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ΣΥΣΤΗΜΑΤΙΚΗ ΑΝΑΣΚΟΠΗΣΗ

Παρεμβάσεις προώθησης της φαρμακευτικής συμμόρφωσης στην τρίτη ηλικία – Συστηματική ανασκόπηση

Μάρκου Παναγιώτα[1], Στάχτιαρη Δήμητρα[2], Στέφου Ασημίνα[3], Γιαννακοπούλου Σοφία[4], Σκρέκα Θεοδώρα[5], Χονδρονικόλα Παρασκευή[6], Μαρκοπούλου Γεωργία – Μαρία[7]

1. *Απόφοιτη του τμήματος Δημόσιας και Κοινοτικής Υγείας - κατεύθυνση Κοινοτική Υγεία, Σχολή Δημόσιας Υγείας, Πανεπιστήμιο Δυτικής Αττικής*
2. *Απόφοιτη του τμήματος Δημόσιας και Κοινοτικής Υγείας - κατεύθυνση Κοινοτική Υγεία, Σχολή Δημόσιας Υγείας, Πανεπιστήμιο Δυτικής Αττικής*
3. *Απόφοιτη του τμήματος Δημόσιας και Κοινοτικής Υγείας - κατεύθυνση Κοινοτική Υγεία, Σχολή Δημόσιας Υγείας, Πανεπιστήμιο Δυτικής Αττικής*
4. *Μεταπτυχιακή φοιτήτρια, Παγκόσμια Υγεία – Ιατρική των Καταστροφών , Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών*
5. *Μεταπτυχιακή φοιτήτρια, Γενική και Εξειδικευμένη Παιδιατρική: Κλινική Πράξη και Έρευνα, Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών*
6. *Λέκτορας εφαρμογών, τμήμα Δημόσια και Κοινοτική Υγεία, Σχολή Δημόσιας Υγείας, Πανεπιστήμιο Δυτικής Αττικής*
7. *Λέκτορας εφαρμογών, τμήμα Δημόσια και Κοινοτική Υγεία, Σχολή Δημόσιας Υγείας, Πανεπιστήμιο Δυτικής Αττικής*

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ΠΕΡΙΛΗΨΗ

Εισαγωγή: Φαρμακευτική συμμόρφωση είναι η ικανότητα του ασθενή να τηρεί τις οδηγίες που αφορούν τη συνέπεια σε σχέση με τη λήψη της φαρμακευτικής αγωγής, τη δοσολογία, την πρόκληση ανεπιθύμητων ενεργειών, την αλληλεπίδραση των φαρμάκων, οδηγίες αποθήκευσης και συντήρησης αλλά και οδηγίες οι οποίες αναγράφονται στο φυλλάδιο οδηγιών, το οποίο περιλαμβάνεται σε κάθε φάρμακο και περιέχει σημαντικές πληροφορίες. Τα άτομα τρίτης ηλικίας είναι πιο επιρρεπή στη μη φαρμακευτική συμμόρφωση διότι συνήθως πάσχουν από πολλές ασθένειες και χρειάζεται να λαμβάνουν πολλαπλές φαρμακευτικές αγωγές.

Σκοπός: Ο σκοπός της παρούσας συστηματικής ανασκόπησης ήταν η μελέτη των παρεμβάσεων που έχουν πραγματοποιηθεί τα τελευταία 5 έτη με στόχο την προώθηση της φαρμακευτικής συμμόρφωσης στους ηλικιωμένους. Τα ερευνητικά ερωτήματα που τέθηκαν ήταν τα εξής: «Ποιες μέθοδοι έχουν χρησιμοποιηθεί στις παρεμβάσεις για την προώθηση της φαρμακευτικής συμμόρφωσης στη τρίτη ηλικία;» και «Ποια είναι η αποτελεσματικότητα αυτών των παρεμβάσεων στην ενίσχυση της φαρμακευτικής συμμόρφωσης στη τρίτη ηλικία;».

Υλικό και Μέθοδος: Πραγματοποιήθηκε αναζήτηση άρθρων στις βάσεις δεδομένων PubMed, Scopus και Google Scholar μεταξύ Μαρτίου και Απριλίου 2024, για το διάστημα 2018 – 2024, χρησιμοποιώντας τις λέξεις κλειδιά «intervention», «elderly», «medication persistence» καθώς και τα συνώνυμά τους.

Αποτελέσματα: Συνολικά συμπεριλήφθηκαν 14 μελέτες οι οποίες και πληρούσαν τα κριτήρια ένταξης της παρούσας συστηματικής ανασκόπησης. Η πλειονότητα των παρεμβάσεων αποδείχθηκε αποτελεσματική στη βελτίωση της φαρμακευτικής συμμόρφωσης στους ηλικιωμένους, ενισχύοντας την ικανότητά τους για αυτοδιαχείριση και διευρύνοντας τις γνώσεις τους σχετικά με τη λογική χρήση των φαρμάκων. Παρεμβάσεις που ενσωμάτωναν τεχνολογικά εργαλεία και καινοτόμες μεθόδους, όπως η χρήση κόμικς, φάνηκαν να αποτελούν επωφελείς στρατηγικές για τη βελτίωση της υγείας των ηλικιωμένων. Ωστόσο, για να είναι αποτελεσματικές, οι παρεμβάσεις απαιτούν συνεχή εποπτεία και υποστήριξη.

