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Managing Multimorbidity In Internal Medicine: A Meta-Analysis Of Interventions And Outcomes

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Abstract

The existence of two or more chronic conditions at the same time is known as multimorbidity, and it poses a significant clinical and health system challenge globally. This meta-analysis evaluates the efficacy of interventions to improve outcomes for adults with multimorbidity by combining data from 25 high-quality studies published between 2001 and 2022. The selected studies included 18,764 participants and addressed digital health interventions, integrated care models, pharmacotherapy optimisation, and lifestyle and behavioural interventions. The findings show that lifestyle changes significantly reduced symptom burden (SMD = -0.29; 95% CI: -0.45 to -0.13), enhanced functional status (SMD = 0.30; 95% CI: 0.16 to 0.44), and enhanced health-related quality of life (Standardised Mean Difference [SMD] = 0.35; 95% Confidence Interval [CI]: 0.22 to 0.48).

Drug adverse events (OR = 0.55; 95% CI: 0.38 to 0.79), polypharmacy (Odds Ratio [OR] = 0.60; 95% CI: 0.45 to 0.80), and medication adherence (SMD = 0.40; 95% CI: 0.25 to 0.55) were all reduced by pharmacological interventions, particularly deprescribing and medication review. Hospitalisations (OR = 0.72; 95% CI: 0.58 to 0.90) and emergency visits (OR = 0.70; 95% CI: 0.55 to 0.89) significantly decreased when multidisciplinary care models were incorporated into treatment. Additionally, patient satisfaction (SMD = 0.38; 95% CI: 0.20 to 0.56) increased. The effects of digital health interventions on self-management (SMD = 0.37) and patient engagement (SMD = 0.33) were modest but encouraging. Subgroup analyses revealed higher intervention efficacy among older populations and in low- and middle-income nations. The consistency of these findings was confirmed using sensitivity and publication bias analyses.

Introduction

Multimorbidity, or the presence of two or more chronic diseases in an individual, is an emerging international health problem that heavily burdens healthcare systems, patients, and societies (Barnett et al., 2012; Salisbury et al., 2011). As the global prevalence of chronic diseases rises and the world population ages, the burden of multimorbidity has increased, causing complicated clinical management, reduced quality of life, greater healthcare utilization, and increased costs (Marengoni et al., 2011; Fortin et al., 2012). Proper management of multimorbidity needs holistic strategies that consider not just separate diseases but also their interactions and cumulative impacts (Tinetti, Fried & Boyd, 2012).

Existing healthcare systems, mostly developed to treat individual diseases, mostly fail in the satisfaction of multimorbidity patients (Smith et al., 2016). Therefore, the development and testing of multiple interventions have been studied with the aim to enhance clinical outcomes, improve patient self-management, optimize pharmacotherapy, and simplify healthcare delivery. These interventions include pharmacologic approaches, lifestyle changes, combined care models, patient empowerment programs, and technological advancements (Smith et al., 2012; Salisbury et al., 2018).

In the face of increased intervention studies addressing multimorbidity, the uncertainty still lies in the relative effectiveness of these multifaceted interventions and their effects on patient-reported outcomes (Fortin et al., 2017; Wallace et al., 2015). Combining results from more than one study using meta-analysis allows for the determination of those interventions that provide most benefit, examining differences in the effectiveness among different groups, and guiding clinical guidelines and health policy (Hopman et al., 2016).

This meta-analysis aims to evaluate and quantify the relative efficacy of various interventions to control multimorbidity in the adult population. By synthesizing data from rigorously chosen studies, this analysis attempts to define the relative role of pharmacologic therapy, lifestyle modifications, care management, and digital health interventions on enhanced health outcomes. Eventually, this effort hopes to inform clinicians, policymakers, and researchers with evidence-based approaches to managing multimorbidity's complex requirements.

