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Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review

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ABSTRACT

Objectives: The aim of this review was to understand *how* and *why* effective multi-chronic disease management (CDM) interventions (identified from a systematic review) influence health outcomes in older adults age 65 years or older.

Design: A realist review.

Data sources: Electronic databases including MEDLINE and EMBASE (inception to Dec 2017); and the grey literature.

Eligibility criteria for selecting studies: We considered any studies (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies) as long as they provided data to explain our programme theories and effectiveness review (published elsewhere) findings. The population of interest was older adults (age ≥ 65 years) with two or more chronic conditions.

Analysis: We used the RAMESES quality and publication criteria for our synthesis aimed at refining our programme theories such that they contained multiple Context-Mechanism-Outcome (CMO) configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography to separate units of data from articles, and to derive explanatory statements across them.

Results: 106 articles contributed to the analysis. We refined our program theories to explain multimorbidity management in older adults: 1) Care coordination interventions are effective because they represent a structured approach; 2) Patients focus on the condition that is associated with the most undesired symptoms; providers focus on the condition that most threatens morbidity and mortality; 3) Effective management requires both clinical management and self-management.

Conclusions: Our realist review contributes to the knowledge of the underlying mechanisms of multi-CDM interventions for older adults. To optimize care, both clinical management and patient self-management need to be considered. To mitigate the complexities of multimorbidity management, patients tend to focus on preserving quality of life while providers are most concerned about reducing morbidity and mortality.

ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first realist review to explain *why* multimorbidity interventions work, *for whom*, and *under what circumstances* to improve outcomes for older adults with multimorbidity – findings can be used to inform practice and policy decisions in the management of older adults with multiple chronic conditions
- Care coordination interventions are effective because they represent a structured approach to holistic care. To mitigate the complexities of multimorbidity management, patients focus on reducing their undesired symptoms and preserving their quality of life, while providers focus on the condition that most threaten a patient's morbidity and mortality
- It is important to ensure that chronic disease management prioritization is undertaken in collaboration with patients
- Many of our included studies did not have complete data to enable optimized Context-Mechanism-Outcome (CMO) investigations
- Incomplete reporting also impacted our ability to fully test our theories and therefore, we could not completely elucidate the interrelationships within and between all of our CMO configurations

BACKGROUND

The global population is aging, with two billion people expected to reach 60 years of age and older by 2050[1,2]. It is now more common for older adults to have multiple chronic diseases than to have single diseases or no chronic medical conditions at all[3]. The burden of chronic disease is also on the rise globally[1,4] with more than half of older adults (age ≥ 65 years) living with high-burden chronic conditions (i.e., highly prevalent and associated with premature death and increased health care utilization)[3,5]. Older adults also have greater health care needs, are at higher risk for adverse health outcomes, and experience more frequent hospitalizations[6], yet only 55% receive appropriate care[7,8]. In response, different chronic disease management (CDM) interventions have been created. For example, a program designed to encourage older adults with COPD and depression to adhere to anti-depressants and pulmonary rehabilitation[9]. Although promising, CDM interventions have shown varying effectiveness[10,11] in part, because they are not usually developed for older adults or created for sustained use; and very few are designed to deliberately address multimorbidity[8,12].

To address these gaps, we conducted a systematic review to identify effective CDM interventions that integrate the care of ≥ 2 high-burden chronic diseases affecting older adults (published elsewhere)[13]. However, a systematic review is not always enough to inform practice and policy decisions, so our objective was to conduct a realist review alongside to explore the underlying mechanisms and contexts by which these CDM interventions work or don't work, for whom, under what circumstances and why[14]. Given our rapidly aging population, there is an urgent need to understand how and why multimorbidity interventions influence health outcomes to optimise patient care.

METHODS

Study Design

Our protocol was published[15], and registered with PROSPERO (registration number CRD42014014489). We applied the RAMESES quality[16] and reporting criteria[17]. The systematic review methods and findings are reported elsewhere[18].

Programme theory development

To identify our initial programme theories (i.e., what multimorbidity interventions are comprised of, how and why they are expected to work and what outcomes they might generate), we used an iterative, consensus-based process. We considered two major sources to identify any published or unpublished literature[19]: 1) Medline and Google Scholar describing models, frameworks, theories of multimorbidity, chronic disease management, and complex interventions; and 2) content and methods experts on our team (geriatricians, family physicians, and health services and realist review experts). Duplicate screening of 97 reports by two reviewers identified 18 initial programme theories. Through team discussions, we narrowed this list to two programme theories to be tested and refined in our realist review:

1. *Complex multi-CDM interventions in different settings [context(s)] may improve patient outcomes such as [outcome(s)] for older adults because of [mechanism(s)].*
2. *Health prioritization is an important aspect of multimorbidity management because of [mechanism(s)] in particular settings [context(s)]. Interventions that consider patient values and circumstances, the evidence, and the clinician's expertise can improve outcomes such as [outcome(s)] in particular settings such as [context(s)] because of [mechanism(s)].*

Search strategy

We identified potentially relevant articles for our realist review (i.e., to test our programme theories) through our systematic review search strategy[18] (inception to December 2017) as well as through additional iterative, targeted searches as needed[16] An experienced information specialist performed these additional searches in Medline and Embase (Appendix 1).

Selection and appraisal of documents

To increase the efficiency of our searching and screening process, reviewer pairs independently screened titles and abstracts simultaneously for both the systematic review and realist review. We considered any study design for inclusion (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies). During full-text screening, we considered all articles that were identified for the systematic review as well through additional targeted searches to explain our programme theories and effectiveness review findings. Two reviewers

independently assessed each article for relevance (*does the source contain any data that could be interpreted as having our relevant context, mechanism or outcome for programme theory development?)* and rigor (*How trustworthy are the data? Does the article provide enough detail on how conclusions were reached irrespective of study design?)*

Data extraction

We created and pilot tested a standardized data extraction form. Data items were driven by our purpose to refine our programme theories through context-mechanism-outcome (CMO) configurations (i.e., if we were able to infer an explanation for the cause [M] for a particular outcome [O] under the influence of one or more particular contexts [C]). For example, computer-based counselling systems (intervention) targeting older adults and providers in primary care (C) are not acceptable (O) if they do not show any relative advantage over the current system (M1) and if inconsistent with providers' current practice workflow (M2). After extracting excerpts in duplicate, reviewer pairs independently assigned an associated concept code and iteratively developed a codebook of concepts (Appendix 2) that was used to code subsequent excerpts; any discrepancies were discussed and resolved as a team.

Analysis and synthesis processes

We used the RAMESES quality[16] and publication[17] criteria to guide the synthesis of our realist review. Our goal was to refine our programme theories such that they contained multiple CMO configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography[20] to separate units of data from articles, and to derive explanatory statements across them. *Step 1*: reviewer pairs independently extracted relevant excerpts from articles. *Step 2*: One reviewer sorted excerpts by concept for each study and developed consolidated statements (groups of CMO configurations) for each. A second reviewer audited the first reviewer's statements by checking for agreement and consistency with their own interpretations. *Step 3*: As a team, we examined and compared consolidated statements *across* studies to derive explanatory statements. These were then used to refine our *programme theories* aimed at explaining the outcome patterns we found within the effectiveness review.

Deviations from our protocol in conducting our realist review

We followed the methods as outlined in our protocol[15] with a few exceptions. First, we switched to an auditing process during *Step 2* of the analysis to make our process more efficient. This involved an auditor checking the work of a primary reviewer. Second, since our process to finalize the list of initial programme theories identified an area that was not covered by our systematic review search (i.e., health prioritization), we added a secondary search strategy to capture this literature as described above.

Patient and Public Involvement

Patients were not involved in the conduct of the review but older adults with multiple chronic conditions are involved in developing key messages for this research. These patients are also part of our broader integrated knowledge translation team to co-design an electronic self-management tool that integrates the care of multiple chronic conditions (KeepWell©); this tool is being informed by this review.

RESULTS

Study characteristics

Figure 1 shows the flow of article selection. Of 2435 potentially relevant citations that were screened for relevance, 124 articles were reviewed in full-text, and 106 articles contributed to the analysis. Studies were published between 2002 and 2016 mostly in the United States (n = 32), the UK (n = 19), Canada (n = 14), Germany (n = 11), and Australia (n = 10). Most of the articles (75%) were about multimorbidity (n = 50) or disease prioritization (n = 29), and 27 studies (25%) addressed specific chronic disease combinations.

Programme theories

Using data from our included studies, we iteratively developed and refined our initial two programme theories as well as a third programme theory that emerged from our data. Detailed descriptions (including all CMO configurations) are in Appendices 3-6.

Programme theory 1: Care coordination interventions for multimorbidity management

Almost one-half of the interventions described in our realist review were "care coordination" interventions (i.e., changes in how healthcare workers interact with each other or patients to ensure timely and efficient delivery of healthcare)[21]. Appendix 3 shows their CMO configurations. Overall, we found that care coordination interventions in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They address multiple conditions through interdisciplinary teams or multidisciplinary disease management, providing specific mechanisms for communication, and establishing formal roles for providers and patients. We identified three specific types of care coordination approaches that have potential for impact: *1) Team-based* or collaborative approaches involve highly trained clinicians[22] providing holistic and coordinated care[23] including spending time with patients to discuss all their concerns, and to prevent care overlap and gaps[24]. Patients are given education, counseling and other support services to address their disease(s), medications, and lifestyle[25]. Team-based approaches can provide access to specialists[22] and a wider range of services, and provide evidence-based care solutions for multiple conditions in parallel (not in tandem)[26]. Optimized care outcomes are most likely to occur through interdisciplinary communication and collaboration[26,27], when teams comprise highly trained and skilled members[22] who understand and accept each other's roles[22], provide opportunities[23,26] and time[22] to share information[27], and collaborate on patient care[22,23,26,28]. Other contexts in which these mechanisms are triggered include teams that have dedicated members who provide additional support to patients[22,26] or providers[27], receive training[22,26,27], and have a robust and well-functioning communication system[26,28]. *2) Disease management* programs follow a "script" for how to provide effective patient care via care protocols or plans, which define the division of tasks, support the follow-up and coordination of action[29,30], and help to sustain a philosophy of common care[28]. Systematized care is achieved through checklists, follow-up timetables[28-30], and treatment targets[28], which can lead to a shared philosophy of care[28,30] and optimized decision making[28]. *3) Case management*: Case managers are trained health care professionals who are the main contact (and conduit of information) between a patient and involved providers[22], and most appropriate for multimorbidity management when there may be multiple and diverse providers involved in a patient's care. When case managers are the primary contact[30,24], care is perceived

by patients as continuous[31,32], coordinated[32] and more individualized[9,24], and fosters the development of the skills and confidence patients need to self-manage their health[31].

Programme theory 2: Disease Prioritization in multimorbidity management

The CMO configurations of disease prioritization are described in Appendix 4. Multimorbidity management is perceived as confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[33], disease and treatment interactions and possible conflicts[34,35], and the difficulty of attributing symptoms to conditions[35]. Multimorbidity can create a cognitive and emotional overload in patients and providers[36], so a common strategy they use is to focus on one condition at a time. Patients and providers focus their attention by prioritizing one condition over another for a specified period of time, or until particular outcomes are achieved[37,36]. However, patients and providers approach prioritization differently. Patients make judgements based on the symptoms they experience and need the most need attention. They identify the most undesired symptoms and focus on their associated condition(s)[38-43] or those that threaten their social activities[39,44,45], limit their independence[37,44] and have potentially severe long-term consequences if not addressed[37,39]. Providers prioritize conditions based on their judgments about the prognosis or severity of the condition and place greater emphasis on conditions with more serious outcomes[35,38,40,41,44,45]; they focus on conditions that threaten a patient's morbidity and mortality[35,38,40,41,44], those they think they are better equipped to address (e.g., physical over emotional[43,46]), and whether the patient is likely to benefit from treatment[35,38,46,47]. What's common among patients and providers, is that they both consider conditions that they feel *capable* of addressing[36-38,46], and both consider the cascading effects of multimorbidity and the interrelatedness of these conditions during the prioritization process[37,48]. For patients, the cascading effects of multimorbidity are particularly challenging. Patients may find it difficult to determine which chronic disease is causing a particular symptom because conditions may share similar symptoms[49] or the treatment of one condition may aggravate the other[37,50-52] or cause other antagonistic effects[36,37,51]. Self-management is therefore a challenge for patients because the diagnosis of (and receipt of information) about a new condition compounds the complexity and uncertainty of what to do[53]. Figure 2 shows our conceptualization of disease prioritization from these perspectives.

Programme theory 3: Patient self-management in multimorbidity

The CMO configurations of multimorbidity self-management are in Appendix 5. Multimorbidity is perceived by patients as a burden because of the volume of information and recommendations provided[54,55] which are often inconsistent or conflicting, and the cognitive and emotional overload required to assimilate this information or to make lifestyle changes[53]. Subsequently, this can lead to confusion and non-adherence to recommendations[34,37,44,56,57] and may also trigger cognitive and emotional overload. Specific explanations to these outcomes include: 1) self-management regimens are designed to fit their condition rather than their health priorities, lifestyle, and available resources[58,59]; 2) prescribed medications are unwieldy (too many, taken often, and difficult to keep track of)[55,60] or mismanaged[61]; 3) difficulties with following the required diet and exercise routine[37,55,62] and to see multiple providers[61]; 4) not knowing how to respond to adverse drug effects[60,61]; and 5) experiencing communication barriers due to linguistic and cultural diversity[61]. Self-management is especially challenging for older adults with cognitive impairment[59] or anxiety[51] in addition to other chronic conditions, as these contexts can interact to increase people's perceived illness burden[39]. In particular, if depression is the additional condition, older adults may choose not to do anything at all because they either consider it a normal part of aging or reluctant to seek treatment due to the stigma associated with mental health problems[63]. Depression, as a context, can therefore also trigger additional mechanisms that reduce a patient's ability to self-manage chronic conditions[36,37,43,53,63-65]: reduced motivation, energy, self-efficacy; and feelings of hopelessness[65], and stress[53]. A number of feedback loops are activated because illness burden can interfere with a person's ability to engage in health promotion (e.g., exercise). This can lead to negative consequences (e.g., weight gain[53], reduced quality of life, functional decline), and in turn impair mood, social networks, and self-management behaviours[50]. Multimorbidity self-management is also influenced by the lack of available resources[36] (e.g., adequate finances[37,50], social supports[23,37,50,59,66] or transportation[37]) or low health literacy[67] or skills to manage adverse effects[51,68]. Older adults are interested in self-management tools that provide health condition information[55]; share, coordinate and synthesize information with and between providers; and connect them with other patients[55]. Physicians can support this by tailoring information to the stage of the patient's condition[69], having interactions with patients[57], providing information[57], and fostering a collaborative approach to care[70].

DISCUSSION

In this realist review we developed and refined our programme theories to explain why coordination of care interventions (found to have the most potential for impact in our systematic review) work to improve outcomes for older adults with multimorbidity. Care coordination interventions have the potential to be effective in primary care because they represent a structured approach to comprehensive care, and address multiple conditions through interdisciplinary teams or multidisciplinary disease management, by providing specific processes for communication, and establishing formal roles for providers and patients. *Team-based approaches* provide the right care at the right time, *disease management* offers a systematized approach to care, and *case management* offers a dedicated case manager as the conduit of care.

In addition to refining our programme theories, we generated explanations associated with these theories. Appendix 6 shows the CMO configurations to explain of multimorbidity management overall. Figure 3 shows our conceptualization of multimorbidity management, which suggests that optimized care requires both clinical management and patient self-management, with the caveat that each needs to consider identified challenges from the perspective of those affected by them (patient, provider, system). From the patient perspective, clinical management can be confusing due to conflicting messages, which is compounded in the presence of depression, impaired cognition, or poor health literacy. Self-management is challenging for patients because of the high burden of required lifestyle changes and adherence to multiple and often conflicting treatment regimens. Multimorbidity can also have cascading effects due to the nature of how chronic diseases are interrelated. From the provider perspective, multimorbidity management may be perceived as overwhelming because evidence to guide clinical decision making is lacking. From a system perspective, even if primary care is the optimal setting for multimorbidity management, it may not always have the infrastructure to support optimal strategies such as care coordination.

Strengths and limitations

To our knowledge, this is the first realist review investigating older adult multimorbidity aimed at explaining *why* effective multi-CDM interventions (identified through a systematic review) work/don't work for whom, under what circumstances and why. This can better inform practice

and policy decisions about multimorbidity management than a systematic review alone. A Cochrane review investigated interventions in multimorbid patients of any age[60] and found mixed results, but concluded that interventions that were integrated with care and targeted specific risk factors or functional difficulties may be more effective[60]. Our findings build on this work by providing *explanations* for why such interventions may be effective. Additionally, we focused exclusively on older adults because they represent a relatively unstudied population, and given their projected population growth, they urgently need our attention to optimize their care. The NICE guidelines on clinical assessment and management of multimorbidity[71] (one of few existing multimorbidity guidelines) support many of our findings. They emphasize the need to find synergies in care regimes and simplifying care where possible. They also describe a preferred approach to care, which involves establishing patient goals, values and priorities, where patients are encouraged to describe their preferred decision making approach and what aspects of their life they prioritize[71]. A recent qualitative systematic review also highlights the need for providers to simplify the burden of care for multimorbid patients[72]. Our findings highlight the importance of focusing multimorbidity management by prioritizing one or more specific condition(s) and ensuring that prioritization is undertaken in collaboration with patients.

Our study has some limitations. First, it is possible that other teams may have identified different programme theories or interpretations. However, we used a rigorous and systematic process, and we let our data guide our interpretations. Second, many of our included studies did not have complete data to enable optimized CMO investigations. This may in part be due to an over-emphasis on effectiveness research in the literature, and an under-representation of qualitative inquiry, particularly about elucidating "mechanisms". For example, the literature rarely addressed the social determinants of health (a potentially significant trigger for multimorbidity outcomes) even though many older adults experience social isolation[73] and financial[74] challenges). Incomplete reporting also impacted our ability to fully test our theories. As such, whilst we developed and refined a number of explanations for our data, we could not completely elucidate the interrelationships within and between all of our CMO configurations.

Conclusions and future directions

Our realist review contributes to the current, limited knowledge of the underlying mechanisms of complex multi-CDM interventions for older adults with multimorbidity. We found that care coordination interventions are effective because they represent a structured approach to holistic care. To mitigate the complexities of multimorbidity management, patients focus on reducing their undesired symptoms and preserving their quality of life, while providers focus on the condition that most threaten a patient's morbidity and mortality. To optimize care, multimorbidity management requires both clinical management and patient self-management, and be considered from multiple perspectives (patient, provider and system).

Abbreviations

CDM: chronic disease management; CMO: context-mechanism-outcome; UK: United Kingdom; COPD: chronic obstructive pulmonary disease; EPOC: effective practice and organization of care.

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Data Statement

We included most of the data generated or analyzed for this study in this published article and associated appendices. Any additional datasets are available from the corresponding author upon request.

Competing Interests

The authors have no competing interests to report.

Author Contributions

MK: Manuscript development, methods, search strategy, data extraction, data analysis, research question development

LH: Manuscript development, data extraction, data analysis

GW: Manuscript development, methods

YL: Manuscript development, data extraction, data analysis, methods

JM: Manuscript development, data extraction, data analysis, methods

VT: Manuscript development, data extraction, data analysis, methods

JC: Manuscript development, data extraction, data analysis

JL: Manuscript development, data extraction, data analysis

NI: Manuscript development, methods, search strategy

JL: Manuscript development, methods, search strategy

SE: Manuscript development, methods, search strategy

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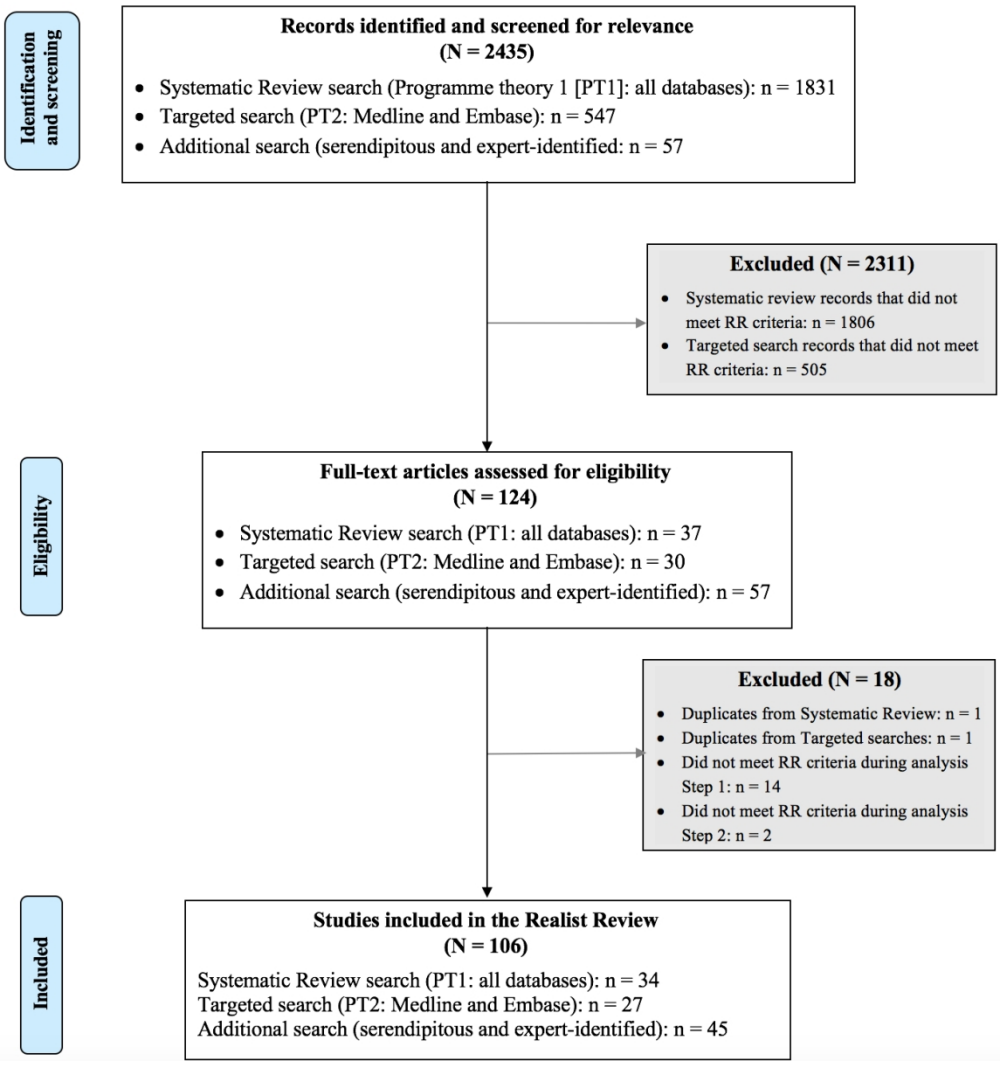

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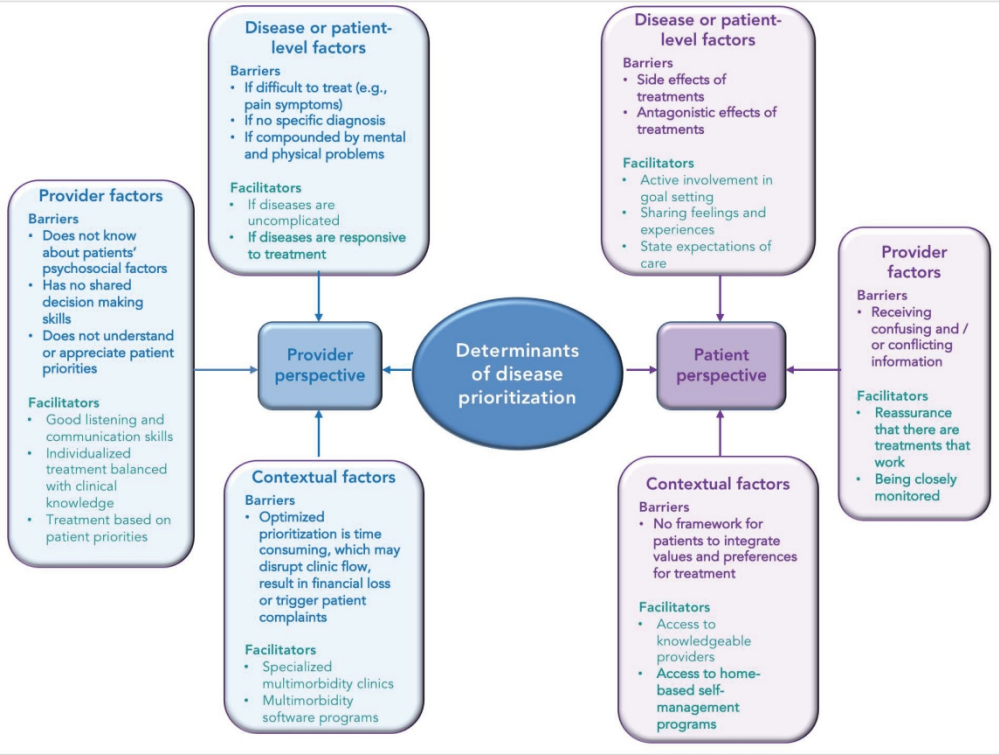
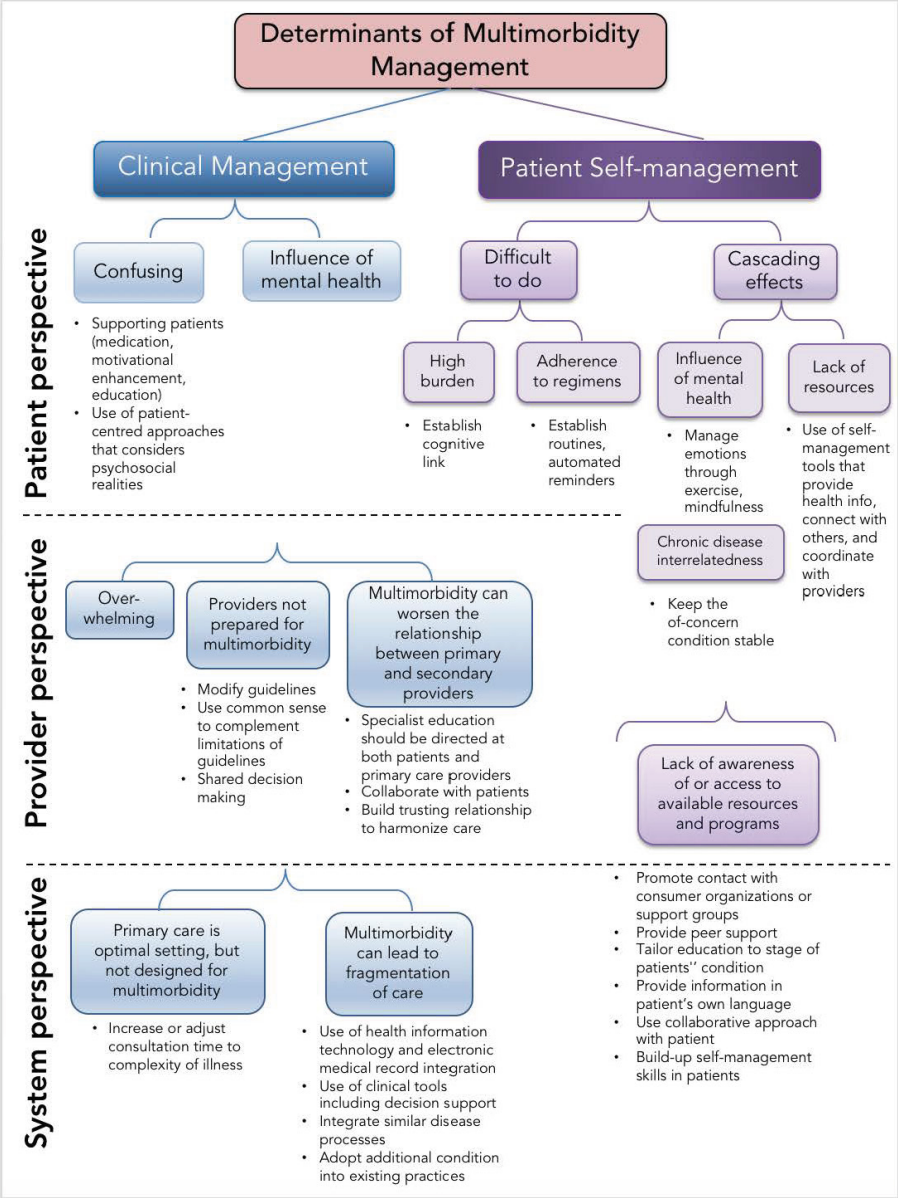


Framework of disease prioritization determinants from the perspective of patients and providers

335x252mm (144 x 144 DPI)



Framework of multi morbidity determinants from the perspective of patients, providers and the system

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Appendix 1

Medline search strategy for rough program theory 2 (health prioritization of multiple chronic conditions)

1. Primary Health Care/
2. Physicians, Family/
3. general practice/ or family practice/
4. (healthcare adj (professional or provider)).tw.
5. or/1-4
6. exp Geriatric Assessment/
7. *"Referral and Consultation"/
8. Decision Making/
9. Decision Support Systems, Clinical/
10. (consult$ or refer$).tw.
11. health planning/ or health planning guidelines/
12. ((Shared or sharing or shares) adj ("decision making" or "decision-making" or "decision making process" or "decision-making process")).tw.
13. Patient Participation/
14. or/6-13
15. 5 and 14
16. (chronic disease$ adj2 management tool$).tw.
17. Chronic Disease/
18. ((chronic* or longterm or long-term) adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)).ti,ab.
19. ((multi or multiple) adj2 (condition* or disabilit* or disease* or disorder* or ill or illness* or morbidit*)).ti,ab.
20. (multimorbid* or multi-morbid*).ti,ab.
21. ((complicated or complex) adj (health or healthcare or illness* or morbidit*)).ti,ab.
22. Comorbidity/
23. (comorbid* or co-morbid*).ti,ab.
24. exp disease management/
25. ((chronic* or (multi* adj chronic*)) adj (disease* or patient$1) adj manag*).ti,ab.
26. ((self or personal*) adj2 (administ* or care or control* or manag* or monitor*)).ti,ab.
27. (17 or 18 or 19 or 20 or 21 or 22 or 23) and 26
28. or/16-25,27
29. (geriatric* or gerontolog*).ti,ab.
30. (elderly or senior? or (old adj age) or (older adj adult?)).ti,ab.
31. Geriatrics/
32. or/29-31
33. Patient Participation/
34. Physician-Patient Relations/
35. Patient Care Planning/
36. *Patient Care Team/
37. ((physician? or doctor? or provider?) adj ((patient? or client*) adj relation*)).tw.
38. "goal-oriented care".ti,ab.
39. ((physician? or doctor? or provider?) adj ((patient? or client*) adj communicat*)).tw.
40. ((Patient?-centred or client*-centered) adj (decision adj mak*)).tw.
41. (Shar* adj ("decision-making" or (decision adj mak*)) adj (process* or proced* or method*)).tw.
42. or/33-41
43. 32 and 42
44. Health Priorities/
45. ("Re-prioritization" or "prioritization" or priorit*).tw.
46. (Priorit* adj guideline?).tw.
47. ("health care" adj priorit*).tw.
48. "pivot point".tw.

49. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
50. (trad* adj off?).ti,ab.
51. or/44-50
52. 15 or 43
53. 52 and 51 and 28

48. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
49. (trade* adj off?).ti,ab.
50. or/44-49
51. 15 or 43
52. 51 and 50 and 28

Appendix 2

Codebook for identifying concept themes – Program Theory 1

Concept	Concept definition	Source
BARRIERS		
Barriers to effective chronic disease management interventions	**GENERAL BARRIERS:** • Barrier factors or challenges to achieving effectiveness, impact, intended performance of chronic disease management interventions. Barriers related to specific types of interventions are described below • These tools can be targeted to clinicians, providers, other health care professionals and patients and used in any setting (e.g., primary care, hospital, home) • Examples: ○ Interventions are not directed to enhance patient self-management **IMPLEMENTATION BARRIERS** • This includes barrier factors related specifically to the implementation of the intervention, which can include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention. • Barriers to positive adaptation to and use of the intervention (emotional, cognitive, or physical dimensions that impede patients' use of the system). • It can also be about the "delivery" mechanisms of the intervention that may hinder its adoption or uptake • Implementation barriers can relate to situations where family members are protective of vulnerable residents (in a LTC setting), which may lead them to withhold permission for their relatives to participate in the study. (McSweeney, 2012 • These intervention designs often presuppose the availability of informal support systems even though the impact of treatment burden on both caregivers and patients with chronic conditions is well documented (Webster, 2015)	• Webster, 2015 • Sun, 2013 • Junius-Walker, 2010 (on applying the Comprehensive Geriatric Assessment) • Infante, 2004
Behavioural interventions • *Cognitive behavioural therapy* • *Self-management interventions*	GENERAL BARRIERS • Factors that negatively influence behavioural interventions • Universal Medication Schedule: The *aim was to standardise prescription labelling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding.* (Kenning, 2015) **<u>Clinic-based self-management interventions for patients</u>** One possibility [for why self-management interventions struggle to achieve reach] is that most forms of intervention, whether provider based or patient based, are outside patients'	• Naik, 2012 • Lamers, 2010 • Kenning, 2015 • Unutzer, 2008 • Smith, 2016 • Wu, 2012 • Zulman, 2009 Self-management interventions • Kenning, 2015 • Kennedy, 2013

	workaday and social activities, so fail to embed themselves into their everyday lives (Kennedy, 2013)	
Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Chronic Care Model* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL BARRIERS** • Factors that negatively influence coordination of care interventions	• Naik, 2012; McSweeney, 2012; Williams, 2004; Eijkelberg, 2002(Prioritization); Starfield, 2011; Fraccaro, 2015; Campbell, 2000; Knowles, 2015; Ricci-Cabello, 2015; Smith, 2010
	IMPLEMENTATION BARRIERS • Factors that negatively influence the implementation of coordination of care interventions **Shared care implementation barriers:** • If care providers are less easily convinced of the feasibility of shared care models because of the traditional professional boundaries they find difficult to give up or change (Eijkel berg, 2002).	• Brodarty, 2003 • Hammill, 2015 • Muller-Staub, 2015 (advanced practice nursing) • Lamothe, 2015 • Knowles, 2015 • Smith, 2016
Health information technology tools: • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL BARRIERS:** • Factors that negatively influence health information technology tools	• Schnipper, 2010; Fraccaro, 2015; Banbury, 2014; Rahimpour 2008; Bowles, 2009; Whitten, 2007; Noel, 2004; Kenning, 2015; Zulman, 2015; Becker, 2010; Collaborative Care; - Wozniakm 2015
	IMPLEMENTATION BARRIERS: • Factors that negatively influence the use of technology based or computer-based tools or systems (e.g., low use). • Factors that influence adaptability of health information technology tools (i.e., factors that affect how people adapt to using the system to manage their chronic conditions) • Issues such as data decentralization, security, and privacy often prevent the implementation of health IT. (Osborn, 2015) **Video-image conferencing implementation barriers:** • Socioeconomic, technological, political and professional barriers • The lack of uniform policies and standards for health care facilities and patient confidentiality issues in the infrastructure at state and national levels • Arbitrary boundaries for services • High costs to support broadband connectivity • Public and private payers' reluctance to establish reimbursement policy at lower levels adds another	• Noel, 2004 • Bowles, 2009 • Zulman, 2015

	obstacle to broader deployment of real world Telemedicine (Noel, 2004) **Computer-based counselling implementation barriers** • Lack of implementation by care staff, which could lead to failure to produce an effect **Telephone/telemonitoring implementation barriers** • Inconsistent interactions with patients (Bowles, 2009); • Completing the minimum number of telephone / telemonitoring calls prior to patient discharge (Bowles, 2009); • Communication and collaboration barriers between nurses and physicians; • Being unaccustomed to modern technology (Rahimpour, 2008); • Fear and avoidance of modern technology ('computer anxiety') which can impede implementation and use of home telecare management system (Rahimpour, 2008). • Nurses had to be assisted with physician communication by other personnel who would send letters for non-urgent requests or calling directly for urgent ones. (Bowles, 2009).	
Barriers to the management of multiple chronic diseases	**GENERAL BARRIERS** • Barriers to the complexity of care required to manage multiple chronic conditions (i.e., multiple prescribers, multiple providers; consumer knowledge gaps about treatment) • Examples: o Having a limited consultation time o Multiple providers o Undefined roles of GPs and specialists (Sinnott, 2013) o The presence of simultaneous care plans for multiple conditions can lead to confusion, which can generate safety hazards [Fraccaro, 2015).	• Williams A, 2012; Eijkelberg, 2002 (Prioritization); Muth, 2014; Luijks, 2012; Sinnott, 2013; Bayliss, 2008; Sondergaard, 2015; Smith, 2007; Infante, 2004; Webster, 2015; Koch, 2015; Lamers, 2010; Harris, 2013; Kennedy, 2013; Starfield, 2011; Cheraghi-Sohi, 2013a; Bower, 2011; Loffler, 2015; Boult, 2008; Hansen, 2015; Onder, 2015; Fracarro, 2015; Van den Bussche, 2011; Williams, 2012a; Zulman, 2013; Sinnott, 2015; Lamothe, 2015; Noel, 2004; Smith, 2012; Vogeli, 2007; Williams, 2004; Wallace, 2015; Cheraghi-Sohi, 2013b; Junius-Walker, 2011; Boyd, 2007; Cheraghi-Sohi, 2014a; Zulman, 2015; Hjelm, 2015b; Knowles, 2015; Hjelm, 2015a; Spoorenberg, 2015; Lee, 2015; Moffatt, 2015; Ricci-Cabello, 2015; Sinnige, 2013; Smith, 2010; Smith, 2007; Smith, 2016
Barriers to effective self-management of multiple chronic conditions	**GENERAL BARRIERS:** • Barriers that patients experience in self-managing their multiple chronic illnesses. • Examples: o Difficulty following exercise and dietary plans o Depression o Fatigue	• Lindsay, 2009 (prioritization) • Smith, 2007 (prioritization) • Eijkelberg, 2002 (prioritization) • Infante, 2004 (prioritization) • Webster, 2015 (prioritization) • Koch, 2015 (MK Found) • Cheraghi-Sohi, 2013a

	○ Poor communication with physicians ○ Lack of social support ○ Pain and physical symptoms ○ Financial problems ○ Lack of awareness ○ Lack of information ○ Emotional impact of having multiple chronic conditions • Multimorbidity reduces the capacity of patients to modify their lifestyle, their ability to seek help and to manage multiple medications [Harris 2015]. • Multimorbidity also has a significant economic impact on patients because of the costs associated with their care, which may be compounded by their inability to work as the conditions progress. (Harris, 2015)	• Bower, 2011 • Fraccaro, 2015 • Tracy, 2013 (MK found) • Banbury, 2014 • Lamers 2010 • Muth, 2014 • Bayliss, 2008 • Fried, 2011 • Hammill, 2015 • Zulman, 2013 • Kenning, 2015 • Unutzer, 2008 • Vogeli, 2007 • Liddy, 2014 • Williams, 2012b • Bratzke, 2015 • Cheraghi-Sohi, 2013b • Harris, 2013 • Junius-Walker, 2010 • Morris, 2011 • Cheraghi-Sohi, 2014a • Zulman, 2015 • Dufour, 2015 • Infante, 2004 • Smith, 2007 • Smith, 2016 • Wu, 2012 • Zulman, 2009
Barriers to using existing guidelines for disease management	**GENERAL BARRIERS** • Barriers or challenges faced by physicians to using existing guidelines for disease management, which tend to focus on a single disease • Lack of guidelines for managing multiple chronic diseases, which may lead to provider lack of knowledge of optimal care pathway	• Junius-Walker, 2010 • Junius-Walker, 2012b • Sinnott, 2013 (Prioritization) • Fried, 2011 (prioritization) • Sondergaard, 2015 (prioritization) • Sinnige, 2013 (prioritization) • Smith, 2007 (prioritization) • Koroukian, 2015 (prioritization) • Luijks, 2015 • Sondergaard, 2015 (prioritization) • Junius-Walker, 2011 (prioritization) • Muth, 2014 • Fraccaro, 2015 • Loffler, 2015 (Prioritization)

		• Fracarro, 2015 • Luijks, 2012 • Zulman, 2013 • Vogeli, 2007 • Wallace, 2015 • Wrede, 2011 • Cheraghi-Sohi, 2014a • Ricci-Cabello, 2015 • Sinnige, 2013 • Smith, 2010 • Smith, 2007
Chronic disease interrelatedness	**GENERAL BARRIERS** • Chronic diseases may be interrelated • The course of one chronic disease may influence the course of the other disease (e.g., Depression and dyspnea-related disability) • The influence of treatment(s) for one chronic disease on the outcomes of other co-existing chronic diseases • The additive impact of one disease to the other • The impact or burden of one disease on the treatment demands of the second disease (e.g., Diabetes magnifies the demands of COPD treatment). • Multimorbidity may present as a collection of long-term conditions that share common risk factors (e.g. chronic obstructive pulmonary disease and cardiovascular disease as a result of smoking) or when one condition leads to another as a complication [Harris 2015] • Quality of life for people with multimorbidity is inversely related to the number of conditions they have and the extent of any disability [Harris 2015].	• Alexopoulos, G.S., 2014 • Unutzer, 2008 • Williams, A., 2011 • Lamers, 2010 • Williams, 2004 • Schafer, 2014 (prioritization) • Bowler • Katon 2006 • Onder, 2015 • Marengoni, 2013 • Lamothe, 2015 • Vogeli, 2007 • Williams, 2012b • Moffat, 2015 • Sinnige, 2015
Depression + Diabetes	The additive impact of depression and diabetes lead to functional impairment including a higher number of cardiac risk factors, increased micro- and macrovascular complications in addition to poor self-care and increased mortality (Katon, 2006).	• Katon, 2006
Diabetes + Chronic Kidney Disease	Irrespective of the cause of kidney disease, the co-existence of diabetes, CKD and hypertension leads to synergistic adverse effects: mortality is higher, quality of life is worse and the burden on healthcare services is increased (Williams, 2012a)	• Williams, 2012a • Naik, 2012 • Williams, 2004 • Morgan, 2013 (Depression + diabetes and/or heart disease)
Depression + Pain	Improved arthritis pain was associated with decreased depression; the concurrent improvement in both conditions supports the close interplay between depression and pain (Lin, 2003).	• Lin 2003
Disease co-management	**GENERAL BARRIERS** • The care or management of two diseases simultaneously • Suggestions on treatment of co-existing diseases (e.g., depression + arthritis) • The need to simultaneously manage multiple chronic conditions complicate care management - escalating challenges of understanding a growing number of different clinical conditions while attempting to monitor combinations of different symptoms, and reporting symptom and functional status	• Alexopoulos, G.S., 2014 • Unutzer, 2008 • Bowler, 2011 • McSweeney, 2012 • Bayliss, 2012 • Zulman, 2013 • Vogeli, 2007

	changes to multiple providers from different specialties, and adhering to different medication administration and other care plans (Koch, 2015)	• Naik, 2012 • Williams, 2004 • Moffat, 2015 • Ricci-Cabello, 2015 • Smith, 2007
FACILITATORS		
Facilitators of effective chronic disease management interventions	**GENERAL FACILITATORS** • Facilitator factors (positive attributes) that contribute to the effectiveness, impact, intended performance of chronic disease management interventions • Impact can directly affect patients or healthcare providers or the system or how patients access or use health services or the management of their diseases • Care plans [in the context of multiple chronic conditions need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. (Fraccaro, 2015) • Participants reported feeling supported and reassured through the intervention because they were in contact with individuals who listened, understood and empathised with them and validated the challenges of living with the many consequences of their health conditions (Webster, 2015) **IMPLEMENTATION FACILITATORS** • This includes facilitator factors related specifically to the implementation of the intervention. These can also include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention.	• Webster, 2015 • Williams, 2012a • Harris, 2013 • Junius-Walker, 2011 • Cheraghi-Sohi, 2014a
Behavioural interventions • *Cognitive behavioural therapy (CBT)* • *Behaviour activation* • *Self-management interventions*	**GENERAL FACILITATORS** Cognitive behavior therapy (CBT) facilitators: • Having trained practice nurses deliver the intervention (Lamers, 2010) Behaviour activation facilitators: • Strategies to activate patients to perform particular health behaviors. (i.e. medication self-efficacy and adherence) Self-management interventions • Universal Medication Schedule: The *aim was to standardise prescription labelling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding*. (Kenning, 2015) • Interventions that target improving patient self-management behavior/skills (Kennedy, 2013)	General • Lamers, 2010 • Infante, 2004 • Smith, 2016 • Wu, 2012 • CBT: • Lamers, 2010 • Lin, 2003 • McSweeney, 2012 Behaviour activation • Unutzer, 2008 • Williams, 2012b Self-management interventions • Kenning, 2015 • Kennedy, 2013 • Williams A, 2012a • Lamers, 2010 • Bond, 2015 • Dufour, 2015 • Smith, 2016 • Wu, 2012

Home based Interventions	**Home-based services that bring multiple disease management services to people with mobility and other barriers to access to care**	• Bleich, 2015
Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Comprehensive Geriatric Assessment* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) coordination of care interventions	• Lemmens, 2009 • Ricci-Cabello, 2015 • Smith, 2016
	IMPLEMENTATION FACILITATORS <u>Case/care-management implementation facilitators</u>**:** • Having a specialist mental health team (Brodarty, 2003) <u>Collaborative care facilitators</u>**:** • A practice nurse who can carry out the intervention • Access to clinical software capable of generating a disease registry from which patients could be selected to participate in the trial were the facilitators of the implementation of the intervention (Morgan 2013) • the design of the intervention which allowed for its easy implementation within general practices and a better use of their existing resources meant that the TrueBlue could be easily applied to patients across general practices at a population level, making the benefit clinically important. (Morgan, 2013) <u>Disease management program facilitators</u>: • Adherence to evidence-based guidelines, which can improve health and cost outcomes • Usefulness (how valuable the users consider the specific features, functions, and data the tool makes available to them) • Value • Satisfaction • Ease of use (how easy it is for a user to complete their desired task with the tool) • Acceptability • Intention to use.	• Brodarty, 2003 • Alexopoulos, 2014 (care management) • Smith, 2007 (prioritization) • Campbell, 2000 • Onder, 2015 • Wallace, 2015 • Hjelm, 2015b (case management) • Hjelm, 2015a (case management) <u>Collaborative Care:</u> • Morgan, 2013 • Knowles, 2015 • Palmer, 2012 <u>Integrated care</u> • Spoorenberg, 2015 • Wozniakm 2015 <u>Coordinated care / Disease management:</u> • Eijkelberg, 2002 (Prioritization) • Harris, 2014 • Cheraghi-Sohi, 2013a • Bower, 2011 • Lemmens, 2009 • Lee, 2015 • Lemmens, 2009 • Ricci-Cabello, 2015 • Lamothe, 2015 <u>Advanced Practice Nursing</u> • Muller-Staub, 2015 <u>Patient-partner approach</u> • Lamothe, 2015

	Health Information Technology Tools • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) health information technology tools • Health information technology can promote coordination of care and improve quality and safety (Osborne, 2015) <u>Telephone/telemonitoring facilitators</u>: • Good disease management combined with the deployment of the technology • Telemonitoring was managed by primary care professionals (GPs and nurses) who regularly see their patients in health centres or at home than if the intervention was in-hospital; • The perception of facilitators in the increasing healthcare professionals' intention to use telemonitoring technology (organisational context is the most important variable); • Paying attention to the proper clinical management of patient's conditions (Martin-Lesande, 2013) • Universal Medication Schedule: The *aim was to standardise prescription labelling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding*. (Kenning, 2015)	• Noel, 2004 • Martin-Lesande, 2013 • Rahimpour 2008 • Bowles, 2009 • Whitten, 2007 • Banbury, 2014 • Osborn, 2015 (MK Found) • Schnipper, 2010 • Kenning, 2015 • Naik, 2012 • Bowles, 2009 • Bond, 2015 • Zulman, 2015 • Becker, 2010 • Bond, 2015
	Self-management interventions?	**GENERAL FACILITATORS** • Factors that facilitate self-management. • Impact on self-management can occur in the emotional, physical, and financial domain, but is not restricted to these	• Naik, 2012 • Franek, 2013 • Noel, 2004 • Smith, 2012 • Boyd, 2007 • Bond, 2015

Facilitators of the <u>management</u> of multiple chronic diseases/multimorbidity • Coordination of care (Lamothe, 2015) • Patient level (Lamothe, 2015)	**GENERAL FACILITATORS** • Factors that facilitate the patient's management of multiple chronic conditions. • "Factors" may include the qualities and components of the intervention that make it easier/simpler to manage a patient's multiple chronic conditions (manage: to stabilize, control, or improve a patient's health or quality of living with multiple chronic conditions). • Care plans that are clear and blend clinical care with self-management are essential in multimorbidity; they need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. (Fraccaro, 2015) • Examples: o Lin (2003) describes how the biopsychosocial approach to care can be applied to patients with both depression and arthritis, and says, "[The biopsychosocial approach in this situation should] include depression screening in a systematic assessment of pain among older patients with symptomatic osteoarthritis. o Medical management of arthritis can integrate evidence-based depression treatment with patient education and support for self-management (eg, exercise) to maximize functional status and quality of life." o The facilitators that are proposed to assist patients with the management of depression and arthritis are 1) the inclusion of depression screening with pain assessment, and 2) the integration of depression treatment with patient education and self-management support. • This concept is different from "Facilitators of effective chronic disease management interventions/programmes" because the latter concept looks at explaining why an intervention/program works o For example, Lamers (2010) explains, "Minimal interventions like our MPI – that (1) may provide patients with the skills to cope with the consequences of their illness and their depressive symptoms, (2) can be incorporated in existing disease and care management programs, (3) can be administered by nurses (e.g. practice nurses)." It is *because* the intervention provides patients with certain skills, and its implementation is favourable, that the MPi is able to be implemented and foster positive patient outcomes.	• Schnipper, 2010; Harris, 2013; Bayliss, 2008; Muth, 2014; Infante, 2004; Maly, 2002; Kennedy, 2013; Tracy, 2013; Jaglal, 2014; Lin, 2003; Bayliss, 2012; Kamerow, 2012; Fried, 2011; Laiteerapong, 2011; Rahimpour, 2008; Fracarro, 2015; Luijks, 2012; Williams, 2012a; Zulman, 2013; Sinnott, 2013; Lamothe, 2015; Smith, 2012; Unutzer, 2008; Vogeli, 2007; Luijks, 2015; Koch, 2015; Arvidsson, 2010; Wallace, 2015; Junius-Walker, 2011; Morris, 2011; Dufour, 2015; Lee, 2015; Moffatt, 2015; Ricci-Cabello, 2015; Sinnige, 2015; Smith, 2010; Smith, 2007; Fortin, 2014; Smith, 2016; Zulman, 2009
Facilitators of effective <u>self-management</u> of multiple chronic conditions	**GENERAL FACILITATORS** • Factors that facilitate self-management of multiple chronic conditions. • Examples: o The support of family, including reminders to take medication and avoidance of eating unhealthy foods, and social relationships serve as motivators for patients to more effectively manage their conditions (Koch, 2015).	• Lindsay, 2009 (prioritization); Kennedy, 2013; Banbury, 2014; Muth, 2014; Eijkelberg, 2002; Rahimpour, 2008; Liddy, 2014; Williams, 2012b; Bratzke, 2015; Maly, 2002; Cheraghi-Sohi, 2013b; Morris, 2011; Bond, 2015; Zulman, 2015; Infante, 2004; Bond, 2015; Dufour, 2015

Facilitators to using existing guidelines for disease management	• Includes examples of situations when practitioners thought it was useful to use or adhere to guidelines
	• Includes suggested ways to improve usefulness or helpfulness of guidelines.
	• Examples:
	  • Adhering to guidelines promotes working transparently
	  • Guidelines would be helpful for multimorbid patients if they provided more details on diagnostic, treatment, and management priorities
	  • Guidelines improve the quality of general practice
	Guidelines provide guidance to medical decision-making
		• Luijks, 2015

Factors influencing the management chronic conditions/multimorbidity	• Factors that influence the management of patients with chronic conditions (directionality not specified). ○ Factors that may influenced doctors' varying views on the preparedness of their practices to manage patients with different types of complex needs include: the organization of primary care, workforce training, use of teamwork, size of practice, payment strategies and incentives, health IT (information technology) capacity, and the availability of community services may play a role. (Osborn, 2015)	• Osborn, 2015 • Harris, 2015 • Fraccaro, 2015 • Kamerow, 2012

Factors which affect treatment adherence	• Factors that influence patient's engagement with the recommendations made by the physician (i.e. factors that cause the patients to follow or not follow the recommendations).
	  ○ A key element influencing patient's engagement with multiple self-management practices was interaction with health professionals, and this was also related to perceived appropriateness of information received (Morris, 2011).
	  ○ The GP's response [TO WHAT?} conflicted with her priorities and had a negative impact on what she felt able to engage with in managing her health. Where self-management instructions and information from the GP were incongruent with personal priorities as illustrated above, respondents remained disengaged from professional advice (Morris, 2011).
	  ○ In our interviews with 34 patients we had enquired about their willingness to be involved. The level of involvement depended on the nature of the problem. If it was a medical theme, patients preferred to follow the professional recommendation of their GP; however, if the theme had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision. In general, patients expressed a need for undivided attention, understandable information, time, and a calm atmosphere in the consultation (Junius-Walker, 2010).
	• Factors that influence the compliance of medication, typically long-term compliance.
	  ○ Strategies that include extrinsic motivators will promote long-term compliance and reduce recidivism (Noel, 2004).	

Risk factors for multimorbidity	• This concept is different from "factors influencing the management of chronic conditions" as they lead to multimorbidity instead of influencing the management of multimorbidity once individuals have it
	• Risk factors may be social determinants of health that put individuals at risk for multimorbidity or predispose individuals to multimorbidity
	• Examples:
	  ○ Being socioeconomically deprived
	  ○ Low income
		• Sinnige, 2013 (prioritization)
		• Koroukian, 2015 (prioritization)
		• Onder, 2015
		• Van den Bussche, 2011
		• Marengoni, 2013
		• Smith, 2012
		• Sinnige, 2013
		• Smith, 2016

	○ Individuals with multiple comorbidities, who frequently experience mental health problems and illnesses, are often of low socioeconomic status and have unmet basic needs, such as housing, employment and transportation.	

Codebook for identifying concept themes – Program Theory 2

Concept	Concept definition	Source
BARRIERS		
Barriers to optimized patient prioritization	• Factors that may hinder a patient with multiple chronic conditions from being able to participate in the act of prioritizing health conditions with his/her provider; this includes their decision making • Factors that may hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization • A patient's family may have a greater influence on the decision than the patient's own preferences [Legare 2011]. • Includes any barriers to patient-centred care	• Zulman, DM, et al. (2009) • Kennedy, 2013 (MK Found) • Wrede, 2011 • Sondergaard, 2015 • Cheraghi-Sohi, 2013a • Bratzke, 2015 • Cheraghi-Sohi, 2014a • Dowdy, 2013
Barriers to optimized provider prioritization	• Factors that may hinder a provider from being able to participate in the act of prioritizing health conditions for a patient with multiple chronic conditions including decision making. This can also include health priorities addressed in the clinic setting • Factors that make it more difficult for health care providers to prioritize the treatment/management of a patient's chronic conditions. For example, factors may include the competing demands of multiple chronic conditions, and challenges of balancing provider and patient priorities. ○ *Psychiatric disorder*: If the patient has a psychiatric disorder, then this may make it more difficult for providers to prioritize treatment/management of the chronic conditions. • Patient-centered care is defined as GPs taking a broader view of the patient, incorporating non-medical or psychosocial issues. Patient-centered care is an over-riding principal for GPs in multimorbidity but trying to achieve this increases the complexity of care in some cases, and can lead the GP into additional conflict with specialist services or evidence-based medicine." [Sinnott, 2013] • Factors that may hinder a provider from being able to apply evidence in the care of their patients. • Clinicians lack a systematic framework for determining patient preferences and synthesizing these preferences with existing evidence to set individual health priorities • Includes the barriers (i.e. time) related specifically to the implementation of training for providers (for example, GPs did not accept shared decision-making and prioritization training sessions of more than 30 min, for fear of organizational disruption , patient complaints, and financial loss). (Wrede, 2011)	• Junius-Walker, U, et al. (2010) • Arvidsson, 2010 • Sondergaard, 2015 • Cheraghi-Sohi, 2013a • Fraccaro, 2015 • Dowdy, 2013 • Wrede, 2011 • Laiteerapong, 2011
Barriers to shared decision making	• Barriers that impede a collaborative process that allows patients and their providers to make health-care decisions together. The collaborative process takes into account the best clinical evidence available, as well as the patient's values and preferences.	• Wrede, 2011 • Sondergaard, 2015 • Sinnott, 2013

	• For example, barriers to shared decision making patients often do not expect to share decisions, in particular older patients may find this SDM process difficult because it is unfamiliar and demanding (Wrede, 2011).	• Sinnott, 2015 • Junius-Walker, 2012blai • Infante, 2004 • Dowdy, 2012
Barriers to the agreement between patients and providers	- Captures any excerpts about the dynamic between the patient and provider (whether that is agreement on prioritization, decision making) - Includes excerpts that mention *both* what patients and providers think. **IN THE PRIORITIZATION OF CHRONIC DISEASES** • Factors that decrease the level of agreement between patient and provider in terms of prioritization of health conditions including health care decision making. For example, when patients present with unrelated or discordant conditions, the patient and provider may disagree about which condition should be prioritized (Zulmn, 2013, JGIM) • Include conflicting views/ranking? Between providers and patients of which diseases should be considered for treatment? – Zulman • Factors that decrease the level of agreement between patient and provider, but not specifically about the prioritization of health conditions. • Factors that decrease the level of agreement between patients and provider, but not specifically about the prioritization of health conditions (Maly, 2002) o For example, communication between the physician and patient can affect agreement. If the physician does not enact enough/ at all information-giving, counseling, quality of question asking and support, and participatory decision-making style (process of negotiation) during consultations with patients, then this many negatively affect agreement.	**PRIORITIZATION** • Zulman, 2009 • Junius-Walker, 2011 • Luijks, 2015 • Hansen, 2015 • Zulman, 2013, JGIM (Additional) • Maly, 2002 Targeted Search (Prioritization)) • Loffler, 2015 (prioritization) • Bratzke, 2015 **HEALTH CARE DECISIONS** • Morris, 2011
Barriers to the patient-provider relationship	• The communication barriers between patient and provider (includes factors that influence poor communication between patient and provider)	• **Junius-Walker, 2012b** • Loffler**, 2015** • Morris, 2011
FACILITATORS		
Facilitators of optimized <u>patient</u> prioritization	• Factors that may promote a patient from taking part in the decision-making process in terms of health prioritization; • Patients engaging with health care workers in health prioritization • What motivates patients to prioritize their conditions. For example, to cope with their health problems and stabilize their health. • The components of a clinical appointment/check up that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making. • The components of a clinical appointment/checkup that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making • Includes any facilitators to patient-centred care (Harris, 2013)	• Harris, 2013 • Bratzke, 2015 • Cheraghi-Sohi, 2014a

Facilitators of optimized <u>provider</u> prioritization	• Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to work with other providers to prioritize multiple chronic conditions. For example, use of an electronic integrated medical records system may facilitate communication and care coordination across providers. (Koch, 2015) • Specifically, how patient-centered communication impacts patients in terms of knowledge, expectations, participation in treatment process and providers in terms of quality of care.	• Arvidsson, 2010 • Luijks, 2015 • Koch, 2015 (MK Found) • Tracy, 2013 (MK found) • Dowdy, 2013 • Harris, 2013 • ion • Junius-Walker, 2010 • Laiteerapong, 2011
Facilitators of the patient-provider relationship	• The concept where physician "accompany the patient, which may contribute to a stable patient-physician relationship. "The physicians saw themselves as doctors who accompany these patients rather than doctors who heal them. This leads to an emphasis on 'little improvements.' […]The physicians stressed that accompanying the patients and witnessing their improvements contributed to a stable doctor-patient-relationship." (Loffler, 2015) • Includes communication facilitators between patient and provider (the factors that influence good communication between patient and provider)	• Loffler, 2015 (prioritization) • Harris, 2013 • Infante, 2004

Facilitators of shared decision making	**GENERAL**
	• Factors that facilitate the collaborative process that allows patients and their providers to make health-care decisions together based on available evidence and clarification of patient preferences.
	• For example:
	  • agreement is a prerequisite of shared decision making and can be achieved using a patient-centred approach (Wrede, 2011).
	  • Sharing personal experiences, and facilitating concise and clear discussions with patients on the interplay between chronic diseases were strategies used by GPs to facilitate SDM. (Sinnott, 2013)
	IMPLEMENTATION
	• Factors that facilitate the implementation of processes, tools, or skills that encourage or foster shared and equitable decision-making between patient and doctor, with decisions based on available evidence and clarification of patient preferences
	• For example:
	  • communication training for GPs can help them facilitate SDM (Wrede, 2011)
	  • If the healthcare provider considers the patient also as an expert in, and partner in the management of, their condition(s), and respects the patient's opinions (Infante, 2004).
	  • Involving patient perspectives and preferences in the patient-provider decision-making process by exploring and mutually explaining each other's ideas (Luijks, 2012).
		GENERAL:
		• Wrede, 2011
		• Luijks, 2012
		• Luijks, 2015
		• Sinnott, 2013
		• Infante, 2004
		• Legare, 2011
		• Hansen, 2015
		• Tracy, 2013 (MK found)
		• Wallace, 2015
		• Junius-Walker, 2012b
		• Hammill, 2015
		• Sinnott, 2015
		IMPLEMENTATION:
		• Wrede, 2011
		• Infante, 2004
		• Luijks, 2015

Facilitators of the agreement between patients and providers	- Captures anything about the dynamic between the patient and provider (whether that agreement on prioritization, decision making) - Includes excerpts that mention *both* what patients and providers think. **IN THE PRIORITIZATION OF CHRONIC DISEASE** • Factors that increase the level of agreement between patients and providers in terms of prioritization of health conditions. • For example, the agreement between patients and providers was higher when ○ Patients have fewer symptoms (Zulman, 2009)	**PRIORITIZATION** • Zulman, 2009 • Morris, 2011 • Hansen, 2015 • Junius-Walker, 2012a • Sinnott, 2015Bratzke, 2015 • Junius-Walker, 2010 **HEALTH CARE DECISIONS**

	The provider was male (Zulman, 2009) **IN HEALTH CARE DECISIONS** • Factors that increase the level of agreement between patients and providers, but not specifically about the prioritization of health conditions. • For example: Having a process of negotiation may ensure collaboration and agreement between patients and their primary care physicians (Maly, 2002).	• Maly, 2002(Targeted Search (Prioritization)) • Loffler, 2015
(Neutral) Factors		
Process of shared decision making between providers and patients	The process of shared and equitable decision-making process between patient and doctor, with decisions based on available evidence and clarification of patient preferences	• Wrede, 2011 • Arvidsson, 2012 • Laiteerapong, 2011 • Wallace, 2015 • Junius-Walker, 2010
Patients' process of prioritizing multiple chronic conditions	• The process used by patients to prioritize their multiple chronic conditions including their decision making and management (anything about *how* patients prioritize) • Includes any "rules of thumb" patients use to prioritize their conditions i.e. pain, functional limitations, new conditions that change up your prioritization • This is different than facilitators or barriers to patients' prioritization of chronic conditions. It spells out the process (steps) that patients go through as well as the factors that they take into account when prioritizing their chronic conditions. • The steps and considerations taken by patients when prioritizing their chronic conditions. For example, Morris et al. (2011) discuss when and why patients reprioritize conditions, and how the new ordering of conditions is determined. • Simply a listing of patients' priorities such as specific diseases or getting informed about their conditions • Factors that may promote or hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization For example, patients tended to follow GP's recommendation if the issue was purely medical; however, if the issue had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision. (Junius-Walker, 2010) • Includes factors that influence prioritization that are not related to specific barriers (challenges) or facilitators, such as the internal processes they use to prioritize multiple chronic diseases • Includes factors that may influence or drive patients' prioritization such as such as pain, fatigue, shortness of breath, or dizziness and have a great impact on quality of life and life satisfaction and thus–likely–on patient preferences. For example: Patients' prioritization and needs were affected by psychosocial factors, previous experiences and the patient's' expectation [Sondergaard 2015]	• Junius-Walker. (2010) • Junius-Walker, 2011 • Lindsay, 2009 • Cheraghi-Sohi, 2013a • Loffler, 2015 (Prioritization) • Junius-Walker, U, et al. (2010) • Zulman, DM, et al. (2009) • Muth, 2014 • Sondergaard, 2015 • Hansen, 2015 • Bratzke, 2015 • Legare, 2011 • Arvidsson, 2012 • Cheraghi-Sohi, 2013b • Morris, 2011 • Cheraghi-Sohi, 2014a
Providers' process of prioritizing multiple chronic conditions	• The process used by providers to prioritize their multiple chronic conditions including their decision making and management • For example: • Providers' priorities were determined by medical aspects of the diseases such as the disease severity and prognosis (Junius-Walker, 2010) • When providers did not feel in charge of a problem or were not aware of suitable treatments, they rated the problem as unimportant (Junius-Walker, 2010)	• Junius-Walker, (2010). • Arvidsson, 2010 • Junius-Walker, 2012 (B) • Junius-Walker, 2011 • Arvidsson, 2012 • Loffler, 2015 (Prioritization) • Zulman, DM, et al.,

	• Instead of symptomatic conditions, providers may focus on the long-term health consequences of asymptomatic hypertension or uncontrolled diabetes (Zulman, 2009)	2009 • Luijks, 2012 • Luijks, 2015 • Hansen, 2015 • Bower, 2011 • Cheraghi-Sohi, 2014a

Appendix 3

Context-Mechanism-Outcome (CMO) configurations of Programme theory 1 (Care coordination interventions)

General CMO configurations to explain Program Theory 1

***Care coordination Interventions** in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They provide a comprehensive and coordinated approach to multimorbidity management by addressing multiple conditions (through interdisciplinary teams and/or multidisciplinary disease management), providing specific mechanisms for communication, and establishing formal roles for providers and patients.	
Team-based approaches	Team-based approaches can lead to a range of outcomes, such as evidence-based care solutions for multiple conditions in parallel (not in tandem) [M][36], a wider range of services [O], more holistic care [O], higher quality of care [O], reduce scheduling complications [O2][33] and increase the flexibility and responsiveness of the team [O3][21]. These outcomes are most likely to occur when team members have mutual respect and confidence [M2][21], are highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M][32] who understand and accept each other's roles [M3][32], provide opportunities[33,36] and time[32] to share information [M][37], and are willing to collaborate on patient care [M5][21,32,33,36]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M]. The contexts in which these mechanisms are triggered include teams that have dedicated members who provide additional support to patients[32,36] or providers[37]. Team members receive official training on the model[32,36,37], including training on team skills[37]. Organizations have a robust and well-functioning communication system[21,36]. Many of the team-based approaches under study were Canadian[21,32,37].
Disease management	Disease management for multimorbidity care consists of the use of a number of discrete intervention strategies with the desired outcome of achieving systematized care. These include: checklists, follow up timetables[21,38,39], and treatment targets [M][21]. Together, these intervention strategies appear to make explicit the roles, expectations, and responsibilities of the health care professionals involved [C], enabling staff to become aware of their roles, expectations, and responsibilities [M] leading to a shared philosophy and platform for care [O][21],[39]. This also permits the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][21]
Case management	Case management intervention strategies are appropriate for managing multimorbidity because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C], a case manager functions as a conduit of information [M] to help improve coordination and information sharing from the patient to providers as well as between providers [O][32]. When improved coordination and information sharing occurs [C] and case managers are in regular contact with the patient [C][34], are the primary point of contact and coordinator of care [C][39] and provide individualized attention [C][22] and information [C][34] to patients, patients perceive that their care is continuous [M][40,41] and coordinated [M][41] and as a result know who is 'in charge' and who to turn to when then have a problem [O]. When patients know who is 'in charge' and who to turn to when then have a problem [C] helps patients to feel safer [M] and trust [M] of their case managers over time[41] resulting in the building of relationships that are more likely be based on confidentiality [O][34,41], and mutual

		equality [O][34] These types pf relationships appear to be the basis of some of the further 'downstream' outcomes that are found with case management, such as helping patients to develop the skills and confidence they need to manage their health [O][40].
Education was a component in 83% of the chronic disease management interventions identified in our systematic review. Education for patients is often a component of care coordination interventions[21,39,42], and can be more effective [O] when combined with active monitoring [M] and provided by a pharmacist[21] [C].		
	Health education	Health education is often combined with self-management support[20,39,43], which is more effective for lifestyle modification than education alone[43]. Patients receive education about their multimorbidity through numerous formats, including: video streaming[44], in-hospital education[45] and the internet[46]. Video streaming may be good for homebound patients[44], whereas in-hospital education may be more effective for those who might become motivated to change their lifestyle after a hospitalization event[45]. Patients with multiple chronic conditions use the internet, but there are few websites that address multiple conditions in an integrated fashion[46].
	Health coaching	Health coaching (helping patients to gain the knowledge, skills and confidence to become active participants in their care aimed at reaching their self-identified health goals)[47]. Health coaches (who could also be case managers) strengthen patient self-management by improving patient self-efficacy by listening and applying patients' challenges and health goals to customize action planning[25]. This allows patients to develop the coping and problem solving skills that support self-management[25,43].
	Web 2.0 technology	Web 2.0 technology (web use that involves more active participation, creation and sharing of information such as through social networking) are examples of interventions captured in our realist review that incorporate education. Web 2.0 technologies may support patient self-efficacy by providing relevant information, and opportunities to learn from other web users. For example, delivering online instructional units (developed and delivered by a multidisciplinary team of healthcare providers), and self-management training workshops staffed by peer moderators (i.e. individuals living with similar chronic conditions as the user)[48].

*This narrative provides only a broad explanation of Programme theory 1, greater detail that explains the outcomes that[37] may be achieved by the different intervention strategies used in the care coordination.

Details of CMO configurations to explain Program Theory 1

Coordination of care element	Definition	Explanation of determinants via Context [C]-Mechanism[M]-Outcome[O] configurations

Teams *The right care at the right time*	Highly trained clinicians[106] who provide holistic and coordinated care, often, but not always, from the same physical location[107]. Teams aim to provide time for the patient to discuss all of their concerns, prevent care overlap and gaps[108], and reduce scheduling complications[107] Patients are taught about their conditions, medications, and how lifestyle affects their health, and given information on health promotion or counseling services and other supporting services[119].	**Why Team-based approaches are appropriate for multimorbidity:** Team-based approaches are appropriate for managing multimorbidity [O1] because they can ideally provide evidence-based care solutions for multiple conditions in parallel (not in tandem) [M1][104]. Collaborative care teams can provide a wider range of services [O1], more holistic care [O2] and higher quality of care [O3] through interdisciplinary communication and collaboration [M1][104,105], and access to specialists [M2][106]. **Facilitators of successful teams:** Successful multidisciplinary teams [O1] are those which comprise highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M1][106] who have mutual respect and confidence [M2][92], understand and accept each other's roles [M3][106], provide opportunities[104,107] and time[106] to share information [M4][105], and collaborate on patient care [M5][92,104,106,107]. These facilitators can also reduce scheduling complications [O2][107] and increase the flexibility and responsiveness of the team [O3][92]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M1]. The use of peer moderators (i.e., individuals also living with a chronic condition who are trained to lead self-management training programs) [M1] can facilitate intervention learning activities such as behavior change, medication management, and disease information [O5].
Disease management *Systematized care (all providers are on the same evidence-based page)*	Disease management programs follow a "script" of how to provide effective (often evidence-based) patient care. Often care protocols or intervention plans define the division of tasks and support the follow-up and coordination of action[62,120], and help sustain the development of a philosophy of common care[92]. Patients may be educated about the disease management system so they know what to expect, and often provided with education and resources about how to properly self-manage their conditions.	**Why Disease management approaches are appropriate for multimorbidity:** Disease management strategies are appropriate for managing multimorbidity [O1] because they can systematically apply evidence-based care to populations of patients [M1] thereby making it more appropriate for managing conditions and combinations of conditions where evidence-based care exists. Care can be systematized [O2] through checklists [M1], follow-up timetables [M2], and treatment targets [M3][62,92,120]. **Facilitators of disease management:** Disease management approaches define the division of tasks [M1][92], support the follow-up and coordination of action [M2][62,92], and help sustain the development of a philosophy[92] and shared platform[62] of care [M3], therefore permitting the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][92].
Case management *Case managers are the primary conduit of care*	Case managers are trained health care professionals who are the contact person between a patient and involved providers. They know how to facilitate care planning and shared decision making; and how to anticipate and address barriers (e.g. to treatment adherence). Case managers work closely with patients and their family/caregivers to provide information (e.g., about the health system or care), and to help them develop the skills and knowledge needed for self-	**Why case management approaches are appropriate for multimorbidity:** Case management are appropriate for managing multimorbidity [O1] because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C1], a case manager acts as a conduit of information [M1] to help improve coordination and information sharing from the patient to providers as well as between providers [O][106]. **Facilitators of case management:** Case management strategies work [O1] because case managers are in regular contact with the patient [M1][108], and provide individualized attention [M2][49] and information [M3][108] to patients. For patients with extensive and diverse care teams [C1], case management can ensure that care is continuous [O2][109,110] and coordinated [O3][110] by enhancing the communication between patients and

	management.	providers [M1] and by being the primary point of contact and coordinator of care [M2][62]. Patients also feel safer [O4] when knowing that their case managers are monitoring their care [M1], and they trust their case managers over time [O5][110] because of regular contact [M1][108], and through a relationship of confidentiality [M2][108,110], and mutual equality [M3][108]. By engaging family/caregivers in proactive care [M1], case managers also help patients develop the skills and confidence they need to manage their health [O6][109].