Συμπεράσματα: Συμπερασματικά, κρίνεται απαραίτητη η διατήρηση κα ενίσχυση της εφαρμογής παρεμβάσεων που στοχεύουν στην προώθηση της φαρμακευτικής συμμόρφωσης, ιδίως στους ασθενείς που πάσχουν από ψυχικές διαταραχές.

Λέξεις Κλειδιά: Φαρμακευτική συμμόρφωση, παρεμβάσεις, ηλικιωμένοι.

Υπεύθυνος αλληλογραφίας: *Θεοδώρα Σκρέκα, τηλέφωνο: 6957461490, Πεζοπούλου 5, 11526, Αθήνα, Ελλάδα, , E-mail: theodoraskreka868@gmail.com*

Markou Panagiota[1], Stachtiari Dimitra[2], Stefou Asimina[3], Giannakopoulou Sofia[4], Skreka Theodora[5], Chondronikola Paraskevi[6], Markopoulou Georgia - Maria[7]

1. *Undergraduate Student, Department of Public and Community Health, School of Public Health, University of West Attica, Athens, Greece*
2. *Undergraduate Student, Department of Public and Community Health, School of Public Health, University of West Attica, Athens, Greece*
3. *Undergraduate Student, Department of Public and Community Health, School of Public Health, University of West Attica, Athens, Greece*
4. *Postgraduate Student, Global Health – Disaster Medicine, Medical School, National and Kapodistrian University of Athens, Greece*
5. *Postgraduate Student, General and Specialized Pediatrics: Clinical Practice and Research, Medical School, National and Kapodistrian University of Athens, Greece*
6. *Lecturer, Department of Public and Community Health, School of Public Health, University of West Attica, Athens, Greece*
7. *Lecturer, Department of Public and Community Health, School of Public Health, University of West Attica, Athens, Greece*

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ABSTRACT

Background: Medication adherence is defined as the extent to which a patient is able to follow prescribed instructions regarding the timing, dosage, and administration of pharmaceutical treatments. This includes adherence to guidelines concerning potential adverse effects, drug interactions, appropriate storage conditions, and additional information provided in the accompanying patient information leaflet, which contains critical safety and usage details. Older adults are particularly vulnerable to medication non – adherence, as they frequently present with multiple comorbidities that necessitate complex and often polypharmaceutical treatment regimens.

Aim: The purpose of this systematic review was to study the interventions that have been carried out in the last 5 years to promote medication compliance to older adults. The research questions are: "Which are the methods that have been used in interventions in order to promote medication adherence?" and "Which is the effectiveness of the interventions in order to promote medication adherence?"

Methods: Articles were searched in PubMed, Scopus and Google Scholar between March 2024 and April 2024 for the years 2018-2024 using the keywords "intervention", "elderly", "medication persistence" as well as synonyms.

Results: A total of 14 studies were included in the systematic review. The majority of interventions were effective in improving medication adherence in the elderly, enhancing their self-management and increasing their knowledge of rational use of medications. Interventions that included technology and innovative methods such as the use of comics were good strategies for improving the health status of the elderly. However, in order to be effective, interventions must be constantly supervised and continually supported.

Conclusion: In conclusion, it is deemed necessary to maintain the implementation of interventions aimed at promoting medication compliance, especially for patient with mental disorders.

Keywords: Medication adherence, interventions, elderly.

Corresponding Author: *Theodora Skreka, phone number: 6957461490, Pezopoulou 5, 11526, Athens, Email: theodoraskreka868@gmail.com*

INTRODUCTION

Medication Adherence is whether a patient can follow a health care provider's instruction regarding the proper use and administration of medications.[1] In other words, it means that the patient follows the instructions regarding consistency taking the medication, the dosage, the occurrence of adverse effects, the interaction of the drugs, storage, maintenance instructions as well as instructions written in the Patient Information Leaflet (PIL), which is included with each medicine and contains

important information. For this to happen requires a full understanding of the guidelines given so that the patient can implement them.[2] Medication adherence is a necessary condition for the success of medication therapy, in the shortest possible time and with the greatest effectiveness.[3] Older adults are more prone to medication non-adherence because they usually suffer from multiple diseases and need to take multiple medications.[4] Major causes of medication non-adherence in the elderly are low education level, lack of clarity, cost of medication and poor communication relationship with the health care providers.[5] The consequences of non-medication adherence are the deterioration of the patient's health, the prolongation of the treatment, the increase in hospitalization, the occurrence of adverse effects, the financial burden on the health system and even the increase in mortality.[6] A study that examined the economic impact of morbidity and mortality due to medication nonadherence concluded that the cost to the health system is 528.4$ billion per year.[7]

Epidemiological Data

Globally, individuals over the age of 60 have some form of disability at a rate more than 46%, while 250 million elderly individuals have a more severe form of disability.[8] Around eight in ten seniors take at least two prescription drugs, while 36% of seniors take five prescription drugs,[9] and individuals over the age of 65 appear to be the largest proportion of non-prescription drug users worldwide.[10] The rate of non-medication adherence is variable, with values starting at 7.1% and reaching 66.2 %. The success of adherence is assessed after the first year of treatment and 50% of medications are usually discontinued during the first six months.[11] A study was conducted in Ireland of elderly patients who had to be admitted to hospital. They investigated 3,760 incidents and concluded that 377 were due to adverse effects of medication. Among them, 268 incidents could not have been caused.[12] Regarding medication adherence in the elderly in Greece there are no sufficient epidemiological data. It is imperative to conduct comprehensive research and studies to ascertain the extent of the problem in Greece.