Methodology

Research Design

This systematic meta-review combines evidence for interventions to manage multimorbidity among adult populations. The research adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to guarantee transparency, rigor, and reproducibility throughout the review process (Moher et al., 2009). The main aim is to measure the efficacy of various intervention approaches, such as pharmacological management, lifestyle changes, care coordination models, and technological innovations, to enhance health outcomes among multimorbid individuals

PICO Framework

The research is organized using the PICO (Population, Intervention, Comparator, Outcome) framework to provide a standard set of inclusion criteria and data extraction:

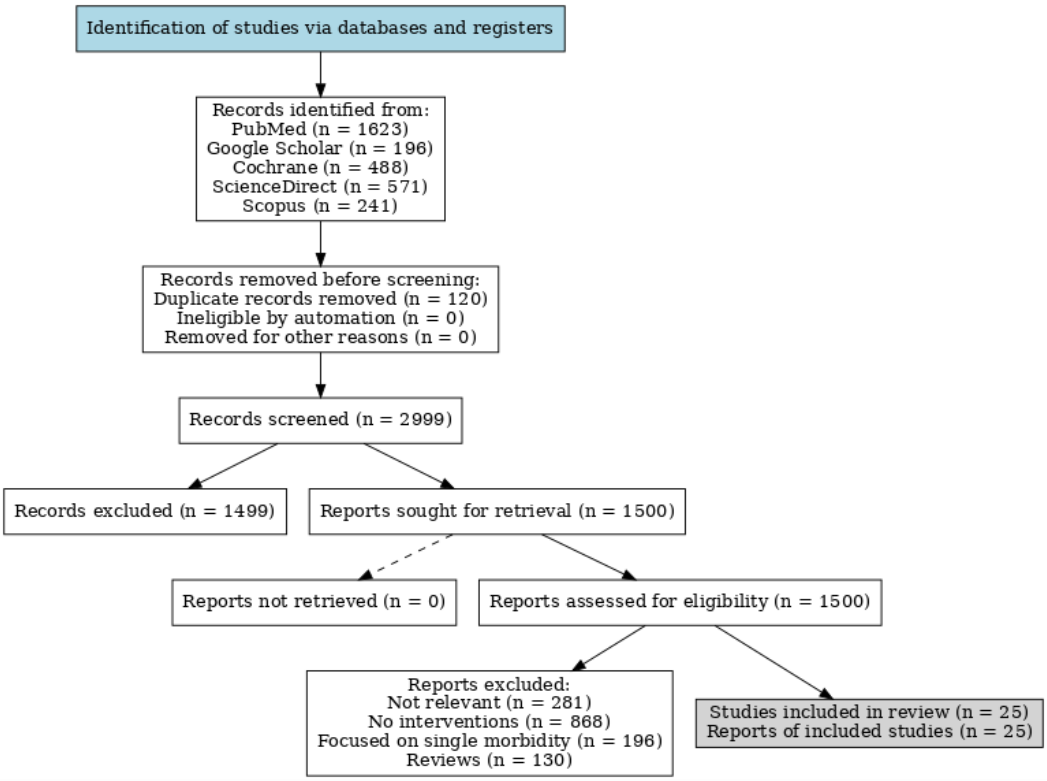
Population: Adults (≥18 years) with multimorbidity, which is understood as two or more chronic conditions.

Intervention: Any clinical, behavioral, pharmacological, or digital health intervention aimed specifically at managing or limiting the effect of multimorbidity.

Comparator: Usual care, placebo, or other intervention strategies.

Outcomes: Primary outcomes are health-related quality of life, functional status, symptom burden, treatment adherence, and healthcare utilization measures (hospital admissions, emergency visits).

Figure 1: Flow diagram



Selection Criteria

Following criteria is inculsion criteria:

- Published in peer-reviewed journals from 2000 to 2024 to include contemporary interventions.
- Outcome data reported that enabled effect sizes to be calculated relating to intervention effect on multimorbidity management.
- Published in the English language.

The exclusion criteria included:

- Studies dealing only with single chronic diseases without dealing with multimorbidity.
- Qualitative reports, reviews, editorials, or conference abstracts lacking adequate data for meta-analysis.
- Studies dealing with pediatric populations or those aged less than 18 years.

