability of medicinal ingredients and may alter their potency.[254] Similarly, increased humidity and moisture in bathrooms can affect drug stability

leading to loss of potency and decreased effectiveness.[254] Some medications have ingredients that are photo sensitive and exposure to light can cause chemical degradation leading to loss of potency or product toxicity.[254,255] A study on in-home storage conditions of medications reported that 53.2% of drugs requiring refrigeration were stored inappropriately.[237] Therefore, awareness of 'what a proper medication storage condition is' is significant and requires special emphasis when dispensing medications and counselling patients by pharmacists. To ensure the effectiveness of medications, they should not be stored in bathrooms or kitchen cabinets that are close to stove, sink or hot appliances.[256] For medications that do not require refrigeration, the most common recommendation provided by pharmacists and manufacturers regarding medication storage is to 'keep [them] in [a] cool, dry place', for instance, in a closet, storage box, dresser drawer or a shelf.[256] When providing instructions, pharmacists should specify what a 'cool and dry place' means.

Another factor that can impact the safe consumption of medications is having expired and discontinued medications at home. This finding has also been previously illustrated in studies where many people tend to store their medications beyond their use and beyond their expiry date.[239] The co-location of discontinued or expired medications with current medications increases the risk of inappropriate medication ingestion, especially among people managing multiple medications.[235,252] The potential to lead to confusion and inappropriate medication administration has been demonstrated to be a significant issue in older adults, who are at risk of medication mismanagement due to polypharmacy and physical and/or cognitive impairments due to ageing.[168,257]

Studies have reported that routines are essential for medication adherence and management especially in patients with chronic diseases.[233] Routines can be defined as 'strategically designed behavioural patterns (conscious and subconscious) used to organize and coordinate activities along different axes of time, duration, social and physical contexts, sequence and order'.[258] Having a routine or system in place for medication management in such populations can help people manage their daily life, on an ongoing basis.[233] This was also highlighted in our study as all participants were living with more than three chronic diseases and on average, were taking more than 10 medications per day (range 5-20). To manage such a high number of medications on a daily basis, all participants adopted some kind of system or routine. To ensure adherence and appropriate medication administration and management at home, patients with chronic diseases often use different strategies to manage their complex regimens on daily basis.[69,74] Some of these strategies include the use of medication management aids or tools (e.g. pharmacy prepared blister packs, dossette boxes, pill boxes, electronic pill bottles, reminders, alarms, etc.) and have proven to be somewhat effective to improve adherence [69]. As shown in our study, 90% of our participants were using some kind of medication adherence aid.

People with chronic diseases, who live independently in their homes face numerous daily challenges with medication management.[233] Everyday management of medications is an ongoing process and not only involves the intake of medications, but also their storage and organization. The themes and sub-themes which emerged from the analysis of our study provide clinicians with a framework to guide the points of discussion with older adults and an opportunity to examine the locations of in-home medication storage by older adults utilising complex medication regimens. Our analysis indicates the decisions behind storage location are driven by individual need for ease

of medication administration, behavioural routines associated with medication intake and privacy. However, storage locations can impact stability of medications and safe administration. Given our findings, it is important for clinicians to investigate and discuss in-home medication storage locations. Our proposed diagram can be used as a tool by health care providers to highlight key points of discussion when addressing in-home medication storage. This can further help clinicians assess the risk factors impacting safe and effective in-home medication use, as well as to identify patient's personal reasons, routines, and systems for their medication intake before advising them about proper medication storage.

Strengths and limitations

A major strength of this study is the use of a comprehensive approach to acquire detailed information on in-home medication management utilising observation protocols, field notes and photographs. We ensured rigour in our study by ensuring independent data analysis and discussions between team members to ensure clarity, and comprehensiveness as well as ensuring context was provided in the data analysis. Since patients were informed during the consent process that researchers would be coming into the home and taking photos of where their medications were kept, they may have altered their storage locations. Although this is unlikely, if this was done consistently by all participants, it may have impacted our results. To address this potential limitation, we used multiple methods of data collection to observe and document the participants' medication management process. Another limitation of this study was its small sample size. Although we collected data on living status as well as educational status, we did not recruit an adequate sample in each sub-group for the analysis to reflect each particular sub-group. Furthermore, we did not aim to recruit participants with different illnesses or socioeconomic status,

which was a significant consideration in this age group. Therefore, future studies should include larger sample sizes with diverse demographics to reflect the whole population.

5.6.Conclusion

In-home medication management is a significant part of everyday life for older adults with chronic diseases. In order to organise and administer their medications, patients develop specific routines and strategies that are personally meaningful to them. Patients also store their medications in different locations depending on multiple factors such as reminders or cues for timely intake, ease of access and/or privacy. The choice of location to store and administer medications can not only drive their medication intake behaviours, but also the safe use of medications. An informational diagram has been proposed to frame the approach to medication management in patients managing long-term therapies for chronic diseases. The proposed diagram outlines the key aspects of medication storage and management at patients' homes and how certain factors of medication management process(es) can impact on medication stability, medication errors and safety, and medication taking behaviour and can be a used by health care providers as a starting point to investigate the in-home medication management for their patients. Further research is needed to assess the validity and usability of the informational diagram in real-world practice setting.

Chapter 6

Integration of a Smart Multidose Blister Package for Medication Intake: A Mixed Method Ethnographic Informed Study of Older Adults with Chronic Diseases

This chapter is published as follows.

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6.1. Overview

Smart adherence products are marketed to assist with medication management. However, little is known about their in-home integration by older adults. It is necessary to investigate the facilitators and barriers older adults face when integrating these products into their medication taking routines before effectiveness can be examined. The aim of this study was to (a) examine the integration of a smart multidose blister package and (b) understand medication intake behaviour of adults with chronic diseases using an integrated theoretical model comprised of the Technology Acceptance Model (TAM), Theory of Planned Behaviour (TPB) and Capability, Opportunity, Motivation and Behaviour (COM-B) Model. An ethnographic-informed study was conducted with older adults using the smart multidose blister package to manage their medications for eight weeks. Data was collected quantitatively and qualitatively using in-home observations, photo-elicitation, field notes, semi-structured interviews, system usability scale (SUS) and net promoter scale (NPS). The interview guide was developed with constructs from the TAM, TPB and COM-B Model. Data were analyzed using the Qualitative Analysis Guide of Leuven (QUAGOL) framework to generate themes and sub-themes which were mapped back to TAM, TPB and COM-B Model. Ten older adults with an average age of 76 years, of which 80% were female, participated in the study. On average, participants reported five medical conditions, while the average number of medications was 11.1. The mean SUS was 75.50 and overall NPS score was 0. Qualitative analysis identified three themes; (1) factors influencing medication intake behaviour (2) facilitators to the product use and, (3) barriers to the product use. The smart blister package was found to be easy to use and acceptable by older adults. Clinicians should assess an older adult's medication intake behavior as well as barriers and facilitators to product use prior to recommending an adherence product for managing medications.

6.2. Introduction

The National Council of Aging, United States of America (USA), reported that 80% of older adults are diagnosed with one chronic medical condition, and 77% have at least two or more chronic medical conditions.[4] A cross-sectional study of the prevalence of multimorbidity highlighted that the number of multiple chronic diseases is directly proportional to age; 64.9% of people aged 65-84 reported two or more, and 81.5% of people aged >85 years reported more than three chronic diseases.[259] The usage of medications increases with the number of chronic diseases a person has. A Canadian study found that the usage of more than five medications increased from 17.8% to 63.8% in patients with the presence of three or more medical conditions.[5] Another USA family residency practice study revealed that 86.1% of patients diagnosed with more than two chronic medical conditions received five or more prescription orders at one office visit.[6] Chronic diseases generally require long term use of medication therapies with multiple medications, especially if multiple chronic conditions exist.[7] Administering multiple medications on a regular basis is a challenging task for older adults with chronic diseases due to increased symptom burden, complex medication regimens, physical and cognitive deficits, and adverse effects leading to treatment non-adherence.[50]

Appropriate medication adherence has been linked to improving health outcomes, quality of life and reducing healthcare system costs in patients with chronic diseases.[18,23,171] Despite this evidence, non-adherence to therapies is still considered one of the major issues that healthcare systems face globally. Approximately half of patients with chronic diseases in developed countries do not adhere to their medications.[1] A recent study examining the prevalence of medication non-adherence in patients with chronic disease in the USA demonstrated that improving adherence to

antihypertensive medications could result in 117,594 fewer emergency room visits and over 7 million fewer inpatient hospital stays annually.[260] The study also reported that adherence to antidiabetic, antihyperlipidemic and antihypertensive therapies can lead to a healthcare cost saving of $ 4.5 billion, $5 billion and $14 billion per year, respectively.[260]

Medication non-adherence is a multidimensional process, and several factors play an essential role when it comes to adherence. A systematic review found 771 determinants of non-adherence based on five factors.[48] These factors are related to patient (attitude, belief and knowledge about medications, forgetfulness), therapy (complex regimen, previous treatment failure, side effects, medication cost), disease (severity of symptoms), healthcare systems (patient-provider relationship, access to treatment resources) and socio-economic determinants (illiteracy, unemployment, social support network).[1,48] Although non-adherence is not directly correlated with age, its prevalence and risks are reported to be higher in older adults due to a combination of factors, including multimorbidity, cognitive impairment, polypharmacy, drug-related adverse effects and drug storage or formulation issues.[30,48] Understanding factors influencing a person's ability to take their medications appropriately is vital to identify patients at risk of non-adherence, assess the reasons for non-adherence and provide individualized adherence interventions.

People with chronic diseases often perform common behaviours to manage multiple medications with complex regimens across a continuum of care.[92,261] To name a few, these behaviours may include preparing, administering and procuring medications, managing side effects, and communicating with health care providers.[92] These behaviours may ultimately impact adherence and as such, it is important to explore facilitators and barriers which influence these behaviours.

Health behaviour theories play an important role in understanding why people do or do not practice health related behaviours, identifying a wide range of factors that can impact patient's medication intake, and designing patient specific interventions to improve medication intake.[262–264]

In the last two decades, the introduction of telehealth technologies has reformed the utilization of and access to healthcare systems and resources. Specifically, to address non-adherence and provide support for in-home medication intake, there has been an increasing development of smart technology-based products. These products range from mobile phone applications, electronic reminders via mobile phone text messages or emails to smart medication dispensing products that offer real-time medication intake monitoring via web or cloud-based portals.[62,70,78,93]A recent review identified 51 smart medication adherence products, of which 38 were commercially available for in-home patient use.[91] Most of these products were marketed by their manufacturers as user-friendly; however, not all of these products were tested with real-world in-home patient use. Another scoping review identified ten studies that evaluated the integration of prototype and commercially available smart oral multidose dispensing systems and reported them to be usable by patients.[265] However, one of the gaps identified by this scoping review was that despite having the capacity to dispense multiple medications, only two studies used a product for more than once daily administration of multiple medication administration.[265] Smart technology-based adherence products may have great potential for supporting patients with their medication management as well as allowing health care providers to monitor patients on a real-time basis, however, it is imperative to understand the barriers and facilitators of integrating these products into patients' homes to achieve their full benefits. Additionally, in order for these technologies to be effective they must be accepted by end users.[266] Different technology adoption models have been identified

in the literature to investigate the usability and acceptance of technology-based systems or products.[103] These theoretical frameworks can help explain the attributes affecting the acceptance or refusal of a technological intervention.

Therefore, we designed a mixed method ethnographic informed study to examine the integration of a prototype smart multidose blister package for in-home patient use to manage complex therapy regimens and to explore their medication intake behaviour by using the Technology Acceptance Model (TAM), Theory of Planned Behaviour (TPB), and Capability, Opportunity, Motivation-Behaviour (COM-B) Model.

Ethical consideration

This study received ethics approval from the University of Waterloo Clinical Research Ethics Committee. All participants provided written informed consent and had the right to withdraw at any stage of the study.

6.3. Materials and methods

6.3.1. Theoretical frameworks

Technology Acceptance Model

The TAM provides a framework to understand a person's intention to use a product versus their actual use. TAM describes that the use of technology depends on a person's perception of ease of use and usefulness of the technology along with external factors such as system characteristics,

user training and implementation.[95] TAM has been used in the healthcare research field to understand technology acceptance in older adults.[104,105]

Theory of Planned Behaviour

The TPB provides a theoretical framework to understand variables that can affect behaviour change.[267] This theory explains that a person's behaviour is constructed on their intention to perform the behaviour. The intention to engage in a behaviour can be driven by an individual's positive and negative estimations about the behaviour, how other people in life approve or disapprove of the behaviour and the beliefs about the resources available or skills needed to perform the behaviour.[268] Various adherence studies have used TPB to identify determinants of non-adherence and improve treatment adherence.[99,269]

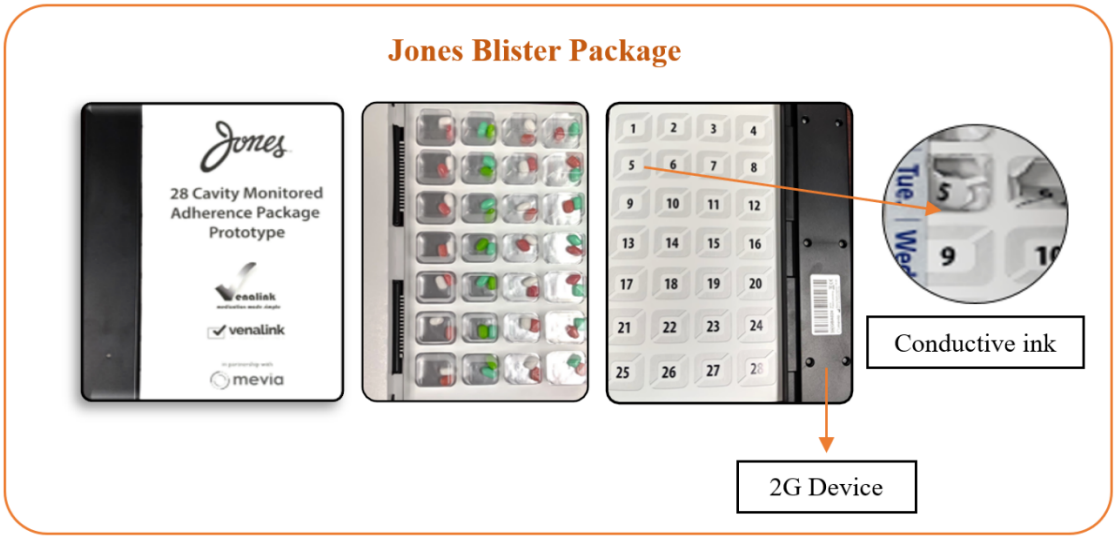
Capability, Opportunity, Motivation-Behaviour (COM-B) Model

The COM-B Model is a comprehensive behaviour system that provides structure to assess different factors affecting the implementation of behaviour change.[101] This model explains that for an individual to be motivated for a behaviour such as medication intake, they must have sufficient capability and opportunity. In addition, various social and environmental factors, (e.g. lack of healthcare resources, access to the medications, cost, and social support for medication management) can influence consistent medication intake.

6.3.2. Smart multidose blister package

The smart multidose blister package is a prototype product with telecommunications technology (see Fig 6-1).

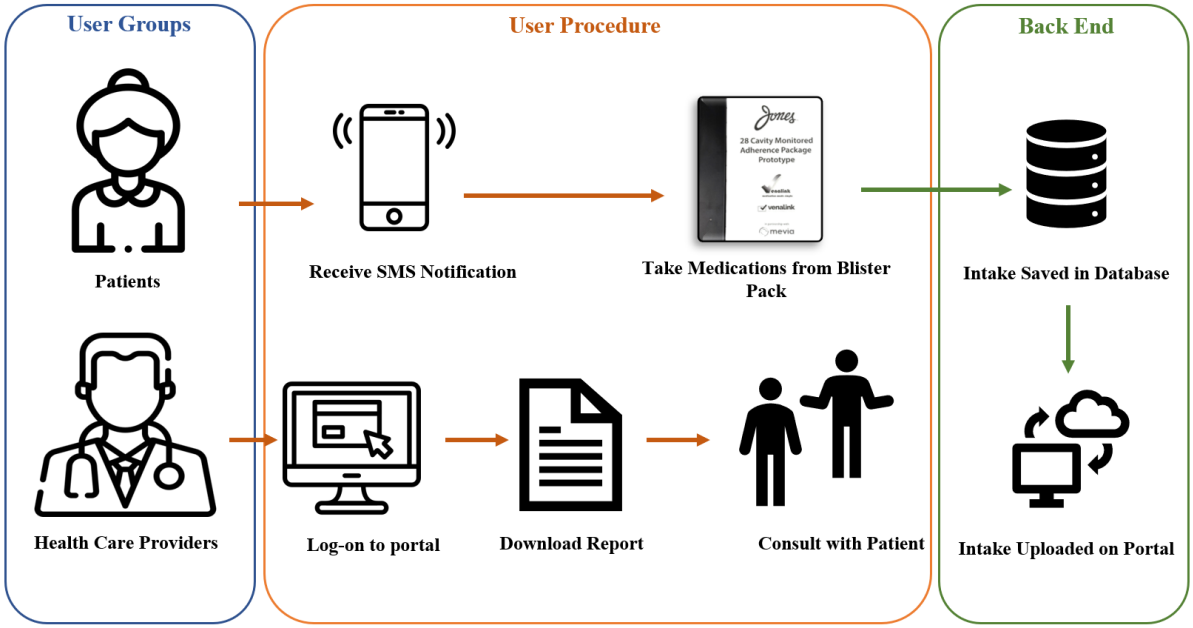
FIGURE 6-1. Smart Multidose Blister Package



The blister package consists of a plastic blister, aluminum foil substrate, and paperboard with conductive ink circuitry that enables the recording of dosage events. The blister package is comprised of 28 cavities and provides up to four times dosing of multiple medications for one week. A telecommunications device is attached to the individual disposable blister pack. The package is pre-filled by the pharmacy. When the cavity is broken to access the medications, the circuitry ink linkage breaks and the telecommunications device records the medication intake event and uploads the data to a cloud-based software portal. The system generates text reminders and notifications via a global system for mobile communications (GSM) and short message service (SMS) technology, to a mobile phone or email address. The software portal is an online interface that can be accessed by a healthcare professional (pharmacist or clinician) or a caregiver. The portal can be used to set patient medication schedules, set up notifications, and obtain a report on patient medication adherence (see Fig 6-2). The portal displays all information transmitted by the telecommunications device and includes a summary page displaying events for all

patients/individuals attached to a user's account. Additionally, each account has a patient profile page providing patient information, device identifier, battery status, service connection status, and date range for monitoring.

Figure 6-2. Process of Utilizing the Smart Multidose Blister Package



6.3.3. Study design

A mixed method ethnographic informed study design was used to examine the integration of the smart multidose blister package and gain an in-depth understanding of the processes, activities and behaviours around medication intake in patients with chronic diseases. Ethnography is a qualitative research method that involves learning about a culture-sharing group of people by being immersed in their natural environment.[111,112] People with chronic diseases are often on multiple medications and have complex medication regimens, which was considered a culture-sharing aspect in this study. For the purpose of this study, we defined integration as the use of the product to support daily medication intake.

6.3.4. Study participants

We used a purposive sampling strategy to recruit participants. A sample size of 5 participants is required to identify 80% of usability issues, while a sample of up to 15 participants enables identification of 100% of usability concerns.[109] We recruited 10 participants to ensure we identified at least 80% of the usability issues that could arise with the product under investigation. We advertised the study through local pharmacies, researchers' professional networks, community environments (e.g. grocery stores, community health care centers and libraries), social media on the University of Waterloo School of Pharmacy's website, Facebook and Twitter page and by approaching previous study participants who had indicated willingness to participate in future studies. Community pharmacists were provided with an approved recruitment script to help them identify potential participants in their practice. If participants were interested in participating, community pharmacist would share their contact information with the research team, after obtaining consent to do so. Since pharmacies were required to dispense medications in the smart blister package, a participant's community pharmacy had to agree to participate in the study, or the participant had to be willing to transfer their prescriptions to a participating pharmacy.

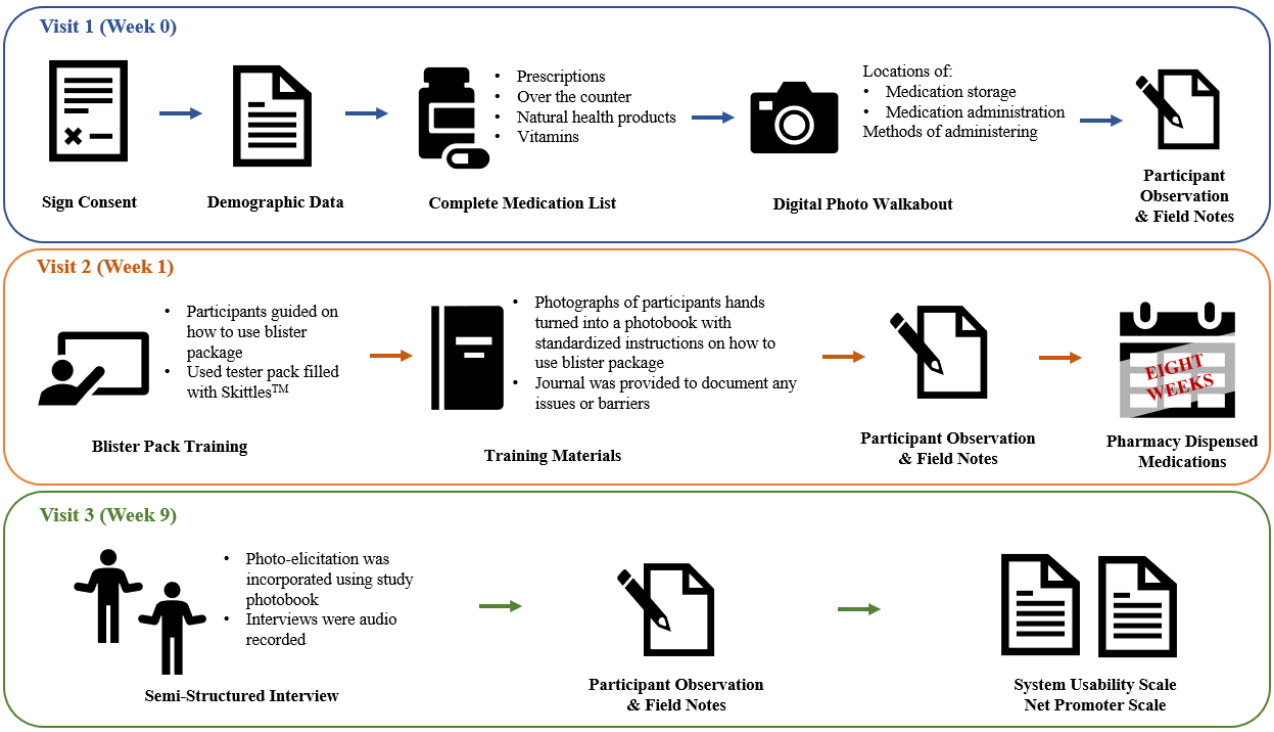
Participants were eligible to take part in the study if they were (1) 18 years of age or older, (2) had more than one chronic disease, (3) on a complex medication regimen (defined as taking five or more oral medications per day, or if taking less than five oral medications per day, taking a more than once-daily dosing schedule for an oral medication), (4) self-managing their medications regularly, (5) able to speak English, and (6) had a cellular phone with SMS messaging capabilities. Participants who were residing in long-term care homes and were on nursing medication administration programs were not eligible to participate due to the potential need to alter their

medication management process. Additionally, since smart multi-dose blister package requires users to respond to prompts written in English in order to use the product, individuals who were unable to speak or read English, or individuals with cognitive impairments were excluded due to their inability to respond to prompts adequately.

6.3.5. Study procedure

Data was collected in 2 large cities in Ontario, from November 2019 to May 2020. Patients were identified by community pharmacies and approached to participate in the study. Participants were asked to complete three in-home patient visits, which ranged from 60 to 90 minutes each. In order to collect data, we used both quantitative and qualitative methods, including in-home participant observations, field notes, digital photo walkabouts (a process of capturing photographs while walking around the place of interest),[118] semi-structured one-on-one interviews using photo-elicitation (a process of utilizing visual methods such as photographs or videos during a participant's interview),[122] and validated tools such as System Usability Scale (SUS) and Net Promoter Score (NPS) (see Fig 6-3). Two of the three researchers (JI, RT and SF) conducted the in-home visits. The coronavirus disease 2019 (COVID-19) pandemic was declared near the end of our study and required us to conduct the last four patient visits virtually.

FIGURE 6-3. Details of Study Visits



Development of semi-structured interview guide

A semi-structured interview guide was developed by using the constructs from three theoretical frameworks. We utilized constructs from TAM to examine the integration and also incorporated constructs of TPB and COM-B Model to explore an older adult's medication intake behaviour. We expected that together, the constructs of these theories would reflect the most common determinants of technology use and in-home medication intake behaviour. Any constructs that were overlapping among these frameworks were used once. Additionally, we added questions regarding the concept of integration. We explored integration by incorporating the following three components: usability, functionality and acceptability in the interview guide.

- Usability refers to how specified users can use a product to achieve defined goals.[120] This was assessed by asking older adults if they were able to remove the tablet from the smart blister package.
- Functionality was defined as "the ability of the product to do what it is intended to do."[121] This was assessed by inquiring questions about the functioning of the alarm and any issues or difficulties related to tablet retrieval from the blister package.
- Acceptability was defined as "acceptance of the product by the end-user."[96] This was assessed by inquiring about the future intention to use the blister package.

The interview guide was initially developed by two researchers (JI and SF) and further reviewed by two researchers (TP and CM) with research and clinical experience in quantitative and qualitative research, and pharmacy, respectively (see S1 File for a mapping of the interview guide to TAM, TPB, and COM-B). Furthermore, we incorporated the photo-elicitation method during one-on-one interviews. The researcher took multiple photographs of the participant's hands while they were using the blister package to administer their medications. These photographs were used during the interview process to discuss any issues related to the use of the blister package. Two researchers (JI and SF) conducted one-on-one interviews. The duration of the interview ranged from 45 to 60 minutes. All interviews were audio-recorded. Field notes were written after each interview.

