2017 Catalyst Grant Competition

Canadian Frailty Network | Réseau canadien des soins aux personnes fragilisées

Section 1 - Administrative Information

CFN File Number:	CAT2017-20
Title of CAT Proposal provided in Intent to Apply:	Team Approach to Polypharmacy Reduction in Long-Term Care (TAPER-LTC). RCT feasibility study: integrating families' experiences
Term of CAT Proposal:	16
Budget:	$100000

Please provide information on the Principal Investigator who will act as Project Leader for proposal

First Name:	Dee	**Last Name:**	Mangin	**Designations:**	MBChB (Otago), DPH (Otago), FRNZCGP (NZ)
Email:	mangind@mcmaster.ca	**Daytime Phone:**	(905) 525-9140 ext. 21685	**Other Phone (optional):**	
Host Institution that will receive and administer funds:		McMaster University			
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CFN Strategic Objective: *Empowering, engaging and supporting patients and their families/caregivers*	**Theme:** *Optimization of community/residential care*
Setting of Care: *Long-term care facility*	**Focus of Impact:** *Patients, their families and informal caregivers/support systems (volunteer)*

Knowledge Activities - Indicate the portion of your project that addresses the following activities on the knowledge continuum:

20 % Knowledge synthesis
70 % Knowledge creation
10 % Knowledge translation/mobilization

Ethics/Environmental Assessment

Please answer the two questions below.

1. **Research Ethics:** *If the proposed research involves biohazards, humans, human embryonic stem cells or animals, AND is funded by CFN, certification of approval by your institutional certification committee must be provided to CFN prior to the release of funds*

   Yes, I expect that this research will require an ethics review

2. **Environmental Assessment:** *Does any phase or part of the research described in this proposal a) take place outside an office or laboratory, or b) involve an undertaking as described in part 1 of Appendix B of the Natural Sciences and Engineering Research Council of Canada (NSERC) Form 101 (http://www.nserc-crsng.gc.ca/OnlineServices-ServicesEnLigne/pdf/F101_e.pdf)?.*

   No, I do not expect that this research will require an environmental impact review

Funding Priority

CFN Medication Optimization Summit identified research priorities areas for funding.

Section 2 - Proposal Summary

2.1: Lay Summary

Provide a non-confidential summary in lay terms of the CAT proposal. A lay summary is an overview of a research project described in a way that can be easily understood by those without prior experience of the subject. See Appendix A for CFN's DRAFT - Guidelines for Writing a Lay Summary

Polypharmacy (the use of many medications) is associated with poorer health and drug side effects in older adults. This makes it a concern in long-term care (LTC). We have developed a program (TAPER) for reducing polypharmacy and drug side effects for older adults living in the community. TAPER combines family doctors and clinical pharmacists, with support from the best medical evidence, and patient preferences for treatment. In this study, we will test TAPER in LTC residents. Our focus is whether using TAPER can reverse medication-related mobility problems and prevent falls. We will also explore family members' perspectives on how best to include their views in the TAPER process.

Study participants from two LTC facilities will be put into either an intervention or comparison group at random. We will assess the logistics of the TAPER process in LTC settings as well as patient outcomes including falls, thinking ability, quality of life, mobility, as well as hospitalizations and number of medications. These measures will be collected before and after the program to see if there have been changes for those receiving TAPER compared to a comparison group.

We will use these results to design and gain funding for a much larger research study to test whether this process can improve outcomes for residents when implemented as part of routine care in multiple settings across Canada. We envision a routine preventive system for screening to reduce polypharmacy and side effects in older adults - one that fits alongside immunizations and other screenings.

2.2: Scientific Summary

Provide a non-confidential scientific summary of the CAT proposal, highlighting the hypothesis, study objectives, milestones and deliverables and potential socioeconomic impact. (For funded CAT proposals, this summary will be used externally in media releases, communications and posted on the CFN's website.)

Our vision is of a routine preventive system in older adults for screening to reduce polypharmacy and adverse drug effects (ADEs). Our previous work in several settings suggest the harms associated with polypharmacy are reversible, and we developed a model, TAPER, that engages pharmacists, family physicians and patients in the primary care setting for community dwelling older adults. We wish to adapt and test this in a LTC setting to see whether, compared to usual care, it could:

- Reduce number of medications
- Improve quality of life, physical and functional ability, and falls
- Reduce unplanned healthcare resource utilization

In this study we will:

1. Examine the feasibility and key signals of effectiveness of TAPER in LTC
2. Talk to families about how best to involve them in this deprescribing process
3. Test outcome measures and processes to inform a larger trial

We will spend 4 months finalising processes and training, then 4 months recruiting participants, and randomising to TAPER or usual care. By 13 months we will complete follow-up data collection, ready to analyse the data and write up results for publication and dissemination to stakeholders in months 14-16.

Potential socioeconomic impact

This program will have important impacts for residents on both physical health and the ability to interact socially if it can mitigate the functional impairments, reduced quality of life and economic costs of ADEs associated with polypharmacy. This scaleable model for sustainable change could substantially reduce the burden on patients, their families and the healthcare system.

Section 3 - Scientific Excellence

3.1: Background, Knowledge Gap(s) and Rationale

- *Provide a comprehensive review of the relevant background literature and identify the knowledge gaps.*
- *Clearly state the rationale for the project and how the results of this proposal may be used to improve the care of older Canadians living with frailty and improve the lives of their family, friends and caregivers.*

Polypharmacy, while sometimes beneficial to individuals, continues to cause great concern, especially among the elderly who are most likely to have multiple comorbid conditions [1-4]. There are substantial associations between polypharmacy and reduced function in older adults and frail older adults both in long-term care and in the community. Specific negative effects include poorer quality of life, and reduced function including poorer mobility, cognition, and nutrition as well as falls, fatigue and reduced medication adherence [5-8] where complicated medication regimes which exceed the patients' ability to cope [9-19]. Overmedication is not only costly in terms of admissions and treatments for adverse drugs effects (ADEs) as well as medication waste [13]. In Canada, ADEs cause an estimated 70,000 preventable hospital admissions per year [14]. In Canada, most older adults on multiple medications have never had a comprehensive medication review, and ADEs requiring medical care affect a substantial proportion of this group (13% of those on ≥5 medications); 1/3 are estimated as preventable [15].

Polypharmacy and Mobility

Polypharmacy in older adults is associated with mobility-related functional decline, increased falls, hospitalization, institutionalization, impaired cognition, and reduced quality of life [10-12]. A higher drug burden has negative associations with bathing, dressing, bladder function, transfers, mobility and stair climbing [16]. In Canada, the burden of polypharmacy and mobility impairment is much higher in long-term care residents. This group stands to gain the most from reduction in polypharmacy. Animal models show polypharmacy affects mobility, balance and strength in older frail animals in ways that are not seen with individual drug treatments, nor in younger animals and this appears to be the case with frail older adults.

Canada's healthcare system lacks a feasible, systematic approach to minimising the negative effects of polypharmacy in routine clinical care, yet morbidity and mortality rates from ADEs in seniors are now higher than many chronic diseases [17-19]. There is little evidence on whether these associations with poorer function are actually reversible if polypharmacy (i.e., the number of medications) is reduced. This is important information, as it determines the type and timing of interventions to address these effects. We propose to test this using an innovative model, TAPER (Team Approach to Polypharmacy Evaluation and Reduction) that we have used successfully in reducing polypharmacy in community-dwelling adults.

TAPER is a structured clinical pathway aimed at reducing the number of medications. It involves integrating evidence tools, an automatic screen for potentially inappropriate medications, and a process developed for integrating patient priorities for care. The "Team" engaged in this intervention is the patient/family, the pharmacist and the physician. The intervention has been specifically structured to address barriers to deprescribing identified in ours and others work with nurses, physicians and patients. (Figure 3 maps TAPER to these identified barriers)

Previous work: Our feasibility study of medication reduction in a cohort of older adults living in the community showed improvements in quality of life, mental status and other morbidity indicators, and has been highly cited [6]. Our CIHR funded RCT, based on an initial feasibility randomised controlled trial, is successfully implementing TAPER for community-dwelling adults in a primary care clinical setting. We have NIHR funding to trial in a hospital setting in Australia.

