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A systematic review of interventions to improve medication adherence in adults with mental-physical multimorbidity in primary care

Lammila-Escalera, Elena; Greenfield, Geva; Pan, Ziyang; Nicholls, Dasha; Majeed, Azeem; Hayhoe, Benedict

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A systematic review of interventions to improve medication adherence in adults with mental-physical multimorbidity in primary care.

Elena Lammila-Escalera MPH (0000-0001-6805-5241); PhD Student, Dr Geva Greenfield (0000-0001-9779-2486); Research Fellow in Public Health, Ziyang Pan MPH, Professor Dasha Nicholls (0000-0002-6457-5458); Professor of Child and Adolescent Psychiatry, Professor Azeem Majeed (0000-0002-6457-5458); Head of the Department of Primary Care and Public Health, Dr Benedict Hayhoe (0000-0002-2645-6191); Clinical Lecturer in Primary Care.

Affiliations: Department of Primary Care and Public Health, School of Public Health, Imperial College London, The Reynolds Building, St Dunstan's Road, London W6 8RP

Address correspondence to: Geva Greenfield, Department of Primary Care and Public Health, School of Public Health, Imperial College London, 314 The Reynolds Building, St Dunstan's Road, London W6 8RP, g.greenfield@ic.ac.uk

How this fits in:

This research builds upon existing knowledge by addressing the uncertainty surrounding the effectiveness of interventions targeting medication adherence in adults with mental-physical multimorbidity in primary care. Prior to this review, the landscape lacked a systematic exploration of such interventions for this complex patient population. Our findings offer a comprehensive synthesis of the literature, addressing a crucial evidential gap. Clinicians will benefit from a clearer understanding of which interventions improve medication adherence in adults with mental-physical multimorbidity, enhancing their ability to tailor care and improve patient outcomes.

Abstract

Background: Medication non-adherence is a significant contributor to healthcare inefficiency, resulting in poor medication management, impaired patient outcomes and ineffective symptom control.

Aim: This review aimed to summarise interventions targeting medication adherence for adults with mental-physical multimorbidity in primary healthcare settings.

Design and setting: A systematic review of the literature was conducted.

Methods: Medline, Embase, PsycInfo, Web of Science, Cochrane Library, and CINAHL were searched for relevant studies. Data were extracted and synthesized using narrative synthesis. The Cochrane Effective Practice and Organisation of Care (EPOC) was used to classify intervention types. Risk of bias was assessed using the National Heart, Lung, and Blood Institute (NHLBI) quality assessment tool.

Results: Eleven studies representing 2,279 patients were included. All interventions examined were classified into one EPOC domain, which was delivery arrangements. All included studies examined patients with a physical condition, alongside depression. Seven studies examining coordination of care and management of care processes interventions reported significant improvements in medication adherence attributed to the intervention. Four studies considering the use of information and communication technology observed no changes in medication adherence.

Conclusion: Interventions that coordinate and manage healthcare processes may help improve how patients adhere to their medication regimes, particularly in patients with mental-physical multimorbidity. However, we still need to better understand how digital health technology can support patients in following their medication regimes. As we face the growing challenges of treating multimorbidity, everyone involved in health services - from providers to policymakers - must be receptive to a more integrated approach to the delivery of healthcare.

Introduction

Medication adherence is "the degree to which the person's behaviour corresponds with the agreed recommendations from a health care provider".(1,2) This description encompasses several behaviours, from seeking medical attention to consuming medication as prescribed. (2,3) Non-adherence, therefore, presents health systems with a multifaceted challenge, imposing a significant economic burden globally.(4) Five interacting dimensions are recognised to affect the ability to adhere to medication, including social and economic factors, healthcare provider-related factors, condition-related factors, therapy-related factors, and patient-related factors.(3,5,6) Socioeconomic status is one of the most frequently explored contributors to poor medication adherence due to illness severity and primary care accessibility.(2,7)