6.3.6. Data analysis

Integration and medication taking behaviour: Semi-structured interview

Each interview was transcribed verbatim by three team members (KP, CH and AP) on Microsoft Word (Microsoft® for Mac version 16.16.13). Two different team members (SF and JI) reviewed

the transcripts for accuracy. Four team members (SF, JI, RT and KP) conducted data analysis. These individuals provided a variety of backgrounds including a pharmacist, systems design engineer and health informatics. These complementary backgrounds provided multiple informative perspectives to data analysis. The Qualitative Analysis Guide of Leuven (QUAGOL) framework was used to analyze interview data.[117] Multiple team members (SF, JI, RT and KP) read, reread and analyzed the interviews independently and created a list of concepts to develop the code list. The NVivo 11 (QSR international, Melbourne, Australia) was used to organize and code the data. Following this, two researchers (JI and SF) independently coded the interviews in detail using the code list. Data saturation was reached at the 7th interview, and no new codes were elicited after that. However, we decided to code all interviews to confirm saturation. Researchers (JI and SF) reread the interviews and linked significant passages with the codes on the code list. Following the review, additional codes were added, and codes without links were removed. A codebook was created containing the name of the code, definition and quotes from the interviews. Researchers (SF, JI, RT and KP) had multiple discussions during the process to ensure consistency. Codes were grouped into overarching themes and sub-themes. Themes and sub-themes were mapped back to TAM, TPB and COM-B Model. To ensure the trustworthiness of the data, we performed member checking with all participants. Member checking is a process of participant validation of research findings.[135] All participants were provided with a document outlining the themes and sub-themes of the study in a layman language. Fifty percent of study participants responded to our member checking process and agreed with the interpretation of the results. No changes were made to themes and sub-themes after their feedback.

Usability: System Usability Scale

The SUS is a validated subjective assessment used to determine a product's usability.[139] It consists of 10 statements (five positive and five negative), scored on a five-point Likert scale. Scores range from 0 to 100, where higher scores indicate that a product is more usable.[139,145] Bangor et al. described scoring systems for the SUS using the following adjectives: *acceptable* (SUS scores above 70), *marginal* (SUS scores between 50 – 69), and *not acceptable* (SUS scores below 50).[145]

Acceptability: Net Promoter Score

The NPS score is a simple tool to assess the overall satisfaction of the user with a product.[146] It consists of a single question with a scale of 0 (very unlikely) to 10 (very likely). The NPS score determines three types of users: (a) Promoters are the users who provided positive comments about the product and respond with a 9 or 10 on NPS scale (b) Passives are the one who are indifferent about the product and respond as 7 or 8, and (3) Detractors are the ones who are not satisfied with the product and answer the NPS question with a 6 or lower. The NPS is calculated by subtracting the percentage of detractors from the percentage of promoters. The score is expressed from -100 to 100.[146] Positive scores indicate that users are satisfied with the product and would most likely recommend the product.[146]

6.4. Results

6.4.1. Demographics

A total of 26 patients were identified by participating pharmacists. Of the 26, one did not have a cellular telephone, eight refused to participate due to personal reasons, and five did not respond to

the researcher's initial contact. One participant withdrew consent due to ongoing health conditions before the study started. No participants were required to transfer their prescriptions to a participating pharmacy. Ten participants were enrolled, with an average age of 76 years (SD: 11.7, range: 57-88), of whom 80% were female. A total of 70% of participants lived with a spouse or partner, 10% lived with a friend, and 20% lived alone. Participants reported 4.9 medical conditions, on average (SD: 1.6, range: 3-8) (see Table 6-1).

TABLE 6-1. Demographic Characteristics of Participants

Variable	(N=10)
Gender (n, %)	
Female	8 (80.00%)
Age (years)	
Mean ± SD	76 ± 11.7
Range	57 - 88
Living Arrangement	
Alone	2 (20.00%)
Spouse/ partner	7 (70.00%)
Others	1 (10.00%)
Level of Education	
<High School	3 (30.00%)
High School	1 (10.00%)
College/University	7 (70.00%)
Reported Medical conditions	
Hypertension	9 (90.00%)
Osteoarthritis	5 (50.00%)
Mood/anxiety disorders	5 (50.00%)
Cancer	4 (40.00%)
Ischemic heart disease	3 (30.00%)
Asthma/chronic obstructive pulmonary disease	3 (30.00%)
Osteoporosis	3 (30.00%)
Diabetes	2 (20.00%)
Other	7 (70.00%)
Number of Medications taken per participant	
Mean ± SD	11.1 ± 5.1
Range	5 – 20
Rx (mean, ± SD, range)	7.4 ± 4.7 (4-16)
OTC/NHP/Vitamins (mean, ± SD, range)	3.7 ± 1.8 (0-6)
Medication aids used (n, %)	
Yes	9 (90.00%)
Pharmacy prepared blister package	5 (55.55%)
Patient prepared dossette	4 (44.44%)
No	1 (10.00%)

6.4.2. Qualitative analysis

Three themes emerged from the qualitative analysis of interviews which are discussed below without any specific hierarchy.

Themes and sub-themes

1. Factors influencing the medication intake behaviour

1.1. Health literacy

When asked, "why is it important to take medications on time" participants responded in many ways. Some participants had a clear understanding of their medical conditions. They were knowledgeable and aware of the importance of taking medications on time, as prescribed by their health care providers.

> "I think the ones in the morning and night are more important because they're the ones [for my] … cholesterol and blood pressure"-011PT

Conversely, some participants did not understand the significance of proper medication intake and lacked the necessary knowledge of dose-time adherence. One participant discussed the importance of taking medications on time in an ambiguous way;

> "I think if you can take your medication on time, you make better use of the medication because… as soon as your body… empties, you're refilling it again and I think that's a good thing because I think it makes the medication stronger and, better for a person"-012PT

1.2. Age-related physical and cognitive changes

The impact of aging was an emerging sub-theme which came about without a probing interview question. Participants mentioned both physical and cognitive age-related changes while discussing their medication intake routines in their homes. One participant described how, with age, they are experiencing deficits associated with vision and hearing:

> "I have a problem with my eye-sight… sometimes … I have to do different things for it. Sometimes I had to get onto the phone and was … having trouble with my ears." -012PT

Almost all participants mentioned forgetfulness and memory issues due to aging as something that impacted their medication intake.

> "As you get older you sometimes think you did something and you turn around [and realize] "oh no I didn't do it"."-002PT

1.3. Social support system

Participants described social supports as an important aspect of their in-home medication intake process. Participants mentioned their spouses, children, friends and pharmacy staff as their social support system.

> "My son-in-law [is my support system] because he works [at the pharmacy]. He was always the one taking care of [me]. He always brings my pills home for me."-008PT

1.4. Mental and physical workload

Participants often mentioned that managing multiple medications regularly was a difficult task requiring both cognitive and physical capabilities. One participant discussed the daily cognitive workload involved with their medication intake by using the following quote:

> "I'd have pill bottles all over the place… Then [to] try to remember to call the pharmacy to order more, or in when my next delivery was…I try to order the pills on the same day my deliveries come in"-011PT

Another participant discussed how accessing medications from the pharmacy is a difficult task to manage:

> "To tell you the truth, it's [a] pain in the neck. Because, especially in [the] wintertime… I'm able to pick up the medication from [the pharmacy], but you know, with ice and snow..."-014PT

Participants identified that pharmacy prepared blister packages are valuable as they reduce the cognitive and physical workload that is involved in managing complex therapies regularly.

> "You gotta take half of this [medication], one or three of this [medication]one or one of this one ugh, it's much better the way it is in the blister pack"-011-PT

2. Facilitators related to product use

2.1. Product simplicity and learnability

When asked about their experience using the smart blister package, all participants felt it was easy to use.

> "I do like that… cause… it was nice and simple to remind you that you did forget which is great"-011PT

Participants found that it was very easy to learn how to use the product and they did not require any ongoing support in terms of the learning process.

> "I just uh went ahead and did it so, you, you showed me, you made it quite clear"012-PT

Some of our participants were using regular pharmacy prepared blister package for their medication management and this familiarity with the blister package design also made it easy for them to learn and use the smart blister package.

Some participants perceived that it would be more beneficial if a user starts using the product before they have a memory issue for better learnability.

> "I would because I can see the problem getting worse. It's bound to. You live longer and you get forgetful so it goes with the territory. So, I think it is a good investment with time to learn to use it when you are younger-001PT

2.2. User satisfaction

Participants had mixed reactions with the overall satisfaction with the product use. Some participants were very satisfied with the product, while others expressed that the product would be better if there were some modifications made to the reminder notification system, product size, and the addition of an audio signal.

> "If it was working--, obviously it was to an extent, if everything was the way it is I-- would be very comfortable with it"-002-PT

Some participants showed intention to use the smart blister package in the future to manage their medications if needed.

2.3. Product induced behaviour change

Participants stated that using a smart blister package changed their behaviour. They became more aware of taking their medications on time. Some of them mentioned that the reminder function kept them alert.

> "It made me more alert to the fact that my medication was waiting for me"-012PT

2.4. Familiarity with the technology

Participants also reported that their understanding of the smart blister package's technological system was impacted by their prior experience or familiarity with technology. Participants who were using some kind of technology such as a computer, smart TV or tablet understood the product quicker as compared to participants who were not using any technology-based devices in their daily routines.

> "I didn't mind [using the smart blister pack] because I am used to … technology for the most part"-009PT

2.5. Feedback from social circle

Another important factor that emerged during the interview analysis was the feedback from the different social circles. Participants reported their spouses or children felt less worried about them as the smart blister package helped manage their medications in a safe and organized manner.

> "I think they will probably be more… satisfied that I that I won't mess up my prescriptions. I do get forgetful and I do get mixed up and sometime I take the medication and then I can't remember if I've taken it and with that I didn't have any question as to whether I took it or no"-009PT

Only one participant mentioned their paid caregiver did not feel the smart blister package was beneficial due to the participant's inexperience and difficulty retrieving tablets appropriately. However, many participants did not care about what other people thought of them while using the device.

"I don't care what other people think of me"-014PT

Participants also mentioned that the use of the device promoted a positive interaction with their pharmacist.

2.6. Product induced positive emotional response

Emotional responses such as a sense of relief, feeling of safety and less worry were reported frequently by most participants.

"Well there again I thought it was good because [….] it is just [like] a little bit of a secure, a security blanket"-002-PT

2.7. Perceived usefulness in other patient populations

All participants showed interest in using the product in the future if they required any assistance with their medication management. Most participants perceived the product's reminder function as most useful for people suffering memory issues and those who forget to administer their medications due to other reasons.

"I don't need that now (ok). But if I had losing my memory or you know when you get older …. I would"- 013-PT

Participants also discussed that one of the potential users of this type of product is nursing home patients. One of the participants quoted;

> "I really think that that would be very useful to be used in nursing homes, for nurses that give out medications. They would probably appreciate the ease of use and the reminder for them"-009-PT

3. Barriers to product use

3.1. Product design

Participants mentioned product features such as device size, ability to lock and portability as factors to consider when incorporating the smart blister package for in-home medication management. Almost all participants said that the device's size affected their ability to store it in the same place where they previously kept their medications or adherence aid.

> "[The blister pack] was too large to-to go where I… normally put my other one"-015PT

Participants also mentioned that the ability to transport the smart blister package was an important aspect for them.

> "When I first started getting ready to book my trip, I was concerned about whether or not I could travel with them on the airplane"- 009PT

During the interview discussion, a participant mentioned the smart blister package did not have a locking feature or notification function if you open the wrong blister cavity.

> "I know that [I made] a mistake but some people, you know…they open it and they go there are my pills and then they take… the wrong one at the wrong time"-014-PT

Participants also reported that while they were opening the blister cavity, tablets would fall out from their hands.

"The only thing is when I was pushing the bubble down to get my pills out, of the package I would always lose it"-012PT

3.2. Product inconsistency

Participants found that the messaging system was inconsistent. There were a few instances where participants received reminder messages to administer their medications when they had already taken them or did not receive the notifications even though the administration time had passed.

"I would not, … I would not rate the system as being reliable."-016PT

3.3. Technology access

The smart blister package required a cell phone that could receive text messages to demonstrate its full functionality. Some participants identified that the availability of the necessary technology to use the smart blister package is of significant importance and can impact its integration for in-home medication management.

"Well if my cell phone isn't working. My husband has a regular little phone but it [cannot receive text messages]. I don't think you can hook up with that"-001-PT

3.4. Financial concerns

Cost was also reported as an essential factor affecting the use of adherence technology. Some participants showed a willingness to pay for these technologies if they needed a reminder for their medication intake. However, some participants did not agree with paying for these technologies if their provincial or private health insurance did not cover them.

"But there is a financial thing involved too […] you know? And a lot of people… older people… they [are] living on a tight budget… and the pension [is] no[t] high [….] And that is an extra burden financial for people"- 014PT

3.5. Product induced negative emotional response

Some participants felt panic and frustrated when retrieving the tablets from the blister package. Most of these feelings were reported earlier in the study due to participants being unfamiliar with the system and having difficulty in tablet retrieval.

"I get very frustrated. I get frustrated if I try different methods of how to get [the tablets] out"-008PT

Some participants felt worried as they did not fully understand how the reminder function worked and who was sending them the reminder messages. For instance, one participant called their pharmacy a few times to inquire about why she is not receiving messages. The community pharmacist then ensured her that since she took her medications before her scheduled time the system did not generate any reminder messages for her.

Some of the participants felt that due to the product use they had lost their autonomy, which was concerning for them.

"It's just that I wouldn't wanna have to rely on somebody"-015-PT

3.6. User's physical and cognitive abilities

Participants reported that utilizing the smart blister package required particular physical and cognitive abilities. Some participants felt that retrieval of the tablets was challenging or not possible for patients with certain medical conditions such as arthritis or Parkinson's disease.

> "Like somebody that was really old and… if their fingers were very… arthritic or something... I think an older… senior would have a terrible time with that"-008PT

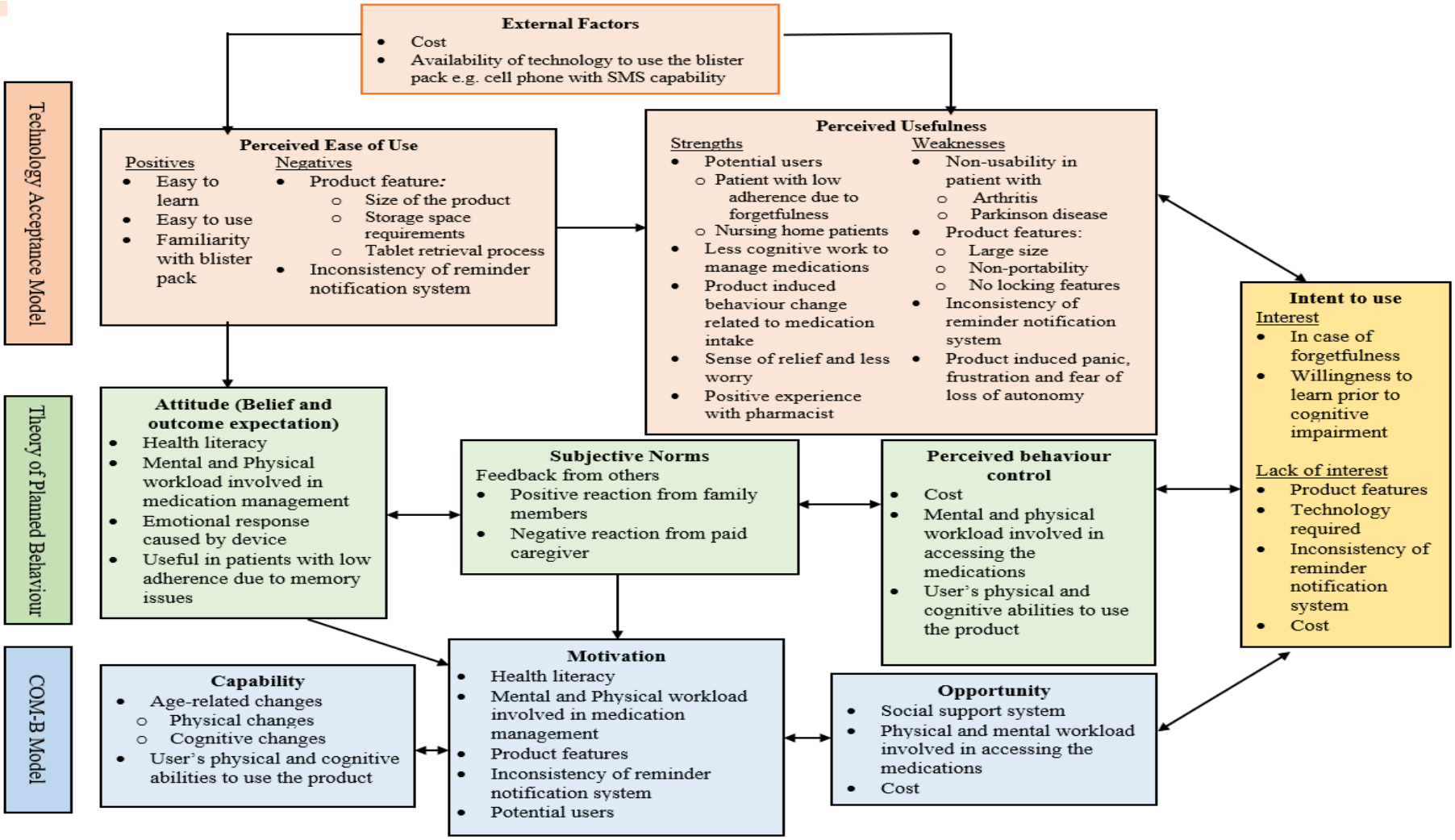
Participants also reported that people needed to have some cognitive capacity to understand and use the technology effectively. They expressed that age may impact these cognitive abilities and, ultimately, the use of the product.

> "The situation would be though that if I were to move to using a blister pack…. it would be because my mental capability had decreased and that in itself would likely decrease my capability of using… technical…. services… if I had to use a blister pack… it would only be because I would have deteriorated and by the deterioration, I would not be able to use…. cell phones… probably"-016PT

Findings mapped to theoretical frameworks

The themes and sub-themes identified by the qualitative analysis of interviews were mapped to TAM, TPB and COM-B Model (see Fig 4).

FIGURE 6-4. Factors Impacting Integration of Smart Packaging



6.4.3. Quantitative analysis

Usability (SUS)

The mean SUS score for the blister package was reported to be 75.50 (range: 37.5-92.50).

Acceptability (NPS)

Of the 10 participants, only eight completed the NPS score, of which 37.5% (N = 3) were detractors, 37.5% (N = 3) were promoters and 25% (N = 2) were passive. The overall NPS score was found to be 0.

6.5. Discussion

6.5.1. Principal findings

The results of this study identified numerous factors affecting the medication intake behaviour as well as barriers and facilitators in using a smart adherence product for in-home medication management. To the best of our knowledge, this is the first study to use an integrated theoretical framework based on TAM, TPB and COM-B Model to investigate the integration of a smart adherence product by exploring the challenges and facilitators to use the product, and outline medication intake behaviour in older adults with chronic diseases.

Medication intake behaviour

The use of TPB and COM-B model further confirmed that an older adult's medication intake behaviour depends on multiple factors. These findings further add to the existing literature focused

on factors affecting the medication adherence.[1] Our study participants reported health literacy, social supports, age-related changes, and mental and physical workload involved in managing complex prescriptions as important determinants to impact medication intake behaviour.

Health literacy can be defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."[270] For medication intake specifically, health literacy not only involves the ability to understand prescription information, but also entails a patient's knowledge of the prescribed drug related to the medical condition it's being used for. Our study results indicated that some older adults were very well informed about medication intake while some lacked this understanding. This lack of understanding has been linked as an important patient related determinant of non-adherence.[1,271] A recent meta-analysis of the role of health literacy in diabetes knowledge, self-care and glycemic control showed that health literacy plays a significant role in disease management.[272]

Besides health literacy, social support was identified as an important factor affecting the in-home medication intake process. We defined social support systems as any individual involved in the medication management process. Studies have shown that social support systems can play an essential role in chronic disease management and improve quality of life by providing patients with helpful resources.[273,274] The availability of social supports has been positively co-related with medication adherence in various chronic conditions.[274–276] Although all of our participants were independently managing their medications, they still identified their spouses, children, friends and even pharmacy staff as their social support system. These people were involved in the participant's

medication management process in various ways ranging from picking up medications from the pharmacy to reminding the participant to take their medications. Participants living alone indicated their community pharmacist as a helpful resource.

People with chronic diseases are often managing complex therapies on a regular basis, requiring both cognitive and physical abilities of the patient.[1,30] In older patients, age-related physical and cognitive changes may impact the medication management and intake process. Our participants indicated age-related forgetfulness as an important change affecting their ability to manage medications. Physical deficits such as hearing loss and vision impairment can affect the ability to read prescription information from the label or hear directions on how to appropriately use medications.[168] Managing multiple therapies requires one's ability to not only remember to take medications, but to also have a system in place for ordering medications from the pharmacy on time.[1,233] Therefore, the clinician should always determine a patient's physical and mental capacity along with other determinants before initiating a complex medication plan to ensure adherence.

Facilitators and barriers

The TAM framework along with TPB and COM-B model assisted us to outline certain facilitators and barriers related to integrating a smart adherence product for in-home patient use.

Facilitators

Two facilitators that were identified in this study include ease of use and ease of learning how to use of the product. Both of these facilitators impact a person's decision to use the technology regularly. Although most of the study participants did not feel they needed the to use the product

at this current time, they all identified the perceived usefulness of this product for patients with memory impairment or unintentional non-adherence due to forgetfulness. Additionally, participants showed their intention to use the product in the future if needed.

Another facilitator identified was the prior exposure or familiarity with the product technology. Participants who had familiarity with the technology embraced the smart blister package quickly and felt comfortable using it. We believe that pre-existing familiarity with technology increased older adults' confidence in using the smart blister package during this study.

Positive feedback from non-participants was identified as another facilitator. Participants reported that their family members' positive responses made them feel motivated to use the smart blister package and using the blister package provided a sense of relief for their family members. Involving family members, if possible, when recommending these technologies should be considered to ensure continuous use. Moreover, participants felt that the product use improved their interaction with their health care providers.

Positive emotions such as experiencing a sense of relief and less worry due to the use of the product was another facilitator found in this study impacting product integration. A study discussing user's perspectives on adherence products has cited similar results. The study reported that patients prefer to use an adherence product for their medication management if it provides them with a feeling of less worry and sense of assurance that they did not miss any doses.[176]

Our analysis also indicated that product-driven behaviour change occurred due to the smart blister package's reminder notification function. Most of our study participants felt obligated to take their medications on time as they perceived that someone was investing time and effort to take care of them. This change in behaviour can be very helpful in addressing unintentional non-adherence due to forgetfulness. However, due to the duration of the study, we are unable to comment on if this behaviour change will be sustained over time. A systematic review of patient reminder systems indicated the importance of measuring sustainability of behaviour change as these patient reminder systems can be recommended as both long and short term solutions to help initiate behaviour change.[79] We recommend future studies assess sustainability of this behaviour change as this will help inform how we should be recommending these tools to patients.

Barriers

Product characteristics such as the large size, limited portability and lack of safety features were identified as barriers impacting the smart blister package's regular use. Additionally, participants found specific issues related to tablet retrieval from the blister package or inconsistencies in the reminder notification system. Previous studies have reported reliability of the technology as a common concern related to technology use in older adults.[62,277,278] For example, a previous study based on older adults' perception about various technologies used in places like home, work and healthcare, reported that participants disliked products that do not function in a reliable manner.[278] A literature review based on daily activity monitoring technologies such as personal alarms, fall detection devices, wearable devices, etc. for older adults discussed non-reliability of the devices as one of the challenges to implement these technologies.[279] Patients and family members often use these products to experience a sense of relief or less worry regarding the medication

management process. Therefore, the product's non-reliability should be addressed as it may very well impact the long-term use of these products.

In order to use the smart blister package, participants needed to have a cellular telephone with the capability of receiving SMS messages. Recruitment of older adults in this study was challenging as many continue to use landline telephones and do not have cellular phones. A 2019 Canadian report on the use of smart technology by Canadian seniors aged 73 years and older has shown that 39% of seniors have no cellular phone at all, 27% own a basic cell phone, and 34% own a smartphone.[280] Some older adults shared one cellular phone between both partners; this would produce a challenge when sending notifications for medication doses. The sharing of a cell phone was a surprising finding as most of the literature suggests that technology use is increasing in older adults. The use of smart phones in Canadian adults aged 25 to 44 years and 45 to 64 years of age has been reported as 97.1% and 87%, respectively.[281] Therefore, the future generation of older adults will likely not face the same challenge as they may be more familiar and well versed with technology use. However, the landscape of medication adherence technologies may also change overtime.

Cost was considered another important barrier to the use of such products. A recent review reported that the cost associated with adherence technologies could vary from a few dollars to a few hundred dollars.[91] Also, some of these products have a cost associated with data charges and connectivity fees. Studies have reported that the inability to pay for medications negatively impacts long-term therapy adherence.[282,283] Generally, older adults are on a fixed income and cannot afford

medications or other health-related devices if public or private insurance plans do not cover them. Therefore, financial implications should be considered when offering these technologies.

The negative emotional responses caused by product use was another critical barrier to consider. Participants reported a range of emotions while using the smart blister package. Although the technology provided them a sense of relief and less worry, they did experience the emotions of being panicked and frustrated at some occasions, more specifically at the start of the study. Studies have reported that older adults like to adopt technologies; however, they perceive themselves as less confident and self-sufficient to use new technology.[284] The lack of confidence can create emotional responses of frustration and panic. However, in our study some participants found the use of the smart blister package became easier over time, thus improving their confidence to use the product. These emotional experiences caused by a product may impact decision making around its continuous use.

Certain medical condition such as arthritis or Parkinson's disease can impact an older adult's ability to retrieve tablets from different packaging.[37,38,168] Additionally, patients with compromised cognitive functioning, may face challenges using the blister package due to a limited understanding the system.[285,286] Both age-related and disease-related decline in sensory and cognitive functioning may significantly impact a person's ability to use the technology. Patients with hearing loss may not hear the sound of a text message if it is not in close proximity. Similarly, patients with cognitive impairment may not remember how to respond or react to the reminder function.

