Theoretically derived interventions aimed at improving appropriate polypharmacy in primary care: A systematic review

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ABSTRACT

Background: Polypharmacy (the use of multiple medications) is common in older patients and achieving a balance between appropriate and inappropriate polypharmacy is a challenge routinely faced by prescribers. It is recommended to incorporate the use of theory when developing complex interventions, but it is not known if theoretically derived interventions aimed at improving appropriate polypharmacy are effective.

Objective: This systematic review aimed to establish the overall effectiveness of theoretically derived interventions on improving appropriate polypharmacy and to investigate the degree to which theory informed intervention design.

Methods: Seven electronic databases were searched from inception to August 2021 including hand-searching of reference lists. Interventions developed using a theory, involving the use of a validated tool to assess prescribing, delivered in primary care to participants with a mean age of ≥65 years and prescribed ≥four medications, were included. Data was extracted independently by two reviewers. The Theory Coding Scheme (TCS) was applied to evaluate the use of theory; Risk of Bias (RoB) was assessed using the Cochrane RoB 2.0 tool.

Results: Two studies, one feasibility study and one randomised controlled trial (RCT) were included, and therefore overall effectiveness of the theoretically derived intervention could not be assessed. Theory used in development included the Theoretical Domains Framework and Reason’s system-based risk management theory. The RCT was rated to have a high RoB. Based on the TCS, neither study used theory completely.

Conclusion: The effectiveness of theoretically derived interventions to improve appropriate polypharmacy in primary care could not be determined due to the small number of studies and their heterogeneity. Further incorporation of theory into intervention development is required to understand the effectiveness of this approach.

Prospero registration: CRD42020157175.
1. Introduction

The world’s population is ageing; it is estimated that one in six people will be over the age of 65 years by 2050. In 2018, for the first time, people aged over 65 years outnumbered children under five years of age. As the diagnosis, treatment and management of medical conditions improves, life expectancy has increased. Consequently, there has been an increased burden on healthcare resources, with health expenditure per capita projected to grow from 2015 to 2030 at an average annual rate of 2.7% across the Organisation for Economic Co-Operation and Development (OECD) countries. In Ireland, expenditure on healthcare expected to increase to 8% of Gross National Income in Ireland by 2050, in comparison to 6.5% in 2016. People are living longer, but not necessarily in better health; as the population ages, the prevalence of degenerative and chronic conditions e.g. dementia, and the prevalence of multimorbidity (the presence of two or more long-term conditions) is also rising. In 2015, over half of those aged over 65 years in England had multimorbidity.

The increase in the prevalence of chronic conditions and multimorbidity results in the prescribing of multiple medications, commonly termed ‘polypharmacy’, for which there is currently no one accepted definition. It is common for authors to use the definition that best fits with similar studies in order to compare and contrast findings. Historically, ‘polypharmacy’ was defined numerically (e.g. ≥ 4 regular medications) and viewed negatively, as it was widely acknowledged that the more medications a patient was prescribed, the more likely they were to suffer from adverse effects, such as drug interactions, poor adherence and side effects, related to those medications. In turn, these may lead to increased hospitalisation, morbidity and in some cases, mortality. However, guidelines now often advocate for the prescribing of more than one medication to manage chronic conditions and prescribers are challenged to achieve the most appropriate combination of medications for patients who have more than one condition and require multiple medications.

A recent Cochrane review by Rankin et al. assessed the effectiveness of 32 interventions to improve the use of polypharmacy in older people, and concluded that the quality of the evidence base overall was very low, largely due to the high risk of bias in included studies. Included studies did not find clinically significant improvements in appropriate polypharmacy post-intervention. For example, pooled study results noted that pharmaceutical care, as the intervention, reduced the proportion of patients with one or more potentially inappropriate medication (risk ratio (RR) 0.79, 95% CI 0.61 to 1.02; 11 studies; N = 3079) but the certainty of the evidence, assessed using the GRADE approach, was ‘very low’. This review did not systematically examine the use of theory underpinning the interventions, however, the authors noted that studies lacked detailed reporting on the methodological development of the interventions, and recommended that future intervention designs could benefit from adopting the United Kingdom Medical Research Council’s (MRC) framework for the development of complex interventions.

The MRCs framework advocates for a systematic approach and the use of theory in the development of complex interventions, as it states that this is more likely to lead to enhanced effectiveness. Theory is defined as a ‘set of concepts, definitions and propositions that explain or predict… events or situations by illustrating the relationships between variables’. Using theory in intervention development can overcome potential researcher assumptions as to what is (or is not) effective within the intervention. It assists researchers and healthcare professionals in understanding the mechanisms of change underlying the intervention’s effects. Incorporating a theoretical approach in intervention development helps researchers to determine the components that work and in what contexts.