Medication non-adherence is particularly challenging for individuals with multimorbidity.(8–10) Multimorbidity is the co-existence of two or more long-term conditions,(11,12) and poses unique clinical challenges since patients suffer from co-existing and potentially interacting diseases which may amplify symptoms and discomfort.(13,14) Managing multimorbidity is complex and interventions to improve outcomes must be multifaceted.(15) Consequently, individuals living with multimorbidity often require multiple medications to achieve optimal treatment.(16,17) This may result in a considerable burden on these individuals. For example, those with five or more chronic conditions could spend between five and eight hours a day managing their conditions. (18,19) This may contribute to treatment burden in those with multimorbidity, reducing medication adherence.(18,19) Patients may also prioritise certain medications over others according to disease progression and severity, acceptability or tolerability, and perceived importance.(2,7,14) Ultimately, this compromises drug safety, leads to inappropriate prescriptions, adverse drug reactions and unnecessary medication interactions.(20–22) Additionally, psychiatric treatments have a lower adherence rate than those for physical conditions. Mental-physical multimorbidity, which includes common mental disorder (CMD), can reduce adherence rates further.(23–26)

Previous studies have proposed many approaches to improving medication non-adherence.(16,27,28) However, it is unclear which and to what extent these interventions effectively address this issue, ultimately informing best practice and service delivery. To date, no systematic review has assessed the evidence on interventions targeting medication adherence in individuals with mental-physical multimorbidity. This systematic review aims to answer this research question: what type of interventions are designed to improve medication adherence for adults with multimorbidity, including CMD, in primary care, and how effective are they?

Methods

This review was conducted in line with recommendations in the Cochrane Collaboration Handbook and reported in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analysis' (PRISMA) Guidelines.(29,30) The protocol for this systematic review was pre-registered on PROSPERO (CRD42022332974).

Eligibility Criteria

Eligibility criteria were formulated using the 'Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework.(31) Studies were not excluded based on published language or country of origin. Studies with a quantitative randomized controlled trial design were eligible for inclusion if they considered adult populations with multimorbidity, including at least one chronic condition and at least one CMD comorbidity, presenting to primary care. Results from pilot studies will also be eligible. Individuals with major depression patients (a severe mental illness (SMI)) were

included in this systematic review for comprehensiveness. Studies were required to compare interventions targeting medication adherence in primary care with usual, standard or care without therapeutic components. Studies were required to consider patient medication/treatment/therapy adherence rate as a primary or secondary outcome. Measures of effect include (a) self-report questionnaires or structured interviews, (b) therapeutic drug monitoring (TDM), (c) electronic devices, and (d) pick-up/refill rates.

Search strategy

Information sources

Articles were identified through searches of the electronic databases Medline, Embase, PsycINFO, Web of Science, Cochrane Library, and Cumulated Index for Nursing and Allied Health Literature (CINAHL) (from January 2000 to May 2022). The search strategy was initially constructed for Medline (Supplementary Table 1) but was later appropriately adapted for use in the other databases searched.

Selection process

After deduplication, the titles and abstracts of the eligible articles were independently screened against the inclusion and exclusion criteria by two reviewers (ZP and ELE). Conflicts were resolved by discussion. This process was repeated for full-text examination.

Data collection process

Data relevant to the study question were independently extracted from each qualified study by ZP and validated by ELE. This data was summarised in a tabular format. Data extracted included the intervention under investigation, sociodemographic factors and intervention effectiveness.