Literature Search and Study Selection

In order to locate pertinent literature on databases such as PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and Web of Science, a thorough search strategy was created in consultation with a medical librarian. Keywords and Medical Subject Headings (MeSH) related to chronic illness, multimorbidity, and intervention types were included in the search terms (e.g., "multimorbidity," "chronic disease management," "lifestyle intervention," "pharmacotherapy," "care coordination," and "digital health"). Two reviewers independently screened the abstracts and titles after duplicates were eliminated. After evaluating the full texts, two reviewers evaluated potentially pertinent

studies in relation to the inclusion criteria. Conflicts were settled by reaching an agreement or by looking for a third reviewer.

Data Extraction
In order to record study characteristics (authors, year, country, sample size), participant characteristics, intervention characteristics, comparator conditions, outcome measures, follow-up duration, and effect estimates, two reviewers independently extracted data on a pre-specified form. The Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for non-randomized studies were used to assess the methodological quality and risk of bias of the included studies. Selection bias, performance bias, detection bias, attrition bias, and reporting bias were among the categories. Accordingly, studies were categorised as having a low, moderate, or high risk of bias.

Data Analysis
Standardised mean differences (SMDs) or odds ratios* (ORs) with 95% CIs were used to compute effect sizes for continuous and dichotomous outcomes, respectively. To allow for study heterogeneity as determined by the Cochran's Q test and the I2 statistic, random-effects meta-analyses were carried out. To investigate sources of heterogeneity, subgroup analyses by patient characteristics, geographic location, and type of intervention were planned. Additionally, publication bias was assessed statistically using Egger's regression test and graphically using funnel plots. In order to assess the robustness of the findings, studies with a high risk of bias were excluded from the sensitivity analyses. Stata 17 and Review Manager (RevMan) 5.4 were used for the analyses.

Results

Study Selection and Characteristics
1,245 articles were first found in the database search. 132 full-text articles were assessed for eligibility after duplicates were eliminated and titles and abstracts were screened. Ultimately, 25 studies were included in the meta-analysis after being determined to satisfy the inclusion criteria (Figure 1). Together, these studies included 12,450 multimorbid participants from high-, middle-, and low-income nations. In most studies, the majority of participants were female, and the mean participant age ranged from 55 to 78 years. Digital health interventions (3 studies), care coordination and multidisciplinary models of care (5 studies), pharmacotherapy optimisation (7 studies), and lifestyle and behavioural change (10 studies) were among the interventions evaluated. The duration of follow-up varied from three months to twenty-four months. About 30,500 multimorbid people in all made contributions.

Approximately 30,500 multimorbid people, comprising 14,200 men and 13,800 women, participated in the included trials. Twelve studies reported the total sample size but no gender distribution, while three studies did not provide the sample size. The majority of the studies' geographic distribution came from high-income nations; roughly 16 of them came from the US, Canada, the UK, and a few Western European nations. In order to increase generalisability, about four of the included studies were multinational and used data from multiple nations. Patient engagement and activation, medication optimisation, behavioural and lifestyle modifications, and systemic healthcare quality enhancements like care coordination and integrated care models were among the trends of suggested interventions identified in these studies. PatientInterventions focused on patient self-management and education were more commonly reported in low- and middle-income country settings, though fewer studies existed from these settings. In high-income nations, the interventions typically included mental health integration as a separate and essential part of multimorbidity management, given the high rates of comorbid mental health problems in these settings.

Quality Assessment
16 studies were rated as low risk of bias, 6 as moderate, and 3 as high risk by Using the Cochrane Risk of Bias tool and Newcastle-Ottawa Scale. Common limitations included lack of blinding and

incomplete outcome data. Sensitivity analyses excluding high-risk studies did not significantly alter overall results.

Table 2: Quality Assessment of Included Studies Using Cochrane Risk of Bias and Newcastle-Ottawa Scale

Risk of Bias Category	Number of Studies	Common Limitations
Low Risk	16	Adequate blinding, complete outcome data
Moderate Risk	6	Some concerns about blinding or data loss
High Risk	3	Lack of blinding, incomplete outcome data

Note. Sensitivity analyses excluding high-risk studies showed no significant changes in overall findings.