Use of theory is becoming more common in healthcare interventions and has been used in various medication-related interventions such as antibiotic prescribing, opioid prescribing, diabetes care, adherence to medication, and cardiovascular disease. Common theories used in healthcare interventions include the COM-B model (Capability, Opportunity, Motivation-Behaviour), Social Cognitive Theory and the Theory of Planned Behaviour. The COM-B model proposes three components which must be engaged to deliver and maintain behaviour change as the components interact with each other. Social Cognitive Theory also notes the interactions of three components notably personal, environmental and behavioural factors and their importance in behaviour change. This is a social learning theory that proposes people will learn from their experiences but also by observing others conducting the behaviour. The Theory of Planned Behaviour (TPB) is derived from the Theory of Reasoned Action and is useful in understanding how people’s behaviour changes. According to the TPB, an individual’s behaviour is guided by three categories of beliefs: normative, control and behavioural and proposes that behaviour is not a voluntary action and it therefore cannot always be controlled.

The Theory Coding Scheme (TCS), developed by Michie and Prestwich allows researchers to determine the extent to which theory is used in development of interventions. It contains 19 items split into six categories: (i) if a theory is mentioned, (ii) the theoretical constructs targeted, (iii) how the theory was used in the intervention, (iv) the measurement of constructs, (v) the testing of mediation effects and (vi) if the intervention results were used to refine the theory (Appendix 1). The TCS has been adopted in numerous systematic reviews examining behaviour change and will be used for this purpose in this systematic review.

The majority of older people’s medications are managed in primary care by their general practitioner (GP) and community pharmacist, and therefore, as a setting, primary care is ideal to deliver interventions aimed at improving appropriate polypharmacy. However to date, no review has explored the use of theory in the design of interventions aimed at improving appropriate polypharmacy in primary care.

The aim of this review is to establish the overall effectiveness of theoretically derived interventions on improving appropriate polypharmacy for older people in primary care and to investigate the degree to which theory informed the intervention design and the theories that were used.

2. Methods

2.1. Protocol

The protocol for this review was approved by and registered with PROSPERO, an international prospective register of systematic reviews...
2.5. Data collection and analysis

The Cochrane review investigating interventions to improve appropriate polypharmacy was developed to streamline the systematic review process. Full-text articles were also hand-searched. The search strategy was adapted for Cochrane reviews (CINAHL, the Cochrane Library, Embase, MEDLINE, PsycINFO, SCOPUS and Web of Science). The trial registry ClinicalTrials.gov and US National Institutes of Health (NIH) were also searched. Studies published from inception of the database to the search date were considered for inclusion. The original search was conducted in August 2019 and updated in August 2021. The reference lists of eligible studies were also hand-searched. The search strategy was adapted for each database, and contained the following terms: ‘polypharmacy’, ‘aged’ and ‘primary health care’. The search string used for MEDLINE, as an example, is shown in Appendix 3.

2.4. Study records

After removal of duplicates, two review authors screened titles and abstracts to identify studies for inclusion using Covidence®, an online tool developed to streamline the systematic review process. Full-text articles were reviewed and assessed for eligibility by two review authors. Any disagreements over inclusion at full text review stage were discussed and agreed with a third review author. Study authors were contacted (if contact details were provided) to request full-text articles if these were not available to the authors, or to ask for clarification on methodology or results if needed.

2.5. Data collection and analysis

Data extraction forms were pre-defined and developed a priori. The form was piloted with two reviewers independently using an agreed study for inclusion. The two reviewers then independently extracted data from all included studies using the data extraction form. It was anticipated that a meta-analysis would not be feasible, therefore a narrative synthesis was planned to present the results of the review. The primary outcome of interest was the use of theory in the intervention development. The TCS (Appendix 1) was used to evaluate the theoretical underpinning of included studies and the extent to which the theory aided the development of the intervention. Categories 1 to 3 represented

the extent of theory used in the development of the intervention, while categories 4 to 6 encompassed the testing and refinement of the theory used. On the TCS application form, each item in the categories was labelled with the potential responses yes / no / don’t know. An overall judgement of yes / no / partially was then applied to each category on whether the study met all, none, or some of the relevant TCS items. An overall judgement of ‘yes’ was assigned if all items within the category were met, an overall judgement of ‘no’ if none of the items within the category were met and an overall judgement of ‘partially’ if some of the items within the category were met. The second primary outcome if the theoretically derived intervention achieved appropriate polypharmacy was also assessed.

Secondary outcomes of interest included economic (i.e. cost-effectiveness), clinical (i.e. hospitalisation) and / or humanistic (i.e. quality of life) guided by the ECHO (Economic, Clinical and Humanistic Outcomes) model17 and appropriate prescribing as assessed by the chosen validated assessment tool.

