

# Rapid Evidence Synthesis: The burdens and management of multiple long-term conditions

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# Rapid Evidence Synthesis:

Rapid Evidence Syntheses (RES) are produced by the National Institute for Health and Care Research (NIHR) Applied Research Collaboration Greater Manchester (ARC-GM). The methods used are based on a framework set out in Norman et al. 2022 and previously registered on the Open Science Framework (OSF).<sup>1,2</sup>

RES use evidence synthesis approaches and draws on the GRADE Evidence to Decision framework<sup>3</sup> to provide rapid assessments of the existing evidence and its relevance to specific decision problems. In the first instance, they focus on evidence from existing evidence syntheses. They are undertaken in a real-time context of decision-making around adoption of innovative health technologies and are designed to provide a “good-enough” answer to inform decision problems in a short timescale. RES methods are flexible and adaptive. They have evolved in response to user feedback and differ depending on the nature of the assessment undertaken.

**RES is not intended to serve as a substitute for a full systematic review.**

We welcome feedback and are particularly interested to hear how you have used this Rapid Evidence Synthesis.

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## Additional information:

This work was undertaken by the National Institute for Health Research (NIHR) Applied Research Collaboration Greater Manchester (ARC-GM). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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<sup>1</sup> Norman, G. *Rapid evidence synthesis to support health system decision making*. OSF registration. 2020 [cited 2023]; Available from: [osf.io/hsxk5](https://osf.io/hsxk5)

<sup>2</sup> Norman, G., et al., *Rapid Evidence Synthesis To Enable Innovation And Adoption in Health and Social Care*. Systematic Reviews, 2022. **11**: p. 250. <https://doi.org/10.1186/s13643-022-02106-z>

<sup>3</sup> Alonso-Coello, P., et al., *GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction*. BMJ, 2016. **353**: p. i2016.

# 1. Summary

There is overwhelming evidence highlighting multiple long-term conditions as a key driver of higher use of health care services. However, there is **limited** evidence about their impacts on health outcomes. There is also **limited** evidence on the contribution of common mental health disorders and severe mental illness (as part of multiple long-term conditions) to poor health outcomes and use of health care services. Where available, the evidence suggests that multiple long-term conditions probably predict a decline in function. The higher the number of conditions and the greater the disease severity, the greater the functional decline. Individuals with comorbid mental health conditions – whether a common mental disorder such as depression or severe mental illness – are at a higher risk of unplanned secondary healthcare use such as hospitalisation and readmission. For those with depression, the greater the depression severity, the higher the probability of secondary health care use.

The evidence suggests that multiple long-term conditions increase total health care costs by 50% to 180% and emergency department use by 12% to 155%. It is **unclear** if multiple long-term conditions lengthen hospital stay or the time of consultations. Combinations of cancer and mental health conditions; diabetes and heart/vascular conditions; and respiratory and mental health conditions were associated with the highest annual direct healthcare costs.

There is much more evidence on clinical effectiveness than cost-effectiveness on the impact of complex interventions for managing multiple long-term conditions on various outcomes. Most clinical effectiveness evidence is of **low or moderate certainty**, thus being acceptably trustworthy. The available evidence is largely for the following three mainstream interventions used in managing multiple long-term conditions, and the evidence suggests that:

- Models of multi-professional healthcare such as care coordination strategies may reduce functional impairment, reduce depression, and improve cognitive functioning and quality of life; but the interventions may not result in additional benefits in mortality. The interventions may be cost-effective for people with the depressive disorder-diabetes cluster in the UK.
- Strategies to improve continuity of care may be beneficial in managing mental health symptoms and improving quality of care and health-related quality of life. However, it is **unclear** if these interventions could reduce use of health services.
- For the various medication management approaches reported, it is largely **unclear** whether they increase medication adherence. **Low-certainty evidence** suggests that the use of multidisciplinary interventions to manage polypharmacy in community-dwelling older adults may increase medication adherence but may not result in additional benefits on mortality, hospital admissions, emergency department or primary care visits compared with control interventions; and that medication review and deprescribing among hospitalised older people may reduce hospital re-admission risk by 8% but not reduce mortality risk.

The evidence appears to suggest that other interventions may achieve the goals that they are designed for, but it is largely **unclear** whether they achieve wider benefits. For example:

- **Low-certainty** evidence suggests that self-management results in little benefit in improving moderate-or-vigorous activity, and general health outcomes such as self-efficacy. However, it is largely **unclear** if self-management could improve other outcomes such as quality of life and mortality.
- Behaviour change interventions may reduce psychological distress such as depression, and anxiety and increase emotional well-being and health-related quality of life.
- Exercise rehabilitation may increase exercise capacity and cardiometabolic outcomes.
- Psychotherapy may reduce comorbid depression in people with chronic physical illness.

The evidence is **limited** for the clinical and cost-effectiveness of most interventions in people with multiple long-term conditions where mental health conditions are a component.

We summarise below the research evidence identified in this area. More details are in [Section 3 Results](#). The colour of Bright Green indicates moderate or high certainty evidence, with Yellow indicating low certainty evidence and Grey for very low-certainty evidence. Where no colour is used, there is no certainty of evidence assessment available.