Long-term care: Our feasibility study in long-term care focussed on a specific medication area (anticholinergic and sedative drugs) showed successful reduction in medication burden, and a statistically significant improvement in the frailty score. [20] Our small pilot "before and after" study looking at all medications, and

aiming to focus in more detail on mobility was carried out in the long-term care facilities selected for this application. This has helped us to understand which elements need adjustment for a LTC setting, in particular the need to understand how to involve families in the process. The study proposed in this application will test the robustness of this signal in improvement of specific functional outcomes and provide the basis for scaling up into a large pragmatic randomized controlled trial if there is a signal of reversibility in this feasibility trial.

3.2: Hypothesis and Research Question(s)

- *State the proposed hypothesis and research question(s) to be addressed in the study.*

Hypotheses

We hypothesize that over 6 months, compared to the usual care group, participants in TAPER will have:

1. no change/fewer number of medications (primary signal of interest).

2. no change/improvements in quality of life, level of physical functioning and performance, activities of daily living, fatigue, sleep, functional ability, and number of falls (secondary outcomes).

3. less healthcare resource utilization.

Research Questions

1. What are the effects of TAPER on numbers/doses of medications and adverse events?
2. What signals indicate that impairments of function associated with polypharmacy are reversible?
3. What are the effects on hospitalizations?
4. How can patient priorities and preferences be successfully integrated in the presence of cognitive impairment and family having power of attorney?
5. What are the experiences of patients and their families undergoing ‘deprescribing’?
6. What are the key aspects to integrating this model as part of routine practice in long-term care?

3.3: Overall Goal and Objectives

- *Describe the overall goal and specific objectives of the study.*

We wish to build on our work developing and testing the effectiveness of an intervention in primary care to reduce polypharmacy. Our pilot and feasibility studies showed TAPER is suitable for use in routine primary care, scaleable, and demonstrated positive health effects of reducing polypharmacy in community dwelling adults [7]. A pilot study testing a narrow range of medications suggest positive health effects in frail older adults also. Our overall project goal is to adapt, implement and test the TAPER process in LTC. The specific objectives are to:

1. Examine important feasibility measures and extent of implementation of the TAPER polypharmacy intervention in 2 LTC facilities
2. Examine signals of effectiveness of TAPER in LTC
3. Test measures for use in a larger randomised controlled trial
4. Collect data from family members to understand how to involve them in the deprescribing process, as well as their perspectives on the deprescribing process

3.4: Methodological Approach

- *Describe how this project will be managed overall and who specifically will manage each major aspect of the study.*
- *Describe the overall study design, approaches, procedures and methods used in the study and why they are appropriate to meet the goals and objectives and deliver upon the proposed output(s).*
- *For example, if relevant, include aspects of participant recruitment, methods and tools used to assess participants for frailty, data collection, statistical analysis, etc.*
  Note: Study protocols must include frailty assessment of all study participants using a published frailty assessment instrument appropriate for the care setting.

Methods

Design

This is a feasibility RCT (1:1 patient randomization to either receive TAPER or usual care). The control group will be offered TAPER after 6-month outcomes are collected. In our experience using a randomized design in a full feasibility study is essential to ensure subsequent effective implementation in a large multi-site pragmatic RCT. This approach enables use of data in subsequent meta-analysis. Detailed testing of the proposed quantitative measures in this population is essential as score distributions may be clustered due to population characteristic similarities. In order to understand how to incorporate family and patient perspectives in priority setting, our experience with developing the approach for integrating patient priorities for TAPER in community-dwelling older adults indicates formal qualitative methods are best in developing the approach and producing publishable information for use by others working in the area.

We will randomize 90 patients (allowing for 10 dropouts). Participants will be 70 years or older and on > 5 medications. Based on our feasibility RCT in community-dwelling adults, this will provide adequate numbers to test feasibility of processes and provide information on outcome measure performance, recruitment rates and sample size calculation for a larger trial.

Patients lists (aged 70 or older and on 5 or more medications) residing at each of the LTC facility will be generated by administrative staff. The study team will work with the LTC facility to develop a consent process. This process will include verbally reviewing expectations of participation, written consent, and confirming inclusion criteria. For those who are unable to provide written consent, consent will be sought by the substitute decision maker. We will provide information evenings for families of all residents considering participation.

Intervention

The intervention as a structured medication review through integrated consultations with a pharmacist and then a physician. The review is based on patient (or family where appropriate) preferences and priorities for treatment and available evidence. A ‘pause and monitor’ plan for medications suitable for discontinuation or dose reduction is developed, including agreed criteria for monitoring and for restarting medications (**see Figure 1 for TAPER diagram**). Key aspects of the intervention include:

1. **Resources, evidence and guidance to support medication discontinuation.** A systematic review of potentially useful tools has been completed and an eHealth platform (TAPERMD) developed for automatic detection of ADEs and screening for potentially inappropriate medications. It combines the Beers List, STOPP criteria, Anticholinergic Burden, hypotension burden, serotonin burden, QT burden and an interaction checker as well as deprescribing guidelines and evidence for benefits in older adults.
2. **Formal incorporation of patient priorities** to empower patients and clinicians to make choices driven by patient’s personal values. A systematic literature review looking for existing tools and approaches and work completed with patient focus groups has informed this [21]. This study will seek family members input into how best to involve them in this process of priority setting.

3. **Collaboration.** The pathway supports collaborative review by pharmacists and physician.
4. **Integration of 'pause and monitor'.** Patient priorities, potential medication side effects, eTools, clinical consultation record and pause and monitor template plan are integrated in a web-based clinical pathway. This has been piloted with clinicians using a small number of patients in the LTC facilities.

Adverse effects will be addressed within the usual care clinical setting. Clinical follow-up will be determined according to the particular drugs discontinued and recorded in the web-based clinical pathway.

Frailty Measure

A validated measure of frailty (Edmonton Frail Scale) will be assessed at baseline and 6-months to determine signals of effectiveness of TAPER compared to usual care. We saw signals of improvements following reduction in polypharmacy with a statistically significant difference in the frailty measure, even in our small pilot sample in LTC [20]

See Table 1 for a full list of outcomes, timing of data collection and analysis.

Management

We have partnered with 2 LTC facilities in Brampton, Ontario, each supported by in-house primary care clinicians and pharmacists. We have an excellent working relationship with these facilities after our pilot study. The Medical Director is a co-investigator and key liaison.DM will manage the operation of the study. Regular team meetings with the McMaster research team, Medical Director (JV) and involved staff, training pharmacists to review progress will occur. Research staff will help to ensure fidelity of data collection, with double data entry among a random sample to test accuracy. Randomization and statistical analysis will be carried out by the Biostatistics Unit at St Joseph's Healthcare Hamilton (LT).

3.5: Research Outcomes, Deliverables and Milestones

- *Describe all milestones and anticipated deliverables, outputs and outcomes for the duration of the project.*
- *Provide a project schedule with dates for all milestones and anticipated deliverables, outputs and outcomes for the duration of the project, including all knowledge translation activities.*
  Note: The project schedule is mandatory and will be used to track progress of the study.
- *Describe how this project will be managed and deliverables tracked.*

Demographic information such as age, sex, gender, date of birth, and ethnicity will be self-reported in the baseline data collection session in order to describe the sample.