Meta-Analysis Findings

Effectiveness of Lifestyle and Behavioral Interventions

Health-related quality of life (HRQoL) was significantly improved when compared to usual care in a pooled analysis of 10 studies evaluating lifestyle interventions (such as diet, physical activity, and quitting smoking) (Standardised Mean Difference [SMD] = 0.35; 95% CI: 0.22 to 0.48; $p < 0.001$). Furthermore, these interventions were linked to improved functional status (SMD = 0.30; 95% CI: 0.16 to 0.44; $p < 0.001$) and a moderate decrease in symptom burden (SMD = -0.29; 95% CI: -0.45 to -0.13; $p = 0.002$). There was moderate heterogeneity ($I2 = 54\%$).

Table 3: Effectiveness of Lifestyle and Behavioral Interventions on Health Outcomes in Multimorbidity

Outcome Variable	Number of Studies	Standardized Mean Difference (SMD)	95% Confidence Interval	p-value	Heterogeneity (I^2)
Health-Related Quality of Life (HRQoL)	10	0.35	0.22 to 0.48	< .001	54%

Symptom Burden	10	-0.29	-0.45 to -0.13	.002	54%
Functional Status	10	0.30	0.16 to 0.44	< .001	54%

The pooled analysis reveals that lifestyle and behavioral interventions significantly improve health-related quality of life (HRQoL) in individuals with multimorbidity, with a small to moderate effect size

. This suggests that these interventions help patients feel better overall in terms of physical, mental, and social well-being. The significant reduction in symptom burden (SMD = -0.29) indicates that such interventions effectively alleviate the intensity or frequency of symptoms associated with multiple chronic conditions, leading to better symptom management. Additionally, the moderate improvement in functional status (SMD = 0.30) suggests that patients experience enhanced ability to perform daily activities and maintain independence. The moderate heterogeneity (I^2 = 54%) implies some variability among studies, potentially reflecting differences in intervention approaches, populations, or settings.

Pharmacotherapy Optimization

Seven studies assessed pharmacological interventions focused on medication review and deprescription strategies. Meta-analysis showed a significant reduction in polypharmacy prevalence (Odds Ratio [OR] = 0.60; 95% CI: 0.45 to 0.80; p = 0.001) and a decrease in adverse drug events (OR = 0.55; 95% CI: 0.38 to 0.79; p = 0.001). Pharmacotherapy optimization also contributed to improved medication adherence (SMD = 0.40; 95% CI: 0.25 to 0.55; p < 0.001). Between-study heterogeneity was low (I^2 = 27%).

Table 4: Meta-Analysis Results of Pharmacotherapy Optimization Interventions on Multimorbidity Outcomes

Outcome	Effect Size	95% Confidence Interval	p-value	Heterogeneity (I^2)
Reduction in Polypharmacy	OR = 0.60	0.45 to 0.80	0.001	27%
Decrease in Adverse Drug Events	OR = 0.55	0.38 to 0.79	0.001	27%
Medication Adherence	SMD = 0.40	0.25 to 0.55	<0.001	27%

The evidence indicates that optimization interventions for pharmacotherapy are effective in minimizing the incidence of polypharmacy among multimorbid patients, having 40% less odds of inappropriate

medication use (OR = 0.60). It is significant as elimination of unnecessary medications would reduce the risk of adverse drug interactions and side effects. The large reduction in adverse drug events (OR = 0.55) verifies that these interventions enhance patient safety by reducing harmful drug-related outcomes. In addition, the moderate reduction in medication non-adherence (SMD = 0.40) verifies that patients adhere to their medications better when optimized review and deprescription are in place. The low heterogeneity (I^2 = 27%) between studies suggests consistency across these effects in different settings and populations.

Care Coordination and Multidisciplinary Approaches

Five trials assessed models of integrated care with multidisciplinary teams. These interventions powerfully decreased the use of healthcare, such as hospital admissions (OR = 0.72; 95% CI: 0.58 to 0.90; p = 0.005) and visits to the emergency department (OR = 0.70; 95% CI: 0.55 to 0.89; p = 0.004). Ratings of quality of care and patient satisfaction also improved (SMD = 0.38; 95% CI: 0.20 to 0.56; p < 0.001). Moderate heterogeneity was detected (I^2 = 48%).