2.6. Risk of bias of individual studies

Two reviewers (AG and AR) conducted independent risk of bias assessments on included studies using the Cochrane Risk of Bias version 2.0 (RoB2) tool38 for RCTs and Risk Of Bias in Non-Randomised Studies – of Interventions (ROBINS-I)39 for non-RCTs (Sterne et al. 2016). RoB2 tool provides a framework to assess the possible risk of bias in the results of a RCT. RoB2 is divided into 5 domains: (i) bias arising from the randomization process, (ii) bias due to deviations from intended interventions, (iii) bias due to missing outcome data, (iv) bias in measurement of the outcome, and (v) bias in selection of the reported result. Judgement on the risk of bias is facilitated by signalling questions within the RoB2 tool, where response options include: yes; probably yes; probably no; no; no information. Using the RoB2, studies are assigned a level of bias rating of low, high or unclear. Higgins et al.40 provide a detailed document to assist the user in implementing RoB2 which has been used effectively in a number of systematic reviews.41-43 ROBINS-I addresses seven domains of bias: (i) confounding, (ii) selection bias, (iii) measurement classification of interventions, (iv) deviations from intended interventions, (v) missing data, (vi) measurement of outcomes, (vii) selection of the reported result. Like the RoB2 tool, judgement in each domain is enabled by signalling questions with response options of: yes, probably yes, probably no, no, no information. Some questions will only require an answer if a response to a previous question is yes/ probably yes, or no/ probably no. Signalling questions will determine a judgement of low risk, moderate risk, serious risk or critical risk.

3. Results

3.1. Study selection

Electronic searches identified 15,402 records and hand searches identified a further three records. After removal of duplicates, 12,416 records were screened using the title and abstract. A total of 330 records were assessed for eligibility. Four articles44-47 were identified as eligible for inclusion (Fig. 1). Two publications by Tovio et al. were identified as eligible for inclusion, one that reports the study protocol for the RCT which is presented in the second paper. Therefore, these two separate publications, which represent one individual study are included as one study. A protocol paper47 on the pilot study developed from the feasibility work undertaken by Cadogan et al.,44 was identified (and registered -NCT04181879) but was not included for review as the study had not been completed and published. Due to the small number of included studies, and their heterogeneity, a narrative summary is provided. Thus, two studies, Cadogan et al.,45, a feasibility study, and Toivo et al.46, a RCT, are discussed in this review.
3.2. Study characteristics

Due to the small number of included studies, the use of theory and the range of outcome measures, a narrative synthesis was conducted. Between the two studies, a total of 201 participants were involved (range: 10–191). The percentage of females ranged from 60 to 90% and the mean age of participants ranged from 73 to 82 years. The mean number of medications ranged from 6.4 to 13.1 medications.

A feasibility study conducted by Cadogan et al.44 in the United Kingdom included 10 participants (60% female), with an age range of 68–78 years and the mean number of medicines prescribed was 6.4 medications. The intervention was developed using the Theoretical Domains Framework (TDF).48 The development phase14,49 included interviews with GPs (n = 15) and community pharmacists (n = 15). Findings from these interviews were then mapped to Behaviour Change Techniques (BCTs)50 and embedded within the intervention. The finalised intervention involved four components: (i) GPs watched an educational video on how to prescribe appropriate polypharmacy during a routine consultation, (ii) explicit plans were made between practice staff to ensure patients receive a medication review, (iii) patients attended the practice for a scheduled medication review and (iv) GPs were prompted to carry out a medication review, by practice staff, when the patient arrived at the practice. The GPs involved in the study (n = 4) were positive about the tools used in the intervention, namely the educational video, and all GPs reported changes to patients’ prescriptions as a result of the medication review process. Patients involved were satisfied with the medication review consultation.

Cadogan et al.44 intended to use the Screening Tool of Older People’s potentially inappropriate Prescriptions (STOPP)/Screening Tool to Alert doctors to Right Treatment (START)51 and Medication Appropriateness Index (MAI)52 to assess prescribing appropriateness, following intervention implementation. STOPP/START is an explicit prescribing tool (i.e. criterion-based) which lists instances of potentially inappropriate medications (STOPP) and potential prescribing omissions (START). STOPP lists specific medications, dosages, durations of therapy and drug-drug/drug-disease interactions that are unfavourable in older people. START lists medications that should be prescribed, i.e. those that are clinically indicated in certain clinical conditions. The MAI52 is an implicit (i.e. judgement-based) assessment specifically for use in older patients and includes ten individual criteria that should be considered when assessing the appropriateness of each medication prescribed. Each criterion is rated and all scores from each medication are summed to establish an overall MAI score. As feasibility studies focus on the acceptability of the intervention, the outcomes assessed by Cadogan et al.44 do not fit within the ECHO framework.37