Appendix 4

Context-Mechanism-Outcome (CMO) configurations of programme theory 2 (Health prioritization in multimorbidity management)

General CMO configurations to explain Program Theory 2

Multimorbidity management is confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[66], disease and treatment interactions and possible conflicts[49,51], and the difficulty of attributing symptoms to conditions[49]. Health prioritization is an important function of the management of multiple chronic diseases in primary care settings because the evidence base is most often single-disease focused and multimorbidity can create a cognitive and emotional overload in patients and health care providers. A common intervention strategy to multimorbidity management is to focus on one condition at a time[28], using a priority setting approach. Prioritizing one condition over the others (for a specified period of time, or until particular outcomes are achieved), allows patients[71] and providers[28] to focus their attention and care.	
Patients' approach to prioritization	Patients with multiple chronic conditions can experience a range of symptoms [C]. These symptoms trigger cognitive and emotional overload [M] for patients and as a result, they resort to prioritization [O]. The prioritization process is influenced by the nature of the symptoms. Patients prioritize their condition [O] by making decisions based on their judgments of the symptoms they experience most need attention [M]. Symptoms which threaten their participation in social activities[68,74,75] [C], limit their independence[71,74] [C] and they believe might have potentially severe long-term consequences if not acted upon[68,71] [C] - examples of these symptoms include pain, fatigue and dizziness. Those diseases that patients prioritize and seek help for [O] are the ones that patients believe are causing with these symptoms[60,63,67,68,72,73] [C] because they do not feel that they have the capacity to engage in self-management behaviors associated with the disease [M]. Multimorbidity can have cascading effects. Patients may find it challenging to determine which chronic disease is causing a particular symptom [O] because conditions may share similar symptoms[29] [M], the treatment of one condition may aggravate the other[61,71,78,79] [M] or cause other antagonistic effects[28,71,79] [M]. The diagnosis of a new condition added to an existing one [C] may impede self-management because information about the new condition adds uncertainty[80] [M]. Patients who are able to identify the main illness that causes the most concern [C], are able to keep their symptoms under control and return to an acceptable way of life[80] [O].
Providers' approach to prioritization	Patients with multiple chronic conditions can present to health care providers with a wide range of symptoms [C]. Dealing with these symptoms trigger cognitive and emotional overload [M] for the providers and as a result, they resort to prioritization [O]. The prioritization process used by providers is influenced by the nature of the symptoms. Providers tend to prioritize conditions [O] based on their judgments about the prognosis or severity of the condition [49,60,72-75] These judgments are influenced by their knowledge or evidence [72,77] about the which conditions are likely to have more serious outcomes [C], whether the patient is likely to benefit from treatment[49,72,76,77] [C] and conditions they feel they are most likely to be able to address (e.g. physical vs. emotional)[67,77]. Providers also tend to prioritize physical conditions over emotional or other conditions [C] (partly because) they consider the interrelatedness of the conditions and any potential cascading effects when prioritizing[64][M].
Associated CMO configurations related to multimorbidity management: We derived explanations of multimorbidity management in the context of primary care from the perspective of patients, providers and the system.	

Patient perspective	The mental health needs of patients add to management challenges and interfere with patient self-care[49]. Some mental health patients with poor communication[C] receive less intensive mental health treatment[50][O] because providers sometimes ignored or normalized [M] their symptoms[36]. A patient-centred approach, which takes into account the patient's psychosocial realities (housing, relationships, income)[51][C] is more likely to meet the needs of complex patients with multimorbidity[30,52] [O].
Provider perspective	Primary care clinicians face a number of challenges when managing patients with multimorbidity. In the contexts of inadequate decision support systems[26], evidence to support their clinical decision making[53], or care protocols or intervention plans that are too rigid[21], they may feel that they lack the skills and/or confidence[54] [M] to simultaneously understand patient subjective experience and biochemical processes of diseases[55] needed to appropriately manage these patients [O]. Another challenge is that most often, only single disease guidelines are available to manage multimorbidity [C], so clinicians are forced to modify them in anticipation of adverse effects[56] [M] or use common sense approaches [M] (to complement the limitations of their application[57]) leading to variations in 'adherence' to single disease guidelines. In the context of few existing multimorbidity guidelines and resulting clinical uncertainty or contradictory information, a promising intervention strategy from our included articles was shared decision making between patients and clinicians, which was described as a useful, and possibly a necessary tool for making individualized treatment decisions[58,59].
System perspective	Multimorbidity can create challenges in the relationship between primary and secondary care. When patients are given more certainty than a primary care practitioner would have provided [C], the primary care practitioner's view of specialists can be negatively affected[60] [O]. There is often poor communication between primary and secondary care providers[61,62], which makes it difficult to coordinate care[58]. From the system perspective, primary care may be the optimal context to deliver multimorbidity care because it is accessible to most patients[54], and tend to be viewed as efficient[54], equitable[54], and having wide reach[54] and good continuity of care[49,54,58,63]. However, the infrastructure of primary care settings may not be optimally designed to handle multimorbidity [C] and can lead to fragmentation of care [O]. This is because multimorbidity demands the involvement of multiple providers[34] [M], multiple care locations[51] [M], and extra consultation and provider time[26,29,36,54,64-67] [M], which can lead to less opportunities for preventative and psychiatric care [O], less care for concurrent conditions[50] [O], inadequate time for building patient-provider relationships[68] [O], and poor follow-up[26][O]. Increasing or adjusting consultation time for multimorbidity management [29,30,69,70] and complexity of illness[58] may provide opportunities to address these challenges.

Details of CMO configurations to explain Program Theory 2

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Disease and patient factors	***Barrier:*** Prioritization in itself is challenging for patients [O1], because of treatment side effects [M1][77], and the patient needs to manage one condition at a time, which may be in conflict with other condition treatment plans that they ought to be having [M1][77] ***Facilitator:*** Patients with multimorbidity optimally prioritize their health conditions [O1] by being actively involved in setting their goals and priorities [M1][92], and by sharing their feelings (with providers) about their illnesss(es) and its effects on their functioning [M2][92] by stating their expectations to providers of medical care [M3][92].
Provider factors	***Barrier:*** Patient prioritization can be hindered for patients [O1] by receiving confusing [M1] and conflicting [M2] treatment recommendations from physicians[77], and by lack of awareness/information regarding the seriousness of a condition [M3][87]. ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to have reassurance that their available treatments work [M2][77], and that their condition is being monitored regularly [M3][77].

	Contextual factors	***Barrier:*** There is currently no framework to assist patients in determining preference and synthesizing these preferences with existing evidence to set individual health priorities and decisions [M][94] ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to use home-based self-management programs [M1][78], and by having access to clinicians who are knowledgeable about their health conditions [M4][77].
Provider perspective		
	Disease and patient level factors	***Barrier:*** Prioritization is difficult for physicians [O1] when aspects of patient health such as when conditions or symptoms (e.g., pain) are difficult to treat and impactful [M1][95], when somatic and mental disorders are combined [M2][96], and when there is no specific diagnosis or the presentation is an asymptomatic condition [M3][93]. ***Barrier:*** The evidence for treating multiple chronic conditions itself [C1] may be problematic [O1] because it may conflict with patients' values, preferences and needs [M1], be insufficient or uncertain regarding effectiveness [M2], or in the case of health economics data, be difficult to interpret and use [M3][93]. ***Facilitator:*** Providers find it easier to prioritize uncomplicated conditions which are responsive to treatment [O2] because they are able to predict patient benefits [M1] and determine if treatment is cost-effective [M2][93]
	Provider factors	***Barrier:*** Prioritization is difficult [O2] when physicians do not know about a patient's psychosocial factors [M1], history [M2] or management expectations [M3][96]. Additionally, physicians themselves may not understand [M4] or be able to adhere to patient priorities [M5][94], and may not have in person-centered communication [M2][82] or shared decision making [M3][97] skills. ***Facilitator:*** Facilitators of optimal provider prioritization [O1] are good listening and communication with patients [M1][82], which also ensures that treatment is individualized to each patient [O2][94]; that priority setting is based on patient's perceptions, concerns, and expectation [O3][82]; that the prioritization has a positive impact on functions of daily living [O3][92], and based on what the patient has identified as their own priorities [O4][82]. This individualized care for the patient [O2] should be balanced with clinical knowledge[94] and provider self-reflection [M1][82].
	Contextual factors	***Barrier***: Optimized provider prioritization is challenging [O1] because it takes an investment in time [M1][82,96,97] which doctors worry might disrupt clinic flow [O2], result in financial loss [O3], and trigger patient complaints [O4][97]. ***Facilitator:*** Physicians can improve the process of prioritizing chronic conditions with the help of specialized multimorbidity clinics [M1] and multimorbidity software programs [M2][82]

Appendix 5

Context-Mechanism-Outcome (CMO) configurations of programme theory 3 (Patient self-management in multimorbidity)

General CMO configurations to explain Program Theory 3

Patient self-management in multimorbidity: We derived explanations via CMO configurations to explain self-management in multimorbidity (Appendix 6).	
Burden of multimorbidity management	Multimorbidity is reported as a burden by patients [O] because of the cognitive and emotional overload [M] required for lifestyle changes [C][80] (which can be inconsistent or conflicting [C][74]), as well as the volume of information and recommendations provided [C][46,81] (which are often confusing and conflicting[51,71,82,83][C]). Adherence to recommended treatment is challenging for patients [O] because: 1) self-management regimens have been designed to fit their condition rather than their health priorities [C], lifestyle [C], available resources [C][43,56]; 2) unwieldy medications (too many, taken often, and difficult to keep track of)[C][42,46]; 3) having to follow a required diet and exercise routine [C][46,71,84]; 4) having to see multiple providers[C][19]; 5) medication mismanagement[C][19]; 6) not knowing how to respond to adverse drug effects[C][19,42]; and 7) communication barriers due to linguistic and cultural diversity[C][19]. These multiple contexts likely trigger cognitive and emotional overload [M].
Influence of cognition and mental health on self-management	Self-management is particularly challenging [O] for older adults who have impaired cognition[56] [C]or suffer from anxiety[79] [C] in addition to chronic conditions [C] as these contexts interact to increase their perceive an increase in illness burden[68]. If the additional condition is depression [C]: older adults may choose not to do anything (such as take medication) [O] because they consider it a normal part of aging [M] or; are reluctant to seek treatment [O] due to stigma[27] [M]. Depression, as a context, appears to also trigger other mechanisms that reduce their ability to self-manage chronic conditions[27,28,45,50,67,71,80] [O]. The mechanism include reduced patient motivation, energy and self-efficacy, feelings of being overwhelmed, hopeless[45] or stressed[80]. There appears to be a number of feedback loops because illness burden can interfere with people's ability to engage in health promotion such as exercise, which can result in negative consequences such as weight gain[80], reduced quality of life, functional decline or ability to work. These in turn, can impact mood, social networks, and self-management behaviours[78].
Influence of resource constraints on self-management	Self-management in multimorbidity is influenced by the lack of resources available to many older adults to help manage this burden[28] including the lack of finances[71,78], social supports[33,56,71,78,87] or transportation[71], as well as the influence of low health literacy[85] or skills to manage and coordinate care and adverse effects[79,82]. Another challenge is that even if resources and programs exist, older adults may not be aware of them[78]. Promoting contact with consumer organizations or support groups[19,55] and having peer support[45] may address these challenges. Older adults are interested in self-management tools that provide health condition information[46]; share, coordinate and synthesize information with and between providers; and connect them with other patients[46]. Physicians can support patient self-management through tailoring of information to the stage of the patient's condition and their adaptation to it[55], as well as through good interaction with patients[83], providing information[83] (including patients' particular language[19]), and a collaborative approach to care[88].

Details of CMO configurations to explain Program Theory 3

Theme	**Sub-theme**	**Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations**
Patient perspective		

Managing multimorbidity is **difficult to do for patients** due to the volume, complexity, and confusing/ contradictory nature of what is required for self-management.	*Burden of self-managing multimorbidity*	***Barrier:*** The burden of self-management is high for people with multimorbidity [O1], and can impair their quality of life life[80] [O2] due to the required lifestyle changes[104], which are sometimes inconsistent or conflicting [M1][105]; the provision of the sheer volume of information provided[100,109] [M2], and the often confusing and conflicting information provided about treatment recommendations [M3][83,87,107,108] (including conflicting dietary advice for different conditions[83] from a multitude of healthcare providers). In fact, self-management becomes more challenging as the number of providers increases [M5][100] along with the numerous appointments required [M6][98,106]. ***Facilitator:*** Having multiple conditions itself can promote self-management [O] because patients may have already developed skills such as self-monitoring and self-advocacy [M1][111,113], and they may be more motivated because of the heightened risk [M2][111]. ***Facilitator:*** When patients can establish a cognitive link between existing self-management practices [M1][83,107,111], and making this link intuitively and over time[83], they can became more successful at self-management [O1].
	Adherence to self-management regimens (treatments and medications)	***Barrier:*** Successful self-management [O1] has been judged by the ability of patients to adhere to prescribed treatment [M1]. However, adherence to recommended treatment has not worked for patients [O2] because self-management regimens have been designed to fit their condition rather than their health priorities, lifestyle, and available resources [M1][78,109,110]. Other factors are unwieldy medications (too many, taken often, and difficult to keep track of) [M2][106,109], having to follow a required diet and exercise routine [M3][55,107,109], having to see multiple providers [M4][71], medication mismanagement [M5][71], not knowing how to respond to adverse drug effects (especially for those who take multiple medications) [M6][71,106], and information communication barriers such as linguistic and cultural diversity [M7][71] ***Barrier:*** Patients do not take prescribed medications [O3] for a variety of reasons: they do not like taking medications [M1][93,107], they believe that the medication will negatively affect their health [M2] or is inappropriate for their underlying condition [M3][107], they do not believe the medication is necessary [M4][107], they experience undesirable side effects from the medication [M5][106,107], the medication information is difficult to read or understand [M6][95], the regimen is too complicated to follow (particularly in culturally and linguistically diverse populations) [M7][71,87,98,109,115], the bottles are difficult to open [M8][95], and they forget to take their medication [M9][95]. Although not being able to understand and receive information can lead to medication noncompliance [O4][111] the provision of better and clearer information about medications alone is unlikely to improve adherence [M1][95]. ***Barrier:*** Medication noncompliance can also result if taking multiple drugs (polypharmacy), which can lead to drug interactions[119] and adverse events [M2][56]. ***Facilitator:*** People with multimorbidity can learn how to take medication strategically to achieve a balance between benefits and side-effects [O4], often based on years of experience of self-managing often antagonistic symptoms and competing goals [M1][93]. Medication adherence [O5] can be facilitated through automated reminder systems [M1][65,98], and switching to medications with modified release formulations [M2][98]. ***Facilitator:*** Medication adherence [O5] is linked to a person's self-efficacy (the confidence or ability to feel "I can do that") [M3][71], which can improve clinical outcomes [O6][65]. Some patients with multiple chronic conditions view their medication as a way of gaining control over their illness management [O7] by establishing routines for taking medications [M1] and seeing it as an opportunity to become more active self-managers [M2]. These patients consider medication management as positive [O8][83].

Cascading effects of multimorbidity: having, experiencing, and managing multimorbidity can cause additional barriers to self-management through **antagonistic** effects, both physical and emotional	The influence of chronic disease interrelatedness	***Barrier:*** Patients with multimorbidity may find it challenging to determine which chronic disease is causing a particular symptom [O1] because chronic diseases may share similar symptoms[103] [M1], the treatment of one condition can also aggravate another condition[92,99,107,111] [M2] or cause other antagonistic effects[107,111,112] (or the fear that it might cause these effects[93]) [M3] – these are major barriers to self-management, which can lead to medication non-adherence [O2][92,107] or low self-management in other lifestyle areas [O3][107]. ***Barrier:*** The diagnosis of an additional condition to an already existing one may also impede self-management [O4] because the new information for the 2nd condition adds uncertainty about what to do[104] [M1]. ***Facilitator:*** Patients who are able to identify the main illness that was causing them the most concern [M1] and keep it stable [M2] helps keep their symptoms under control [O1] and return to an acceptable way of life within the limitations of their illness [O2][104].
	The influence of mental and emotional health on self-management	***Barrier:*** Multimorbidity management challenges are exacerbated [O1] in patients with mental and emotional health problems (low cognition[78], anxiety[111]) because the limitations of one condition may impact the ability to look after another condition [M1][83,104]. The ability to self-manage for these people are influenced by the interaction of conditions [M2], which may also contribute to a perceived increase in illness burden [O2][113]. It is a cascading effect because if illness burden prevents exercise [M3], this can cause an increase in weight [104] [M3], and reduce quality of life, relationships, and ability to work [O3], which in turn can impact mood, social networks, and self-management behaviours[92] [O4]. In patients who have large discrepancies between current and past physical and cognitive functional abilities and activities (i.e., previous energy, endurance, strength, memory, ability to concentrate) [M1] may be unable to reconcile the difference and embrace self-management [O3][104]. ***Barrier:*** Cascading effects on self-management ability are also seen in multimorbidity patients with depression. In older adults, depression may be a barrier to effective self-management [O1] or a result of previous failures with self-management[116] [O2] because they may choose not to treat depression because they consider it a normal part of aging [M1], do not want to take medications [M2], or are reluctant to seek treatment due to stigma [M3][68]. Additionally, depression can reduce patient motivation, energy and self-efficacy [M4], causing them to feel overwhelmed [M5], hopeless [M6][74] or stressed [M7][104], which in turn can reduce their ability to self-manage[68,74,104,107,112,114,115]. Chronic pain[115] [C2] experienced by older adults with multimorbidity works similarly in that it can be disruptive to self-management [O3] because it can reduce motivation [M1] and cause significant emotional distress [M2]. ***Facilitator:*** Factors that influence better self-care [O1] and better experience of illness [O2] of patients with multimorbidity are learning how to manage their emotions through exercise [M1][93], spending time being outdoors [M2][93], having a change of scenery [M3][93], reframing their situation [M4][111], prioritizing certain conditions [M5][111], staying positive [M6][104], doing their best [M7][104] and to consider mindfulness-based stress reduction [M8][110].
	Lack of resources	***Barrier:*** Self-management of patients with multimorbidity [O1] is influenced by the lack of resources to manage the burden of multimorbidity[112] such as insufficient knowledge and information [M1][28,104,107], low health literacy [M2][95]; low skills to manage and coordinate care and side effects [M3][108,111]; and lack of finances [M4][92,107], social support [M5][78,92,107,117,118], or access to transportation [M6][107]. Caregivers [C] may find self-care especially difficult [O2] because of the time [M1] and finances [M2] they are already using to care for others[92]. Even if resources and programs exist to help patients self-manage multimorbidity, they may not be aware of them [M1][92]. ***Barrier:*** Self-management regimens can impede one's ability to work. Although continuing to work for those with

		multimorbidity may be difficult, it provides financial stability, health insurance and identity to patients[92]. ***Facilitator:*** Self-management can be improved for patients with multimorbidity [O1] if they have contact with consumer organizations or support groups [M1][71,120] and peer support [M2][74]. ***Facilitator:*** Patients are interested in self-management tools [O1] that provide health condition information [M1][109]; can share, coordinate and synthesize information with and between providers [M2]; help them access new research findings [M3], connect them with other patients [M4], help them sort health records [M5], consult with remote specialists [M6], and coordinate with local providers [M7][109]. Telehome care systems can improve patient self-management [O1] through the provision of health information [M8][65].
Provider perspective		
Communication between providers and patients		***Barrier:*** Providers (particularly specialists) [C] can themselves be a barrier to patient self-management [O1][99]. Patients may be dissatisfied with the way the provider communicates [M1][107,108], and family physicians (who are the primary contacts for patients) may fail to provide valuable information about self-management resources such as patient advocacy and self-help groups and other resources [M3][120]. ***Facilitator:*** Physicians can support patient self-management [O1] and have a positive impact on patient self-management [O2] through tailoring information-giving to the stage of the patient's condition and their adaptation to it [M1]***[120],*** through good interaction with patients [M1][83], information provision [M2][83] (including information in the patient's own language and adequate time to review it[71]), a collaborative approach to care [M3][84], encouraging active engagement in self-management [M4][71], motivating patients and providing a behavioural model [M5][74], and empowering patients by providing them with skills and confidence to manage their own conditions [M6][110].

Appendix 6

Details of Context-Mechanism-Outcome configurations to explain multimorbidity management overall

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Confusing for patients	***Barrier:*** Multimorbidity management in primary care [C] is confusing to patients [O2][80] due to the heterogeneous nature of multimorbidity [M1][81], disease and treatment interactions and possible conflicts [M2][77,82], and the difficulty of attributing symptoms to conditions [M3][77]. ***Facilitator:*** Supporting patient self-management is a critical aspect of multimorbidity care[93,94] and to achieve optimal health outcomes. These include medication support [68,72] [M1], motivational enhancement[92],43 [M2], and education [M3], which is a key aspect of optimal medication [O2] [95] and disease management [O3], particularly for people with arthritis and depression [C2][59]. ***Facilitator:*** A patient-centred approach, that takes into account the patient's psychosocial realities (housing, relationships, income, etc.) [M1][87] is more likely to meet the needs [O1] of complex patients with multimorbidity [C1][88,89]. Patient-centred approaches [M2] can help patients adopt healthy lifestyles [O2] if they have adequate adoption readiness [M2], and target additional behaviours once change in one behaviour is achieved [M3][90] 23. For complex patients [C1], patient-centered care may be promoted [O4] by enhanced communication [M3] although this may or may not improve disease-specific self-care and outcomes [O5][91]
Mental health needs of patients add to complexity	***Barrier:*** In primary care, mental health needs of patients in the context of multimorbidity management can be a barrier to patient self-care [O1][77], can create communication issues with providers (i.e., patient complaints may not be clear) [O2][77], are often ignored or normalized since physical health issues take precedent [O3][78], and can lead to patients receiving less intensive treatment [O4][79].
Provider perspective	
Overwhelming for providers	***Barrier:*** Multimorbidity management in primary care [C] may be overwhelming for providers [O1][83] due to the heterogeneous nature of multimorbidity [M1][81], disease and treatment interactions and possible conflicts [M2][77,82], and the difficulty of attributing symptoms to conditions [M3][77].
Not prepared for managing multimorbidity	***Barrier:*** Primary care clinicians are inadequately prepared for multimorbidity [O1] due to their lack of skills and confidence in addressing multimorbidity [M1][84], not having adequate decision support systems [M2][73] or evidence [M3][85] to support their clinical decision making, and having care protocols or intervention plans that are too rigid [M4][86]. These make it difficult for primary care physicians to simultaneously understanding patient subjective experience and biochemical processes of chronic conditions [O2][87]. ***Facilitator:*** Many general practitioners have identified the need for guidelines that address multimorbidity[77]. When only single disease guidelines are available to manage multimorbidity [C1], clinicians sometimes modify guidelines [M1] in anticipation of adverse effects[78], use common sense to complement the limitations of their application [M2][79], and work with patients to help them understand guidelines [M3] so they can make informed treatment decisions [O1][79]. Collaboration with patients is needed [M4] when the single disease guidelines being used are contradictory [C2][80]. In situations where few guidelines exist and there is significant clinical uncertainty [C3], shared decision making between patients and clinicians is a useful, and possibly a necessary tool [M5] for making individualized treatment decisions [O2][81]

	Multimorbidity can worsen the relationship between primary and secondary care (including care transitions)	***Barrier:*** An effective relationship between primary and secondary care (and in consequence, the transition between primary and specialist care) is difficult [O] for patients with multimorbidity because: patients are susceptible to exaggerated instructions by specialists and overly influenced by diagnostics [M1][99], specialists do not acknowledge primary care [M2][33,100], and there is often poor communication between primary and secondary care providers [M3][33,100]. This is compounded by the emphasis each specialist puts on 'their' guideline, which makes it difficult for primary care providers to coordinate care [M4][96]. The lack of cooperation between primary and secondary care [O2] also makes it difficult for patients [O3] because their needs are often episodic requiring both primary and specialist care either simultaneously or in succession [M4][55]. ***Facilitator:*** Patient-primary care physician concordance on health-related attitudes and perceptions [M1] appears to be a powerful predictor of primary care physician implementation of [O1] and patient adherence to [O2] to recommended geriatric health care[84]. This implies that specialist education regarding recommended care should be directed at both primary care physicians and their patients[85]. Additionally, trusting relationships between primary care physicians and specialists [M2] promotes collective and harmonized approaches to care [O3][86]
System perspective		
	Primary care is the optimal context to deliver multimorbidity care, but it is not designed to handle it	***Facilitator:*** Primary care may be the optimal context to deliver multimorbidity care [C] because it is accessible to most patients [M1][96], efficient [M2][96], equitable [M3][96], has reach [M4][96], has good continuity of care [M4][80,96-98], and primary care providers general know their patients well [M5][96-98] and they have a generalist and patient-centred approach to care [M6][98]. Relational continuity [M7] in primary care helps providers better understand patient needs [O1] and enhances multimorbidity care [O2][80]. ***Barrier:*** Primary care is not designed to handle multimorbidity [O1] because it demands extra consultation and provider time [M1][73,78,81,84,88-91]. This in turn can lead to inadequate care patients (i.e., less preventative care, psychiatric care, less care for concurrent conditions) [O2][79], inadequate time for building patient-provide relationships [O3][92], the complexities of primary care clinics requiring to schedule multiple appointments for multiple issues [O3][88], poor follow-up practices by clinicians [O4][73], and the tendency to maintain the status quo for complex patients rather than changing the management plan [O5][93]. ***Facilitator:*** Increasing consultation time for multimorbidity [M1][77,89,102,103], adjusting consultation time to complexity of illness [M2][80], and allowing for time to discuss health issues [M3][103] and build a relationship [M4][80] have all been identified as opportunities to improve multimorbidity management [O].
	Multimorbidity can lead to fragmentation of care	***Barrier:*** Multimorbidity can lead to fragmented care [O1][94,95] because it often leads to the involvement of multiple providers [M1][94], territorial specialists [M2][96] and multiple care locations [M3][82]. This complexity of care can lead to poor communication between primary and secondary care [O2][33,55,82,94,96,97], duplication of efforts [O3][82], confusion about what has been done (i.e., tests, treatments, and medications) [O4][94], treatment errors [O5][94], impaired treatment participation (i.e., lack of understanding of what is happening with a patient's care due to fragmentation, so the provider may not add to the care because they don't want to confuse things more) [O6][94]; high use of specialty services [O7][97], and lack of care coordination or the consideration of a holistic approach to care [O8][98]. ***Facilitator:*** Health information technology tools, including integrated EMRs and telehealth solutions [M1], can help with patient care coordination [O1][65,67,80,92]. ***Facilitator:*** Clinical tools (including those that focus providers on functional, rather than disease-related outcomes) [M1][99], and those that provide multi-morbidity decision support [M2][100] and assessment [M3][78,87]) can help providers more optimally manage patients with multiple chronic conditions [O1][100] and can optimize medication management [O2][101]. ***Facilitator:*** Multimorbidity can be better managed [O] through integrating similar disease processes[82] [M1], adopting additional health conditions into existing management practices [M2][83], and highlighting links between management practices [M3][83]

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			1
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			2
Structured summary	2	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.	2
INTRODUCTION			4
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			4-7
Protocol and registration	5	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.	4
Eligibility criteria	6	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.	5-6
Information sources	7	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.	6-7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5; Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	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.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			7-10
Study selection	17	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.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Not applicable
Results of individual studies	20	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.	7-10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8-10
DISCUSSION			11-13
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			13
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

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Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review

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Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review

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Word count: 3881

ABSTRACT

Objectives: To understand *how* and *why* effective multi-chronic disease management (CDM) interventions influence health outcomes in older adults 65 years of age or older.

Design: A realist review.

Data sources: Electronic databases including MEDLINE and EMBASE (inception to Dec 2017); and the grey literature.

Eligibility criteria for selecting studies: We considered any studies (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies) as long as they provided data to explain our programme theories and effectiveness review (published elsewhere) findings. The population of interest was older adults (age ≥ 65 years) with two or more chronic conditions.

Analysis: We used the RAMESES quality and publication criteria for our synthesis aimed at refining our programme theories such that they contained multiple Context-Mechanism-Outcome (CMO) configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography to separate units of data from articles, and to derive explanatory statements across them.

Results: 106 articles contributed to the analysis. We refined our programme theories to explain multimorbidity management in older adults: 1) Care coordination interventions with the best potential for impact are *team-based* strategies, *disease management* programs and *case management*; 2) optimized disease prioritization involves ensuring that clinicans work with patients to identify what symptoms are problematic and why, and to explore options that are acceptable to both clinicians and patients; and 3) optimized patient self-management is dependent on patients' capacity for self care and to what extent, and establishing what patients need to enable self care.

Conclusions: To optimize care, both clinical management and patient self-management need to be considered from multiple perspectives (patient, provider and system). To mitigate the complexities of multimorbidity management, patients focus on reducing symptoms and preserving quality of life while providers focus on the condition that most threaten morbidity and mortality.

ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first realist review to explain *why* multimorbidity interventions work, *for whom*, and *under what circumstances* to improve outcomes for older adults with multimorbidity – findings can be used to inform practice and policy decisions in the management of older adults with multiple chronic conditions
- Our search strategy was in part informed by a Systematic Review investigating the effectiveness of multimorbidity interventions for older adults that we conducted alongside this Realist Review
- We created a 3-step synthesis process drawn from in meta-ethnography to separate units of data from articles, and to derive explanatory statements across them
- Many of our included studies did not have complete data to enable optimized Context-Mechanism-Outcome (CMO) investigations
- Incomplete reporting also impacted our ability to fully test our theories and therefore, we could not completely elucidate the interrelationships within and between all of our CMO configurations

BACKGROUND

The global population is aging, with two billion people expected to reach 60 years of age and older by 2050[1,2]. It is now more common for older adults to have multiple chronic diseases than to have single diseases or no chronic medical conditions at all[3]. The burden of chronic disease is also on the rise globally[1,4] with more than half of older adults (age ≥ 65 years) living with high-burden chronic conditions (i.e., highly prevalent and associated with premature death and increased health care utilization)[3,5]. Older adults also have greater health care needs, are at higher risk for adverse health outcomes, and experience more frequent hospitalizations[6], yet only 55% receive appropriate care[7,8]. In response, different chronic disease management (CDM) interventions have been created. For example, a programme designed to encourage older adults with COPD and depression to adhere to anti-depressants and pulmonary rehabilitation[9]. Although promising, CDM interventions have shown varying effectiveness[10,11] in part, because they are not usually developed for older adults or created for sustained use; and very few are designed to deliberately address multimorbidity[8,12].

Given our rapidly aging population, there is an urgent need to understand how and why multimorbidity interventions influence health outcomes to optimise patient care. To address these gaps, we conducted a systematic review to identify effective CDM interventions that integrate the care of ≥ 2 high-burden chronic diseases affecting older adults (published elsewhere)[13]. However, a systematic review is not always enough to inform practice and policy decisions as knowing "what" works seldom reveals which desired outcomes may occur under different contexts. Our objective was to conduct a realist review alongside to explore the underlying mechanisms and contexts by which these CDM interventions work or do not work, for whom, under what circumstances and why[14]. Realist review is particularly relevant for making sense of complex interventions (such as those focusing on CDM) that have context-sensitive outcomes. It can add important contextual and mechanistic detail to existing knowledge on this topic[15]. Such detail is likely to contribute to the limited existing clinical practice guidelines on multi-morbidity management such as those developed by NICE[16], by explaining the contexts in which intended and unintended outcomes are likely to occur. Additional resources about realist reviews can be found the RAMESES Project website[17]. Our overall objective of this

review is to: understand *how* and *why* effective CDM interventions influence health outcomes in older adults 65 years of age or older.

METHODS

Study Design

Our protocol was published[18], and registered with PROSPERO (registration number CRD42014014489). We applied the RAMESES quality[19] and reporting criteria[20]. The systematic review methods and findings are reported elsewhere[13].

Programme theory development

To identify our initial programme theories (i.e., what multimorbidity interventions are comprised of, how and why they are expected to work and what outcomes they might generate), we used an iterative, consensus-based process. We considered two major sources to identify any published or unpublished literature[21]: 1) Medline and Google Scholar describing models, frameworks, theories of multimorbidity, chronic disease management, and complex interventions; and 2) content and methods experts on our team (geriatricians, family physicians, and health services and realist review experts). Duplicate screening of 97 reports by two reviewers identified 18 documents that contained data that helped us to understand CDM interventions. Through team discussion and a Delphi survey amongst our team, we indentified that our initial programme theory would have to incorporate the following concepts: 1) CDM interventions are complex interventions that do provide different outcomes in different settings; 2) health prioritization is an important aspect of multimorbidity and; 3) interventions that consider patient values and circumstances, the evidence and the clinician's expertise were more likely to produce desired outcomes. We then used the data from our included studies to gradually refine our understanding of these concepts and how(if at all) they fit into our more refined programme theory developed from this review.

Search strategy

Since we performed our realist review alongside our systematic review of multimorbidity interventions[13], the search strategy was done simultaneously for both reviews. As such, we identified potentially relevant articles for our realist review (i.e., to provide data to test our

programme theories) through our systematic review search strategy (inception to December 2017)[13] and performed additional iterative, targeted searches as needed for the realist review[19]. An experienced information specialist performed these additional searches in Medline and Embase (Appendix 1).

Selection and appraisal of documents

To increase the efficiency of our searching and screening process, reviewer pairs independently screened titles and abstracts simultaneously for both the systematic review and realist review. We considered any study design for inclusion (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies). During full-text screening, we considered all articles that were identified for the systematic review as well through additional targeted searches to explain our programme theories and effectiveness review findings. Two reviewers independently assessed each article for relevance (*does the source contain any data that could be interpreted as having our relevant context, mechanism or outcome for programme theory development?)* and rigor (*How trustworthy are the data? Does the article provide enough detail on how conclusions were reached irrespective of study design?)*

Data extraction

We created and pilot tested a standardized data extraction form. Data items were driven by our purpose to refine our programme theories through context-mechanism-outcome (CMO) configurations (i.e., if we were able to infer an explanation for the cause [M] for a particular outcome [O] under the influence of one or more particular contexts [C]). For example, computer-based counselling systems (intervention) targeting older adults and providers in primary care (C) are not acceptable (O) if they do not show any relative advantage over the current system (M_1) and if inconsistent with providers' current practice workflow (M_2). After extracting excerpts in duplicate, reviewer pairs independently assigned an associated concept code and iteratively developed a codebook of concepts (Appendix 2) that was used to code subsequent excerpts; any discrepancies were discussed and resolved as a team.

Analysis and synthesis processes

We used the RAMESES quality[19] and publication[20] criteria to guide the synthesis. Our goal was to refine our programme theories such that they contained multiple CMO configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography[22] to separate units of data from articles, and to derive explanatory statements across them. *Step 1*: reviewer pairs independently extracted relevant excerpts from articles. *Step 2*: One reviewer sorted excerpts by concept for each study and developed consolidated statements (groups of CMO configurations) for each. A second reviewer audited the first reviewer's statements by checking for agreement and consistency with their own interpretations. *Step 3*: As a team, we examined and compared consolidated statements *across* studies to derive explanatory statements. These were then used to refine our *programme theories* aimed at explaining the outcome patterns we found within the effectiveness review. When the consolidated statements seemed to disagree, we unpacked the concepts and further examined them, consulting our literature and content experts as necessary for additional data and insights.

Deviations from our protocol in conducting our realist review

We followed the methods as outlined in our protocol[18] with a few exceptions. First, we switched to an auditing process during *Step 2* of the analysis to make our process more efficient. This involved an auditor checking the work of a primary reviewer. Second, since our process to finalize the list of initial programme theories identified an area that was not covered by our systematic review search (i.e., health prioritization), we added a secondary search strategy to capture this literature as described above.

Patient and Public Involvement

Patients were not involved in the conduct of the review but older adults with multiple chronic conditions are involved in developing key messages for this research. These patients are also part of our broader integrated knowledge translation team to co-design an electronic self-management tool that integrates the care of multiple chronic conditions (KeepWell™); this tool is being informed by this review.