6.5.2. Usability and acceptability

The SUS is a popular subjective assessment used to determine the usability of a product.[139] For example, the mean SUS score for microwave is reported to be 86.9, for Microsoft Word ® is 76.2 and for using an ATM is 81.8.[140] Some research has been conducted in assessing the usability of electronic medication adherence products such as the smart multidose blister package tested in this study, however, there is no benchmark for SUS scores of such products. One usability and workload study determined the mean SUS score for 21 electronic products was 52.28 (SD: 28.52; range: 0-100).[94] Our study reported a higher mean SUS score for the smart multidose blister package. As per Bangor et al.'s acceptability scale, this product is acceptable to use.[145]

The NPS score is used to evaluate the overall satisfaction of the user about the product.[146] The NPS score was reported as 0. The score indicated that the smart adherence product had an equal number of detractors and promoters. Participants who were detractors on the NPS scale reported that they would recommend the product if its design and reliability were improved.

Strengths and limitations:

The most significant strength of this study is the methodology used. Use of ethnography-based data collection methods has provided detailed, comprehensive and in-depth information about the complexities related to in-home medication intake behaviours. To the best of our knowledge, this is the first study that used an ethnographic data collection methodology to understand medication intake behaviours and examine the integration of a smart adherence technology for in-home use in older adults with chronic diseases by utilizing a combination of TAM framework along with two health behaviour theories, i.e. TPB and COM-B Model. It has been argued that TAM does not

adequately address the acceptance of health-related technology, and certain other factors can influence the incorporation of technologies into daily patient use; therefore, two health behaviour theories were used to identify additional factors. Additionally, the photo-elicitation method was used during the one-on-one interviews to enhance participation and gather richer data. Furthermore, the use of the team-based approach with complementary backgrounds in pharmacy, systems design engineering and health informatics to conduct the data analysis provided interprofessional triangulation and added rigour to the study. In addition to strengths, this study has limitations such as brief duration of in-home observations and the change of interviewing atmosphere from in-person to over-the-phone due to COVID-19.

6.6. Conclusion

This study's findings support existing literature and further document barrier and facilitator determinants which can be incorporated into adherence technologies for in-home patient use. The integrated use of TAM, TPB, and COM-B Model, highlighted how the identified barriers and facilitators in this study are interconnected and can impact an older adult's intention to incorporate such technology-based products into their daily medication intake routine. Our study results indicate that the smart adherence technology was easy to use, acceptable by older adults and can be a useful tool for in-home medication management. However, particular areas of improvement regarding product design and reliability should be considered. These findings provide an opportunity for industry partners to improve product design and reliability in a real-world context. Moreover, future studies should be planned to assess the healthcare outcomes, cost saving and sustainable product driven behaviour change by implementing these technologies in older adults

who are at high risk of non-adherence. A study with this focus may lead to a discussion with policymakers to identify new cost models that promote affordable access to these technologies.

Chapter 7

Implementation of a Real-Time Medication Intake Monitoring Technology Intervention in Community Pharmacy Settings: A Mixed-Method Pilot Study

This chapter is published as follow:

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7.1. Overview

Innovative dispensing products offering real-time medication intake monitoring are being developed to address medication non-adherence. However, implementation of these interventions within the workflow of a community pharmacy is unknown. The purpose of this study was to explore factors affecting implementation of a real-time adherence-monitoring, multi-dose-dispensing system in community pharmacies. A mixed-method study was conducted with pharmacy staff, who packaged and dispensed medications in smart multidose packages and monitored real-time medication intake via web-portal. Pharmacy staff participated in semi-structured interviews. The Technology Acceptance Model, Theory of Planned Behaviour and Capability, Opportunity, Motivation, Behaviour Model informed the interview guide. Interview transcripts were analyzed thematically and findings were mapped back to the frameworks. The usability was assessed by the System Usability Scale (SUS). Three pharmacists and one pharmacy assistant with a mean of 19 years of practice were interviewed. Three themes and 12 subthemes were generated. Themes included: pharmacy workflow factors, integration factors, and pharmacist-perceived patient factors. The mean SUS was found to be 80.63. Products with real-time adherence monitoring capabilities are valued by pharmacists. A careful assessment of infrastructure—including pharmacy workload, manpower and financial resources is imperative for successful implementation of such interventions in a community pharmacy setting.

Keywords:

medication adherence; pharmacists; real-time monitoring; medication dispensing technology

7.2. Introduction

Non-adherence to therapies is a global healthcare challenge. In developed countries, medication adherence is reported to be approximately 50% in patients with chronic illnesses.[1] Medication non-adherence has been linked to negative health outcomes for patients as well as increased costs to healthcare systems. For example, a population-based cohort study in patients with hypertension, reported a higher risk of stroke (1.13 and 1.27 times respectively) with intermediate and poor adherence to antihypertensive medication, as compared to those with high adherence.[21] Another study examining the effect of medication non-adherence on healthcare costs in diabetic patients demonstrated that improving adherence can save approximately $661 million to $1.16 billion annually.[287] Assessing adherence is important not only to determine the extent of non-adherence, but also to identify factors and patterns of non-adherence.[63,68] Medication adherence can be determined directly by measuring drug or metabolite levels in the bodily fluids or indirectly by assessing prescription records, pill counts, patient self-reports through interviews, questionnaires or diaries, and/or electronic medication packaging devices.[63]

Obtaining adherence data electronically can be a useful approach to provide patients with feedback to improve non-adherent behaviour.[67] The data obtained through this method documents the date and time the medication was accessed.[78] Several studies have reported on the impact of electronic medication adherence feedback on medication adherence, clinical outcomes and hospitalization.[67,288] A systematic review assessing the effect of electronic adherence monitoring feedback on adherence and clinical outcomes reported a positive impact on adherence.[67] Although in this systematic review, the impact of electronic monitoring and feedback on clinical outcomes was found to be inconclusive, in another randomized controlled study, electronic monitoring and feedback significantly decreased the need for oral steroids ($p=0.008$) and hospital admissions ($p \leq$

0.0010) in the active arm compared to the control group among pediatric asthma patients.[288] Real time medication intake monitoring is an innovative approach of adherence monitoring. It offers health care providers a unique opportunity to monitor patients for their medication intake and intervene in a timely manner.

Health care providers, especially pharmacists, are in an ideal position to address and assist patients in improving adherence. Pharmacists are highly accessible and trusted professionals with expertise in medication management.[289] Community pharmacists see their patients face-to-face regularly, which provides opportunities for building relationships and communicating directly with patients.[86] A recent study in Canada reported that approximately 55% of Canadians visit their community pharmacy at least once weekly.[87] Numerous interventions are offered by pharmacists to improve medication adherence for their patients. These interventions range from patient education and counselling, simplifying dosage regimens, packaging medications for convenient administration, conducting medication reviews and many more.[35,88,290,291] Studies indicate that these interventions impact adherence in a positive manner. For example, a systematic review examining the impact of community pharmacist-led interventions on medication adherence and health outcomes reported that improvement in adherence resulted in improvements in blood pressure, cholesterol, asthma and chronic obstructive pulmonary disease control.[292] Another randomized controlled study evaluating the impact of community pharmacist-led adherence interventions on adherence, healthcare utilization and costs showed that the intervention group reported 3% higher medication adherence, 1.8% fewer hospital admissions, 2.7% less emergency room visits as compared to the control group.[90] In yet another randomized controlled trial assessing the impact of pharmacist intervention on adherence in low income heart failure patients, the intervention improved adherence to 78.8% compared to 67.9% in the usual care group. The

improvement in adherence results in 19.4% fewer emergency room visits and hospital admissions and reduced annual healthcare costs. Of note, medication adherence was measured through the use of Medication Event Monitoring System (MEMS) prescription container lids, which enables monitoring of medication intake.[293]

Innovative medication-based technologies, such as automated dispensers, electronic dossette or pill boxes, electronic blister packs, electronic inhaler devices and electronic injectors have been developing over the years.[62,78,91] This growth in development has led to an abundance of adherence products with the capability of real-time adherence monitoring in the market for in-home patient use.[62,78,91] These adherence products have a variety of features; however, their most notable feature is the ability to send notifications and reminders to the patient and/or caregivers when a dose is due to be ingested. Some of these products require pharmacies to package and dispense the medications, while other products require that the caregiver or patient fill the device with medication doses.[204,214,225]

The impact of packaging and dispensing medications to meet the requirements of these new technologies and feasibility of monitoring real-time medication intake within community pharmacy settings is not known. Several barriers and facilitators have been identified related to implementation of clinical services and programs in pharmacies.[294–297] It is necessary to identify and understand factors that can enable or hinder the successful implementation of an innovative clinical service at the pharmacy level.

The usability of a product can be defined as "the extent to which a product can be used by a specified user."[120] For the successful adoption of any innovative system, usability should be

determined to identify problems with the product design or how easy or difficult the product is to use as it can drive the intention to use the product. Therefore, we conducted a pilot study using mixed methods, with community pharmacies dispensing a prototype smart medication adherence product with the capability of real-time medication intake monitoring. The purpose of this study was to understand the factors which may impact community pharmacies offering these products to their non-adherent patients and explore the usability of a prototype smart adherence technology system.

7.3. Materials and Methods

7.3.1. Theoretical Framework

Three validated frameworks were used to inform this research: (1) the Technology Acceptance Model (TAM), (2) Theory of Planned Behaviour (TPB), and (3) Capability, Opportunity, Motivation, Behaviour (COM-B) Model. It has been argued that TAM alone cannot predict health care providers' beliefs about the use of health related technology [95], therefore we used an integrated approach of combing two behaviour theories: TPB and COM-B Model with TAM framework to explore the factors affecting the implementation of a technology based adherence intervention in community pharmacy setting and to add rigour to the study.

The TAM framework is a validated framework frequently used in pharmacy research to assess a user's acceptance and intention to adopt a technology.[103,298,299] The framework suggests that a user's actual use of a technology depends on their intention to adopt the technology. This intention to use a technology can be based on a user's perceived usefulness and perceived ease of use along with other external factors.[103] The TPB is one of the health behaviour theories which posits that an

individual's engagement in a behaviour can be influenced by their intention, their own beliefs about the behaviour, others' attitudes toward the behaviour, and factors that can facilitate or impede the behaviour.[267] The COM-B model is a framework to identify and understand the factors that can affect a behaviour change.[101] This model describes that any behaviour is dependent on the capability of an individual to perform a behaviour and available opportunities and motivation to engage in the behaviour. Both TPB and COM-B Model have been used in pharmacy research to understand and predict behaviour.[300–305]

7.3.2. System Usability Scale

The system usability scale (SUS) is a validated tool used to measure the usability of a product.[139] The tool has been used to assess the usability of, cell phones, appliances such as TV and microwaves and websites.[140] Recently, SUS has been utilized in healthcare to evaluate the usability of internet based healthcare interventions used by professionals, electronic health records, home healthcare devices, mobile health applications, and electronic medication adherence products.[141,142,144,306,307]

7.3.3. Study Design

A mixed-method study design was used for this study. This study was part of a larger ethnographic informed study focusing on the integration of a smart multidose blister package for in-home medication management in older adults with chronic disease.

7.3.4. Study Material

Smart adherence technology system

The smart adherence technology system comprised of a smart multidose blister package and a web-based portal to monitor the patient's medication intake remotely (see figure 7-1 for a description of the adherence technology system).

(1) Smart multidose blister package

The smart multidose blister package is a prototype product using telecommunication technology. The blister package consists of a plastic blister, aluminum foil substrate, and a paperboard with conductive ink circuitry that enables recording of dosage events. The blister pack is comprised of 28 cavities and provides up to four times dosing of multiple medications for the duration of one week. A telecommunications device is attached to the individual disposable adherence blister package. The package is pre-filled by the pharmacy. When a cavity is broken to access the medications, the telecommunications device records the medication intake event and uploads the data to a cloud-based software portal. The system generates reminders and notifications via global system for mobile communications (GSM) and short message service (SMS) technology which are sent as text to a mobile phone or an email address.

(2) Cloud-based Software Portal

The software portal is the online interface that can be accessed by a healthcare professional. The portal can be used to set patient medication schedules, set up notifications and obtain a report on patient medication adherence. The portal displays all information transmitted by the telecommunications device and includes a summary page displaying events for all patients attached to a user's account. Additionally, each account has a patient profile page providing

patient information, device, battery status, service connection status and date range for monitoring (see figure 7-2 for the process of the smart adherence technology system).

FIGURE 7-1: Description of Adherence Technology System

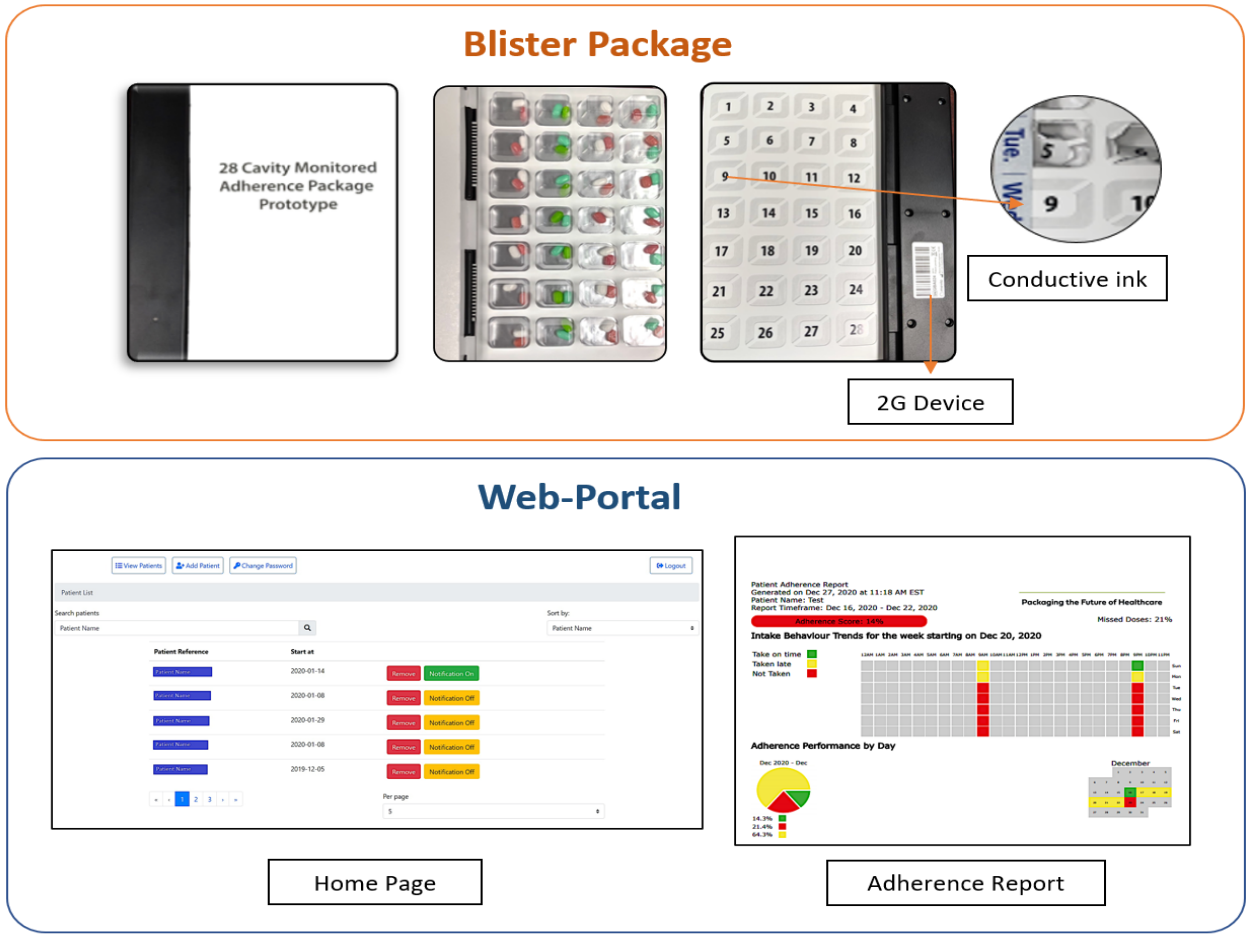

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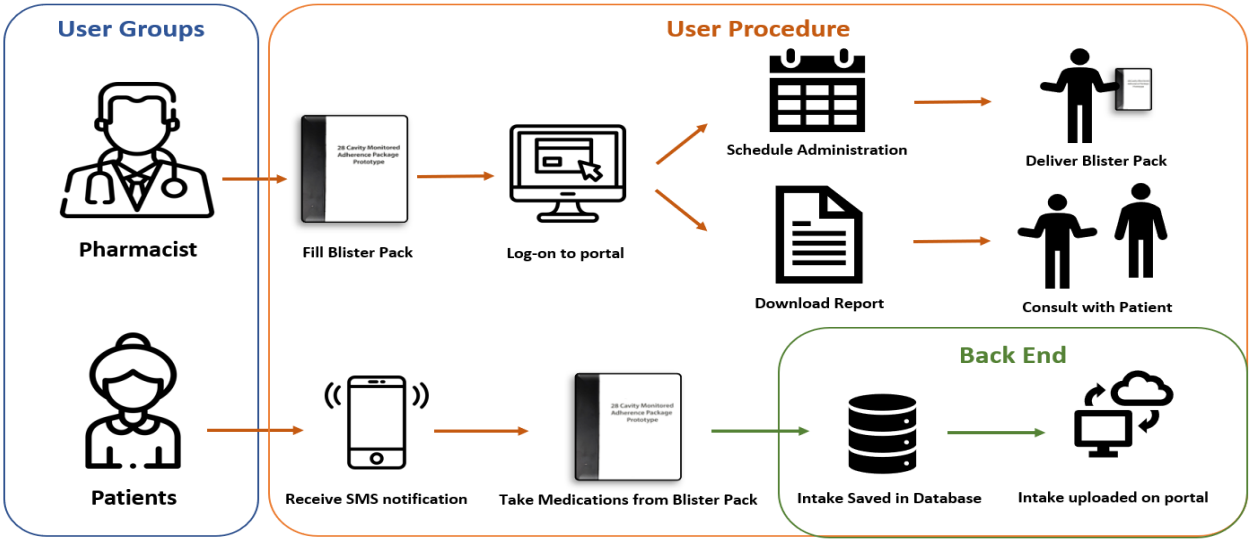
FIGURE 7-2: Smart Adherence Technology System Process



Ethical Consideration

The study received ethics approval from the University of Waterloo Clinical Research Ethics Committee, (ORE# 41015) Canada. All participants provided written consent prior to the start of study. The study was conducted in three community pharmacies located in two major cities in Ontario, Canada between November 2019 to June 2020.

7.3.5. Study Participants

Pharmacists and pharmacy assistants who packaged and dispensed medications in smart multidose packages and monitored real-time medication intake via a web-portal remotely for older adults were recruited. Recruitment flyers, patient participants and professional networks of researchers were used to recruit the pharmacies.

7.3.6. Study Procedures

Once older adult participants provided permission to contact their respective pharmacies. Information letters and consent forms were sent to the pharmacy staff. Pharmacists and pharmacy assistants were provided with in-person training on how to set up and use the smart adherence system, including the physical device and web-based portal. Training was provided over 45 to 60 minutes. Following the training session, community pharmacies packaged and dispensed each participant's regular medications in the smart blister package for eight weeks and monitored real time medication intake remotely. Each patient was assigned with three telecommunication devices to be attached to each individual weekly disposable blister package. At the end of the study, pharmacy staff were asked to participate in a one-on-one interview and complete the System Usability Scale (SUS).

7.3.7. Data Collection

Qualitative: Semi-structured interviews

At the end of the study period, pharmacy staff were asked to partake in one-on-one semi-structured interviews to provide their feedback and experience related to the implementation of the smart adherence system. The interview guide was developed based on the constructs of the TAM, TPB, and COM-B Model. The guide was initially developed by two researchers (SF and JI) with backgrounds in pharmacy and health informatics. One other researcher (TP), with pharmacy practice research experience, reviewed the interview guide prior to finalizing it through discussion and agreement (see Appendix A for the complete interview guide). Three team members (JI, RT and SF) conducted the interviews. Each interview lasted from 60 to 90 minutes. Due to the coronavirus disease 2019 (COVID-19) pandemic declaration, all interviews were conducted

virtually via telephone or video conferencing software. All interviews were audio recorded by using Sony IC recorder ICD-PX470 and transcribed verbatim by four team members (AS, DJ, KP, and AP) using Microsoft Word (Microsoft® for Mac version 16.16.13). One of the four team members reviewed the transcripts for accuracy. Interview transcripts were entered into NVivo 11 software (QSR international, Melbourne, Australia) to manage and analyze data.

Quantitative: System Usability Scale

At the end of the study, all participants were asked to complete the SUS questionnaire. The SUS questionnaire is comprised of 10 questions on a five-point Likert scale ranging from "Strongly Disagree" to "Strongly Agree." The scores range from 0 to 100 and higher score indicates that product is more usable.

7.3.8. Data Analysis

The Braun & Clark's framework (2006) of thematic analysis was used to analyze the interviews[128]. Two team members (SF and JI) read and reread the interviews to become familiar with data. The NVivo 11 (QSR international, Melbourne, Australia) was used to organize and code the data. Both team members coded the first interview independently, and came together to discuss the codes, to ensure the consistency of codes and establish the code book. All three remaining interviews were coded independently by both researchers (JI and SF) based on the established code book by two researchers. To add rigour to the study, we also calculated the inter relater reliability between the two coders, which is a benchmark of qualitative studies. The inter-rater reliability was found to be 88.6%. Finally, to even add more rigour, four researchers (KP, JI, RT, SF) reviewed the code book together. Any disagreements were resolved by discussion. Codes were grouped into themes and sub-themes. Once themes were finalized, four researchers (KP, JI, SF and RT) reviewed them

again. Since the frameworks were guiding this research themes and sub-themes were mapped back to the TAM, TPB and COM-B Model to understand the meanings of results.

Member checking was performed to ensure the trustworthiness of the data. Member checking is a process of asking participants review the research findings and confirm the validity of the data.[135] A document containing summarized details of the themes, sub-themes and de-identified participant quotations were sent to all participants via e-mail. Fifty percent of study participants responded to our member checking process and agreed with the interpretation of the results. No disagreements were noted by participants and as such, no changes were made to the original themes and sub-themes.

7.4. Results:

7.4.1. Demographic Characteristics

Five participants were recruited; however, one participant was lost to follow up and did not participate in the final one-on-one interview. Three pharmacists and one pharmacy assistant participated in the one-on-one semi-structured interview. All participants recommended medication adherence aid(s) to their patients (see Table 7-1).

TABLE 7-1: Demographic characteristics of participants

Variable	(N=4)
Gender (n, %)	
Male	3 (75.00%)
Age (years)	
Mean ± SD/Range	43 ± 7.9/30-50
Years of Practice	
Mean ± SD/Range	19 ± 9.7/5-30

7.4.2. Themes and Sub-themes

Our interview analysis identified three themes and 12 sub-themes, which are described below without any hierarchy related to their importance.

Theme 1: Pharmacy workflow related factors

Sub-theme 1.1: Pharmacy Workload

Pharmacy workload (due to added steps involved in packaging the medications in smart blister package and entering patient data on the web-portal) was another sub-theme identified by the interview analysis. Participants compared the workload involved in adopting this system to their usual system of pharmacy prepared regular blister packs.

> "You have to assign the devices to every patient, you have to make sure that the devices are charged and ready to go. You have to keep an inventory of the devices to make sure that they're going and coming back and the patient is not just keeping them at home. So... there's more work involved around the managing of this whole system as a smart blister pack for the pharmacy team"-004HCP

Participants also discussed the perceived workload if they decided to implement the system for all of their patients.

> "Right now, I have ninety patients on blister packs. If I were to add fifteen minutes every week for ninety patients, you can imagine how much extra time it would take and that's not taking the conversations that will happen because I am seeing the compliance reports. So that in itself is a huge undertaking for any pharmacy"-004HCP

Sub-theme 1.2: Staff availability, training and role

When asked if there were any resources needed to adopt the system in their pharmacies, participants stated that additional staff or manpower would be required to maintain this system adequately to not only fill the blister package, but also enter and regularly review data from the portal.

> "Let's say 10 or 15 patients… just from an actual delivery and keeping track of all those things… that would be a little bit tricky from a …. again, more staff time needed that's all" -005HCP

In addition to manpower, staff training was indicated as another factor. Participants mentioned that due to the novelty of this system, pharmacy staff would require additional training. Some of the pharmacy staff showed hesitation in filling the smart blister packages, despite the fact that they were filling regular blister packs which looked exactly similar to the smart blister package but without the paperboard with conductive ink circuitry and connectivity device for non-study patients. In other cases, some pharmacists did not feel comfortable involving the pharmacy staff in the process of preparing smart blister package.

> "Although my assistant would have done it…I wasn't very comfortable in, in letting her do it" -004HCP

Another important aspect identified during the interview analysis was the role differentiation among health care providers in the pharmacy.

> "For filling we had a pharmacy assistant who was filling the blister pack. Other than that, everything else was done by a pharmacist. So, printing it…keeping you know … the schedule that … you know, they have to be printed then they have to

> be made. If there's any changes … with the setting it up initially and then copying it over for the next week, all of those things were done by a pharmacist in the pharmacy. So, the only thing that was left for the pharmacy assistant to do was just with filling of the blister packs"-004HCP

Sub-theme 1.3: Pharmacy Workflow Organization

Participants mentioned they needed to make some changes in their pharmacy workflow that involved dedicating a specific place for blister pack storage, charging the batteries and preparing the blister packs.

> "You would want to make sure that you have a dedicated area to keep track of the charge units, what's charged, [and] what's not. Because of… packaging …is different from the other packaging that we have at the store, it needed its own little area as well so maybe some space in that, you know some planning around that"-005HCP

They also mentioned that additional support was required from delivery staff to collect the old blister packs and deliver the new ones. This also led to multiple trips to patients' homes and required planning.

> "We just have to do those little nuances to figure out that system ahead of time and maybe it means that family has to drop... that box off in the middle of the week to the pharmacy and it's not delivered"-004HCP

Sub-theme 1.4: Cost associated to set up the system

Due to additional staff, workload and time requirement for system implementation, associated cost was mentioned as an important factor.

