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Review article

# Outcome measures for health interventions targeting multimorbid older adults: A systematic review

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## ABSTRACT

*Background:* Older adults with multimorbidity are often excluded from clinical trials. Traditional disease-centered endpoints may be inadequate for this population, presenting unique challenges related to frailty, functional decline and disability.

*Objectives:* To systematically review the literature on outcomes considered relevant in interventions targeting older adults with multimorbidity, based on both patient and healthcare professionals' perspectives.

*Methods:* This systematic review followed PRISMA 2020 guidelines and was registered in PROSPERO (CRD42023478249). We searched five electronic databases for primary quantitative and qualitative studies including patients aged $\geq 60$ years with $\geq 2$ chronic conditions. Outcomes were categorized into six domains: 1) Physical conditions/outcomes; 2) Mental conditions/outcomes; 3) Psychosocial outcomes/general health; 4) Healthcare utilization and costs; 5) Patients' behaviors; 6) Care process outcomes. We conducted a narrative synthesis and compared outcomes across qualitative and quantitative studies.

*Results:* Seventy-one studies were included (53 quantitative, 16 qualitative, 2 mixed-methods). The most frequently reported outcomes fell under Psychosocial outcomes / General health (69.0 %), followed by Care process outcomes (52.1 %) and Healthcare utilization and costs (49.3 %). Qualitative studies more often addressed Mental health outcomes (43.8 %). Maintaining independence, physical function, and quality of life emerged as most important outcomes for older adults.

*Conclusions:* In intervention studies involving older adults with multimorbidity, outcomes should move beyond disease-specific measures to include independence, physical function and quality of life. Outcome selection should account for patient clinical heterogeneity, frailty, and life expectancy to ensure relevance and impact in this complex population.

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## 1. Introduction

Multimorbidity, defined as the co-occurrence of two or more chronic conditions (van den Akker et al., 1996), is common and increasingly prevalent, with significant implications for health-care systems worldwide (Navickas et al., 2016). A recent systematic review and meta-analysis evaluating data from 126 peer-reviewed studies, encompassing nearly 15.4 million individuals (weighted mean age of about 57 years), reported a global multimorbidity prevalence of 37.2 % (95 % CI = 34.9–39.4 %), rising to 51.0 % (95 % CI, 44.1–58.0 %) among adults aged over 60 (Chowdhury et al., 2023). Other studies reported a prevalence of multimorbidity in people over 65 as high as 93 % (Nicholson et al., 2024) or 95 % (Violan et al., 2014). Older adults with multimorbidity have a 44 % higher mortality risk than those without multimorbidity (Nunes et al., 2016). Moreover, multimorbidity has been associated with polypharmacy (Menditto et al., 2019; Zhao et al., 2023), more frequent hospital admissions, longer hospital stays and higher healthcare costs (Vogeli et al., 2007), disability and functional decline (Marengoni et al., 2011), with a poor health-related quality of life (Fortin et al., 2004; Kanesarajah et al., 2018; Makovski et al., 2019). Multimorbidity has also a significant impact on health-care costs (Vogeli et al., 2007).

The management of older adults with multimorbidity is difficult for physicians (Kimura et al., 2024; Mc Namara et al., 2017) since scientific evidence is limited, being those individuals often excluded from randomized clinical trials (Cherubini et al., 2024; Crome et al., 2014). Clinical guidelines are usually focused on single diseases and provide recommendations that often do not consider the coexistence of multiple chronic diseases in the same patient. Indeed, applying disease-specific recommendations to multimorbid adults may be difficult or even counterproductive (Hughes et al., 2013; Muth et al., 2019).

Furthermore, multimorbid patients are often cared by different healthcare providers and services without coordination, while they would be more likely to need a highly integrated healthcare system (Vogeli et al., 2007).

One of the most challenging issues is how to select clinically important outcomes related to interventions in these complex patients. While traditional outcomes, e.g. blood pressure levels, acute worsening of a chronic condition or hospitalization, are disease centered, they do not work well for older adults with multimorbidity (Reuben and Tinetti, 2012).

Indeed, older multimorbid adults are extremely heterogeneous, having various degrees of clinical complexity, frailty, functional and cognitive decline, disability as well as socio-economic issues. Therefore, it is important to identify which outcomes are relevant for multimorbid older adults.

The aim of this study is to perform a systematic review of the literature concerning outcomes that should be investigated in interventions targeting older multimorbid adults, based on both expert and patient perspectives.