	<b>Health outcomes</b>				<b>Health care use/ costs</b>	
Q1: Burdens of MLTCs	INCREASE: functional decline (greater decline in people with higher numbers of conditions and greater disease severity)				INCREASE: twice hospitalisation risk in older adults INCREASE: 1.07 times hospital readmission risk INCREASE: total costs by 50% to 180%, and top three clusters associated with the highest annual direct medical costs: <ul style="list-style-type: none"> <li>cancer and mental health condition clusters within the first year of cancer diagnosis,</li> <li>clusters of diabetes and heart/vascular conditions,</li> <li>clusters of respiratory and mental health conditions</li> </ul> INCREASE: hospital costs INCREASE: care transition costs INCREASE: primary care use INCREASE: dental care use by on average 156% INCREASE: emergency department use by on average of 12% to 155% UNCERTAIN: length of hospital stays UNCERTAIN: health care consultation time	
Q2: Burdens of MLTCs people with mental health conditions	NA				Depression and severe mental illness: INCREASE: risk of unplanned secondary healthcare use such as hospitalisation, and readmission <ul style="list-style-type: none"> <li>a higher risk in those with a greater severity of depression</li> </ul>	
<b>Q3 &amp; Q4: Intervention evidence</b>	<b>Physiological/ physical outcomes</b>	<b>Mental &amp; psychosocial outcomes</b>	<b>Medication-related outcomes &amp; care process outcomes</b>	<b>General health, or mortality</b>	<b>Health care use/ costs</b>	<b>Cost effectiveness</b>
<i>A range of service delivery interventions</i>						
Complex interventions that were specified e.g.,	REDUCE: glycated haemoglobin (HbA1c) REDUCE: systolic blood pressure	NA	INCREASE: care process outcomes	NA	REDUCE: healthcare use	NA

holistic patient review; organisational models of care and formal training of healthcare workers	REDUCE: total cholesterol					
Patient-level interventions	NA	INCREASE: mental outcomes and psychosocial outcomes	NA	INCREASE: general health	NA	NA
Complex interventions as a general category	NO CHANGE: physiological outcomes such as glycaemic control	INCREASE: mental health outcomes such as reducing mean depression scores for those with depression INCREASE: patient-related health behaviours	INCREASE: medication adherence INCREASE: health provider's behaviour in terms of prescribing behaviour INCREASE: quality of care	INCREASE: quality of life	NO CHANGE: health service use	
<b>Models of multi-professional healthcare</b> such as care coordination strategies	REDUCE: glycated haemoglobin (HbA1c) by 0.51 on average (depression-COPD, or cardiovascular disease-diabetes clusters)	<b>MLTCs:</b> REDUCE: depression scores by 0.41 on average (depression-COPD or cardiovascular disease-diabetes clusters)  <b>MLTCs plus mental health conditions:</b> REDUCE: comorbid depression in people with chronic physical illness	NA	<b>MLTCs:</b> NO CHANGE: mortality (depression-COPD, or cardiovascular disease-diabetes clusters)  REDUCE: functional impairment (quality of life) by 0.82 (arthritis-depression cluster) or by 3.21 (diabetes-depression cluster)  INCREASE: cognitive functioning (quality of life) by 2.44 (diabetes-depression) or by unknown amount (heart failure-COPD cluster)	INCREASE: the use of mental health services by on average of 157% (diabetes-cardiovascular disease/ depression cluster)	May be cost-effective for depressive disorder-diabetes, comorbid major depression-cancer, and depression-multiple long-term conditions clusters (UK data: £12,656 per QALY gained in England in adults with depressive disorder and diabetes)

				<b>MLTCs plus mental health conditions:</b> INCREASE: quality of life for managing comorbid depression in people with chronic physical illness		
<b>Strategies to improve continuity of care</b>						
Case management	NA	INCREASE: depression symptoms (at least one chronic medical condition and depression)	NA	NA	UNCERTAIN: health care use	NA
Care models involving primary care teams or nurse practitioner-delivered primary care	UNCERTAIN: physiological outcomes	INCREASE: mental and psychological outcomes	NA	INCREASE: quality of care, health-related quality of life UNCERTAIN: mortality	UNCERTAIN: hospitalisations, costs and resource use	NA
Transitional care models that support transitions between hospital and home	NA	NA	NA	INCREASE: quality of life INCREASE: satisfaction during discharge	REDUCE: hospital readmissions and financial costs	NA
<b>Medication management</b>						
Polypharmacy interventions as a general category	NA	NA	UNCERTAIN: inappropriate prescribing, medication adherence	UNCERTAIN: quality-of-life outcomes including health-related quality of life	UNCERTAIN: health and care resource use and expenditure	NA
The use of multidisciplinary	NO CHANGE: functional status, falls	UNCERTAIN: cognitive status	INCREASE: medication appropriateness,	NO CHANGE: mortality, patient satisfaction	REDUCE: medication costs	NA