RESULTS

Study characteristics

Figure 1 is our PRISMA diagram, which shows the flow of article selection. Of 2435 potentially relevant citations that were screened for relevance, 124 articles were reviewed in full-text, and 106 articles contributed to the analysis[3,9,15,23-125]. Studies were published between 2002 and 2016 mostly in the United States (n = 32), the UK (n = 19), Canada (n = 14), Germany (n = 11), and Australia (n = 10). Most of the articles (75%) were about multimorbidity (n = 50) or disease prioritization (n = 29), and 27 studies (25%) addressed specific chronic disease combinations.

Programme theories

Using data from our included studies, we iteratively developed and refined our initial two programme theories and a third programme theory that emerged from our data. To make our findings more succint, in the following paragraphs, we have provided narratives that summarise the most important aspects of our programme theories. This approach obscures the detailed CMO configurations that underpin these narratives and may make our manuscript less useful for those interested in realist review methodology. To address this issue, we have provided indications of the CMO configurations that our narratives are based on. For those interested in seeing the links between our data and CMO configurations, please see Appendices 3-6 that explains the outcomes that may be achieved by the different intervention strategies used in care coordination under different contexts.

Programme theory 1: Care coordination interventions for multimorbidity management

Almost one-half of the interventions described in our realist review were "care coordination" interventions (i.e., changes in how healthcare workers interact with each other or patients to ensure timely and efficient delivery of healthcare)[126]. Appendix 3 shows their detailed CMO configurations that underpin this programme theory. Overall, we found that care coordination interventions in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They address multiple conditions through interdisciplinary teams or multidisciplinary disease management, providing specific processes for communication, and establishing formal roles for providers and patients. We identified three types of care coordination approaches that health care providers may wish to use that have

potential for impact: *1) Team-based* or collaborative approaches involve highly trained clinicians[53] providing holistic and coordinated care[88] including spending time with patients to discuss all their concerns, and to prevent care overlap and gaps[80]. Patients are given education, counseling and other support services to address their disease(s), medications, and lifestyle[44]. Team-based approaches can provide access to specialists[53] and a wider range of services, and provide evidence-based care solutions for multiple conditions in parallel (not in tandem)[38]. Optimized care outcomes are most likely to occur through interdisciplinary communication and collaboration[38,81], when teams comprise highly trained and skilled members[53] who understand and accept each other's roles[53], provide opportunities[38,88] and time[53] to share information[81], and collaborate on patient care[38,45,53,88]. Other contexts in which mechanisms are likely to be triggered include teams that have dedicated members who provide additional support to patients[38,53] or providers[81], receive training[38,53,81], and have a robust and well-functioning communication system[38,45]. *2) Disease management* programs follow a "script" for how to provide effective patient care via care protocols or plans, which define the division of tasks, support the follow-up and coordination of action[103,110], and help to sustain a philosophy of common care[45]. Systematized care is achieved through checklists, follow-up timetables[45,103,110], and treatment targets[45], which can lead to a shared philosophy of care[45,103] and optimized decision making[45]. *3) Case management*: Case managers are trained health care professionals who are the main contact (and conduit of information) between a patient and involved providers[53], and most appropriate for multimorbidity management when there may be multiple and diverse providers involved in a patient's care. When case managers are the primary contact[103,80], care is perceived by patients as continuous[78,79], coordinated[79] and more individualized[9,80], and fosters the development of the skills and confidence patients need to self-manage their health[78].

Programme theory 2: Disease Prioritization in multimorbidity management

The detailed CMO configurations of disease prioritization that underpin this programme theory are described in Appendix 4. Multimorbidity management is perceived as confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[102], disease and treatment interactions and possible conflicts[57,92], and the difficulty of attributing symptoms to conditions[57]. Multimorbidity can create a cognitive and emotional overload in patients and

providers[64], so a common strategy they use is to focus on one condition at a time. Patients and providers focus their attention by prioritizing one condition over another for a specified period of time, or until particular outcomes are achieved[91,64]. However, patients and providers approach prioritization differently. Patients make prioritization judgements based on the symptoms they experience and need the most attention. They identify the most undesired symptoms and focus on their associated condition(s)[32,56,63,66,68,125] or those that threaten their social activities[25,63,76], limit their independence[25,91] and have potentially severe long-term consequences if not addressed[63,91]. Providers prioritize conditions based on their judgments about the prognosis or severity of the condition and place greater emphasis on conditions with more serious outcomes[25,57,66,68,76,125]; they focus on conditions that threaten a patient's morbidity and mortality[25,57,66,68,125], those they think they are better equipped to address (e.g., physical over emotional[32,124]), and whether the patient is likely to benefit from treatment[57,114,124,125]. What's common among patients and providers, is that they both consider conditions that they feel *capable* of addressing[64,91,124,125], and both consider the cascading effects of multimorbidity and the interrelatedness of these conditions during the prioritization process[65,91]. For patients, the cascading effects of multimorbidity are particularly challenging. Patients may find it difficult to determine which chronic disease is causing a particular symptom because conditions may share similar symptoms[72] or the treatment of one condition may aggravate the other[61,62,90,91] or cause other antagonistic effects[64,90,91]. Self-management is therefore a challenge for patients because the diagnosis of (and receipt of information) about a new condition compounds the complexity and uncertainty of what to do[87]. Figure 2 shows our conceptualization of optimized disease prioritization from the perspective of providers and patients.

Programme theory 3: Patient self-management in multimorbidity

The detailed CMO configurations of multimorbidity self-management that underpin this programme theory are in Appendix 5. Multimorbidity is perceived by patients as a burden because of the volume of information and recommendations provided[51,74] which are often inconsistent or conflicting, and the cognitive and emotional overload required to assimilate this information or to make lifestyle changes[87]. Subsequently, this can lead to confusion and non-adherence to recommendations[25,43,91-93] and may also trigger cognitive and emotional overload. Specific explanations to these outcomes include: 1) self-management regimens are designed to

fit their condition rather than their health priorities, lifestyle, and available resources[89,94]; 2) prescribed medications are unwieldy (too many, taken often, and difficult to keep track of)[15,51] or mismanaged[71]; 3) difficulties with following the required diet and exercise routine[36,51,91]; and to see multiple providers[71]; 4) not knowing how to respond to adverse drug effects[15,71]; and 5) experiencing communication barriers due to linguistic and cultural diversity[71]. Self-management is especially challenging for older adults with cognitive impairment[89] or anxiety[90] in addition to other chronic conditions, as these contexts can interact to increase people's perceived illness burden[63]. In particular, if depression is the additional condition, older adults may choose not to do anything at all because they either consider it a normal part of aging or reluctant to seek treatment due to the stigma associated with mental health problems[30]. Depression, as a context, can therefore also trigger additional mechanisms that reduce a patient's ability to self-manage chronic conditions[30-32,59,64,87,91]: reduced motivation, energy, self-efficacy; and feelings of hopelessness[31], and stress[87]. A number of feedback loops are activated because illness burden can interfere with a person's ability to engage in health promotion (e.g., exercise). This can lead to negative consequences (e.g., weight gain[87], reduced quality of life, functional decline), and in turn impair mood, social networks, and self-management behaviours[62]. Multimorbidity self-management is also influenced by the lack of available resources[64] (e.g., adequate finances[62,91], social supports[23,62,88,89,91] or transportation[91]) or low health literacy[29] or skills to manage adverse effects[43,90]. Older adults are interested in self-management tools that provide health condition information[51]; share, coordinate and synthesize information with and between providers; and connect them with other patients[51]. Physicians can support this by tailoring information to the stage of the patient's condition[26], having interactions with patients[93], providing information[93], and fostering a collaborative approach to care[115].

DISCUSSION

In this realist review we developed and refined our programme theories to explain why coordination of care interventions (found to have the most potential for impact in our systematic review) work to improve outcomes for older adults with multimorbidity. Care coordination interventions may be effective in primary care because they represent a structured approach to comprehensive care, and address multiple conditions through interdisciplinary teams or multidisciplinary disease management by providing specific processes for communication, and

establishing formal roles for providers and patients. *Team-based approaches* provide the right care at the right time, *disease management* offers a systematized approach to care, and *case management* offers a dedicated case manager as the conduit of care.

In addition to refining our programme theories, we generated explanations associated with these theories. Appendix 6 shows the CMO configurations to explain of multimorbidity management overall. Figure 3 shows our conceptualization of multimorbidity management, which suggests that optimized care requires both clinical management and patient self-management, with the caveat that each needs to consider identified challenges from the perspective of those affected by them (patient, provider, system). From the patient perspective, clinical management can be confusing due to conflicting messages, which is compounded in the presence of depression, impaired cognition, or poor health literacy. The mental health needs of patients can further complicate clinical management by impeding self-care, creating communication barriers with providers (e.g., patient complaints may not be clear), and patients receiving less intensive treatment. Self-management is difficult for patients because of the high burden of required lifestyle changes and adherence to multiple and often conflicting treatment regimens. Multimorbidity can also have cascading effects due to the nature of how chronic diseases are interrelated and the influence of a patient's mental and emotional health on self-management. From the provider perspective, clinical management of multimorbidity may be perceived as overwhelming because of the heterogeneous nature of multimorbidity, and conflicting or lack of evidence to guide clinical decision making. Lack of skills and confidence, not having decision support systems and protocols that are too rigid can also lead to inadequate preparation to manage multimorbidity. From a system perspective, even if primary care is the optimal setting for multimorbidity management, it may not always have the infrastructure to support optimal strategies such as care coordination and can also lead to fragmentation of care.

Recommendations

Findings from programme theory 1 suggests that health care providers may wish to use care coordination interventions that are: *1) Team-based* or collaborative approaches that involve highly trained clinicians providing holistic and coordinated care through effective interdisciplinary communication and collaboration, and the provision of education and

counseling to patients to address their disease(s), medications, and lifestyle; *2) Disease management* programs via care protocols or plans, checklists, follow-up timetables, and treatment targets; and *3) Case management* strategies for situations when there may be multiple and diverse providers involved in a patient's care. For programme theory 2, the specific types of disease prioritization approaches that health care providers may wish to consider is to work with patients to identify what symptoms are bothering them and why, and exploring options that are acceptable to both clinicians and patients for addressing their symptoms. For programme theory 3, the specific types of self management approaches that health care providers may wish to consider include not assuming that all patients are capable of self care, identifying who is capable of self care and to what extent, and establishing with the patient what they need (eg. informtion, support) to enable self care.

Strengths and limitations

To our knowledge, this is the first realist review investigating older adult multimorbidity aimed at explaining *why* effective multi-CDM interventions (identified through a systematic review[13]) work/do not work for whom, under what circumstances and why. This can better inform practice and policy decisions about multimorbidity management than a systematic review alone. A Cochrane review investigated interventions in multimorbid patients of any age[15] and found mixed results, but concluded that interventions that were integrated with care and targeted specific risk factors or functional difficulties may be more effective[15]. A rapid realist review investigating the underlying mechanisms of care planning strategies found that the mechanisms driving positive outcomes for people with long-term conditions are those that motivate them and promote an understanding of their role in self-management and how their lifestyle affects their conditions[127]. Our findings build on these studies by providing *explanations* for why multimorbidity interventions may be effective for older adults. Additionally, we focused exclusively on older adults because they represent a relatively unstudied population, and given their projected population growth, they urgently need our attention to optimize their care. The NICE guidelines on clinical assessment and management of multimorbidity[16] (one of few existing multimorbidity guidelines) support many of our findings. They emphasize the need to find synergies in care regimes and simplifying care where possible. They also describe a preferred approach to care, which involves establishing patient goals, values and priorities,

where patients are encouraged to describe their preferred decision making approach and what aspects of their life they prioritize[16]. A recent qualitative systematic review also highlights the need for providers to simplify the burden of care for multimorbid patients[128]. Our findings highlight the importance of focusing multimorbidity management by prioritizing one or more specific condition(s) and ensuring that prioritization is undertaken in collaboration with patients.

Our study has some limitations. First, it is possible that other teams may have identified different programme theories or interpretations. However, we used a rigorous and systematic process, and we let our data guide our interpretations. Second, many of our included studies did not have complete data to enable optimized CMO investigations. This may in part be due to an over-emphasis on effectiveness research in the literature, and an under-representation of qualitative inquiry, particularly about elucidating "mechanisms". For example, the literature rarely addressed the social determinants of health (a potentially significant trigger for multimorbidity outcomes) even though many older adults experience social isolation[129] and financial[130] challenges). Incomplete reporting also impacted our ability to fully test our theories. As such, whilst we developed and refined a number of explanations for our data, we could not completely elucidate the interrelationships within and between all of our CMO configurations. Finally, it is important to note that since this analysis was interpretive and inductive, it is possible that another team of researchers would have arrived at a different set of programme theories that incorporate the mechanisms and contexts of multi-CDM interventions for older adults. Thus, these findings should only be used as potential mid-range theories to explore and interrogate.

Conclusions and future directions

Our realist review contributes to the current, limited knowledge of the underlying mechanisms of complex multi-CDM interventions for older adults with multimorbidity. We found that care coordination interventions are effective because they represent a structured approach to holistic care. To mitigate the complexities of multimorbidity management, patients focus on reducing their undesired symptoms and preserving their quality of life, while providers focus on the condition that most threaten a patient's morbidity and mortality. To optimize care, multimorbidity management requires both clinical management and

patient self-management, and be considered from multiple perspectives (patient, provider and system).

Abbreviations

CDM: chronic disease management; CMO: context-mechanism-outcome; UK: United Kingdom; COPD: chronic obstructive pulmonary disease; EPOC: effective practice and organization of care.

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Data Statement

We included most of the data generated or analyzed for this study in this published article and associated appendices. Any additional datasets are available from the corresponding author upon request.

Competing Interests

The authors have no competing interests to report.

Author Contributions

MK: Manuscript development and final approval, methods design, data acquisition, data extraction, data analysis, research question development

LH: Manuscript development and final approval, data extraction, data analysis

GW: Manuscript development and final approval, methods design, and data interpretation

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Figure legends

Figure 1: Flow of article selection

Figure 2: Framework of optimized multimorbidity management

Figure 3: Framework of optimized chronic disease prioritization

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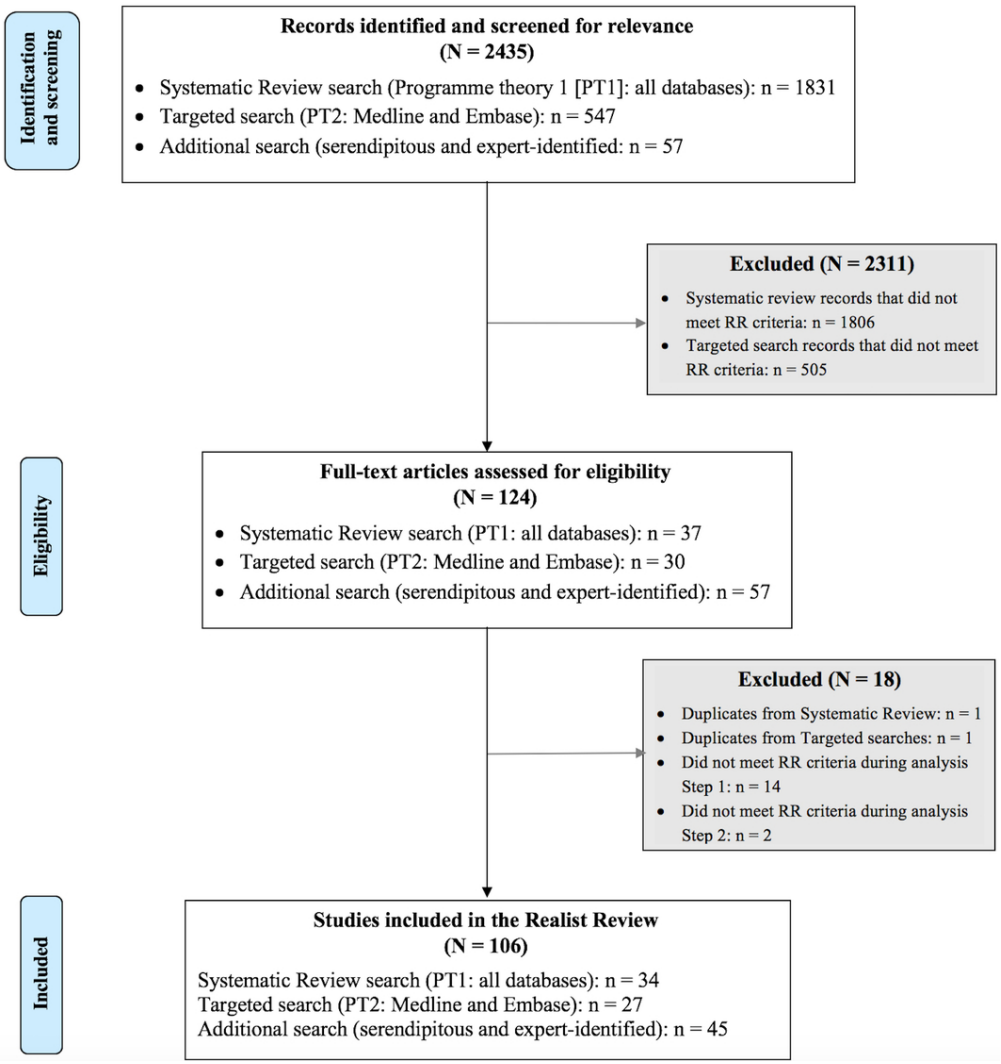

Flow of article selection

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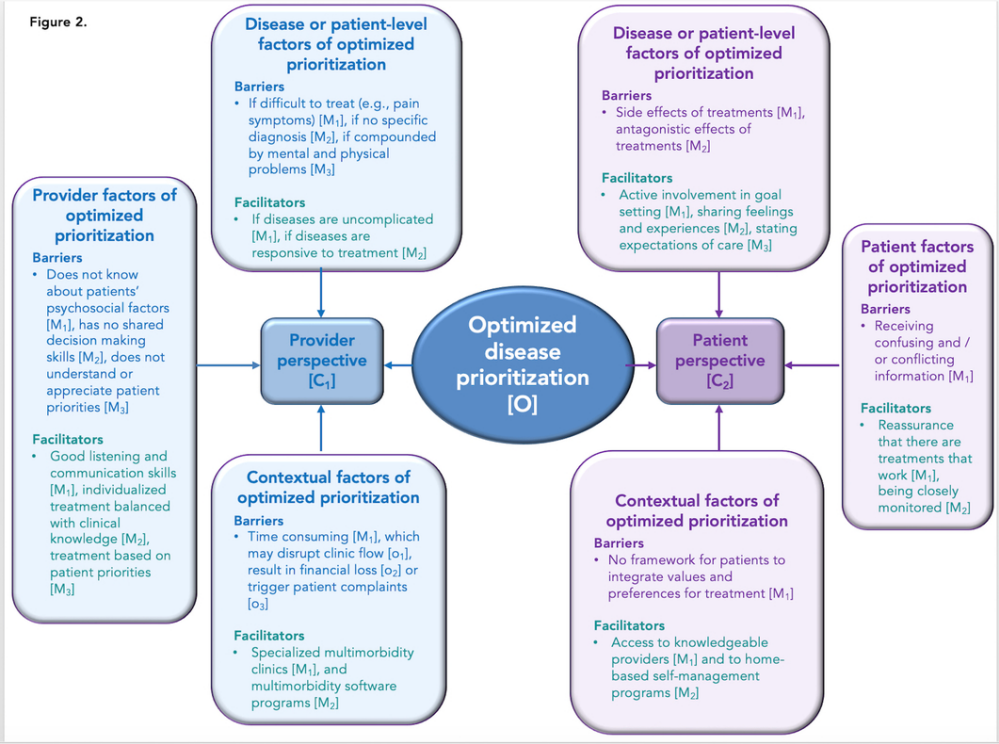

Framework of optimized multi morbidity management

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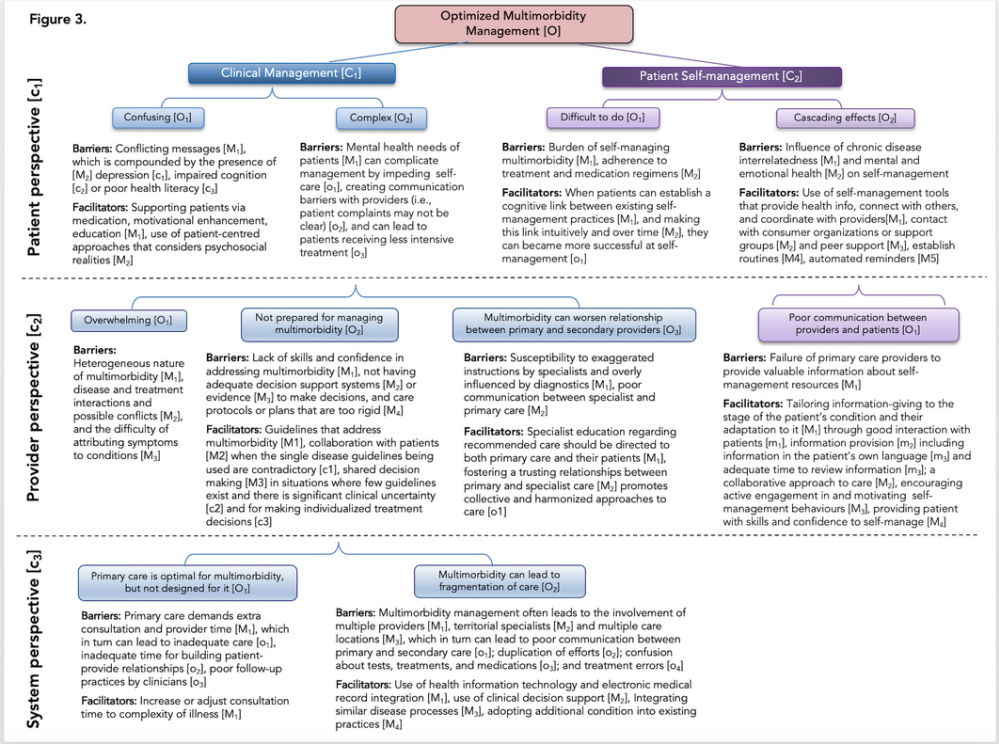

Framework of optimized chronic disease prioritization

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Appendix 1

Medline search strategy for rough program theory 2 (health prioritization of multiple chronic conditions)

1. Primary Health Care/
2. Physicians, Family/
3. general practice/ or family practice/
4. (healthcare adj (professional or provider)).tw.
5. or/1-4
6. exp Geriatric Assessment/
7. *"Referral and Consultation"/
8. Decision Making/
9. Decision Support Systems, Clinical/
10. (consult$ or refer$).tw.
11. health planning/ or health planning guidelines/
12. ((Shared or sharing or shares) adj ("decision making" or "decision-making" or "decision making process" or "decision-making process")).tw.
13. Patient Participation/
14. or/6-13
15. 5 and 14
16. (chronic disease$ adj2 management tool$).tw.
17. Chronic Disease/
18. ((chronic* or longterm or long-term) adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)).ti,ab.
19. ((multi or multiple) adj2 (condition* or disabilit* or disease* or disorder* or ill or illness* or morbidit*)).ti,ab.
20. (multimorbid* or multi-morbid*).ti,ab.
21. ((complicated or complex) adj (health or healthcare or illness* or morbidit*)).ti,ab.
22. Comorbidity/
23. (comorbid* or co-morbid*).ti,ab.
24. exp disease management/
25. ((chronic* or (multi* adj chronic*)) adj (disease* or patient$1) adj manag*).ti,ab.
26. ((self or personal*) adj2 (administ* or care or control* or manag* or monitor*)).ti,ab.
27. (17 or 18 or 19 or 20 or 21 or 22 or 23) and 26
28. or/16-25,27
29. (geriatric* or gerontolog*).ti,ab.
30. (elderly or senior? or (old adj age) or (older adj adult?)).ti,ab.
31. Geriatrics/
32. or/29-31
33. Patient Participation/
34. Physician-Patient Relations/
35. Patient Care Planning/
36. *Patient Care Team/
37. ((physician? or doctor? or provider?) adj ((patient? or client*) adj relation*)).tw.
38. "goal-oriented care".ti,ab.
39. ((physician? or doctor? or provider?) adj ((patient? or client*) adj communicat*)).tw.
40. ((Patient?-centred or client*-centered) adj (decision adj mak*)).tw.
41. (Shar* adj ("decision-making" or (decision adj mak*)) adj (process* or proced* or method*)).tw.
42. or/33-41
43. 32 and 42
44. Health Priorities/
45. ("Re-prioritization" or "prioritization" or priorit*).tw.
46. (Priorit* adj guideline?).tw.
47. ("health care" adj priorit*).tw.
48. "pivot point".tw.

49. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
50. (trad* adj off?).ti,ab.
51. or/44-50
52. 15 or 43
53. 52 and 51 and 28

48. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
49. (trade* adj off?).ti,ab.
50. or/44-49
51. 15 or 43
52. 51 and 50 and 28

Appendix 2

Codebook for identifying concept themes – Program Theory 1

Concept	Concept definition	Source (Reference number)
BARRIERS		
Barriers to effective chronic disease management interventions	**GENERAL BARRIERS:** • Barrier factors or challenges to achieving effectiveness, impact, intended performance of chronic disease management interventions. Barriers related to specific types of interventions are described below • These tools can be targeted to clinicians, providers, other health care professionals and patients and used in any setting (e.g., primary care, hospital, home) • Examples: ○ Interventions are not directed to enhance patient self-management **IMPLEMENTATION BARRIERS** • This includes barrier factors related specifically to the implementation of the intervention, which can include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention. • Barriers to positive adaptation to and use of the intervention (emotional, cognitive, or physical dimensions that impede patients' use of the system). • It can also be about the "delivery" mechanisms of the intervention that may hinder its adoption or uptake • Implementation barriers can relate to situations where family members are protective of vulnerable residents (in a LTC setting), which may lead them to withhold permission for their relatives to participate in the study. • These intervention designs often presuppose the availability of informal support systems even though the impact of treatment burden on both caregivers and patients with chronic conditions is well documented.	• 23-26
Behavioural interventions • *Cognitive behavioural therapy* • *Self-management interventions*	GENERAL BARRIERS • Factors that negatively influence behavioural interventions • Universal Medication Schedule: The *aim was to standardize prescription labeling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding*.	• 15,27-32 Self-management interventions • 29,33

		Clinic-based self-management interventions for patients One possibility [for why self-management interventions struggle to achieve reach] is that most forms of intervention, whether provider based or patient based, are outside patients' workaday and social activities, so fail to embed themselves into their everyday lives.	
	Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Chronic Care Model* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL BARRIERS** • Factors that negatively influence coordination of care interventions	• 27,34-41
		IMPLEMENTATION BARRIERS • Factors that negatively influence the <u>implementation</u> of coordination of care interventions **<u>Shared care implementation barriers:</u>** • If care providers are less easily convinced of the feasibility of shared care models because of the traditional professional boundaries they find difficult to give up or change.	• 15,38,42-45
	Health information technology tools: • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL BARRIERS:** • Factors that negatively influence health information technology tools	• 29,37,46-53
		IMPLEMENTATION BARRIERS: • Factors that negatively influence the use of technology based or computer-based tools or systems (e.g., low use). • Factors that influence adaptability of health information technology tools (i.e., factors that affect how people adapt to using the system to manage their chronic conditions) • Issues such as data decentralization, security, and privacy often prevent the implementation of health IT. **<u>Video-image conferencing implementation barriers:</u>** • Socioeconomic, technological, political and professional barriers • The lack of uniform policies and standards for health care facilities and patient confidentiality issues in the infrastructure at state and national levels • Arbitrary boundaries for services • High costs to support broadband connectivity	• 48,50,51,54

	• Public and private payers' reluctance to establish reimbursement policy at lower levels adds another obstacle to broader deployment of real world Telemedicine. **Computer-based counselling implementation barriers** • Lack of implementation by care staff, which could lead to failure to produce an effect **Telephone/telemonitoring implementation barriers** • Inconsistent interactions with patients. • Completing the minimum number of telephone / telemonitoring calls prior to patient discharge. • Communication and collaboration barriers between nurses and physicians. • Being unaccustomed to modern technology. • Fear and avoidance of modern technology ('computer anxiety') which can impede implementation and use of home telecare management system. • Nurses had to be assisted with physician communication by other personnel who would send letters for non-urgent requests or calling directly for urgent ones.	
Barriers to the management of multiple chronic diseases	**GENERAL BARRIERS** • Barriers to the complexity of care required to manage multiple chronic conditions (i.e., multiple prescribers, multiple providers; consumer knowledge gaps about treatment) • Examples: o Having a limited consultation time o Multiple providers o Undefined roles of GPs and specialists o The presence of simultaneous care plans for multiple conditions can lead to confusion, which can generate safety hazards.	• 15,23,26,33,35-40,45,50,51,55-86
Barriers to effective self-management of multiple chronic conditions	**GENERAL BARRIERS:** • Barriers that patients experience in self-managing their multiple chronic illnesses. • Examples: o Difficulty following exercise and dietary plans o Depression o Fatigue o Poor communication with physicians o Lack of social support o Pain and physical symptoms o Financial problems o Lack of awareness o Lack of information	• 15,23,25,26,28-32,36,43,51, 55,56,59,61-65,72,74,85,87-95

	○ Emotional impact of having multiple chronic conditions • Multimorbidity reduces the capacity of patients to modify their lifestyle, their ability to seek help and to manage multiple medications. • Multimorbidity also has a significant economic impact on patients because of the costs associated with their care, which may be compounded by their inability to work as the conditions progress.	
Barriers to using existing guidelines for disease management	**GENERAL BARRIERS** • Barriers or challenges faced by physicians to using existing guidelines for disease management, which tend to focus on a single disease • Lack of guidelines for managing multiple chronic diseases, which may lead to provider lack of knowledge of optimal care pathway	• 25,37,39,40,56-58,60,61, 63,66,72,74-76,83,86,89,96-99
Chronic disease interrelatedness	**GENERAL BARRIERS** • Chronic diseases may be interrelated • The course of one chronic disease may influence the course of the other disease (e.g., Depression and dyspnea-related disability) • The influence of treatment(s) for one chronic disease on the outcomes of other co-existing chronic diseases • The additive impact of one disease to the other • The impact or burden of one disease on the treatment demands of the second disease (e.g., Diabetes magnifies the demands of COPD treatment). • Multimorbidity may present as a collection of long-term conditions that share common risk factors (e.g. chronic obstructive pulmonary disease and cardiovascular disease as a result of smoking) or when one condition leads to another as a complication. • Quality of life for people with multimorbidity is inversely related to the number of conditions they have and the extent of any disability.	• 3,9,28,30,35,45,55,65,69,71,74,82,92,100-102
Depression + Diabetes	The additive impact of depression and diabetes lead to functional impairment including a higher number of cardiac risk factors, increased micro- and macrovascular complications in addition to poor self-care and increased mortality.	• 101
Diabetes + Chronic Kidney Disease	Irrespective of the cause of kidney disease, the co-existence of diabetes, CKD and hypertension leads to synergistic adverse effects: mortality is higher, quality of life is worse and the burden on healthcare services is increased.	• 27,35,55,103
Depression + Pain	Improved arthritis pain was associated with decreased depression; the concurrent improvement in both conditions supports the close interplay between depression and pain (Lin, 2003).	• 104
Disease co-management	**GENERAL BARRIERS** • The care or management of two diseases simultaneously • Suggestions on treatment of co-existing diseases (e.g., depression + arthritis)	• 9,27,30,34,35,39,61,62,65,72,74, 82,105

	• The need to simultaneously manage multiple chronic conditions complicate care management - escalating challenges of understanding a growing number of different clinical conditions while attempting to monitor combinations of different symptoms, and reporting symptom and functional status changes to multiple providers from different specialties, and adhering to different medication administration and other care plans.	
FACILITATORS		
Facilitators of effective chronic disease management interventions	**GENERAL FACILITATORS** • Facilitator factors (positive attributes) that contribute to the effectiveness, impact, intended performance of chronic disease management interventions • Impact can directly affect patients or healthcare providers or the system or how patients access or use health services or the management of their diseases • Care plans [in the context of multiple chronic conditions need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. • Participants reported feeling supported and reassured through the intervention because they were in contact with individuals who listened, understood and empathized with them and validated the challenges of living with the many consequences of their health conditions. **IMPLEMENTATION FACILITATORS** • This includes facilitator factors related specifically to the implementation of the intervention. These can also include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention.	• 23,37,55,63,76,92,106
Behavioural interventions • *Cognitive behavioural therapy (CBT)* • *Behaviour activation* • *Self-management interventions*	**GENERAL FACILITATORS** <u>Cognitive behavior therapy (CBT) facilitators</u>: • Having trained practice nurses deliver the intervention. <u>Behaviour activation facilitators</u>: • Strategies to activate patients to perform particular health behaviors. (i.e. medication self-efficacy and adherence) <u>Self-management interventions</u> • Universal Medication Schedule: The aim was to standardize prescription labeling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding. • Interventions that target improving patient self-management behavior/skills.	General • 15,26,28,31,107 CBT: • 28,34,104 Behaviour activation • 30,71 Self-management interventions • 15,28,29,31,33,55,94,108

	Home based Interventions	Home-based services that bring multiple disease management services to people with mobility and other barriers to access to care	• 109
	Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Comprehensive Geriatric Assessment* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) coordination of care interventions	• 15,39,110
		IMPLEMENTATION FACILITATORS <u>Case/care-management implementation facilitators</u>**:** • Having a specialist mental health team. <u>Collaborative care facilitators</u>**:** • A practice nurse who can carry out the intervention • Access to clinical software capable of generating a disease registry from which patients could be selected to participate in the trial were the facilitators of the implementation of the intervention. • The design of the intervention which allowed for its easy implementation within general practices and a better use of their existing resources meant that the TrueBlue could be easily applied to patients across general practices at a population level, making the benefit clinically important. <u>Disease management program facilitators</u>: • Adherence to evidence-based guidelines, which can improve health and cost outcomes • Usefulness (how valuable the users consider the specific features, functions, and data the tool makes available to them) • Value • Satisfaction • Ease of use (how easy it is for a user to complete their desired task with the tool) • Acceptability • Intention to use.	• 9,41,42,61,69,75,78,79,111 <u>Collaborative Care:</u> • 38,103,112 <u>Integrated care</u> • 53,80 <u>Coordinated care / Disease management:</u> • 36,39,45,63,65,81, 92,110 <u>Advanced Practice Nursing</u> • 44 <u>Patient-partner approach</u> • 45

	Health Information Technology Tools • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) health information technology tools • Health information technology can promote coordination of care and improve quality and safety. <u>Telephone/telemonitoring facilitators</u>: • Good disease management combined with the deployment of the technology • Telemonitoring was managed by primary care professionals (GPs and nurses) who regularly see their patients in health centres or at home than if the intervention was in-hospital; • The perception of facilitators in the increasing healthcare professionals' intention to use telemonitoring technology (organizational context is the most important variable); • Paying attention to the proper clinical management of patient's conditions. • Universal Medication Schedule.	• 27,29,46-52,54,108,113
	Self-management interventions?	**GENERAL FACILITATORS** • Factors that facilitate self-management. • Impact on self-management can occur in the emotional, physical, and financial domain, but is not restricted to these	• 27,50,77,84,108,114

Facilitators of the management of multiple chronic diseases/multimorbidity	**GENERAL FACILITATORS** • Factors that facilitate the patient's management of multiple chronic conditions. • "Factors" may include the qualities and components of the intervention that make it easier/simpler to manage a patient's multiple chronic conditions (manage: to stabilize, control, or improve a patient's health or quality of living with multiple chronic conditions). • Care plans that are clear and blend clinical care with self-management are essential in multimorbidity; they need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. • Examples: o The biopsychosocial approach to care can be applied to patients with both depression and arthritis; it should include depression screening in a systematic assessment of pain among older patients with symptomatic osteoarthritis.[104] o Medical management of arthritis can integrate evidence-based depression treatment with patient education and support for self-management (eg, exercise) to maximize functional status and quality of life." o The facilitators that are proposed to assist patients with the management of depression and arthritis are 1) the inclusion of depression screening with pain assessment, and 2) the integration of depression treatment with patient education and self-management support. • This concept is different from "Facilitators of effective chronic disease management interventions/programmes" because the latter concept looks at explaining why an intervention/program works o For example, Lamers[28] explains, "Minimal interventions like our MPI – that (1) may provide patients with the skills to cope with the consequences of their illness and their depressive symptoms, (2) can be incorporated in existing disease and care management programs, (3) can be administered by nurses (e.g. practice nurses)." It is *because* the intervention provides patients with certain skills, and its implementation is favourable, that the MPi is able to be implemented and foster positive patient outcomes.	• 15,26,30,32,33,37,39, 40,45-47, 55-59,61,62,72,74-76,81,82, 84,86,88,89,92-94,98,102,104, 105,115-120
Facilitators of effective self-management of multiple chronic conditions	**GENERAL FACILITATORS** • Factors that facilitate self-management of multiple chronic conditions. • Examples: o The support of family, including reminders to take medication and avoidance of eating unhealthy foods, and social relationships serve as motivators for patients to more effectively manage their conditions.[62]	• 26,33,36,47,51,56,64,71,85,87,90, 91,93-95,108,115

Facilitators to using existing guidelines for disease management	• Includes examples of situations when practitioners thought it was useful to use or adhere to guidelines
	• Includes suggested ways to improve usefulness or helpfulness of guidelines.
	• Examples:
	  • Adhering to guidelines promotes working transparently
	  • Guidelines would be helpful for multimorbid patients if they provided more details on diagnostic, treatment, and management priorities
	  • Guidelines improve the quality of general practice
	Guidelines provide guidance to medical decision-making
		• 98

Factors influencing the management chronic conditions/multimorbidity	• Factors that influence the management of patients with chronic conditions (directionality not specified). ○ Factors that may influenced doctors' varying views on the preparedness of their practices to manage patients with different types of complex needs include: the organization of primary care, workforce training, use of teamwork, size of practice, payment strategies and incentives, health IT (information technology) capacity, and the availability of community services may play a role.[54]	• 37,54,92,117

Factors which affect treatment adherence	• Factors that influence patient's engagement with the recommendations made by the physician (i.e. factors that cause the patients to follow or not follow the recommendations).
	  ○ A key element influencing patient's engagement with multiple self-management practices was interaction with health professionals, and this was also related to perceived appropriateness of information received[93].
	  ○ The GP's response conflicted with her priorities and had a negative impact on what she felt able to engage with in managing her health. Where self-management instructions and information from the GP were incongruent with personal priorities as illustrated above, respondents remained disengaged from professional advice[93].
	  ○ In our interviews with 34 patients we had enquired about their willingness to be involved. The level of involvement depended on the nature of the problem. If it was a medical theme, patients preferred to follow the professional recommendation of their GP; however, if the theme had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision. In general, patients expressed a need for undivided attention, understandable information, time, and a calm atmosphere in the consultation[25].
	• Factors that influence the compliance of medication, typically long-term compliance.
	  ○ Strategies that include extrinsic motivators will promote long-term compliance and reduce recidivism.[50]
		• 25,50,93

Risk factors for multimorbidity	• This concept is different from "factors influencing the management of chronic conditions" as they lead to multimorbidity instead of influencing the management of multimorbidity once individuals have it	• 3,15,69,70,83,84,97,121

	• Risk factors may be social determinants of health that put individuals at risk for multimorbidity or predispose individuals to multimorbidity
	• Examples:
	  ○ Being socioeconomically deprived
	  ○ Low income
	  ○ Individuals with multiple comorbidities, who frequently experience mental health problems and illnesses, are often of low socioeconomic status and have unmet basic needs, such as housing, employment and transportation.	