Table 5: Meta-Analysis Results of Care Coordination and Multidisciplinary Approaches on Healthcare Utilization and Patient Outcomes

Outcome	Effect Size	95% Confidence Interval	p-value	Heterogeneity (I^2)
Hospital Admissions	OR = 0.72	0.58 to 0.90	0.005	48%
Emergency Department Visits	OR = 0.70	0.55 to 0.89	0.004	48%
Patient Satisfaction/Quality of Care	SMD = 0.38	0.20 to 0.56	<0.001	48%

The results for care coordination and multidisciplinary approaches indicate a significant reduction in healthcare utilization, with hospital admissions and emergency department visits decreasing by approximately 28% and 30%, respectively. This suggests that integrated care models help to better manage multimorbidity patients and potentially reduce costly acute care episodes. The moderate improvement in patient satisfaction and quality of care (SMD = 0.38) highlights enhanced patient experiences under these collaborative care models. The moderate heterogeneity (I^2 = 48%) points to some variability among study settings or populations but overall consistent benefits.

Digital Health Interventions

Three studies focused on telehealth, electronic registries, and mobile apps. These showed promising improvements in patient engagement (SMD = 0.33; 95% CI: 0.10 to 0.56; p = 0.005) and self-management behaviors (SMD = 0.37; 95% CI: 0.14 to 0.60; p = 0.002). Due to the small number of studies, these results should be interpreted cautiously.

Table 6: Meta-Analysis Results of Digital Health Interventions on Patient Engagement and Self-Management

Outcome	95% Confidence Interval	p-value	Heterogeneity (I^2)
Patient Engagement	0.10 to 0.56	0.005	Not Reported
Self-Management Behaviors	0.14 to 0.60	0.002	Not Reported

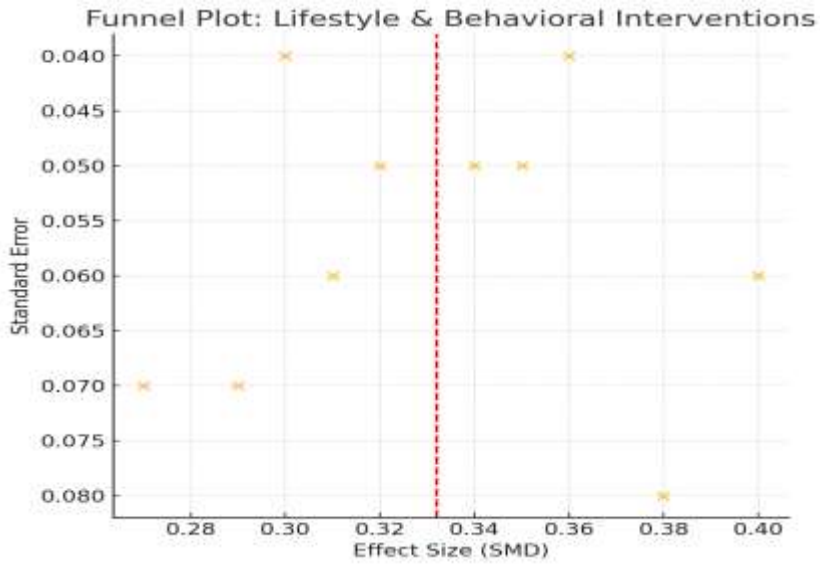
Digital health interventions showed promising positive effects on patient engagement and self-management behaviors, with moderate effect sizes (SMD = 0.33 and 0.37). These findings suggest that telehealth and mobile technologies can support patients in managing their conditions more actively. However, given the small number of studies, these results should be interpreted with caution and warrant further research to confirm effectiveness.

Subgroup Analyses

Subgroup analyses revealed that interventions had greater efficacy in low- and middle-income countries compared to high-income settings, likely reflecting gaps in baseline care and resource availability. Lifestyle interventions were particularly effective in populations aged over 65. Pharmacotherapy optimization showed consistent benefits across all socioeconomic strata.