> "At this point it would have to be […] economically viable [be]because it does take more time on a pharmacy stand point just you know- even from the delivery stand point"-005HCP

Pharmacists also mentioned additional remuneration for added workload when monitoring the real-time medication intake remotely.

> "If you didn't have some sort of remuneration system I don't see any …advantage to a pharmacy to actually take this on unless they are getting paid more. Just from a time standpoint again, it only takes a couple minutes to set up a card, no big deal, but if I'm gonna start going back and analyzing it, that's just going to take a lot more time"-005HCP

Sub-theme 1.5: Regulatory implication

Pharmacists stated that having the ability to monitor real-time medication intake put them in a position where they needed to know about the regulatory implications of this data.

> "You have to think about the pharmacist, the position that this data will put the pharmacist in. You cannot, if you have a printed report in front of you, and of course we want to have that printed report as you want to see what the compliance is, but you cannot then to choose to ignore that report if there's a compliance issue. Because that would put the pharmacist in a very bad position legally, that they had printed report in front of them that the patient was not complying, and they failed

to act on that. Right now, we don't have that information, so we don't know"-004HCP

Sub-theme 1.6: Feedback from others

Participants mentioned they received variable feedback from others around including pharmacy staff and patients with the technology. Pharmacy staff who were not involved in the study commented on the additional workload and did not want to participate.

> "I think the only comments they made was thinking that it was a lot of work because I was trimming all the stickers, I had to cut both sides and the top and bottom, so that took a while they saw me working on that"-018HCP

When asked about the response from the physicians, participants thought they would embrace this technology as it will help their patients to adhere to medications.

> "Absolutely, yeah absolutely, I think. Physicians you know, they love it that the medications that they're prescribing, the patients are taking those medications and they're compliant…I think there's nothing more they love than that, you know, they prescribe a prescription medication and the patient doesn't take it for two months they go back and see the physician and the physician thinks that they're medications are not working and they increase the dose and they keep doing it and the patient's just not taking the medication. So, for them to know exactly what's going on I think it can help them quite a bit in…treating their patient. So, I think the physician would be very receptive--004HCP

Sub-theme 1.7: Improved patient interaction

Participants mentioned they felt their interactions with their patients was improved due to the system.

> "People were happy that we had called them, they were interested in being involved in a study, they were interested in being involved in something new"-005HCP

Theme 2: Integration related factors

Sub-theme 2.1: Product design factors

When asked about their experience related to dispensing medications using the smart blister package, participants felt that the system was easy to implement and they did not experience any issues while dispensing the medications in the blister package. However, the size and bulkiness of the blister package was not appreciated by both pharmacy staff and the patients.

> "One thing was that I think most of the patients found it to be quite… you know they have to keep it somewhere because of the device it's, you know, and for us to, to store it, to keep it, send it, it's always a bulkier item to send"-004HCP

Since each patient was assigned with three telecommunication devices thus the limited availability of these devices created some logistics issue for the pharmacy. Pharmacy delivery staff had to make extra trips to patients' homes to pick up the devices. Some patients prefer to have their medications on monthly basis rather than weekly basis and due to limited quantity of devices, it was not possible for the pharmacy to deliver four blister packs.

> "I think considering we had the two weeks supply…you're gonna need more of those black boxes because some of the patients would go to monthly"-005HCP

Sub-theme 2.2: Portal factors

Difficulty in setting up patient profiles on the software portal were identified as a problem by all participants. The initial portal set up included adding patient information, setting up the text message reminder and creating a dosing schedule. Pharmacists were also required to create a dosing schedule every week which could be manually completed or cloned from the previous week.

> "I don't think you need any extra special skills, I think um as, as a pharmacist you're always um dealing with software in pharmacies, so it's just a, just a maybe a quick overview of software"-004HCP

However, once the initial set-up was done, participants found the system easy to use.

The access of real-time medication intake data was found to be useful by all the participants. Pharmacists found that this feature can be very useful in addressing medication non-adherence while conducting medication reviews or in cases in which if the family members or caregivers expressed any concerns related to non-adherence of their patients.

> "The benefits of it…you know uh not just for that patients, there's the pharmacist, the health care provider can see the compliance, the patient can see the compliance, their family members can see the compliance so there's, there's definitely benefit"-004HCP

Participants faced a few challenges regarding the reliability of the real-time medication intake data. The system experienced some technical difficulties during the study period and did not report the adherence accurately. This was identified as a huge concern by the participants.

> "My concern is … about the software.…if I can trust the software a 100% and if I know that the software is working 100% is what I'm seeing of the software uh that the compliance is not 100%. If I'm, if I trust the software 100% then having that conversation with the, with the patient is definitely not the problem, I have that conversation all the time with for people who are on regular dossette when they have not been taking their medications" -004HCP

The portal had the ability to show the adherence percentage as well as show the adherence record in different colors to differentiate if a participant is adherent, or non-adherent. Pharmacists found this feature quite useful.

> "It's a you know, the colour coding when they have not taken their medication on time or when they have taken their medications on time. I think that's kind of gives you right at one glance you can see the compliance. If the compliance is not there on a person's page you can just see that they did not take most of their medications on time. That's one thing… I mean it gives you that- that snapshot of the patient. Uh, it gives you that percentage compliance as well as you know what's going on"-004HCP

Overall, participants expressed their satisfaction with the system and commented on their intention to use it in the future.

> "If it was available we would offer it"-007HCP
>
> "I actually enjoyed it I was very satisfied with it"-005HCP

Theme 3: Pharmacist perceived patient related factors

Sub-theme 3.1: Potential users

Pharmacists identified that not only patients but also family members can be potential users of this system. They mentioned that such a system can offer people an opportunity for independent living.

> "If you have your mom or dad or grandparents living by themselves in a retirement home but they're still independent, or if they're living at home [and] they're taking their own medications… you are not going to go see them every day or maybe not maybe even every week"-004HCP

Sub-theme 3.2: Concerns for users

Pharmacists also expressed concerns for some users with cognitive and physical deficits to use the product appropriately. The system sends text reminders to the patients at their scheduled dosing time, however, pharmacists felt that people with advanced stages of cognitive impairment may not be able to process that information and would not be able to respond to the reminder function. Pharmacists identified that for such situations it would be beneficial to involve family members.

> "We had patients on blisters for a reason because usually some sort of cognitive decline so the question is: is the notification to a patient's cellphone, is that going to be enough to make a difference or does the notification have to go somewhere else, having a family member involved. Where does the bang for our buck come in do we have a better bang by just have a patient on a smart blister getting notified themselves? You know what if they are with it, then maybe that's what they want"-005 HCP

Another concern identified by pharmacists was the ability of patients with physical challenges to access medications from the blister package. The blister package requires a certain process to punch the medications out and it may not be feasible for such patients.

> "It was hard to punch for some patients especially with some arthritis or if they have, they have Parkinson's or their hands are shaking"-004 HCP

Sub-theme 3.3: Cost to the end-users

Cost associated with the system use was another important concern expressed by pharmacists prior to offering this product to the patients. However, pharmacist felt that system is still an affordable option for patients compared to the cost of nurse-led medication administration services for those who wish to live independently in their homes.

> "You know, for the whole package including the connectivity fees, [and] pharmacy fees… [would be] less than what they would pay a nurse to come in and give the medications"-004HCP

Sub-theme3.4: Technology access for the end-user

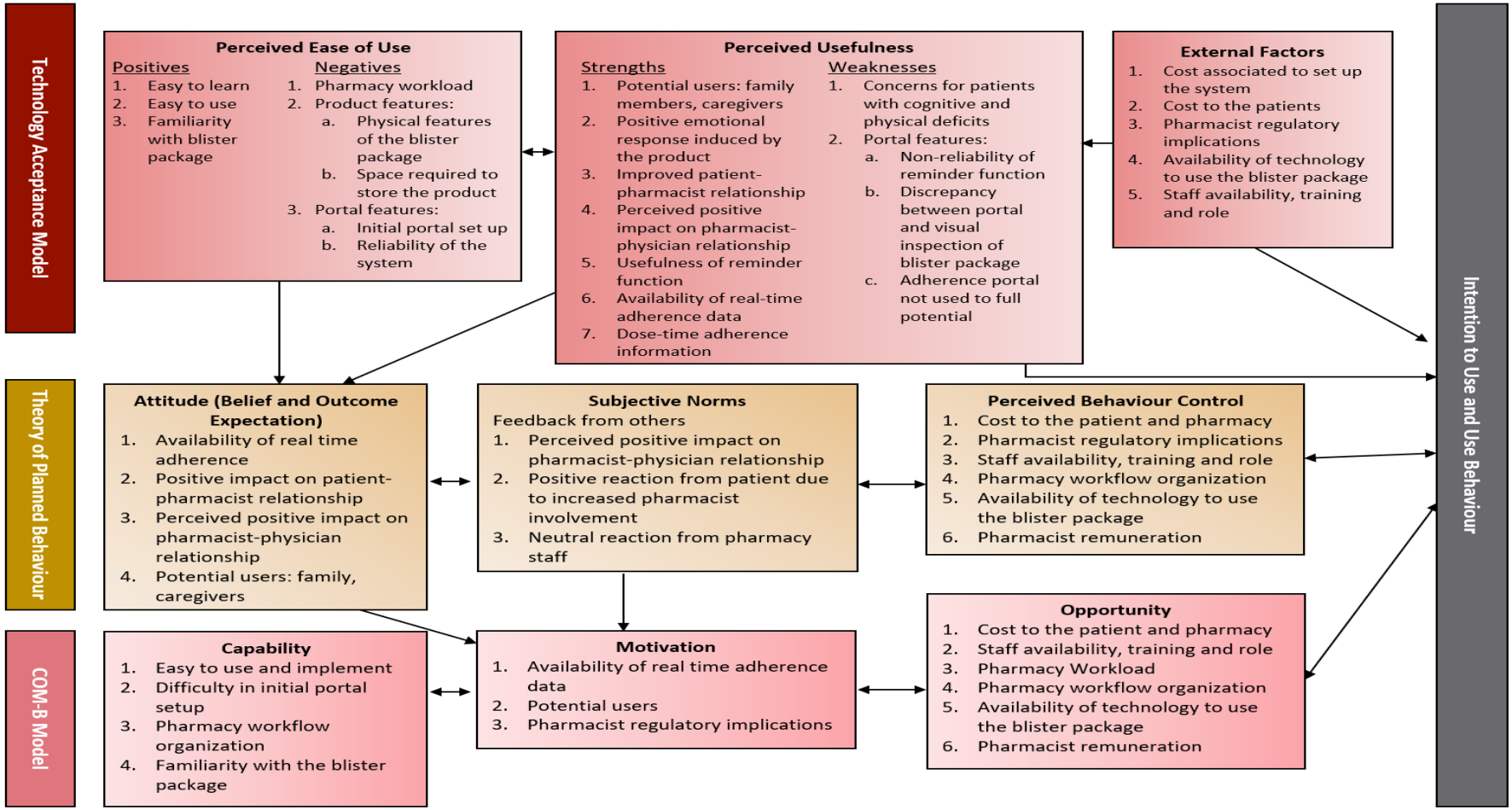
Another important patient factor that was identified by participants was the availability and access of the technology required for the functionality of the smart blister package. The blister package requires a cell phone with the capability of receiving SMS text messages for the reminder function. Participants mentioned that most of the older adults in their practice did not carry a cellphone, however, older adults who did, had limited data plans, which were not very feasible to accommodate the messaging services.

> "Well with our two patients'…I don't know if we had a good sample size, but I don't think…they had the technology…to fully use the device"-007HCP

Themes and sub-themes mapped to theoretical frameworks

The identified themes and sub-themes were mapped back to the theoretical frameworks (see Figure 7-3).

FIGURE 7-3: Themes and Sub-themes Mapped to Theoretical Frameworks



7.4.3. System Usability Scale

The mean SUS score was found to be 80.63 with a range of 70-87.5.

7.5. Discussion:

7.5.1. Principal Findings

To the best of our knowledge, this is the first study to examine the factors that may impact the implementation of a prototype smart adherence system in community pharmacies in Ontario, Canada. Our study results indicated that pharmacists valued the availability of real-time medication intake data and perceived that it can be a useful tool to make clinical decisions related to therapy. We identified numerous factors that are not solely related to pharmacy workflow but also include pharmacists' perceived patient determinants and product features which may impact the implementation such interventions in community pharmacy settings.

Previously, studies have identified pharmacy workflow and time constraints as critical barriers to offering medication management interventions at community pharmacies.[308–311] A systematic review of pharmacy clinical care services identified pharmacy workflow and space availability, time constraint, low remuneration cost and extensive paperwork as potential barriers for pharmacists to adopt clinical services.[312] The interview analysis for this study provided additional and new insights from pharmacists and pharmacy assistants regarding pharmacy workflow related factors. Although participants perceived that the system was easy to use, the initial set up and staff training was discovered as a necessary step to implement these services effectively and perceived as a barrier. The additional required steps within the traditional pharmacy workflow organization include switching between the portal screen and the pharmacy software screen, securing the blister packages' connectivity devices, labelling the blister package's using date and time stickers and

additional delivery scheduling. Furthermore, pharmacy staff required a larger space and specific storage locations for the smart blister package than traditional blister packs. The pharmacies in this study were dispensing smart blister packages for a small number of patients (one pharmacy dispensed for 5 patients, one for three and one for two patients), and storage of the devices was already a concern. If a pharmacy chooses to use this service for dispensing to a large number of patients, it is important to support pharmacies in identifying effective methods for managing storage that maintains their current workflow. Moreover, to fully implement the service, pharmacies may require additional staffing or personnel resources. Personnel requirements may include more pharmacy assistants to package the blister pack, pharmacists to monitor and address real-time adherence intake and personnel responsible for delivering the packages to the patients who cannot commute to the pharmacy. The cost associated with increased staffing, training and workload must be considered before offering such services.

In our study, pharmacists perceived the usefulness of access to the real-time adherence data. They expressed that this access would provide them with the confidence to address non-adherence issues with their patients and positively influence physician-pharmacist interaction. However, given all of the new data available to them, this also places a regulatory implication on pharmacists. Pharmacists were concerned about balancing the constraints of implementing this system with the time required to identify adherence issues and patterns to intervene if needed effectively. Additionally, pharmacists expressed that there should be reasonable remuneration for the additional time and resources needed to monitor the real-time adherence and follow up with the patients and physicians. Several studies have identified that lack of financial remuneration or poor remuneration is a barrier for pharmacists in offering clinical services in healthcare systems.[313–315] Canada has a universal healthcare funding model.[316] In Ontario, the Ontario Drug Benefit (ODB)

program covers the cost of most prescription medications, few over the counter medications and some monitoring devices (such as glucometers for specific age groups and populations).[317] Currently, this program reimburses pharmacies for identifying a potential drug related problem while dispensing, conducting medication reviews, and supporting smoking cessation for their patients.[318] However, they do not provide reimbursement for pharmacists or pharmacies that offer real-time medication monitoring services. Similarly, none of the private insurance plans provide reimbursement for these kinds of clinical services. If pharmacists were to monitor real-time medication intake for their patients and intervene in a timely manner, this may lead to prevention of hospitalization, emergency room visits and potential healthcare cost savings related to non-adherence. However, currently pharmacist will not be remunerated for their effort. Therefore, policymakers should analyze the current pharmacy funding model in both public and private sectors for the successful implementation of such services.

By using the integrated model with three different frameworks, we also identified critical patient and product determinants that were perceived by pharmacists related to the safe and effective use of such products. These determinants could help pharmacists identify and recommend the appropriateness of an adherence intervention for their patient population. Medication adherence interventions should be individualized based on patient characteristics.[319] In our study, pharmacists perceived that the smart adherence product can be usable in patients with unintentional non-adherence. However, due to the smart blister package's physical features, pharmacists indicated that the product might not be suitable for all users, especially those experiencing dexterity issues related to aging or disease state. In those cases, family caregivers were identified as potential users of the system, especially if they live in a different geographical location than their loved one. The prototype smart adherence system provides an opportunity for caregivers to receive notifications

about missed doses. The reminder functionality is a valuable feature and can be utilized to address non-adherence promptly.

The cost to the patients and patient access to technology were some of the barriers identified by the pharmacists. The smart blister package requires a cell phone with the ability to receive SMS reminders. Similarly, this system's costs may include monthly connectivity fees and expenses associated with a more capable cell phone plan. Most of the pharmacies in Ontario, Canada, offer blister packaging as a free service, while some may charge a minimal monthly fee. In this study, the pharmacists raised concerns with costs associated with cell phone plans as most of their patients either had a basic cell phone or had a cell phone with a limited plan that had a cap on messaging services.

During this study, both patients and pharmacists encountered some technical challenges with the portal and its reminder functionality. This induced panic and worried both patients and pharmacists, who feared that they were doing something wrong with regard to the system. As mentioned above, product features and design can affect a product's usability in specific patient populations. This could very well impact the integration of such devices into patient's homes. Therefore, pharmacists should carefully evaluate patient and device-related factors to match them appropriately before offering these types of interventions.

7.5.2. System Usability Scale

The SUS scale is a validated tool to assess the usability of a product subjectively.[139] There is no cut off value available to indicate the usability of a product, however Bangor et al. interpreted the SUS score by using adjectives. SUS scores higher than 70 indicate that the product is acceptable

by the users, scores between 50-69 represent that product is marginally acceptable and score lower than 50 demonstrate that it is not acceptable.[140] The SUS score for the smart adherence system in this study was reported to be 80.63 with a range of 70 to 87.5. This score indicates that the product was rated acceptable to use by pharmacy staff.

Strengths and Limitations

This is the first study that specifically explored and outlined the implementation of smart adherence interventions at the community pharmacy in Canada (to the best of our knowledge). The study adds to the existing literature related to the barriers and facilitators affecting adherence interventions at the community pharmacy. We used three frameworks to develop the interview guide and analyze the data, which provides rigour to the study. A limitation of the study was the small sample size. Although the research was conducted in three community pharmacies, we could only interview three pharmacists and one pharmacy assistant.

7.6. Conclusion

Products that offer real time medication intake monitoring are valued by health care providers especially pharmacists. However, essential determinants related to pharmacy workflow —along with patients and product factors —must be considered before implementing a technology-based adherence intervention program in a community pharmacy setting. The careful evaluation of these factors will help pharmacy teams and management to continuously integrate these services successfully. Future studies should be designed with larger sample sizes and structured as randomized controlled trials comparing healthcare systems' cost-savings due to the delivery of such adherence interventions via community pharmacies.

CHAPTER 8

Lessons in Reflexivity of a Pharmacist conducting Ethnographic Research

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8.1. Abstract

The practice of reflexivity is widely recognized in ethnographic research as a strategy to identify and explore a researcher's self- knowledge, beliefs, experiences, and their influence on research. In this article, I explore my journey from a practising pharmacist to a researcher within an ethnographic informed study pertaining to patients with chronic diseases and their medication intake behaviour. Ethnography allowed me to explore the lived experiences of ten participants using a smart medication adherence product. Through in-depth at home observations, photo-elicitation and semi-structured interviews over a period of 6 months, I was able to gather the invisible meanings associated with their in-home medication intake process. Extensive field notes were written after each home visit in addition to a reflexive journal documenting my inner thoughts, questions and reflections. A key finding of this activity was the intersectionality of my profession with race and gender, something I had not anticipated. Secondly, my social location as a woman and person of colour resulted in questions being asked of me that was unexpected and at times left me feeling uncertain and uncomfortable. I entered this study believing that the boundary I erected between my roles of pharmacist and researcher would ensure clarity, and perhaps a sense of protection to some degree. I now realize this may have been naive and by relinquishing control of these roles, I was able to gain a deeper understanding of myself, my role as a clinician/researcher, and the older adults I serve as a pharmacist. Being reflexive during the study period offered me an opportunity to first identify and then analyze my beliefs and how they may impact the information I gathered during fieldwork. The practice of reflexivity is a critical tool for clinician-researchers and should be practiced throughout the course of fieldwork.

Keywords

Ethnography, reflexivity, pharmacist, lived experience, chronic illness, medication adherence

8.2. Introduction

Originating from social anthropology, ethnography involves "learning about people from people" by immersing oneself into another's natural environment or culture.[111,112] As a qualitative research method, ethnography focuses on learning through mindful observation of the lived habitat from the standpoint of social relations and the meanings and protocols associated with rituals, habits, and behavioural norms. It involves "hands on, on the scene learning" that requires a high degree of self-awareness and self-reflection. The ethnographic research method usually involves a single setting with detailed data collection through participant observations, field notes, in-depth interviews, and focus groups.[112] Moreover, ethnography also aims to interpret social reality through in-depth analysis.[111] The ethnographic research method was first employed in the field of healthcare in 1961, when Becker et al. studied the lived experience of students in medical school in *"Boys in White"* by collecting data through participant observations and interviews.[320] Later on, Goffman's "*Asylums"* reported "the social world of the hospital inmate" based on year-long fieldwork at a psychiatric hospital with non-specified methodology.[321] Glaser and Strauss's "*Awareness of Dying"* was based on rigorous fieldwork involving a combination of observations and interviews at six hospitals, where researchers observed various aspects of dying and described how health care providers and patients' level of understanding of the dying process can impact patients' end-of-life care experience.[322] From there onward, numerous ethnographic studies have been conducted in nursing and healthcare.[114]

As mentioned, the main focus of ethnography is to learn about a culture through the lived experience of the people by observing them, before drawing a conclusion about their attitudes and behaviors.[112] Culture can be defined as a "set of guidelines which individuals inherit as members of a particular society."[113] In ethnography, the cultural aspects of the research are generally

associated with things such as language, ethnicity, cuisine, customs, etc.[114] In terms of healthcare-related research, the culture-based approach can also involve a particular disease condition such as heart disease, diabetes, and/or cancer.[112,113] By applying an ethnographic approach, one can not only understand the lived experiences of patients suffering from particular illnesses, but can also illustrate and discover the complexities, attitudes, and behaviours of that shared culture and its impact on patients' illness in a detailed and thorough manner.[323]

The role of the researcher is one of three key principles of ethnographic research, along with the nature of knowledge and investigating cultures.[114] The role of the researcher emphasizes that when a researcher enters into a culture, he or she "does not arrive empty minded in the field" and can never investigate a culture without incorporating their own knowledge of the world.[114] These influences can impact several aspects of research, ranging from the selection of methodology to writing up the study findings for publication.[324] Though the researcher's personal beliefs, experiences, and knowledge can have a profound effect on the research, their position in society and the socio-cultural circumstances of the study can deeply influence the research as well.[325] An important aspect of ethnographic research is reflexivity: a process of self-reference or self-explanation that involves examining one's personal reactions to situations that occur while working in the field.[326] Reflexivity also shows that the researcher is self-aware of their social and worldly role where knowledge is being co-constructed and can have an impact on the research process and findings.[325,326] By incorporating the practice of reflexivity in ethnography, the researcher can recognize, address, and describe these possible influences on their findings.[327] This acknowledgment of the researcher's influence using reflexivity practices is particularly important for ethnographic studies due to the close relationship between the researcher and the culture they are studying.[325] Therefore, acknowledging the researcher's influence through reflexivity not only

enhances the accuracy of the research process but also increases the transparency, trustworthiness, and accountability of the research.[326]

This article draws upon my reflections of a study conducted by myself as part of my Ph.D. thesis project at the University of Waterloo, School of Pharmacy in Canada. The study aimed to understand the medication intake behaviour of older adults diagnosed with chronic diseases such as hypertension, ischemic heart disease, diabetes, etc. who were integrating a smart medication adherence product into their medication intake routines. In this article, I will describe my reflections as a researcher, specifically during the ethnographic field phase. First, I will explain how my professional position as a pharmacist allowed me to become an insider, helped me gain access to participants, and aided me in obtaining their trust. Secondly, I will describe how the intersectionality of being a woman and an immigrant informed and impacted the social relationships developed between myself and the participants. Third, I will share some of the complexities related to my dual identities as a pharmacist and a researcher during the home visits and how I navigated my role as a clinician-researcher in patients' homes. Finally, I will reflect on the struggles I faced while drawing boundaries between myself and participants in terms of discussing my multiple roles.

8.3. Context and project background

Chronic diseases contribute to 70% of deaths worldwide.[2] The risk of chronic disease increases with age and is often linked with cognitive impairment, functional disability, falls and injuries, and psychological issues.[328] For optimal management of chronic diseases, medication adherence is extremely important. Studies have shown that almost half of chronic disease patients do not adhere to their medications.[1] Non-adherence to therapies causes sub-optimal management of disease

symptoms, resulting in an increase in morbidity and mortality, and poor quality of life.[329,330] Furthermore, non-adherence leads to increased utilization of medical resources and costs to the healthcare system.[18]

This study was based on a qualitative design and specifically, the ethnographic approach was used to understand the medication intake behaviour in patients with chronic diseases. People with chronic diseases are often on multiple medications and have a complex medication regimen to follow.[7] Managing complex medication regimens on a regular basis was considered to be a cross-cultural aspect of the study participants. The use of the ethnographic method allowed for the opportunity to observe this culture-sharing group, to better understand the process, activities, and behaviours of their medication management, and to explore their personal experiences pertaining to their medication intake routines — all within their natural environment, their homes. Throughout the study period, participants were asked to use a prototype smart multidose blister packaging that had the ability to record medication intake events on a web-based portal, to manage their medications.

The study received ethics approval from The Office of Research Ethics, University of Waterloo. All participants provided written consent prior to home visits.

I visited patients in their homes multiple times to understand and explore their lived experiences relating to medication management. Framed by ethnography, I used multiple methods to collect data. For example, digital photography walkabouts (a process of taking pictures while walking around the place of interest,)[118] permitted me to document participants' medication storage locations in their homes. I also collected data via participant observations and wrote field notes

after each home visit. Moreover, during the semi-structured interview process, I incorporated photo-elicitation (a process of involving photos, videos, or other forms of visual methods during a participant's interview)[122] to generate discussions with participants on the use of smart multidose blister packaging. At the end of each visit, I wrote detailed and reflective field notes to capture additional and nuanced details. I also kept a reflexive journal, which was kept separate from the data, to record my thoughts, feelings, and frustrations after each participant interaction. The journal was extremely important as it allowed me to not only capture details of participant home visits but also prompted me to critically reflect on my thoughts and emotions.