Codebook for identifying concept themes – Program Theory 2

Concept	Concept definition	Source
BARRIERS		
Barriers to optimized patient prioritization	• Factors that may hinder a patient with multiple chronic conditions from being able to participate in the act of prioritizing health conditions with his/her provider; this includes their decision making • Factors that may hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization • A patient's family may have a greater influence on the decision than the patient's own preferences.[122] • Includes any barriers to patient-centred care	• 32,33,60,63,64,91,99, 122,123
Barriers to optimized provider prioritization	• Factors that may hinder a provider from being able to participate in the act of prioritizing health conditions for a patient with multiple chronic conditions including decision making. This can also include health priorities addressed in the clinic setting • Factors that make it more difficult for health care providers to prioritize the treatment/management of a patient's chronic conditions. For example, factors may include the competing demands of multiple chronic conditions, and challenges of balancing provider and patient priorities. ○ *Psychiatric disorder*: If the patient has a psychiatric disorder, then this may make it more difficult for providers to prioritize treatment/management of the chronic conditions. • Patient-centered care is defined as GPs taking a broader view of the patient, incorporating non-medical or psychosocial issues. Patient-centered care is an over-riding principal for GPs in multimorbidity but trying to achieve this increases the complexity of care in some cases, and can lead the GP into additional conflict with specialist services or evidence-based medicine.[58] • Factors that may hinder a provider from being able to apply evidence in the care of their patients. • Clinicians lack a systematic framework for determining patient preferences and synthesizing these preferences with existing evidence to set individual health priorities • Includes the barriers (i.e. time) related specifically to the implementation of training for providers (for example, GPs did not accept shared decision-making and prioritization training sessions of more than 30 min, for fear of organizational disruption , patient complaints, and financial loss).[99]	• 25,37,58,60,63,99, 118,119,123
Barriers to shared decision making	• Barriers that impede a collaborative process that allows patients and their providers to make health-care decisions together. The collaborative process takes into account the best clinical evidence available, as well as the patient's values and preferences. • For example, barriers to shared decision making patients often do not expect to share decisions, in particular older patients may find this SDM process difficult because it is unfamiliar and demanding.[99]	• 26,58,60,73,96,99, 123

Barriers to the agreement between patients and providers	- Captures any excerpts about the dynamic between the patient and provider (whether that is agreement on prioritization, decision making) - Includes excerpts that mention *both* what patients and providers think. **IN THE PRIORITIZATION OF CHRONIC DISEASES** • Factors that decrease the level of agreement between patient and provider in terms of prioritization of health conditions including health care decision making. For example, when patients present with unrelated or discordant conditions, the patient and provider may disagree about which condition should be prioritized.[72] • Include conflicting views/ranking? Between providers and patients of which diseases should be considered for treatment?[32] • Factors that decrease the level of agreement between patient and provider, but not specifically about the prioritization of health conditions. • Factors that decrease the level of agreement between patients and provider, but not specifically about the prioritization of health conditions.[115] o For example, communication between the physician and patient can affect agreement. If the physician does not enact enough/ at all information-giving, counseling, quality of question asking and support, and participatory decision-making style (process of negotiation) during consultations with patients, then this many negatively affect agreement.	**PRIORITIZATION** • 32,66,68,72,76,91,98,115 **HEALTH CARE DECISIONS** • 93
Barriers to the patient-provider relationship	• The communication barriers between patient and provider (includes factors that influence poor communication between patient and provider)	• 66,93,96
FACILITATORS		
Facilitators of optimized <u>patient</u> prioritization	• Factors that may promote a patient from taking part in the decision-making process in terms of health prioritization; • Patients engaging with health care workers in health prioritization • What motivates patients to prioritize their conditions. For example, to cope with their health problems and stabilize their health. • The components of a clinical appointment/check-up that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making. • The components of a clinical appointment/checkup that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making • Includes any facilitators to patient-centred care.[92]	• 63,91,92
Facilitators of optimized <u>provider</u> prioritization	• Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to work with other providers to prioritize multiple chronic conditions. For example, use of an electronic integrated medical records system may facilitate communication and care coordination across providers.[62]	• 25,62,88,92,98,118,119, 123

	• Specifically, how patient-centered communication impacts patients in terms of knowledge, expectations, participation in treatment process and providers in terms of quality of care.	
Facilitators of the patient-provider relationship	• The concept where physician "accompany the patient, which may contribute to a stable patient-physician relationship. "The physicians saw themselves as doctors who accompany these patients rather than doctors who heal them. This leads to an emphasis on 'little improvements.' […]The physicians stressed that accompanying the patients and witnessing their improvements contributed to a stable doctor-patient-relationship."[66] • Includes communication facilitators between patient and provider (the factors that influence good communication between patient and provider)	• 26,66,92

Facilitators of shared decision making	**GENERAL**
	• Factors that facilitate the collaborative process that allows patients and their providers to make health-care decisions together based on available evidence and clarification of patient preferences.
	• For example:
	  • Agreement is a prerequisite of shared decision making and can be achieved using a patient-centred approach.[99]
	  • Sharing personal experiences, and facilitating concise and clear discussions with patients on the interplay between chronic diseases were strategies used by GPs to facilitate SDM.[58]
	IMPLEMENTATION
	• Factors that facilitate the implementation of processes, tools, or skills that encourage or foster shared and equitable decision-making between patient and doctor, with decisions based on available evidence and clarification of patient preferences
	• For example:
	  • Communication training for GPs can help them facilitate SDM.[99]
	  • If the healthcare provider considers the patient also as an expert in, and partner in the management of, their condition(s), and respects the patient's opinions.[26]
	  • Involving patient perspectives and preferences in the patient-provider decision-making process by exploring and mutually explaining each other's ideas[57].
		GENERAL:
		• 26,43,57,58,68,73,75,88,96,98,99,122
		IMPLEMENTATION:
		• 26,98,99

Facilitators of the agreement between patients and providers	- Captures anything about the dynamic between the patient and provider (whether that agreement on prioritization, decision making)
	- Includes excerpts that mention *both* what patients and providers think.
	
	IN THE PRIORITIZATION OF CHRONIC DISEASE
	• Factors that increase the level of agreement between patients and providers in terms of prioritization of health conditions.
	• For example, the agreement between patients and providers was higher when
	  ○ Patients have fewer symptoms.[32]
	  ○ The provider was male.[32]
	IN HEALTH CARE DECISIONS
	• Factors that increase the level of agreement between patients and providers, but not specifically about the prioritization of health conditions.
		PRIORITIZATION
		• 25,32,68,73,91,93, 124
		HEALTH CARE DECISIONS
		• 66,115

	• For example: Having a process of negotiation may ensure collaboration and agreement between patients and their primary care physicians.[115]	
(Neutral) Factors		
Process of shared decision making between providers and patients	The process of shared and equitable decision-making process between patient and doctor, with decisions based on available evidence and clarification of patient preferences	• 25,75,99,118,125
Patients' process of prioritizing multiple chronic conditions	• The process used by patients to prioritize their multiple chronic conditions including their decision making and management (anything about *how* patients prioritize) • Includes any "rules of thumb" patients use to prioritize their conditions i.e. pain, functional limitations, new conditions that change up your prioritization • This is different than facilitators or barriers to patients' prioritization of chronic conditions. It spells out the process (steps) that patients go through as well as the factors that they take into account when prioritizing their chronic conditions. • The steps and considerations taken by patients when prioritizing their chronic conditions. For example, Morris and colleagues[93] discuss when and why patients reprioritize conditions, and how the new ordering of conditions is determined.[93] • Simply a listing of patients' priorities such as specific diseases or getting informed about their conditions • Factors that may promote or hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization For example, patients tended to follow GP's recommendation if the issue was purely medical; however, if the issue had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision.[25] • Includes factors that influence prioritization that are not related to specific barriers (challenges) or facilitators, such as the internal processes they use to prioritize multiple chronic diseases • Includes factors that may influence or drive patients' prioritization such as such as pain, fatigue, shortness of breath, or dizziness and have a great impact on quality of life and life satisfaction and thus–likely–on patient preferences. For example: Patients' prioritization and needs were affected by psychosocial factors, previous experiences and the patient's' expectation.[60]	• 25,32,56,60,63,64,66, 68,76,87,91,93,122,125
Providers' process of prioritizing multiple chronic conditions	• The process used by providers to prioritize their multiple chronic conditions including their decision making and management • For example: ○ Providers' priorities were determined by medical aspects of the diseases such as the disease severity and prognosis.[25] ○ When providers did not feel in charge of a problem or were not aware of suitable treatments, they rated the problem as unimportant.[25] ○ Instead of symptomatic conditions, providers may focus on the long-term health consequences of asymptomatic hypertension or uncontrolled diabetes.[32]	• 25,32,57,63,65, 66,68, 76,96,98,119, 125

Appendix 3

Context-Mechanism-Outcome (CMO) configurations of Programme theory 1 (Care coordination interventions)

General CMO configurations to explain Program Theory 1

***Care coordination Interventions** in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They provide a comprehensive and coordinated approach to multimorbidity management by addressing multiple conditions (through interdisciplinary teams and/or multidisciplinary disease management), providing specific mechanisms for communication, and establishing formal roles for providers and patients.	
Team-based approaches	Team-based approaches can lead to a range of outcomes, such as evidence-based care solutions for multiple conditions in parallel (not in tandem) [M][38], a wider range of services [O], more holistic care [O], higher quality of care [O], reduce scheduling complications [O2][88] and increase the flexibility and responsiveness of the team [O3][45]. These outcomes are most likely to occur when team members have mutual respect and confidence [M2][45], are highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M][53] who understand and accept each other's roles [M3][53], provide opportunities[38,88] and time[53] to share information [M][81], and are willing to collaborate on patient care [M5][38,45,53,88]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M]. The contexts in which these mechanisms are triggered include teams that have dedicated members who provide additional support to patients[38,53] or providers[81]. Team members receive official training on the model[38,53,81], including training on team skills[81]. Organizations have a robust and well-functioning communication system[38,45]. Many of the team-based approaches under study were Canadian[45,53,81].
Disease management	Disease management for multimorbidity care consists of the use of a number of discrete intervention strategies with the desired outcome of achieving systematized care. These include: checklists, follow up timetables[45,103,110], and treatment targets [M][45]. Together, these intervention strategies appear to make explicit the roles, expectations, and responsibilities of the health care professionals involved [C], enabling staff to become aware of their roles, expectations, and responsibilities [M] leading to a shared philosophy and platform for care [O][45],[103]. This also permits the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][45]
Case management	Case management intervention strategies are appropriate for managing multimorbidity because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C], a case manager functions as a conduit of information [M] to help improve coordination and information sharing from the patient to providers as well as between providers [O][53]. When improved coordination and information sharing occurs [C] and case managers are in regular contact with the patient [C][80], are the primary point of contact and coordinator of care [C][103] and provide individualized attention [C][9] and information [C][80] to patients, patients

		perceive that their care is continuous [M][78,79] and coordinated [M][79] and as a result know who is 'in charge' and who to turn to when then have a problem [O]. When patients know who is 'in charge' and who to turn to when then have a problem [C] helps patients to feel safer [M] and trust [M] of their case managers over time[79] resulting in the building of relationships that are more likely be based on confidentiality [O][79,80], and mutual equality [O][80] These types pf relationships appear to be the basis of some of the further 'downstream' outcomes that are found with case management, such as helping patients to develop the skills and confidence they need to manage their health [O][78].
Education was a component in 83% of the chronic disease management interventions identified in our systematic review. Education for patients is often a component of care coordination interventions[15,45,103], and can be more effective [O] when combined with active monitoring [M] and provided by a pharmacist[45] [C].		
	Health education	Health education is often combined with self-management support[94,103,104], which is more effective for lifestyle modification than education alone[94]. Patients receive education about their multimorbidity through numerous formats, including: video streaming[50], in-hospital education[31] and the internet[51]. Video streaming may be good for homebound patients[50], whereas in-hospital education may be more effective for those who might become motivated to change their lifestyle after a hospitalization event[31]. Patients with multiple chronic conditions use the internet, but there are few websites that address multiple conditions in an integrated fashion[51].
	Health coaching	Health coaching (helping patients to gain the knowledge, skills and confidence to become active participants in their care aimed at reaching their self-identified health goals)[27]. Health coaches (who could also be case managers) strengthen patient self-management by improving patient self-efficacy by listening and applying patients' challenges and health goals to customize action planning[27]. This allows patients to develop the coping and problem solving skills that support self-management[27,94].
	Web 2.0 technology	Web 2.0 technology (web use that involves more active participation, creation and sharing of information such as through social networking) are examples of interventions captured in our realist review that incorporate education. Web 2.0 technologies may support patient self-efficacy by providing relevant information, and opportunities to learn from other web users. For example, delivering online instructional units (developed and delivered by a multidisciplinary team of healthcare providers), and self-management training workshops staffed by peer moderators (i.e. individuals living with similar chronic conditions as the user)[95].

*This narrative provides only a broad explanation of Programme theory 1, greater detail that explains the outcomes that[81] may be achieved by the different intervention strategies used in the care coordination.

Details of CMO configurations to explain Program Theory 1

Coordination of care element	Definition	Explanation of determinants via Context [C]-Mechanism[M]-Outcome[O] configurations
Teams *The right care at the right time*	Highly trained clinicians[53] who provide holistic and coordinated care, often, but not always, from the same physical location[88]. Teams aim to provide time for the patient to discuss all of their concerns, prevent care overlap and gaps[80], and reduce scheduling complications[88] Patients are taught about their conditions, medications, and how lifestyle affects their health, and given information on health promotion or counseling services and other supporting services[44].	**Why Team-based approaches are appropriate for multimorbidity:** Team-based approaches are appropriate for managing multimorbidity [O1] because they can ideally provide evidence-based care solutions for multiple conditions in parallel (not in tandem) [M1][38]. Collaborative care teams can provide a wider range of services [O1], more holistic care [O2] and higher quality of care [O3] through interdisciplinary communication and collaboration [M1][38,81], and access to specialists [M2][53]. **Facilitators of successful teams:** Successful multidisciplinary teams [O1] are those which comprise highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M1][53] who have mutual respect and confidence [M2][45], understand and accept each other's roles [M3][53], provide opportunities[38,88] and time[53] to share information [M4][81], and collaborate on patient care [M5][38,45,53,88]. These facilitators can also reduce scheduling complications [O2][88] and increase the flexibility and responsiveness of the team [O3][45]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M1]. The use of peer moderators (i.e., individuals also living with a chronic condition who are trained to lead self-management training programs) [M1] can facilitate intervention learning activities such as behavior change, medication management, and disease information [O5].
Disease management *Systematized care (all providers are on the same evidence-based page)*	Disease management programs follow a "script" of how to provide effective (often evidence-based) patient care. Often care protocols or intervention plans define the division of tasks and support the follow-up and coordination of action[103,110], and help sustain the development of a philosophy of common care[45]. Patients may be educated about the disease management system so they know what to expect, and often provided with education and resources about how to properly self-manage their conditions.	**Why Disease management approaches are appropriate for multimorbidity:** Disease management strategies are appropriate for managing multimorbidity [O1] because they can systematically apply evidence-based care to populations of patients [M1] thereby making it more appropriate for managing conditions and combinations of conditions where evidence-based care exists. Care can be systematized [O2] through checklists [M1], follow-up timetables [M2], and treatment targets [M3][45,103,110]. **Facilitators of disease management:** Disease management approaches define the division of tasks [M1][45], support the follow-up and coordination of action [M2][45,103], and help sustain the development of a philosophy[45] and shared platform[103] of care [M3], therefore permitting the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][45].
Case management	Case managers are trained health care professionals who are the contact person between a patient and involved providers. They know how to facilitate	**Why case management approaches are appropriate for multimorbidity:** Case management are appropriate for managing multimorbidity [O1] because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C1], a case manager acts as a

Case managers are the primary conduit of care	care planning and shared decision making; and how to anticipate and address barriers (e.g. to treatment adherence). Case managers work closely with patients and their family/caregivers to provide information (e.g., about the health system or care), and to help them develop the skills and knowledge needed for self-management.	conduit of information [M1] to help improve coordination and information sharing from the patient to providers as well as between providers [O][53]. **Facilitators of case management:** Case management strategies work [O1] because case managers are in regular contact with the patient [M1][80], and provide individualized attention [M2][9] and information [M3][80] to patients. For patients with extensive and diverse care teams [C1], case management can ensure that care is continuous [O2][78,79] and coordinated [O3][79] by enhancing the communication between patients and providers [M1] and by being the primary point of contact and coordinator of care [M2][103]. Patients also feel safer [O4] when knowing that their case managers are monitoring their care [M1], and they trust their case managers over time [O5][79] because of regular contact [M1][80], and through a relationship of confidentiality [M2][79,80], and mutual equality [M3][80]. By engaging family/caregivers in proactive care [M1], case managers also help patients develop the skills and confidence they need to manage their health [O6][78].

Appendix 4

Context-Mechanism-Outcome (CMO) configurations of programme theory 2 (Health prioritization in multimorbidity management)

General CMO configurations to explain Program Theory 2

Multimorbidity management is confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[102], disease and treatment interactions and possible conflicts[57,92], and the difficulty of attributing symptoms to conditions[57]. Health prioritization is an important function of the management of multiple chronic diseases in primary care settings because the evidence base is most often single-disease focused and multimorbidity can create a cognitive and emotional overload in patients and health care providers. A common intervention strategy to multimorbidity management is to focus on one condition at a time[64], using a priority setting approach. Prioritizing one condition over the others (for a specified period of time, or until particular outcomes are achieved), allows patients[91] and providers[64] to focus their attention and care.		
	Patients' approach to prioritization	Patients with multiple chronic conditions can experience a range of symptoms [C]. These symptoms trigger cognitive and emotional overload [M] for patients and as a result, they resort to prioritization [O]. The prioritization process is influenced by the nature of the symptoms. Patients prioritize their condition [O] by making decisions based on their judgments of the symptoms they experience most need attention [M]. Symptoms which threaten their participation in social activities[25,63,76] [C], limit their independence[25,91] [C] and they believe might have potentially severe long-term consequences if not acted upon[63,91] [C] - examples of these symptoms include pain, fatigue and dizziness. Those diseases that patients prioritize and seek help for [O] are the ones that patients believe are causing with these symptoms[32,56,63,66,68,125] [C] because they do not feel that they have the capacity to engage in self-management behaviors associated with the disease [M]. Multimorbidity can have cascading effects. Patients may find it challenging to determine which chronic disease is causing a particular symptom [O] because conditions may share similar symptoms[72] [M], the treatment of one condition may aggravate the other[61,62,90,91] [M] or cause other antagonistic effects[64,90,91] [M]. The diagnosis of a new condition added to an existing one [C] may impede self-management because information about the new condition adds uncertainty[87] [M]. Patients who are able to identify the main illness that causes the most concern [C], are able to keep their symptoms under control and return to an acceptable way of life[87] [O].
	Providers' approach to prioritization	Patients with multiple chronic conditions can present to health care providers with a wide range of symptoms [C]. Dealing with these symptoms trigger cognitive and emotional overload [M] for the providers and as a result, they resort to prioritization [O]. The prioritization process used by providers is influenced by the nature of the symptoms. Providers tend to prioritize conditions [O] based on their judgments about the prognosis or severity of the condition [25,57,66,68,76,125] These judgments are influenced by their knowledge or evidence [124,125] about the which conditions are likely to have more serious outcomes [C], whether the patient is likely to benefit from treatment[57,114,124,125] [C] and conditions they feel they are most likely to be able to address (e.g. physical vs. emotional)[32,124]. Providers also tend to prioritize physical conditions over emotional or other conditions [C] (partly because) they consider the interrelatedness of the conditions and any potential cascading effects when prioritizing[65][M].

Associated CMO configurations related to multimorbidity management: We derived explanations of multimorbidity management in the context of primary care from the perspective of patients, providers and the system.		
	Patient perspective	The mental health needs of patients add to management challenges and interfere with patient self-care[57]. Some mental health patients with poor communication[C] receive less intensive mental health treatment[59][O] because providers sometimes ignored or normalized [M] their symptoms[38]. A patient-centred approach, which takes into account the patient's psychosocial realities (housing, relationships, income)[92][C] is more likely to meet the needs of complex patients with multimorbidity[82,117] [O].
	Provider perspective	Primary care clinicians face a number of challenges when managing patients with multimorbidity. In the contexts of inadequate decision support systems[35], evidence to support their clinical decision making[60], or care protocols or intervention plans that are too rigid[45], they may feel that they lack the skills and/or confidence[33] [M] to simultaneously understand patient subjective experience and biochemical processes of diseases[26] needed to appropriately manage these patients [O]. Another challenge is that most often, only single disease guidelines are available to manage multimorbidity [C], so clinicians are forced to modify them in anticipation of adverse effects[89] [M] or use common sense approaches [M] (to complement the limitations of their application[98]) leading to variations in 'adherence' to single disease guidelines. In the context of few existing multimorbidity guidelines and resulting clinical uncertainty or contradictory information, a promising intervention strategy from our included articles was shared decision making between patients and clinicians, which was described as a useful, and possibly a necessary tool for making individualized treatment decisions[58, 118].
	System perspective	Multimorbidity can create challenges in the relationship between primary and secondary care. When patients are given more certainty than a primary care practitioner would have provided [C], the primary care practitioner's view of specialists can be negatively affected[68] [O]. There is often poor communication between primary and secondary care providers[61,84], which makes it difficult to coordinate care[58]. From the system perspective, primary care may be the optimal context to deliver multimorbidity care because it is accessible to most patients[33], and tend to be viewed as efficient[33], equitable[33], and having wide reach[33] and good continuity of care[33,56-58]. However, the infrastructure of primary care settings may not be optimally designed to handle multimorbidity [C] and can lead to fragmentation of care [O]. This is because multimorbidity demands the involvement of multiple providers[80] [M], multiple care locations[92] [M], and extra consultation and provider time[32,33,35,38,65,72,102,105] [M], which can lead to less opportunities for preventative and psychiatric care [O], less care for concurrent conditions[59] [O], inadequate time for building patient-provider relationships[63] [O], and poor follow-up[35][O]. Increasing or adjusting consultation time for multimorbidity management [40,72,75,82] and complexity of illness[58] may provide opportunities to address these challenges.

Details of CMO configurations to explain Program Theory 2

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Disease and patient factors	***Barrier:*** Prioritization in itself is challenging for patients [O1], because of treatment side effects [M1][64], and the patient needs to manage one condition at a time, which may be in conflict with other condition treatment plans that they ought to be having [M1][64]

		Facilitator: Patients with multimorbidity optimally prioritize their health conditions [O1] by being actively involved in setting their goals and priorities [M1][92], and by sharing their feelings (with providers) about their illnesss(es) and its effects on their functioning [M2][92] by stating their expectations to providers of medical care [M3][92].
	Provider factors	***Barrier:*** Patient prioritization can be hindered for patients [O1] by receiving confusing [M1] and conflicting [M2] treatment recommendations from physicians[64], and by lack of awareness/information regarding the seriousness of a condition [M3][32]. ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to have reassurance that their available treatments work [M2][64], and that their condition is being monitored regularly [M3][64].
	Contextual factors	***Barrier:*** There is currently no framework to assist patients in determining preference and synthesizing these preferences with existing evidence to set individual health priorities and decisions [M][123] ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to use home-based self-management programs [M1][91], and by having access to clinicians who are knowledgeable about their health conditions [M4][64].
Provider perspective		
	Disease and patient level factors	***Barrier:*** Prioritization is difficult for physicians [O1] when aspects of patient health such as when conditions or symptoms (e.g., pain) are difficult to treat and impactful [M1][118], when somatic and mental disorders are combined [M2][60], and when there is no specific diagnosis or the presentation is an asymptomatic condition [M3][119]. ***Barrier:*** The evidence for treating multiple chronic conditions itself [C1] may be problematic [O1] because it may conflict with patients' values, preferences and needs [M1], be insufficient or uncertain regarding effectiveness [M2], or in the case of health economics data, be difficult to interpret and use [M3][119]. ***Facilitator:*** Providers find it easier to prioritize uncomplicated conditions which are responsive to treatment [O2] because they are able to predict patient benefits [M1] and determine if treatment is cost-effective [M2][119]
	Provider factors	***Barrier:*** Prioritization is difficult [O2] when physicians do not know about a patient's psychosocial factors [M1], history [M2] or management expectations [M3][60]. Additionally, physicians themselves may not understand [M4] or be able to adhere to patient priorities [M5][123], and may not have in person-centered communication [M2][25] or shared decision making [M3][99] skills. ***Facilitator:*** Facilitators of optimal provider prioritization [O1] are good listening and communication with patients [M1][25], which also ensures that treatment is individualized to each patient [O2][123]; that priority setting is based on patient's perceptions, concerns, and expectation [O3][25]; that the prioritization has a positive impact on functions of daily living [O3][92], and based on what the patient has identified as their own priorities [O4][25]. This individualized care for the patient [O2] should be balanced with clinical knowledge[123] and provider self-reflection [M1][25].
	Contextual factors	***Barrier***: Optimized provider prioritization is challenging [O1] because it takes an investment in time [M1][25,60,99] which doctors worry might disrupt clinic flow [O2], result in financial loss [O3], and trigger patient complaints [O4][99]. ***Facilitator:*** Physicians can improve the process of prioritizing chronic conditions with the help of specialized multimorbidity clinics [M1] and multimorbidity software programs [M2][25]

Appendix 5

Context-Mechanism-Outcome (CMO) configurations of programme theory 3 (Patient self-management in multimorbidity)

General CMO configurations to explain Program Theory 3

Patient self-management in multimorbidity: We derived explanations via CMO configurations to explain self-management in multimorbidity (Appendix 6).	
Burden of multimorbidity management	Multimorbidity is reported as a burden by patients [O] because of the cognitive and emotional overload [M] required for lifestyle changes [C][87] (which can be inconsistent or conflicting [C][25]), as well as the volume of information and recommendations provided [C][51,74] (which are often confusing and conflicting[43,91-93][C]). Adherence to recommended treatment is challenging for patients [O] because: 1) self-management regimens have been designed to fit their condition rather than their health priorities [C], lifestyle [C], available resources [C][89,94]; 2) unwieldy medications (too many, taken often, and difficult to keep track of)[C][15,51]; 3) having to follow a required diet and exercise routine [C][36,51,91]; 4) having to see multiple providers[C][71]; 5) medication mismanagement[C][71]; 6) not knowing how to respond to adverse drug effects[C][15,71]; and 7) communication barriers due to linguistic and cultural diversity[C][71]. These multiple contexts likely trigger cognitive and emotional overload [M].
Influence of cognition and mental health on self-management	Self-management is particularly challenging [O] for older adults who have impaired cognition[89] [C]or suffer from anxiety[90] [C] in addition to chronic conditions [C] as these contexts interact to increase their perceive an increase in illness burden[63]. If the additional condition is depression [C]: older adults may choose not to do anything (such as take medication) [O] because they consider it a normal part of aging [M] or; are reluctant to seek treatment [O] due to stigma[30] [M]. Depression, as a context, appears to also trigger other mechanisms that reduce their ability to self-manage chronic conditions[30-32,59,64,87,91] [O]. The mechanism include reduced patient motivation, energy and self-efficacy, feelings of being overwhelmed, hopeless[31] or stressed[87]. There appears to be a number of feedback loops because illness burden can interfere with people's ability to engage in health promotion such as exercise, which can result in negative consequences such as weight gain[87], reduced quality of life, functional decline or ability to work. These in turn, can impact mood, social networks, and self-management behaviours[62].
Influence of resource constraints on self-management	Self-management in multimorbidity is influenced by the lack of resources available to many older adults to help manage this burden[64] including the lack of finances[62,91], social supports[23,62,88,89,91] or transportation[91], as well as the influence of low health literacy[29] or skills to manage and coordinate care and adverse effects[43,90]. Another challenge is that even if resources and programs exist, older adults may not be aware of them[62]. Promoting contact with consumer organizations or support groups[26,71] and having peer support[31] may address these challenges. Older adults are interested in self-management tools that provide health condition information[51]; share, coordinate and synthesize information with and between providers; and connect them with other patients[51]. Physicians can support patient self-management through tailoring of information to the stage of the patient's condition and their adaptation to it[26], as well as through good interaction with patients[93], providing information[93] (including patients' particular language[71]), and a collaborative approach to care[115].

Details of CMO configurations to explain Program Theory 3

Theme	Sub-theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective		
Managing multimorbidity is **difficult to do for patients** due to the volume, complexity, and confusing/ contradictory nature of what is required for self-management.	*Burden of self-managing multimorbidity*	***Barrier:*** The burden of self-management is high for people with multimorbidity [O1], and can impair their quality of life life[92] [O2] due to the required lifestyle changes[87], which are sometimes inconsistent or conflicting [M1][25]; the provision of the sheer volume of information provided[51,74] [M2], and the often confusing and conflicting information provided about treatment recommendations [M3][43,91-93] (including conflicting dietary advice for different conditions[93] from a multitude of healthcare providers). In fact, self-management becomes more challenging as the number of providers increases [M5][74] along with the numerous appointments required [M6][15,56]. ***Facilitator:*** Having multiple conditions itself can promote self-management [O] because patients may have already developed skills such as self-monitoring and self-advocacy [M1][63,90], and they may be more motivated because of the heightened risk [M2][90]. ***Facilitator:*** When patients can establish a cognitive link between existing self-management practices [M1][90,91,93], and making this link intuitively and over time[93], they can became more successful at self-management [O1].
	Adherence to self-management regimens (treatments and medications)	***Barrier:*** Successful self-management [O1] has been judged by the ability of patients to adhere to prescribed treatment [M1]. However, adherence to recommended treatment has not worked for patients [O2] because self-management regimens have been designed to fit their condition rather than their health priorities, lifestyle, and available resources [M1][89,94]. Other factors are unwieldy medications (too many, taken often, and difficult to keep track of) [M2][15,51], having to follow a required diet and exercise routine [M3][36,51,91], having to see multiple providers [M4][71], medication mismanagement [M5][71], not knowing how to respond to adverse drug effects (especially for those who take multiple medications) [M6][15,71], and information communication barriers such as linguistic and cultural diversity [M7][71] ***Barrier:*** Patients do not take prescribed medications [O3] for a variety of reasons: they do not like taking medications [M1][85,91], they believe that the medication will negatively affect their health [M2] or is inappropriate for their underlying condition [M3][91], they do not believe the medication is necessary [M4][91], they experience undesirable side effects from the medication [M5][15,91], the medication information is difficult to read or understand [M6][29], the regimen is too complicated to follow (particularly in culturally and linguistically diverse populations) [M7][32,51,56,71,92], the bottles are difficult to open [M8][29], and they forget to take their medication [M9][29]. Although not being able to understand and receive information can lead to medication noncompliance [O4][90] the provision of better and clearer information about medications alone is unlikely to improve adherence [M1][29]. ***Barrier:*** Medication noncompliance can also result if taking multiple drugs (polypharmacy), which can lead to drug interactions[124] and adverse events [M2][101].

		Facilitator: People with multimorbidity can learn how to take medication strategically to achieve a balance between benefits and side-effects [O4], often based on years of experience of self-managing often antagonistic symptoms and competing goals [M1][85]. Medication adherence [O5] can be facilitated through automated reminder systems [M1][47,56], and switching to medications with modified release formulations [M2][56]. ***Facilitator:*** Medication adherence [O5] is linked to a person's self-efficacy (the confidence or ability to feel "I can do that") [M3][71], which can improve clinical outcomes [O6][47]. Some patients with multiple chronic conditions view their medication as a way of gaining control over their illness management [O7] by establishing routines for taking medications [M1] and seeing it as an opportunity to become more active self-managers [M2]. These patients consider medication management as positive [O8][93].
Cascading effects of multimorbidity: having, experiencing, and managing multimorbidity can cause additional barriers to self-management through **antagonistic** effects, both physical and emotional	The influence of chronic disease interrelatedness	***Barrier:*** Patients with multimorbidity may find it challenging to determine which chronic disease is causing a particular symptom [O1] because chronic diseases may share similar symptoms[72] [M1], the treatment of one condition can also aggravate another condition[61,62,90,91] [M2] or cause other antagonistic effects[64,90,91] (or the fear that it might cause these effects[85]) [M3] – these are major barriers to self-management, which can lead to medication non-adherence [O2][62,91] or low self-management in other lifestyle areas [O3][91]. ***Barrier:*** The diagnosis of an additional condition to an already existing one may also impede self-management [O4] because the new information for the 2nd condition adds uncertainty about what to do[87] [M1]. ***Facilitator:*** Patients who are able to identify the main illness that was causing them the most concern [M1] and keep it stable [M2] helps keep their symptoms under control [O1] and return to an acceptable way of life within the limitations of their illness [O2][87].
	The influence of mental and emotional health on self-management	***Barrier:*** Multimorbidity management challenges are exacerbated [O1] in patients with mental and emotional health problems (low cognition[89], anxiety[90]) because the limitations of one condition may impact the ability to look after another condition [M1][87,93]. The ability to self-manage for these people are influenced by the interaction of conditions [M2], which may also contribute to a perceived increase in illness burden [O2][63]. It is a cascading effect because if illness burden prevents exercise [M3], this can cause an increase in weight [87] [M3], and reduce quality of life, relationships, and ability to work [O3], which in turn can impact mood, social networks, and self-management behaviours[62] [O4]. In patients who have large discrepancies between current and past physical and cognitive functional abilities and activities (i.e., previous energy, endurance, strength, memory, ability to concentrate) [M1] may be unable to reconcile the difference and embrace self-management [O3][87]. ***Barrier:*** Cascading effects on self-management ability are also seen in multimorbidity patients with depression. In older adults, depression may be a barrier to effective self-management [O1] or a result of previous failures with self-management[65] [O2] because they may choose not to treat depression because they consider it a normal part of aging [M1], do not want to take medications [M2], or are reluctant to seek treatment due to stigma [M3][30]. Additionally, depression can reduce patient motivation, energy and self-efficacy [M4], causing them to feel overwhelmed [M5], hopeless [M6][31] or stressed [M7][87], which in turn can reduce their ability to self-manage[30-32,59,64,87,91].