interventions to manage polypharmacy in community-dwelling older adults			medication adherence  REDUCE: the number of medications, medication-related problems	UNCERTAIN: quality of life	NO CHANGE: hospital admissions, emergency department or primary care visits	
Use of generic management interventions	NA	NA	UNCERTAIN: medication adherence	NA	NA	NA
General practice-based pharmacists' services to optimise medicines management (medication review)	NA	NA	UNCERTAIN: medication adherence	NA	NA	In general, the benefit might outweigh costs (UK data: the cost per QALY gained varied from £11,885 to £32,466)
Deprescribing i.e. the gradual withdrawal from medications with supervision by a healthcare professional	NA	NA	UNCERTAIN: medication adherence	NO CHANGE: mortality (hospitalised older adults)	REDUCE: hospital re-admissions by 8% (hospitalised older adults)	NA
<b>Self management</b> and expert patient programmes such as trained lay navigators	<b>MLTCs:</b> INCREASE: walking per week (comorbid physical and mental health conditions)  NO CHANGE: moderate or vigorous activity (comorbid physical and mental health conditions)	NA	<b>MLTCs plus mental health conditions:</b> UNCERTAIN: self-management skills and behaviours, self-management attitudes	UNCERTAIN: mortality, health-related quality of life, self-rated health, psychological wellbeing, health distress, self-efficacy, positive and active engagement in life, disability, role activities limitations, and social role activities (multiple physical conditions)	UNCERTAIN: hospital admissions (multiple physical conditions)  REDUCE: use of emergency department (comorbid physical and mental health conditions)	NA



	<p><b>MLTCs plus mental health conditions:</b>          UNCERTAIN: biological outcomes, functional status</p>			<p><b>INCREASE:</b> health-related quality of life physical component, and patient activation (comorbid physical and mental health conditions)</p> <p><b>NO CHANGE:</b> health-related quality of life mental component, overall health-related quality of life, and self-efficacy (comorbid physical and mental health conditions)</p>		
<p><b>Interventions used to support care delivery:</b>          digital telemedicine</p>	<p><b>REDUCE:</b> systolic blood pressure (diabetes mellitus and hypertension)</p> <p><b>REDUCE:</b> HbA1c (diabetes and chronic kidney disease)</p> <p><b>REDUCE:</b> the total cholesterol (diabetes and hypertension)</p>	<p><b>MLTCs plus mental health conditions:</b>  <b>REDUCE:</b> comorbid depression in people with chronic physical illness</p>		<p><b>MLTCs:</b>          UNCERTAIN: self-perceived health status</p> <p><b>MLTCs plus mental health conditions:</b>  <b>INCREASE:</b> quality of life for managing comorbid depression in people with chronic physical illness</p>		
<p><b>Other interventions</b></p>						
<p>Interventions to involve older adults with MLTCs in decision-making about their health cares</p>	NA	NA	NA	<p>UNCERTAIN: self-rated health and patient enablement</p>	NA	NA

Behaviour change interventions targeting lifestyle behaviours	UNCERTAIN: physical activity and weight loss outcomes	REDUCE: Psychological distress outcomes (i.e., depression and anxiety)	NA	INCREASE: emotional well-being, health-related quality of life	NA	NA
Exercise rehabilitation	INCREASE: exercise capacity, and cardiometabolic outcomes	NA	NA	INCREASE: health-related quality of life	NA	NA
Co-designed health interventions	UNCERTAIN: functional status	UNCERTAIN: anxiety, depression	NA	UNCERTAIN: quality of life, self-efficacy, well-being, and mortality	UNCERTAIN: healthcare use	NA
Goal-oriented care	NA	NA	NA	UNCERTAIN: quality of life, patient satisfaction, caregiver burden	UNCERTAIN: hospital admission	NA
Psychotherapy	<b>MLTCs plus mental health conditions:</b> UNCERTAIN: somatic health-related outcomes such as glycaemic control, pain	<b>MLTCs plus mental health conditions:</b> REDUCE: comorbid depression in people with chronic physical illness		<b>MLTCs plus mental health conditions:</b> INCREASE: quality of life for managing comorbid depression in people with chronic physical illness  UNCERTAIN: mortality		

**Notes:**

- Where the phrase ‘**MLTCs plus mental health conditions**’ is noted, the evidence is for Q4 in relation to people with MLTCs including mental health conditions. Otherwise, the evidence is for Q3 regarding MLTCs in general.
- All data cited in the table are estimates as reported in the included reviews, and these data were used for illustrative purposes and their precision cannot be assured.

## 2. Methods

### 2.1 Description of the Intervention

About 14 million people in England live with multiple long-term conditions (MLTCs). These might be physical or mental conditions, or both. Caring for people with MLTCs accounts for more than half of NHS primary and secondary care costs. Delivering health care to people with MLTCs is challenging; they will often be taking multiple medicines, sometimes alongside non-pharmacological treatments. People with MLTCs frequently have a sub-optimal experience of uncoordinated and fragmented care with numerous, separate appointments with different services.

Effective service delivery models for people with MLTCs are needed to enhance patient experience of care, improve health outcomes such as health-related quality of life and functioning and reduce use of health and care services.