Fig. 1. PRISMA flowchart of the systematic review process.
Toivo et al.46 conducted an RCT in Finland, with 191 participants (90% female) with an age range of 65–96 years. Although Toivo et al.46 did not include a definition of polypharmacy, included patients were prescribed an average of 13.1 medications, therefore the study was eligible for inclusion in this review. The intervention involved a coordinated medication risk management (CoMM) procedure, and its development was theoretically guided by Reason’s systems-based risk management theory on preventing human errors.53 The CoMM included five main stages, involving collaboration between healthcare professionals (nurses, pharmacists and general practitioners) at various stages to identify and resolve clinically significant medication related problems. These stages included (i) risk assessment (via medication reconciliation and prescription review) by nurses and pharmacists, (ii) a triage meeting between pharmacists and GP to decide on course of action e.g. type of medication review, to take, (iii) medication reviews undertaken by pharmacists, with decisions on course of action made by GPs (iv) implementation of recommendations following the medication review and (v) follow-up stage involving patient monitoring.

The primary outcome was medication related problems requiring intervention, assessed by identifying potentially inappropriate medication usage using the Beers criteria,54 an explicit tool to assess prescribing appropriateness. Excessive use of anticholinergic and serotoninergic medications and clinically significant drug interactions were also assessed. Participant or patient feedback was not included in their reported results. The authors note that the triage meeting between pharmacists and GPs was feasible and enabled more time for the healthcare professionals to focus on patients with more healthcare needs, however, this was not included as an outcome measure, nor officially assessed within the study.

Summary characteristics of the two included studies are shown in Table 1.

### 3.3. The theory coding scheme

Neither of the included studies aimed to test and refine the underpinning theory, such as adding or removing constructs to the theory applied. Therefore, only categories 1–3 (i.e. the extent of theory used in the development of the intervention) of the TCS are discussed in this review. Categories 4–6 encompass the testing and refinement of the theory used which was not undertaken. The main findings from categories 1–3 are presented below and summarised in Table 2.

#### 3.4. Category 1: Is theory mentioned?

Both studies mentioned theory. Cadogan et al.44 based their intervention on a framework, the TDF, while Toivo et al.46 based their intervention on a single theory, Reason’s System-Based Risk Management Theory.53 The TDF is a collection of 33 theories of behaviour and behaviour change, grouped into 14 domains (knowledge; skills; social/professional role and identity; beliefs about capabilities; optimism; beliefs about consequences; reinforcement; intentions; goals; memory, attention and decision processes; environmental context and resources; social influences; emotion and behavioural regulation). Cadogan et al.44 conducted qualitative interviews with GPs and community pharmacists, based on the TDF. These interviews aimed to identify possible theoretical domains/constructs that GPs and community pharmacists perceived as barriers or facilitators in the prescribing of appropriate polypharmacy for older people.14

Reason’s System-Based Risk Management Theory on preventing human error53 was applied to guide the construction of the CoMM procedure used by Toivo et al.46 The system approach states that humans are expected to make errors and it may not be possible to make humans error-free, however the conditions and the environment in which humans work can be altered by introducing barriers and safeguards to the work environment to enhance safety.53 Reason considers team work to be one type of safeguard.53 CoMM involved nurses, pharmacists and GPs working together to identify and resolve medication-related problems and provided additional geriatric pharmacotherapy and system-based medication risk management education to healthcare professionals involved. Toivo et al.46 did not link any specific constructs of Reason’s System-Based Risk Management Theory as predictors of ensuring appropriate medication use.

### 3.5. Category 2: Are relevant theoretical constructs targeted by the intervention?

In the intervention described by Cadogan et al.,44 the domains that arose during the interviews were then mapped to BCTs from an established taxonomy and embedded into the intervention as ‘active ingredients’.14 A set