## 2. Methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021a, 2021b). The study protocol was registered on PROSPERO (www.crd.york.ac.uk/prospero), with the registration number CRD42023478249. The review question investigated in this systematic review is: What are the opinions and preferences of both experts and older multimorbid adults in terms of health outcomes resulting from an intervention?

### 2.1. *Eligibility criteria*

Eligibility criteria were defined according to the PICOS framework (Population, Intervention, Comparator, Outcomes, and Study design) and are detailed in the following sections.

#### 2.1.1. *Population*

We included all types of primary studies, both quantitative and qualitative, including older adults (age $\geq$ 60 years) living with two or more chronic conditions that currently cannot be cured but can be controlled through medications or other treatments. We also included studies where most patients ($\geq$ 70 %) had $\geq$60 years and multimorbidity, and studies that reported separate analyses in a subgroup of multimorbid participants who are $\geq$60 years old. We excluded studies that considered comorbidity, i.e. the burden of illness co-existing with a specific disease of interest, instead of multimorbidity as defined above, and studies focusing on end-of-life care. Although comorbidity and multimorbidity are related concepts, comorbidity refers to additional diseases co-occurring with a specific index disease, while multimorbidity considers all chronic conditions equally. As our review focused on outcomes relevant to overall health and functioning rather than disease-specific outcomes, we excluded comorbidity-focused studies.

#### 2.1.2. *Interventions and comparators*

We included studies considering any type of intervention and comparator, because we were interested in the outcomes deemed important by patients and/or healthcare providers, regardless of the treatment they received.

#### 2.1.3. *Outcomes*

We sought to identify outcome measures that were considered relevant to their own health by multimorbid older adults or considered relevant by clinicians and researchers to measure the effects of an intervention in older multimorbid adults.

#### 2.1.4. *Context*

We considered studies conducted worldwide in primary, secondary or tertiary care settings.

#### 2.1.5. *Type of studies*

We included all types of primary studies, both quantitative and qualitative. Quantitative studies comprised randomized controlled trials (RCTs), non-randomized controlled studies, cohort studies, cross-sectional studies, case–control studies, before–after studies, and case series. Qualitative studies included those using interviews, focus groups, observations, or other qualitative methodology to explore experiences, preferences, and perceptions. We also included mixed-methods studies combining both quantitative and qualitative approaches.

Quantitative studies were included to capture the outcome measures assessed when evaluating the effectiveness of interventions for multimorbid older adults, particularly in RCTs. Qualitative studies were included to identify outcomes perceived as important by older adults, caregivers, and healthcare professionals, providing insights into the value and relevance of outcomes beyond what is typically measured in trials. Mixed-methods studies contributed to both perspectives.

We excluded review articles, study protocols, editorials, letters, comments, case reports, conference proceedings, and books.

#### 2.1.6. *Language*

We considered only studies written in English.

### 2.2. *Information sources*

We performed searches in the following databases: PubMed, Embase, Scopus, Web of Science, and CINAHL. We also screened the reference lists of included studies to find additional articles fulfilling our inclusion criteria.

### 2.3. Search strategy

The full search strategy for all databases is reported in Supplementary Table 1. The original search was conducted on 05/07/2023 and an updated search was conducted on 08/11/2024.

### 2.4. Selection process

We used Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org.), a web-based collaboration software platform that streamlines the production of systematic and other literature reviews, to manage search results, remove duplicates, and screen titles, abstracts, and full-text articles. Couples of reviewers independently screened titles and abstracts, and full texts of potentially eligible studies. Disagreements were resolved through consultation with a third reviewer. Reasons for article exclusion after full-text reading were documented and resumed in the PRISMA 2020 flow diagram (Fig. 1).

### 2.5. Data collection process

A data extraction form was developed, pilot tested on the first five included articles and then refined. After finalizing the data extraction form, one reviewer performed the initial data extraction for all included studies and a second reviewer checked all extracted data. Disagreements were solved through consensus or involving a third reviewer.