Study risk of bias assessment

The two authors independently assessed the included studies for risk of bias using the National Heart, Lung, and Blood Institute (NHLBI) Study Quality Assessment Tools for Controlled Intervention Studies.(32) Studies were not excluded based on quality assessment.
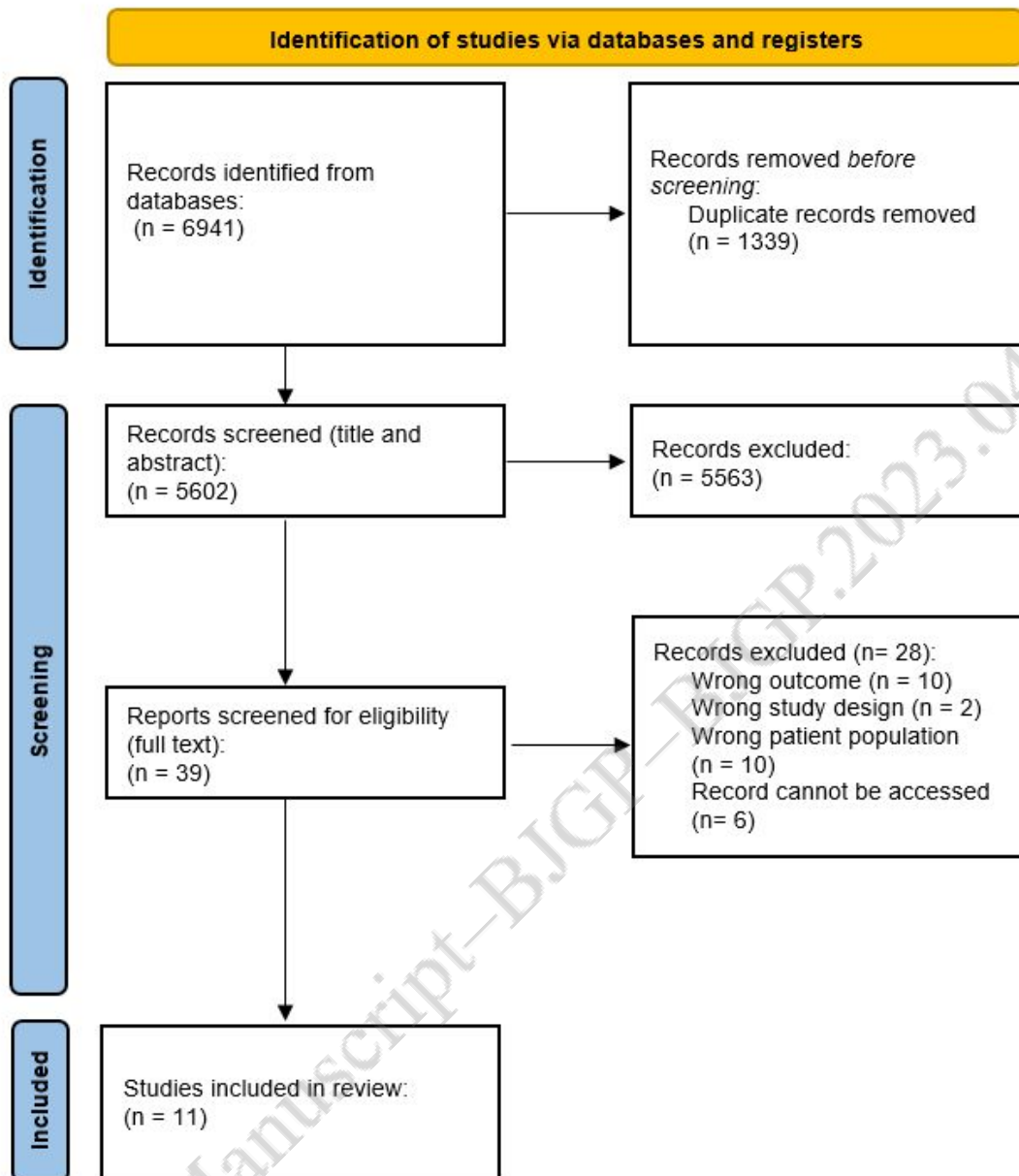
Synthesis methods

A meta-analysis was considered impractical due to the anticipated heterogeneity of intervention. Consequently, a narrative synthesis approach was conducted, utilising the Cochrane Effective Practice and Organisation of Care (EPOC) Taxonomy to classify the interventions reported. There are four categories: (I) delivery arrangements, (II) financial arrangements, (III) governance arrangements and (IV) implementation strategies.(33)