PURPOSE OF SYSTEMATIC REVIEW

The purpose of this systematic review is to examine interventions about Medication adherence in elderly that have been implemented worldwide from 2018 to 2024. The review questions were formulated based on PICO (Population, Intervention, Comparison and Outcomes)[13] and are as follows:

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1. Which are the interventions that have been conducted in order to promote medication adherence?
2. Which are the methods that have been used in interventions in order to promote medication adherence?
3. Which is the effectiveness of the interventions in order to promote medication adherence?

METHODS

The systematic review was conducted using three databases: PubMed, Scopus and Google Scholar. The query was based on the PICO model[13] (Fig. 1) and the selected articles were those that have been published from 2018 until 2024. Literature research lasted from 18th of April 2024 to 10th of May 2024, and was conducted by 3 researchers. The query that was used for PubMed was:

(elderly or aged or aging or old* or "elderly people" or "older people" or "older patient" or "elderly patient") AND ("medication adherence" or "medication compliance" or "medication persistence" or "drug* adherence" or "drug compliance") AND (intervention or action* or program* or "health promotion" or "prevention and control" or interference*)

Additionally, the query that was used for Scopus was:

(elderly) OR (aged) OR (aging) OR (old*) OR ("elderly people") OR ("older people") OR ("older patient") OR ("elderly patient") AND ("medication adherence") OR ("medication compliance") OR ("medication persistence") OR ("drug* adherence") OR ("drug compliance") AND (intervention) OR (action*) OR (program*) OR ("health promotion") OR ("prevention and control") OR (interference*)

The relevant one that was used for Google Scholar:

(elderly OR aged OR aging OR old OR "elderly people" OR "older people") AND ("older patient" AND "elderly patient") AND ("medication adherence" OR "medication compliance" OR "medication persistence" OR "drug adherence" OR "drug compliance") AND (intervention OR action OR program OR "health promotion" OR "prevention and control" OR interference)

This systematic review was conducted and reported using the PRISMA guidelines[14] (Fig. 2). The included criteria for the literature search were: 1) Articles that include interventions with aim to promote medication adherence only in elderly (>60 years old), 2) Articles that include interventions for elderly with chronic diseases, 3) Articles published in English language, 4) Articles that include interventions which contain evaluation methods. Nevertheless, exclusion criteria for the research were: 1) Articles that include interventions which participate caregivers or relatives, 2) Articles that include interventions which participants live in

hospital or nursing homes, 3) Articles that include interventions which participants have been diagnosed with cancer or HIV, 4) Articles that were part of dissertations, systematic reviews and meta-analyzes. Moreover, the strategy of research contained conditions as "AND/OR".

OUTCOMES

Firstly, they were identified 8.017 articles (5396 from Scopus, 2.444 from PubMed and 177 from Google Scholar). After that 2.554 articles were duplicates and as a result, they were excluded. The rest 5.463 were chosen to be checked for eligibility. 4.869 articles were discarded after the title and abstract screening and 594 stood out as potentially relevant to the topic. Nevertheless, 9 of them were not retrieved, so they were also rejected. The final selection was made based on determined criteria: 1) 18 articles were not in English, 2) 36 articles focused on Medication Adherence on patients with cancer, 3) 277 articles were excluded due to age criteria (under 60 years old), 4) 79 articles were systematic reviews, 5) 96 were focused on HIV patients, 6) 18 articles included participation of caregivers or relatives, 7) 38 articles were conducted in Hospitals or nursing homes and 8) 9 of them were not related to chronic conditions.

Overall, 14 articles met the inclusion criteria. All of the above are presented in the flow chart. (fig.2)

RESULTS

Based on table 1 the studies of Zárate-Bravo E. et al.,[25] Desteghe L. et al.,[15] and Leung A.Y.M. et al.[28] had the most significant results. More specifically, in the study conducted by Zárate-Bravo E. et al.,[25] the treatment group's medication adherence increased with the use of MAD (Medication Ambient Display) from 80% at baseline to 95.97%. The treatment group's medication adherence was higher than that of the control group (95.97% vs. 88.18%). The study revealed that the external cues provided by MAD not only enhanced medication adherence in seniors but also enabled family caregivers to take on a more proactive role. The study by Desteghe L. et al.[15] shows that telemonitoring-based feedback can greatly enhance medication adherence, particularly in individuals who had previously had lower levels of adherence. This Intervention can be cost-effective, especially when paired with less expensive telemonitoring devices and advanced software. That way the cost per prevented stroke can be reduced. Telemonitoring had a significant improvement in medication and regimen adherence rates (97.4% vs. 93.8%, respectively). Also, direct feedback improved further those results, with a decrease in unprotected days to 1.5 and raised regimen and taking adherence to 96.8% and 99.0%, respectively. While unprotected days were