### 2.6. Data items

The following information was extracted by the included studies: study identifier (first author last name and publication year), study design, country in which the study was conducted, setting (e.g., primary,

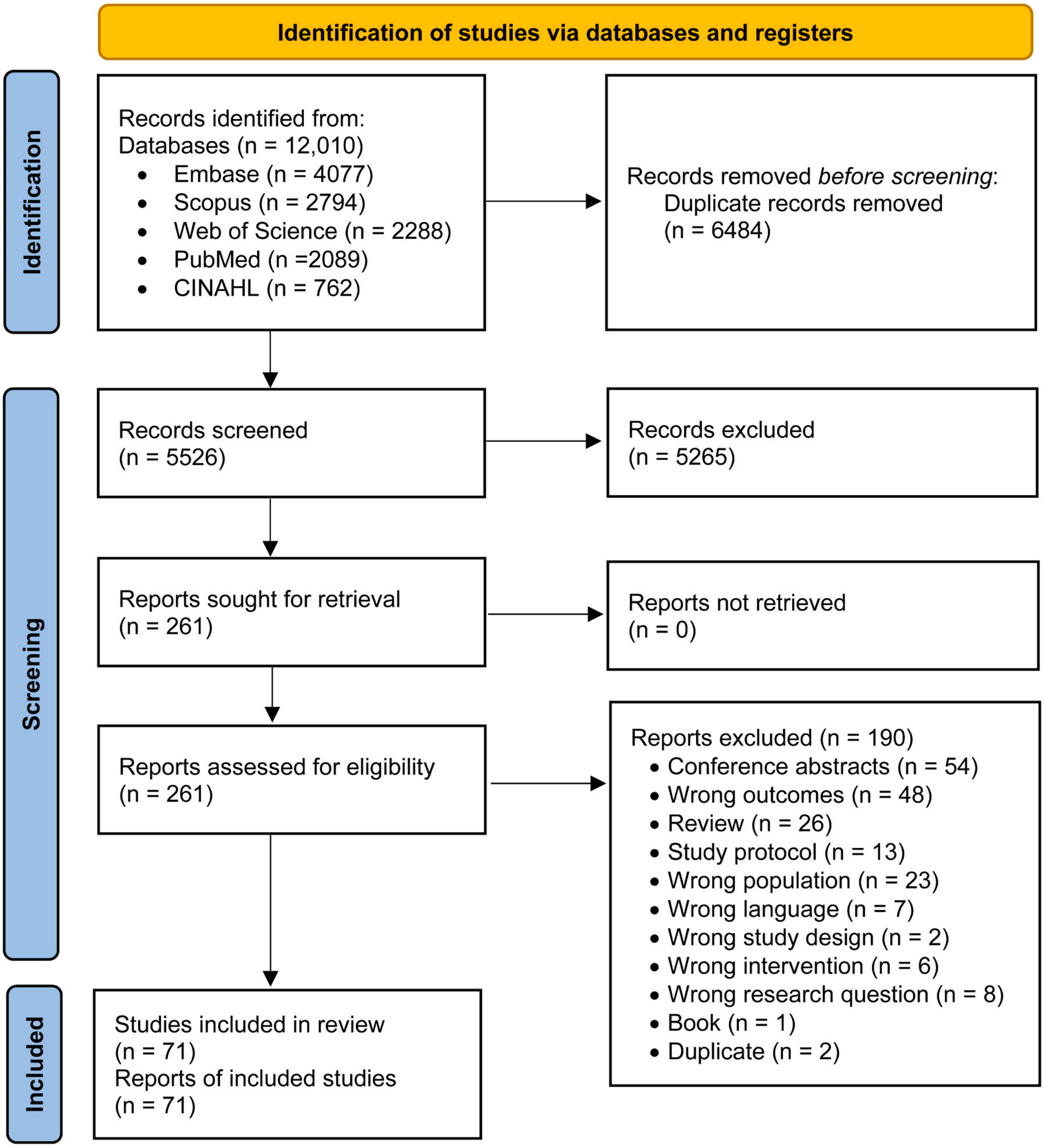

**Fig. 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.** Source: Page MJ, et al# BMJ 2021;372:n71. doi: 10.1136/bmj.n71. This work is licensed under CC BY 4.0. To view a copy of this license, visit https://creativecommons.org/licenses/by/4.0/.

secondary, or tertiary), study population (number of participants, age, sex), study aim as stated in the papers, definition of multimorbidity, and outcome measures investigated.

### 2.7. Study risk of bias assessment

The methodological quality of included studies was assessed using the following tools: the revised Cochrane risk of bias tool (RoB 2) for randomized clinical trials (Sterne et al., 2019); the Methodological Index for NOn-Randomized Studies (MINORS) for non-randomized studies, both comparative and non-comparative (Slim et al., 2003); the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for analytical cross-sectional studies (Moola et al., 2020); the CASP Qualitative Studies Checklist for qualitative research (Critical Appraisal Skills Programme, 2024). Quality assessment was conducted independently by couples of reviewers. Any disagreements were resolved by a third review author.