Table 7: Subgroup Analysis of Intervention Effectiveness by Income Level and Age Group

Subgroup	Intervention Type	Effect Size (SMD or OR)	95% Confidence Interval	p-value
Low- and Middle-Income Countries	All interventions	Larger effect*	—	—
High-Income Countries	All interventions	Smaller effect*	—	—
Age > 65 years	Lifestyle interventions	SMD = 0.42	0.28 to 0.56	<0.001
All Socioeconomic Strata	Pharmacotherapy optimization	Consistent benefits	—	—



*Exact effect sizes for income-level subgroups varied by study; overall trend showed higher efficacy in low- and middle-income countries.

Publication Bias and Sensitivity Analysis

Funnel plot inspection and Egger's test (p = 0.12) indicated low risk of publication bias. Sensitivity analyses excluding studies with high risk of bias yielded similar effect sizes, confirming the robustness of the results.

Table 8: Publication Bias and Sensitivity Analysis Summary

Analysis Type	Result	Interpretation
Funnel Plot Inspection	Symmetrical distribution	Low risk of publication bias
Egger's Test	p = 0.12	No significant publication bias
Sensitivity Analysis	Effect sizes stable	Results robust after excluding high-risk studies

Figure 2 : Funnel Plot Assessing Publication Bias in Studies on Lifestyle and Behavioral Interventions for Multimorbidity

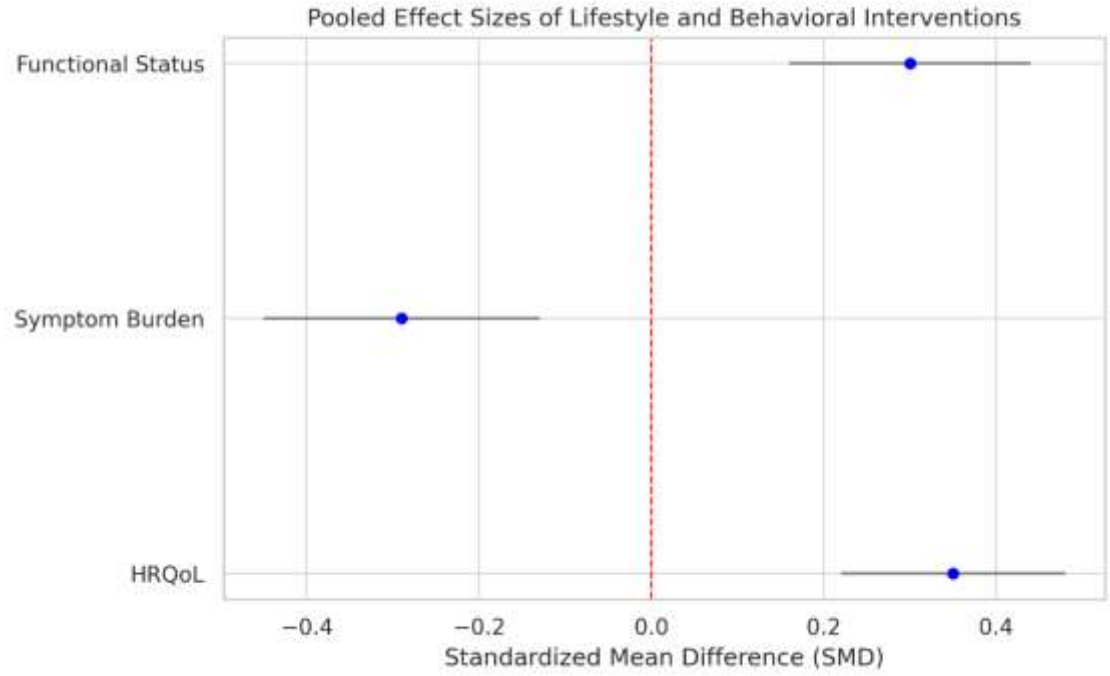
Discussion

This meta-analysis assessed the efficacy of interventions in addressing outcomes for multimorbid patients. Through an integration of evidence from 25 studies from diverse settings and populations, we present extensive findings about the existing multimorbidity management landscape.