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similar, adherence was much higher with the once-daily (OD) NOAC (non-vitamin K antagonist oral anticoagulants) than with the BID (bis in die or twice a day) NOAC ($P = 0.272$ respectively $P = 0.251$). The use of comic books as an educational tool had really important improvements in medication compliance, reducing both knowledge deficiencies and storage problems. This was evident from the study conducted by Leung A.Y.M. et al.[28] All measured areas (Medication compliance, Knowledge deficiency, Drug storage problems) had highly significant p-values supporting the statistical analysis that showed compelling evidence for these changes. With clear reductions in medication non-compliance (−0.273, $p < 0.001$), knowledge deficiency (−0.161, $p < 0.05$), and drug storage concerns (−0.180, $p < 0.001$), verbal advise decreased the mean total MCKS (Medication Compliance, Knowledge and Storage) score from 1.55 to 0.94, indicating better compliance. Also, the comic book intervention reduced the mean total MCKS score from 1.88 to 1.40, showing significant improvements in medication compliance (total score) (coefficient = −1.018, $p < 0.001$), reduced knowledge deficiency (coefficient = −0.236, $p < 0.05$), and reduced storage problems (coefficient = −0.293, $p = 0.001$).

Data Extraction and Quality Assessment

The articles that were included in this systematic review, were evaluated in terms of risk of bias using the revised tool Cochrane risk of Bias (RoB-2),[29] (Fig.3) for randomized studies, the National Institutes of Health (NIH),[30] quality assessment tool for non-randomized and observational studies (Fig.4),(Fig.5) and finally the Joanna Briggs Institute (JBI),[31] critical appraisal checklist tool for experimental studies (Fig.6).

DISCUSSION

A general overview of the interventions suggests that the majority of older patients exhibited medication adherence. From the fourteen studies, there are three in which a significant increase in medication adherence throughout the intervention was observed and one that had the same positive outcomes at the follow up.[15,19,24,28] Similarly, five interventions were also effective, but in those studies the medication adherence was notable higher in the intervention groups than the control groups.[16,20,22,23,27] On the other side, Delavar F. et al, proved that through “self-management education tailored to health literacy” medication adherence can be increased but there were no significant differences between the intervention and the control group.[17] The study by Zárate-Bravo E. et al, was quite effective during the intervention phase, but afterwards in the postintervention phase there was an obvious decrease. [25] As a final point, there are three

interventions that did not improve medication adherence at elders at all. [18,21,26]

Among the studies examining medication adherence in older adults with cardiovascular diseases, four report a positive effect on adherence, whereas one shows no improvement.[15-19] By contrast, studies focusing on individuals with bipolar disorder and multiple sclerosis consistently demonstrate positive outcomes. However, in other neurological problems, such as Mild Cognitive Impairment, the beneficial effects appear to be confined to the duration of the intervention and decline thereafter.[25,27,28,] Similarly, among the studies investigating medication adherence in patients experiencing polypharmacy, three—one involving comorbidities and two involving multimorbidity—indicate positive results, while one reports no response. [21,22,23,24] Finally, the study addressing medication adherence in individuals with glaucoma did not demonstrate any improvement.[26]

Regarding the methodology, of the 14 interventions studied, eight of them focused on the education of the elderly respecting medication adherence by providing educational sessions on a monthly or weekly basis. Of these, five demonstrated positive outcomes, whereas three showed no improvement.[16,17,19,21,22,25,26,27] Similarly, four interventions incorporated telephone communication, either to provide guidance or to monitor participants' adherence. [15,17,18,22] Notably, three of these resulted in improved medication adherence, while one did not. Two interventions successfully enhanced adherence promoted the use of an application, which reminds the seniors to take their medication.[19,24] As well positive effects seem to have the use of materials to enhance the organization of medicines, such as specialized carrying bags or pill storage boxes.[19,23] Three interventions employed multimodal approach that combined several strategies to promote medication adherence, two of them were successful, while one was not.[20,25,28] The intervention by Raj JP et al.,[20] included systematic training, phone calls at regular intervals, and a patient diary to record the day of medicine intake.[20] The intervention by Leung AYM et al.,[28] was conducted in two phases. As part of the educational process, educational comics were also used, which had information about the proper management of medicines. Furthermore, 2 home visits were implemented in each phase of the intervention. [28] In contrast, the intervention by Zárate-Bravo E et al.[25] Despite combining educational sessions, home visits, and the use of the MAD (Medication Ambient Display) application, exhibited a different trajectory: although initially effective, adherence declined after the end of the study (participants during the intervention were trained to be able to use the MAD application,

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which helps the elderly to take their medication at the right dosage and at the right time of the day).[25]

Limitations

There are some limitations that probably have resulted in missing some relevant articles. First and foremost, three databases (PubMed, Scopus, Google Scholar) were used for the literature investigation, and it is possible that some articles were not included in any of those. Furthermore, the research was restricted only to English language. Also, there is a possibility that the keywords used in the search may not have retrieved all the necessary studies, leading to an incomplete representation of existing literature. An important limitation constitutes the fact that a small number of articles were eliminated while they were not retrieved.

CONCLUSION

The objective of this systematic review was to investigate the interventions that have been used globally to enhance medication adherence in the older population. Most of them were extremely successful in improving medication adherence rates among the elderly. The intervention conducted by Leung AYM et al.[28] was notably groundbreaking and unique. They used instructional comics to enhance medication adherence, setting it apart from prior programs that lacked a comparable approach. Nevertheless, the global tally of treatments done indicates a dearth of research and actions aimed at resolving this issue. Very few interventions have been carried out in Europe, and no interventions have been found in Greece specifically aimed at promoting medication adherence among the elderly. Ultimately, it is crucial for the scientific community to do further research and implement interventions on a worldwide scale to enhance medication adherence among the elderly. The available data clearly indicate that this is a significant public health concern, however there is a lack of adequate information and initiatives addressing this issue.