Results

Study selection

Searches identified 6,941 studies (Figure 1). Of 39 studies selected for full-text screening, 28 were excluded due to intervention, outcomes, patient population, and study design. Therefore, 11 randomised controlled trials were included in this review.(34–44)

Figure 1. Systematic review flow chart

Identification of studies via databases and registers

Identification

Records identified from databases:
(n = 6941)

Records removed *before screening*:
Duplicate records removed
(n = 1339)

Screening

Records screened (title and abstract):
(n = 5602)

Records excluded:
(n = 5563)

Reports screened for eligibility (full text):
(n = 39)

Records excluded (n= 28):
Wrong outcome (n = 10)
Wrong study design (n = 2)
Wrong patient population
(n = 10)
Record cannot be accessed
(n= 6)

Included

Studies included in review:
(n = 11)

Study characteristics

Of the 11 trials (Supplementary Table 2), nine were conducted in the United States,(34–36,38–42,44) one in Australia,(37) and one in South Africa.(43) Six articles targeted medication adherence as a primary outcome.(34–36,38,43,44) These studies recruited 2,279 adults with multimorbidity and CMD. Disease combinations include hypertension, diabetes, HIV/AIDS, and coronary heart disease, all in combination with depression.

Three included studies were deemed as good quality,(40,42,44) five studies were of fair quality,(36,37,39,41,43) and three studies were of poor quality (34,35,38) (Supplementary Table 3). Reasons for the poorer rating include a failure to meet an adequate randomisation requirement, not specifying the randomisation method, not specifying the treatment allocation concealment, or not reporting the blinding of the researchers.

Intervention classification

All 11 trials assessed interventions that could be classified as delivery arrangement interventions. (34–44) according to EPOC. Of the interventions reported, the most frequent EPOC sub-categories of the delivery arrangement domain explored were the coordination of care and management of care processes (34–36,40,41,43,44) and the use of information and communication technology (37–39,42).

Coordination of care and management of care processes interventions

Seven studies examined interventions that targeted the coordination of care and the management of care processes.(34–36,40,41,43,44) These interventions were multifaceted, with several components spanning EPOC subcategories. These include case management, integration, shared care, shared decision-making and teams. For instance, three studies assessed an integrated depression and chronic disease treatment intervention by utilising an integrated care manager as a liaison between the physician and patients.(34–36) The role of this intermediary case management is to work with the patient to address the factors of adherence and effectively communicate the rationale behind antidepressant and antihypertension medication use. Similarly, the multi-condition collaborative care management intervention proposed by Lin *et al* aimed to co-ordinate care using a care manager.(41)

The nurse-led intervention, detailed in the studies authored by Safren *et al*, integrated adherence counselling with traditional CBT techniques for treating depression and antiretroviral therapy adherence.(43,44) This program commenced with problem-solving, employing case studies (Life-Steps) to prepare participants for subsequent CBT sessions. Additional resources offered to participants include reminders, graphic aids, self-care and physical activity techniques. Katon *et al* instead focused on shared care, decision-making and team collaboration.(40) Nurses collaborated with other health professionals, such as psychiatrists, who would co-review medication use, provide recommendations and work closely with patients to establish patient-centred goals. A stepped care algorithm was also employed, where participants who did not initially meet goals had to choose their next treatment plan during a second phase of the intervention.

Information and communication technology interventions

Four studies utilised information and communication technology (ICT) and telemedicine to deliver care. (37–39,42) For example, Clarke *et al* assessed the delivery of their self-management CBT program through a web-based platform.(37) Targeting the improvement of social and occupational functioning, participants were required to complete a minimum set of CBT modules. Moreover, the platform offered self-monitoring reminders, home practice activities and motivational statements. This intervention was entirely self-guided, whilst the other ICT interventions were guided by healthcare professionals. Both Himelhoch *et al* and Piette *et al* examined the impact of CBT-based intervention delivered via telephone.(39,42) In contrast, another trial assessed an intervention consisting of electronic device monitoring and consultation. (38) This program was a pharmacist-led telehealth management program involving the deployment of an electronic device (Health Buddy®) to facilitate communication, sending individualised daily reminders to patients to take their medications.

