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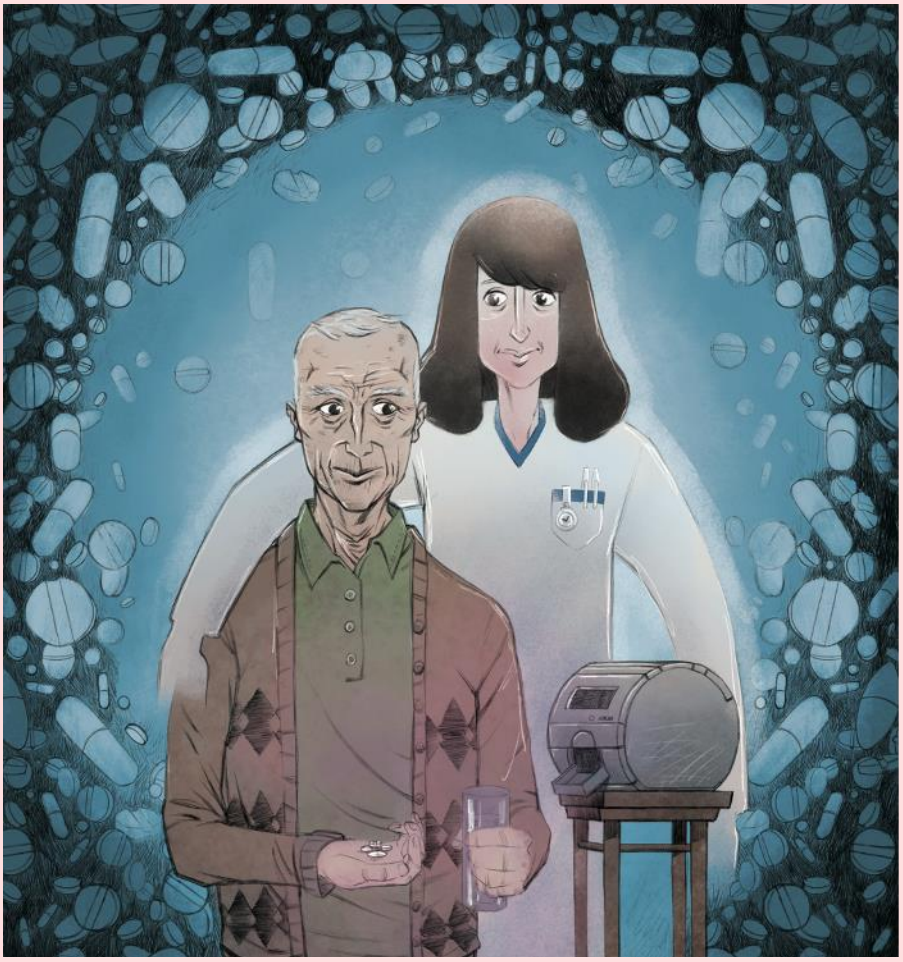
Masteroppgave

Automatic medical dispensers and adherence in home dwelling adults: A scoping review.

THE RIGHT MEDICINE?



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Avansert Geriatrisk Sykepleie

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Institutt for helse og samfunn,
Avdeling for folkehelsevitenskap.
Det medisinske fakultet

UNIVERSITETET I OSLO
DET MEDISINSKE FAKULTETET
Institutt for helse og samfunn, Avdeling for folkehelsevitenskap.
Boks 1130 Blindern, 0318 Oslo

Navn:	**Dato:**
Gro Oscarsson-Nagel	15.11.2023

Tittel og undertittel:

Automatic medical dispensers and adherence in home dwelling adults: A scoping review.

The right medicine?

Sammendrag: **Bakgrunn:** Manglende etterlevelse av medisininntak er en utfordring for enkeltpasienter og helsevesenet. Helseteknologi blir systematisk tatt i bruk i kommunale helsetjenester for å spare ressurser. Automatiske medisindispensere plassert i pasienters hjem er et tiltak for å redusere medisinfeilene, øke etterlevelse, og spare ressurser i hjemmesykepleien, men det er begrenset kunnskap om effekten.

Formål: Hensikten med denne scoping reviewen er å kartlegge kvantitativ forskningslitteratur om automatiske medisindispensere og etterlevelse hos hjemmeboende voksne, og å beskrive metodene studiene anvender for målinger av etterlevelse.

Metode: Relevante databaser ble søkt for artikler på engelsk og skandinaviske språk. Inklusjonskriteriene var artikler publisert fra 2013 som undersøkte automatiske medisindispensere med lys og/eller lydsignaler som leverer multidose medisiner, etterlevelsesutfall, voksne hjemmeboende ≥ 18 år. Søket identifiserte 119 studier hvorav 10 ble inkludert. Arksey og O´Malley´s teoretiske rammeverk for scoping reviews ble brukt. Dataekstraksjon ble gjort og resultatene er presentert som en narrativ syntese.