### 2.8. Synthesis methods

Considering the nature of our review question, data from the quantitative and qualitative studies were synthesized using a narrative synthesis approach.

The outcomes considered in the included studies were categorized in the following groups, as proposed by Zhou et al. (2023): 1) physical conditions/outcomes, 2) mental conditions/outcomes, 3) psychosocial outcomes/general health, 4) healthcare utilization and costs, 5) patients' behaviors, and 6) care process outcomes.

To assess whether there were statistically significant differences between the expected and observed values for the types of outcomes investigated in quantitative and qualitative studies, both Pearson's chi-squared test and Fisher's exact test were applied. In addition, we explored which outcome categories were most frequently considered as primary outcomes among quantitative studies that clearly defined at least one primary outcome.

### 2.9. Reporting bias assessment

Considering the nature of our review question, the assessment of reporting bias was considered not applicable.

### 2.10. Certainty assessment

Considering the nature of our review question, the certainty assessment using methods such as the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (Balshem et al., 2011) was considered not applicable.

## 3. Results

### 3.1. Study selection

We found 12,010 records in databases searching. After removing duplicates, we screened 5526 records, from which we reviewed 261 full-text documents, and finally included 71 papers. We also screened the reference lists of included studies, but we did not find additional articles fulfilling our inclusion criteria. The literature selection process is depicted in Fig. 1 (PRISMA 2020 flow diagram).

### 3.2. Study characteristics

Among the 71 included studies, there were 53 quantitative studies, 16 qualitative studies, and two mixed-method studies (Junius-Walker et al., 2012; Rijken et al., 2021). It is worth noting that two studies (Steele Gray et al., 2021; Stewart et al., 2021) were described by the authors as mixed-methods, but were classified as quantitative in this review, since their design, analysis, and primary objectives were primarily quantitative. Quantitative studies, included: 24 randomized controlled trials (RCTs) (Boult et al., 2011; Carballeira et al., 2021; Chow and Wong, 2014; Fisher et al., 2020; Ford et al., 2019; Garvey et al., 2015; Gonzalez-Ortega et al., 2017; Hall et al., 2010; Khunti et al., 2021; Kirwan et al., 2022; Lanzeta et al., 2016; Lee et al., 2024; Martin et al., 2012; Mazya et al., 2019; McCarthy et al., 2022; O'Mahony et al., 2020; O'Toole et al., 2021; Park and Chang, 2014; Read et al., 2020; Reed et al., 2018; Salisbury et al., 2018; Steele Gray et al., 2021; Stewart et al., 2021; Yang et al., 2022), 21 observational studies (de Gans et al., 2023; Freytag et al., 2020; Fried et al., 2011a, 2011b; García-Fernández et al., 2014; Islam et al., 2021; Kogan et al., 2013; Lo et al., 2024; Melchiorre et al., 2018; Mofina et al., 2024; Moye et al., 2022; Ng et al., 2023; Ong et al., 2017; Rozsnyai et al., 2020; Sommers et al., 2000; Soto-Gordoa et al., 2019; Tent et al., 2023; Valdivieso et al., 2018; van Summeren et al., 2016; Varela et al., 2023; Zamorano et al., 2022), three controlled clinical trials (Berntsen et al., 2019; Dorr et al., 2008; Steinman et al., 2018), three quasi-experimental studies (Low et al., 2015; Mateo-Abad et al., 2020; Shah et al., 2019), one development and testing study (Lang et al., 2022), and one discrete choice experiment study (Hoedemakers et al., 2022). Qualitative studies, included: 13 qualitative studies (Caughey et al., 2017; DiNapoli et al., 2016; Fried et al., 2008; Kuluski et al., 2013, 2019; Leijten et al., 2018; Lim et al., 2017; Llop-Medina et al., 2022; Löffler et al., 2012; Spiers et al., 2023; Vermunt et al., 2018; Visser et al., 2024; Wyman et al., 2020), two observational studies (Schäfer et al., 2023; Tisminetzky et al., 2017), and one development and testing study (Eidam et al., 2022).