Feasibility Measures (Research Question 2)

Feasibility measures will be assessed using recommendations of Thabane et al. (2010) [22]. Process, resources, management, and scientific areas of feasibility will be assessed through research team and administrative records for the study, and will include:

1. Long-term care recruitment rate
2. Participant recruitment, retention, refusal rates
3. Number of cancelled-scheduled appointments
4. Proportion meeting eligibility criteria from lists generated by administrative personnel (>70 years and 5+ medications)
5. Proportion needing substitute decision maker involvement
6. Time needed for enrolment target of 80 participants

7. Length of time to complete measures
8. Performance of measures, looking for floor and ceiling effects and change over time
9. Research team's description of appropriateness of the collection surveys and process of data collection
10. Changes to process to meet context demands and needs

Study Measures (Research Questions 1,3,4,5)

Main outcome measures will be collected at baseline and 6-months post-intervention. Additional follow-up by the research team will occur at 1-week, 3-months, and 6-months after initial appointments to facilitate recall and recording of any immediate effects revealed by discontinuation. Study measures include:

1. *Mean number of medications per participant* (primary outcome of interest).
2. *Adverse events* will be collected by solicited enquiry as well as spontaneous patient or clinician report, and serious adverse events reported as a subgroup.
3. *Quality of life* will be measured by the EQ-5D-5L and SF-36 [23]. The EQ5D-5L survey will also be used in our economic analysis [7].
4. *Level of physical functioning impairment* will be measured using the Manty.
5. *Timed Up and Go* and timed 8-foot walk test will be used as performance measures of physical functioning [24].
6. *Number of falls* (minor and those resulting in injury) will be recorded by self-report and from electronic medical record review.
7. *Pain* will be measured using the Brief Pain Inventory (short-form) [25].
8. *Performance in activities of daily living* (ADL) will be measured using the Barthel Index [26].
9. *Mobility-related fatigue* will be measured by the Avlund Mob-T Scale [27,28].
10. *Sleep* will be measured by a single item on the 15-D quality of life scale [29].
11. *Grip strength* will be assessed using a hand grip dynamometer as per standard testing procedures [30].
12. *Functional ability* will be measured using the Functional Ability Scale for the Elderly [31].
13. *Frailty* will be measured by the Edmonton Frail Scale [32].
14. *Healthcare resource utilization* data will include number of hospitalizations and emergency department and urgent care visits, as well as visits to the family physician.
15. *Perceived change in side-effects and medication related symptoms* will be self-reported at 1-week, 3-month, and 6-month follow-up.

Semi-structured interview (Research Question 6)

Patients and family members will be asked to participated in a semi-structured interview to explore their experience with deprescribing, and their views on how to incorporate families' perspectives into deprescribing and strategies to address polypharmacy in LTC residents

Data Analysis

Means and standard deviations or proportions will be calculated for demographic information and study outcomes where appropriate. Analysis will involve t-tests or Chi-squared statistics where appropriate. Qualitative data will be analyzed by descriptive methods. See Table 1 for a full list of outcomes, timing of data collection and analysis.

Project Schedule

The project will be carried out over a 16 month period. All research, analysis and KT activities will be carried out in this time period. The project PI and the Research Associate will oversee all activities and will ensure the project schedule is followed **(See Figure 2 for the Project Schedule)**

Section 4 - Project Feasibility

4.1: Feasibility

- *Identify all feasibility issues, barriers, challenges and limitations to the successful execution and completion of the study. Specifically address issue related to budget constraints, time constraints, structural issues, and organizational and personnel challenges that may delay or derail timely completion of the study.*
- *Describe how the investigative team plans on mitigating and overcoming these barriers, challenges and limitations.*

We have experience in conducting studies on reducing polypharmacy in community and LTC settings, and have chosen an adequate and achievable sample size and time frame to answer the research questions, considering expected recruitment rates from our previous studies, and available population. RCTs are complex to implement in community settings, and full feasibility trials such as the one proposed are essential, to ensure success in implementation of both the intervention model and the research elements in larger RCTs. Our previous experience in successful conduct of RCTs in the community setting gives us the awareness of the logistics, pragmatism, and meticulous attention to detail required.We are aware of the costs, including KT, and have budgeted appropriately, and have additional support from students that to ensure adequate study personnel and time to complete the study.

The TAPER intervention model has been specifically designed to address the known barriers to polypharmacy reduction: We have mapped this in Figure 3, and we believe the success of our previous feasibility studies reflects this. **(see Figure 3 for diagram)**.

We are currently undertaking a small pilot study in a LTC facility. Our learnings identified several challenges working in a long-term care facility that we have put processes in place to mitigate.

Personnel requirements

During the pilot, we found that a dedicated assessor was required for the mobility assessments who is experienced in working with with frail older adults and can ensure patients' safety during physical assessments. To address this, in addition to the research associate and assistant, we propose to hire a trained physiotherapist for physical assessments at the LTC sites. We have identified a local physiotherapist who is experienced in working with frail older adults, and received training on the study procedures and data collection methods during piloting. This reduces time and resources required for specialised training and avoids mileage costs associated with sending a research assistant or physiotherapist from McMaster in Hamilton Ontario to Brampton to carry out the assessments.

Partnerships

Finding a long-term care facility willing and able to partner with us was important. We have found and successfully partnered with long-term care facilities in Brampton, Ontario, taking into account the context and needs of the facility workflows, and residents needs in designing the trial processes. Key staff have good understanding and experience of requirements of a randomized feasibility trial and have worked with the team to develop processes to facilitate this. The partnership allows us to have access to a large population of LTC residents when recruiting participants, which will provide more than ample sample size given our anticipated response rate. There is no competing research at this location and the facility also includes a pharmacy, pharmacists who are interested and engaged with the project, and the residents' primary physicians. As a result, the research team, physiotherapist and the medical team will be able to easily and relatively seamlessly communicate and implement the project protocol as evidenced in our pilot.

We have piloted several patients through the processes to assess how best to organize processes of the intervention and measurement. We discovered that testing needs to be done at a consistent time of day at baseline and 6 months, as residents tend to fatigue as the day progresses. Consequently, we have identified a

2.5 hour morning window for all testing that will ensure residents are not fatigued, data collection is consistent and unbiased, and there is no interference with facility workflows around mealtimes, dressing etc.

The intervention is already designed to partner with patients as an explicit part of the 'Team' aspect of the TAPER intervention, and this is working successfully in community-dwelling adults. An important partnership in LTC facilities is with families, particularly where the resident may have cognitive impairment. Families carry a lot of responsibility for overseeing and participating in care decisions for family members in LTC. In order to engage families, to prepare for the smooth running of TAPER for the study, and for wider implementation if proven successful, we have planned specifically in this feasibility trial to study how best to include families in the process.

Structural issues

Finding space to carry out the assessments in a consistent way, in particular the physical function assessments, is a challenge when working with residents of a long-term care facility. We have scoped and secured a dedicated space in the Brampton long-term care facility to carry out the assessments with the residents. The space is within the facility, allowing for easy access for the participants.

4.2: Expertise and Experience of Research team

- *Please describe the expertise and experience of each Principal Investigator, Co-investigator, Partner and other critical team members to demonstrate that the team is capable of delivering on the proposed outputs and achieve the goals and objectives of this proposal.*
- *Please provide an estimate on the number of hours per week (contribution) for each Principal Investigator, Co-investigator, Partner and other critical team member that will be working on the study and describe why this is an appropriate level of engagement and/or commitment to deliver the proposed outputs and achieve the goals and objectives of this proposal. (Note: All Individuals participating as project team members will also need to be listed in the Project Team List document).*
- *For each Principal Investigator, Co-investigator, Partner and other critical team member please describe why the environment (academic institution and/or other organization) is appropriate to enable the conduct and success of the project.*

Our team members have a breadth of experience in various disciplines including pharmacology and therapeutics, family medicine, pharmacy, nursing, polypharmacy, epidemiology, sociology, evidence review and synthesis, research design, and extensive experience in successful RCT implementation in primary care. Our collaboration builds on existing relationships within a team, all committed to the goals of this research. The intervention and processes will follow those that were successfully used in our just-completed RCT of antidepressant discontinuation, our previously published general medication reduction feasibility study, and our RCT in community-dwelling adults as well as our pilot work in LTC.

Our team has a demonstrated track record of collaboration. We have worked collaboratively on Canadian Polypharmacy projects and tools including TAPER and MedStopper, and JT, DM, JM and AC specifically have collaborated on knowledge translation projects in polypharmacy, and DM PR and LG collaborate in the Canadian Longitudinal Study on Aging (CLSA) Medicines Working Group. Our team has also published widely on research design (LT), polypharmacy and drug discontinuation (DM JM JH SG), research on how clinical evidence on medications gets communicated to policy-makers, prescribers (AC DM) and consumers (AC JT WB DM) and effective interventions to change prescribing.