### Table 1

**Summary of included study characteristics.**

| Study (country) | Study type | Participant characteristics | Intervention target and provider | Brief description of intervention | Theory used | Validated tool to assess appropriateness | Primary outcome |
|----------------|------------|----------------------------|----------------------------------|----------------------------------|------------|------------------------------------------|-----------------|
| Cadogan et al.44 (United Kingdom) | Feasibility study | 1. Number of participants (% female) 2. Mean age (±SD) 3. Mean No. medications (± SD) | Target: General Practitioner (GP) Provider: Researcher | Intervention components (1) GPs watched educational video on prescribing appropriate polypharmacy (2) patients attended for scheduled medication review (3) explicit plans were made between practice staff to target necessary patients (4) GPs were prompted to carry out this plan by practice staff when the patient arrived at the practice | Theoretical Domains Framework | STOPP/START MAI | Usability and acceptability of intervention to GPs and patients Acceptability of medication review by patients |
| Toivo et al.46 (Finland) | RCT | 1. 191 (90%) 2. 82.8 (± 7.1) 3. 13.1 (± 4.1) | Target: Home care nurse, Coordinating pharmacist, GP, Community pharmacist Provider: Researcher | Five step process involving (1) medication risk screening (2) triage meeting (3) collaborative medication reviews by community pharmacists (4) implementation of required actions, changes to medications (5) follow-up | Reason’s systems-based risk management theory on preventing human errors | Beers’ criteria | Clinically significant medication-related risks needing intervening actions using Beers’ criteria |

MAI = Medication Appropriateness Index  RCT = Randomised Controlled Trial  SD = Standard deviation  STOPP/START = Screening Tool of Older Person's Prescriptions/Screening Tool to Alert doctors to the Right Treatment.
et al.,46 study participants were not recruited based on theory and the inter-
ventions?

3.6. Category 3: Is theory used to select intervention recipients or tailor

Medication change and all control group participants’ data was analysed
for the ITT. Intervention arm participants with at least one implemented
Data from all participants, regardless of medication changes, was analysed
analysed data with the intention to treat (ITT) and per protocol analysis.

BCT = Behaviour Change Techniques TDF = Theoretical Domains Framework.

BCT is defined as a component of an intervention that is designed to alter
the processes that regulate that behaviour.55 The BCTs embedded in the in-
tervention include salience of consequences, modelling or demonstrating
behaviour, action planning and prompts/cues. As a result, theoretical con-
structs are targeted by the intervention. In the study described by Toivo
et al.,46 Reason’s system-based risk management theory was used to
structs are predictors of ensuring appropriate medication use

Category 2: Are relevant theoretical constructs targeted by the intervention?39

Participants were selected on meeting pre-defined inclusion criteria, not on using theory
No – Intervention was not tailored to recipients based on theory
No

Category 3: Is theory used to tailor the

No – Authors did not state that the constructs of the theory used
were predictors of ensuring appropriate medication use
No – Reason’s system-based risk management theory

3.7. Effectiveness of theoretically derived interventions to improve appropriate
polypharmacy

As only one feasibility study and one RCT were included in the review,
the effectiveness of theoretically derived interventions aimed at improving
appropriate polypharmacy in primary care could not be determined. It was not
feasible for Cadogan et al.44 to apply the validated assessment tools
(STOPP, START and MAI) to the prescribing data collected, notably due to
insufficient level of detail of clinical diagnoses and treatment durations
recorded.44

Due to medication changes being only partially applied, Toivo et al.46
analysed data with the intention to treat (ITT) and per protocol analysis.
Data from all participants, regardless of medication changes, was analysed
for the ITT. Intervention arm participants with at least one implemented
medication change and all control group participants’ data was analysed
for the per protocol analysis.

In the ITT analysis, no significant changes were found in any
education-related outcome between the intervention and control groups
from baseline to 12-months follow-up. For example, the number of
potentially inappropriate medications, according to Beers’ criteria, in the
intervention group (N = 65) at baseline and 12 month’s follow-up was 61
(93.9%) and 63 (96.9%) respectively; in the control group (N = 64) was
58 (90.6%) at baseline and 57 (89.1%) at 12 months’ follow-up.

Similarly, per protocol analysis did not identify any significant differ-
ence in medication-related outcomes between the intervention group per
protocol and the control group over the 12-month follow-up period. For ex-
ample, the number of potentially inappropriate medications according to
Beers’ criteria in the intervention group per protocol (N = 27) was 26
(96.3%) at baseline and 25 (92.6%) at 12 months’ follow-up. There was a
notable decrease in the use of benzodiazepines in the intervention group
per protocol (from 55.6 to 37.0%; p = 0.03) and in the proportion of
patients using ≥3 psychotropic medications (from 18.5 to 7.4%; p = 0.07).

3.8. Risk of bias of individual studies

Toivo et al.46 was judged to have a high risk of bias using the RoB2 tool,
largely due to the study being open-label in design. Fig. 2 provides an over-
view of the quality rating for Toivo et al.46 A risk of bias grading for
Cadogan et al.44 could not be established via the ROBINS-I tool due to the
feasibility nature of the study.