8.4. The Social position(s) and intersectionality: pharmacist, woman, and immigrant

Positionality can be defined as the "position of the researcher in relation to social and political context of the study."[331] The social position of the researcher and the participant can bring status and power and may influence the way the participant perceives the researcher or vice versa during interactions.[332] This mutuality is fluid and shifts according to social positions of gender, race, knowledge, background, culture, and education of both parties.[326,333] As a result, the researcher must adjust in the moment of how such positions may impact the establishment of trustworthiness, which are benchmarks of ethnographic research. This power shift among researcher and participant can very well impact the knowledge created during the research process.[332,333] Social positions affect the researcher's access to the research field, shape the nature of the relationship that is formed between the researcher and the participants, and influences how the respondents share information. The researcher's background knowledge about the phenomena also impacts the way they frame the research question and analyze the data.[334] I brought several social positions to the study; pharmacist, women, immigrant, and person of colour.

8.4.1. My social position as a pharmacist

Establishing trust plays a crucial role in an ethnographic informed study and can impact deep and genuine data collection, especially in the context of studying complex health behaviour such as medication management behaviours.[335] The need to reach stories that perhaps have not been shared before requires implicit respect, trust, and the ability to receive questions and hear experiences without judgment. For all participants, my social position as a pharmacist aided in a sort of *fiduciary trust* described as the trust that the person will act in others' interest before their own,[336] perhaps assuming that since I already had their best interests as a health care professional, this would continue in my role as a researcher. This awareness was starkly visible when the participants granted me entry into their homes without condition, which left me feeling overwhelmed and internally grateful.

At the time of study enrollment, all study participants were informed of my position as a practising pharmacist for the reason of transparency. Some participants had an existing relationship with me through the community pharmacy where I practice, raising the initial issue of whether individuals felt obligated to participate in the study. To avoid the perception of possible coercion, I followed several steps. If individuals expressed an interest in the study, I arranged for the initial contact to be made by another researcher who accompanied me for the home visits during the study. My colleague described the study process to the participants and emphasized I would continue to be their pharmacist regardless if they participated in the study or not. I was not involved in obtaining the consent to participate in the study with these participants. As mentioned, my pre-existing role as a pharmacist to the individuals who participated was advantageous in that a degree of trust was already present, but also contained a caveat that I needed to be mindful of; I often found it challenging to remain within the parameters of a researcher, especially when interacting with the

participants to whom I was also a health care provider-pharmacist. Keeping myself from slipping into the role of a pharmacist while remaining focused on the research proved to be more complicated during these interactions than I had anticipated.

Once the participants consented to the study, this pre-existing relationship lessened the amount of time needed to create an environment of trust. This existing relationship facilitated a culture of openness during the home visits that allowed for conversations to be quickly initiated upon my arrival at their house. Similarly, participants who I was not familiar with before starting the study also established a trusting relationship with me quite quickly once they learned that I was a pharmacist. They accepted my role of researcher in a positive manner as they did not see my questioning of their medication management as judgment, but rather as a pharmacist helping them share their views and thoughts in a detailed and non-judgmental manner.

8.4.2. My social position as a woman

Besides my social role as a pharmacist, I am also a woman. Eighty percent of study participants were female. While I am unable to claim that my gender influenced the interactions I had with the male participants, I do feel my gender allowed for conversations about the impact of aging on societal beauty standards with the female participants. I felt that they were eager to discuss issues specific to gender and aging e.g. how age can influence the physical appearance of a woman's hands. Many of the female participants also commented on how their male partners did not seem to notice these cosmetic changes. I suppose our shared gender gave them a sense of familiarity or 'knowing' and allowed them to share more personal thoughts without much hesitation. After those visits, I did wonder how the female participants would have responded to a male researcher; would they have been as comfortable or open to speaking on these gender-aging specific issues? I also

wondered if or what the male participants would have chosen to share and if their concerns related to aging would have been on cosmetic or physical health.

I became acutely aware of how gender created a space that I had not entered in before as a researcher or pharmacist. For example, while conducting interviews, I listened to some opinions that I felt strongly against, experienced internal discomfort with, but in the end, remained silent. One of the male participants made it known to me of his high comfort with technology, extending his point to say that *"women know nothing about computers or cell phones."* As a researcher, I was obliged to record his opinion the way he expressed himself while being mindful to contain my disagreement for the sake of the relationship. Ironically, this statement was said to someone whose study is informed by the use of technology to aid in medication adherence. I had an intense urge to correct him at that point with statistical data available regarding women currently working in STEM (science, technology, engineering, mathematics) fields. However, due to the fear of negatively impacting my relationship with the participant, I decided not to. I felt that this process of keeping myself silent brought a sense of powerlessness to me resulting in value dissonance. I consider myself to be a feminist and in my personal and professional life, I advocate for the rights of women within science and technology related careers, and yet this one statement silenced me and left me feeling disempowered and passive.

Studies have reported similar situations where researchers found themselves in awkward situations during an interview. A study based on the reflections from a medical education researcher discussed a similar situation where one participant took the interview question as an opportunity to express personal grievances.[337] The researcher felt unsure of how to act - if making a response or correcting the interviewee was appropriate at that time and how it may have affected the

interview process. Therefore, to maintain the quality of the interview, the researcher navigated the conversation back to the question.[337] Another study describing the experiences of a female researcher with an East Asian background reported that while conducting interviews, one of the interviewees expressed negative feelings about females of the researcher's ethnicity.[338] However, the study did not report how the researcher handled the situation.[338] Later, when recording and reflecting on this situation, I realized that I should have tried to have a respectful discussion with the participant. This discussion may have changed his mind about "women and technology", rather than validating his beliefs. However, as a researcher, I do not believe that I would have gained anything related to my research project by changing their views. Looking back, I should have tried to steer the conversation back to the interview questions. This is something I can practice for future encounters.

8.4.3. My social location as an immigrant and person of color

As both a person of color and an immigrant, I've had many friendly and unfriendly encounters throughout my personal and professional life because of my ethnicity and immigrant status. All of the study participants were Caucasian and natural-born citizens of Canada. I migrated to Canada 16 years ago, and I have friends from different ethnic backgrounds, visiting participants in their homes still made me feel that I was not "one of them."

As an immigrant, I have always noticed significant differences existed between my culture- South Asian and Canadian culture, and doing in-home interviews accentuated these differences. For example, in the environment I grew up in, one cannot address elders by their first name and must instead use terms such as Mr./Mrs. before using their name. In Canadian culture, however, people are much more casual and address each other by their first names regardless of the age difference.

This was something that I have always struggled with, and I felt the same way during the interviews, as the participants insisted I address them by their first names. This again, created a value dissonance for me, as participants assumed this was a gesture of acceptance toward me as an outsider, when in fact it challenged my values and upbringing as a South Asian person. Another difference I noted was that in my culture, direct eye contact with elders is considered to be disrespectful, whereas in Canadian culture, not making proper eye contact is considered to be rude. These cultural differences were especially difficult for me, resulting in multiple value dissonance situations that at times, left me feeling groundless. This feeling of groundless has been used in social research and describes a feeling of discomfort, anxiety, fear, anger, etc.[339] During this study, in certain situations, these differences in the cultural norms left me confused, and produced feelings of anxiety. This made me feel like my feet were not firmly planted to rules by which I had been brought to live by and left me feeling groundless.

When one interacts with their patients in the capacity of a pharmacist, the conversations are exclusively related to health or medical issues. However, when you visit a participant in the capacity of a researcher, the conversations are not as specific. To develop rapport with participant, one may have to create a comfortable space where the participant can share their lived experiences. In order to compensate for the cultural differences and create a comfortable interviewing environment, I started to familiarize myself with current affairs (politics, sports, tv shows) before each study visit, so I could initiate conversations with participants during home visits. However, I found this to be quite emotionally exhausting; to adjust my personality depending on each participant's lifestyle and interests and assume a persona that was not my own. I have never watched ice hockey and do not know much about current political affairs, and so keeping myself updated on Canadian culture was additional emotional work that I had to do before each home

visit. I was also not aware of body language and social cues with which a native Canadian researcher would have been familiar with. Therefore, I had to be extra vigilant during these interactions to pick up on social cues that I may not as familiar with, due to the different backgrounds and origins of the participants. Again, even though it was exhausting, I adapted to these emerging situations as I have been living in Canada for some time. Concealing these feelings from participants evolved into a role I submerged myself in only for the time of the interview and this became a coping strategy.

Some participants were very interested in my story, such as, where I was born, my religion, and my reasons for migrating to Canada. Others were familiar with me due to our previous interactions at the community pharmacy and therefore, already knew my race and background. During encounters at the pharmacy, patients do not have the opportunity to partake in long discussions, therefore these background talks are usually limited to questions about my country of origin. When I visited these patients as study participants, I found we discussed a great deal about my background ranging from the place where I was born to my reasons for migrating to Canada. One of the male participants even discussed the politics of the country where I migrated from. The participants with whom I was not previously acquainted with viewed me as an "exotic", or a "never-before-seen" being. These participants were living in mostly a white community and having a person of color and an immigrant in their home was something that they were not familiar with and viewed the visit as an 'experience.' As a first-generation immigrant, I am quite acquainted with answering questions regarding my race, nationality, and religion. Yet as a researcher, this was my first experience answering such personal questions while also attempting to maintain professional boundaries. While having these non-research related conversations made participants

more comfortable during the home visits, it did feel like uncharted territory for me and I experienced many moments of uncertainty in how to respond, if at all.

8.5. Being an insider while an outsider

While conducting ethnographic research, it is important to consider another aspect of the researcher's position — are they an 'insider' or an 'outsider'? If the researcher is not a member of a certain culture, yet engages in observing and describing that culture or the phenomenon under investigation, they are considered an outsider.[111,114] Alternatively, researchers who are members of the community or culture being studied are considered insiders.[335] Both approaches offer a rich and detailed collection of data and require the researcher to reflect on their own perspective and beliefs in order to provide legitimacy to their findings.[111,335]

At the start of my project, being a practising pharmacist allowed me to map out the data collection process in a detailed manner. As I was already aware of the medication management issues in the older adult population, I made sure to collect every possible detail about their in-home medication management process in this study. For example, it is a very common practice that patients do not discard their medications once they finish the therapy; therefore, during home visits I asked participants to show me all of the medications they had in their homes, rather than only asking for their current medications. I believe that if I was not a practising pharmacist, I would have only collected data on their current medications. Moreover, my positionality as a practising pharmacist also improved my accessibility to recruit potential participants, both from my own workplace and outside, as I have professional connections with many other practising pharmacists. Additionally, I had developed careful listening skills due to my experience as a pharmacist, which helped me in my research while making conversations with participants.

In the end, I viewed myself as both an outsider and an insider. As someone who is not an older adult, does not have any diagnosed chronic condition, and is not taking medications on a regular basis, I cannot relate to those whose shared culture is chronic medical conditions and the management of these conditions. Therefore, I would consider myself to be an outsider. On the other hand, due to my years of experience as a practising pharmacist, I can also view myself as an insider. To be specific, my time as a practising pharmacist has allowed me to observe various medication management issues within the geriatric patient population, and I have dealt with older, chronically ill adults on a regular basis. I have a strong understanding of the Canadian healthcare system, patient language, and how older adults process daily issues regarding medication management. I am also familiar with the challenges and barriers experienced by older adults when trying to manage their medications.

Moreover, I understand the kinds of solutions that may be used to help plan and manage medications regularly. For instance, the use of reminders, alarms, pill boxes, and blister packages to aid in the management of medications is not a new concept for me. I often recommend these medication administration aids to patients. This familiarity I have with the medical world and culture relating to individuals with chronic medical conditions and the management of these conditions made me feel at home when conducting my research study. During my research project, I continuously self-evaluated myself. I repeatedly asked myself questions — am I understanding the situation in the same way as these participants are, or what would I do if I had to manage so many medications on a daily basis? Though I was clearly not an older adult who manages medications, I was very well aware of the challenges and issues related to medication management due to the experiences of both my 65-year-old mother and many of my patients.

8.6. Negotiating the space between the researcher and the pharmacist

Managing dual identities as a pharmacist and as a researcher was a dilemma that I faced during my fieldwork. While this is a common finding of many reflexivity practices that clinician-researchers face when conducting ethnographic studies, I felt that my role as a pharmacist ushered in different kinds of challenges. Arber mentioned her experience of managing the dual identities of a researcher and practitioner while conducting an ethnographic study in the hospice setting as challenging, especially when she had to choose between the role of a researcher and a nurse during her fieldwork.[340] Similar experiences were shared by Hiller and Vears, two trained healthcare professionals, who discussed the dual role researchers exhibit, by describing how patient participants expected feedback regarding a clinical situation because they were aware of the researchers' status as healthcare professionals.[341]

Similarly, during my fieldwork, I encountered numerous situations where participants expected me to address a medication-related question such as clinical advice about their treatment efficacy or managing side effects of their medications. On multiple occasions, participants inquired about prescription and non-prescription drug usage and expected me to provide them advice. At that point, I struggled with how to respond. I was there as a researcher and not as a pharmacist, but participants were hoping to get an answer from me. I did not want to advise them about their medications as I was not their regular pharmacist and did not want to compromise the relationship they had with their pharmacist. More importantly, I did not feel comfortable giving them advice because I did not have all the health-related information necessary to provide a proper recommendation. I addressed this issue in several ways. In a few instances, if the participant insisted on receiving advice regarding their medications, I told the participant that I would speak to them about their medication-related concerns following the study visit, and would remind them

to also speak with their pharmacist should there be any additional concerns. I come across this very situation often in my personal life, where my friends and relatives ask for my advice about their medication usage and demonstrate displeasure if I do not provide them an answer. However, my past experiences in addressing these types of situations made it somewhat easier to manage these discussions with the participants.

For example, one of the memos I wrote in my reflexivity journal, after visiting a participant, highlights this issue:

> *"During the home visit, [patient name] asked me a question that I was not sure how to respond to. She told me that she is losing a lot of hair and her nails are breaking easily, her friend suggested to buy a natural supplement. She is planning to buy [name of the natural supplement], and she asks me if it is okay for her to take it with her other medications. I wanted to answer her from my clinical knowledge but felt uncertain of how to react. I knew that the supplement would interact with her medications. At the same time, I was there as a researcher and not as a pharmacist. I told her gently to contact her community pharmacist before purchasing the supplement as it may likely interact with the medications she is currently taking."*

I questioned myself numerous times during the fieldwork of this study as to when and how to shift my role between being a researcher and a pharmacist. As per the Code of Ethics from the Ontario College of Pharmacists, it is my ethical obligation to follow the principle of "Non-Maleficence" defined as the "obligation to protect patients and society from harm."[336] The Code of Ethics applies to all pharmacy practice and related research.[336] There were some instances where I came across

situations where I felt that participants were at risk of harm. In these situations, I felt obligated to intervene and I shifted my role from being a researcher to a pharmacist. For example, some participants were not storing their medications in appropriate locations or in suitable conditions, something which is vital for the effectiveness and potency of medications.

Similarly, some participants were storing their expired and/or discontinued medications alongside their current medications, which may lead to wrongful ingestion of medications. As a pharmacist, it was my ethical obligation to ensure that the medications within the participants' homes were being managed in a safe and effective way. Yet, even so, I did not want to outwardly address these issues as I had been invited into their home as a researcher and did not want to breed panic or concern. Here, I looked through the lens of the pharmacist and I advised them to take their expired medications to the pharmacy so that they can be properly disposed of. When I work as a pharmacist in the dispensary, I counsel patients regularly about medication use and often advise them to store their medication in a cool, dry place and warn them to keep it away from moisture and heat. However, I never expected that after dispensing medications, patients would choose to store them in places such as over the kitchen stove, in bathrooms, or alongside their cleaning supplies. I did not want participants to feel that I was judging their choice of location for medication storage, yet as a pharmacist, I felt the urge to counsel them on medication storage. However, I was there as a researcher, so I refrained from intervening as their choice of storage was not causing any immediate harm, and instead politely advised them to call their regular pharmacist and ask about the proper storage of medications.

While I spent time with study participants as a researcher, I was still observing their lives through the lens of a pharmacist. As an ethnographic researcher, I was able to learn about and better

understand the participants' lived experiences through a pharmacist-informed perspective. These experiences that I witnessed first-hand, helped change my practice as a pharmacist. Before I conducted this study, I have often asked patients during my work at the community pharmacy *"where do you store your medications?*", yet I have never asked "*why did you choose this specific location?*" or observed their daily medication storage. After observing the lived experience of study participants, I hope to include the aspect of *"why*" in my encounters with patients.

Another situation, where I felt that being a pharmacist provided me a different outlook into the lived experience of participants' medication management was when one participant was storing used insulin needles in an open container rather than a Sharps container. The risk that comes from the unsafe disposal of needles was obvious to me as a pharmacist. Upon inquiry, the participant explained that she did not get any counseling from her pharmacist about the disposal of used needles and she was not offered a Sharps container from her pharmacy. This response upset me because as pharmacists, it is our duty to properly counsel our patients. This participant was unaware of what a Sharps container was, and so I felt it was my professional obligation to advise her as a pharmacist on how to obtain a Sharps container and the importance of having one. When I later reflected on this incident with the research team member who was accompanying me during the home visit, she later confessed that she would not have noticed this safety concern due to her non-pharmacist background. During my fieldwork, I looked through the perspective of a clinician-researcher and realized that numerous of the aforementioned occasions would have been missed if I had lacked the clinical background I have as a pharmacist.

8.7. Drawing the boundaries between my personal and public life

Another facet that emerged related to reflexivity is how participants showed an interest in my personal life. I assumed that reason for this interest lies in participants wanting to become more comfortable with the researcher before opening up about their medical concerns. Yet, I was left with thoughts of uncertainty regarding which parts of my life to share with them and to what degree. Almost all participants were curious to know why I decided to go back to school and pursue graduate studies when I was already a practising pharmacist. One participant even asked me "*will it affect the amount of money you make as a pharmacist"?*

I was surprised to be asked this question as I never thought about pursuing my graduate studies simply for a pay raise. People often ask me what I am going to do career-wise following my Ph.D., but no one ever outrightly asked me about my income. It led me to wonder if other people also assumed that I was pursuing my graduate studies in order to earn more money.

People usually do not ask about my religion so openly when I am working as a community pharmacist; however, one of the participants asked me this question in a very direct manner. The participant asked me "Which religion do you follow?" and before I answered her, she continued her conversation as follows:

> *"It does not matter to me, which religion you are from…. I do not judge people, I do not care which God you follow, (she touches the wood table), your God can be a table, I don't care, as far as you follow one"*

In another home visit, I had an interesting conversation with a participant. As I am not a native English speaker, the participant inquired about my origin of country due to my accent. I was not sure how to respond to her at that point. I captured this interaction in my field notes as follows:

> *Participant: I hear you got an accent, It's a nice accent by the way. What country were you born?*
>
> *Me: I'm from Pakistan.*
>
> *Participant: Oh beautiful. I followed the real nice story on Pakistan in the last couple of days, my husband joined me to watch it. It was a very, very nice story about the life. I'm not talking about the life of the dictators and the people like that we have in Ottawa. They are honest straightforward everyday people, they believe in what they have been brought up to believe. They believe in their families and children. I think that film and I can't to this minute remember the name exactly, should be shown all over. It was a fantastic movie. They, the people that had nothing, how kind and how generous they were. And you know, really how hard life must be for them. So, I don't care where you're born, it doesn't matter to me, besides I've got some good friends that are from Pakistan. They made a nice business here in town and you will do fine too here.*

My reflexivity notes after that visit are below:

> *The patient participant questioned me about my origin because she noticed that I had an accent, but she asked about it in a very polite manner. I think that if she did not ask me about my origin in such a nice way, I would have felt a little upset.*

Furthermore, she shared her own experience of interacting with people belonging to that particular geographical region. She mentioned that she was very happy to have good friends who are from Pakistan and pointed out that since they have done very well for themselves, I will do fine too. I was not sure how to respond to that. I have been living in Canada for the last 16 years and I am doing very well professionally, socially, and financially. So why is she thinking that I am not doing well? But I felt very comfortable during the home visit after this little chit-chat. I believe these types of conversations help the researcher and the participant connect on a very intimate level and help build rapport between researcher and participant.

This posed a dilemma to me as a researcher and also as a person of color. In this instance, I was being questioned about my origin, and my ethnicity. I was unsure of how much I wished to discuss this with a stranger, yet at the same time I was thinking, "*was the participant considering herself a stranger at that point?*". She had welcomed me into her home and shown me the most intimate and private places of her home such as the bedroom and bathrooms. Perhaps if she can trust me to explore her medication drawers and take pictures, I should trust her and share aspects of my personal life.

Despite thinking that creating clear boundaries prior to embarking on this study would serve me well, I found myself in many murky areas of how to conduct myself. I reflected upon how my answers to questions asked by the participants would have been different if asked when I was filling their prescription at the pharmacy. I wondered if participants would have asked these questions if I was Caucasian or Canadian-born, and how I would have reacted to these questions if I looked more similar to them in terms of race. Creating the reflexivity journal and documenting

my thoughts post home visit helped to unpack my views, beliefs, and assumptions embedded in these questions, and while not necessarily providing an answer, pushed me deeper into understanding myself as a researcher.

This research examines the reflections of a practicing pharmacist conducting ethnographic research to understand the medication management of patients with chronic conditions. By using a reflexivity strategy during fieldwork, I learned that it helped me overcome the challenges that occurred due to my dual identity, my social position as a pharmacist, and my own beliefs and assumptions. Although the social position as a pharmacist can help the researcher build a trusting relationship with the participant, it is important to consider the difficulties faced by pharmacists when they disclose their identity to their participants. The ethical and legal implications caused by the 'clinician-researcher' dual identity should be carefully considered and reported.

A researcher's social identity, whether it is based on their gender, profession, and race, among other things, may color their expectations and interactions with others as well as influence how participants perceive the researcher. Ultimately, perceptions and interactions can impact the knowledge being produced. I have summarized the key lessons learned during my fieldwork in Table 8-1.

TABLE 8-1: Lessons Learned during Fieldwork:

• The social identity and position as a pharmacist enabled a researcher to obtain the status of an insider while conducting healthcare research. • Shifting the dual identity of pharmacist-researchers during fieldwork is challenging and requires significant self-management. • Researchers should note that boundaries related to race, gender, and profession will be challenged during fieldwork. • Self-reflection not only helps the researcher identify their assumptions, beliefs, and perceptions towards others, but also their impact on others.

8.8. Conclusion

It is essential that a researcher, who is also a practitioner, is reflective throughout their fieldwork, as it not only contributes to building knowledge according to contextual situations and understanding how that knowledge was created, but also provides rigour and transparency to the study findings. There is limited literature on the experiences and reflexivity of practising pharmacists in ethnography fieldwork, much less as a woman and person of color. Other pharmacists involved in qualitative research should consider writing their reflections on their interactions with participants, their dilemmas about managing dual identities, and the struggles to draw boundaries between their personal and professional lives during fieldwork.

Chapter 9

Summary, Discussion, Implication, and Conclusion

9.1. Summary and Discussion

Medications are one of the most frequently used treatments to manage chronic diseases. However, more than half of the patients with chronic illness do not take their medications as prescribed by their health care providers leading to non-optimal management of their chronic diseases, increased costs to the healthcare systems, poor quality of life for the patient, and increased caregiver burden.[1,18,291,329] As discussed in Chapter 1, medication adherence is one of the biggest challenges of healthcare systems, and various factors impact adherence, including forgetfulness, physical and cognitive limitations, patient's knowledge and belief about disease severity and medication usage, medication regimen complexity, and many more.[33,48–50] Numerous interventions are available to aid in managing complex medication regimens and improve adherence, such as reminders, patient education, pharmacy prepared blister packages, dossettes, and electronic adherence products.[66,81,342] In the last two decades, there has been an influx of development and utilization of technology-based adherence products to improve medication management.[62,78,91,343]

The research presented in this thesis focused on understanding and exploring the in-home medication management process and medication intake behaviour of people with chronic diseases who manage complex therapy regimens regularly and identifying the barriers and facilitators to using a technology-based adherence product through the integration of a prototype adherence product for in-home medication management. Furthermore, this research explored the feasibility

of community pharmacies to implement and offer smart adherence products to their patients in the future.

The scoping review, described in Chapter 3, identified various innovative dispensing products such as automated dispensers, smart blister packs, and electronic medication trays to address non-adherence and support medication intake. The scoping review identified various gaps in the existing literature. One significant gap reported was the limited research related to the in-home integration of SOMDS. This review identified that most of the research done in this area discussed the impact of SOMDS on adherence. Although the primary purpose of these adherence products is to improve patient adherence, it is equally important to evaluate the factors that can facilitate or hinder the in-home use of these products. If products are not deemed usable and acceptable by the patients in their homes, no matter how positively they impact adherence, patients may not be open to utilizing them for their in-home medication management process. Therefore, more research is needed to holistically examine the integration of technology-based adherence products.

Another vital gap highlighted was the marked variability related to how adherence was defined and the methods used to measure and report adherence. Only two out of 11 studies used a standardized medication adherence scale to measure adherence.[143,164] The rest of the studies measured and reported adherence using broad and variable descriptions. For example, McGillicuddy et al. reported complete adherence if medications were taken within a 3-hour window of the prescribed dosing time, while Siu et al. considered taking medications within a 2-hour window to be completely adherent. Therefore, patients who were adherent in the McGillicuddy et al. study would be considered non-adherent in Siu et al. study. The novelty of smart dispensing products lies in their ability to record and report medication adherence in real-

time; however, if inconsistent adherence parameters are being used to measure and report adherence, one cannot compare which product use improved the adherence outcome in a true manner. Therefore, future work should develop a standardized definition of medication adherence and the recommended methodologies to measure adherence.

Another important aspect to highlight about these products is their ability to measure medication adherence. These products can record the medication intake event with date and time stamp. This type of adherence data can provide clinicians with detailed insight into their patient's medication intake pattern when compared to traditional methods such as pill counts or patient self-report. However, some data errors may be caused through technical issues related to data transmission. Our scoping review identified two studies where adherence data recorded via the product was reported to be low when compared with pill counts and patient self-reports.[165,166] Haberer et al. reported that 9.8% of medication intake events were not recorded by the product due to technical failures which may have led to low adherence captured by the device. Similarly, Orrell et al. reported that a total of 10.1% of events were not captured due to the product's battery issues. These data transmission errors can raise questions about the integrity of the adherence data that is being collected by these products.