### 2.2 Search

We searched Medline (Ovid) for English literature in July 2024 based on the components of MLTCs, multimorbidity, cost-of-illness, health outcomes, and service delivery and management. The search strategy combined terms used in the National Institute for Health and Care Excellence (NICE) multimorbidity guidelines, and existing systematic reviews on MLTCs and multimorbidity. We also searched websites of NICE and searched the reference lists of key studies.

### 2.3 Key Questions

Q1. What does current evidence tell us about the role of combinations of MLTCs as drivers of poor health outcomes and high use of health care services in the UK?

Q2. When common mental health disorders or severe mental illness are a component of MLTCs, what is their contribution to poor health outcomes and use of health care services in the UK?

Q3. What is the evidence for clinically- and cost-effective service delivery interventions for preventing or managing MLTCs?

Q4. Are particular complex intervention components clinically- and cost-effective in preventing or managing multiple long term conditions (a) in general and (b) where conditions include mental health conditions?

### 2.4 Inclusion Criteria

#### 2.4.1 Participants

We included evidence about adults (aged 18 years old and over) who had two or more long-term conditions. We acknowledge that there is ongoing discussion but no widely agreed consensus about

the definition of MLTCs, what conditions should be included in that definition, and whether MLTCs should be described in terms of numbers of conditions or particular 'clusters'. We accepted the definitions of MLTCs given by the authors of the included studies unless the definitions diverged significantly from either physical or mental conditions often considered (see the list of often considered MLTCs in Ho and colleagues[1]). These include but are not limited to:

- physical and mental health conditions such as cardiovascular disease, diabetes hypertension, cancer, lung disease, stroke, arthritis, Parkinson's disease, dementia, common mental health disorders (e.g., anxiety and depression), and severe mental illness (e.g., schizophrenia)
- persistent conditions such as learning disability
- symptom complexes such as frailty or chronic pain
- sensory impairment such as sight or hearing loss.
- alcohol and drug misuse.

We excluded (1) studies in children and people younger than 18 years old; and (2) studies of a single long-term condition, or specific clusters of conditions instead of overall multimorbidity; (3) studies of comorbidity indexes such as the Charlson Co-morbidity Index; and (4) studies of multimorbidity with involved different mental health disorders only.

#### **2.4.2 Interventions**

Where applicable, we included studies of any service delivery intervention that aimed to (1) prevent MLTCs and/or (2) manage MLTCs to improve patient outcomes.

Interventions were broadly grouped as below[2]:

- Models of multi-professional healthcare
  - Multi-professional team working
  - Collaborative care
  - Integrated care
- Strategies to improve the continuity of care:
  - Case management
  - Provider continuity model that is to use the same care provider to facilitate regular appointments
  - Care plans
  - Interventions to improve continuity of information (including health information exchange across healthcare settings; patient held medical records; discharge planning)
  - Co-location of care services
- Medication management
- Self-management, expert patient programmes and lay navigators-led interventions
- Support for model delivery. That is, to change supporting infrastructure, such as workforce, technology, or funding/incentives for improving the organisation of care delivery.
  - Education of professionals including upskilling of primary care workforce

- Telephone management
- Funding/payment change such as incentivising care providers to change their behaviours in organising care delivery
- Primary care provider network
- A combination of any of the above

We excluded studies of pharmacological treatments, symptomatic treatment, management of health and care services for individual conditions, and palliative and end-of-life care.

In terms of the evidence about the prevention of MLTCs, we only included studies of interventions targeted at the prevention of MLTC clusters, particularly the prevention of a new long-term condition in people with one long-term condition or with existing MLTCs.

### 2.4.3 Comparators

Where applicable, we considered any comparator groups that include no intervention, care or service as usual, and alternative interventions.

### 2.4.4 Outcomes

We considered the incidence of MLTCs as the key outcome for strategies aimed at prevention.

For questions related to management strategies, we considered any health outcome, in line with the results of the NICE consultation exercise[2]. The outcomes that were considered critical included: health-related quality of life, mortality, functional outcomes (e.g., mobility, activities of daily living), patient and carer satisfaction.

For Q1 and Q2, we also considered the use of health care services such as unplanned hospital admissions or unscheduled care, admission to care facilities, length of hospital stays, number of primary care appointment, patient/carer burden, and related costs of illness.

### 2.4.5 Study design

We recognised the extensive evidence available on this topic. In the first instance we considered existing overviews of reviews for this RES. Where relevant overviews of reviews had no eligible evidence, we included systematic reviews of primary studies. We used a broad definition of systematic reviews as having a systematic search, clear inclusion criteria and critical appraisal of the included studies.

We planned to consider primary studies where needed, but we identified sufficient evidence syntheses for this RES.

In summarising the evidence identified, we followed the GRADE approach to categorising the certainty of evidence into four levels:

- **high** certainty, indicating we are confident that the research findings reflect a true effect;
- **moderate** certainty, indicating we are fairly confident that the finding reflect a true effect;

- **low** certainty, indicating we have limited confidence in the findings, and more research is likely to change them;
- **very low** certainty, indicating there are no clear findings.