		Chronic pain[32] [C2] experienced by older adults with multimorbidity works similarly in that it can be disruptive to self-management [O3] because it can reduce motivation [M1] and cause significant emotional distress [M2]. ***Facilitator:*** Factors that influence better self-care [O1] and better experience of illness [O2] of patients with multimorbidity are learning how to manage their emotions through exercise [M1][85], spending time being outdoors [M2][85], having a change of scenery [M3][85], reframing their situation [M4][90], prioritizing certain conditions [M5][90], staying positive [M6][87], doing their best [M7][87] and to consider mindfulness-based stress reduction [M8][94].
	Lack of resources	***Barrier:*** Self-management of patients with multimorbidity [O1] is influenced by the lack of resources to manage the burden of multimorbidity[64] such as insufficient knowledge and information [M1][87,91,95], low health literacy [M2][29]; low skills to manage and coordinate care and side effects [M3][43,90]; and lack of finances [M4][62,91], social support [M5][23,62,88,89,91], or access to transportation [M6][91]. Caregivers [C] may find self-care especially difficult [O2] because of the time [M1] and finances [M2] they are already using to care for others[62]. Even if resources and programs exist to help patients self-manage multimorbidity, they may not be aware of them [M1][62]. ***Barrier:*** Self-management regimens can impede one's ability to work. Although continuing to work for those with multimorbidity may be difficult, it provides financial stability, health insurance and identity to patients[62]. ***Facilitator:*** Self-management can be improved for patients with multimorbidity [O1] if they have contact with consumer organizations or support groups [M1][26,71] and peer support [M2][31]. ***Facilitator:*** Patients are interested in self-management tools [O1] that provide health condition information [M1][51]; can share, coordinate and synthesize information with and between providers [M2]; help them access new research findings [M3], connect them with other patients [M4], help them sort health records [M5], consult with remote specialists [M6], and coordinate with local providers [M7][51]. Telehome care systems can improve patient self-management [O1] through the provision of health information [M8][47].
Provider perspective		
Communication between providers and patients		***Barrier:*** Providers (particularly specialists) [C] can themselves be a barrier to patient self-management [O1][61]. Patients may be dissatisfied with the way the provider communicates [M1][43,91], and family physicians (who are the primary contacts for patients) may fail to provide valuable information about self-management resources such as patient advocacy and self-help groups and other resources [M3][26]. ***Facilitator:*** Physicians can support patient self-management [O1] and have a positive impact on patient self-management [O2] through tailoring information-giving to the stage of the patient's condition and their adaptation to it [M1]***[26],*** through good interaction with patients [M1][93], information provision [M2][93] (including information in the patient's own language and adequate time to review it[71]), a collaborative approach to care [M3][115], encouraging active engagement in self-management [M4][71], motivating patients and providing a behavioural model [M5][31], and empowering patients by providing them with skills and confidence to manage their own conditions [M6][94].

Appendix 6

Details of Context-Mechanism-Outcome configurations to explain multimorbidity management overall

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Confusing for patients	***Barrier:*** Multimorbidity management in primary care [C] is confusing to patients [O2][120] due to the heterogeneous nature of multimorbidity [M1][102], disease and treatment interactions and possible conflicts [M2][57,92], and the difficulty of attributing symptoms to conditions [M3][57]. ***Facilitator:*** Supporting patient self-management is a critical aspect of multimorbidity care[37,85] and to achieve optimal health outcomes. These include medication support [30,55] [M1], motivational enhancement[62],43 [M2], and education [M3], which is a key aspect of optimal medication [O2] [29] and disease management [O3], particularly for people with arthritis and depression [C2][104]. ***Facilitator:*** A patient-centred approach, that takes into account the patient's psychosocial realities (housing, relationships, income, etc.) [M1][92] is more likely to meet the needs [O1] of complex patients with multimorbidity [C1][82,117]. Patient-centred approaches [M2] can help patients adopt healthy lifestyles [O2] if they have adequate adoption readiness [M2], and target additional behaviours once change in one behaviour is achieved [M3][120] 23. For complex patients [C1], patient-centered care may be promoted [O4] by enhanced communication [M3] although this may or may not improve disease-specific self-care and outcomes [O5][105]
Mental health needs of patients add to complexity	***Barrier:*** In primary care, mental health needs of patients [M1] in the context of multimorbidity management can be a barrier to patient self-care [O1][57], can create communication issues with providers (i.e., patient complaints may not be clear) [O2][57], are often ignored or normalized since physical health issues take precedent [O3][38], and can lead to patients receiving less intensive treatment [O4][59].
Provider perspective	
Overwhelming for providers	***Barrier:*** Multimorbidity management in primary care [C] may be overwhelming for providers [O1][56] due to the heterogeneous nature of multimorbidity [M1][102], disease and treatment interactions and possible conflicts [M2][57,92], and the difficulty of attributing symptoms to conditions [M3][57].
Not prepared for managing multimorbidity	***Barrier:*** Primary care clinicians are inadequately prepared for multimorbidity [O1] due to their lack of skills and confidence in addressing multimorbidity [M1][33], not having adequate decision support systems [M2][35] or evidence [M3][60] to support their clinical decision making, and having care protocols or intervention plans that are too rigid [M4][45]. These make it difficult for primary care physicians to simultaneously understanding patient subjective experience and biochemical processes of chronic conditions [O2][26]. ***Facilitator:*** Many general practitioners have identified the need for guidelines that address multimorbidity[75]. When only single disease guidelines are available to manage multimorbidity [C1], clinicians sometimes modify guidelines [M1] in anticipation of adverse effects[89], use common sense to complement the limitations of their application [M2][98], and work with patients to help them understand guidelines [M3] so they can make informed treatment decisions [O1][98]. Collaboration with patients is needed [M4] when the single disease guidelines being used are contradictory [C2][58]. In

		situations where few guidelines exist and there is significant clinical uncertainty [C3], shared decision making between patients and clinicians is a useful, and possibly a necessary tool [M5] for making individualized treatment decisions [O2][118]
	Multimorbidity can worsen the relationship between primary and secondary care (including care transitions)	***Barrier:*** An effective relationship between primary and secondary care (and in consequence, the transition between primary and specialist care) is difficult [O] for patients with multimorbidity because: patients are susceptible to exaggerated instructions by specialists and overly influenced by diagnostics [M1][68], specialists do not acknowledge primary care [M2][61,84], and there is often poor communication between primary and secondary care providers [M3][61,84]. This is compounded by the emphasis each specialist puts on 'their' guideline, which makes it difficult for primary care providers to coordinate care [M4][58]. The lack of cooperation between primary and secondary care [O2] also makes it difficult for patients [O3] because their needs are often episodic requiring both primary and specialist care either simultaneously or in succession [M4][36]. ***Facilitator:*** Patient-primary care physician concordance on health-related attitudes and perceptions [M1] appears to be a powerful predictor of primary care physician implementation of [O1] and patient adherence to [O2] to recommended geriatric health care[115]. This implies that specialist education regarding recommended care should be directed at both primary care physicians and their patients[109]. Additionally, trusting relationships between primary care physicians and specialists [M2] promotes collective and harmonized approaches to care [O3][45]
System perspective		
	Primary care is the optimal context to deliver multimorbidity care, but it is not designed to handle it	***Facilitator:*** Primary care may be the optimal context to deliver multimorbidity care [C] because it is accessible to most patients [M1][33], efficient [M2][33], equitable [M3][33], has reach [M4][33], has good continuity of care [M4][33,56-58], and primary care providers general know their patients well [M5][33,56,57] and they have a generalist and patient-centred approach to care [M6][56]. Relational continuity [M7] in primary care helps providers better understand patient needs [O1] and enhances multimorbidity care [O2][58]. ***Barrier:*** Primary care is not designed to handle multimorbidity [O1] because it demands extra consultation and provider time [M1][32,33,35,38,65,72,102,105]. This in turn can lead to inadequate care patients (i.e., less preventative care, psychiatric care, less care for concurrent conditions) [O2][59], inadequate time for building patient-provide relationships [O3][63], the complexities of primary care clinics requiring to schedule multiple appointments for multiple issues [O3][65], poor follow-up practices by clinicians [O4][35], and the tendency to maintain the status quo for complex patients rather than changing the management plan [O5][73]. ***Facilitator:*** Increasing consultation time for multimorbidity [M1][40,72,75,82], adjusting consultation time to complexity of illness [M2][58], and allowing for time to discuss health issues [M3][72] and build a relationship [M4][58] have all been identified as opportunities to improve multimorbidity management [O].
	Multimorbidity can lead to fragmentation of care	***Barrier:*** Multimorbidity can lead to fragmented care [O1][75,80] because it often leads to the involvement of multiple providers [M1][80], territorial specialists [M2][58] and multiple care locations [M3][92]. This complexity of care can lead to poor communication between primary and secondary care [O2][15,36,58,80,84,92], duplication of efforts [O3][92], confusion about what has been done (i.e., tests, treatments, and medications) [O4][80], treatment errors [O5][80], impaired treatment participation (i.e., lack of understanding of what is happening with a patient's care due to fragmentation, so the provider may not add to the care because they don't want to confuse things more) [O6][80]; high use of specialty services [O7][15], and lack of care coordination or the consideration of a holistic approach to care [O8][79].

		Facilitator: Health information technology tools, including integrated EMRs and telehealth solutions [M1], can help with patient care coordination [O1][46,47,58,62]. ***Facilitator:*** Clinical tools (including those that focus providers on functional, rather than disease-related outcomes) [M1][61], and those that provide multi-morbidity decision support [M2][74] and assessment [M3][89,92]) can help providers more optimally manage patients with multiple chronic conditions [O1][74] and can optimize medication management [O2][86]. ***Facilitator:*** Multimorbidity can be better managed [O] through integrating similar disease processes[73] [M1], adopting additional health conditions into existing management practices [M2][93], and highlighting links between management practices [M3][93]

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
Title			
1		In the title, identify the document as a realist synthesis or review	1
Abstract			
2		While acknowledging publication requirements and house style, abstracts should ideally contain brief details of: the study's background, review question or objectives; search strategy; methods of selection, appraisal, analysis and synthesis of sources; main results; and implications for practice	2
Introduction			
3	Rationale for review	Explain why the review is needed and what it is likely to contribute to existing understanding of the topic area	4-5
4	Objectives and focus of review	State the objective(s) of the review and/or the review question(s). Define and provide a rationale for the focus of the review	4-5
Methods			
5	Changes in the review process	Any changes made to the review process that was initially planned should be briefly described and justified	7
6	Rationale for using realist synthesis	Explain why realist synthesis was considered the most appropriate method to use	4

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
7	Scoping the literature	Describe and justify the initial process of exploratory scoping of the literature	5
8	Searching processes	While considering specific requirements of the journal or other publication outlet, state and provide a rationale for how the iterative searching was done. Provide details on all of the sources accessed for information in the review. Where searching in electronic databases has taken place, the details should include, for example, name of database, search terms, dates of coverage and date last searched. If individuals familiar with the relevant literature and/or topic area were contacted, indicate how they were identified and selected	5-6
9	Selection and appraisal of documents	Explain how judgements were made about including and excluding data from documents, and justify these	6
10	Data extraction	Describe and explain which data or information were extracted from the included documents and justify this selection	6
11	Analysis and synthesis processes	Describe the analysis and synthesis processes in detail. This section should include information on the constructs analysed and describe the analytic process	7
Results			
12	Document flow diagram	Provide details on the number of documents assessed for eligibility and included in the review, with reasons for exclusion at each stage, as well as an indication of their source of origin (e.g. from searching databases, reference lists and so on). You may consider using the example templates (which are likely to need modification to suit the data) that are provided	8; Fig 1

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
13	Document characteristics	Provide information on the characteristics of the documents included in the review	8
14	Main findings	Present the key findings with a specific focus on theory building and testing	8-11
Discussion			
15	Summary of findings	Summarise the main findings, taking into account the reviews objective(s), research question(s), focus and intended audience(s)	11-12
16	Strengths, limitations and future research directions	Discuss both the strengths of the review and its limitations. These should include (but need not be restricted to) (a) consideration of all the steps in the review process and (b) comment on the overall strength of evidence supporting the explanatory insights which emerged The limitations identified may point to areas where further work is needed	13
17	Comparison with existing literature	Where applicable, compare and contrast the reviews findings with the existing literature (e.g. other reviews) on the same topic	12-13
18	Conclusion and recommendations	List the main implications of the findings and place these in the context of other relevant literature. If appropriate, offer recommendations for policy and practice	14
19	Funding	Provide details of funding source (if any) for the review, the role played by the funder (if any) and any conflicts of interests of the reviewers	15

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Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review

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Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review

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ABSTRACT

Objectives: To understand *how* and *why* effective multi-chronic disease management (CDM) interventions influence health outcomes in older adults 65 years of age or older.

Design: A realist review.

Data sources: Electronic databases including MEDLINE and EMBASE (inception to Dec 2017); and the grey literature.

Eligibility criteria for selecting studies: We considered any studies (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies) as long as they provided data to explain our programme theories and effectiveness review (published elsewhere) findings. The population of interest was older adults (age ≥ 65 years) with two or more chronic conditions.

Analysis: We used the RAMESES quality and publication criteria for our synthesis aimed at refining our programme theories such that they contained multiple Context-Mechanism-Outcome (CMO) configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography to separate units of data from articles, and to derive explanatory statements across them.

Results: 106 articles contributed to the analysis. We refined our programme theories to explain multimorbidity management in older adults: 1) Care coordination interventions with the best potential for impact are *team-based* strategies, *disease management* programs and *case management*; 2) optimized disease prioritization involves ensuring that clinicans work with patients to identify what symptoms are problematic and why, and to explore options that are acceptable to both clinicians and patients; and 3) optimized patient self-management is dependent on patients' capacity for self care and to what extent, and establishing what patients need to enable self care.

Conclusions: To optimize care, both clinical management and patient self-management need to be considered from multiple perspectives (patient, provider and system). To mitigate the complexities of multimorbidity management, patients focus on reducing symptoms and preserving quality of life while providers focus on the condition that most threaten morbidity and mortality.

ARTICLE SUMMARY

Strengths and limitations of this study

- To our knowledge, this is the first realist review to explain *why* multimorbidity interventions work, *for whom*, and *under what circumstances* to improve outcomes for older adults with multimorbidity – findings can be used to inform practice and policy decisions in the management of older adults with multiple chronic conditions
- Our search strategy was in part informed by a Systematic Review investigating the effectiveness of multimorbidity interventions for older adults that we conducted alongside this Realist Review
- We created a 3-step synthesis process drawn from in meta-ethnography to separate units of data from articles, and to derive explanatory statements across them
- Many of our included studies did not have complete data to enable optimized Context-Mechanism-Outcome (CMO) investigations
- Incomplete reporting also impacted our ability to fully test our theories and therefore, we could not completely elucidate the interrelationships within and between all of our CMO configurations

BACKGROUND

The global population is aging, with two billion people expected to reach 60 years of age and older by 2050[1,2]. It is now more common for older adults to have multiple chronic diseases than to have single diseases or no chronic medical conditions at all[3]. The burden of chronic disease is also on the rise globally[1,4] with more than half of older adults (age ≥ 65 years) living with high-burden chronic conditions (i.e., highly prevalent and associated with premature death and increased health care utilization)[3,5]. Older adults also have greater health care needs, are at higher risk for adverse health outcomes, and experience more frequent hospitalizations[6], yet only 55% receive appropriate care[7,8]. In response, different chronic disease management (CDM) interventions have been created. For example, a programme designed to encourage older adults with COPD and depression to adhere to anti-depressants and pulmonary rehabilitation[9]. Although promising, CDM interventions have shown varying effectiveness[10,11] in part, because they are not usually developed for older adults or created for sustained use; and very few are designed to deliberately address multimorbidity[8,12].

Given our rapidly aging population, there is an urgent need to understand how and why multimorbidity interventions influence health outcomes to optimise patient care. To address these gaps, we conducted a systematic review to identify effective CDM interventions that integrate the care of ≥ 2 high-burden chronic diseases affecting older adults (published elsewhere)[13]. However, a systematic review is not always enough to inform practice and policy decisions as knowing "what" works seldom reveals which desired outcomes may occur under different contexts. Our objective was to conduct a realist review alongside to explore the underlying mechanisms and contexts by which these CDM interventions work or do not work, for whom, under what circumstances and why[14]. Realist review is particularly relevant for making sense of complex interventions (such as those focusing on CDM) that have context-sensitive outcomes. It can add important contextual and mechanistic detail to existing knowledge on this topic[15]. Such detail is likely to contribute to the limited existing clinical practice guidelines on multi-morbidity management such as those developed by NICE[16], by explaining the contexts in which intended and unintended outcomes are likely to occur. Additional resources about realist reviews can be found the RAMESES Project website[17]. Our overall objective of this

review is to: understand *how* and *why* effective CDM interventions influence health outcomes in older adults 65 years of age or older.

METHODS

Study Design

Our protocol was published[18], and registered with PROSPERO (registration number CRD42014014489). We applied the RAMESES quality[19] and reporting criteria[20]. The systematic review methods and findings are reported elsewhere[13].

Programme theory development

To identify our initial programme theories (i.e., what multimorbidity interventions are comprised of, how and why they are expected to work and what outcomes they might generate), we used an iterative, consensus-based process. We considered two major sources to identify any published or unpublished literature[21]: 1) Medline and Google Scholar describing models, frameworks, theories of multimorbidity, chronic disease management, and complex interventions; and 2) content and methods experts on our team (geriatricians, family physicians, and health services and realist review experts). Duplicate screening of 97 reports by two reviewers identified 18 documents that contained data that helped us to understand CDM interventions. Through team discussion and a Delphi survey amongst our team, we indentified that our initial programme theory would have to incorporate the following concepts: 1) CDM interventions are complex interventions that do provide different outcomes in different settings; 2) health prioritization is an important aspect of multimorbidity and; 3) interventions that consider patient values and circumstances, the evidence and the clinician's expertise were more likely to produce desired outcomes. We then used the data from our included studies to gradually refine our understanding of these concepts and how(if at all) they fit into our more refined programme theory developed from this review.

Search strategy

Since we performed our realist review alongside our systematic review of multimorbidity interventions[13], the search strategy was done simultaneously for both reviews. As such, we identified potentially relevant articles for our realist review (i.e., to provide data to test our

programme theories) through our systematic review search strategy (inception to December 2017)[13] and performed additional iterative, targeted searches as needed for the realist review[19]. An experienced information specialist performed these additional searches in Medline and Embase (Appendix 1).

Selection and appraisal of documents

To increase the efficiency of our searching and screening process, reviewer pairs independently screened titles and abstracts simultaneously for both the systematic review and realist review. We considered any study design for inclusion (i.e., experimental quasi-experimental, observational, qualitative and mixed-methods studies). During full-text screening, we considered all articles that were identified for the systematic review as well through additional targeted searches to explain our programme theories and effectiveness review findings. Two reviewers independently assessed each article for relevance (*does the source contain any data that could be interpreted as having our relevant context, mechanism or outcome for programme theory development?)* and rigor (*How trustworthy are the data? Does the article provide enough detail on how conclusions were reached irrespective of study design?)*

Data extraction

We created and pilot tested a standardized data extraction form. Data items were driven by our purpose to refine our programme theories through context-mechanism-outcome (CMO) configurations (i.e., if we were able to infer an explanation for the cause [M] for a particular outcome [O] under the influence of one or more particular contexts [C]). For example, computer-based counselling systems (intervention) targeting older adults and providers in primary care (C) are not acceptable (O) if they do not show any relative advantage over the current system (M_1) and if inconsistent with providers' current practice workflow (M_2). After extracting excerpts in duplicate, reviewer pairs independently assigned an associated concept code and iteratively developed a codebook of concepts (Appendix 2) that was used to code subsequent excerpts; any discrepancies were discussed and resolved as a team.

Analysis and synthesis processes

We used the RAMESES quality[19] and publication[20] criteria to guide the synthesis. Our goal was to refine our programme theories such that they contained multiple CMO configurations describing the ways different mechanisms fire to generate outcomes. We created a 3-step synthesis process grounded in meta-ethnography[22] to separate units of data from articles, and to derive explanatory statements across them. *Step 1*: reviewer pairs independently extracted relevant excerpts from articles. *Step 2*: One reviewer sorted excerpts by concept for each study and developed consolidated statements (groups of CMO configurations) for each. A second reviewer audited the first reviewer's statements by checking for agreement and consistency with their own interpretations. *Step 3*: As a team, we examined and compared consolidated statements *across* studies to derive explanatory statements. These were then used to refine our *programme theories* aimed at explaining the outcome patterns we found within the effectiveness review. When the consolidated statements seemed to disagree, we unpacked the concepts and further examined them, consulting our literature and content experts as necessary for additional data and insights.

Deviations from our protocol in conducting our realist review

We followed the methods as outlined in our protocol[18] with a few exceptions. First, we switched to an auditing process during *Step 2* of the analysis to make our process more efficient. This involved an auditor checking the work of a primary reviewer. Second, since our process to finalize the list of initial programme theories identified an area that was not covered by our systematic review search (i.e., health prioritization), we added a secondary search strategy to capture this literature as described above.

Patient and Public Involvement

Patients were not involved in the conduct of the review but older adults with multiple chronic conditions are involved in developing key messages for this research. These patients are also part of our broader integrated knowledge translation team to co-design an electronic self-management tool that integrates the care of multiple chronic conditions (KeepWell™); this tool is being informed by this review.

RESULTS

Study characteristics

Figure 1 is our PRISMA diagram, which shows the flow of article selection. Of 2435 potentially relevant citations that were screened for relevance, 124 articles were reviewed in full-text, and 106 articles contributed to the analysis[3,9,15,23-125]. Studies were published between 2002 and 2016 mostly in the United States (n = 32), the UK (n = 19), Canada (n = 14), Germany (n = 11), and Australia (n = 10). Most of the articles (75%) were about multimorbidity (n = 50) or disease prioritization (n = 29), and 27 studies (25%) addressed specific chronic disease combinations.

Programme theories

Using data from our included studies, we iteratively developed and refined our initial two programme theories and a third programme theory that emerged from our data. To make our findings more succint, in the following paragraphs, we have provided narratives that summarise the most important aspects of our programme theories. This approach obscures the detailed CMO configurations that underpin these narratives and may make our manuscript less useful for those interested in realist review methodology. To address this issue, we have provided indications of the CMO configurations that our narratives are based on. For those interested in seeing the links between our data and CMO configurations, please see Appendices 3-6 that explains the outcomes that may be achieved by the different intervention strategies used in care coordination under different contexts.

Programme theory 1: Care coordination interventions for multimorbidity management

Almost one-half of the interventions described in our realist review were "care coordination" interventions (i.e., changes in how healthcare workers interact with each other or patients to ensure timely and efficient delivery of healthcare)[126]. Appendix 3 shows their detailed CMO configurations that underpin this programme theory. Overall, we found that care coordination interventions in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They address multiple conditions through interdisciplinary teams or multidisciplinary disease management, providing specific processes for communication, and establishing formal roles for providers and patients. We identified three types of care coordination approaches that health care providers may wish to use that have

potential for impact: *1) Team-based* or collaborative approaches involve highly trained clinicians[53] providing holistic and coordinated care[88] including spending time with patients to discuss all their concerns, and to prevent care overlap and gaps[80]. Patients are given education, counseling and other support services to address their disease(s), medications, and lifestyle[44]. Team-based approaches can provide access to specialists[53] and a wider range of services, and provide evidence-based care solutions for multiple conditions in parallel (not in tandem)[38]. Optimized care outcomes are most likely to occur through interdisciplinary communication and collaboration[38,81], when teams comprise highly trained and skilled members[53] who understand and accept each other's roles[53], provide opportunities[38,88] and time[53] to share information[81], and collaborate on patient care[38,45,53,88]. Other contexts in which mechanisms are likely to be triggered include teams that have dedicated members who provide additional support to patients[38,53] or providers[81], receive training[38,53,81], and have a robust and well-functioning communication system[38,45]. *2) Disease management* programs follow a "script" for how to provide effective patient care via care protocols or plans, which define the division of tasks, support the follow-up and coordination of action[103,110], and help to sustain a philosophy of common care[45]. Systematized care is achieved through checklists, follow-up timetables[45,103,110], and treatment targets[45], which can lead to a shared philosophy of care[45,103] and optimized decision making[45]. *3) Case management*: Case managers are trained health care professionals who are the main contact (and conduit of information) between a patient and involved providers[53], and most appropriate for multimorbidity management when there may be multiple and diverse providers involved in a patient's care. When case managers are the primary contact[103,80], care is perceived by patients as continuous[78,79], coordinated[79] and more individualized[9,80], and fosters the development of the skills and confidence patients need to self-manage their health[78].

Programme theory 2: Disease Prioritization in multimorbidity management

The detailed CMO configurations of disease prioritization that underpin this programme theory are described in Appendix 4. Multimorbidity management is perceived as confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[102], disease and treatment interactions and possible conflicts[57,92], and the difficulty of attributing symptoms to conditions[57]. Multimorbidity can create a cognitive and emotional overload in patients and

providers[64], so a common strategy they use is to focus on one condition at a time. Patients and providers focus their attention by prioritizing one condition over another for a specified period of time, or until particular outcomes are achieved[91,64]. However, patients and providers approach prioritization differently. Patients make prioritization judgements based on the symptoms they experience and need the most attention. They identify the most undesired symptoms and focus on their associated condition(s)[32,56,63,66,68,125] or those that threaten their social activities[25,63,76], limit their independence[25,91] and have potentially severe long-term consequences if not addressed[63,91]. Providers prioritize conditions based on their judgments about the prognosis or severity of the condition and place greater emphasis on conditions with more serious outcomes[25,57,66,68,76,125]; they focus on conditions that threaten a patient's morbidity and mortality[25,57,66,68,125], those they think they are better equipped to address (e.g., physical over emotional[32,124]), and whether the patient is likely to benefit from treatment[57,114,124,125]. What's common among patients and providers, is that they both consider conditions that they feel *capable* of addressing[64,91,124,125], and both consider the cascading effects of multimorbidity and the interrelatedness of these conditions during the prioritization process[65,91]. For patients, the cascading effects of multimorbidity are particularly challenging. Patients may find it difficult to determine which chronic disease is causing a particular symptom because conditions may share similar symptoms[72] or the treatment of one condition may aggravate the other[61,62,90,91] or cause other antagonistic effects[64,90,91]. Self-management is therefore a challenge for patients because the diagnosis of (and receipt of information) about a new condition compounds the complexity and uncertainty of what to do[87]. Figure 2 shows our conceptualization of optimized disease prioritization from the perspective of providers and patients. For this simplefied overall programme theory, we have analysed and interpreted our findings in such a way as to provide a programme theory that presents out findings in a more familiar format using the concepts of 'barriers' and 'facilitators'. The programme theory sets out the factors that need to be taken into account if providers and patients wish to optimize disease prioritzation. In particular we provide an overview of factors that health care providers may need to address to help patients to: 1) identify what symptoms are bothering them; 2) why they bother them and; 3) exploring options that are acceptable to them for addressing their symptoms.

Programme theory 3: Patient self-management in multimorbidity

The detailed CMO configurations of multimorbidity self-management that underpin this programme theory are in Appendix 5. Multimorbidity is perceived by patients as a burden because of the volume of information and recommendations provided[51,74] which are often inconsistent or conflicting, and the cognitive and emotional overload required to assimilate this information or to make lifestyle changes[87]. Subsequently, this can lead to confusion and non-adherence to recommendations[25,43,91-93] and may also trigger cognitive and emotional overload. Specific explanations to these outcomes include: 1) self-management regimens are designed to fit their condition rather than their health priorities, lifestyle, and available resources[89,94]; 2) prescribed medications are unwieldy (too many, taken often, and difficult to keep track of)[15,51] or mismanaged[71]; 3) difficulties with following the required diet and exercise routine[36,51,91]; and to see multiple providers[71]; 4) not knowing how to respond to adverse drug effects[15,71]; and 5) experiencing communication barriers due to linguistic and cultural diversity[71]. Self-management is especially challenging for older adults with cognitive impairment[89] or anxiety[90] in addition to other chronic conditions, as these contexts can interact to increase people's perceived illness burden[63]. In particular, if depression is the additional condition, older adults may choose not to do anything at all because they either consider it a normal part of aging or reluctant to seek treatment due to the stigma associated with mental health problems[30]. Depression, as a context, can therefore also trigger additional mechanisms that reduce a patient's ability to self-manage chronic conditions[30-32,59,64,87,91]: reduced motivation, energy, self-efficacy; and feelings of hopelessness[31], and stress[87]. A number of feedback loops are activated because illness burden can interfere with a person's ability to engage in health promotion (e.g., exercise). This can lead to negative consequences (e.g., weight gain[87], reduced quality of life, functional decline), and in turn impair mood, social networks, and self-management behaviours[62]. Multimorbidity self-management is also influenced by the lack of available resources[64] (e.g., adequate finances[62,91], social supports[23,62,88,89,91] or transportation[91]) or low health literacy[29] or skills to manage adverse effects[43,90]. Older adults are interested in self-management tools that provide health condition information[51]; share, coordinate and synthesize information with and between providers; and connect them with other patients[51]. Physicians can support this by tailoring information to the stage of the patient's condition[26], having interactions with patients[93], providing information[93], and fostering a collaborative approach to care[115].

DISCUSSION

In this realist review we developed and refined our programme theories to explain why coordination of care interventions (found to have the most potential for impact in our systematic review) work to improve outcomes for older adults with multimorbidity. Care coordination interventions may be effective in primary care because they represent a structured approach to comprehensive care, and address multiple conditions through interdisciplinary teams or multidisciplinary disease management by providing specific processes for communication, and establishing formal roles for providers and patients. *Team-based approaches* provide the right care at the right time, *disease management* offers a systematized approach to care, and *case management* offers a dedicated case manager as the conduit of care.

In addition to refining our programme theories, we generated explanations associated with these theories. Appendix 6 shows the CMO configurations to explain of multimorbidity management overall. Figure 3 shows our conceptualization of multimorbidity management, which suggests that optimized care requires both clinical management and patient self-management, with the caveat that each needs to consider identified challenges from the perspective of those affected by them (patient, provider, system). From the patient perspective, clinical management can be confusing due to conflicting messages, which is compounded in the presence of depression, impaired cognition, or poor health literacy. The mental health needs of patients can further complicate clinical management by impeding self-care, creating communication barriers with providers (e.g., patient complaints may not be clear), and patients receiving less intensive treatment. Self-management is difficult for patients because of the high burden of required lifestyle changes and adherence to multiple and often conflicting treatment regimens. Multimorbidity can also have cascading effects due to the nature of how chronic diseases are interrelated and the influence of a patient's mental and emotional health on self-management. From the provider perspective, clinical management of multimorbidity may be perceived as overwhelming because of the heterogeneous nature of multimorbidity, and conflicting or lack of evidence to guide clinical decision making. Lack of skills and confidence, not having decision support systems and protocols that are too rigid can also lead to inadequate preparation to manage multimorbidity. From a system perspective, even if primary care is the optimal setting

for multimorbidity management, it may not always have the infrastructure to support optimal strategies such as care coordination and can also lead to fragmentation of care.

Recommendations

Findings from programme theory 1 suggests that health care providers may wish to use care coordination interventions that are: *1) Team-based* or collaborative approaches that involve highly trained clinicians providing holistic and coordinated care through effective interdisciplinary communication and collaboration, and the provision of education and counseling to patients to address their disease(s), medications, and lifestyle; *2) Disease management* programs via care protocols or plans, checklists, follow-up timetables, and treatment targets; and *3) Case management* strategies for situations when there may be multiple and diverse providers involved in a patient's care. For programme theory 2, the specific types of disease prioritization approaches that health care providers may wish to consider is to work with patients to identify what symptoms are bothering them and why, and exploring options that are acceptable to both clinicians and patients for addressing their symptoms. For programme theory 3, the specific types of self management approaches that health care providers may wish to consider include not assuming that all patients are capable of self care, identifying who is capable of self care and to what extent, and establishing with the patient what they need (eg. informtion, support) to enable self care.

Strengths and limitations

To our knowledge, this is the first realist review investigating older adult multimorbidity aimed at explaining *why* effective multi-CDM interventions (identified through a systematic review[13]) work/do not work for whom, under what circumstances and why. This can better inform practice and policy decisions about multimorbidity management than a systematic review alone. A Cochrane review investigated interventions in multimorbid patients of any age[15] and found mixed results, but concluded that interventions that were integrated with care and targeted specific risk factors or functional difficulties may be more effective[15]. A rapid realist review investigating the underlying mechanisms of care planning strategies found that the mechanisms driving positive outcomes for people with long-term conditions are those that motivate them and promote an understanding of their role in self-management and how their lifestyle affects their

conditions[127]. Our findings build on these studies by providing *explanations* for why multimorbidity interventions may be effective for older adults. Additionally, we focused exclusively on older adults because they represent a relatively unstudied population, and given their projected population growth, they urgently need our attention to optimize their care. The NICE guidelines on clinical assessment and management of multimorbidity[16] (one of few existing multimorbidity guidelines) support many of our findings. They emphasize the need to find synergies in care regimes and simplifying care where possible. They also describe a preferred approach to care, which involves establishing patient goals, values and priorities, where patients are encouraged to describe their preferred decision making approach and what aspects of their life they prioritize[16]. A recent qualitative systematic review also highlights the need for providers to simplify the burden of care for multimorbid patients[128]. Our findings highlight the importance of focusing multimorbidity management by prioritizing one or more specific condition(s) and ensuring that prioritization is undertaken in collaboration with patients.

Our study has some limitations. First, it is possible that other teams may have identified different programme theories or interpretations. However, we used a rigorous and systematic process, and we let our data guide our interpretations. Second, many of our included studies did not have complete data to enable optimized CMO investigations. This may in part be due to an over-emphasis on effectiveness research in the literature, and an under-representation of qualitative inquiry, particularly about elucidating "mechanisms". For example, the literature rarely addressed the social determinants of health (a potentially significant trigger for multimorbidity outcomes) even though many older adults experience social isolation[129] and financial[130] challenges). Incomplete reporting also impacted our ability to fully test our theories. As such, whilst we developed and refined a number of explanations for our data, we could not completely elucidate the interrelationships within and between all of our CMO configurations. Finally, it is important to note that since this analysis was interpretive and inductive, it is possible that another team of researchers would have arrived at a different set of programme theories that incorporate the mechanisms and contexts of multi-CDM interventions for older adults. Thus, these findings should only be used as potential mid-range theories to explore and interrogate.

Conclusions and future directions

Our realist review contributes to the current, limited knowledge of the underlying mechanisms of complex multi-CDM interventions for older adults with multimorbidity. We found that care coordination interventions are effective because they represent a structured approach to holistic care. To mitigate the complexities of multimorbidity management, patients focus on reducing their undesired symptoms and preserving their quality of life, while providers focus on the condition that most threaten a patient's morbidity and mortality. To optimize care, multimorbidity management requires both clinical management and patient self-management, and be considered from multiple perspectives (patient, provider and system).

Abbreviations

CDM: chronic disease management; CMO: context-mechanism-outcome; UK: United Kingdom; COPD: chronic obstructive pulmonary disease; EPOC: effective practice and organization of care.

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Data Statement

We included most of the data generated or analyzed for this study in this published article and associated appendices. Any additional datasets are available from the corresponding author upon request.

Competing Interests

The authors have no competing interests to report.