Another essential finding of this scoping review was that despite having the capacity to dispense multiple daily dosing schedules, only two out of ten studies utilized a SOMDS for multiple daily dosing administration. Approximately 44% of Canadians aged 20 years and older reported having at least one chronic disease, which increases to 73% in those 65 years and older, who are among the highest users of medications.[3,230,344] Patients diagnosed with chronic diseases often take multiple medications with complex therapy regimens, including multiple medications, variable dosing, different dosage forms, and more than once daily medication administration, especially if

comorbidities exist.[92,261] Managing such regimens on a daily basis is a complex task and may lead to non-adherence.[57,59] Additionally, individuals with physical and cognitive disorders may find use of these products more challenging. Our scoping review identified very few studies investigating limitation-based usability and impact on adherence. Since SOMDS has the capability of dispensing multiple medications and sending reminders and notifications to patients and caregivers when the dose is due, they may be a potential solution to managing complex regimens and if designed appropriately could address medication management challenges that arise form physical and cognitive limitations, therefore impact medication adherence. Moreover, the ability to track real-time medication intake data through SOMDS can identify the medication-taking pattern and allow health care providers to discuss the medication-taking behaviours with their patients and find effective adherence solutions. Therefore, future studies should explore the utilization of these products amongst patients who are on complex therapy regimens, have physical and cognitive limitations and explore impact on adherence.

Since the scoping review identified three types of SOMDS, we decided to explore further what other types and features of smart adherence products are available. The literature review discussed in Chapter 4 identified both prototype and marketed smart adherence products available globally. Additionally, we classified and compared features of these products, including storage capacity, the number of compartments, alarm or reminder functions, portability, locking ability, and any additional features such as product notifications, including the type of notification (e.g., telephone call, SMS reminder or email), notification recipient (patient, caregiver, and health care provider), the requirement for a cellular device for optimal product functionality and real-time medication intake information. The results of this study provide a comprehensive review of the types and features of available smart adherence products and may be used as a resource for clinicians to

make an informed decision when recommending these products to their patients based on their patient's needs and limitations. This research highlighted a critical gap that not all the products available to purchase were tested by the patients prior to marketing. Therefore, there is limited to no evidence of how usable these products are for end-users in the real-world setting. The product developers should consider real-world testing of these innovative technologies so the usability of the products can be determined and product functionality issues can be identified and resolved prior to making them available for purchase, which may also improve the product uptake and integration into daily medication management by end-users.

Smart dispensing products are innovative products that can dispense and track real-time medication intake events remotely to address and potentially improve medication intake behavior for patients.[91] The dispensing of medications via the product, opening the product or breaking the conductive ink of the blister pack to access medications acts as a proxy measure of medication ingestion, therefore, these products do not confirm that a patient has actually ingested the medication. These products are available in many different types and offer a variety of features that may or may not be suitable for all patients. Therefore, it is imperative to examine their usability, acceptability, and integration for in-home medication management among different patient populations for their successful adoption. This thesis describes emerging research related to in-home medication management routines and strategies of older adults, integration of a smart technology-based adherence product to manage medications in the real-world setting as well as feasibility and perceptions of community pharmacy staff, including pharmacists and pharmacy assistants, about offering such technology to their patients who are on complex therapy regimens. This holistic approach makes this research innovative in highlighting the gaps not identified by previous research.

In-Home Medication Management

To gain holistic insight into medication management practices in patients' homes, the first phase of this project was developed, as described in Chapter 5. This phase involved visiting participants in their natural environment-their homes, observing their medication storage and administration practices, and collecting their narratives about their daily medication management routines and practices. This research identified that older adults experiencing chronic diseases develop specific routines and strategies to administer their complex regimens and store their medications. These routines and processes are personalized and depend on the ease of access and visibility of their medications. In some cases, medications were stored in hidden places to address the older adult's concerns or views about the privacy associated with their medication usage, while for some older adults where their health was the center of their daily life, medications were stored out in the open. This indicated that older adults treat their medications management practices variably in their homes. A recent study investigating the medication management among older adults on complex therapy regimens highlighted that medication management in such individuals is not a simple process, but rather a complex phenomenon which involves various steps and processes.[43] Our study reported similar findings related to in-home medication management. Maidment et al. also reported that not only older adults but their family caregivers also find it burdensome to manage complex regimens on daily basis. In our study, we did not aim to explore older adults' views about their medication burden when managing complex regimens, however we highly recommend future studies to explore this significant aspect.

A previous study identified that patients prefer adherence products that are smaller in size because they are not visible in their homes and provide them with the privacy of their medication

management.[176] Therefore, if a patient is concerned about their medication routine privacy, the size of the adherence product needs to be considered as they may not be willing to use an automated dispenser with a large size for their daily medication intake. On the contrary, patients who need a visual cue to remember their medication intake may be more willing to use a product visible on a kitchen counter or would like to place the product in an area where they can hear the reminder alarm. Previous qualitative research has reported that the portability of a product is also a necessary consideration for patients who have an active social life and would like to carry their medications with them when leaving their homes.[228,343] Smart adherence products are available with different sizes and may not all be kept hidden. Therefore, the understanding and knowledge of an older adult's personal privacy concern about their medication management and places where they store and administer their medications is highly important to find and offer the most suitable adherence product.

This study further identified that older adults stored their medications at variable storage locations, and few of those were inappropriate and could affect the stability and efficacy of medications. Previous research also identified that only half of older adults store their medications at appropriate locations.[236,252] Some smart adherence products such as blister packs are comprised of plastic cavities sealed by adhesive paper.[91,265] The adhesive paper may absorb the moisture if stored in high moisture areas such as bathrooms, and may impact the stability and efficacy of the medications being stored in them. There is a need of more research about the storage requirements for these products. The product developers should test the stability of medications packaged in these products under high temperature and humid areas to provide specific recommendations for ideal product storage.

To find an adherence product that can fit into an older adult's daily medication taking routine, it is vital to understand what goes on in patient's homes related to their medication management processes, administration routines and storage conditions. An informational diagram in Chapter 5 summarizes these aspects. This proposed diagram may be used as a resource for health care providers to initiate discussions around medication management and storage with their patients, identify their preferences and medication routines, assess the risks associated with inappropriate storage, and educate how inappropriately stored medications may impact medication stability. Furthermore, in-home medication management information gathered from a patient may help clinicians to identify an adherence product that can align with their personal preferences, practices, and daily routines.

Patient: Technology Integration and Medication Intake Behaviour

The second phase of this research project described the integration of a prototype SMBP for in-home medication intake for patients who manage complex therapy regimens daily. This phase of the research project employed various data collection methods, including quantitative and qualitative data, and utilized constructs from three validated theoretical frameworks (TAM, TPB, and COM-B Model) to inform our interview guide and analysis. Usability is an important concept to establish before integrating a product. If users find a product too challenging to learn or use appropriately due to its features, it may very well impact their intention to incorporate the product into their daily medication management routine. The data analysis utilizing the TAM, TPB, and COM-B model identified facilitators (e.g., ease of use, the familiarity of the product, positive feedback from social circle and sense of relief and less worry due to product use) as well as barriers (e.g., large size, limited portability, inability to access medications from the product, associated costs and necessity of having a smart cell phone related to the integration of SMBP.

With the help of the TAM, key factors affecting the acceptance of the SMBP technology by older adults were reported. For example, ease of use and learnability can increase acceptance; however, product design features such as size and difficulty in tablet retrieval can decrease acceptance. Older adults described that the product use reduced their worry and offered them a sense of relief about remembering to administer their medications and perceived its usefulness in situations where forgetfulness causes non-adherence. However, external factors such as cost and the availability of required technology, such as a cell phone to use the product to its full capacity, can very well influence an older adult's intention to use a product.

This research informed us that when offering such products to older adults, health care providers should not only consider the simplicity and ease of use of the product but also explore the affordability and the technology access required to utilize the product for their patients. To utilize fully, some smart adherence products require access to a cellular phone with SMS capability or a smart phone to set up the product or utilize the adherence portal via mobile application.[91] The use of smart phones is becoming more common among older adults. A 2020 survey reported that approximately 65% of Canadians aged 65 and older own a smart phone, and 19% of them used it to manage their health and wellness via fitness or activity app/tracker.[345] These findings are promising and indicate that more and more older adults are using technology to manage their health and stay independent, however we also need to pay attention to those who are unable to afford it. The cost of smart adherence products varies from a few dollars to a few hundred dollars, additionally some products require additional monthly or yearly subscription fees.[91] Most of older adults live on fixed income and may not be able to afford the cost of these products if they are not

covered by their insurance plans. Policy makers and product developers should work collaboratively to make these products more affordable and accessible for older adults.

Using TPB, we identified how product use could drive behavior change related to medication taking and the factors that drive or impede that change, such as feedback from others, cost, and one's physical or cognitive ability to use the product. The study participants identified that the use of the product made them more aware of their medication taking. However, due to the short duration of this study, we cannot claim the sustainability of this behaviour change. There is a need for research including studies with a longer duration to assess the sustainability of this behaviour change. With the COM-B Model, we identified factors that can drive medication-taking behaviors, such as the physical and cognitive ability to manage medications and use a product or the ability to afford the product financially. Specific product features, patients' understanding of disease and treatment knowledge, patients' physical and cognitive capability to manage medications and use a technology-based adherence product, and the amount of work involved in managing medications can also impact the motivation to use the product. A majority of older adults face challenges related to their medication management due to physical and cognitive limitations.[168,285] Future studies should focus on recruiting older adults with physical and cognitive limitations, in particular, to better understand the integration of technology-based products into their daily medication management routine.

The findings of this phase reassured that factors, including knowledge about disease and medications, a patient's physical and cognitive ability to manage medications, available social support, and the work involved in managing complex therapy regimens, can impact an individual's medication intake behavior. Health literacy has been identified as one of the important determinant

impacting adherence.[271,272] Health care providers must identify the level of disease and treatment knowledge an older adult has and discuss the importance of treatment adherence to improve adherence. Similarly, an older adult's cognitive and physical capacity to administer medications and utilize a smart adherence product as well as the available social support system for picking up the medications or providing help in administering medications should be considered prior to recommending a technology-based product for their patients to ensure successful product integration. This research provided real-world usage and feedback of the product which in turn provides product developers with an excellent opportunity to learn from these identified factors, specifically those relating to product design, reliability, and cost, to allow for product improvement and provide an opportunity to make the product more affordable for its users.

Community Pharmacy: Feasibility and Implementation

The third phase of this research project, described in Chapter 7, discussed the findings of a pilot study that took place in three community pharmacies. During this phase, researchers interviewed community pharmacists and pharmacy assistants who packaged and dispensed their patient's medications in the SMBP and monitored their real-time medication intake for the study duration. Additionally, the usability of the adherence system was assessed via the SUS. Community pharmacies are an essential component of a patient's medication management process, not only because of their vital role related to medication dispensing but also due to the established role of pharmacists to address and support medication adherence.[86,90,292]

This pilot study identified factors that can affect the implementation of a technology-based adherence system within a community pharmacy workflow. By using the integrated approach of three validated frameworks TAM, TPB, and COM-B Model, researchers were able to identify that

pharmacists found the technology based-adherence system to be easy to learn and use. The community pharmacists identified the perceived usefulness of the product for specific patient populations, family members, and caregivers. However, this ease of use and perceived usefulness can be influenced by additional workload, which is a vital factor for the successful implementation of a new intervention. Before a community pharmacy decides to offer these products to its non-adherent patients, it needs to evaluate the pharmacy workflow and organization structurally. Moreover, it is crucial to identify the potential need for additional staff so pharmacists can delegate the packaging and dispensing tasks to their staff and can utilize their time to monitor real-time medication intake for clinical decision-making instead of packaging and dispensing.

Pharmacists in this study believed that having the real-time medication information available could improve their interaction with patients when discussing adherence concerns and positively impact their relationship with physicians. However, they were worried about regulatory and ethical implications that they could face with having all this information available to them. The availability of real-time medication intake data would place ethical obligation on pharmacists to monitor their patients' adherence and how and when to act on such information. It is time for pharmacy regulatory bodies and pharmacy professional organizations to start a discussion related to the regulatory implications, including ethical and legal obligations about reporting non-adherence and provide guidance to community pharmacists about the time frame on when to act on the available adherence information. Additionally, pharmacist remuneration for providing this clinical service may impact their willingness to offer this system to their patients and should be addressed by pharmacy professional organizations, private and public health insurance providers, and regulatory bodies.

Reflexivity

The content of chapter 8 discusses the experience and views of a practicing pharmacist conducting ethnography-informed fieldwork. This chapter describes how the reflexivity practice during fieldwork helped the pharmacist-researcher identify their beliefs and assumptions and their impact on data collection and analysis. Additionally, the social position of the researcher as a pharmacist helped gain access to participants more intimately, which allowed study participants to share their medication management stories and experiences without hesitation. This study identified different challenges that the researcher experienced during the fieldwork related to her gender, social and racial background, and dual identity as a pharmacist and as a researcher. Writing reflexive notes and jotting down thoughts after each interaction helped the researcher navigate these situations. The reflexivity practice provided the context of how knowledge was created during this project and provided rigor and transparency to the study findings. Pharmacist-researchers may use the lessons learned during this endeavor to navigate similar situations that may arise during ethnography-informed fieldwork.

Rigor of the Study

As discussed in Chapter 2, Lincoln and Gaba's trustworthiness criteria were utilized to ensure the rigor of this research. Utilizing a team-based approach with members from diverse professional backgrounds, including pharmacy, system design engineering, health informatics, and qualitative research, added interprofessional triangulation and rigor to the research findings. To ensure the creditability of study findings, method triangulation was employed by using multiple methods to collect data, by visiting participants multiple times during the study period and through the member checking process. Although qualitative research is not generalizable, we provided a thick description of our study setting, sampling strategy, participant characteristics, data collection, and

analytic process to provide context. The inter-coder agreement was calculated and reported during the data analysis process, where only two coders were coding the data.

Additionally, a few other approaches were used to ensure reliability included: using one system to code data (e.g., using paper-based initial coding and NVivo Software for final coding), developing the initial codebook among coders, comparing coding across multiple researchers, further revising and finalizing the codebook, and using the member checking process. The COREQ checklist was used to report and document the reporting for projects described in Chapters 5, 6, and 7. Furthermore, the reflexivity technique provided study context and documented and assumptions from the researcher that could impact the study process.

Strengths and limitations

To the best of our knowledge, this is the first study that has used an integrated approach of using three validated frameworks- TAM, TPB, and COM-B model to explore the in-home integration of a smart adherence product. The themes and sub-themes identified via the qualitative interview analysis were mapped back to the key constructs of these frameworks. This integrated approach of using three validated frameworks permitted us to assess a user's intention to use and adopt the technology. It helped us identify additional factors related to health behavior and incorporate the technology-based product into a patient's daily medication management routine. Another strength of this research project was the mixed-method approach, allowing for data triangulation from qualitative and quantitative approaches. Moreover, we employed ethnography-based data collection methods, which allowed us to capture the lived experience of older adults and provided in-depth and detailed information about a complex phenomenon of medication management.

The current study contributes to the existing knowledge about the medication-taking behaviour of people with chronic diseases and provides new knowledge related to usability and patient perspectives about innovative medication management technologies. This research is the first study to explore the feasibility of implementing a smart technology-based adherence system in community pharmacies to the best of our knowledge. The results of this pilot project can be used to design future studies to further test products in other practice settings such as hospitals and primary care clinics and with other health care providers, including physicians, nurse practitioners, and nurses.

There were a few limitations of this study. A purposive sampling strategy was used to recruit participants, leading to selection bias and under-representation of participants with specific demographic characteristics. Another limitation of the study was the small sample size for both patients and pharmacy staff. Although three community pharmacies participated in the study, we could only interview three pharmacists and one pharmacy assistant. Future studies should include a larger sample size to reflect the diversity of patient populations and their health care providers. In addition to pharmacists, other health care providers such as family physicians and nurse practitioners could have been ideal participants to provide feedback about the usability of such products. We intended to recruit family physicians; however, we could not recruit them. Therefore, future studies should include a wide range of health care providers to assess their views about these products and real-time medication intake data usability. Caregivers play an integral part in the medication management of chronic disease patients.[169,346] We did not recruit any caregivers in our study and thus could not provide their perspective about the utilization of smart adherence products for their patients. Future studies should also assess the impact and sustainability of such adherence

interventions on caregiver burden and explore the perspective of family physicians about the availability of real-time medication intake data and its utilization in clinical decision-making.

Another limitation of this project was the inability to analyze the real-time intake data of study participants due to portal software issues. This information would have been critical to determining the impact and effectiveness of such interventions on adherence. We hope to conduct a study to show the impact of the SMBP on adherence in the future. The short duration of the study was another limitation of the study. Participants utilized the SMBP for eight weeks and reported that it made them more aware of their medication intake and induced a behaviour change. Future studies should be designed with a longer study duration to assess product-induced behavior change's sustainability. In this study, we did not intend to explore the outcome of such products on patients' medication adherence. Future research by utilizing study designs such as randomized controlled trials should be designed comparing adherence and healthcare cost-savings utilizing such interventions. We recruited required participants to assess the usability via SUS however we had a small sample size for the NPS assessment which can also be noted as another limitation of our study.

9.2. Implications and Future Research:

Smart technology-based adherence products are emerging to assist patients in their daily medication management. The results of this thesis project provide data relevant to various stakeholders, including patients, health care providers, especially community pharmacists, product developers, and policymakers, and demonstrate that although these products may be an option to help patients manage their complex medication regimen, there are vital factors that need to be addressed for successful integration.

The findings of Chapter 3 and Chapter 4 identified a variety of smart technology-based adherence products with variable features. There is an opportunity to educate health care providers about these innovative technologies so they can help their patients make informed decisions about utilizing these products for their in-home medication management.

The research findings of the in-home medication storage and administration study described in Chapter 5 have several implications for health care providers. Health care providers should be mindful of an individual's concerns and beliefs related to the preference and privacy of their medication usage and should devise patient-specific strategies when offering adherence products and adherence solutions. Similarly, health care providers should inquire and educate patients routinely about the proper medication storage conditions, as inappropriately storing medication can impact the safety of the patients and others around them and can lessen the potency of medications resulting in less effectiveness and ultimately therapeutic failure. The product developers should identify the specific storage requirements for these products to ensure the stability of medications being dispensed in these products. There is a need for future research to assess the validity and usability of the informational diagram based on in-home medication management and storage (presented in Chapter 5) in a real-world setting. It is also vital for healthcare providers to explore the individuality of an older adult related to their in-home medication management as well as assess the medication burden that they experience when offering a medication management solution.

To fully understand the effectiveness of smart adherence products on medication adherence, it is imperative to test their in-home usability. The qualitative interviews of patient participants in this research project provided patient perspective and a real-world experience using a smart

technology-based product for medication management. These findings highlight that although the product must be simple and easy to use for its end-users, it does not guarantee that patients will utilize it in their daily lives. Other determinants such as cost and the availability of the required technology to use the product to its full capacity can very well drive a person's intention to use or not use a product. Therefore, product developers should also consider ways to make these products more affordable for patients, especially older adults, who mostly live on a fixed income and cannot afford out-of-pocket payments associated with such products. The functionality and reliability of a product are other essential features that need to be addressed by product developers. This research project found that users like a reliable product and offer easy access to medications. Product developers can use these findings to improve product design and enhance the system's reliability related to the reminder function. More research is needed to understand the effectiveness and impact of these products on health outcomes such as disease progression and hospitalization due to non-adherence. If found effective, policymakers should consider making these products available through government and private drug plans. The results of this project identified that participants became more aware of their medication intake, and the product use induced a change in their medication intake behaviour; however, due to the short duration of the study, we were unable to identify if this behaviour changed be sustained over time. Future research should examine the sustainability of product-induced behaviour change.

The pilot feasibility study based in the community pharmacy setting, discussed in Chapter 7, provided important information about the determining factors that can impact a community pharmacy to offer such products for their patients. There is a need for full-scale implementation studies to explore this aspect further. The finding of this research project can be used as a step toward creating a framework for community pharmacies to offer such services. The pharmacy

professional organizations, pharmacy owners, and regulatory bodies should work collaboratively to address pharmacy workflow, staff training, education opportunities, regulatory implications of real-time medication intake data access, and remuneration of clinical pharmacy services. The product developers should involve health care providers, including pharmacists and physicians, during the early stage of product development to identify the type and extent of real-time medication intake data provided by these products.

9.3. Conclusion

The smart multidose blister package was easy to use and acceptable by patients, and it could potentially be incorporated into their daily medication management routine. However, before recommending smart adherence products, it is vital to identify and address medication-taking behaviors among patients with chronic diseases. Moreover, facilitators and barriers impacting the use of a product should be considered by clinicians to successfully integrate such products into a patient's daily medication management routine. Community pharmacists value products with the capability to record real-time medication intake; however, pharmacy workflow-related determinants, product features, pharmacist remuneration for providing clinical services, and regulatory implications should be addressed for the successful implementation of such products. Suppose these products can be found usable and successful in medication management studies with large sample sizes, in that case, they may potentially improve adherence and quality of life for patients, reducing caregiver burden and providing an opportunity for clinicians to respond to non-adherence promptly.

9.4. Current Research Projects

Smart adherence products and technologies can impact patients, caregivers, and health care providers such as pharmacists and physicians due to the availability of real-time medication intake data. Additionally, pharmacy owners may need to adjust their pharmacy infrastructure and budgeting to implement these technologies in their practice. Moreover, both public and private insurance providers may need to evaluate their funding models to make these products more accessible to patients. Therefore, to understand the views of different stakeholders regarding the availability of real-time medication intake data, a qualitative study has been designed using Schwartz's theory of values framework to explore stakeholders' values, including patients, caregivers, physicians, community pharmacists, pharmacy owners, and public and private insurance providers. The results of this study will allow us to provide a multidimensional perspective about smart adherence products.

Both older adults and pharmacists who participated in this thesis project identified that patients with cognitive and physical limitations might not be ideal users of some technology-based products. Therefore, to better understand medication management capacity, beliefs, and behaviours related to medication taking and knowledge of medication adherence technologies within older adults diagnosed with Alzheimer's disease and Parkinson's disease, we are conducting a survey-based study in Ontario. The primary objective of this research is to explore how older adults manage their medications in their homes, what are their beliefs and behaviours related to medication taking, what knowledge and experience they have with medication adherence aids and technologies, and how did the COVID-19 pandemic affect their access to medications, pharmacist, and physicians. The secondary objective is to provide population-based information on prescription and non-prescription medications (e.g., over-the-counter drugs, vitamins and

minerals, and herbal preparations/natural supplements). The survey questions are based on the three constructs of the Theory of Planned Behaviour. The results of this study will inform the medication management challenges faced by patients diagnosed with Alzheimer's disease and Parkinson's disease and the adherence aids they use to manage these issues.

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Appendices

Appendix A

Team Members

Name	Discipline
Dr. Tejal Patel	Pharmacy
Ms. Jessica Ivo	Health Informatics
Mr. Ryan Tennant	System Design Engineer
Dr. Kelsey-Ann Poirier	Pharmacy
Dr. Kelly Grindrod	Pharmacy
Dr. Colleen McMillan	Social Work
Ms. Sadaf Faisal	Pharmacy

Appendix B

Ethics Documents- Recruitment Material

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Pharmacy

Recruitment Poster

PARTICIPANTS NEEDED FOR RESEARCH in a Usability and Impact Study Using Smart Multi-Dose Blister Packaging

We are conducting a study to determine how easy and impactful it is to use a smart multi-dose blister package to help you take your medications. We are inviting English speaking individuals who are 18 years of age or older, and taking multiple medications.

As a participant in this study, you will be asked to:

- Use one of two smart multi-dose blister packages for 8 weeks
- Complete questionnaires
- Participate in a one-on-one interview

Your participation will involve 3 in-home visits
where each session will take approximately 60-90 minutes.

In appreciation for your time, you will receive $25 gift card.

For more information about this study, please contact:

Sadaf Faisal
School of Pharmacy
519-888-4567 ext.21371 Email: sadaf. faisal@uwaterloo.ca

This study has been reviewed by and received ethics clearance
through a University of Waterloo Research Ethics Committee

Email Script for Patient Participant

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

Are you 18 years of age or older? Do you take multiple medications on a regular basis for a long-term condition? Would you like to be among those who help us improve medication taking strategies in people with long-term conditions? The University of Waterloo invites you to join our study.

My name is [*researcher name]* and I am working with Dr. Tejal Patel (PharmD), the study's principal investigator, and a faculty member from the University of Waterloo, School of Pharmacy. I am contacting you because we are currently seeking participants for a study as part of a PHD Thesis project.

We are inviting you to participate in a study to test one of two smart products: the "Jones Blister Pack" or "Jones NFC Label" to see how usable and impactful they are in taking medications. We are looking for English speaking individuals aged 18 or older who are taking multiple medications on a regular basis for one or more long-term medical conditions. If you decide to participate in this study, you will be asked to use one of the smart products for 8 weeks and will meet researchers three times in your home. During these visits, researchers will observe how you interact with the products, ask you to complete questionnaires and interview you about your experience with the products. Each visit will take approximately 60-90 minutes. If you receive help taking your medications, you are welcome to invite that individual to attend the in-home visits. All information collected as part of this study will be considered confidential and will be kept in a secure location and disposed of in a minimum of seven years.

If you agree to participate in this study, your pharmacy will be contacted, and invited to participate in this study to dispense your medications in one of the smart products for 8 weeks. If your pharmacy does not choose to participate in the study you will be asked if you are willing to transfer your medications to another participating pharmacy for the duration of the study. In either scenario you will not incur any additional cost as a result of this study. You will however, be expected to continue paying for your medications as per usual. We will also invite your physician to participate in the study to provide feedback about the impact of these product on your medication intake. If your physician does not choose to participate in this study, you can still be eligible to participate.

In appreciation of your time commitment, you will receive a $25 gift card.

This study is being funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label. Adherence information, such as when the product was opened, and your phone number will be shared with Jones Packaging Inc to ensure the device is working. Your name, and any medical and or prescription information will not be provided.