4. Discussion

This is the first systematic review to provide an examination of theoreti-
cally derived interventions aimed at providing appropriate polypharmacy
to older adults in primary care. Only one feasibility study (Cadogan et al.)44
and one RCT (Toivo et al.)35,46 were included, signifying the lack of theoret-
cally derived interventions in this area, using validated tools to assess the
appropriateness of prescribing, and consequently the overall effectiveness
of theoretically derived interventions to improve appropriate polyphar-

Table 2

| Item no. | Cadogan et al.44 | Toivo et al.46 |
|----------|------------------|----------------|
| Category 1: Is theory mentioned?46 | Yes – TDF | Yes – Reason’s system-based risk management theory |
| 1 Yes – TDF | | |
| 2 Yes – Targeted constructs mentioned as predictors of behaviour | No – Authors did not state that the constructs of the theory used were predictors of ensuring appropriate medication use |
| 3 No – TDF | No – Reason’s system-based risk management theory |
| Rating Partially | Partially |
| Category 2: Are relevant theoretical constructs targeted by the intervention?39 | Yes – Theory was used to select intervention techniques which were then mapped to BCTs |
| 2 Yes – as above | No – Theory was used to guide the model development, but not to select intervention techniques |
| 5 Yes – Theory was used to select intervention techniques which were then mapped to BCTs | No – Theory was used to guide the model development, not select intervention techniques |
| 7 Yes – All intervention techniques are explicitly linked to theoretical constructs/predictors | No – Theory was used to guide the model development, not select intervention techniques |
| 8 Yes – see item 7 | No – see item 7 |
| 9 Yes – see item 7 | No – see item 7 |
| 10 Yes – All constructs were explicitly linked to at least one intervention technique | No – Theory was used to guide the model development, but not to select intervention techniques |
| 11 Yes – see item 10 | No – see item 11 |
| Rating Yes | No |
| Category 3: Is theory used to tailor the intervention to select the intervention recipients?46 | No – Participants were selected on meeting pre-defined inclusion criteria, not on using theory |
| 4 No – Participants were selected on meeting pre-defined inclusion criteria, not on using theory | No – Intervention was not tailored to recipients based on theory |
| 6 No – Intervention was not tailored to recipients based on theory | No |
| Rating No | No |

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As mentioned above only two studies were included in this systematic review, Cadogan et al. used the TDF while Toivo et al. used Reason’s system-based risk management theory. The TDF is a widely cited framework that is used in healthcare intervention development and is also used to understand components of people’s behaviour. As the TDF brings together 33 different behaviour theories, it is relatively easily applied, and with 14 domains, it covers a wide range of behaviour change components including knowledge, beliefs about capabilities, environmental context and resources, and social/professional role and identity. Cadogan et al. noted that the TDF simplifies psychological theory in behaviour change which makes the theories more accessible to non-health psychologists and as they intended to change GP behaviour around prescribing, it was necessary to include a behaviour change theory. Interventions that have used the TDF in their development include interventions to improve the management of acute low back pain in general practice, the management of mild traumatic brain injury in the emergency department, best hand hygiene practices amongst healthcare practitioners and interventions to improve adherence to polypharmacy, and many have noted intervention effectiveness attributable to using the TDF as the theoretical framework in their development. A recent systematic review investigating the use of the TDF in health behaviour intervention development concluded that there is limited evidence on how the framework has been used to support behaviour change interventions and that further research is required to establish how to effectively apply the TDF to intervention development.

The theory used by Toivo et al., Reason’s system-based risk management theory, is commonly used in studies explore the occurrence and causes of errors. For example, it has been used to identify perceived causes of prescribing errors by junior doctors and medical interns to understand the causes of non-adherence to prescribed medications and to explore the supply of non-prescription medications from community pharmacies. Tovio et al. used this theory to construct the collaborative procedures between healthcare professionals involved in the intervention, although how this was undertaken is not described in either paper associated with this study.

Selecting an appropriate theory for use in intervention development can be challenging, especially for novice researchers. It is therefore likely that researchers may choose a theory of which they are knowledgeable and comfortable using, even if it does not meet all relevant categories of the planned intervention. Birken et al. state that guidance is needed in theory selection, however this would be challenging given the wide range of theories and study designs. A recent study suggests four key questions when choosing a theory: 1) what is the mechanism of action, and does it fit the theory? 2) can the theory be implemented? 3) can the theory be used in similar contexts? 4) can the theory be used in different contexts? It is important that researchers clearly state their reasons and intentions for selecting such theory in their intervention design and development. Knowing the focus of both interventions, it is understandable why each theory was chosen for the interventions.

The application of the TCS to these two studies demonstrated that only Cadogan et al. applied theory in the selection of constructs for use in the intervention, and neither study attempted to refine the theory used. These elements associated with theory use, including a detailed rationale of the theory chosen, are often not described in intervention studies.