We followed general GRADE criteria in assessing the certainty of evidence without performing a full GRADE assessment of the evidence.

## 3. Results

### 3.1 Results of search

We identified 3749 records from the searches. After screening, we considered the following evidence syntheses eligible for inclusion in this RES:

- six systematic reviews for Q1[3-8];
- two systematic reviews for Q2[9, 10];
- three overviews of reviews [11-13] and 21 systematic reviews for Q3[2, 14-33]; and
- one overview of reviews [13] and seven systematic reviews for Q4 [34-40].

As there were several existing evidence syntheses, we did not include primary studies in this RES. We report evidence below by intervention types and, where applicable, different outcomes. In some sections, multiple reviews were included on the same topics, but this may not mean multiple distinct bodies of primary research. Due to time limitations, we were unable to explore the overlap of evidence between different reviews.

### 3.2 The role of MLTCs as a driver of poor health outcomes and high use of health care services (Q1)

#### 3.2.1 Health outcomes

Ryan (2015) is the only systematic review on this topic [4], and it focused on the impacts of having more than two chronic medical conditions on functional decline in community-dwelling adults. [4]

This review of 28 cross-sectional and 9 cohort studies found **consistent** evidence that MLTCs predicted future functional decline, with greater decline in people with higher numbers of conditions and greater disease severity. However, it is not reported if the more conditions and greater severity have a linear or non-linear relationship with greater decline. We considered the evidence to be of **moderate certainty** as the methodological quality of the included studies was rated **good** in general. The evidence is **directly relevant** to the UK context as almost all studies were from high-income countries.

#### 3.2.2 Use of health services

Five systematic reviews report evidence of the following aspects of health service use [3, 5-8]:

- **hospitalisation in older adults.** Older adults with MLTCs had on average at least twice the hospitalisation risk and 1.07 times hospital readmission risk than those without MLTCs (**moderate certainty evidence** from one review of 21 cross-sectional and 12 cohort studies).[3] The association between MLTCs and length of hospital stay is unclear.

- **consultation time.** It is **unclear** if people with MLTCs have longer health care consultations than those without (**very low-certainty evidence** from one review of one cross-sectional study with 404 participants).[6]
- **healthcare costs and use or wider economic burdens.** Having MLTCs may be associated with a considerable economic burden (**low or moderate certainty evidence** from three reviews).[5, 7, 8] Of the three relevant reviews, only one included UK-based studies (17 studies). This review [5] suggested that MLTCs might increase total costs, hospital costs, care transition costs, primary care use, dental care use (risk increased by on average 156%), emergency department use (risk increased by on average 12% to 155% depending on the number of conditions), and hospitalisations (risk increased by 77% to 333% depending on the number of conditions) (**low to moderate certainty evidence**).[5] In terms of the costs, those with one to three conditions had 1.5 to 2.8 times the mean total cost of those without morbidities. [5] Another review reports evidence of health care-associated costs by chronic condition clusters.[7] This review suggested that people with cancer and mental health condition clusters within the first year of cancer diagnosis had the highest average annual direct medical costs (85,820 in 2021 International Dollars), followed by those with clusters of diabetes and heart/vascular condition (37,090), and those with clusters of respiratory and mental health conditions (36,840) (**low to moderate certainty evidence**). Generally, people with clusters involving hypertension were among the least expensive to manage (the costs ranging from 13,270 to 17,880 in 2021 International Dollars depending on the types of comorbidities; **low to moderate certainty evidence**).[7]

Among all the evidence above, where we considered the quality to be of **low or very low**, this was largely due to methodological limitations of the included studies and variations in the findings across studies. All the evidence is **directly relevant** to the UK context as most studies were from high-income countries.

### 3.3 The contribution of common mental health disorders and severe mental illness as part of MLTCs to poor health outcomes and use of health care services (Q2)

Two systematic reviews report evidence on this topic[9, 10], both looking at secondary care use such as hospitalisation. Of the two reviews, Cicek (2022) focused on the association between depression and unplanned secondary healthcare use among adults aged 19 years old with at least one other long-term condition in addition to **depression** (6 cross-sectional and 14 longitudinal studies).[9] The other review (50 observational studies) looked at hospital service use in <75-years adults who had **severe** mental illness managed in the community and one or more comorbid physical long-term conditions.[10]

In general, the two reviews suggested that people with mental health conditions, regardless of severe mental illness or depression, may have a higher risk of unplanned secondary healthcare use such as hospitalisation and readmission. This association increased with greater severity of depression.[9] We considered the evidence to be of **low or moderate certainty** due to the **fair or**



**good** methodological quality of the included studies. All the evidence is **directly relevant** to the UK context as most studies are from high-income countries.

### 3.4 The clinical- and cost-effectiveness of service delivery interventions for preventing or managing MLTCs (Q3)

#### 3.4.1 Service delivery interventions for preventing or managing MLTCs

We identified one overview of reviews[13] and a Cochrane Review[28] covering any service delivery interventions used in managing MLTCs.