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participating is yours. There will not be any negative consequences if you choose not to participate.

If you are interested in participating in this study, please contact Sadaf Faisal by email at sadaf.faisal@uwaterloo.ca or by telephone at 519-888-4567 ext.21371. The information letter and consent form is attached to this email for your convenience.

Thank you very much!
Sincerely,

[Emailing researcher]

WRAP Email Script-for Patient Participant

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

My name is [*researcher name]* and I am a [researcher's position], working with Dr. Tejal Patel (PharmD), the study's principal investigator, and a faculty member from the University of Waterloo, School of Pharmacy. I am contacting you because you recently provided your name and contact details to the Waterloo Research in Aging Participant Pool (WRAP) and indicated you would be interested in being contacted about studies needing participants. The reason I am contacting you is to inform you that we are conducting a study to test one of two smart products: the "Jones Blister Pack" or "Jones NFC Label" to see how usable and impactful they are in taking medications. we are currently seeking volunteers from the Waterloo Research in Aging Pool as participants in this study.

We are looking for English speaking individuals aged 18 or older who are taking multiple medications on a regular basis for one or more long-term medical conditions. If you decide to participate in this study, you will be asked to use one of the smart products for 8 weeks and will meet researchers three times in your home. During these visits, researchers will observe how you interact with the products, ask you to complete questionnaires and interview you about your experience with the products. Each visit will take approximately 60-90 minutes. If you receive help taking your medications, you are welcome to invite that individual to attend the in-home visits. All information collected as part of this study will be considered confidential and will be kept in a secure location and disposed of in a minimum of seven years.

If you agree to participate in this study, your pharmacy will be contacted, and invited to participate in this study to dispense your medications in one of the smart products for 8 weeks. If your pharmacy does not choose to participate in the study you will be asked if you are willing to transfer your medications to another participating pharmacy for the duration of the study. In either scenario you will not incur any additional cost as a result of this study. You will however, be expected to continue paying for your medications as per usual. If you agree to participate in this study, your physician will be contacted and invited to participate in this study to provide feedback on the product. If your physician does not agree to participate you are still eligible to take part in this study.

In appreciation of your time commitment, you will receive a $25 gift card.

This study is being funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label. Adherence information, such as when the product was opened, and your phone number will be shared with Jones Packaging Inc to ensure the device is working. Your name, and any medical and or prescription information will not be provided.

I would like to assure you that your participation is voluntary and you are under no obligation to participate. This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participating is yours.

If you are interested in participating in this study, please contact Sadaf Faisal by email at sadaf.faisal@uwaterloo.ca or by telephone at 519-888-4567 ext.21371. The information letter and consent form is attached to this email for your convenience.

Thank you very much!
Sincerely,

[Emailing researcher]

Verbal/Telephone Script Patient Participant

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

Hello, [*participant name*]

My name is [*research name*], and I am working with Dr. Tejal Patel from the University of Waterloo, School of Pharmacy. I am contacting you because we are currently seeking participants for a study that is testing two smart products designed to help people take their medication on time. We are looking to get feedback on how usable and impactful the products are as part of a PHD Thesis project. I wanted to know if you would be interested in hearing more about it."

If says "No", say "Thank you for your time and good bye."
If says "Yes", continue on with the call.

The purpose of this study is to test one of two smart products known as either "Jones blister pack" or "Jones NFC label" for daily use in adults, aged 18 and older. If you agree to take part in this study, you will be asked to use one of these products for 8 weeks for your medications and will meet with researchers three times during the study period in your home. During in-home study visits, the researcher will observe how you take your medications and ask you fill out questionnaires and take part in a one-on-one interview. Each in home visit will take approximately 60-90 minutes. If you have someone who helps you take your medications, you are welcome to invite them to the scheduled in-home visits. All information collected as part of this study will be considered confidential and will be kept in a secure location and disposed of in a minimum of seven years.

If you agree to participate in this study, your pharmacy will be contacted, and invited to participate in this study to dispense your medications in one of the smart products for 8 weeks. If your pharmacy does not choose to participate in the study you will be asked if you are willing to transfer your medications to another participating pharmacy for the duration of the study. In either scenario you will not incur any additional costs as a result of this study. You will however, be expected to continue paying for your medications as per usual. We will also invite your physician to participate in the study to provide feedback about the impact of these product on your medication intake. If your physician does not choose to participate in this study, you can still be eligible to participate.

In appreciation of your time commitment, you will receive a $25 gift card.

This study is being funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label. Adherence information, such as when the product was opened, and your phone number will be shared with Jones Packaging Inc to ensure the device is working. Your name and any medical and or prescription information will not be provided.

I would like to assure you that your participation is voluntary and you are under no obligation to participate. There will not be any negative consequences if you choose not to participate. This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee.

Would you be interested in participating?"

If says “No”, say “Thank you for your time and good bye.”
If says “Yes”, continue on with the call.

Administer eligibility checklist using eligibility checklist script.

Email Script-Pharmacist

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

My name is [researcher name], and I am a [researcher title] working with Dr. Tejal Patel from the University of Waterloo, School of Pharmacy. I am contacting you because we are currently seeking participants for a study as part of a PhD thesis project.

We are inviting you to participate in a study to test one of two smart products: the "Jones Blister Pack" or "Jones NFC Label", which are designed to help people take their medications on time. Each product is linked to a software portal which tracks patient's medication intake and can develop reports to assess medication adherence.

As part of this study, you will be asked dispense your patent's medications in one of two smart products: the "Jones Blister Pack" or "Jones NFC Label" for the duration of 8 weeks. You will only be dispensing medications to patient participants who have signed consent to participate in this study. At this time, one patient from your pharmacy has already contacted us and shown interest in taking part in this study. You will also be asked to use the cloud software portal during the study. We will provide complete training in regards to dispensing medications in smart products along with interacting with the cloud software portal. At the end of the study, you will be asked to take part in a one-on-one interview, which will take approximately 30-60 minutes. We will also invite patient participant's physician to take part in the study to provide feedback about the impact of these products on the patient participant's medication intake. If patient participant's physician does not choose to participate in this study, the patient participants can still be eligible to participate.

All information collected as part of this study will be considered confidential and will be kept in a secure location and disposed of in a minimum of seven years.

If you are interested in referring any patient from your practice to this study, we are recruiting patients who are:

- Able to speak and read English,
- Aged 18 or older,
- Are taking 5 medications on a regular basis, or less than 5 medications with multiple daily dosing, and
- Have more than one long-term medical condition.

If you have any patients that may fit this criterion, please let us know and we will forward you a patient recruitment poster with more details along with a recruitment script. Once you receive the poster and script, you may reach out to any patients who may be interested in participating in this study. Once the individual has provided consent for you to share their contact information with us, please let us know.

You and your pharmacy will not incur any additional costs as a result of this study. In appreciation of your time commitment, you will receive $150.00 cheque.

This study is being funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label. Adherence information, such as when the product was opened, and patient participant's phone number will be shared with Jones Packaging Inc. to ensure the device is working. Patient participant's name, and any medical and or prescription information will not be provided.

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participating is yours.

If you are interested in participating in this study, please contact Sadaf Faisal by email at sadaf.faisal@uwaterloo.ca or by telephone at 519-888-4567 ext.21371. The information letter and consent form is attached to this email for your convenience.

Thank you very much!
Sincerely,

[emailing researcher]

Verbal/Telephone Script to contact Pharmacist (when patient has signed consent)

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

Hello [potential participant name]

My name is [researcher name], and I am a [researcher title] working with Dr. Tejal Patel from the University of Waterloo, School of Pharmacy. I am contacting you because one of your patients is interested in participating in our study and we are seeking pharmacist participation as part of this PhD thesis project.

We are inviting you to participate in a study in which your patient is willing to test one of two smart products: the "Jones Blister Pack" or "Jones NFC Label", which are designed to help people take their medications on time. Each product is linked to a software portal which tracks patient's medication intake and can develop reports to assess medication adherence. Would you be interested in hearing more about this study?

If says "No" Thank you for your time and good bye.
If says "Yes"

As part of this study, you will be asked dispense your patient's medications in one of two smart products: the "Jones Blister Pack" or "Jones NFC Label" for the duration of 8 weeks. You will only be dispensing medications in the Jones Products to patients who have signed a consent form to participate in this study. You will also be asked to use the cloud software portal during the study. We will provide complete training to you that will include medication dispensing or interacting with the cloud software portal. At the end of the study, you will be asked to take part in a one-on-one interview, which will take approximately 30-60 minutes. We will also invite patient participant's physician to take part in the study to provide feedback about the impact of these product on patient participant's medication intake. If the patient participant's physician does not choose to participate in this study, the patient participant is still be eligible to participate.

All information collected as part of this study will be considered confidential and will be kept in a secure location and disposed of in a minimum of seven years.

If you are interested in referring any other patients from your practice to this study, we are recruiting patients who are:

- Able to speak and read English,
- Aged 18 or older,
- Are taking 5 medications on a regular basis, or less than 5 medications with multiple daily dosing, and
- Have more than one long-term medical condition.

If you have any patients that may fit this criterion, please let us know and we will forward you a patient recruitment poster and a recruitment script. Once you receive the poster and script you may

reach out to any patients who may be interested in participating in this study. Once the individual has provided consent for you to share their contact information with us, please let us know.

You and your pharmacy will not incur any additional costs as a result of this study. In appreciation of your time commitment, you will receive $150.00 cheque.

This study is being funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label. Adherence information, such as when the product was opened, and patient participant's phone number will be shared with Jones Packaging Inc to ensure the device is working. Patient participant's name, and any medical and or prescription information will not be provided.

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participating is yours.

Would you be interested in participating?"

If says "No" Thank you for your time and good bye.
If says "Yes"

Thank you for your intertest. (Get name, contact information and email information letter and consent form)

Pharmacist Verbal/Telephone Script

Note: If they are interested, we are asking participating pharmacists to refer to the researchers any patients from their practice to this study. The criteria for recruitment are patients who are:

- Able to speak and read English,
- Aged 18 or older,
- Are taking 5 medications on a regular basis, or less than 5 medications with multiple daily dosing, and
- Have more than one long-term medical condition.

If the pharmacist identifies any patients that may fit this criterion, they will ask the patient if they are interested in the study and if so, they will also ask for their consent to share their contact information with the researchers to learn more about the study.

a. **Pharmacist Telephone Script to Recruit Patient Participants**

Hello, [*participant name*]
My name is [*pharmacist name*], and I am a pharmacist at your pharmacy. I am contacting you because a study you may be interested in is currently recruiting participants. This study is seeking participants to test two smart products designed to help people take their medication on time, to get feedback on how usable and impactful the products are. Are you interested in knowing more about this study?

If says "No", say "Thank you for your time and good bye."
If says "Yes", continue on with the call.
This study is being conducted by the researchers at the School of Pharmacy, University of Waterloo. The aim of the study is to test one of two smart products known as either "Jones blister pack" or "Jones NFC label" for daily use in adults, aged 18 and older. During the study you will be asked to use one of these products for 8 weeks for your medications and will meet with researchers three times during the study period in your home. If you are interested in knowing more about this study, I can forward your contact details to the researchers so that they may explain the study in further detail to you. Do you give your consent for me to share your contact information with the researchers?
If says "No", say "Thank you for your time and good bye."
If says "Yes", record contact information and thank the participant. [The pharmacist will then share the contact information with one of the researchers so that they may contact the patient regarding study eligibility].

b. **Pharmacist Verbal Script (in-person) to Recruit Patient Participants**

Hello, [*participant name*]
My name is [*pharmacist name*], and I am wondering if you have a few minutes to talk about a study. This study is seeking participants to test two smart products designed to help people take their medication on time, to get feedback on how usable and impactful the products are. Are you interested in knowing more about this study?

If says “No”, say “Thank you for your time and good bye.”
If says “Yes”, continue on. [feel free to use the study poster as a reference]
This study is being conducted by the researchers at the School of Pharmacy, University of Waterloo. The aim of the study is to test one of two smart products known as either “Jones blister pack” or “Jones NFC label” for daily use in adults, aged 18 and older. During the study you will be asked to use one of these products for 8 weeks for your medications and will meet with researchers three times during the study period in your home.
If you are interested in knowing more about this study, I can forward your contact details to the researchers so that they may explain the study in further detail to you. Do you give your consent for me to share your contact information with the researchers?
If says “No”, say “Thank you for your time and good bye.”
If says “Yes”, record contact information and thank the participant. [The pharmacist will then share the contact information with one of the researchers so that they may contact the patient regarding study eligibility].

Patient Participant Verbal/Telephone Script for Eligibility

Smart Multi-dose Blister Packaging: Integration and Impact on medication intake behavior

"Prior to me scheduling a meeting with the research team, we have a few questions for you to determine whether you are eligible to participate in our study. Would you mind if I asked these questions now? It should take no more than 5 minutes."

If says "No", say "When would you be next available to call?"
If says "Yes", continue on with the call.

"Are you able to read English comfortably?" [record response]

"What is your current living situation? Are you living at home, with family or in a retirement home or long-term care home?" [record response]

"Do you mind having research staff come to your home during the study?" [record response]

"Do you have a cell phone with SMS messaging or a cell phone with NFC technology? A phone with SMS messaging is a phone that can receive or send out text messages. NFC technology is a scanning function that some smart phones have. If you know the type of phone you have, I can help you determine if you have the NFC technology on your phone." [record response]

"Have you been diagnosed with any chronic conditions? And if so, which ones?" [record response]

"How many medications are you currently taking?" [record response]

"Do you have help taking your mediations? How do you receive help?" [record response]

"Have you ever been diagnosed with a cognitive impairment, like dementia, or Alzheimer's disease?" [record response]

"If your pharmacy is not interested in participating in this study, would you be willing to transfer your prescriptions to one of our participating pharmacies? You would not incur any extra charges in this transfer and we would transfer your prescriptions back to your original pharmacy at the end of the study, unless otherwise requested" [record response]

"These are all of the questions I have for you today. Thank you very much for answering them."

If eligible: "You are eligible to participate in the study. With your permission, I would like to email/ mail you an information letter and consent form which has all of the details we discussed, along with contact names and numbers, to help assist you in making a decision about your participation in the study. [Ask for contact information of participant]. Thank you very much for your time. May I call you in 2 to 3 days to see if you are interested in participating in this study? Once again, do not hesitate to contact me at ***[researcher phone number]*** if you have any questions or concerns.

If ineligible: “Unfortunately, you are ineligible to participated in this study. Thank you for taking the time to speak with me today. If there are future studies regarding smart medication adherence products, would you like to be contacted? [Record response] Have a nice day”.

Sample text for School of Pharmacy Website and Facebook

Patient Participant:

We are currently seeking participants for a study to test two smart products designed to help people take their medications on time. We are inviting participants who are English speaking, 18 years or age or older, taking multiple medications, and who manage their own medications.

As a patient in this study, you will be asked to use a smart multi-dose blister package for 8 weeks, complete questionnaires, participate in a one-on-one interview and provide your feedback. Your participation will involve 3 in-home sessions; where each session will take 60-90 minutes. In appreciation for your time, you will receive $25 gift card.

This study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee.

For more information about this study, or to volunteer for this study, please contact: Sadaf Faisal at sadaf.faisal@uwaterloo.ca

Healthcare Provider Pharmacist Participants:

We are currently seeking pharmacists for a study to test two smart products designed to help people take their medications on time. To participate in this study, you must have at least one patient who has enrolled in the patient segment of this study. As a health care provider in this study, you will be asked to use the cloud software portal, complete questionnaires, participate in a one-on-one interview, and provide your opinion and feedback. Your participation will involve 2 sessions; where each session will take 30-45 minutes. In appreciation for your time, you will receive $150.00 cheque. We will also ask if you know any potential patients who would be interested in participating in the patient segment study.

This study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee.

For more information about this study, or to volunteer for this study, please contact: Sadaf Faisal at sadaf.faisal@uwaterloo.ca

Sample Text for School of Pharmacy Twitter- Patient Participants:

We are currently seeking patients to participate in a study to test two smart products designed to help people take their medications on time. This study has received ethics clearance. Learn more here: [link to School of Pharmacy Website Post about the study].

Sample Text for School of Pharmacy Twitter- Health care Provider-Pharmacist Participants:

We are currently seeking pharmacists to participate in a study to test two smart products designed to help people take their medications on time. This study has received ethics clearance. Learn more here: [link to School of Pharmacy Website Post about the study].

Appendix C

Eligibility Checklist

Participant ID: _____ Date**: _____**

Inclusion Criteria	
Able to speak and read English	□ Yes | □ No
Allows for in home visits	□ Yes | □ No
Cell phone with SMS messaging or cell phone with NFC technology	□ Yes | □ No
Has been diagnosed with >1 chronic condition	□ Yes | □ No
Has been prescribed ³ 5 chronic oral medications; OR Has been prescribed < 5 medications, with multiple daily dosing	□ Yes | □ No

Exclusion Criteria	
Currently residing in long term care or on nursing medication administration?	□ Yes | □ No
Self-identified mild, moderate or severe cognitive impairment including MCI, dementia or any other cognitive disease	□ Yes | □ No
Are not willing to change their pharmacy/ are not currently part of a pharmacy has agreed to participate in the study/ their pharmacy is not willing to participate in the study	□ Yes | □ No

Is participant eligible to participate? □ Yes | □ No

Investigator Name: _____

Date of Decision: _____

Appendix D

Information Letter and Consent Form (Patient)

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Pharmacy

Title of the study: Smart Multi-dose Blister Packaging: Integration and impact on medication intake behaviour

Faculty Supervisor: Dr. Tejal Patel, Assistant Professor, Pharm D, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21337, Email: t5patel@uwaterloo.ca

Student Investigator: Sadaf Faisal, PhD student, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21371, Email: sadaf.faisal@uwaterloo.ca

Research Assistant: Jessica Ivo, School of Pharmacy, University of Waterloo.
Email: jarivo@edu.uwaterloo.ca

To help you make an informed decision regarding your participation, this letter will explain what the study is about, the possible risks and benefits, and your rights as a research participant. If you do not understand something in the letter, please ask one of the investigators prior to consenting to the study. You will be provided with a copy of the information and consent form if you choose to participate in the study.

What is the study about?
You are invited to participate in a research study about smart multidose blister packaging. The purpose of this study is to test the use of two smart multi-dose blister packages not currently available for purchase to see if they can impact medication intake behavior in adults over the age of 18, taking multiple medications for chronic condition(s). This study will achieve this goal by recruiting patient participants, and their health care providers (e.g. pharmacists and physicians) to provide feedback on one of two smart multi-dose blister packages. Patient participants will be asked to use one of these smart multi-dose blister packages for 8 weeks and provide feedback on how usable and impactful the product is on how they take their medications.
The study is being undertaken as part of my (Sadaf Faisal) PhD research.

What does participation involve?
As a participant of this study, you will be using one of two smart multidose blister packages to help with taking your medications based on the type of smartphone you have. You will meet researchers for three in-home visits. If you have help with taking your medications, you are welcome to invite that person to these meetings as well. You will be asked to use one of the following smart multi-dose blister packages for 8 weeks.

1. Jones Blister Pack: This device is a 28-cavity blister pack. Each cavity is labelled with numbers ranging from 1 to 28. When the cavity is broken to access the

medications, the event is recorded and sent to a cloud software portal. This software can also send reminders or notifications to the user's phone through messaging or email if desired.

2. Jones NFC Label: The Jones NFC labels are tags that are physically encoded with a unique ID number and unique URL. Each time you take your medications out of the blister pack, you will have to touch the tag with an NFC enabled smart phone. This will send a radio signal to the phone and record the event on a secure cloud software portal.

During your first visit, you will be asked to complete a brief background survey gather data about your age, gender, medication aid use, and names and contact information of your pharmacy, family physician, specialists or other health care providers within your circle of care. You will also be asked to provide a complete list of your medications that you are currently taking. During this visit, the researcher will take multiple photographs of your pill bottles and the place(s) where they are being stored in your home to better understand how you manage and store your medications on a daily basis. All identifiable information will be removed from these photos. This visit will take approximately 60-90 minutes.

Following your first visit, we will contact your pharmacy to invite them to participate in this study to dispense your medications in one of the smart multi-dose blister packages for 8 weeks. We will also review the complete medication list you provide us to the one provided by your dispensing pharmacy. If any discrepancies are found in the medication records (i.e. doses or dosing times are recorded differently), they will be discussed with you and your dispensing pharmacist. These discrepancies will be addressed prior to your medications being dispensed in the smart multi-dose blister package, to ensure you are receiving the most benefit from your medications.

Your second visit will take place one week following your first visit. During this visit, you will be trained on how to use the smart multi-dose blister package by using a sample package containing sugar pills. You will receive an instruction guide (with photos) on how to use the smart package along with the emergency contact information of the researchers. All of your regular medications will be dispensed in smart blister pack for the next 8 weeks. The researcher will ask to watch you take a dose from the product. While you are using the product, the researcher will take notes and photograph you as you do so. The researcher is interested in seeing how you interact with the product to take your medications. The photographs that the researcher takes while you are using the product will be provided back to you in a photo-book. These photographs can be used as a reference, along with the instruction guide provided but should not be used as a replacement for the instruction guide, with either the Jones Blister Pack or the Jones NFC label, as you use either of these at home during the study. The photographs that are taken during this visit will be printed in a photobook and delivered to you as soon as possible. As you use the products, we will only take photographs of your hands; no images of your face will be captured during this process. This visit will be approximately 60 minutes.

The third and last visit will be scheduled after 8 weeks of study visit two. During this visit, a researcher will ask to watch you take a dose from the smart multi-dose blister packaging. The researcher is interested in seeing how you handle the product and the effect of this product on your medication intake. You will then take part in a one-on-one interview to provide a reflection on your experience and any issues or barriers you observed while using the smart multi-dose blister packaging. Your voice will be recorded during these interviews to ensure an accurate record of what you said during the interview. Visual images from the photo book will be used

during the interview, which will provide reflective information during the interview. You will then be asked to complete a questionnaire on the usability of the smart pack. The duration of the visit will be approximately 60 minutes.
At the completion of the study researcher will retrieve all the supplies from patient participant' home and the dispensing pharmacy and will send the connectivity device attached to the product back to the manufacturer (Jones Packaging Inc.) in the condition they were delivered.

If your pharmacy does not choose to participate in the study, you will be asked if you will be willing to transfer your medications to another participating pharmacy for the study duration with your consent. In either scenario, you will not incur any additional costs as a result of this study. However, you will be expected to continue paying for your medications as per usual.

Who may participate in the study?
In order to participate in the study, you must be at least 18 years of age, able to speak and understand English, have a cell phone with messaging service or NFC enabled technology, and must be regularly taking medications for a chronic medical condition.

Is participation in the study voluntary?
Participation in this study is voluntary and you are under no obligation to participate. Participants may decline to answer any of the questions they do not wish to answer. Furthermore, participants may decide to withdraw from this study at any time, without any negative consequences, simply by letting us know your decision.

Will I receive anything for participating in the study?
To thank participants for their time, participants will receive a $25 gift card. The gift card can be redeemed at coffee or food retailers such as Tim Hortons, McDonalds, and/or ultimate dining cards. Additional remuneration will not be provided to those who accompany a participant. Please be advised that the amount received is taxable. It is the participant's responsibility to report this amount for income tax purposes.

What are the possible benefits of the study?
There is no direct benefit to participants from participating in this study. However, the results from participation will help the research team better understand how patients and their health care providers manage their care using smart multi-dose blister packages for their medication management.

What are the risks associated with the study?
Participating in the study may cause some anxiety, or discomfort due to use of an unfamiliar product and audio recording while using the smart multi-dose blister pack. You may also be anxious about recording your voice during one-on-one interview. In all instances however, we will try to make it as comfortable for you as possible.

Will my information be kept confidential?
During this study, data will be collected using three different avenues:

1. Data collected for the purpose of this research study
2. Data collected by the pharmacy as part of standard of care
3. Data collected by the Jones Device you are using

Data collected for the purpose of this research study:
We would like to assure participants that their identity and its association with the research data obtained in the study will be kept confidential. In order to understand your medication management process and track your adherence, research data will be stored with the researchers at the University of Waterloo. All study related data will be securely stored in a password protected datasheet within a password-protected computer and in a locked office at the University of Waterloo, School of Pharmacy for a minimum of seven years. For your protection, we will assign each participant a code number that will be used to label all information and responses. Anonymous quotations may also be used with your permission. The results of the study will be published for scientific purposes, but we will not include identifying information such as names or your home address. You can withdraw your consent to participate and request that your data be removed from the study by contacting the researchers within this time period. Please note that data cannot be withdrawn once study results are submitted for publication. Additionally, the data set that has identifiable personal information removed may be shared publicly (e.g. in data repositories), however only the researchers will have access to identifying information.

Data collected by the pharmacy:
Medication dispensing data will be stored with the dispensing pharmacy as per standard of care for the particular pharmacy. As per Ontario Legislation, only health care providers who are involved in your care will have access to your information. Since pharmacists are setting up the Jones device for you, they will also have access to the Jones packaging adherence portal or otherwise known as cloud software portal.

Data collected by the Jones Device you are using:
Data collected through the Jones Blister Pack or the Jones NFC Label will be securely stored using an online server called Amazon Web Service (AWS), Canada, during this study.

Jones will only have access to dosage events and your telephone number designated for notifications. No identifiable medical information including your name will be shared with Jones Packaging Inc. They will only be able to see your ID chosen by the research associate. Once the study has been completed, all data will be deleted from AWS, including any backups. After the completion of the study, a study report indicating the findings will be shared with Jones Packaging Inc, however no patient identifiable data will be presented in that report.

Who is sponsoring/funding this study?
This study is funded by Jones Packaging Inc, the developer of the Jones Blister Pack and Jones NFC Label, of which both products will be tested and monitored during this study.

Disclosures:
Tejal Patel and Sadaf Faisal are both pharmacists and are bound to the Code of Ethics of the Ontario College of Pharmacists and conducts all of their business and professional services accordingly. As such, they are required to report any therapy related concerns or discrepancies found during the study to the dispensing pharmacy or the family physician to ensure safe and accurate dispensing of medications for the patient participants.