We actively provide consumer medication information through engagement with patient groups, in NGO and internet information sites (DM JT), health journalism and books for consumers (AC), translating research for prescribers and residency training programs/postgraduate CME (DM AH JL JH JT). Our team is formally linked with national and provincial pharmacy organizations through the Ontario Pharmacy Research Collaboration (DM scientific advisory board), the Canadian College of Family Physicians leadership (DM SG), and the Medication Leads Group for the Integrated Patient Safety Action Plan (Canadian Patient Safety Institute) (JT DM).

Two critical additions to our research team expertise should be highlighted in carrying out this project. First, our partnership with DataBasedMedicine has been very effective and efficient in developing the electronic platform (TAPERMD) for TAPER in our community-based trial, and they have adapted it for use in Australia as well as for this study in LTC setting. The format and function has been extremely well received by clinicians, with requests

for access beyond the trial. Second, we have added partners from the LTC facilities, and chosen LTC facilities where the director (JV) has academic experience and understanding of the requirements of research, in addition to implementation of new clinical models of care. The integration of expertise in trials focused on specific patient level outcomes, in service delivery change models, in sociological perspectives on clinical care and health services, in the epidemiology of aging within the CLSA, as well as partners in the LTC context makes this a well- informed and strongly cohesive team making success of this project likely.

Hours and Roles

See Table 2 for the hours committed to the project and roles for the PI, CO-Is and other team members.

Section 5 - Project Relevance and Impact

- *Describe the relevance and the importance of the proposed project to CFN's mission and strategic research programme goals, priorities, and potential to assist CFN in achieving a positive impact on policy and practice.*
- *Identify how the proposed study meets the specific objectives of the Catalyst Grant Program to foster novel, innovative projects demonstrating potential for significant socio-economic benefits related to the care of Canadians living with frailty.*
- *Describe how sex as a biological variable and/or gender as a social determinant of health have been considered and integrated into the research plan.*

This study aligns closely with CFNs strategic priorities and patient-orientated research themes. Polypharmacy is associated with poorer quality of life due to adverse drug effects (e.g. falls, cognitive impairment, malnutrition), drug interactions, and poorer medication adherence due to inability to manage exhaustive medication regimes [9-12]. TAPER is designed to safely reduce polypharmacy, to improve clinical outcomes and care across the continuum, and empower and support patients and their families by incorporating their treatment priorities and preferences at its core. TAPER was designed with the help of patients, patient groups and caregivers after a systematic review failed to show a deprescribing process which formally incorporated patients' views.
A key component of this study is input from, and analysis of, families' experience of deprescribing. This is a unique and important contribution to emerging literature relating to medication burden and will provide unmatched qualitative insight.

Additionally, we will determine if introducing TAPER to usual care results in improved clinical outcomes in LTC residents. Little is known about structured deprescribing in LTC settings. We know that the majority of LTC residents experience multi-morbidity [33]. From 1998-2008 the percentage of Canadian seniors taking >5 prescription medications rose from 13% to 30% overall; the percentage for LTC residents is >50%. [34-36]. Canadian seniors take a median of 7 regular medications [37,38]. Resulting hospital admissions and other treatments for ADEs are costly [13].
Our 2 feasibility studies, in primary care and LTC settings, have strongly signaled the beneficial impact on clinical outcomes. One of the purposes of this study is to confirm these findings, with a view to upscaling to a large pragmatic randomized national trial. Despite increasing morbidity and mortality rates associated with ADEs, Canada's healthcare system currently lacks a feasible, systematic approach to reducing the overmedication [17- 19]. In frail older adults, the decision to stop medications may be as important as the decision to start. Our TAPER approach to deprescribing is ready for upscaling, provided the early signals indicating success are confirmed and implementation is deemed feasible. We believe TAPER has the potential to transform clinical care in the LTC setting.

Sex and Gender Considerations
Women experience more ADEs compared to men, regardless of age and rate of exposure [39]. Women also have a greater risk of certain ADEs. The FDA does not require analysis of sex in terms of efficacy and safety outcomes, and women are underrepresented in drug trials [39].
Prescribing patterns differ according to gender: on average, US women are prescribed more medications than men (5 versus 3.7) [39] and evidence demonstrates certain drugs are prescribed more often to women, especially psychotropic and pain medications [39].
In this feasibility study, we will describe data on baseline characteristics, clinical outcomes, and patient experiences, according to sex and gender. We will not have power in this feasibility study to test hypotheses in subgroups, but we plan to use these data to determine power and sample size calculations for sex and gender analyses for the larger trial.

Section 6 - Capacity Building - Highly Qualified Personnel

CFN funded proposals must contribute to the development of Highly Qualified Personnel (HQP) through their inclusion as project team members in a meaningful manner.

- *Briefly summarize the number and level of HQP required and the experience/expertise afforded by involvement in Network-funded research.*
- *Specify expected contributions to HQP studies.*

Two highly qualified personnel (HQP) will be involved in this study. Alison Ross, a PhD student in sociology will help to develop and carry out the semi-structured interviews to explore experiences of deprescribing among family members. Involvement in this study will expand Alison's knowledge of polypharmacy, a new area for her. Also, this involvement will provide her experience working with frail older adults and their family, which will refine her interview skills. She will be involved in analysis and write up of the data and in translating the results in adapting the TAPER process for long term case based on the findings. Jenna Parascandalo is a Master of Public Health student. She will be involved in using this data in the process of adapting TAPER to fit a LTC context as well as the data collection for analysis and publication. Her engagement in the process of adapting and implementing TAPER for a LTC setting will give her experience in knowledge translation activities and factors involved in scaling up an intervention. Jenna will also be involved in translating the results of this study into consumable mediums for a variety of audiences. Jenna will be responsible for monitoring our use of the Knowledge-to-Action framework throughout the study. Other funds will cover the human resource cost of Alison and Jenna.

Section 7 - Project Networking and Engagement

7.1: Project Networking

A funded project must represent a collaborative effort of different Investigators in more than one discipline (e.g., combinations of biomedical science, natural sciences and/or the social sciences) and at more than one Institution and with involvement of partners and stakeholders from other sectors.

- *Describe the networking and engagement planned for the project across disciplines, research sites (universities, hospitals, institutes) and sectors.*

The TAPER team consists of patients, their caregivers, patient advocates, and experienced investigators representing multiple disciplines and institutions across several Canadian provinces - Family Medicine (McMaster University; University of Alberta; University of British Columbia), Geriatric Medicine (McMaster University; Geriatric Medicine, Kitchener Waterloo), Pharmacy (McMaster Family Health Team; University of British Columbia), Sociology (Department of Health, Aging and Society, McMaster University), and Biostatistics and Epidemiology (McMaster University/St. Joseph's Hospital, Hamilton). This project will help evolve this multidisciplinary engagement and build on recently-established relationships with caregivers at our Brampton LTC sites. This project will also continue a partnership with Data Based Medicine Americas Ltd. (DBMA) in order to modify and develop our e-tool TAPERMD. DBMA, in partnership with the TAPER team, are committed to the safe and efficient incorporation of TAPERMD into the LTC setting. TAPERMD has also been selected by MaRS (MaRS Discovery District, Toronto) for development support. We plan to have weekly investigator meetings, with remote members attending via Webex and Skype. To date we have found this mode of meeting a successful means of communication and collaboration. It is time-efficient and removes necessity of travel for those working remotely (including investigators working at the LTC facility). As a team, we are excited about potential TAPER has towards improving safe prescription of medications, and overall clinical care, across Canada.

7.2: Citizen Engagement

CFN is committed to empowering and engaging older adults living with frailty and their families and caregivers and other knowledge users.