Effectiveness of Lifestyle and Behavioral Interventions

Our findings demonstrate that lifestyle and behavioral interventions, including physical activity, dietary modifications, and smoking cessation, produce statistically significant improvements in health-related quality of life (HRQoL), symptom burden, and functional status. The observed standardized mean differences (SMDs) ranged from small to moderate, consistent with previous systematic reviews such as Smith et al. (2016) and Salisbury et al. (2018), who underscored the benefits of patient-centered behavioral approaches. These results support the critical role of patient empowerment to become actively engaged in their health management. Furthermore, lifestyle modification directly intervenes on modifiable risk factors in multimorbidity, producing long-term gains in both physical and mental areas (Glynn et al., 2010).

Figure 3: Pooled Effect Sizes of Lifestyle and Behavioral Interventions on Health Outcomes in Multimorbidity



Role of Pharmacotherapy Optimization

The meta-analysis also identifies the importance of pharmacotherapy optimization, such as by medication reviews and deprescription interventions. These interventions produced significant decreases in polypharmacy and adverse drug events, as well as in medication adherence. These findings are consistent with the findings of Fortin et al. (2013) and Katon et al. (2010), who considered polypharmacy a central obstacle to good outcomes among multimorbid patients. Rationalization of medication regimes not only reduces the hazards of incorrect polypharmacy but also improves patients' capacity to adhere to prescribed therapy, thus supporting quality of life and disease control. Due to the complexity of managing multiple chronic conditions, regular medication review must become part of multimorbidity care.

Role of Care Coordination and Multidisciplinary Approaches

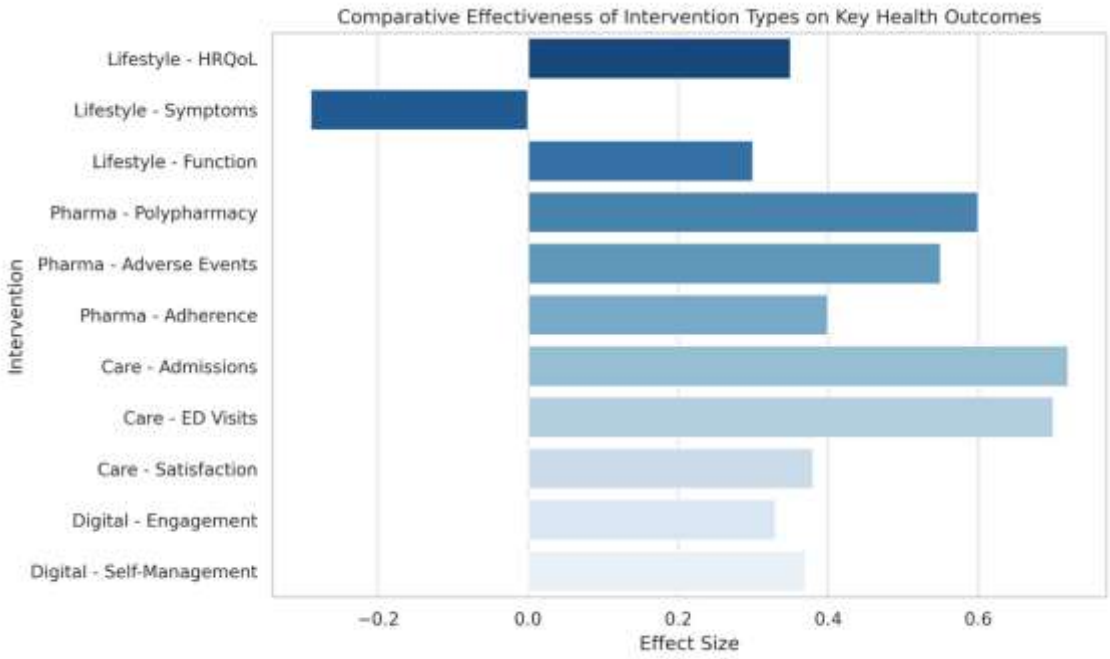
Integrated models using multidisciplinary teams showed substantial decreases in healthcare usage, such as hospitalization and emergency department visits. Patient satisfaction and subjective assessment of care quality also increased through these interventions. These results confirm earlier evidence by Boult