The included studies were conducted in Europe (n = 37), North America (n = 19), Asia (n = 9), Oceania (n = 3), South America (n = 2), and North America/Oceania (n = 1). The sample size of the quantitative studies ranged from 15 to 16,603 patients, while that of the qualitative studies ranged from 12 to 130 participants, mainly focused on patients' opinions. Two qualitative studies (Caughey et al., 2017; Schäfer et al., 2023) included both general practitioners and patients; two studies (Lim et al., 2017; Wyman et al., 2020) included patients and their caregivers; one study (Llop-Medina et al., 2022) involved patients, caregivers, and healthcare professionals; another study (Vermunt et al., 2018) included general practitioners and geriatricians; and one study (Visser et al., 2024) involved nursing home physicians and pharmacists. Key characteristics of included studies are reported in Supplementary Table 2.

### 3.3. Risk of bias in studies

The overall risk of bias assessment for each included study is summarized in Supplementary Table 3. Among the RCTs, one was judged having a low risk of bias, 12 with some concerns, and 11 with a high risk of bias. Among the non-randomized studies, eight studies fulfilled $\geq 80$ % of the checklist items, 17 studies $\geq 60$ % and $< 80$ % of the checklist items, and nine studies fulfilled $< 60$ % of the checklist items. Among the qualitative studies, 9 studies fulfilled $\geq 80$ % of the checklist items, while 4 studies $\geq 60$ % and $< 80$ % of the checklist items.

### 3.4. Results

Table 1 provides an overview of the outcomes identified in both the quantitative and qualitative included studies, which were grouped into six domains. These domains reflect the multidimensional nature of care and outcomes relevant to older adults with multimorbidity, encompassing clinical, functional, psychological, behavioral, and care delivery aspects.

The first domain, i.e. Physical Conditions/Outcomes, includes traditional clinical endpoints such as disease prevention, stabilization, symptom management, and mortality. It also comprises physiological and biological measurements (e.g., blood pressure, lipid profiles, HbA1c), as well as indicators of frailty, disability, and comorbidity, key factors in the assessment of older adults.

**Table 1**

Brief description of the main outcomes for each category.

| **1) Physical conditions/outcomes: including physical conditions/diseases and related biomarkers, symptoms and mortality.** | **2) Mental conditions/outcomes: including mental conditions/diseases and their symptoms and severity.** |
|---|---|
| 1. **Disease prevention, stabilization and monitoring**:<br>Prevention of disease onset or prevention of worsening of existing disease; stabilization of chronic conditions; achievement of disease-specific or symptom-specific treatment goals; clinical effectiveness.<br>2. **Symptom management and relief**:<br>Management of symptoms; alleviating complaints; symptom burden; disease-specific measures.<br>3. **Mortality and life extension**:<br>Mortality; extending life; staying alive.<br>4. **Physical and biological measurements**:<br>Body composition changes; hemodynamic changes; laboratory biomarkers (e.g., lipid profile, kidney function, glycated hemoglobin [HbA1c]).<br>5. **Physical conditions**:<br>Frailty; physical conditions; sensory impairments (e.g., vision, hearing); pressure ulcers risk; comorbidity index. | 1. **Mental health status and disorders**:<br>Mental illness; presence or absence of a depressive disorder; anxiety; mental slowing / fogginess / behavior change; symptom severity and psychological well-being.<br>2. **Treatment and clinical effectiveness**:<br>Preferences for mental health treatment; clinical effectiveness. |
| **3) Psychosocial outcomes/general health: including physical function, well-being, social activity, and general health status (e.g., 36-item Short-Form [SF−36] score).** | **4) Healthcare utilization and costs: including visits to health providers, hospital, and emergency department (ED) admissions, and costs of healthcare.** |
| 1. **Quality of life and general well-being**:<br>Quality of life (QoL); general well-being (physical, psychological, social); health-related quality of life (HRQoL); satisfaction with life; quality-adjusted life years (QALYs); pain (reduction/elimination of pain).<br>2. **Physical functioning and independence**:<br>Functional status and performance; improvement of gait instability and fear of falling; self-rated health; maintaining independence; disability.<br>3. **Cognitive and psychological functioning**:<br>Cognitive functioning; cognitive impairment; psychological well-being.<br>4. **Social relationships and participation**:<br>Preservation of social functioning; having satisfying and effective relationships.<br>5. **Emotional well-being and support**:<br>Feeling heard, appreciated, and comfortable; feeling safe; principles and aspirations. | 1. **Hospital and facilities admissions**:<br>Hospital admissions and readmissions, emergency department (ED) visits and urgent care utilization, facilities admissions, and length of stay.<br>2. **Primary and secondary care utilization**:<br>Primary care visits; specialist visits; primary care service use; radiological procedures; home care visits.<br>3. **Economic and cost analysis**:<br>Cost-effectiveness; cost-efficiency; economic cost analysis; resource utilization and costs. |
| **5) Patients' behaviors: physical activity, diet habits, medication adherence, and other objective behaviors of patients.** | **6) Care process outcomes: including behaviors of healthcare providers, and perceptions of healthcare providers, caregivers, and patients.** |
| 1. **Physical activity and lifestyle**:<br>Physical activity; frequency of activity participation; activities: pursuits, things people do for work or leisure.<br>2. **Health behaviors and self-management**:<br>Health behaviors (i.e. smoking habits, exercise); self-management activities and support; self-efficacy; behavior and psychological changes. | 1. **Medication management and deprescribing**:<br>Medication added, avoided or stopped; number of changes to the medication regimen; deprescribing.<br>2. **Treatment burden**:<br>Treatment burden; adverse drug reactions (ADR); drug-related problems (DRP).<br>3. **Access to care**:<br>Access to care; early prevention; care planning and clinical management; integration of care; management of care; quality of care.<br>4. **Patient and caregiver experience, and patient-centered care**:<br>Patient satisfaction with care and care continuity; palliative care needs; support for both the patient and their caregiver; caregiver burden; patient-centered care; coordination of care.<br>5. **Professional training and care process improvement**. |