- *Describe how knowledge users (e.g. patients/families, decision makers, stakeholders, practitioners) will be involved in the research in a meaningful manner. For clarity, meaningfully involved participation of knowledge users includes assisting in the planning and execution of the research project and/or in assisting in the interpretation and translation/mobilization of research findings.*

Johanna Trimble has been a partner in knowledge translation and a key co-investigator in our TAPER program for many years. She is a consumer advocate who has had personal experiences with navigating medications and care of frail older adults, and contributes to a number of provincial and national committees working on polypharmacy. Her work focuses on the frail elderly, and issues surrounding pharmacology, polypharmacy and medication safety. A consumer advisory group lead by Johanna Trimble has been involved in developing the TAPER intervention, and will be involved in the planning and execution of this research project. The group is comprised of patients and caregivers with lived experience in deprescribing and other aspects of the healthcare system. The group has been involved in the development and selection of tools to be used in the data collection for the feasibility study as well as knowledge translation of findings, and will continue this role in the RCT feasibility study. The advisory group will meet via skype with the research team once a month to discuss the study and provide feedback.

Focus groups will be carried out with families and caregivers of participants to gather feedback of their lived experience with the study process and gather their input into processes for incorporating their views into the TAPER process for their family member. Three focus groups will be held with 7 family members and/or caregivers in each group. The findings from the focus groups will be used to inform the future RCT.

Section 8 - Knowledge Translation

8.1: Potential for Knowledge Translation/Knowledge Mobilization/Commercialization

Describe the opportunities for knowledge translation and exchange and/or technology transfer or commercialization of the research proposed along a continuum leading to social or economic impacts or policy and practice change. If there are specific companies or organizations that will be involved, list in Section 3 (Partnerships) and ensure that a letter of support is included.

The project has integrated knowledge translation (KT) at a micro-level with clinicians and consumers participating in the design and implementation of the study. They contributed through focus groups and individual comments, to tool development around patients priorities and challenges, and to the web-based evidence support, and pathway. This has created a model and tool that is immediately scalable and responsive to emerging evidences. Knowledge will be shared at the LTC site level and with the regional network of LTC facilities, with whom we have a close collaboration (DM JV and HS) in order to disseminate fundings and initiate processes and policy changes with a wider reach. At the macro-level, TAPER investigators work closely with the Canadian National Deprescribing Network (CaDeN) to inform development of the national strategy for deprescribing. We will present findings to CaDeN to distribute learnings and influence national policy. Study findings will be made available to the research community through open access journal publications and conference presentations.

The team uses social media as part of an integrated KT strategy. Polypharmacy videos describing the rationale, and model for TAPER have a high number of views on YouTube (2700 and more recently 700). TAPER is a pathway designed so the 'Team' stakeholders can initiate the approach to polypharmacy evaluation: we have developed the TAPER tool with consumer initiation of the process in mind. A consumer health information site (RxISK.org) has been used to disseminate information about polypharmacy [40)], and this will be a vehicle for KT to consumers. The website receives >200,000 visits/month. Testing interest with a "Could you be on too many drugs" questionnaire for consumers to take to their pharmacist or family physician, generated 1000 completions in the first month.

Our partnership with DBMA has been very successful. The TAPER tool is designed to easily integrate additional evidence resources, as they become available, and designed for seamless scale-up. If successful it is planned to progress to commercialisation, in partnership with DBMA, to support scalability and sustainability at provincial national and international levels as part of routine clinical care. (support letter attached)

8.2: KT Framework/Platform

Please identify the KT framework that will be used and how it will be implemented. The framework should be one from the April 2012 Knowledge Translation Framework for Ageing and Health from the World Health Organization (http://www.who.int/ageing/publications/knowledge_translation.pdf).

The Knowledge-to-Action framework will allow us to guide the process of adapting what we already know about TAPER in primary care as we move to test its feasibility in a different context, LTC. Tailoring knowledge to a new setting is a strength of this framework. Focus of implementing each phase of the framework will occur.

A systematic look at our outcome and process data collected during our feasibility study in primary care will be used to help inform how to adapt TAPER to LTC (*adapt knowledge to local context*). For example, key learnings have and will be shared with our partners at the LTC facility with discussion of how to use these learning in the LTC setting. Examples of learnings include the best way to support family doctors and pharmacists in using TAPERMD: in the primary care setting, partnering during first time use, using peer to peer learning was very successful in addition to training sessions. Further, learnings from our feasibility pilot in LTC will also be discussed, assessing feasibility of certain data collection tools and the process of patient consent and family engagement. This will provide rich information before implementation of this study in order to *assess barriers* beforehand and develop processes to overcome these barriers (see Section 4.1 for some barriers already identified). This ultimately will involve *tailoring* the intervention to suit the context before *implementing* the intervention. We will also have a process for identifying and addressing barriers online to course-correct the intervention as a way to *monitor knowledge use*. Our plan is to *evaluate outcomes* at baseline and 6-months as well as collate process outcomes at the end of the intervention. We would plan to use these key learnings in designing and implementing our larger RCT, using the RE-AIM framework to then study reach, effectiveness, adoption, implementation, and maintenance and including a policy environmental assessment of barriers and

facilitators to implementation in routine care. Throughout this process we will leverage the opportunities described in section 8.1 to maximise KT.

Section 9 - Supporting Information

Provide tables and figures and a list of references as necessary to support sections above.

Document appended to the end of the application

Section 10 - Partnerships & Letters of Support

- *Complete the table below.*
- *In a single PDF document please provide letters of support for each partner, collaborator etc. Upload this document below. Make sure that each letter of support within the PDF is on the organization's letterhead, detailing the partnership and specifically indicating their cash and/or in-kind contribution. The letter should specifically include reference to CFN, the proposed study, and any conditions placed on funding. See Application Instructions for guidance on allowable expenses and eligible partners and contributions.*
- *Individuals from the partner organizations that will be participating as project team members must be listed in the submitted Project Team Information document.*
- *All financial information provided in the table below must also appear in the submitted budget document.*
- *Where a researcher has a "financial interest" (as defined by NCE Conflict of Interest Guidelines) in a partner, the potential conflict of interest should be declared in the table. This does not preclude the partnership in any way, but provides transparency during the review process. Please see CFN Conflict of Interest Policy and Guidelines for additional guidance http://www.cfn-nce.ca/media/23963/cfn-conflict-of-interest-policy.pdf*

Partner Organization/Research Receptor	Potential Conflict of Interest	Role in Project and Specific Use of Contribution in Project	Nature of Contribution	Contribution Amount (CDN$)
Data Based Medicine Americas Ltd.	No	Time, custom web development, database design, secure platform hosting, software licensing, and out-of-pocket expenses	In-Kind	100000

Letters of Support

Download **CAT2017-20_Mangin_Partners.pdf**

Section 11 - Other Funding

For all Principal Investigators please provide details on grants currently planned, being applied for, pending and awarded, for the entire period covered by this application.

Status of Grant	Funding Source	Budget Amount of Grant	Title of Grant	% Scientific Overlap	% Financial Overlap
Awarded	CIHR	974737	Team Approach to Polypharmacy Evaluation and Reduction (TAPER)	10	0
Awarded	Labarge Optimal Aging Initiative	81500	Team Approach to Polypharmacy Evaluation and Reduction (TAPER)- Long term care (Pilot)	50	10

Supporting Documents

Project team Information

Download **CAT2017-20_Mangin_TeamList.xlsx**

Budget

Download **CAT2017-20_Mangin_Budget.xlsx**

Principal Investigator CV(s)

Download **CAT2017-20_Mangin_PI_CV.pdf**

Team Member CVs

Download **CAT2017-20_Mangin_TeamCVs.pdf**

Required Signatures

Download **CAT2017-20_Mangin_Signatures.pdf**

Proof of Study Submission to Research Ethics Board

Download **CAT2017-20_Mangin_REB.pdf**

Proof of Completion of one of CIHR Institute of Gender and Health's (IGH) online sex- and gender-based analysis training modules