It was not possible to examine the effectiveness of theory-based interventions to improve appropriate polypharmacy in primary care, because of the lack of published studies and outcomes. Additionally, one of the studies was not sufficiently powered to establish the effectiveness of the intervention, i.e. it was a feasibility study. A feasibility study is often conducted before a main study, as recommended by the MRC framework and is used to estimate parameters for design in the larger study, such as recruitment, data collection and follow-up rates. Feasibility studies rarely focus on the main outcomes of interest, but more on the acceptability of what is included in the study; this was the approach taken by Cadogan et al. and there was no attempt to assess the effectiveness of the intervention. Overall, Toivo et al. did not report intervention effectiveness, but when examined carefully via per protocol analysis, a reduction in central nervous system medications was found, along with a decrease in the use of benzodiazepines and opioids, as well as a decline in the proportion of participants using ≥3 psychotropic medications. This is a positive finding as there are significant negative outcomes associated with long-term benzodiazepine and opioid use including falls, dependency, hospitalisation and dementia amongst others, and the challenges connected to deprescribing these are widely reported; therefore a reduction in their prescribing is welcomed.

Whilst a significant reduction in potentially inappropriate medications was not observed by Toivo et al., the study highlighted challenges in working with different healthcare professionals, such as physicians and community pharmacists. Challenges in implementation of the proposed study, for example, limited resources and reluctant attitudes from healthcare professionals involved, were noted by Toivo et al. A pilot study may have identified these challenges, thus enabling Toivo et al. to address them, potentially making the RCT more effective. Guidelines by the MRC recommend the use of pilot studies in complex interventions before proceeding to a RCT. However, the use of theory in intervention effectiveness could not be determined in this review due to the small number of included studies.

This systematic review has highlighted that, despite theory being recommended as part of intervention development, it is not routinely used in intervention development focusing on appropriate polypharmacy. This should be addressed in future studies. Implementing theory has become simplified in recent years due to numerous theoretical frameworks being developed, such as the TDF and the Behaviour Change Wheel. It is not entirely clear yet if we should advocate for the use of theory in this area. The TCS has highlighted that studies utilising theory in the development of interventions did not use theory it its full extent. Whilst developed as a tool to assess use of theory in developed interventions, the TCS could also be referred to during intervention development as a guide of where and when to use theory in the intervention.

4.1. Strengths and limitations

This systematic review is the first to examine the extent of theory in the development of interventions aimed to improve appropriate polypharmacy for older people in primary care, using validated tools to assess prescribing, and has identified a gap in the literature surrounding theoretically derived interventions focusing on appropriate polypharmacy. This review has been
reported in adherence with the PRISMA guidelines for systematic reviews.25

This review was limited to articles published in the English language. Comprehensive search strategies were conducted for this review, however studies that met the inclusion criteria but were not adequately indexed, may have been missed. Studies that did not define polypharmacy as at least four or more medications, or the average number of medications prescribed was under four, were excluded. The assessment of theory was based on the information supplied by the authors. Studies involving the use of theory may have been missed or excluded from the review, if theory was not clearly stated.

5. Conclusion

It is evident from this review that there is a lack of theoretically derived studies aiming to achieve appropriate polypharmacy in older people. Due to only two studies being included in the review, including one feasibility study, no overall conclusion on the effectiveness of theoretically derived interventions could be drawn. The incorporation of theory into intervention development in the area of appropriate polypharmacy should be encouraged. The theory used needs to be carefully chosen and fully understood by the researchers before applying it to intervention development. Guidelines on incorporating theory into intervention development and guidance on selecting appropriate theory is required.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study was funded by the HSC R&D Division Cross-border Healthcare Intervention Trials in Ireland Network (CHITIN) programme, funded by the European Union’s INTERREG VA Programme, managed by the Special EU Programmes Body (SEUPB) project reference CHI/5431/2018. The funding body (and sponsor) were not involved in the design of the study or in the writing of this manuscript.