The second domain, i.e. Mental Conditions/Outcomes, includes the presence and severity of mental health disorders such as depression, anxiety, and behavioral or cognitive changes. Outcomes in this domain also include psychological well-being and preferences related to mental health treatments.

The third domain, i.e. Psychosocial Outcomes/General Health, is particularly well-represented in the literature. It includes quality of life (QoL), physical functioning, independence, pain, and emotional well-being, along with social participation, cognitive functioning, and self-rated health. These outcomes reflect aspects of life that are especially valued by older adults, such as maintaining autonomy, feeling safe and supported, and engaging in meaningful social relationships.

The fourth domain, i.e. Healthcare Utilization and Costs, encompasses outcomes related to the use of health services—such as hospital admissions, emergency department visits, outpatient consultations, and home care—and associated healthcare costs. Some studies also evaluated cost-effectiveness and economic implications of interventions.

The fifth domain, i.e. Patient Behaviors, includes physical activity, lifestyle habits (e.g., smoking, diet), adherence to treatment plans, self-management capabilities, and changes in behavior or health-related routines. These outcomes are closely linked to health maintenance and long-term disease control.

Finally, the sixth domain, i.e. Care Process Outcomes, reflects the structure, coordination, and perceived quality of care. This includes aspects such as medication management, treatment burden, care accessibility, patient and caregiver experiences, and the degree of patient-centeredness in care delivery. Additionally, outcomes related to professional training and care improvement strategies were also included in this category.

Together, these domains offer a detailed picture of the diverse outcome measures used in studies involving older adults with multimorbidity.

In Table 2, for each outcome category we reported the numbers and percentages of studies including outcomes that fell into that specific category. The most frequently studied outcomes were Psychosocial outcomes / General health (69.0 %), outcomes related to the Process of care (52.1 %) and Healthcare utilization and costs (49.3 %). We found significant differences between quantitative and qualitative studies (Pearson's chi-squared 15.7, $p = 0.008$; Fisher's exact test, $p = 0.001$). The outcome categories showing the greatest differences between

**Table 2**
Outcome category prevalence in qualitative and quantitative research.

| Outcome category | Total studies, N (%) | Quantitative studies, N (%) | Qualitative studies, N (%) |
|---|---|---|---|
| 1) Physical conditions/ outcomes | 28 (39.4) | 20 (37.7) | 7 (43.8) |
| 2) Mental conditions/ outcomes | 18 (25.4) | 10 (18.9) | 7 (43.8) |
| 3) Psychosocial outcomes/general health | 49 (69.0) | 36 (67.9) | 12 (75.0) |
| 4) Healthcare utilization and costs | 35 (49.3) | 34 (64.2) | 0 (0.0) |
| 5) Patients' behaviors | 19 (26.8) | 12 (22.6) | 4 (25.0) |
| 6) Care process outcomes | 37 (52.1) | 23 (43.4) | 12 (75.0) |

Percentages are column-wise proportions (Total studies: N = 71; Quantitative studies: N = 53; Qualitative studies: N = 16). In the Total studies column, we also included the two mixed-methods studies; however, these were not considered in the statistical comparison between quantitative and qualitative studies.

groups were #4 "Healthcare utilization and costs" (chi-squared contribution = 10.6), #2 "Mental conditions/outcomes" (chi-squared contribution = 2.9), and #6 "Care process outcomes" (chi-squared contribution = 2.2).