STATEMENTS AND DECLARATIONS

Disclosure Statement

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ΠΑΡΑΡΤΗΜΑ

Title	Authors	Country	Population	Type of study	Method	Evaluation	Results
Elderly with Cardiovascular Diseases							
Telemonitoring-based feedback improves adherence to non-vitamin K antagonist oral anticoagulants intake in patients with atrial fibrillation (2018) [15]	Desteghe L, et al	Finland	48 patients with atrial fibrillation who were receiving medication (mean age 72 ± 9 years) (male)	Randomized controlled trial	Daily Telemonitoring, observation without intervention, telephone communication **There was no Control group**	47 filled out the Eight-item Morisky Medication Adherence Scale and a questionnaire about their experience	Telemonitoring-only already led to very high taking and regimen adherence (97.4% vs 93.8%, respectively). However, direct feedback further improved both to 99.0% and 96.8%, respectively ($P < 0.001$ respectively $P = 0.002$). Observation without daily monitoring resulted in a significant waning of taking adherence (94.3%; $P = 0.049$). Taking adherence was significantly higher for OD (once daily) compared to BID (bis in die or twice a day) NOAC (non-vitamin K antagonist oral anticoagulants), although unprotected days were similar.
Effect of an Educational Program based on Health Belief Model on Medication Adherence in Elderly Patients with Hypertension (2019) [16]	Yazdanpanah Y. et al	Iran	60 people 60 years old with hypertension (male/female)	Randomized controlled trial in groups	**Intervention group:** Education on medication adherence through conferences, Medication leaflets **Control group:** typical routine services provided by the centers	2 questionnaries were distributed to 60 people [Morisky Medication Adherence Scale (MMA-8) and demographic- medical questionnaire]	The mean medication compliance score was 6.7 ± 0.5 (significantly higher than the control group (3.7±1.0) (P<0.001)). The mean medication adherence score in the intervention group increased significantly (P<0.001).

The effects of self-management education tailored to health literacy on medication adherence and blood pressure control among elderly people with primary hypertension: A randomized controlled trial (2020) [17]	Delavar F et al	Iran	118 elderly people with uncontrolled primary hypertension and insufficient health literacy (male/female)	Randomized controlled trial in groups	**Intervention group**:Weekly Sessions, phone sessions, educational materials, exclusive provision of assistance services **Control group:** Usual care	54 from intervention group and 58 from control group: Demographic questionnaire, eight-item Morisky medication adherence scale, data sheet	After the intervention, between-group comparisons adjusted for pretest scores showed a significant decrease in mean systolic and diastolic blood pressure scores and an increase in medication adherence due to intervention ($P < 0.05$). However, the proportions of controlled systolic and diastolic blood pressure were not statistically significantly different between groups ($P > 0.05$).
Randomized trial of telephone counselling to improve participants ' adherence to prescribed drugs in a vascular screening trial (2020) [18]	Qvist I. et al	Denmark	1446 participants, 65- to 74-year-old men diagnosed with abdominal aortic aneurysm (AAA), peripheral arterial disease (PAD) or high blood pressure (HB) (male)	Randomized controlled trial in groups	**Intervention group:** Telephone interview, consultation. **Control group:** usual care	1446 people were evaluated. The assessment was done by telephone.	There were no differences between the groups in relation to composite PDC (proportion of days covered) (P = .10; adjusted P = .20). PDC to statin was significantly higher in the intervention group over the first 6 months of follow-up (P = .04; adjusted P = .03). 63.2% and 53.4% of participants were classified as adherent in the intervention group and the control group, respectively (difference: proportion difference (PD) 9.8% (95% CI: 0.5-19.0); adjusted: 10.1% (95% CI: 0.9-19.4)) (Table 2). There were no differences between the groups in relation to the composite PDC for adherence or to antithrombotic treatment (P = .84; adjusted P = .70) or

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							antihypertensive treatment (P = .64; adjusted P = .83).
The use of an electronic medication organizer device with alarm to improve medication adherence of older adults with hypertension (2021) [19]	Vieira LB et al	Brazil	32 elderly patients diagnosed with hypertension (male/female)	Quali-quantitative, prospective, before-and-after study	Conducted using 2 methodological approaches: qualitative-quantitative, use of Supermed as a medication reminder device, monthly meetings with the elderly, provision of a bag to carry medicine boxes. **There was no Control group.**	32 participants completed the Morisky Medication Adherence Scale, semi-structured interview, self-report questionnaires	Regarding medication adherence, 78.1% of patients changed from "less adherent" to "more adherent" after the Supermed intervention (p<0.001). Accordingly, the differences between mean systolic and diastolic blood pressure between before and after the intervention were 21.6mmHg (p<0.001) and 4.7mmHg (p<0.001) respectively.
Elderly with either one disease or with multimorbidity							
Effect of behavioral intervention on medication adherence among elderly with select non-communicable diseases (ENDORSE): Pilot randomized controlled trial (2020) [20]	Raj JP, Mathews B.	India	46 elders with select non-communicable diseases (mean age 69) (male)	Randomized controlled trial in groups	**Intervention group:** systematic education, patient diary to mark daily medicine intake, periodic telephone reminders **Control group:** Usual care	46 participants completed a standardized semistructured case record format	The reported pill count (RPC) in control and intervention arms at the third month were 78.20% and 91.88% (*P* = 0.007), whereas at 6 months they were 68.64% and 83.08% (*P* = 0.003), respectively. Similarly, change in RPC in intervention arm between baseline and the third month (mean difference 24.08%, *P* = 0.001), and between baseline and the sixth month (mean difference 15.280%, *P* = 0.006) were statistically significant. However, the RPC between the third and sixth month showed a significant decline (mean