Download **CAT2017-20_Mangin_IGH.pdf**

Figure 1: TAPER process

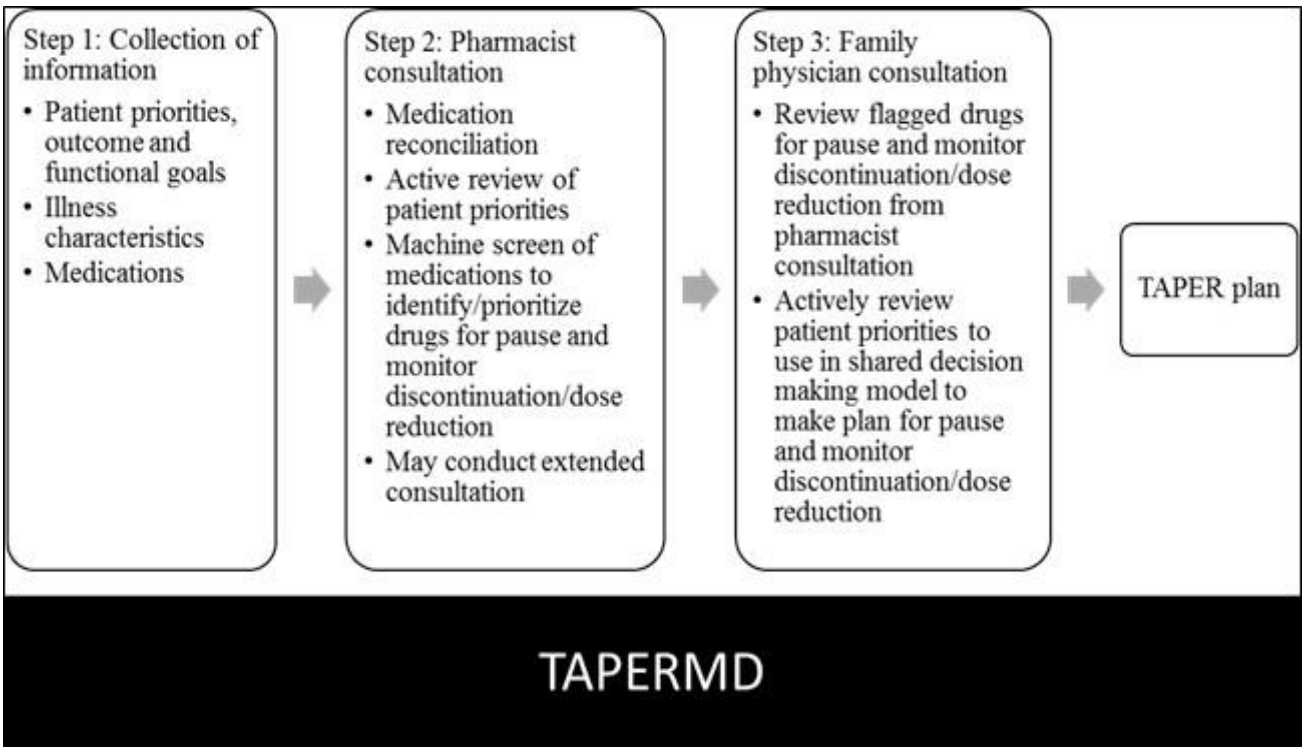

Figure 2: Project Schedule

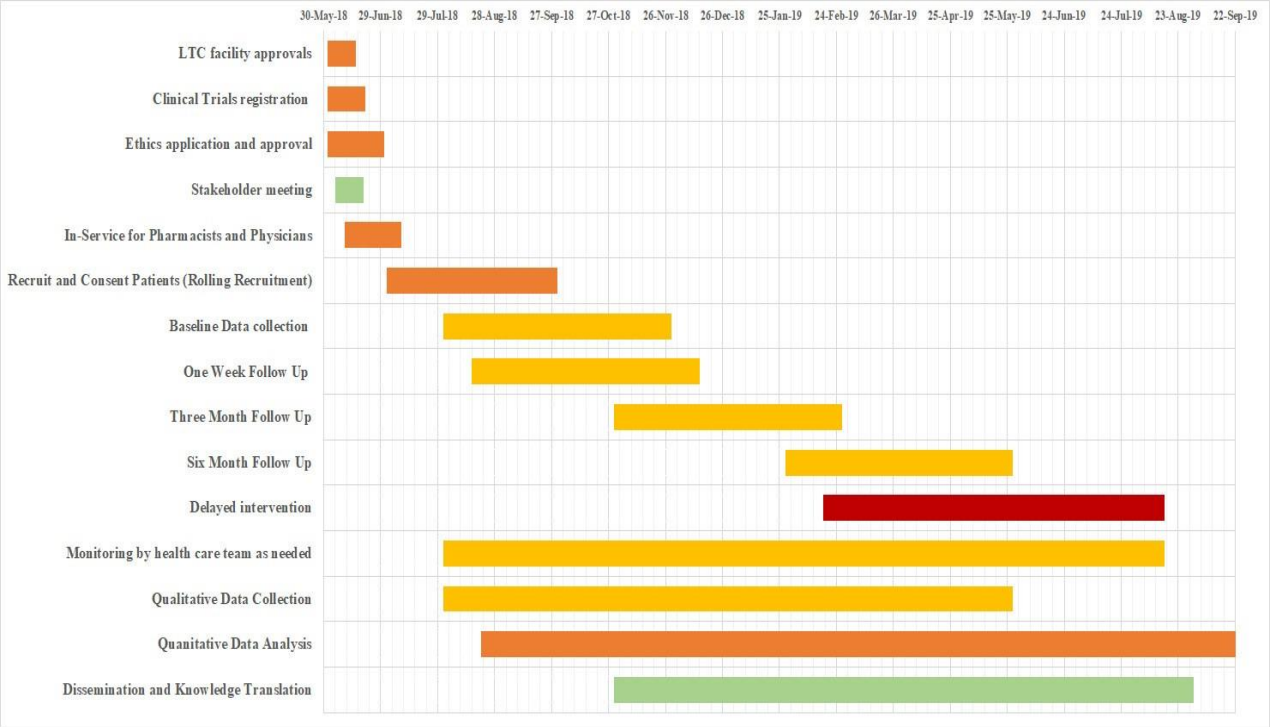

Figure 3: Map of barriers

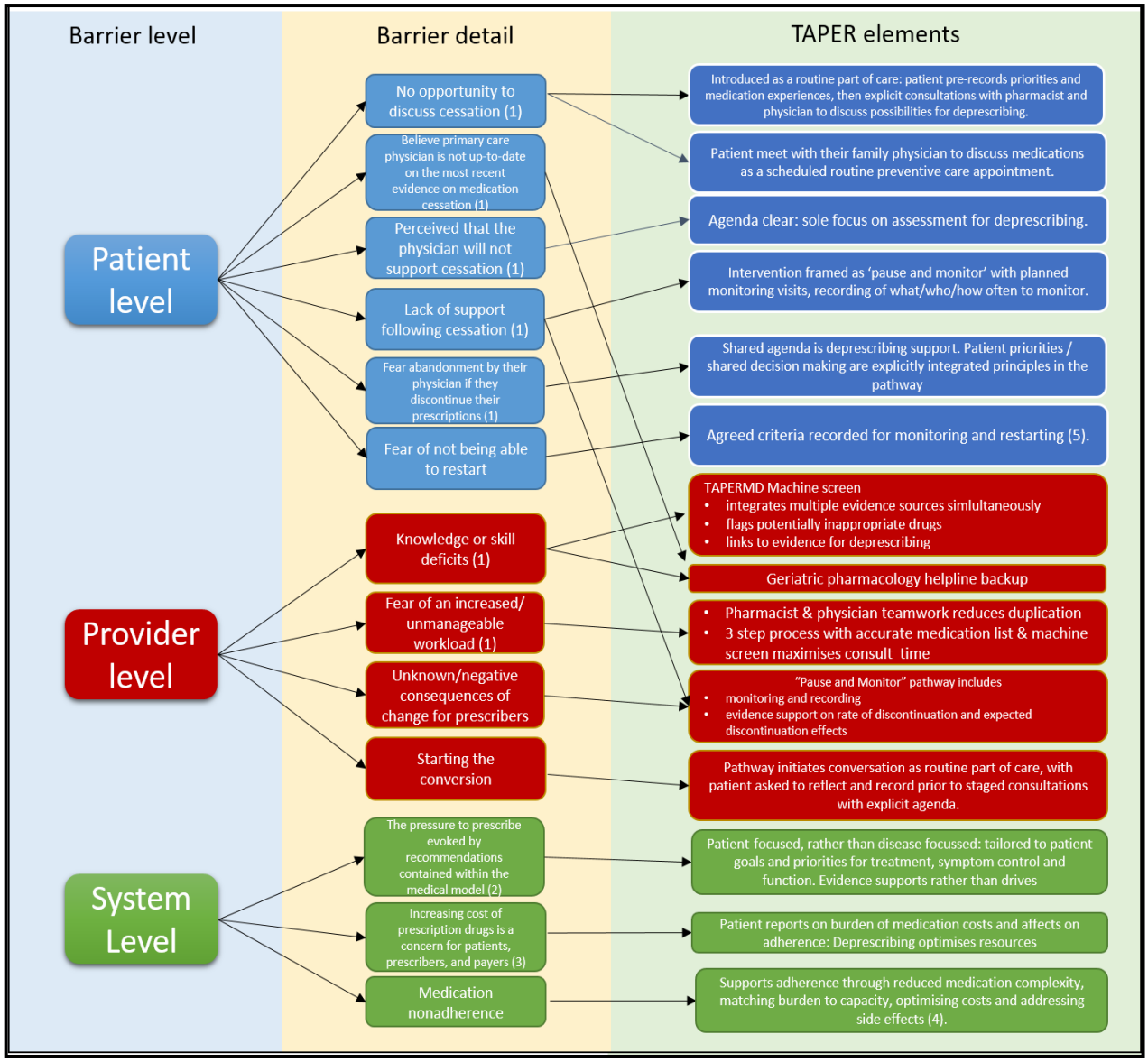