Reported outcomes

All 11 studies collated reported medication adherence as an outcome, (34–44) eight reported mental health outcomes (34–39,42,44) and five reported physical health outcomes (34–37,42) (**Table 1**). Of the seven studies assessing coordination of care and management of care processes, six reported improved medication adherence,(34–36,44) four reported improvements in mental health outcomes (34–36,44) , and three reported improvements in physical health outcomes(34–36). Of the four studies

examining ICT interventions, two reported improved medication adherence (38,39) and two reported improved mental health outcomes only (37,42).

Table 1: Reported outcome by EPOC Taxonomy Intervention category(33)

	Medication adherence	Mental health outcomes	Physical health outcomes
Coordination of care and management of care processes interventions	Three studies reported that for their respective outcome assessments, the intervention group exhibited higher proportion of patients who had 80% or greater adherence to medication, compared to their usual control participants.(34–36) Three further studies reported that intervention participants had significantly greater medication adherence than the control group. (40,43,44) One of these studies recorded that adherence gains were not maintained at 8 months.(44) A further study reported that whilst there were no differences observed for medication adherence, adjustment rates were higher among the intervention group, relative to the control.(41)	Four studies reported significant reductions in depression status and depressive symptoms, compared to their usual control participants.(34–36,44)	Three studies reported better physical chronic disease indexes compared to their usual control participants.(34–36)
Information and communication technology interventions	Two studies observed that medication adherence was maintained in the intervention participants, in comparison to the control.(38,39) Two studies reported no differences in medication adherence between intervention and control participants.(37,40)	Two studies reported significant reductions in depressive symptoms. (37,42) In contrast, one study observed that both intervention and control group participants experienced significant reductions in depressive symptoms.(39) One study reported there were no significant changes for both groups in	One study observed that intervention participants experienced no differences in blood glucose monitoring.(37) Another reported no differences in Hba1c levels between the intervention and control groups.(42)

			terms of the depression scores.(38)	

Discussion

Summary

Current interventions show potential to improve medication adherence in adults with mental-physical multimorbidity in primary care despite substantial heterogeneity in participant and intervention characteristics.(34–44) Trials which assessed the coordination of care and care process interventions showed improvements across all outcomes, supporting the implementation of this intervention type for this complex patient population.(34–36,40,41,43,44) In contrast, studies examining the efficacy of ICT interventions reported conflicting findings.(37–39,42)

Strengths and Limitations

To our knowledge, this is the first systematic review to examine the effectiveness of interventions to improve medication adherence for adults with multimorbidity, including CMD. This review addresses a crucial evidential gap for this group, presenting valuable insight to improve service delivery. Moreover, the focus on RCTs ensured that the evidence generated was high quality, as RCTs are recommended when establishing a causal relationship.(45)

Despite an extensive search, only 11 articles were included due to strict eligibility criteria. Only depression plus a limited number of physical comorbidities were trialled in the studies eligible, restricting applicability across other chronic diseases and mental disorders. Few counties were represented, with all trials conducted in countries with English as their primary language; variation in terminology and intervention description due to language or culture differences may have led to some studies being overlooked in the search. This review is also vulnerable to the limitations of the various methods used to quantify adherence, such as self-report measures.(46)

There are recognised limitations in employing the EPOC Taxonomy as a guide in synthesis,(47) and interventions to improve outcomes for individuals with multimorbidity are often multifaceted with a potential for overlap in categorisation. Furthermore, the interventions demonstrated a broad range of characteristics, varying from significant structural changes in the healthcare team to patient-level amendments. Consequently, causality on any outcome cannot be attributed to a specific intervention component. Finally, no studies from the UK were identified. This may have an impact on the contextual adaptability of the interventions proposed, limiting generalisability for widespread implementation in UK settings.