							difference 8.8%, *P* = 0.016).
Elderly with Polypharmacy							
The Effect of a Comprehensive, Interdisciplinary Medication Review on Quality of Life and Medication Use in Community Dwelling Older People with Polypharmacy (2021) [21]	Bosch-Lenders D et al	Netherlands	770 patients aged 60 years and older with polypharmacy (mean age 75 years) (male/female)	Randomized controlled trial in groups	**Intervention group:** A comprehensive mobilization-education program was implemented out for one month. **Control group:** Routine clinical care, measuring patients' medication adherence, before, after and two months after the intervention	508 elders completed the Measurement of quality of life using the Short Form 36 Health Survey (SF-36) and EuroQol 5-Dimension five-level (EQ-5D), as well as the patient's functional status using the Activities of Daily Living Scale.	A positive effect on SF-36 mental health (estimated mean was stable in the intervention, but decreased in the control condition by -6.1, p = 0.009,) was found with reduced number of medications at follow-up compared to the control condition. No significant effects were found on other subscales of QoL, ADL, iADL, or medication adherence
Effects of a nurse-led medication self-management intervention on medication adherence and health outcomes in older people with multimorbidity: A randomized controlled trial (2022) [22]	Yang C, et al	China	136 elderly with multimorbidity (male/female)	Randomized controlled trial in groups	**Intervention group:** They received a medication self-management intervention programme: Training sessions, 2 follow-up phone calls **Control group:** Usual care	107 answered the Questionnairie [Medication Adherence Report Scale (MARS-5) AMS)	Improved medication adherence was observed in the intervention group at a 3-month follow-up compered to baseline, although between group differences were not significant [medication adherence (β = 1,63, p = 0,034), in the knowledge of medication (β = 2,61, p < 0,001 and β = 2,26, p < 0,001 after 3 months), in medication self-efficacy (β = 3,22, p < 0,001 and β = 1,87, p = 0,015 after 3 months)]
Rational medication management mode and	Tang Q. et, al	China	618 elderly patients with multimorbidity, aged 65-	Cohort Study	**Intervention group:** Implementation of	618 Adjusted knowledge-belief-	**Primary Outcome:** At 90 days, the number of medications was achieved by 3.88 in the

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its implementation effect for the elderly with multimorbidity: A prospective cohort study in China (2022) [23]			75 years (male/female)		rational medication management involving physicians, pharmacists, assistants, nurses, elderly and families. Guidance was provided through a handbook and a pillbox. **Control group:** Implementation of conventional medication management.	behavior scales for rational medication were completed	intervention group, while 4.32 in the control group, which had a significant difference between the two groups ($P = 0.001$). And patients with polypharmacy were reduced by 59.55% in the intervention group having a significant difference compared with the control group ($P < 0.001$).
NPS MedicineWise application in supporting medication adherence in chronic heart failure: an acceptability and feasibility pilot study(2023) [24]	Chapman-Goetz J. et al	Australia	55 individuals (mean age 63 years) with comorbidities (male/female)	Randomized controlled trial	**Intervention group:** Use of an application for medication reminders at each dosing interval. **Control group:** Received standard care without access to the application throughout the study.	49 questionnaires were completed, including the Self-care of Heart Failure Index (SCHFI), SEAMS (Self-Efficacy for Appropriate Medication Use Scale), medication adherence and knowledge scales, EQ-5D-5L, Short Form 36 Health Survey version 2 (SF-36v2),	Approximately half of respondents reported managing HF and medications better by using the MedicineWise app. Most respondents expressed satisfaction with the in-app messages and pharmacists' phone calls. The intervention participants demonstrated a significant improvement in the SEAMS (Self-Efficacy for Appropriate Medication Use Scale) between baseline and 6-months follow-up.