The overview included a total of 30 systematic reviews (with 464 unique primary studies) [13]. This overview grouped interventions at four levels: patient-level interventions, provider-level interventions, organisation-level interventions, and interventions involving two or three levels. The overview presents **moderate or high-certainty evidence** favouring the use of:

- specific complex interventions for improving physiological outcomes such as glycated haemoglobin (HbA1c). Of these interventions, the effective ones included: holistic patient review with practitioner training and organisational change; digital telehealth interventions; quality improvement strategies; implementation of organisational models of care and formal training of healthcare workers.
- patient-level interventions for improving mental conditions/outcomes and psychosocial outcomes/general health.
- organisation-level and combined interventions for reducing healthcare use and improving care process outcomes.

There is **limited** evidence on the effectiveness of provider-level interventions.

The Cochrane Review, Smith (2021), included 17 RCTs evaluating a range of complex interventions for people with MLTCs. The interventions included have two predominant components: (1) a change to the organisation of care delivery, usually through case management or enhanced multidisciplinary teamwork; and (2) patient-oriented activities, for example, educational or self-management support-type interventions delivered directly to participants. Compared with other interventions, the complex interventions may result in no additional benefits in physiological outcomes such as glycaemic control, and health service use (**low or moderate certainty evidence**). The interventions may slightly improve patient-reported outcomes such as quality of life, medication adherence, and patient-related health behaviours (**low or moderate certainty evidence**). The interventions probably improve mental health outcomes, reduce mean depression scores for those with depression, and improve health provider's behaviour in terms of prescribing behaviour and quality of care (**moderate or high certainty evidence**). Cost effectiveness data were **limited**. The evidence is **directly relevant** to the UK context as most studies are from high-income countries.

As noted above, the overview and the Cochrane Review both grouped interventions at a higher level. We believe it is valuable to present more granular evidence by specific intervention types below.

### 3.4.2 Models of multi-professional healthcare

**Health outcomes.** We included one review on this topic [20], and this review included any interventions used for managing multiple high-burden chronic diseases in older adults [20]. Most interventions included were versions of ‘collaborative care’, i.e., a complex intervention with a multidisciplinary care approach, structured care plans, scheduled follow-ups, and inter-professional communication. This review (of 25 RCTs) suggests that, in patients with depression-COPD or cardiovascular disease-diabetes clusters, care-coordination strategies may improve depressive symptoms (standardised score of depression reduced by 0.41 on average) and reduce glycated haemoglobin (HbA1c) levels by on average 0.51 but not mortality (**low or moderate evidence**). In terms of quality of life outcomes, care coordination strategies may also reduce functional impairment in people with arthritis-depression (on average reduced by 0.82) or diabetes-depression (on average reduced by 3.21) clusters; improve cognitive functioning in patients with diabetes-depression (by on average 2.44) or heart failure-COPD clusters (**low or moderate evidence**).

**Costs.** Compared with controls, care coordination strategies may increase the use of mental health services in those with the diabetes-cardiovascular disease/depression cluster by on average 157% (**low or moderate evidence**).

The low or moderate certainty of the evidence above is largely due to methodological limitations and/or small sample sizes of the included studies. All evidence above is **directly relevant** to the UK context as most studies of the above reviews are from high-income countries.

### 3.4.3 Strategies to improve the continuity of care

We identified one overview [12] and four systematic reviews [14, 23-25] on this topic, and these reviews included the following interventions:

- Case management

Baker (2018) reviewed 15 RCTs of care management interventions [14]. The interventions were effective in improving depression symptoms in those with at least one chronic medical condition and depression (**low certainty evidence**). The evidence is however **inconsistent** as to whether the interventions could reduce healthcare use.

- Provider continuity models that use the same care provider to facilitate regular appointments

Three reviews summarised evidence on care models involving primary care teams or nurse practitioner-delivered primary care for people with MLTCs. [23-25] These care models are largely designed to provide comprehensive care and increase continuity and coordination of care. Key intervention components identified are: involving nurses in advanced practice, interdisciplinary team-based care, case management, supporting self-management, discharge planning/ transitional care, and activities for improving continuity of care. The three reviews **consistently** suggested that the interventions may improve the quality of care, health-related quality of life, and mental and psychological outcomes (**low certainty evidence**). The evidence is **inconclusive** for physiological outcomes and other outcomes such as hospitalisations, mortality, costs and resource use.

The low certainty of the above evidence is largely due to methodological limitations of the included studies and variations of effects between studies. All the evidence above is **directly relevant** to the UK context as most studies are from high-income countries.

- Co-location of care services

One overview (of five systematic reviews) focused on transitional care models that included elements to support transitions between hospital and home in people with MLTCs.[12] The transitional care activities aim to achieve the coordination, communication, collaboration and continuity of care in transitions, organised information and education for patients and pre-arranged structured post-discharge follow-ups. The reviews **consistently** suggest that transitional care interventions may reduce hospital readmissions and financial costs and increase patients' quality of life and satisfaction during discharge. The quality of two of the included reviews was rated by the authors of the overview (Berthelsen and colleagues) as **low**. We however cannot judge the certainty of evidence and its relevance to the UK context as such information is not available in the overview.