Has the study received ethics clearance?
We would like to assure you that this study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE# 41015). If you have any questions for the committee, contact the Office of Research Ethics, at 519-888-4567 ext. 36005 or ore-ceo@uwaterloo.ca.

Who should I contact if I have questions regarding my participation in the study?
Should you have any questions about the study, or would like additional information to assist you in reaching a decision about participation, please contact Sadaf Faisal by phone at 519-888-4567 ext.21371 or by email at sadaf.faisal@uwaterloo.ca or Tejal Patel by phone at 519-888-4567 ext. 21337 or by email at t5patel@uwaterloo.ca. Thank you for your assistance in this project.

Dr. Tejal Patel, Pharm D
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University of Waterloo
1-519-888-4567 ext. 21337
t5patel@uwaterloo.ca

Sadaf Faisal
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1-519-888-4567 ext. 21371
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CONSENT FORM

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

Title of the study: Smart multidose blister packaging: Integration and impact on medication intake behaviour

I have read the information presented in the information letter about a study being conducted by Dr. Tejal Patel, a faculty member at University of Waterloo, School of Pharmacy. All the procedures and any risks and benefits relating to my participation have been explained. I have had the opportunity to ask any questions related to this study (if any), to receive satisfactory answers to my questions, and any additional details I wanted.

I am aware that:

□ I may withdraw my consent for any of the above statements or withdraw my study participation at any time without penalty by advising the researcher.

□ audio-recordings of my voice will be taken as I test the usability of the products.

□ my responses will be audio-recorded during all of the one-on-one interviews.

□ with my permission, anonymous quotations, may be used for publications and educational purposes.

This study has been reviewed by, and received ethics clearance, through a University of Waterloo Research Ethics Committee (ORE#41015). If you have questions for the Committee, contact the Office of Research Ethics, at 519-888-4567 ext. 36005 or ore-ceo@uwaterloo.ca.

With full knowledge of all foregoing, I agree, of my own free will, to the following:

I agree to participate in this study
□ Agree □ Disagree
I agree to use: □ Jones blister packaging □ Jones NFC label packaging

I agree to have my medications transferred to another pharmacy should my pharmacy choose not to participate in the study:
□ Agree □ Disagree

I agree to the use of anonymous quotations in any presentation or report that comes of this study
□ Agree □ Disagree

Participant Name (Please print)	Witness Name (Please print)
Participant Signature	Witness Signature
Date	Date

Companion Document re: Data Storage- Smart Multidose Blister Packaging (Jones 28-Cavity Blister Pack and Jones NFC Labels)

What is Amazon Web Services?
Amazon Web Services is a computing service that provides the structures, organization and capacity needed to store a lot of information over the internet (also called a cloud computing platform).

What data is being stored on Amazon Web Services from this study? Why it is being stored on Amazon Web Services?
There are multiple types of data being collected in this project. Please refer to the attached document called, "Jones Packaging Data Collection Avenues." As you will note in this graphic, there are three types of data being collected in this study. The data being collected from the Jones Packaging adherence platform or otherwise known as Cloud software portal (for more details see page 4 of the User guide) is listed in the first column in the graphic (colored bright yellow). The data that is collected in this column will be stored on Amazon Web Services. The data in this column is being collected to allow your pharmacist to set up your Jones smart blister pack/NFC label to work as it should – that is allow the Jones smart blister pack/NFC label to dispense the right medication at the right dose and at the right time. This information also allows your pharmacist to see if you are having any concerns with how you are taking your medications, in particular which medication and/or which doses you may be having trouble with. This information can help them trouble shoot possible solutions with you to help you with your medication taking. This information is collected through Jones smart blister pack and/or NFC labels which the pharmacist has access to. The information is stored on Amazon Web Services because this information requires a secure storage space that is large enough and secure.

Is the data being stored on Amazon Web Services secure?
Amazon Web Services stores all the information it receives securely. They provide security for the data (information) they receive by encrypting (or coding) the data, only allowing access to the people who provide the data Jones Packaging adherence platform. They provide assurances for the security they provide and indicate that the security measures have been verified by several independent reviews.
In Canada, Amazon Web Services is also required to follow PIPEDA. PIPEDA stands for Personal Information Protection and Electronic Documents Act. This is a Canadian law that protects personal information, including health information. Amazon Web Services also continuously reviews any new privacy laws that come into effect to make sure that they meet the requirements of PIPEDA as well as any new laws.

Who has access and control of the data on Amazon Web Services?
The information that is stored on Amazon Web Services can only be accessed by Jones Packaging Inc. Amazon Web Services indicates that it will not access the data that it is storing for Jones Packaging Inc. The data will be stored on Amazon Web Services for the study duration. Once the study has been completed, all data will be deleted from Amazon Web Services, including any backups.

Appendix E

Information Letter and Consent Form (Pharmacist)

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Pharmacy

Title of the study: Smart Multi-dose Blister Packaging: Integration and impact on medication intake behaviour

Faculty Supervisor: Dr. Tejal Patel, Assistant Professor, Pharm D, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21337, Email: t5patel@uwaterloo.ca

Student Investigator: Sadaf Faisal, PhD student, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21371, Email: sadaf.faisal@uwaterloo.ca

Research Assistant: Jessica Ivo, School of Pharmacy, University of Waterloo.
Email : jarivo@edu.uwaterloo.ca

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(e.g. pharmacists and physicians) to provide feedback on one of two smart multi-dose blister packages. Patient participants will be asked to use one of these smart multi-dose blister packages for 8 weeks and provide feedback on how usable and impactful the product is on how they take their medications.
The study is being undertaken as part of my (Sadaf Faisal) PhD research.

What does participation involve?
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its impact on your clinical decision-making process. There are two types of smart multi-dose packaging being used in this study:

1. Jones Blister Pack: This device is a 28-cavity blister pack. Each cavity is labelled with numbers ranging from 1 to 28. When the cavity is broken to access the medications, the event is recorded and sent to a cloud software portal. This software can also send reminders or notifications to the user's phone through messaging or email if desired.
2. Jones NFC Label: The Jones NFC labels are tags that are physically encoded with a unique ID number and unique URL. Each time your patient takes their medications out of the blister pack, they will have to touch the tag with an NFC enabled smart phone. This will send a radio signal to the phone and record the event on a secure cloud software portal.

As a health care provider, you will dispense your patient's medication in one of the two smart multidose packaging options for the duration of 8 weeks. You will also have access to the secure cloud software portal and real-time drug intake data of your patient. You will meet with researchers for two visits during the study.

- During the first visit, researchers will meet you at your office and will ask you fill out a background survey. This survey will collect information on your age, gender, type of profession and practice duration. You will then be trained on how to access the secure cloud software portal. This visit will take approximately 30 minutes.
- The second visit will take place at the end of the study (i.e. after your patient has used the smart product for 8 weeks). During this visit, you will be asked to complete a questionnaire about the usability of the secure cloud software portal and partake in a one -on-one interview regarding your experience as a health care provider. These interviews will occur in-person, at the School of Pharmacy, University of Waterloo or at your office. During these interviews, you will be asked a number of questions about the impact of smart blister pack on your patient's medication intake process and the significance of having real-time drug intake data for your patient. Your voice will be audio-recorded during these interviews. The data collected from these interviews will be used to determine your, and other participants' satisfaction and additional comments (positive or negative) that can be used to improve the medication management process in non-adherent patients. This visit will take approximately 30-45 minutes.

All pharmacy dispensing supplies (e.g. NFC labels, blister package) will be supplied to the dispensing pharmacy without additional cost. Patients will not incur any additional costs to their medications by participating in this study. They will be expected to continue paying for their medications as they have been prior to participating in this study. At the completion of the study researcher will retrieve all the supplies from patient participant' home and the dispensing pharmacy and will send the connectivity device attached to the product back to the manufacturer (Jones Packaging Inc.) in the condition they were delivered.

Who may participate in the study?

For this study, we are looking for pharmacists of patients who have agreed to take part in this study. Participants must be able to speak and understand English in order to participate in this study.

Is participation in the study voluntary?

Participation in this study is voluntary and you are under no obligation to participate. Participants may decline to answer any of the questions they do not wish to answer. Furthermore, participants

may decide to withdraw from this study at any time, without any negative consequences, simply by letting us know your decision.

Will I receive anything for participating in the study?
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What are the possible benefits of the study?
There is no direct benefit to participants from participating in this study. However, the results from participation will help the research team better understand how patients and their health care providers manage their care using smart products for their medication management.

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Participating in the study may cause some anxiety, or discomfort due to the recording of the voice during one-on-one interview. You may experience some stress or anxiety due to the learning process of using the portal or change in your current workflow by incorporating a new device. However, in all instances we will try to make it as comfortable for you as possible.

Will my information be kept confidential?
We would like to assure participants that their identity and its association with the research data obtained in the study will be kept confidential. In order to understand your patient's medication management process and track adherence, research data will be stored with the researchers at the University of Waterloo, medication dispensing data will be stored at your pharmacy as per standard of care and adherence data will be stored with Jones through an online server associated with AWS (Amazon Web Service) during this study.

For your protection, we will assign each participant a code number that will be used to label all information and responses. Anonymous quotations may also be used with your permission. The results of the study will be published for scientific purposes, but we will not include identifying information such as names or your pharmacy address. All study related data will be securely stored on a password-protected computer and in a locked office at the University of Waterloo, School of Pharmacy for a minimum of seven years. You can withdraw your consent to participate and request that your data be removed from the study by contacting the researchers within this time period. Please note that data cannot be withdrawn once study results are submitted for publication. Additionally, the data set that has identifiable personal information removed may be shared publicly (e.g. in data repositories), however only the researchers will have access to identifying information.

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Disclosures:
Tejal Patel and Sadaf Faisal are both pharmacists and are bound to the Code of Ethics of the Ontario College of Pharmacists and conducts all of their business and professional services accordingly. As such, they are required to report any therapy related concerns or discrepancies found during the study to the dispensing pharmacy or the family physician to ensure safe and accurate dispensing of medications for the patient participant.

Has the study received ethics clearance?
We would like to assure you that this study has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE# 41015). If you have any questions for the committee, contact the Office of Research Ethics, at 519-888-4567 ext. 36005 or ore-ceo@uwaterloo.ca.

Who should I contact if I have questions regarding my participation in the study?
Should you have any questions about the study, or would like additional information to assist you in reaching a decision about participation, please contact Sadaf Faisal by phone at 519-888-4567 ext.21371 or by email at sadaf.faisal@uwaterloo.ca or Tejal Patel by phone at 519-888-4567 ext. 21337 or by email at t5patel@uwaterloo.ca. Thank you for your assistance in this project.

Dr. Tejal Patel, Pharm D
School of Pharmacy
University of Waterloo
1-519-888-4567 ext. 21337
t5patel@uwaterloo.ca

Sadaf Faisal
School of Pharmacy
University of Waterloo
1-519-888-4567 ext. 21371

CONSENT FORM

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

Title of the study: Smart multidose blister packaging: Integration and impact on medication intake behaviour

I have read the information presented in the information letter about a study being conducted by Sadaf Faisal PhD student under the supervision of Dr. Tejal Patel, a faculty member at University of Waterloo, School of Pharmacy. All the procedures and any risks and benefits relating to my participation have been explained. I have had the opportunity to ask any questions related to this study (if any), to receive satisfactory answers to my questions, and any additional details I wanted.

I am aware that:

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With full knowledge of all foregoing, I agree, of my own free will, to the following statements:

I agree to participate in this study.
□ Agree □ Disagree

I agree to the use of anonymous quotations in presentations or reports that comes of this study.
□ Agree □ Disagree

Participant Name (Please print)	Witness Name (Please print)
Participant Signature	Witness Signature
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Appendix F
Information Letter and Consent Form (Pharmacy Assistant/Technician)

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Pharmacy

Title of the study: Smart Multi-dose Blister Packaging: Integration and impact on medication intake behaviour

Faculty Supervisor: Dr. Tejal Patel, Assistant Professor, Pharm D, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21337, Email: t5patel@uwaterloo.ca

Student Investigator: Sadaf Faisal, PhD student, School of Pharmacy, University of Waterloo. Phone: 1-519-888-4567 ext. 21371, Email: sadaf.faisal@uwaterloo.ca

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□ Agree □ Disagree

I agree to the use of anonymous quotations in presentations or reports that comes of this study.
□ Agree □ Disagree

Participant Name (Please print)	Witness Name (Please print)
Participant Signature	Witness Signature
Date	Date

Appendix G

Background Survey for Patient Participant

Participant ID: _____ Date**: _____ Visit: _____**

1. Age at the last birthday: _____ years

2. Gender: □ Male □ Female □ Other: _____

3. Highest degree or level of school you have completed:
   □ Less than a high school diploma □ High School diploma or equivalent
   □ Some College/University, no degree □ College/University Degree
   □ Other: _____

4. Living Situation: □ Alone □ Spouse □ Partner □ Family members
   □ Other: _____

5. Pharmacy Name: _____ Phone number: _____

6. Family Physician Name: _____ Phone number: _____

7. Any other specialist or health care providers (HCP) involved in care? □ Yes □ No

If yes, please list the name and phone number:

Name	Type of HCP	How often you visit them

8. Current medical problems: please check off all that apply
□ Hypertension □ Ischemic heart disease □ Diabetes □ Cancer □ Osteoarthritis □ Asthma

□ Osteoporosis □ Mood and/or anxiety disorder □ Chronic obstructive pulmonary disease □ Other: _____

9. Do you use any medication administration aid(s)? □ Yes □ No

If yes, what is it? □ Blister Pack □ Dossette □ Pill bottle □ Alarm/Reminder □ Other:

_____

_____

If yes, why do you use a medication administration aid?

_____

_____

10. Is there a caregiver involved in helping you manage your medications: □ Yes □ No

If yes, who and how?

_____

_____

Appendix H

Background Survey for Health care Provider Participant

Participant ID: _____ Date: _____

1. Age: _____ years

2. Gender: □ Male □ Female □ Other

3. Years of practice: _____

4. Profession: _____

5. Do you recommend any medication administration aid to your patients: □ Yes □ No

If yes what is it? □ Blister Pack □ Dossette □ Pill bottle □ Alarm/Reminder □ Other: _____

If yes, why do you choose to recommend these products? _____
_____
_____
_____

Appendix I

Complete Medication List

Participant ID: _____ Date**: _____Visit: _____**

List all the current medications. This includes: prescriptions, over the counter medications, and herbal medications/supplements.

Type of Drug	Drug Name	Dose and frequency	Indication	Additional Instructions: How to take it?
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				
□ Prescription □ OTC □ NPH □ Vitamins				

Appendix J

Observational Protocol- Study Visit one

Participant ID : _____Date : _____Visit : _____Duration : _____	
Descriptive Notes	**Reflective Notes**
□Photos of pill bottles and the area of medication storage Photo ID: _____ 1)Physical location of medication storage in home □ Kitchen □ Bathroom □ Bedroom □Others_____ 2) Where does the patient administer medication □ Kitchen □ Family room □ Bedroom □ Others _____ 3) Regular medications are in □ Vials □ Blister packs from pharmacy □ Dossette box made by patient or caregivers 4) PRN medications are present □ Yes □ No If yes method of administration_____ _____ 5) OTC/ NHP medications are present □ Yes □ No If yes method of administration_____ _____ 6) Cues for medication administration □ Alarm □ Calendar □ Others	
Patient/product user's medication intake process walkthrough	

Appendix K

Observational Protocol- Study Visit two and three

Participant ID : _____Date : _____ Visit : _____Duration: _____	
Descriptive Notes	**Reflective Notes**
□Photos of medication retrieval process Photo ID: _____ 1. Medication retrieval process from the smart product OR process of NFC labels tagging for dose administration.	
2) Participant ‘s response to the reminder function	

Appendix L

System Usability Scale

Participant ID: _____ Date**:** _____**Visit**_____

	Strongly disagree				Strongly agree
1. I think that I would like to use this system frequently	1	2	3	4	5
2. I found the system unnecessarily complex	1	2	3	4	5
3. I thought the system was easy to use	1	2	3	4	5
4. I think that I would need the support of a technical person to be able to use this system	1	2	3	4	5
5. I found the various functions in this system were well integrated	1	2	3	4	5
6. I thought there was too much inconsistency in this system	1	2	3	4	5
7. I would imagine that most people would learn to use this system very quickly	1	2	3	4	5
8. I found the system very cumbersome to use	1	2	3	4	5
9. I felt very confident using the system	1	2	3	4	5
10. I needed to learn a lot of things before I could get going with this system	1	2	3	4	5

Appendix M

NET Promoter Score

Participant ID : _____Date : _____Visit : _____Duration :_____

How likely is it that you would recommend our company to a friend or colleague?

Not all likely Extremely likely

0 1 2 3 4 5 6	7 8	9 10
Detractor	Passive	Promoter

NPS = % Promoters - % Detractors

Appendix N

Interview Guide for Patient Participant

Participant ID: _____Date: _____Visit: _____ Duration: _____

Theory	Construct	Domain	Questions
Theory of Planned Behaviour	Attitude **(beliefs about the advantages or disadvantages of the behavior)**	Belief	What do you think will happen if you take your medications on time? What do you think will happen if you don't take your medications on time?
		Outcomes expectation	What do you see as? a. Advantages of using the smart blister pack? b. Disadvantages of using the smart blister pack? What else comes to your mind when you think about using the smart blister pack?
	Subjective norm **(beliefs about what others think about the behavior)**	Normative Beliefs	What do the people around you think/feel about using the smart blister pack for your medication intake? If you take your medications using the smart blister pack, how will it affect people around you?
	Perceived behavioral control **(belief about the resources or Skills required to perform the action)**	Skills or capability	What skills do you think you need use the smart blister pack? Probe for: additional training
		Resources	What would make it difficult or prevent you from using this smart blister pack? Probe with the following: Cost, training, product characteristics (likes or dislikes), network or internet connection issues, use of technology
COM-B Model	Capability **(Ability to engage in an activity)**	**Physical** Dexterity Vision Hearing	How would you describe your physical ability to manage your medications through the smart blister pack? Probe with the following: Removing medicine from the smart blister pack (use of knife/fork?), reading the label on the smart blister pack, hearing the reminder
		Cognitive Knowledge Memory Capacity to plan	How would you describe your ability to manage your medication through the smart pack? Probe with the following: Understanding of how to use the blister pack, remembering to arrange for the smart pack to pick up from the pharmacy/delivered?
	Opportunity **(factors that lie outside the individual that make the behaviour possible or prompt it)**	**Physical**	How do you get your medications? Probe with the following: Drive to the pharmacy, delivered by the pharmacy, need someone to help with the task Could you describe any obstacle(s) using the smart blister pack? Probe with the following: Cost, training, product characteristics (likes or dislikes), network or internet connection issues, use of technology
		Social Cultural or religious beliefs	Could you describe any stigma or fear related to the use of the smart pack? How would you describe any available social support in terms of using the smart blister pack? How do you think the use of the smart blister pack affected your interaction with your physician? How do you think the use of the smart blister pack affected your interaction with your pharmacist?
	Motivation **(brain processes that**	**Beliefs** Treatment	What do you think will happen if you take your medications on time?

	energize and direct behaviour)		What do you think will happen if you don't take your medications on time?
		Outcome expectation	What do you see as? • Advantages of using the smart blister pack? • Disadvantages of using the smart blister pack? What else comes to your mind when you think about using the smart blister pack?
	Behaviour		How has the use of the smart blister pack affected the way you take your medication?
Technology Acceptance Model	Perceived usefulness ***("potential user's subjective likelihood that the use of a certain system will improve his/her action")***	Usability	How useful the product was? Probe with the following: • Most useful • Least useful • Cumbersome • Irritating How has the use of the smart blister pack affected the way you take your medication?
	Perceived ease of use **(*"the degree to which the potential user expects the target system to be effortless")***	Functionality	How would you describe your experience with the smart blister pack? Probe with the following: Taking the medication out of the smart blister pack? reminder function, feedback system via SMS What do you think in terms of any problems you experienced with the smart blister pack? How did you resolve those problems?
		Learnability	Over the past few weeks, how have your interactions with the smart blister pack changed? • Describe what was easier to do. • Describe what was giving you problems. How did you find the training that was provided for the use of smart blister pack? Describe if there was any additional information you wish you were told in the training.
		Satisfaction	How would you describe the overall satisfaction with the smart blister pack?
	Behavior intention **(A conscious decision to perform a behaviour)**	Intention	Would you consider using this smart blister pack in the future? Why or why not?
	External factors		What factors would you consider when considering to use smart blister pack in the future? Probe with following: Cost, training, product characteristics (likes or dislikes), network or internet connection issues, use of technology
Photo elicitation			How was your experience with using the photos during the study? How did you feel when I took the photo? Probe with following: was it useful, irrelevant, cumbersome, etc. How did you use the photos other than during the study visit? Would you consider using the photos if you are using the product in the future?
Home Visit			How was your experience with the home visit? Probe with: comfortable, worried, felt pressured/relaxed etc.

Appendix O

Interview Guide for Pharmacist and Pharmacy Assistant/Technician

ID: _____Date: _____Visit: _____ Duration: _____

Questions	Constructs	Framework
What do you see as advantages/disadvantages of using the smart blister pack by your patient? What did you hear back from your patient regarding the bister pack? What did you see as advantage/disadvantage of access to medication adherence information for your patients	Attitude	Technology Acceptance Model
How did the use of smart blister pack affect your interaction with your patients? What did people around you (other pharmacy staff) think about the smart blister pack?	Subjective Norm	
What skills do you think you need to dispense the smart blister pack or access the portal? How would you explain any planning that was required to use the system?	Perceived behaviour control- Skills	
What type of resources would you need to adopt this system in your pharmacy?	Perceived behaviour control- Resources	
How would you explain your ability to use the system in your pharmacy? What skills do you think you need to dispense the smart blister pack or access the portal?	Capability- Physical	COM-B Model
How would you explain any planning that was required to use the system?	Capability-Cognitive	
Would there be any factors that will affect your ability to offer this system for your patient in your current work environment?	Opportunity-Physical	
How did the use of smart blister pack affect your interaction with your patients? How did using the new smart bluster pack for your patients affected your interaction with your pharmacy staff and superiors i.e. managers?	Opportunity- Social	
What do you see as advantages/disadvantages of using the smart blister pack by your patient? What did you see as advantage/disadvantage of access to medication adherence information for your patients? Did it become easier after you start doing it? If you have to do this how would you plan your workload and workflow around this? How would you explain any support you received from organization if any? How did you feel when you were providing the service?	Motivation	
How did you incorporate this adherence data into your practice? Was it useful and How? On average how often did you check each patient's portal after giving them their blister pack? On average how long did it take to set up a patient with a new blister pack? Please compare this to your process for your regular non-smart blister packs. What was the longest time you spent looking at a single patient's profile and why? What was the shortest time you spend looking at a single patient's profile and why? Which patients did you check and why?	Behaviour	
What did you find most useful about the availability of real-time drug intake data and Why? What did you find least useful about the availability of real-time drug intake data and Why? Which features of portal did you like/dislike? Which features of portal provided value to you? Which features on portal provided limited to no value? What did you think about the presentation of the information in the portal?	Perceived Usefulness	Technology Acceptance Model
How was your experience with this blister back? How did you like dispensing the medications in smart product? Please describe any problems you experienced with the product? How did you resolve those problems?	Perceived ease of use	

Did you use the reminder function for yourself in addition to the patient and how did you find it? What did you hear back from your patients regarding the reminder? How did you resolve any patient concerns related to the reminder function?		
Would you recommend this product for your patients in the future? Why or Why not?	Intention to use	
Would there be any barriers to offer this system for your patient?	External factor	

Appendix P

Thank You Letter

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Pharmacy

Smart multi-dose blister pack: Integration and impact on medication intake behaviour

Dear Participant,

Thank you for your participants in our "**Smart multi-dose blister pack: Integration and impact on medication intake behaviour"** study. As a reminder, the purpose of this study was to evaluate the use of Jones blister pack and determine if it can impact the medication intake behavior in adults over the age of 18, taking multiple medications for chronic condition(s).

Please remember that any data pertaining to you as an individual participant will be kept confidential. The results of the study may be published for scientific purposes. If you would like any further information about the study, including a copy of our findings when they become available, please contact us at the contact information below.

If you have any questions about the study, please contact Dr. Tejal Patel, faculty member, School of Pharmacy, University of Waterloo or Sadaf Faisal, graduate student, School of Pharmacy, University of Waterloo at (519) 888-4567 ext.21371 or via email at sadaf.faisal@uwaterloo.ca for assistance.

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE# 41015). Should you have any comments or concerns resulting from your participation in this study, please contact the Office of Research Ethics, at 519-888-4567 ext. 36005 or ore-ceo@uwaterloo.ca.

Sincerely,

Sadaf Faisal, B. Pharm, BCGP, M. Sc(c)
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School of Pharmacy
University of Waterloo
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Phone: 519-888-4567 ext. 21371

Appendix Q

UNIVERSITY OF WATERLOO
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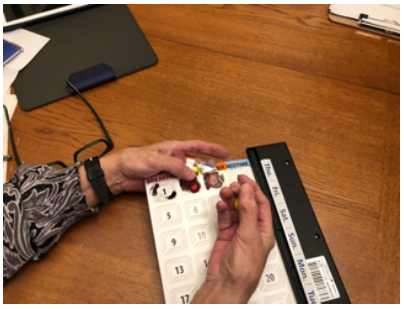
School of Pharmacy

How to use your Jones Blister Package

1. Identify the blister cavity to take, and pierce the cavity with your index finger

2. Pinch the number printed on the card between your index finger and pull the barrier out of the package



3. Remove the medications from the package

Appendix R

Thank You Letter from a study participant

Hello Sadat, Jessica and Ryan.

Hello to all thank you your gift is appreciated
I will make sure its spent on healthy food
University of Waterloo officials to know what excellent.
Representative you are for school of pharmacy
I enjoyed meeting with you.

As mentioned before I do hope a push to all sector our government
That we produce Medicine and supply Canadian population
As well as other countries if requested this is a requirement
that all Canadian should stand and demand.
Its a shame our great country
Leaders have been thoughtless and lazy not to have
Realized how important this is (too all
Leaders) work for Canadians thats is your responsible

Its imperative that the horse and the cart in your barn
before you open your mouth and shout demands

MADE IN CANADA. Build in Canada.