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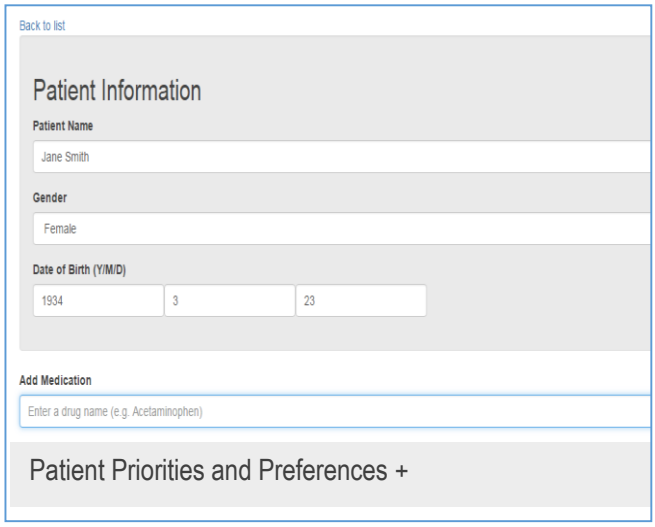
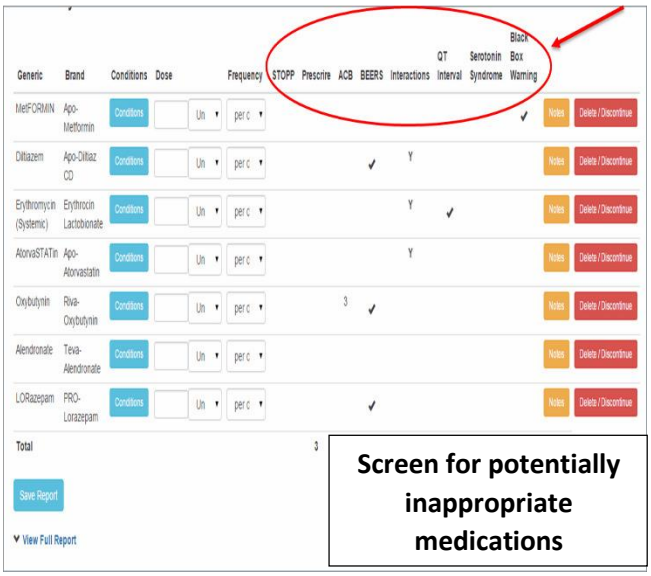
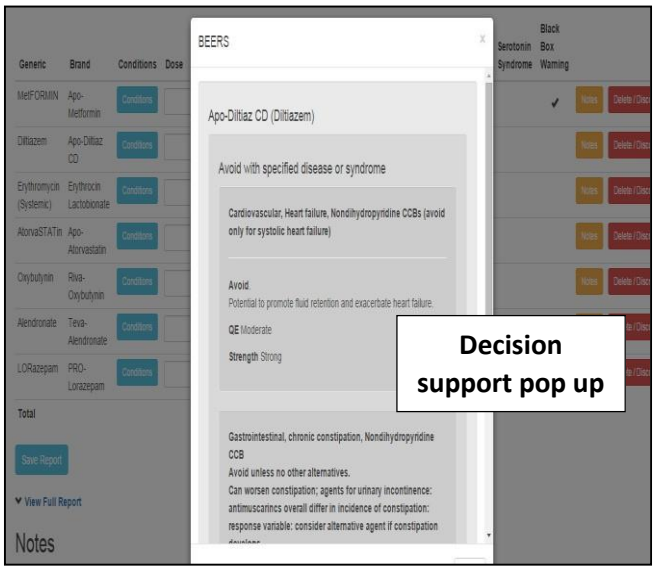
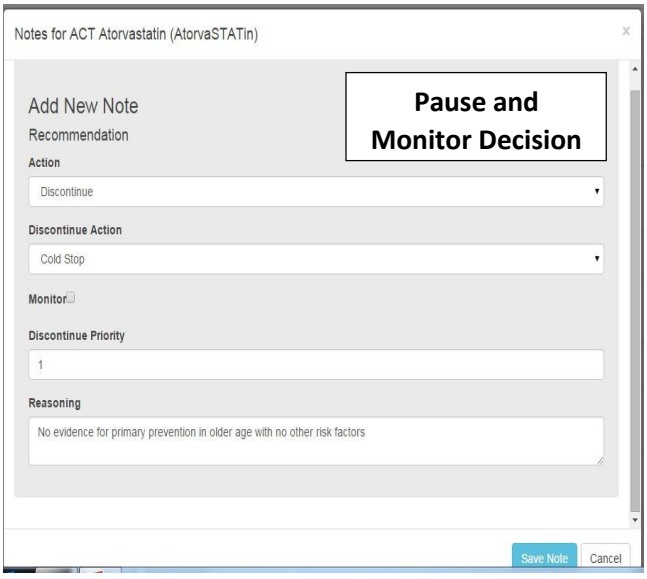
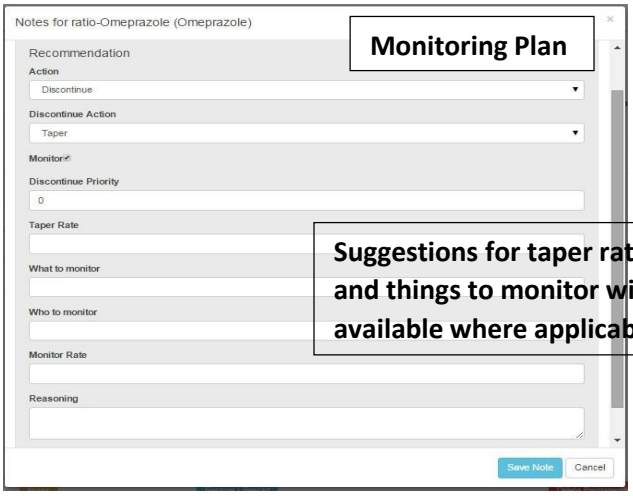
Figure 4: TAPERMD Screen Shots