#### **3.4.4 Medication management**

We included one overview of reviews [11] and six systematic reviews [19, 26, 30-33] on this topic. The overview grouped specific medication management interventions in a general intervention group. The six systematic reviews presented the evidence of specific interventions that was not included in the overview. We present the evidence from both the overview and the six reviews below.

**Health outcomes.** The overview suggested **low or very low-certainty** evidence that polypharmacy interventions reduced potentially inappropriate prescribing; improved medication adherence; and reduced health and care resource usage and expenditure [11]. The evidence is **limited** and, where available, **inconsistent** about the effectiveness of polypharmacy interventions on clinical and intermediate outcomes and quality-of-life outcomes including health related quality of life. Due to the lack of information, we cannot comment on the relevance of the evidence to the UK context.

Roncal-Belzunce (2024) summarised evidence (17 RCTs) on the use of multidisciplinary interventions to manage polypharmacy in community-dwelling older adults.[26] This review suggests that multidisciplinary interventions may reduce medication costs, improve medication appropriateness, reduce the number of medications, prevent medication-related problems, and improve medication adherence (**low or moderate-certainty evidence**). However, there may be no additional benefits of using multidisciplinary interventions compared with other interventions on functional status, falls, mortality, patient satisfaction, hospital admissions, emergency department or primary care visits (**low or moderate-certainty evidence**). It is **unclear** if the interventions are effective in improving quality of life and cognitive status.

Carollo (2024) reviewed the evidence (21 RCTs and 9 non-randomised studies) on medication review and deprescribing interventions that targeted hospitalised older adults with polypharmacy.[33] This review suggests that medication review and deprescribing among hospitalised older people may reduce the frequency of hospital re-admission by 8% but may not reduce the risk of death (**low-certainty evidence**).

The evidence from the other four systematic reviews is generally **unclear** or **insufficient** about whether the following interventions could improve medication adherence:

- use of generic MLTCs management interventions in improving medication adherence in community-dwelling older people with MLTCs (two reviews, **very low certainty evidence**) [31, 32]. The specific interventions included are: self-management interventions, digital health interventions, and medication review.
- general practice-based pharmacists' services to optimise medicines management in older people with multimorbidity and polypharmacy, that is, use of medication review led by general practice-based pharmacists (one review, **very low certainty evidence**).[19]
- deprescribing i.e. the gradual withdrawal from medications with supervision by a healthcare professional (one review, **limited** RCT evidence)[30].

The uncertainties of the above evidence are due to the availability of **limited** data, or where available, the methodological limitations of the included studies. The evidence is overall **directly relevant** to the UK context as most studies were from high-income countries.

**Cost effectiveness.** Laberge (2021) reviewed 11 economic studies of interventions intended at optimising medication use in older adults with multimorbidity and polypharmacy. [22] Most interventions included a medication review with the involvement of a multidisciplinary team, with a pharmacist and a general practitioner, in the decision-making process. The evidence suggests that the interventions to optimise medication use might provide benefits that outweigh their implementation costs. Cost-utility and cost-effectiveness analyses suggested that incremental cost-effectiveness ratios were generally within the willingness-to-pay thresholds of the countries where the studies were conducted. For example, the cost-utility analysis of data from the UK suggested that the cost per QALY gained varied from £11,885 to £32,466. However, the evidence is **limited** and of **low certainty** as the included studies generally had low quality. We are **unsure** about the relevance of the evidence to the UK context as only one economic study was from the UK, although most studies were from high-income countries.

### **3.4.5 Self-management, expert patient programmes, and lay navigators-led interventions**

We only identified one systematic review on this topic, and it was conducted to inform the NICE guidance *Multimorbidity: clinical assessment and management*. [2] It is **unclear** if, compared with usual care, self-management interventions could improve the clinical outcomes of people with multiple physical conditions in mortality, hospital admissions, health-related quality of life, self-rated health, psychological wellbeing, health distress, self-efficacy, positive and active engagement in life, disability, role activities limitations, and social role activities (**very low-certainty evidence**).

In people with comorbid physical and mental health conditions, the evidence suggested that self-management may be effective in health-related quality of life physical component, change in walking per week, use of emergency department, and patient activation compared with usual care (**low or moderate-certainty evidence**). The evidence suggested no difference between self-management and usual care for health-related quality of life mental component, overall health related quality of life,

moderate or vigorous activity, and self-efficacy (**moderate or high-certainty evidence**). The evidence is **directly relevant** to the UK context as most studies were from high-income countries.

### 3.4.6 Interventions used to support care delivery

We only identified one review on this topic,[21] and it reviewed six studies (699 participants) that evaluated the effectiveness of digital telemedicine interventions in improving clinical outcomes in people with multimorbidity.[21] The review reported **moderate-certainty evidence** that digital interventions reduced systolic blood pressure in people with diabetes mellitus and hypertension; HbA1c in people with diabetes and chronic kidney disease as indicator diseases; and the total cholesterol in people with diabetes and hypertension. The evidence is **unclear** for self-perceived health status (**low certainty evidence**). The evidence is **directly relevant** to the UK context as all studies are from high-income countries.