Comparison with Existing Literature

This review reaffirms previous conclusions that despite successes with care coordination and care management processes, evidence for widespread implementation of these interventions remains undeveloped. However, unlike previous work, this review investigates the efficacy of interventions to improve medication adherence for this unique patient population.(48–51)

Some of the interventions examined, reported as successful at improving medication adherence, have also been successful when assessed for suitability in other contexts across a variety of outcomes. For example, team care has been used in the treatment and management of other conditions and has fostered improved outcomes in participants, contributing to the potential usefulness of the intervention

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throughout the health care system.(52) Previous research has explored the relationship between care coordination and medication adherence.(53,54) While the exact mechanism of association is not fully understood, it is likely influenced by fostering a robust relationship between the patient and the professional.(55,56) Plus, evidence indicates that an ongoing partnership may improve patient satisfaction, trust and communication.(57)

Implications for Research and/or Practice
To mitigate the impending challenges associated with multimorbidity, health services, providers, and policymakers must be receptive to adopting alternative approaches to care.(70) National guidelines and policies should be reviewed to ensure alignment with best practices for this complex patient population and to support the implementation of novel ideas for change. This review presents several interventions that could be utilised to improve medication adherence, either as a reference for care delivery or as a foundational basis for additional development. Primary care providers should embrace the evidence presented in this review to reinforce care management processes and coordinate efforts to improve outcomes. The patient-provider relationship should also be prioritised when formulating strategies to enhance medication adherence for this complex patient population. The benefit of investment in medication non-adherence could significantly outweigh any associated short-term expenses associated with staffing, cost and capacity constraints.(4,58)

Decision-makers should also grasp the opportunity to use and integrate digital health technologies into usual service delivery. Despite conflicting evidence, the 'MyCompass' platform and the 'Health Buddy®' (37,38) device explored in this review represent how digital health technologies may improve outcomes and alleviate associated burdens for the provider. However, comprehensive training, acceptance, communication, and organisational stability must be given special consideration to support the successful implementation of digital health technologies and ensure optimal outcomes.(59)

Further research is urgently required to expand the sparse evidence base for interventions supporting the care of this complex group of patients. Most of the studies collated in this review focused solely on a specific combination of chronic disease and CMD. Subsequently, more trials should actively include participants with various comorbidity combinations. This would provide greater insight into the viability of the widespread implementation, whereby adults with multimorbidity will present to primary care with varied combinations of chronic disease. Future research should also assess the impact of variables associated with adults with multimorbidity on the efficacy of these interventions, conducting sub-group analyses. For example, only one study in this review recruited African American participants. Special focus should also be given to age, ethnicity, and socioeconomic status, as the literature on these factors is limited. By neglecting to incorporate these variables into the analysis, appropriate evidence will not be generated, potentially resulting in inadequate care.

Furthermore, the interventions trialled in this review may not be suitable for implementation across all global contexts. It would be advantageous if trials examined efficacy in other contexts and countries to ensure the interventions' contextual adaptability. Economic evaluations to determine cost-effectiveness also provide decision-makers with additional operational information for reaching a consensus on feasibility.

Conclusion

There is a lack of evidence concerning which and to what extent existing interventions improve medication adherence for adults with mental-physical multimorbidity in primary care. This systematic review identified that the dominant intervention type assessed targeted service delivery arrangements.

Trials assessing coordination of care interventions reported improvements in medication adherence and mental and physical health outcomes. In contrast, information and communication technology interventions failed overall to improve outcomes for trial participants. Additional resources must consequently be allocated to foster the creation, testing, and implementation of interventions that aim to integrate care to improve outcomes for this complex group of patients.

Other information

Registration and protocol

PROSPERO 2022 CRD42022332974

Competing interests

No competing interests

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