						Depression Anxiety and Stress Scales (DASS-21), and SCHFI.	
Elderly with Neurological Problems							
Supporting the Medication Adherence of Older Mexican Adults Through External Cues Provided with Ambient Displays: Feasibility Randomized Controlled Trial (2020) [25]	Zárate-Bravo E. et al	Mexico	16 seniors over 60 who were taking at least 3 prescribed medications (polypharmacy) with mild cognitive impairment (male/female)	Randomized controlled trial in groups	**Intervention group:** Pill Counting Technique, Training and System personalization, MAD (Medication Ambient Display), Home Visit **Control group:** Usual care, Pills counting.	16 participants completed the 10-item Short Portable Mental Status Questionnaire, Morisky Medication Adherence Scale-8 (MAQ-8), Medication Management Instrument for Deficiencies in the Elderly (MedMaIDE)	The treatment group improved adherence behavior from 80.9% at baseline to 95.97% using MAD (Medication Ambient Display) in the intervention phase. This decreased to 76.71% in the post-intervention phase, when MAD was no longer used. Furthermore, the medication adherence rate of the treatment group (95.97%) was greater than that of the control group (88.18%) during the intervention phase
Elderly with Glaucoma							
The Effect of an Educational Intervention on Adherence to Intraocular Pressure-Lowering Medications in a Large Cohort of Older Adults with Glaucoma (2018) [26]	Fiscella R. et al	United States of America	1800 patients aged 65–89 years who had ≥ 1 diagnosis of glaucoma, they had received at least 1 relevant medication in the last 6 months and enrolled in the MAPD program during the 6-month follow-up and in the	Randomized controlled trial	Patients and physicians were randomized to cohorts A (no interventions), B (physician intervention), and C (patient and physician interventions) Physicians in cohorts B and C received information on the	Control of the administration days IOP-lowering medication	The mean PDC (proportion of days covered) was 0.54–0.56 in all cohorts. At 12 months, ≥ 90.5% of physicians and ≥ 75.5% of patients remained in the study. The mean PDC was 0.53–0.54 in all cohorts. No statistically significant differences were observed between cohorts in PDC and adherence.

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			previous 12 months. (male/female)		model, adherence, and patient profiles at baseline and months 3, 6, and 9. Patients in cohort C received educational materials on glaucoma and adherence (same schedule). **There was no Control group**		
Elderly with Mental Disorders							
The effect of comprehensive individual motivational-educational program on medication adherence in elderly patients with bipolar disorders: An experimental study (2023) [27]	Tahghighi H. et al	Iran	62 elderly individuals (aged 60 years and older) with bipolar disorders who have been admitted to a specific hospital (male/female	Experimental study	**Intervention group:** 1 month of mobilization program - (four sessions of 30-45 minutes). **Control group:** routine clinical care was provided	62 participants completed the Demographic-Medical Information Questionnaire and the Morisky Medication Adherence Inventory.	There was a significant difference in the mean medication adherence score of the elderly by time (P < 0.001), group (P < 0.001), and the crossover between group and time (P < 0.001). In the intervention group, paired t-tests showed significant differences before and after the intervention (P < 0.001), as well as between different time points. In the control group, no significant differences were observed between the intervention and post time points.
Elderly with Multiple Sclerosis							
Improving health literacy and medication compliance through comic	Leung AYM. et al	China	165 people (mean age 81.7 years) with multiple sclerosis (male/female)	Quasi-experimental study	**Two intervention phases:** Two home visits per phase, counseling	165 individuals completed the Geriatric Depression Scale,	There was a significant improvement in medication compliance (total score) (coefficient = −1.018, p < 0.001), reduced knowledge deficiency (coefficient =

books: a quasi-experimental study of Chinese community-dwelling older adults (2018) [28]					of elderly individuals regarding reading, understanding, and interpreting medication labels, and proper storage of medications. Two assessments (T2, T3), educational comics, re-evaluation (T4), use of the Chinese Health Education Scale for Chronic Care, evaluation of medication adherence through the Medication Adherence, Knowledge, and Storage Scale, and Generalized Linear Mixed Models. **There was no Control group.**	assessed cognitive function using the Montreal Cognitive Assessment (MoCA), and used the Medication Compliance, Knowledge, and Storage (MCKS) Scale and the Chinese Health Literacy Scale for Chronic Care (CHLCC).	−0.236, $p < 0.05$), and reduced storage problems (coefficient = −0.293, $p = 0.001$) after using comic books.

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FIGURE 1: PICO Framework Guiding selection criteria for Evaluating Medication Adherence in Elderly.

PICOs framework guiding selection criteria	
Population:	("elderly" OR "aged" OR "aging" OR "old" OR "elderly people" OR "older people" OR "older patient" OR "elderly patient")
Interventions:	(intervention OR action OR program OR "health promotion" OR "prevention and control" OR interference)
Comparators:	Elderly people (>60 years old) with chronic diseases
Outcomes:	("medication adherence" OR "medication compliance" OR "medication persistence" OR "drug adherence" OR "drug compliance")
Studies	Randomized Controlled Studies, non-randomized studies, Observational studies. Publication date 2018 – 2024 Available in English language

FIGURE 2. PRISMA flow diagram.