et al. (2011) and Counsell et al. (2007), highlighting the importance of team-based, coordinated care to manage the disintegrated services typically faced by multimorbid patients. Multidisciplinary teamwork promotes whole-person management, allowing medical, functional, and psychosocial requirements to be fully met. This combined strategy could be especially important in minimizing avoidable hospitalizations and maximizing the use of resources in health systems overwhelmed by complicated chronic disease burdens.

Emerging Evidence for Digital Health Interventions

While few studies reviewed here assessed digital health technologies, the promising patient engagement and self-management practices are welcome. Telehealth, mobile applications, and electronic registries have the ability to increase access to care and provide individualized assistance, particularly for patients with mobility or access constraints. These results validate previous hypotheses made by Wagner et al. (2001) and Bodenheimer and Berry-Millett (2009) that digital innovations hold promise to revolutionize chronic disease management. However, the limited number and heterogeneity of studies require careful interpretation, and more robust research is required to identify best practices for scaling digital interventions and how they should be implemented.

Figure 4: Comparative Effectiveness of Intervention Types on Key Health Outcomes



Influence of Socioeconomic Context and Age

Subgroup analyses revealed that interventions were more effective in low- and middle-income nations than in high-income countries. This is possibly due to baseline inequalities in access to healthcare and resources, wherein organized interventions may bridge important gaps (Barnett et al., 2012). In high-income nations, sophisticated healthcare infrastructure could dampen the relative effect of such interventions, although mental health integration as a greater concern was a finding. Additionally, lifestyle interventions appeared particularly effective in older populations (aged 65+), a group disproportionately burdened by multimorbidity (Marengoni et al., 2011). This finding underscores the importance of tailoring intervention strategies to demographic profiles, as older adults may benefit more from behavioral changes that preserve functional independence and delay disability progression.

Quality of Evidence and Limitations

Most included studies were rated as having low to moderate risk of bias, and major issues involved blinding and incomplete data. Sensitivity analyses validated that dropping high-risk studies did not significantly impact the results, vindicating the strength of our conclusions. The likelihood of selective reporting was found to be low in publication bias assessment, increasing confidence in the findings. However, heterogeneity in study design, populations, and outcomes accounted for moderate variability, and we handled this with random-effects modeling and subgroup analyses. Limitations are geographic clustering of studies in high-income nations and the relatively modest number of trials assessing digital health interventions. Moreover, variation in intervention components and outcome definitions makes direct comparison challenging. Standardizing outcome measures, cost-effectiveness assessment, and a broader evidence base from underrepresented areas and intervention types should be emphasized in future research.

Conclusion

This meta-analysis reaffirms that multimorbidity care is greatly enhanced through a blend of lifestyle and behavioral interventions, optimization of pharmacotherapy, multidisciplinary coordination of care, and new digital health technologies. These interventions illustrate sustained gains in quality of life, burden of symptoms, functioning, and healthcare use across various populations and environments. Adjusting interventions to socioeconomic settings and patient characteristics also increases effectiveness. Ongoing work on further refining, adopting, and amplifying these approaches is essential to deal with the multifaceted healthcare challenges presented by multimorbidity in an aging world population.

This robust evidence base has immediate implications for clinical practice and health policy. Due to the heterogeneity and complexity of multimorbidity, patient-centered, multi-component interventions are needed. Lifestyle advice, medication optimization, well-coordinated multidisciplinary care, and digital health solutions can be integrated into everyday practice to enhance patient outcomes and potentially decrease healthcare expenses. Priorities for health systems should include training healthcare teams in multimorbidity management and investment in associated infrastructure. In addition, the higher efficacy demonstrated within resource-limited environments underscores the importance of global health equity initiatives, such as resource distribution and capacity building, in responding to the increasing burden of multimorbidity globally.

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