### 3.4.7 Other interventions

Five reviews report evidence on the following interventions that are not grouped into the above categories. All evidence below is **directly relevant** to the UK context as most studies are from high-income countries.

- interventions to involve older adults with MLTCs in decision-making about their care

Butterworth (2019) presented a Cochrane Review of three RCTs (1879 participants) on this topic.[18] The components of the included interventions were: patient workshop and individual coaching using behaviour change techniques; individual patient coaching utilising cognitive-behavioural therapy and motivational interviewing; and holistic patient review, multi-disciplinary practitioner training, and organisational change. It is **unclear** whether the included interventions are effective in self-rated health and patient enablement (**very low-certainty evidence**).[18]

- behaviour change interventions targeting lifestyle behaviours

Two recent reviews report the relevant evidence,[17, 27] and they generally suggested that behaviour change interventions may be effective in improving emotional well-being and health-related quality of life and reducing psychological distress outcomes (i.e., depression and anxiety) in people with MLTCs (**low certainty evidence**). Large reductions in psychological distress outcomes were reported for interventions targeting those with physical and mental health conditions, and those with cognitive and/or behavioural activation approaches. It is unclear if the interventions are effective in physical activity and weight loss outcomes (**very low-certainty evidence**).

- exercise rehabilitation

A review of 38 RCTs and non-randomised studies reports evidence on this topic.[16] The review suggested that exercise rehabilitation may improve exercise capacity, health-related quality of life, and cardiometabolic outcomes in people with MLTCs.[16] The evidence is of **low certainty** due to some methodological limitations in the included studies and the inconsistency of results as reported across individual studies.

- co-designed health interventions

Evidence from a systematic review of co-designed health interventions for people living with MLTCs was **unclear** if the interventions could improve quality of life, self-efficacy, well-being, anxiety, depression, functional status, healthcare use and mortality.[29] The evidence is of **very low certainty** due to methodological limitations and small sample sizes of the included studies.

- goal-oriented care

Barbato (2022) included goal-oriented care[15], an approach of engaging patients, establishing personal goals, and setting targets for patients and clinicians to plan a course of action, with the goal achieved via collaboration among professionals and patients. The evidence is of **very low certainty** for hospital admission and quality of life and **low certainty** for patient satisfaction and caregiver burden, meaning that it is **unclear** about the impact of using goal-oriented care on these outcomes.

### 3.5 The clinical- and cost-effectiveness of service delivery interventions for preventing or managing MLTCs including mental health conditions (Q4)

#### 3.5.1 The clinical effectiveness of service delivery interventions for preventing or managing MLTCs including mental health conditions

Six systematic reviews report evidence of clinical effectiveness of interventions for managing MLTCs in people with comorbid mental health conditions [35-40].

These reviews suggest that **collaborative care** interventions,[36, 38] **psychotherapy**,[37, 39], and **web-based interventions** [35] may be effective in reducing depression and/or improving quality of life for managing comorbid depression in people with chronic physical illness. The evidence is of **low or moderate-certainty** largely due to methodological limitations and/or small sample sizes of the included studies.

The evidence is **limited** for use of **psychotherapy** in managing somatic health-related outcomes (i.e. glycaemic control, pain), or mortality. [37, 39] For adults with severe mental illness and general medical comorbidity, it is **unclear** if integrated general medical and psychiatric self-management interventions are effective in improving self-management skills and behaviours, self-management attitudes, biological outcomes, service use, and functional status (**very low-certainty evidence**) [40]

All the evidence above is **directly relevant** to the UK context as most studies are from high-income countries.

Kappelin (2022) also analysed the components of collaborative care interventions included for managing comorbid depression in people with chronic conditions. The components identified are:

- a stepped care model, involving medication and psychotherapy delivered by a nurse or psychologist care manager focusing on problem-solving techniques;

- follow-up including monitoring of symptoms and function, and relapse prevention strategies;
- and scheduled care manager supervision.

### **3.5.2 The cost effectiveness of service delivery interventions for preventing or managing MLTCs with mental health conditions**

One systematic review reports on economic evaluations [34]. With a total of 19 studies, the review identified four types of interventions: collaborative care, self-management, telephone-based and antidepressant treatment. Most interventions were suggested to be potentially cost-effective, particularly, the collaborative care for people with depressive disorder and diabetes, those with comorbid major depression and cancer, and those with depression and MLTCs. For example, collaborative care programmes cost £206 per quality-adjusted life year (QALY) gained in the USA in older adults with diabetes and depression at primary care clinics, and the intervention cost £12,656 per QALY gained in England in adults with depressive disorder and diabetes. The cost is within the decision threshold of £20 000 per QALY gained. We considered the evidence to be of **low certainty** as, in most of the evidence syntheses reported, Banstola and colleagues rated half of the included economic analyses to have **serious limitations**. The evidence is **directly relevant** to the UK context as all included studies are from high-income countries.

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