Resultater: De ti inkluderte studiene viser gjennomgående at automatiske medisindispensere ser ut til å føre til bedre etterlevelse. Pasienter som i utgangspunktet hadde god etterlevelse virker å få enda høyere etterlevelse ved bruk av automatisk medisindispenser. Pasienter med mer kompleks sykdom ser ut til å ha best nytte av automatisk dispenser når denne kombineres med andre tiltak, for eksempel regelmessig oppfølging rettet mot manglende etterlevelse, riktig medisinbruk (inkludert legemiddelgjennomganger), og helseutfordringer generelt. De inkluderte studiene var små, karakterisert av stor heterogenitet og brukte svake design, som begrenser muligheten til å trekke konklusjoner. Etterlevelse blir definert og målt forskjellig som begrenser muligheten til sammenligning på tvers av studiene.

Konklusjon: Pasienter som i utgangspunktet hadde god etterlevelse fikk enda bedre etterlevelse ved bruk av automatisk medisindispenser. De med komplekse kroniske sykdommer kan trenge personlig oppfølging i tillegg for å ha nytte av automatiske medisindispensere. Det er behov for flere studier med høy kvalitet for å undersøke nytte og effekt av medisindispensere på etterlevelse, spesielt hos eldre.

Nøkkelord: hjemmeboende voksne, automatiske medisin/multidose dispensere, etterlevelse

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Name:	**Date:**
Gro Oscarsson-Nagel	15.11.2023

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Abstract: **Background**: Medication non-adherence represent a challenge for health-care systems globally. Technological innovations are systematically introduced into home health care services to increase sustainability. Automatic medical dispensers are placed in patient´s homes to reduce non-adherence and medication errors, enhance patient autonomy and save home-carers time, but the evidence for their effectiveness is limited.

Purpose: The aim of this scoping review is to map the last ten years of quantitative reasearch studies on medication packaging devices and adherence in home-dwelling adults, and to describe the methods used for measuring adherence.

Method: A comprenensive search was done in relevant databases for articles in English and Scandinavian languages. Inclusion criteria: articles published from 2013 examining automated medical devices with visual and/or audio reminder signals delivering multimedication, medical adherence outcomes, home dwelling adults $\geq$ 18 years. From a total of 119 articles, 10 were included. Arksey and O´Malleys ~~(2005)~~ Theoretical Framework for Scoping Reviews was used. After data extraction, a narrative synthesis was done.

Results: The ten included studies indicated overall positive outcomes on medical adherence. Patients with small non-adherence problems seem to benefit even more from an EMD . Patients with more complex chronic illness, seemed to benefit the most from EMD´s when used in combination with other supplementary interventions and regular follow ups addressing non-adherence, medication use (including pharmacy screens) and health issues in general. The included studies were small, characterized large heterogeneity, and weak designs, which may affect the ability to draw conclusions. Adherence was defined and measured differently between the studies which leaves it challenging to compare adherence outcomes, and to conclude.

Conclusion: Patients who are already adherent, became more adherent using EMDs. Those with complex chronic illnesses may need personal follow-up in addition to the EMDs to benefit from such tools. Future high quality studies are needed on EMDs usefulness and effect on adherence, especially in in the elderly.

Key words: home-dwellers, automatic medical dispensers, adherence, non-adherence

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Contents

Introduction

Medication non-adherence is one of the largest challenges of health-care systems globally, and WHO (2003) notes approximately 50% of people with chronic disease in western countries do not take medication as prescribed. Consequences of poor medication-taking ability may be treatment failure of chronic disease and adverse drug reactions leading to physician-visits, acute and long-term hospitalizations, increased healthcare-costs and poor quality of life, all of which avoidable (DiMatteo et al., 2004). According to the UN Report «World Population Prospects 2022», the proportion of aged persons 65 years and older in Europe and North America will double to 22% by 2050 and individuals aged 80 years and over are expected to triple, representing the fastest growing segment of the population. With a growing aged population prescription usage and related health care expenses are inticipated to increase proportionally (Miller & Solai, 2013). As governments seek to rig sustainable health care systems for ongoing and future needs, technological innovations are systematically introduced into home care health services in Norway (NOU 2011:11; Meld. St.29 (2012-2013); Velferdsteknologiprogrammet, 2023). One of the suggested solutions to improve medication adherence in an aging population are automatic medical dispensers placed in peoples´ homes.

Adherence to a medication regimen involves the right medication in the right quantity being taken at the right time, *and* for the right duration of time (Lam et al., 2015). A person is generally considered adherent if he or she takes between 80% and 120% of medication over a given time period, in other words can non-adherence lead to both under- and overutilization of medication (WHO, 2003). There are two broad understandings of non-adherence: Intentional non-adherence associated with poor motivation and negative beliefs and/or negative experiences with treatment, and non-intentional adherence which is associated with demographic and socioeconomic factors complicating access to, and use of medication (Lam et al., 2015). Age and/or stage of illness may generate practical problems due to poor instructions, complexity and quantity of regimen, poor memory, cognitive defects or difficulty in opening packaging (DiMatteo et al., 2004; Horne et al., 2005). The most acknowledged factors for non-adherence are doses missed because of busy lifestyles, changing medication

schedules and forgetfulness (Stone, 2001). A review by Osterberg et al. (2005) identified strategies to improve adherence including simplifying regimen dosing, the use of pillboxes to organize daily doses, and cues to remind patients to take medications.