Additional analyses on primary outcomes are reported in Supplementary Tables 4a and 4b. Twenty-two quantitative studies clearly defined at least one primary outcome. As shown in Supplementary Table 4b, the two most frequently reported primary outcome categories were Psychosocial outcomes/general health and Healthcare utilization and costs.

## 4. Discussion

### *4.1. General interpretation of the results in the context of other evidence*

Findings from this systematic review found that, based on the analysis of both qualitative and quantitative data, outcomes other than disease-centered measures are relevant in research involving older adults with multi morbidity.

In particular, more than two-thirds of the included studies reported at least one outcome related to the "Psychosocial outcomes/General health" category. This category primarily includes outcomes related to physical function and quality of life (Table 1), marking a clear departure from traditional disease-specific outcomes, such as blood pressure or glycaemia levels, commonly used in clinical trials.

Maintaining independence has been found to be the most important domain for the majority of older adults in the literature, with physical function consistently identified as the highest priority (Strout et al., 2018). Independence and quality of life are key issues for older adults, as they strongly influence well-being and the ability to participate meaningfully in daily life, to maintain social connections, to live according to personal desires, to remain in their homes, and to enjoy life (Strout et al., 2018; Wiles et al., 2012). When asked to prioritize the outcomes they valued most, older adults overwhelmingly chose maintaining independence. Even in the minority of cases where survival was prioritized, independence remained a very close second choice (Fried et al., 2011b).

This aspect is particularly relevant in the context of multimorbidity, where treatments can sometimes lead to adverse effects or interact negatively, producing unintended negative events that can be considered competing outcomes.

In the 2008 study by Fried et al. (2008), the authors used qualitative focus groups with purposefully sampled participants to explore this issue. Participants were informed that some disease-specific treatments might conflict with each other or exacerbate other conditions, leading to undesirable side effects, that could be classified as competing outcomes. Once this concept was well understood, many participants shifted their preferences away from traditional disease-specific goals (e.g., blood pressure control or cardiovascular risk reduction) toward broader, cross-disease outcomes more aligned with quality of life, such as maintenance of functional independence or pain control. This led the authors to conclude that the process of prioritizing outcomes rather than discussing the pros and cons of different, even complex, therapeutic strategies would be the best strategy to use in the management of older adults with multimorbidity, as it is more understandable for the patients, and it can be applied to treatments that are also very different from each other.

"Care process outcomes" is the second most common category found in our study. This is a heterogenous category, including outcomes related to the perceptions of health care providers, caregivers, and patients regarding health care processes as well as outcomes related to polypharmacy and treatment burden, conditions strictly linked to multimorbidity. Managing multiple chronic conditions according to disease-specific guidelines can be particularly difficult in older adults, often requiring numerous medications, frequent visits to different specialists, and substantial time and energy spent on health-related activities. These demands can significantly impair daily life and overall well-being (Buffel du Vaure et al., 2016; Dobler et al., 2018). Polypharmacy, in particular, is associated with an increased risk of adverse drug reactions, e.g. falls, and cognitive impairment in older adults, which can negatively affect patient's independence (Davies et al., 2022). Moreover, caregiver burden, also included in the "Care process outcomes" category, represents a critical outcome. As highlighted by García-Fernández et al. (2014), high caregiver strain may contribute to increased dependency and hospital readmissions in patients with multimorbidity.

The third most frequently represented outcome category was "Healthcare utilization and costs", examined in approximately half of the studies. This is an issue of growing concern for healthcare systems worldwide, especially in the context of an aging population. There is a clear relationship between multimorbidity and increased healthcare resource utilization (Skou et al., 2022). Multimorbidity accounts for 78 % of all consultations in primary care, higher specialist consultation rates and less continuity of care (Salisbury et al., 2011). Hospital admissions are also more frequent, with longer hospital stays, and an almost exponential relationship between the number of chronic conditions and their associated costs because of increased healthcare utilization (Frølich et al., 2019; Skou et al., 2022; Vogeli et al., 2007). Moreover, hospitalization often results in functional decline for older adults, further complicating the clinical conditions of older adults being highly relevant in geriatric care (Brown et al., 2004).