Author Contributions

MK: Manuscript development and final approval, methods design, data acquisition, data extraction, data analysis, research question development

LH: Manuscript development and final approval, data extraction, data analysis

GW: Manuscript development and final approval, methods design, and data interpretation

YL: Manuscript development and final approval, data extraction, data analysis, methods

JM: Manuscript development and final approval, data extraction, data analysis, methods

VT: Manuscript development and final approval, data extraction, data analysis, methods design

JC: Manuscript development and final approval, data extraction, data analysis

JL: Manuscript development and final review, data extraction, data analysis

NI: Manuscript development and final approval, methods design, data acquisition

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Figure legends

Figure 1: Flow of article selection

Figure 2: Framework of optimized multimorbidity management

Figure 3: Framework of optimized chronic disease prioritization

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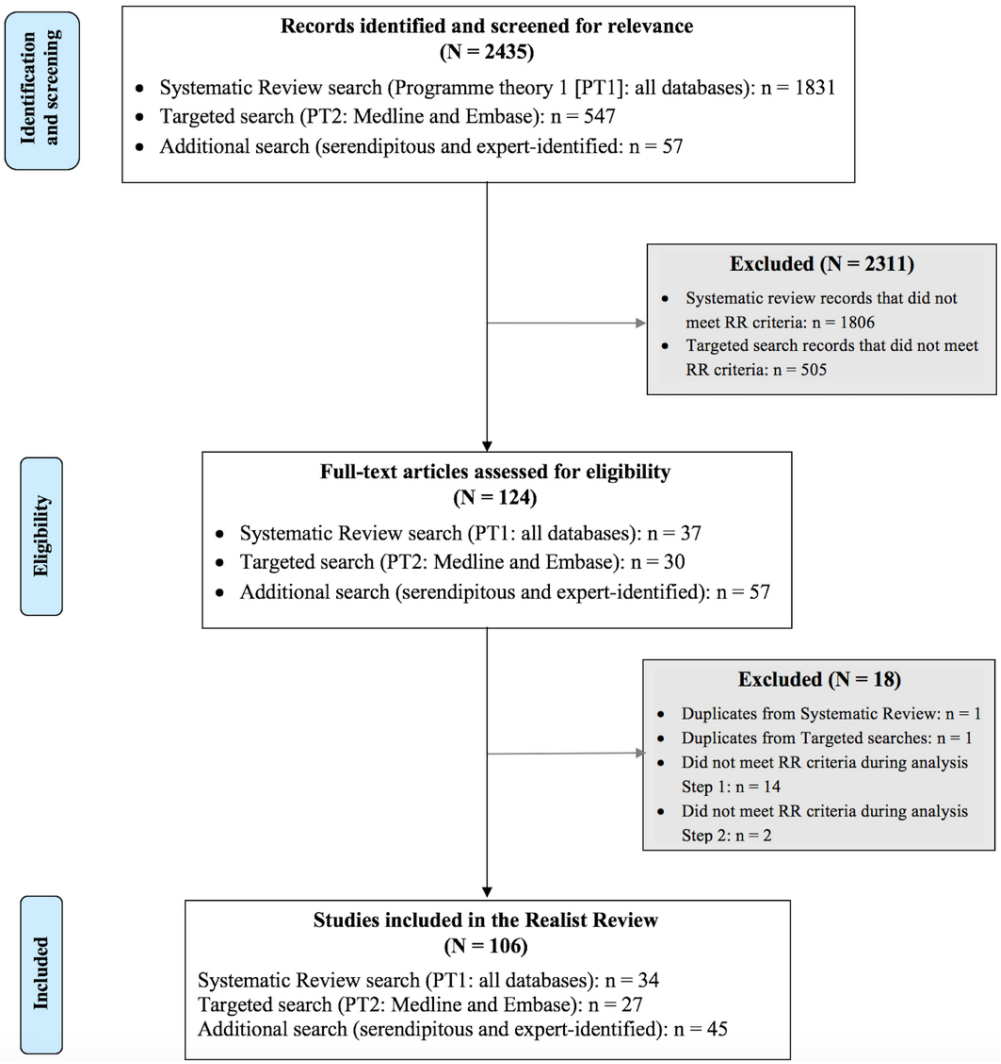

Flow of article selection

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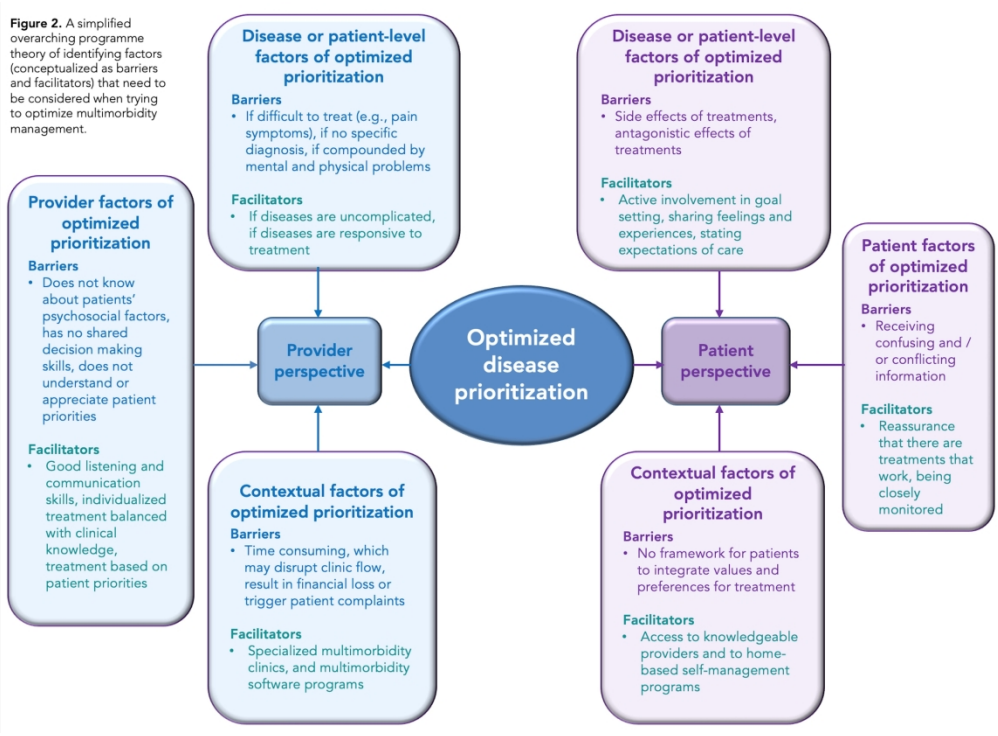
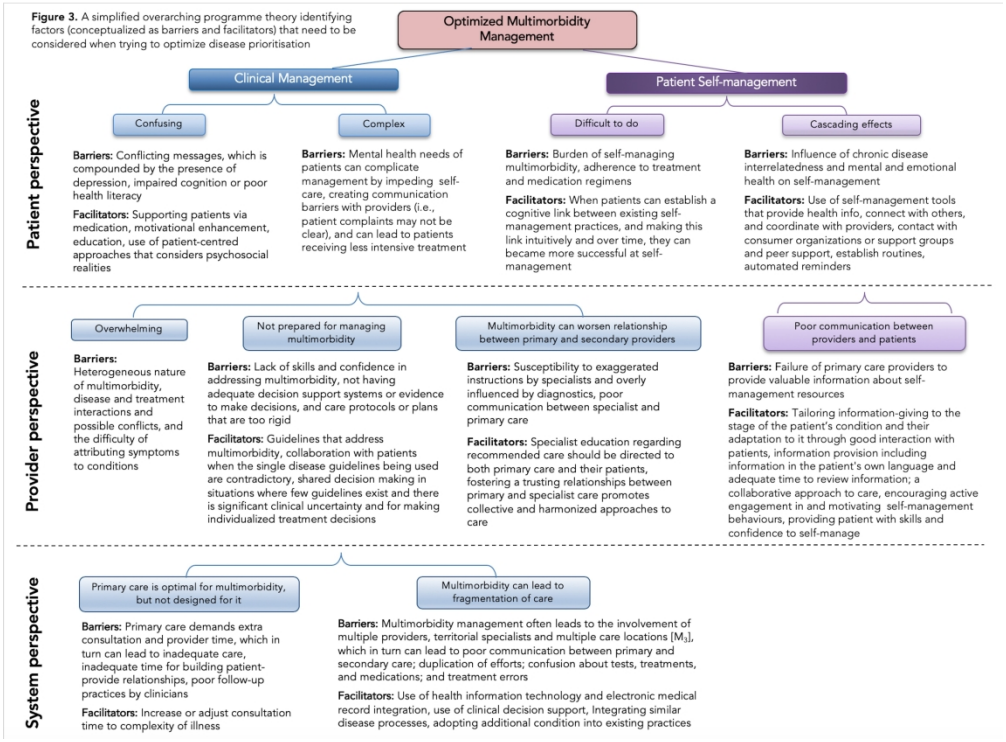


Optimized disease prioritization

338x247mm (300 x 300 DPI)



Optimized multimorbidity management

353x259mm (300 x 300 DPI)

Appendix 1

Medline search strategy for rough program theory 2 (health prioritization of multiple chronic conditions)

1. Primary Health Care/
2. Physicians, Family/
3. general practice/ or family practice/
4. (healthcare adj (professional or provider)).tw.
5. or/1-4
6. exp Geriatric Assessment/
7. *"Referral and Consultation"/
8. Decision Making/
9. Decision Support Systems, Clinical/
10. (consult$ or refer$).tw.
11. health planning/ or health planning guidelines/
12. ((Shared or sharing or shares) adj ("decision making" or "decision-making" or "decision making process" or "decision-making process")).tw.
13. Patient Participation/
14. or/6-13
15. 5 and 14
16. (chronic disease$ adj2 management tool$).tw.
17. Chronic Disease/
18. ((chronic* or longterm or long-term) adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)).ti,ab.
19. ((multi or multiple) adj2 (condition* or disabilit* or disease* or disorder* or ill or illness* or morbidit*)).ti,ab.
20. (multimorbid* or multi-morbid*).ti,ab.
21. ((complicated or complex) adj (health or healthcare or illness* or morbidit*)).ti,ab.
22. Comorbidity/
23. (comorbid* or co-morbid*).ti,ab.
24. exp disease management/
25. ((chronic* or (multi* adj chronic*)) adj (disease* or patient$1) adj manag*).ti,ab.
26. ((self or personal*) adj2 (administ* or care or control* or manag* or monitor*)).ti,ab.
27. (17 or 18 or 19 or 20 or 21 or 22 or 23) and 26
28. or/16-25,27
29. (geriatric* or gerontolog*).ti,ab.
30. (elderly or senior? or (old adj age) or (older adj adult?)).ti,ab.
31. Geriatrics/
32. or/29-31
33. Patient Participation/
34. Physician-Patient Relations/
35. Patient Care Planning/
36. *Patient Care Team/
37. ((physician? or doctor? or provider?) adj ((patient? or client*) adj relation*)).tw.
38. "goal-oriented care".ti,ab.
39. ((physician? or doctor? or provider?) adj ((patient? or client*) adj communicat*)).tw.
40. ((Patient?-centred or client*-centered) adj (decision adj mak*)).tw.
41. (Shar* adj ("decision-making" or (decision adj mak*)) adj (process* or proced* or method*)).tw.
42. or/33-41
43. 32 and 42
44. Health Priorities/
45. ("Re-prioritization" or "prioritization" or priorit*).tw.
46. (Priorit* adj guideline?).tw.
47. ("health care" adj priorit*).tw.
48. "pivot point".tw.

49. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
50. (trad* adj off?).ti,ab.
51. or/44-50
52. 15 or 43
53. 52 and 51 and 28

48. ((chronic* adj (care or condition* or disabilit* or disease* or disorder* or health* or ill or illness* or morbidit* or syndrom* or symptom*)) and (manag* adj priorit*)).tw.
49. (trade* adj off?).ti,ab.
50. or/44-49
51. 15 or 43
52. 51 and 50 and 28

Appendix 2

Codebook for identifying concept themes – Program Theory 1

Concept	Concept definition	Source (Reference number)
BARRIERS		
Barriers to effective chronic disease management interventions	**GENERAL BARRIERS:** • Barrier factors or challenges to achieving effectiveness, impact, intended performance of chronic disease management interventions. Barriers related to specific types of interventions are described below • These tools can be targeted to clinicians, providers, other health care professionals and patients and used in any setting (e.g., primary care, hospital, home) • Examples: ○ Interventions are not directed to enhance patient self-management **IMPLEMENTATION BARRIERS** • This includes barrier factors related specifically to the implementation of the intervention, which can include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention. • Barriers to positive adaptation to and use of the intervention (emotional, cognitive, or physical dimensions that impede patients' use of the system). • It can also be about the "delivery" mechanisms of the intervention that may hinder its adoption or uptake • Implementation barriers can relate to situations where family members are protective of vulnerable residents (in a LTC setting), which may lead them to withhold permission for their relatives to participate in the study. • These intervention designs often presuppose the availability of informal support systems even though the impact of treatment burden on both caregivers and patients with chronic conditions is well documented.	• 23-26
Behavioural interventions • *Cognitive behavioural therapy* • *Self-management interventions*	GENERAL BARRIERS • Factors that negatively influence behavioural interventions • Universal Medication Schedule: The *aim was to standardize prescription labeling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding*.	• 15,27-32 Self-management interventions • 29,33

		Clinic-based self-management interventions for patients One possibility [for why self-management interventions struggle to achieve reach] is that most forms of intervention, whether provider based or patient based, are outside patients' workaday and social activities, so fail to embed themselves into their everyday lives.	
	Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Chronic Care Model* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL BARRIERS** • Factors that negatively influence coordination of care interventions	• 27,34-41
		IMPLEMENTATION BARRIERS • Factors that negatively influence the <u>implementation</u> of coordination of care interventions **<u>Shared care implementation barriers:</u>** • If care providers are less easily convinced of the feasibility of shared care models because of the traditional professional boundaries they find difficult to give up or change.	• 15,38,42-45
	Health information technology tools: • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL BARRIERS:** • Factors that negatively influence health information technology tools	• 29,37,46-53
		IMPLEMENTATION BARRIERS: • Factors that negatively influence the use of technology based or computer-based tools or systems (e.g., low use). • Factors that influence adaptability of health information technology tools (i.e., factors that affect how people adapt to using the system to manage their chronic conditions) • Issues such as data decentralization, security, and privacy often prevent the implementation of health IT. **<u>Video-image conferencing implementation barriers:</u>** • Socioeconomic, technological, political and professional barriers • The lack of uniform policies and standards for health care facilities and patient confidentiality issues in the infrastructure at state and national levels • Arbitrary boundaries for services • High costs to support broadband connectivity	• 48,50,51,54

	• Public and private payers' reluctance to establish reimbursement policy at lower levels adds another obstacle to broader deployment of real world Telemedicine. **Computer-based counselling implementation barriers** • Lack of implementation by care staff, which could lead to failure to produce an effect **Telephone/telemonitoring implementation barriers** • Inconsistent interactions with patients. • Completing the minimum number of telephone / telemonitoring calls prior to patient discharge. • Communication and collaboration barriers between nurses and physicians. • Being unaccustomed to modern technology. • Fear and avoidance of modern technology ('computer anxiety') which can impede implementation and use of home telecare management system. • Nurses had to be assisted with physician communication by other personnel who would send letters for non-urgent requests or calling directly for urgent ones.	
Barriers to the management of multiple chronic diseases	**GENERAL BARRIERS** • Barriers to the complexity of care required to manage multiple chronic conditions (i.e., multiple prescribers, multiple providers; consumer knowledge gaps about treatment) • Examples: o Having a limited consultation time o Multiple providers o Undefined roles of GPs and specialists o The presence of simultaneous care plans for multiple conditions can lead to confusion, which can generate safety hazards.	• 15,23,26,33,35-40,45,50,51,55-86
Barriers to effective self-management of multiple chronic conditions	**GENERAL BARRIERS:** • Barriers that patients experience in self-managing their multiple chronic illnesses. • Examples: o Difficulty following exercise and dietary plans o Depression o Fatigue o Poor communication with physicians o Lack of social support o Pain and physical symptoms o Financial problems o Lack of awareness o Lack of information	• 15,23,25,26,28-32,36,43,51, 55,56,59,61-65,72,74,85,87-95

	○ Emotional impact of having multiple chronic conditions • Multimorbidity reduces the capacity of patients to modify their lifestyle, their ability to seek help and to manage multiple medications. • Multimorbidity also has a significant economic impact on patients because of the costs associated with their care, which may be compounded by their inability to work as the conditions progress.	
Barriers to using existing guidelines for disease management	**GENERAL BARRIERS** • Barriers or challenges faced by physicians to using existing guidelines for disease management, which tend to focus on a single disease • Lack of guidelines for managing multiple chronic diseases, which may lead to provider lack of knowledge of optimal care pathway	• 25,37,39,40,56-58,60,61, 63,66,72,74-76,83,86,89,96-99
Chronic disease interrelatedness	**GENERAL BARRIERS** • Chronic diseases may be interrelated • The course of one chronic disease may influence the course of the other disease (e.g., Depression and dyspnea-related disability) • The influence of treatment(s) for one chronic disease on the outcomes of other co-existing chronic diseases • The additive impact of one disease to the other • The impact or burden of one disease on the treatment demands of the second disease (e.g., Diabetes magnifies the demands of COPD treatment). • Multimorbidity may present as a collection of long-term conditions that share common risk factors (e.g. chronic obstructive pulmonary disease and cardiovascular disease as a result of smoking) or when one condition leads to another as a complication. • Quality of life for people with multimorbidity is inversely related to the number of conditions they have and the extent of any disability.	• 3,9,28,30,35,45,55,65,69,71,74,82,92,100-102
Depression + Diabetes	The additive impact of depression and diabetes lead to functional impairment including a higher number of cardiac risk factors, increased micro- and macrovascular complications in addition to poor self-care and increased mortality.	• 101
Diabetes + Chronic Kidney Disease	Irrespective of the cause of kidney disease, the co-existence of diabetes, CKD and hypertension leads to synergistic adverse effects: mortality is higher, quality of life is worse and the burden on healthcare services is increased.	• 27,35,55,103
Depression + Pain	Improved arthritis pain was associated with decreased depression; the concurrent improvement in both conditions supports the close interplay between depression and pain (Lin, 2003).	• 104
Disease co-management	**GENERAL BARRIERS** • The care or management of two diseases simultaneously • Suggestions on treatment of co-existing diseases (e.g., depression + arthritis)	• 9,27,30,34,35,39,61,62,65,72,74, 82,105

	• The need to simultaneously manage multiple chronic conditions complicate care management - escalating challenges of understanding a growing number of different clinical conditions while attempting to monitor combinations of different symptoms, and reporting symptom and functional status changes to multiple providers from different specialties, and adhering to different medication administration and other care plans.	
FACILITATORS		
Facilitators of effective chronic disease management interventions	**GENERAL FACILITATORS** • Facilitator factors (positive attributes) that contribute to the effectiveness, impact, intended performance of chronic disease management interventions • Impact can directly affect patients or healthcare providers or the system or how patients access or use health services or the management of their diseases • Care plans [in the context of multiple chronic conditions need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. • Participants reported feeling supported and reassured through the intervention because they were in contact with individuals who listened, understood and empathized with them and validated the challenges of living with the many consequences of their health conditions. **IMPLEMENTATION FACILITATORS** • This includes facilitator factors related specifically to the implementation of the intervention. These can also include factors/processes/obstacles that are identified as possible points of modification for future implementation of a similar intervention.	• 23,37,55,63,76,92,106
Behavioural interventions • *Cognitive behavioural therapy (CBT)* • *Behaviour activation* • *Self-management interventions*	**GENERAL FACILITATORS** <u>Cognitive behavior therapy (CBT) facilitators</u>: • Having trained practice nurses deliver the intervention. <u>Behaviour activation facilitators</u>: • Strategies to activate patients to perform particular health behaviors. (i.e. medication self-efficacy and adherence) <u>Self-management interventions</u> • Universal Medication Schedule: The aim was to standardize prescription labeling and to provide a simple chart bringing all medicines in a patients' regimen together over 4 dosing periods through the day and which also explains the purpose of each medication to improve understanding. • Interventions that target improving patient self-management behavior/skills.	General • 15,26,28,31,107 CBT: • 28,34,104 Behaviour activation • 30,71 Self-management interventions • 15,28,29,31,33,55,94,108

	Home based Interventions	Home-based services that bring multiple disease management services to people with mobility and other barriers to access to care	• 109
	Coordination of care interventions • *Collaborative care* • *Case/care-management* • *Consultations/consultation services* • *Multidisciplinary care* • *Shared care* • *Teams* • *Stepped-care strategies* • *Comprehensive Geriatric Assessment* • *Advanced Practice Nursing* • *Patient-partner approach*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) coordination of care interventions	• 15,39,110
		IMPLEMENTATION FACILITATORS <u>Case/care-management implementation facilitators</u>**:** • Having a specialist mental health team. <u>Collaborative care facilitators</u>**:** • A practice nurse who can carry out the intervention • Access to clinical software capable of generating a disease registry from which patients could be selected to participate in the trial were the facilitators of the implementation of the intervention. • The design of the intervention which allowed for its easy implementation within general practices and a better use of their existing resources meant that the TrueBlue could be easily applied to patients across general practices at a population level, making the benefit clinically important. <u>Disease management program facilitators</u>: • Adherence to evidence-based guidelines, which can improve health and cost outcomes • Usefulness (how valuable the users consider the specific features, functions, and data the tool makes available to them) • Value • Satisfaction • Ease of use (how easy it is for a user to complete their desired task with the tool) • Acceptability • Intention to use.	• 9,41,42,61,69,75,78,79,111 <u>Collaborative Care:</u> • 38,103,112 <u>Integrated care</u> • 53,80 <u>Coordinated care / Disease management:</u> • 36,39,45,63,65,81, 92,110 <u>Advanced Practice Nursing</u> • 44 <u>Patient-partner approach</u> • 45

	Health Information Technology Tools • *Clinical decision support systems (CDSSs* • *Computer-based counseling systems (CBCSs)* • *Health information technology (IT) tools* • *SmartForm* • *Telecare / Telemedicine* • *Telemonitoring* • *Videoconferencing systems*	**GENERAL FACILITATORS** • Factors that facilitate (positively influence) health information technology tools • Health information technology can promote coordination of care and improve quality and safety. <u>Telephone/telemonitoring facilitators</u>: • Good disease management combined with the deployment of the technology • Telemonitoring was managed by primary care professionals (GPs and nurses) who regularly see their patients in health centres or at home than if the intervention was in-hospital; • The perception of facilitators in the increasing healthcare professionals' intention to use telemonitoring technology (organizational context is the most important variable); • Paying attention to the proper clinical management of patient's conditions. • Universal Medication Schedule.	• 27,29,46-52,54,108,113
	Self-management interventions?	**GENERAL FACILITATORS** • Factors that facilitate self-management. • Impact on self-management can occur in the emotional, physical, and financial domain, but is not restricted to these	• 27,50,77,84,108,114

Facilitators of the management of multiple chronic diseases/multimorbidity	**GENERAL FACILITATORS** • Factors that facilitate the patient's management of multiple chronic conditions. • "Factors" may include the qualities and components of the intervention that make it easier/simpler to manage a patient's multiple chronic conditions (manage: to stabilize, control, or improve a patient's health or quality of living with multiple chronic conditions). • Care plans that are clear and blend clinical care with self-management are essential in multimorbidity; they need to incorporate not only biomedical but also psychosocial factors, such as mood, informal care network, and patient income/finances. • Examples: o The biopsychosocial approach to care can be applied to patients with both depression and arthritis; it should include depression screening in a systematic assessment of pain among older patients with symptomatic osteoarthritis.[104] o Medical management of arthritis can integrate evidence-based depression treatment with patient education and support for self-management (eg, exercise) to maximize functional status and quality of life." o The facilitators that are proposed to assist patients with the management of depression and arthritis are 1) the inclusion of depression screening with pain assessment, and 2) the integration of depression treatment with patient education and self-management support. • This concept is different from "Facilitators of effective chronic disease management interventions/programmes" because the latter concept looks at explaining why an intervention/program works o For example, Lamers[28] explains, "Minimal interventions like our MPI – that (1) may provide patients with the skills to cope with the consequences of their illness and their depressive symptoms, (2) can be incorporated in existing disease and care management programs, (3) can be administered by nurses (e.g. practice nurses)." It is *because* the intervention provides patients with certain skills, and its implementation is favourable, that the MPi is able to be implemented and foster positive patient outcomes.	• 15,26,30,32,33,37,39, 40,45-47, 55-59,61,62,72,74-76,81,82, 84,86,88,89,92-94,98,102,104, 105,115-120
Facilitators of effective self-management of multiple chronic conditions	**GENERAL FACILITATORS** • Factors that facilitate self-management of multiple chronic conditions. • Examples: o The support of family, including reminders to take medication and avoidance of eating unhealthy foods, and social relationships serve as motivators for patients to more effectively manage their conditions.[62]	• 26,33,36,47,51,56,64,71,85,87,90, 91,93-95,108,115

Facilitators to using existing guidelines for disease management	• Includes examples of situations when practitioners thought it was useful to use or adhere to guidelines
	• Includes suggested ways to improve usefulness or helpfulness of guidelines.
	• Examples:
	  • Adhering to guidelines promotes working transparently
	  • Guidelines would be helpful for multimorbid patients if they provided more details on diagnostic, treatment, and management priorities
	  • Guidelines improve the quality of general practice
	Guidelines provide guidance to medical decision-making
		• 98

Factors influencing the management chronic conditions/multimorbidity	• Factors that influence the management of patients with chronic conditions (directionality not specified). ○ Factors that may influenced doctors' varying views on the preparedness of their practices to manage patients with different types of complex needs include: the organization of primary care, workforce training, use of teamwork, size of practice, payment strategies and incentives, health IT (information technology) capacity, and the availability of community services may play a role.[54]	• 37,54,92,117

Factors which affect treatment adherence	• Factors that influence patient's engagement with the recommendations made by the physician (i.e. factors that cause the patients to follow or not follow the recommendations).
	  ○ A key element influencing patient's engagement with multiple self-management practices was interaction with health professionals, and this was also related to perceived appropriateness of information received[93].
	  ○ The GP's response conflicted with her priorities and had a negative impact on what she felt able to engage with in managing her health. Where self-management instructions and information from the GP were incongruent with personal priorities as illustrated above, respondents remained disengaged from professional advice[93].
	  ○ In our interviews with 34 patients we had enquired about their willingness to be involved. The level of involvement depended on the nature of the problem. If it was a medical theme, patients preferred to follow the professional recommendation of their GP; however, if the theme had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision. In general, patients expressed a need for undivided attention, understandable information, time, and a calm atmosphere in the consultation[25].
	• Factors that influence the compliance of medication, typically long-term compliance.
	  ○ Strategies that include extrinsic motivators will promote long-term compliance and reduce recidivism.[50]
		• 25,50,93

Risk factors for multimorbidity	• This concept is different from "factors influencing the management of chronic conditions" as they lead to multimorbidity instead of influencing the management of multimorbidity once individuals have it	• 3,15,69,70,83,84,97,121

	• Risk factors may be social determinants of health that put individuals at risk for multimorbidity or predispose individuals to multimorbidity
	• Examples:
	  ○ Being socioeconomically deprived
	  ○ Low income
	  ○ Individuals with multiple comorbidities, who frequently experience mental health problems and illnesses, are often of low socioeconomic status and have unmet basic needs, such as housing, employment and transportation.	

Codebook for identifying concept themes – Program Theory 2

Concept	Concept definition	Source
BARRIERS		
Barriers to optimized patient prioritization	• Factors that may hinder a patient with multiple chronic conditions from being able to participate in the act of prioritizing health conditions with his/her provider; this includes their decision making • Factors that may hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization • A patient's family may have a greater influence on the decision than the patient's own preferences.[122] • Includes any barriers to patient-centred care	• 32,33,60,63,64,91,99, 122,123
Barriers to optimized provider prioritization	• Factors that may hinder a provider from being able to participate in the act of prioritizing health conditions for a patient with multiple chronic conditions including decision making. This can also include health priorities addressed in the clinic setting • Factors that make it more difficult for health care providers to prioritize the treatment/management of a patient's chronic conditions. For example, factors may include the competing demands of multiple chronic conditions, and challenges of balancing provider and patient priorities. ○ *Psychiatric disorder*: If the patient has a psychiatric disorder, then this may make it more difficult for providers to prioritize treatment/management of the chronic conditions. • Patient-centered care is defined as GPs taking a broader view of the patient, incorporating non-medical or psychosocial issues. Patient-centered care is an over-riding principal for GPs in multimorbidity but trying to achieve this increases the complexity of care in some cases, and can lead the GP into additional conflict with specialist services or evidence-based medicine.[58] • Factors that may hinder a provider from being able to apply evidence in the care of their patients. • Clinicians lack a systematic framework for determining patient preferences and synthesizing these preferences with existing evidence to set individual health priorities • Includes the barriers (i.e. time) related specifically to the implementation of training for providers (for example, GPs did not accept shared decision-making and prioritization training sessions of more than 30 min, for fear of organizational disruption , patient complaints, and financial loss).[99]	• 25,37,58,60,63,99, 118,119,123
Barriers to shared decision making	• Barriers that impede a collaborative process that allows patients and their providers to make health-care decisions together. The collaborative process takes into account the best clinical evidence available, as well as the patient's values and preferences. • For example, barriers to shared decision making patients often do not expect to share decisions, in particular older patients may find this SDM process difficult because it is unfamiliar and demanding.[99]	• 26,58,60,73,96,99, 123

Barriers to the agreement between patients and providers	- Captures any excerpts about the dynamic between the patient and provider (whether that is agreement on prioritization, decision making) - Includes excerpts that mention *both* what patients and providers think. **IN THE PRIORITIZATION OF CHRONIC DISEASES** • Factors that decrease the level of agreement between patient and provider in terms of prioritization of health conditions including health care decision making. For example, when patients present with unrelated or discordant conditions, the patient and provider may disagree about which condition should be prioritized.[72] • Include conflicting views/ranking? Between providers and patients of which diseases should be considered for treatment?[32] • Factors that decrease the level of agreement between patient and provider, but not specifically about the prioritization of health conditions. • Factors that decrease the level of agreement between patients and provider, but not specifically about the prioritization of health conditions.[115] o For example, communication between the physician and patient can affect agreement. If the physician does not enact enough/ at all information-giving, counseling, quality of question asking and support, and participatory decision-making style (process of negotiation) during consultations with patients, then this many negatively affect agreement.	**PRIORITIZATION** • 32,66,68,72,76,91,98,115 **HEALTH CARE DECISIONS** • 93
Barriers to the patient-provider relationship	• The communication barriers between patient and provider (includes factors that influence poor communication between patient and provider)	• 66,93,96
FACILITATORS		
Facilitators of optimized <u>patient</u> prioritization	• Factors that may promote a patient from taking part in the decision-making process in terms of health prioritization; • Patients engaging with health care workers in health prioritization • What motivates patients to prioritize their conditions. For example, to cope with their health problems and stabilize their health. • The components of a clinical appointment/check-up that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making. • The components of a clinical appointment/checkup that patients deem valuable and want to receive. For example, being given sufficient adequate medical information from the healthcare provider, particularly to empower patient decision making • Includes any facilitators to patient-centred care.[92]	• 63,91,92
Facilitators of optimized <u>provider</u> prioritization	• Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to prioritize multiple chronic conditions • Factors that promote health care providers to work with other providers to prioritize multiple chronic conditions. For example, use of an electronic integrated medical records system may facilitate communication and care coordination across providers.[62]	• 25,62,88,92,98,118,119, 123

	• Specifically, how patient-centered communication impacts patients in terms of knowledge, expectations, participation in treatment process and providers in terms of quality of care.	
Facilitators of the patient-provider relationship	• The concept where physician "accompany the patient, which may contribute to a stable patient-physician relationship. "The physicians saw themselves as doctors who accompany these patients rather than doctors who heal them. This leads to an emphasis on 'little improvements.' […]The physicians stressed that accompanying the patients and witnessing their improvements contributed to a stable doctor-patient-relationship."[66] • Includes communication facilitators between patient and provider (the factors that influence good communication between patient and provider)	• 26,66,92

Facilitators of shared decision making	**GENERAL**
	• Factors that facilitate the collaborative process that allows patients and their providers to make health-care decisions together based on available evidence and clarification of patient preferences.
	• For example:
	  • Agreement is a prerequisite of shared decision making and can be achieved using a patient-centred approach.[99]
	  • Sharing personal experiences, and facilitating concise and clear discussions with patients on the interplay between chronic diseases were strategies used by GPs to facilitate SDM.[58]
	IMPLEMENTATION
	• Factors that facilitate the implementation of processes, tools, or skills that encourage or foster shared and equitable decision-making between patient and doctor, with decisions based on available evidence and clarification of patient preferences
	• For example:
	  • Communication training for GPs can help them facilitate SDM.[99]
	  • If the healthcare provider considers the patient also as an expert in, and partner in the management of, their condition(s), and respects the patient's opinions.[26]
	  • Involving patient perspectives and preferences in the patient-provider decision-making process by exploring and mutually explaining each other's ideas[57].
		GENERAL:
		• 26,43,57,58,68,73,75,88,96,98,99,122
		IMPLEMENTATION:
		• 26,98,99

Facilitators of the agreement between patients and providers	- Captures anything about the dynamic between the patient and provider (whether that agreement on prioritization, decision making)
	- Includes excerpts that mention *both* what patients and providers think.
	
	IN THE PRIORITIZATION OF CHRONIC DISEASE
	• Factors that increase the level of agreement between patients and providers in terms of prioritization of health conditions.
	• For example, the agreement between patients and providers was higher when
	  ○ Patients have fewer symptoms.[32]
	  ○ The provider was male.[32]
	IN HEALTH CARE DECISIONS
	• Factors that increase the level of agreement between patients and providers, but not specifically about the prioritization of health conditions.
		PRIORITIZATION
		• 25,32,68,73,91,93, 124
		HEALTH CARE DECISIONS
		• 66,115

	• For example: Having a process of negotiation may ensure collaboration and agreement between patients and their primary care physicians.[115]	
(Neutral) Factors		
Process of shared decision making between providers and patients	The process of shared and equitable decision-making process between patient and doctor, with decisions based on available evidence and clarification of patient preferences	• 25,75,99,118,125
Patients' process of prioritizing multiple chronic conditions	• The process used by patients to prioritize their multiple chronic conditions including their decision making and management (anything about *how* patients prioritize) • Includes any "rules of thumb" patients use to prioritize their conditions i.e. pain, functional limitations, new conditions that change up your prioritization • This is different than facilitators or barriers to patients' prioritization of chronic conditions. It spells out the process (steps) that patients go through as well as the factors that they take into account when prioritizing their chronic conditions. • The steps and considerations taken by patients when prioritizing their chronic conditions. For example, Morris and colleagues[93] discuss when and why patients reprioritize conditions, and how the new ordering of conditions is determined.[93] • Simply a listing of patients' priorities such as specific diseases or getting informed about their conditions • Factors that may promote or hinder a patient from taking part in the decision-making process in terms of health prioritization; engaging with health care workers in health prioritization For example, patients tended to follow GP's recommendation if the issue was purely medical; however, if the issue had a direct impact on their daily lives (e.g. changes at home), the patients themselves wanted to make the decision.[25] • Includes factors that influence prioritization that are not related to specific barriers (challenges) or facilitators, such as the internal processes they use to prioritize multiple chronic diseases • Includes factors that may influence or drive patients' prioritization such as such as pain, fatigue, shortness of breath, or dizziness and have a great impact on quality of life and life satisfaction and thus–likely–on patient preferences. For example: Patients' prioritization and needs were affected by psychosocial factors, previous experiences and the patient's' expectation.[60]	• 25,32,56,60,63,64,66, 68,76,87,91,93,122,125
Providers' process of prioritizing multiple chronic conditions	• The process used by providers to prioritize their multiple chronic conditions including their decision making and management • For example: ○ Providers' priorities were determined by medical aspects of the diseases such as the disease severity and prognosis.[25] ○ When providers did not feel in charge of a problem or were not aware of suitable treatments, they rated the problem as unimportant.[25] ○ Instead of symptomatic conditions, providers may focus on the long-term health consequences of asymptomatic hypertension or uncontrolled diabetes.[32]	• 25,32,57,63,65, 66,68, 76,96,98,119, 125

Appendix 3

Context-Mechanism-Outcome (CMO) configurations of Programme theory 1 (Care coordination interventions)

General CMO configurations to explain Program Theory 1

***Care coordination Interventions** in primary care are effective for older adults with multimorbidity because they represent a structured approach to holistic care. They provide a comprehensive and coordinated approach to multimorbidity management by addressing multiple conditions (through interdisciplinary teams and/or multidisciplinary disease management), providing specific mechanisms for communication, and establishing formal roles for providers and patients.	
Team-based approaches	Team-based approaches can lead to a range of outcomes, such as evidence-based care solutions for multiple conditions in parallel (not in tandem) [M][38], a wider range of services [O], more holistic care [O], higher quality of care [O], reduce scheduling complications [O2][88] and increase the flexibility and responsiveness of the team [O3][45]. These outcomes are most likely to occur when team members have mutual respect and confidence [M2][45], are highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M][53] who understand and accept each other's roles [M3][53], provide opportunities[38,88] and time[53] to share information [M][81], and are willing to collaborate on patient care [M5][38,45,53,88]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M]. The contexts in which these mechanisms are triggered include teams that have dedicated members who provide additional support to patients[38,53] or providers[81]. Team members receive official training on the model[38,53,81], including training on team skills[81]. Organizations have a robust and well-functioning communication system[38,45]. Many of the team-based approaches under study were Canadian[45,53,81].
Disease management	Disease management for multimorbidity care consists of the use of a number of discrete intervention strategies with the desired outcome of achieving systematized care. These include: checklists, follow up timetables[45,103,110], and treatment targets [M][45]. Together, these intervention strategies appear to make explicit the roles, expectations, and responsibilities of the health care professionals involved [C], enabling staff to become aware of their roles, expectations, and responsibilities [M] leading to a shared philosophy and platform for care [O][45],[103]. This also permits the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][45]
Case management	Case management intervention strategies are appropriate for managing multimorbidity because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C], a case manager functions as a conduit of information [M] to help improve coordination and information sharing from the patient to providers as well as between providers [O][53]. When improved coordination and information sharing occurs [C] and case managers are in regular contact with the patient [C][80], are the primary point of contact and coordinator of care [C][103] and provide individualized attention [C][9] and information [C][80] to patients, patients

		perceive that their care is continuous [M][78,79] and coordinated [M][79] and as a result know who is 'in charge' and who to turn to when then have a problem [O]. When patients know who is 'in charge' and who to turn to when then have a problem [C] helps patients to feel safer [M] and trust [M] of their case managers over time[79] resulting in the building of relationships that are more likely be based on confidentiality [O][79,80], and mutual equality [O][80] These types pf relationships appear to be the basis of some of the further 'downstream' outcomes that are found with case management, such as helping patients to develop the skills and confidence they need to manage their health [O][78].
Education was a component in 83% of the chronic disease management interventions identified in our systematic review. Education for patients is often a component of care coordination interventions[15,45,103], and can be more effective [O] when combined with active monitoring [M] and provided by a pharmacist[45] [C].		
	Health education	Health education is often combined with self-management support[94,103,104], which is more effective for lifestyle modification than education alone[94]. Patients receive education about their multimorbidity through numerous formats, including: video streaming[50], in-hospital education[31] and the internet[51]. Video streaming may be good for homebound patients[50], whereas in-hospital education may be more effective for those who might become motivated to change their lifestyle after a hospitalization event[31]. Patients with multiple chronic conditions use the internet, but there are few websites that address multiple conditions in an integrated fashion[51].
	Health coaching	Health coaching (helping patients to gain the knowledge, skills and confidence to become active participants in their care aimed at reaching their self-identified health goals)[27]. Health coaches (who could also be case managers) strengthen patient self-management by improving patient self-efficacy by listening and applying patients' challenges and health goals to customize action planning[27]. This allows patients to develop the coping and problem solving skills that support self-management[27,94].
	Web 2.0 technology	Web 2.0 technology (web use that involves more active participation, creation and sharing of information such as through social networking) are examples of interventions captured in our realist review that incorporate education. Web 2.0 technologies may support patient self-efficacy by providing relevant information, and opportunities to learn from other web users. For example, delivering online instructional units (developed and delivered by a multidisciplinary team of healthcare providers), and self-management training workshops staffed by peer moderators (i.e. individuals living with similar chronic conditions as the user)[95].