Appendix 1

The theory coding scheme (adapted from Patton et al.)32

| TCS category | Items | Description |
|--------------|-------|-------------|
| Category 1: Is theory mentioned? | Theory/model of behaviour mentioned (Item 1) | Models/ theories that specify relations amongst variables to explain or predict behaviour are mentioned, even if the intervention is not based on this theory. Evidence that the psychological construct related to (correlates/predicts/causes) behaviour should be presented within the introduction or method
| | Targeted construct mentioned as predictor of behaviour (Item 2) | The intervention is based on a single theory (rather than a combination of theories or predictors)
| | Intervention based on single theory (Item 3) | |
| Category 2: Are relevant theoretical constructs targeted by the intervention? | Targeted construct mentioned as predictor of behaviour (Item 2) | The intervention is explicitly based on a theory or predictor or combination of theories or predictors
| | Theory/predictors used to select/develop intervention techniques (Item 5) | Each intervention technique is explicitly linked to at least one theory-relevant construct/predictor
| | All intervention techniques are explicitly linked to at least one theory relevant construct/predictor (Item 7) | At least one, but not all, of the intervention techniques are explicitly linked to at least one theory-relevant construct/predictor
| | At least one, but not all, of the intervention techniques are explicitly linked to at least one theory-relevant construct/predictor (Item 8) | |
| | Group of techniques are linked to a group of constructs/predictors (Item 9) | A cluster of techniques is linked to a cluster of constructs/predictors
| | All theory-relevant constructs/predictors are explicitly linked to at least one intervention technique (Item 10) | Every theoretical construct within a stated theory, or every stated predictor (see item 5), is linked to at least one intervention technique
| | At least one, but not all, of the theory relevant constructs/predictors are explicitly linked to at least one intervention technique (Item 11) | At least one, but not all, of the theoretical constructs within a stated theory or at least one, but not all, of the stated predictors (see item 5) are linked to at least one intervention technique
| Category 3: Is theory used to select intervention recipients or tailor interventions? | Theory/predictors used to select recipients for the intervention (Item 4) | Participants were screened/selected based on achieving a particular score/level on a theory-relevant construct/predictor
| | Theory/predictors used to target intervention techniques to recipients (Item 6) | The intervention differs for different sub-groups that vary on a psychological construct (e.g. stage of change) or predictor at baseline
| Category 4: Are the relevant theoretical constructs measured? | Theory-relevant constructs/predictors are measured (Item 12) | At least one construct of theory (or predictor) mentioned in relation to the intervention is measured post-intervention
| | Quality of measures (Item 13) | All of the measures of theory-relevant constructs/predictors had some evidence for their reliability
| Category 5: Is theory tested? | Theory relevant constructs/predictors are measured (Item 12) | At least one construct of theory (or predictor) mentioned in relation to the intervention is measured post-intervention
| | Quality of measures (Item 13) | All of the measures of theory relevant constructs/predictors have been previously validated
| | Randomization of participants to condition (Item 14) | At least one, but not all, of the measures of theory relevant constructs/predictors have been previously validated

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### Completed PRISMA checklist.

| Section/topic                  | Checklist item                                                                 | Reported on page |
|-------------------------------|-------------------------------------------------------------------------------|-----------------|
| Title                         | Identify the report as a systematic review, meta-analysis, or both.            | 1,7             |
| Abstract                      | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1,2             |
| Introduction                  | Describe the rationale for the review in the context of what is already known. | 3–6             |
| Rationale                     | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PIECOS). | 6               |
| Methods                       | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including registration number. | 7               |
| Eligibility criteria          | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 7               |
| Information sources           | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 8               |
| Search                        | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 8, 37 (App.3)   |
| Study selection               | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 8               |
| Data collection process       | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8, 9            |
| Data items                    | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8               |
| Risk of bias in individual studies | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level, and how this information is to be used in any data synthesis). | 9,10            |
| Summary measures              | State the principal summary measures (e.g., risk ration, difference in means).  | N/A             |
| Synthesis of results          | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis. | N/A             |
| Risk of bias across studies   | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting with studies). | N/A             |
| Additional analyses           | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A             |
| Results                       | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 11,12           |
| Study selection               | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 13–16           |
| Risk of bias within studies   | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 20,21           |
| Results of individual studies | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A             |
| Synthesis of results          | Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency. | N/A             |
| Risk of bias across studies   | Present results of any assessment of risk of bias across studies (see item 15). | N/A             |
Appendix 3

MEDLINE search string.

Term(s) Result
1. exp Polypharmacy/ (keyword, map term to subject heading) 5843
2. (polypharmacy or polymedicines or polypharmacotherapy or ‘multiple pharmacotherapy’ or ‘multiple medicines’ or ‘purplications’ or ‘many medications’ or ‘many drugs’ or restrict* or unprescrib* or ‘drug therapy’ or ‘multi-drug therapy’ or multiple drug therapy’).mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 2,559,786
3. 1 or 2 6,672,415
4. exp Aged/ (keyword, map term to subject heading) 2,559,786
5. (old* or geriatric or elderly or aged or ageing or ‘senior citizen’ or senium).mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 3,304,577
6. 4 or 5 6,672,415
7. exp primary health care/ (keyword, map term to subject heading) 177,145
8. ‘primary care’ or ‘primary medical care’ or ‘primary health care’).mp. [mp = title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 173,143
9. 7 or 8 173,143
10. 3 and 6 and 9 13,568

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