Although less represented in general (25.4 %), the category "Mental conditions/outcomes" is however well represented in qualitative studies (43.8 %), that mainly represent the older adults' view. This category includes a whole series of outcomes regarding depression associated with multimorbidity, a condition that certainly has a great impact on the quality of life of the older adult with multimorbidity (Sieber et al., 2023).

Our review showed a partial misalignment between the outcomes valued by older adults, caregivers, and healthcare professionals and those commonly measured in intervention studies. Qualitative studies more often highlighted outcomes related to mental health and care processes, such as treatment burden, care coordination, and caregiver strain, which reflect aspects that strongly influence daily life and the management of multimorbidity. In contrast, quantitative studies, particularly RCTs, tended to focus more on healthcare utilization and costs, outcomes more relevant to healthcare systems and policymakers than to patients. While psychosocial/general health outcomes were frequently assessed in both study types, mental well-being and patient-experienced care processes remain underrepresented in trial-based research and are often included only as secondary outcomes. This gap suggests that the outcomes most meaningful to older adults with multimorbidity are not consistently prioritized in intervention evaluations. Future studies should incorporate outcomes that better reflect patient priorities to strengthen the person-centeredness of trial design.

To the best of our knowledge, there is only another systematic review investigating outcomes considered important by both clinicians and older adults with multimorbidity (Sathanapally et al., 2020). The main difference between our study and that of Sathanapally et al. lies in the study population: we exclusively included studies involving older adults, whereas their review included studies on adults of all ages.

In addition, we included intervention studies targeting older adults with multimorbidity, with the aim of identifying which outcomes are considered important by trialists, in order to assess whether these align with or differ from those deemed relevant by patients and caregivers in qualitative studies.

Thus, our review offers added value by focusing specifically on older adults with multimorbidity and incorporating more recent evidence, thus providing more targeted and up-to-date insights for improving care for older multimorbid adults.

### *4.2. Limitations*

This review has some limitations. First, the heterogeneity and frequent lack of consistency in the terminology as well as in the criteria used in different studies to define multimorbidity and related outcomes, made the review process difficult and prone to subjective judgment.

Further, not all multimorbid older adults have the same characteristics, and the expectations about outcomes can change depending on the type/severity of multimorbidity (Boyd et al., 2019; NICE, 2016), while the studies that we included were often unable to capture such extreme heterogeneity. Managing two relatively treatable diseases, such as hypertension and asthma, in a fit older adult with long life expectancy is not the same as dealing with two severe conditions, such as heart failure and cancer, in an older adult with functional impairment and lower life expectancy. In fact, although the category "Psychosocial outcomes/general health" is the most represented in the studies included in our review, it is equally true that in some studies there was a portion of older multimorbid adults who declared that reduction of mortality was their priority, confirming that among this population priorities and values may be diverse (Fried et al., 2008, 2011b; Ng et al., 2023; van Summeren et al., 2016).

Since there is no universally accepted definition of multimorbidity, many studies that declared to include multimorbid older adults indeed focused on an index disease associated with other diseases. In our review process, these studies were considered as studies investigating comorbidity rather than multimorbidity and were therefore excluded. Otherwise, other studies may have focused on multimorbid older adults but without clearly stating this in their methodology and therefore could have been missed in the review process.

## 5. Conclusions

The outcomes to be considered in intervention studies targeting multimorbid older adults should focus on the dimensions of functioning, quality of life and other related aspects, such as treatment burden, rather than on disease-specific outcomes as in most clinical studies. Unlike multimorbid adults, older adults with multimorbidity often face complex challenges, such as managing difficulties alone, experiencing socioeconomic hardships, having limited social support, being frail, or living with disabilities (Tazzeo et al., 2024). Therefore, for many of them, maintaining their independence is an absolute priority.

Since the multimorbid older population is extremely heterogeneous, the selection of outcomes to be included in intervention studies targeting this population should be carefully conducted, considering also other features, such as life expectancy and frailty.

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## Declaration of Competing Interest

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

## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.arr.2025.102940.

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