*This narrative provides only a broad explanation of Programme theory 1, greater detail that explains the outcomes that[81] may be achieved by the different intervention strategies used in the care coordination.

Details of CMO configurations to explain Program Theory 1

Coordination of care element	Definition	Explanation of determinants via Context [C]-Mechanism[M]-Outcome[O] configurations
Teams *The right care at the right time*	Highly trained clinicians[53] who provide holistic and coordinated care, often, but not always, from the same physical location[88]. Teams aim to provide time for the patient to discuss all of their concerns, prevent care overlap and gaps[80], and reduce scheduling complications[88] Patients are taught about their conditions, medications, and how lifestyle affects their health, and given information on health promotion or counseling services and other supporting services[44].	**Why Team-based approaches are appropriate for multimorbidity:** Team-based approaches are appropriate for managing multimorbidity [O1] because they can ideally provide evidence-based care solutions for multiple conditions in parallel (not in tandem) [M1][38]. Collaborative care teams can provide a wider range of services [O1], more holistic care [O2] and higher quality of care [O3] through interdisciplinary communication and collaboration [M1][38,81], and access to specialists [M2][53]. **Facilitators of successful teams:** Successful multidisciplinary teams [O1] are those which comprise highly trained and skilled (fast learners, effective communicators, motivated, capable, well organized) members [M1][53] who have mutual respect and confidence [M2][45], understand and accept each other's roles [M3][53], provide opportunities[38,88] and time[53] to share information [M4][81], and collaborate on patient care [M5][38,45,53,88]. These facilitators can also reduce scheduling complications [O2][88] and increase the flexibility and responsiveness of the team [O3][45]. Successful teams [O4] also require that patients and team members be educated about how the team functions and the role of each member [M1]. The use of peer moderators (i.e., individuals also living with a chronic condition who are trained to lead self-management training programs) [M1] can facilitate intervention learning activities such as behavior change, medication management, and disease information [O5].
Disease management *Systematized care (all providers are on the same evidence-based page)*	Disease management programs follow a "script" of how to provide effective (often evidence-based) patient care. Often care protocols or intervention plans define the division of tasks and support the follow-up and coordination of action[103,110], and help sustain the development of a philosophy of common care[45]. Patients may be educated about the disease management system so they know what to expect, and often provided with education and resources about how to properly self-manage their conditions.	**Why Disease management approaches are appropriate for multimorbidity:** Disease management strategies are appropriate for managing multimorbidity [O1] because they can systematically apply evidence-based care to populations of patients [M1] thereby making it more appropriate for managing conditions and combinations of conditions where evidence-based care exists. Care can be systematized [O2] through checklists [M1], follow-up timetables [M2], and treatment targets [M3][45,103,110]. **Facilitators of disease management:** Disease management approaches define the division of tasks [M1][45], support the follow-up and coordination of action [M2][45,103], and help sustain the development of a philosophy[45] and shared platform[103] of care [M3], therefore permitting the formalization of decisions (about which health care professionals have agreed upon) preferably in discussion with patients and their family and/or friends [O][45].
Case management	Case managers are trained health care professionals who are the contact person between a patient and involved providers. They know how to facilitate	**Why case management approaches are appropriate for multimorbidity:** Case management are appropriate for managing multimorbidity [O1] because in collaborative care interventions where there may be diverse and many providers involved in a patient's care [C1], a case manager acts as a

Case managers are the primary conduit of care	care planning and shared decision making; and how to anticipate and address barriers (e.g. to treatment adherence). Case managers work closely with patients and their family/caregivers to provide information (e.g., about the health system or care), and to help them develop the skills and knowledge needed for self-management.	conduit of information [M1] to help improve coordination and information sharing from the patient to providers as well as between providers [O][53]. **Facilitators of case management:** Case management strategies work [O1] because case managers are in regular contact with the patient [M1][80], and provide individualized attention [M2][9] and information [M3][80] to patients. For patients with extensive and diverse care teams [C1], case management can ensure that care is continuous [O2][78,79] and coordinated [O3][79] by enhancing the communication between patients and providers [M1] and by being the primary point of contact and coordinator of care [M2][103]. Patients also feel safer [O4] when knowing that their case managers are monitoring their care [M1], and they trust their case managers over time [O5][79] because of regular contact [M1][80], and through a relationship of confidentiality [M2][79,80], and mutual equality [M3][80]. By engaging family/caregivers in proactive care [M1], case managers also help patients develop the skills and confidence they need to manage their health [O6][78].

Appendix 4

Context-Mechanism-Outcome (CMO) configurations of programme theory 2 (Health prioritization in multimorbidity management)

General CMO configurations to explain Program Theory 2

Multimorbidity management is confusing for patients and overwhelming for providers due to the heterogeneous nature of multimorbidity[102], disease and treatment interactions and possible conflicts[57,92], and the difficulty of attributing symptoms to conditions[57]. Health prioritization is an important function of the management of multiple chronic diseases in primary care settings because the evidence base is most often single-disease focused and multimorbidity can create a cognitive and emotional overload in patients and health care providers. A common intervention strategy to multimorbidity management is to focus on one condition at a time[64], using a priority setting approach. Prioritizing one condition over the others (for a specified period of time, or until particular outcomes are achieved), allows patients[91] and providers[64] to focus their attention and care.		
	Patients' approach to prioritization	Patients with multiple chronic conditions can experience a range of symptoms [C]. These symptoms trigger cognitive and emotional overload [M] for patients and as a result, they resort to prioritization [O]. The prioritization process is influenced by the nature of the symptoms. Patients prioritize their condition [O] by making decisions based on their judgments of the symptoms they experience most need attention [M]. Symptoms which threaten their participation in social activities[25,63,76] [C], limit their independence[25,91] [C] and they believe might have potentially severe long-term consequences if not acted upon[63,91] [C] - examples of these symptoms include pain, fatigue and dizziness. Those diseases that patients prioritize and seek help for [O] are the ones that patients believe are causing with these symptoms[32,56,63,66,68,125] [C] because they do not feel that they have the capacity to engage in self-management behaviors associated with the disease [M]. Multimorbidity can have cascading effects. Patients may find it challenging to determine which chronic disease is causing a particular symptom [O] because conditions may share similar symptoms[72] [M], the treatment of one condition may aggravate the other[61,62,90,91] [M] or cause other antagonistic effects[64,90,91] [M]. The diagnosis of a new condition added to an existing one [C] may impede self-management because information about the new condition adds uncertainty[87] [M]. Patients who are able to identify the main illness that causes the most concern [C], are able to keep their symptoms under control and return to an acceptable way of life[87] [O].
	Providers' approach to prioritization	Patients with multiple chronic conditions can present to health care providers with a wide range of symptoms [C]. Dealing with these symptoms trigger cognitive and emotional overload [M] for the providers and as a result, they resort to prioritization [O]. The prioritization process used by providers is influenced by the nature of the symptoms. Providers tend to prioritize conditions [O] based on their judgments about the prognosis or severity of the condition [25,57,66,68,76,125] These judgments are influenced by their knowledge or evidence [124,125] about the which conditions are likely to have more serious outcomes [C], whether the patient is likely to benefit from treatment[57,114,124,125] [C] and conditions they feel they are most likely to be able to address (e.g. physical vs. emotional)[32,124]. Providers also tend to prioritize physical conditions over emotional or other conditions [C] (partly because) they consider the interrelatedness of the conditions and any potential cascading effects when prioritizing[65][M].

Associated CMO configurations related to multimorbidity management: We derived explanations of multimorbidity management in the context of primary care from the perspective of patients, providers and the system.	
Patient perspective	The mental health needs of patients add to management challenges and interfere with patient self-care[57]. Some mental health patients with poor communication[C] receive less intensive mental health treatment[59][O] because providers sometimes ignored or normalized [M] their symptoms[38]. A patient-centred approach, which takes into account the patient's psychosocial realities (housing, relationships, income)[92][C] is more likely to meet the needs of complex patients with multimorbidity[82,117] [O].
Provider perspective	Primary care clinicians face a number of challenges when managing patients with multimorbidity. In the contexts of inadequate decision support systems[35], evidence to support their clinical decision making[60], or care protocols or intervention plans that are too rigid[45], they may feel that they lack the skills and/or confidence[33] [M] to simultaneously understand patient subjective experience and biochemical processes of diseases[26] needed to appropriately manage these patients [O]. Another challenge is that most often, only single disease guidelines are available to manage multimorbidity [C], so clinicians are forced to modify them in anticipation of adverse effects[89] [M] or use common sense approaches [M] (to complement the limitations of their application[98]) leading to variations in 'adherence' to single disease guidelines. In the context of few existing multimorbidity guidelines and resulting clinical uncertainty or contradictory information, a promising intervention strategy from our included articles was shared decision making between patients and clinicians, which was described as a useful, and possibly a necessary tool for making individualized treatment decisions[58, 118].
System perspective	Multimorbidity can create challenges in the relationship between primary and secondary care. When patients are given more certainty than a primary care practitioner would have provided [C], the primary care practitioner's view of specialists can be negatively affected[68] [O]. There is often poor communication between primary and secondary care providers[61,84], which makes it difficult to coordinate care[58]. From the system perspective, primary care may be the optimal context to deliver multimorbidity care because it is accessible to most patients[33], and tend to be viewed as efficient[33], equitable[33], and having wide reach[33] and good continuity of care[33,56-58]. However, the infrastructure of primary care settings may not be optimally designed to handle multimorbidity [C] and can lead to fragmentation of care [O]. This is because multimorbidity demands the involvement of multiple providers[80] [M], multiple care locations[92] [M], and extra consultation and provider time[32,33,35,38,65,72,102,105] [M], which can lead to less opportunities for preventative and psychiatric care [O], less care for concurrent conditions[59] [O], inadequate time for building patient-provider relationships[63] [O], and poor follow-up[35][O]. Increasing or adjusting consultation time for multimorbidity management [40,72,75,82] and complexity of illness[58] may provide opportunities to address these challenges.

Details of CMO configurations to explain Program Theory 2

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Disease and patient factors	***Barrier:*** Prioritization in itself is challenging for patients [O1], because of treatment side effects [M1][64], and the patient needs to manage one condition at a time, which may be in conflict with other condition treatment plans that they ought to be having [M1][64]

		Facilitator: Patients with multimorbidity optimally prioritize their health conditions [O1] by being actively involved in setting their goals and priorities [M1][92], and by sharing their feelings (with providers) about their illnesss(es) and its effects on their functioning [M2][92] by stating their expectations to providers of medical care [M3][92].
	Provider factors	***Barrier:*** Patient prioritization can be hindered for patients [O1] by receiving confusing [M1] and conflicting [M2] treatment recommendations from physicians[64], and by lack of awareness/information regarding the seriousness of a condition [M3][32]. ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to have reassurance that their available treatments work [M2][64], and that their condition is being monitored regularly [M3][64].
	Contextual factors	***Barrier:*** There is currently no framework to assist patients in determining preference and synthesizing these preferences with existing evidence to set individual health priorities and decisions [M][123] ***Facilitator:*** Strategies to help patients prioritize their conditions [O1] are to use home-based self-management programs [M1][91], and by having access to clinicians who are knowledgeable about their health conditions [M4][64].
Provider perspective		
	Disease and patient level factors	***Barrier:*** Prioritization is difficult for physicians [O1] when aspects of patient health such as when conditions or symptoms (e.g., pain) are difficult to treat and impactful [M1][118], when somatic and mental disorders are combined [M2][60], and when there is no specific diagnosis or the presentation is an asymptomatic condition [M3][119]. ***Barrier:*** The evidence for treating multiple chronic conditions itself [C1] may be problematic [O1] because it may conflict with patients' values, preferences and needs [M1], be insufficient or uncertain regarding effectiveness [M2], or in the case of health economics data, be difficult to interpret and use [M3][119]. ***Facilitator:*** Providers find it easier to prioritize uncomplicated conditions which are responsive to treatment [O2] because they are able to predict patient benefits [M1] and determine if treatment is cost-effective [M2][119]
	Provider factors	***Barrier:*** Prioritization is difficult [O2] when physicians do not know about a patient's psychosocial factors [M1], history [M2] or management expectations [M3][60]. Additionally, physicians themselves may not understand [M4] or be able to adhere to patient priorities [M5][123], and may not have in person-centered communication [M2][25] or shared decision making [M3][99] skills. ***Facilitator:*** Facilitators of optimal provider prioritization [O1] are good listening and communication with patients [M1][25], which also ensures that treatment is individualized to each patient [O2][123]; that priority setting is based on patient's perceptions, concerns, and expectation [O3][25]; that the prioritization has a positive impact on functions of daily living [O3][92], and based on what the patient has identified as their own priorities [O4][25]. This individualized care for the patient [O2] should be balanced with clinical knowledge[123] and provider self-reflection [M1][25].
	Contextual factors	***Barrier***: Optimized provider prioritization is challenging [O1] because it takes an investment in time [M1][25,60,99] which doctors worry might disrupt clinic flow [O2], result in financial loss [O3], and trigger patient complaints [O4][99]. ***Facilitator:*** Physicians can improve the process of prioritizing chronic conditions with the help of specialized multimorbidity clinics [M1] and multimorbidity software programs [M2][25]

Appendix 5

Context-Mechanism-Outcome (CMO) configurations of programme theory 3 (Patient self-management in multimorbidity)

General CMO configurations to explain Program Theory 3

Patient self-management in multimorbidity: We derived explanations via CMO configurations to explain self-management in multimorbidity (Appendix 6).	
Burden of multimorbidity management	Multimorbidity is reported as a burden by patients [O] because of the cognitive and emotional overload [M] required for lifestyle changes [C][87] (which can be inconsistent or conflicting [C][25]), as well as the volume of information and recommendations provided [C][51,74] (which are often confusing and conflicting[43,91-93][C]). Adherence to recommended treatment is challenging for patients [O] because: 1) self-management regimens have been designed to fit their condition rather than their health priorities [C], lifestyle [C], available resources [C][89,94]; 2) unwieldy medications (too many, taken often, and difficult to keep track of)[C][15,51]; 3) having to follow a required diet and exercise routine [C][36,51,91]; 4) having to see multiple providers[C][71]; 5) medication mismanagement[C][71]; 6) not knowing how to respond to adverse drug effects[C][15,71]; and 7) communication barriers due to linguistic and cultural diversity[C][71]. These multiple contexts likely trigger cognitive and emotional overload [M].
Influence of cognition and mental health on self-management	Self-management is particularly challenging [O] for older adults who have impaired cognition[89] [C]or suffer from anxiety[90] [C] in addition to chronic conditions [C] as these contexts interact to increase their perceive an increase in illness burden[63]. If the additional condition is depression [C]: older adults may choose not to do anything (such as take medication) [O] because they consider it a normal part of aging [M] or; are reluctant to seek treatment [O] due to stigma[30] [M]. Depression, as a context, appears to also trigger other mechanisms that reduce their ability to self-manage chronic conditions[30-32,59,64,87,91] [O]. The mechanism include reduced patient motivation, energy and self-efficacy, feelings of being overwhelmed, hopeless[31] or stressed[87]. There appears to be a number of feedback loops because illness burden can interfere with people's ability to engage in health promotion such as exercise, which can result in negative consequences such as weight gain[87], reduced quality of life, functional decline or ability to work. These in turn, can impact mood, social networks, and self-management behaviours[62].
Influence of resource constraints on self-management	Self-management in multimorbidity is influenced by the lack of resources available to many older adults to help manage this burden[64] including the lack of finances[62,91], social supports[23,62,88,89,91] or transportation[91], as well as the influence of low health literacy[29] or skills to manage and coordinate care and adverse effects[43,90]. Another challenge is that even if resources and programs exist, older adults may not be aware of them[62]. Promoting contact with consumer organizations or support groups[26,71] and having peer support[31] may address these challenges. Older adults are interested in self-management tools that provide health condition information[51]; share, coordinate and synthesize information with and between providers; and connect them with other patients[51]. Physicians can support patient self-management through tailoring of information to the stage of the patient's condition and their adaptation to it[26], as well as through good interaction with patients[93], providing information[93] (including patients' particular language[71]), and a collaborative approach to care[115].

Details of CMO configurations to explain Program Theory 3

Theme	Sub-theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective		
Managing multimorbidity is **difficult to do for patients** due to the volume, complexity, and confusing/ contradictory nature of what is required for self-management.	*Burden of self-managing multimorbidity*	***Barrier:*** The burden of self-management is high for people with multimorbidity [O1], and can impair their quality of life life[92] [O2] due to the required lifestyle changes[87], which are sometimes inconsistent or conflicting [M1][25]; the provision of the sheer volume of information provided[51,74] [M2], and the often confusing and conflicting information provided about treatment recommendations [M3][43,91-93] (including conflicting dietary advice for different conditions[93] from a multitude of healthcare providers). In fact, self-management becomes more challenging as the number of providers increases [M5][74] along with the numerous appointments required [M6][15,56]. ***Facilitator:*** Having multiple conditions itself can promote self-management [O] because patients may have already developed skills such as self-monitoring and self-advocacy [M1][63,90], and they may be more motivated because of the heightened risk [M2][90]. ***Facilitator:*** When patients can establish a cognitive link between existing self-management practices [M1][90,91,93], and making this link intuitively and over time[93], they can became more successful at self-management [O1].
	Adherence to self-management regimens (treatments and medications)	***Barrier:*** Successful self-management [O1] has been judged by the ability of patients to adhere to prescribed treatment [M1]. However, adherence to recommended treatment has not worked for patients [O2] because self-management regimens have been designed to fit their condition rather than their health priorities, lifestyle, and available resources [M1][89,94]. Other factors are unwieldy medications (too many, taken often, and difficult to keep track of) [M2][15,51], having to follow a required diet and exercise routine [M3][36,51,91], having to see multiple providers [M4][71], medication mismanagement [M5][71], not knowing how to respond to adverse drug effects (especially for those who take multiple medications) [M6][15,71], and information communication barriers such as linguistic and cultural diversity [M7][71] ***Barrier:*** Patients do not take prescribed medications [O3] for a variety of reasons: they do not like taking medications [M1][85,91], they believe that the medication will negatively affect their health [M2] or is inappropriate for their underlying condition [M3][91], they do not believe the medication is necessary [M4][91], they experience undesirable side effects from the medication [M5][15,91], the medication information is difficult to read or understand [M6][29], the regimen is too complicated to follow (particularly in culturally and linguistically diverse populations) [M7][32,51,56,71,92], the bottles are difficult to open [M8][29], and they forget to take their medication [M9][29]. Although not being able to understand and receive information can lead to medication noncompliance [O4][90] the provision of better and clearer information about medications alone is unlikely to improve adherence [M1][29]. ***Barrier:*** Medication noncompliance can also result if taking multiple drugs (polypharmacy), which can lead to drug interactions[124] and adverse events [M2][101].

		Facilitator: People with multimorbidity can learn how to take medication strategically to achieve a balance between benefits and side-effects [O4], often based on years of experience of self-managing often antagonistic symptoms and competing goals [M1][85]. Medication adherence [O5] can be facilitated through automated reminder systems [M1][47,56], and switching to medications with modified release formulations [M2][56]. ***Facilitator:*** Medication adherence [O5] is linked to a person's self-efficacy (the confidence or ability to feel "I can do that") [M3][71], which can improve clinical outcomes [O6][47]. Some patients with multiple chronic conditions view their medication as a way of gaining control over their illness management [O7] by establishing routines for taking medications [M1] and seeing it as an opportunity to become more active self-managers [M2]. These patients consider medication management as positive [O8][93].
Cascading effects of multimorbidity: having, experiencing, and managing multimorbidity can cause additional barriers to self-management through **antagonistic** effects, both physical and emotional	The influence of chronic disease interrelatedness	***Barrier:*** Patients with multimorbidity may find it challenging to determine which chronic disease is causing a particular symptom [O1] because chronic diseases may share similar symptoms[72] [M1], the treatment of one condition can also aggravate another condition[61,62,90,91] [M2] or cause other antagonistic effects[64,90,91] (or the fear that it might cause these effects[85]) [M3] – these are major barriers to self-management, which can lead to medication non-adherence [O2][62,91] or low self-management in other lifestyle areas [O3][91]. ***Barrier:*** The diagnosis of an additional condition to an already existing one may also impede self-management [O4] because the new information for the 2nd condition adds uncertainty about what to do[87] [M1]. ***Facilitator:*** Patients who are able to identify the main illness that was causing them the most concern [M1] and keep it stable [M2] helps keep their symptoms under control [O1] and return to an acceptable way of life within the limitations of their illness [O2][87].
	The influence of mental and emotional health on self-management	***Barrier:*** Multimorbidity management challenges are exacerbated [O1] in patients with mental and emotional health problems (low cognition[89], anxiety[90]) because the limitations of one condition may impact the ability to look after another condition [M1][87,93]. The ability to self-manage for these people are influenced by the interaction of conditions [M2], which may also contribute to a perceived increase in illness burden [O2][63]. It is a cascading effect because if illness burden prevents exercise [M3], this can cause an increase in weight [87] [M3], and reduce quality of life, relationships, and ability to work [O3], which in turn can impact mood, social networks, and self-management behaviours[62] [O4]. In patients who have large discrepancies between current and past physical and cognitive functional abilities and activities (i.e., previous energy, endurance, strength, memory, ability to concentrate) [M1] may be unable to reconcile the difference and embrace self-management [O3][87]. ***Barrier:*** Cascading effects on self-management ability are also seen in multimorbidity patients with depression. In older adults, depression may be a barrier to effective self-management [O1] or a result of previous failures with self-management[65] [O2] because they may choose not to treat depression because they consider it a normal part of aging [M1], do not want to take medications [M2], or are reluctant to seek treatment due to stigma [M3][30]. Additionally, depression can reduce patient motivation, energy and self-efficacy [M4], causing them to feel overwhelmed [M5], hopeless [M6][31] or stressed [M7][87], which in turn can reduce their ability to self-manage[30-32,59,64,87,91].

		Chronic pain[32] [C2] experienced by older adults with multimorbidity works similarly in that it can be disruptive to self-management [O3] because it can reduce motivation [M1] and cause significant emotional distress [M2]. ***Facilitator:*** Factors that influence better self-care [O1] and better experience of illness [O2] of patients with multimorbidity are learning how to manage their emotions through exercise [M1][85], spending time being outdoors [M2][85], having a change of scenery [M3][85], reframing their situation [M4][90], prioritizing certain conditions [M5][90], staying positive [M6][87], doing their best [M7][87] and to consider mindfulness-based stress reduction [M8][94].
	Lack of resources	***Barrier:*** Self-management of patients with multimorbidity [O1] is influenced by the lack of resources to manage the burden of multimorbidity[64] such as insufficient knowledge and information [M1][87,91,95], low health literacy [M2][29]; low skills to manage and coordinate care and side effects [M3][43,90]; and lack of finances [M4][62,91], social support [M5][23,62,88,89,91], or access to transportation [M6][91]. Caregivers [C] may find self-care especially difficult [O2] because of the time [M1] and finances [M2] they are already using to care for others[62]. Even if resources and programs exist to help patients self-manage multimorbidity, they may not be aware of them [M1][62]. ***Barrier:*** Self-management regimens can impede one's ability to work. Although continuing to work for those with multimorbidity may be difficult, it provides financial stability, health insurance and identity to patients[62]. ***Facilitator:*** Self-management can be improved for patients with multimorbidity [O1] if they have contact with consumer organizations or support groups [M1][26,71] and peer support [M2][31]. ***Facilitator:*** Patients are interested in self-management tools [O1] that provide health condition information [M1][51]; can share, coordinate and synthesize information with and between providers [M2]; help them access new research findings [M3], connect them with other patients [M4], help them sort health records [M5], consult with remote specialists [M6], and coordinate with local providers [M7][51]. Telehome care systems can improve patient self-management [O1] through the provision of health information [M8][47].
Provider perspective		
Communication between providers and patients		***Barrier:*** Providers (particularly specialists) [C] can themselves be a barrier to patient self-management [O1][61]. Patients may be dissatisfied with the way the provider communicates [M1][43,91], and family physicians (who are the primary contacts for patients) may fail to provide valuable information about self-management resources such as patient advocacy and self-help groups and other resources [M3][26]. ***Facilitator:*** Physicians can support patient self-management [O1] and have a positive impact on patient self-management [O2] through tailoring information-giving to the stage of the patient's condition and their adaptation to it [M1]***[26],*** through good interaction with patients [M1][93], information provision [M2][93] (including information in the patient's own language and adequate time to review it[71]), a collaborative approach to care [M3][115], encouraging active engagement in self-management [M4][71], motivating patients and providing a behavioural model [M5][31], and empowering patients by providing them with skills and confidence to manage their own conditions [M6][94].

Appendix 6

Details of Context-Mechanism-Outcome configurations to explain multimorbidity management overall

Theme	Explanations using Context [C]-Mechanism[M]-Outcome[O] configurations
Patient perspective	
Confusing for patients	***Barrier:*** Multimorbidity management in primary care [C] is confusing to patients [O2][120] due to the heterogeneous nature of multimorbidity [M1][102], disease and treatment interactions and possible conflicts [M2][57,92], and the difficulty of attributing symptoms to conditions [M3][57]. ***Facilitator:*** Supporting patient self-management is a critical aspect of multimorbidity care[37,85] and to achieve optimal health outcomes. These include medication support [30,55] [M1], motivational enhancement[62],43 [M2], and education [M3], which is a key aspect of optimal medication [O2] [29] and disease management [O3], particularly for people with arthritis and depression [C2][104]. ***Facilitator:*** A patient-centred approach, that takes into account the patient's psychosocial realities (housing, relationships, income, etc.) [M1][92] is more likely to meet the needs [O1] of complex patients with multimorbidity [C1][82,117]. Patient-centred approaches [M2] can help patients adopt healthy lifestyles [O2] if they have adequate adoption readiness [M2], and target additional behaviours once change in one behaviour is achieved [M3][120] 23. For complex patients [C1], patient-centered care may be promoted [O4] by enhanced communication [M3] although this may or may not improve disease-specific self-care and outcomes [O5][105]
Mental health needs of patients add to complexity	***Barrier:*** In primary care, mental health needs of patients [M1] in the context of multimorbidity management can be a barrier to patient self-care [O1][57], can create communication issues with providers (i.e., patient complaints may not be clear) [O2][57], are often ignored or normalized since physical health issues take precedent [O3][38], and can lead to patients receiving less intensive treatment [O4][59].
Provider perspective	
Overwhelming for providers	***Barrier:*** Multimorbidity management in primary care [C] may be overwhelming for providers [O1][56] due to the heterogeneous nature of multimorbidity [M1][102], disease and treatment interactions and possible conflicts [M2][57,92], and the difficulty of attributing symptoms to conditions [M3][57].
Not prepared for managing multimorbidity	***Barrier:*** Primary care clinicians are inadequately prepared for multimorbidity [O1] due to their lack of skills and confidence in addressing multimorbidity [M1][33], not having adequate decision support systems [M2][35] or evidence [M3][60] to support their clinical decision making, and having care protocols or intervention plans that are too rigid [M4][45]. These make it difficult for primary care physicians to simultaneously understanding patient subjective experience and biochemical processes of chronic conditions [O2][26]. ***Facilitator:*** Many general practitioners have identified the need for guidelines that address multimorbidity[75]. When only single disease guidelines are available to manage multimorbidity [C1], clinicians sometimes modify guidelines [M1] in anticipation of adverse effects[89], use common sense to complement the limitations of their application [M2][98], and work with patients to help them understand guidelines [M3] so they can make informed treatment decisions [O1][98]. Collaboration with patients is needed [M4] when the single disease guidelines being used are contradictory [C2][58]. In

		situations where few guidelines exist and there is significant clinical uncertainty [C3], shared decision making between patients and clinicians is a useful, and possibly a necessary tool [M5] for making individualized treatment decisions [O2][118]
	Multimorbidity can worsen the relationship between primary and secondary care (including care transitions)	***Barrier:*** An effective relationship between primary and secondary care (and in consequence, the transition between primary and specialist care) is difficult [O] for patients with multimorbidity because: patients are susceptible to exaggerated instructions by specialists and overly influenced by diagnostics [M1][68], specialists do not acknowledge primary care [M2][61,84], and there is often poor communication between primary and secondary care providers [M3][61,84]. This is compounded by the emphasis each specialist puts on 'their' guideline, which makes it difficult for primary care providers to coordinate care [M4][58]. The lack of cooperation between primary and secondary care [O2] also makes it difficult for patients [O3] because their needs are often episodic requiring both primary and specialist care either simultaneously or in succession [M4][36]. ***Facilitator:*** Patient-primary care physician concordance on health-related attitudes and perceptions [M1] appears to be a powerful predictor of primary care physician implementation of [O1] and patient adherence to [O2] to recommended geriatric health care[115]. This implies that specialist education regarding recommended care should be directed at both primary care physicians and their patients[109]. Additionally, trusting relationships between primary care physicians and specialists [M2] promotes collective and harmonized approaches to care [O3][45]
System perspective		
	Primary care is the optimal context to deliver multimorbidity care, but it is not designed to handle it	***Facilitator:*** Primary care may be the optimal context to deliver multimorbidity care [C] because it is accessible to most patients [M1][33], efficient [M2][33], equitable [M3][33], has reach [M4][33], has good continuity of care [M4][33,56-58], and primary care providers general know their patients well [M5][33,56,57] and they have a generalist and patient-centred approach to care [M6][56]. Relational continuity [M7] in primary care helps providers better understand patient needs [O1] and enhances multimorbidity care [O2][58]. ***Barrier:*** Primary care is not designed to handle multimorbidity [O1] because it demands extra consultation and provider time [M1][32,33,35,38,65,72,102,105]. This in turn can lead to inadequate care patients (i.e., less preventative care, psychiatric care, less care for concurrent conditions) [O2][59], inadequate time for building patient-provide relationships [O3][63], the complexities of primary care clinics requiring to schedule multiple appointments for multiple issues [O3][65], poor follow-up practices by clinicians [O4][35], and the tendency to maintain the status quo for complex patients rather than changing the management plan [O5][73]. ***Facilitator:*** Increasing consultation time for multimorbidity [M1][40,72,75,82], adjusting consultation time to complexity of illness [M2][58], and allowing for time to discuss health issues [M3][72] and build a relationship [M4][58] have all been identified as opportunities to improve multimorbidity management [O].
	Multimorbidity can lead to fragmentation of care	***Barrier:*** Multimorbidity can lead to fragmented care [O1][75,80] because it often leads to the involvement of multiple providers [M1][80], territorial specialists [M2][58] and multiple care locations [M3][92]. This complexity of care can lead to poor communication between primary and secondary care [O2][15,36,58,80,84,92], duplication of efforts [O3][92], confusion about what has been done (i.e., tests, treatments, and medications) [O4][80], treatment errors [O5][80], impaired treatment participation (i.e., lack of understanding of what is happening with a patient's care due to fragmentation, so the provider may not add to the care because they don't want to confuse things more) [O6][80]; high use of specialty services [O7][15], and lack of care coordination or the consideration of a holistic approach to care [O8][79].

		Facilitator: Health information technology tools, including integrated EMRs and telehealth solutions [M1], can help with patient care coordination [O1][46,47,58,62]. ***Facilitator:*** Clinical tools (including those that focus providers on functional, rather than disease-related outcomes) [M1][61], and those that provide multi-morbidity decision support [M2][74] and assessment [M3][89,92]) can help providers more optimally manage patients with multiple chronic conditions [O1][74] and can optimize medication management [O2][86]. ***Facilitator:*** Multimorbidity can be better managed [O] through integrating similar disease processes[73] [M1], adopting additional health conditions into existing management practices [M2][93], and highlighting links between management practices [M3][93]

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
Title			
1		In the title, identify the document as a realist synthesis or review	1
Abstract			
2		While acknowledging publication requirements and house style, abstracts should ideally contain brief details of: the study's background, review question or objectives; search strategy; methods of selection, appraisal, analysis and synthesis of sources; main results; and implications for practice	2
Introduction			
3	Rationale for review	Explain why the review is needed and what it is likely to contribute to existing understanding of the topic area	4-5
4	Objectives and focus of review	State the objective(s) of the review and/or the review question(s). Define and provide a rationale for the focus of the review	4-5
Methods			
5	Changes in the review process	Any changes made to the review process that was initially planned should be briefly described and justified	7
6	Rationale for using realist synthesis	Explain why realist synthesis was considered the most appropriate method to use	4

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
7	Scoping the literature	Describe and justify the initial process of exploratory scoping of the literature	5
8	Searching processes	While considering specific requirements of the journal or other publication outlet, state and provide a rationale for how the iterative searching was done. Provide details on all of the sources accessed for information in the review. Where searching in electronic databases has taken place, the details should include, for example, name of database, search terms, dates of coverage and date last searched. If individuals familiar with the relevant literature and/or topic area were contacted, indicate how they were identified and selected	5-6
9	Selection and appraisal of documents	Explain how judgements were made about including and excluding data from documents, and justify these	6
10	Data extraction	Describe and explain which data or information were extracted from the included documents and justify this selection	6
11	Analysis and synthesis processes	Describe the analysis and synthesis processes in detail. This section should include information on the constructs analysed and describe the analytic process	7
Results			
12	Document flow diagram	Provide details on the number of documents assessed for eligibility and included in the review, with reasons for exclusion at each stage, as well as an indication of their source of origin (e.g. from searching databases, reference lists and so on). You may consider using the example templates (which are likely to need modification to suit the data) that are provided	8; Fig 1

RAMESES Checklist

Reporting item		Description of item	Reported on page(s)
13	Document characteristics	Provide information on the characteristics of the documents included in the review	8
14	Main findings	Present the key findings with a specific focus on theory building and testing	8-11
Discussion			
15	Summary of findings	Summarise the main findings, taking into account the reviews objective(s), research question(s), focus and intended audience(s)	11-12
16	Strengths, limitations and future research directions	Discuss both the strengths of the review and its limitations. These should include (but need not be restricted to) (a) consideration of all the steps in the review process and (b) comment on the overall strength of evidence supporting the explanatory insights which emerged The limitations identified may point to areas where further work is needed	13
17	Comparison with existing literature	Where applicable, compare and contrast the reviews findings with the existing literature (e.g. other reviews) on the same topic	12-13
18	Conclusion and recommendations	List the main implications of the findings and place these in the context of other relevant literature. If appropriate, offer recommendations for policy and practice	14
19	Funding	Provide details of funding source (if any) for the review, the role played by the funder (if any) and any conflicts of interests of the reviewers	15