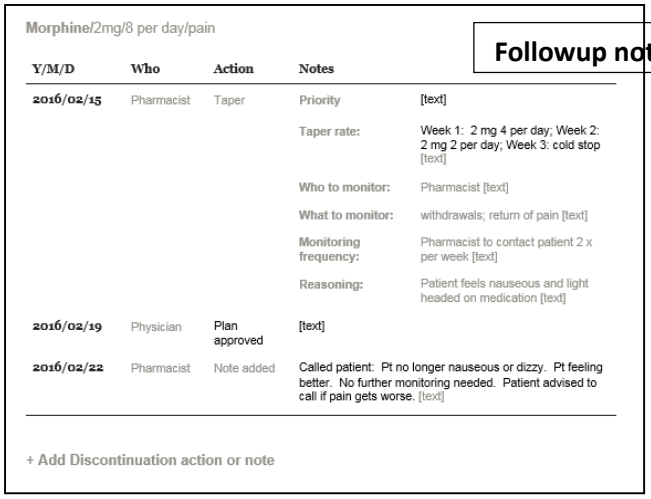


Table 1: **Summary of proposed data analysis methods for quantitative outcomes**

Research question	Hypothesis	Outcome	Outcome measure/data collection	Timing	Method of analysis
What is the effect of a structured medication discontinuation clinical pathway designed to reduce polypharmacy on mean number of medications and patterns of discontinuation compared to usual practice?	Reduction in mean number of medications	Medication from reconciliation list	Mean number of medications	T_0, T_6	t-test
			Proportion with successful reduction in medication number or dose	T_6	Chi Square
			Composite variable of mean number of medication discontinuations or dose reductions	T_6	t-test
What is the effect of a structured medication discontinuation clinical pathway designed to reduce polypharmacy on patient quality of life, frailty, cognition, mobility-related fatigue, nutritional status, physical function capacity, pain, sleep, patient enablement, medication self-efficacy, medication confusion, grip	*Improved* frailty, disease and treatment burden, quality of life, cognition, fatigue, nutritional status, physical function capacity and ability, pain, sleep, patient enablement, medication self-efficacy and	Frailty	Edmonton Frail Scale	T_0, T_6	t-test
		Disease burden	Bayliss Disease Burden	T_0, T_6	t-test
		Treatment burden	Brief Treatment Burden Scale	T_0, T_6	t-test
		Quality of life	EQ5D-5L (economic analysis)	T_0, T_6	t-test for all Chi squared for proportions
			SF36v2	T_0, T_6	
		Cognition	Mini Mental State Exam	T_0, T_6	

strength, falls and adverse events, and hospital admissions compared to usual practice?	*lower/fewer* falls, healthcare utilization, and adverse events will be reported in the intervention arm compared to the control arm at 6-months	Fatigue	Avlund Mob-T and Limb-T scale	T_0, T_6	
		Nutritional status	Mini Nutritional Assessment Short-Form	T_0, T_6	
		Physical function capacity and ability	Mänty survey	T_0, T_6	
			Timed up and go	T_0, T_6	
			Global rating of change (balance)	T_0, T_6	
			Grip strength	T_0, T_6	
		Falls	Number	T_0, T_6	
		Pain	Brief Pain Inventory	T_0, T_6	
		Sleep	15-D (sleep item)	T_0, T_6	
		Patient enablement	Patient Enablement Index	T_0, T_6	
		Medication self-efficacy	Self-efficacy for appropriate medication use scale	T_0, T_6	
		Healthcare utilization	Number of hospitalizations	T_0, T_6	
			Number of ED visits	T_0, T_6	
			Urgent care visits	T_0, T_6	
			Proportion of patients with at least one hospitalizati	T_0, T_6	

			on		
		Serious adverse events	Number	T_0, T_6	
What is the cost-effectiveness of the structured medication discontinuation clinical pathway designed to reduce polypharmacy?	Not applicable	Cost per QALY	Data collection survey developed for study, EQ5D	T_6	Cost Utility Analysis
What is the experience of patients as they go through a structured medication discontinuation clinical pathway designed to reduce polypharmacy? What trajectories do patients follow in deprescribing? Does deprescribing transform their bio/psycho/social experience of chronic disease and its management? Are there social side effects of deprescribing?	Not applicable	Lived experience with deprescribing process	Semi-structured interview/patient diaries	T_6	Descriptive analysis
		Satisfaction with the intervention	5-point Likert scale developed for study	T_6	t-test
		Satisfaction with care around medications	5-point Likert scale developed for study	T_0, T_6	t-test
		Strength and weakness of intervention	Open-ended question	T_6	Descriptive analysis
What are the experiences of the pharmacist and family physician of managing patients	Not applicable	Lived experience with deprescribing process	Semi-structured interview, field notes	T_6	Thematic analysis

through the deprescribing process?		Confidence in medication discontinuation	5-point Likert scale developed for study	T_0, T_6	t-test
		Five best/worst aspects of intervention	Open-ended question	T_6	Descriptive analysis
		Implementation processes	NoMAD	T_0, after 3 of their patients have reached T_3 and after all intervention group patients have completed T6 mark T_3, T_6	Descriptive analysis

Table 2: Team contributions

Role	First name	Last Name	Contribution of hours per week (based on 35hr work week)	Role
Project Leader	Dee	Mangin	7	Team lead; co-ordinate investigator and steering committee meetings; oversee the day-to-day operations; leading weekly meetings with the operational research team; supervise the research assistants in the day-to-day activites with weekly meetings including both sites; provide input into functional outcomes assessment and analysis; lead patient/family stakeholder engagement in design and KT aspects of study
Co-Investigator	Gina	Agarwal	1.75	Provide input into functional outcomes assessments
Co-Investigator	Henry	Siu	1.75	Provide input into functional outcomes assessments within LTC setting and engagement of family members as potential substitute decision makers
Co-Investigator	Lehana	Thabane	3.5	Provide input into functional outcomes assessment and analysis; overseeing analysis and randomization

Co-Investigator	Julie	Richardson	3.5	Provide input into functional outcomes assessment and analysis
Co-Investigator	Mat	Savelli	1.75	Lead and oversee the qualitative research aspects of the study
Co-Investigator	Parmind er	Raina	1.75	Provide input into functional outcomes assessments; provide broader context of LTC within Canada
Co-Investigator	Justin	Lee	1.75	coordinate the expert advisory committee of clinical pharmacologists, and the associated geriatric/pharmacologist advice service for clinicians
Co-Investigator	Jane	Jurcic-Vrataric	3.5	Clinical Pharmacist
Co-Investigator	Alan	Cassels	1.75	Lead and oversee the qualitative research aspects of the study; Assist with KT activities
Co-Investigator	Scott	Garrison	1.75	Assist in analysis and randomization
Co-Investigator	Anne	Holbrook	1.75	coordinate the expert advisory committee of clinical pharmacologists, and the associated geriatric/pharmacologist advice service for clinicians; Assist in analysis and randomization

Co-Investigator	Diana	Sherifali	1.75	Provide input into functional outcomes assessments
Co-Investigator	Cathy	Risdon	1.75	lead patient/family stakeholder engagement in design and KT aspects of study
Co-Investigator	James	Gillett	3.5	Lead and oversee the qualitative research aspects of the study
Co-Investigator	Kiska	Colwill	3.5	Clinical Pharmacist
Co-Investigator	Joanne	Ho	3.5	coordinate the expert advisory committee of clinical pharmacologists, and the associated geriatric/pharmacologist advice service for clinicians
Co-Investigator	Jobin	Varughese	5.25	lead at LTC sites; oversee adapting of TAPER in LTC sites; attend weekly operations meetings; provide input on operational aspects including consenting and assessment of residents; engagement of KT within LTC sites.
Co-Investigator	Johanna	Trimble	1.75	lead patient/family stakeholder engagement in design and KT aspects of study
Co-Investigator	Lauren	Griffith	1.75	Provide input into functional outcomes assessments
Co-Investigator	Kristina	Frizzle	3.5	Clinical Pharmacist

Co-Investigator	James	McCormack	1.75	Provide input into functional outcomes assessment and analysis
Collaborator	Larkin	Lamarche	5.25	Provide input into functional outcomes assessments, provide support for day-to-day operation of study
HQP	Alison	Ross	3.5	Assist with the qualitative research aspects of the study
HQP	Jenna	Parascandalo	5.25	Provide support for operational aspects of trial in LTC
Partner	Peter	Wood	7	Adapt TAPERMD tool for LTC setting

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