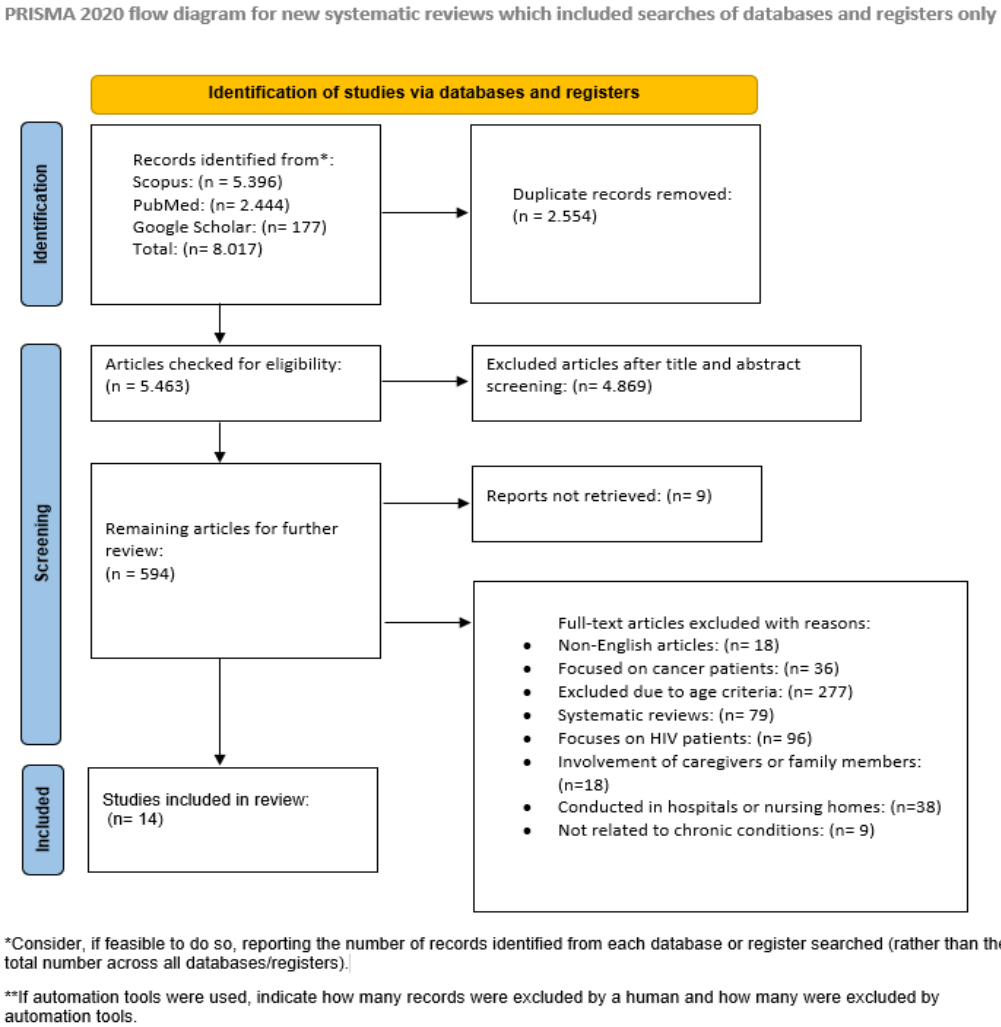

FIGURE 3. Evaluation of randomized controlled trials with Cochrane risk of Bias (RoB-2) tool.

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Desteghe et al. 2018	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns
Yazdanpanah et al. 2019	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns
Delavar et al. 2019	Low	Some concerns	Low	Low	Some concerns	Some concerns
Qviot et al. 2020	Low	Some concerns	Low	High	Some concerns	High
Raj et al. 2020	Some concerns	Some concerns	Low	High	Some concerns	High
Boch-Lenders et al. 2021	Some concerns	High	Low	High	Some concerns	High
Zavate-Bravo et al. 2020	Some concerns	Some concerns	Low	High	Some concerns	High
Chapman-Goetz et al. 2023	High	High	Low	High	Some concerns	High
Yang et al. 2022	Low	High	Low	High	Some concerns	High
Fiscella et al. 2018	Some concerns	High	Low	High	Some concerns	High

FIGURE 4. Quality Assessment for Before and After Studies by National Institutes of Health (NIH) tool.

NIH Quality Assessment Tool for Before and After Studies

Study	Vieira et. al (2021)
Question	Answer
1. Was the study question or objective clearly stated?	YES
2. Were eligibility/selection criteria for the study population prespecified and clearly described?	YES
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	CD
4. Were all eligible participants that met the prespecified entry criteria enrolled?	YES
5. Was the sample size sufficiently large to provide confidence in the findings?	NO
6. Was the test/service/intervention clearly described and delivered consistently across the study population?	NR
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	YES
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	NR
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	NR
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	YES
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	YES
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	YES

*CD = Cannot Determine ** NA = not applicable ***NR = not reported

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FIGURE 5. Quality Assessment for Cohort Studies by National Institutes of Health (NIH) tool.

NIH Quality Assessment Tool for Cohort Studies

Study	Tang et. al (2022)
Question	Answer
1. Was the research question or objective in this paper clearly stated?	YES
2. Was the study population clearly specified and defined?	YES
3. Was the participation rate of eligible persons at least 50%?	YES
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	YES
5. Was a sample size justification, power description, or variance and effect estimates provided?	YES
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	CD
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	YES
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	NA
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES
10. Was the exposure(s) assessed more than once over time?	YES
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES
12. Were the outcome assessors blinded to the exposure status of participants?	NO
13. Was loss to follow-up after baseline 20% or less?	NO
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	YES

*CD = Cannot Determine ** NA = not applicable ***NR = not reported

FIGURE 6. Critical Appraisal for Experimental Studies with the Joanna Briggs Institute (JBI) tool.

JBI critical appraisal tool for the assessment of risk of bias for quasi-experimental

Studies	Tahghighi et. al (2023)	Leung et. al (2018)
Question	Answer	Answer
1. Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	YES	YES
2. Was there a control group?	YES	NO
3. Were participants included in any comparisons similar?	YES	YES
4. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	NO	NO
5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	YES	YES
6. Were the outcomes of participants included in any comparisons measured in the same way?	YES	YES
7. Were outcomes measured in a reliable way?	YES	YES
8. Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	YES	YES
9. Was appropriate statistical analysis used?	YES	YES