Manual pillboxes or dosettes are widely used, they are cheap and useful tools for managing single and multimedication regimens. The dispensers have developed from simple plastic containers *(ill. 1*) to technically advanced solutions (*ill. 2)* to target non-adherence due to forgetfulness and problems with dexterity and vision. Features may be light and sound alarm, display with written instructions and the possibility of sending electronic messages to a caregiver when a dose is not removed (Faisal et al., 2021).

Ill. 1: Example pillbox «Dosett ®)»

The latest and most advanced electronic multidose dispensers on the market in Norway contain a roll of small plastic pouches *(ill. 4*) with medications prepacked from a specific pharmacy, called automatic or multidose drug-dispensing (ADD or MDD) (Apotek1, 2023). Technical programming and medicine installation for home use are set up individually by home care nurses. Rolls of 1-2 weeks of medications are installed in the dispenser and a pouch of medicine is discharged when the patient push a button at a preprogrammed hour, promted by a light and sound alarm (music or a voice with instructions to take the medicine). When a pouch is not removed within a set time limit it is automatically moved to a separate unreachable (for the patient) chamber and an electronic message is sent to a caregiver. Some dispensers have a display with written instructions (*ill. 3).* They have become widely in use in Scandinavia, and some other European countries. The multidose dispensers were introduced in Norway 2014-2015, with the intention to enhance patient safety by minimizing medication errors and non-adherence, enhance patient autonomy, and finally save home care nurses time (OE-report, 2021). Home care visits to patients who only require help in the form of delivery of medication can now be substituted with a dispenser. According to statistics from The Norwegian Directorate for Health (2020),

Ill. 2: Example electronic pillbox «Pilly ®)»

Ill. 3: Example dispenser with multidose bag «Evondos ®».

Ill 4: Multidose bag

there were approximately 5712 dispensers in use in Norway 2020, an increase of 215% from 2019.

A systematic review on electronic medication devices´effect on medication adherence found mixed results suggesting both increase and decrease in adherence, and devices recording a dosing event and integration into the care delivery system were associated with better adherence (Checchi et al., 2014). In another systematic review, Paterson and colleagues (2016) studied multi-compartment medication devices in a sample of older adults and found varied but positive effect on adherence. Both noted that small samples and poor methodological quality urges a need for higher quality evidence. A more recent scoping review by Kurup et al., published in 2020 examined effectiveness of electronic medication packaging devices on medication adherence and found that although such devices may improve adherence no strong conclusions could be drawn, especially for the older population. None of the above mentioned reviews included studies evaluating multidose dispensers with sachets. Furthermore, two Norwegian studies published on health care workers experiences with automatic medicine dispensers in patient´s homes argue that such devices can improve efficiency in healthcare services and contribute to patient independence when implemented in the right way. However safety of medication practices and quality of care remains concerns (Nakrem, 2018; Kleiven, 2020). The current state of knowledge on automatic medical dispensers and adherence in adult home dwellers suggests varying evidence for their effect. Since technology development is rapid and health care practices are modified accordingly, there is a need for an updated review of the literature that includes modern medical dispensers. The purpose of this scoping review is 1) to map the last ten years of quantitative research studies on automatic or electric multimedication dispenser devices (EMD´s) and their impact on adherence in home dwelling adults, and 2) to describe the methods used for measuring adherence.

Method

This scoping review is conducted according to The Arksey and O´Malley 5 stage scoping review framework: (1) identifying the research question, (2) identifying the relevant studies, (3) selecting the studies for inclusion, (4) charting the data, and (5) collating, summarizing and reporting the results (Arksey and O'Malley 2005).

Identifying research questions

The research purpose is formulated in the introduction section. Research gaps are sought outlined and future research is feasibly informed, according to the first stage of Arksey and O'Malley´s (2005) methodological framework for scoping studies.

Identifying relevant studies

A comprehensive search was conducted by the help of a professional librarian November 9th 2022, and repeated January 9th 2023. The main search was done in English in PubMed and Ovid covering entries in MedLine and Cochrane, identifying 119 articles which were imported to EndNote. SveMed+ and Oria were searched superficially for missed articles by the librarian. Key terms in English were «welfare technology», «e-Health», «medic*/automat*/electronic dispenser», «medic* compliance/adherence», «patient safety», «adults» and «living at home» (in MeSH terms where applicable). «Electronic» and «automatic» is used interchangeably in the literature. Norwegian national websites were searched by hand by the author for useful policy documents or reports. Google Scholar and reference lists were searched for relevant studies. One additional study met inclusion critera and was included (Marek et. al., 2013). Medical dispensers examined in the studies were looked up in their web sites and searched for useful material. Denomination of medical dispensers in English language vary in different countries, are fondly abbreviated and were sought covered through the broad search. See Appendix 1 for Boolean search and PICO.

Selecting studies for inclusion

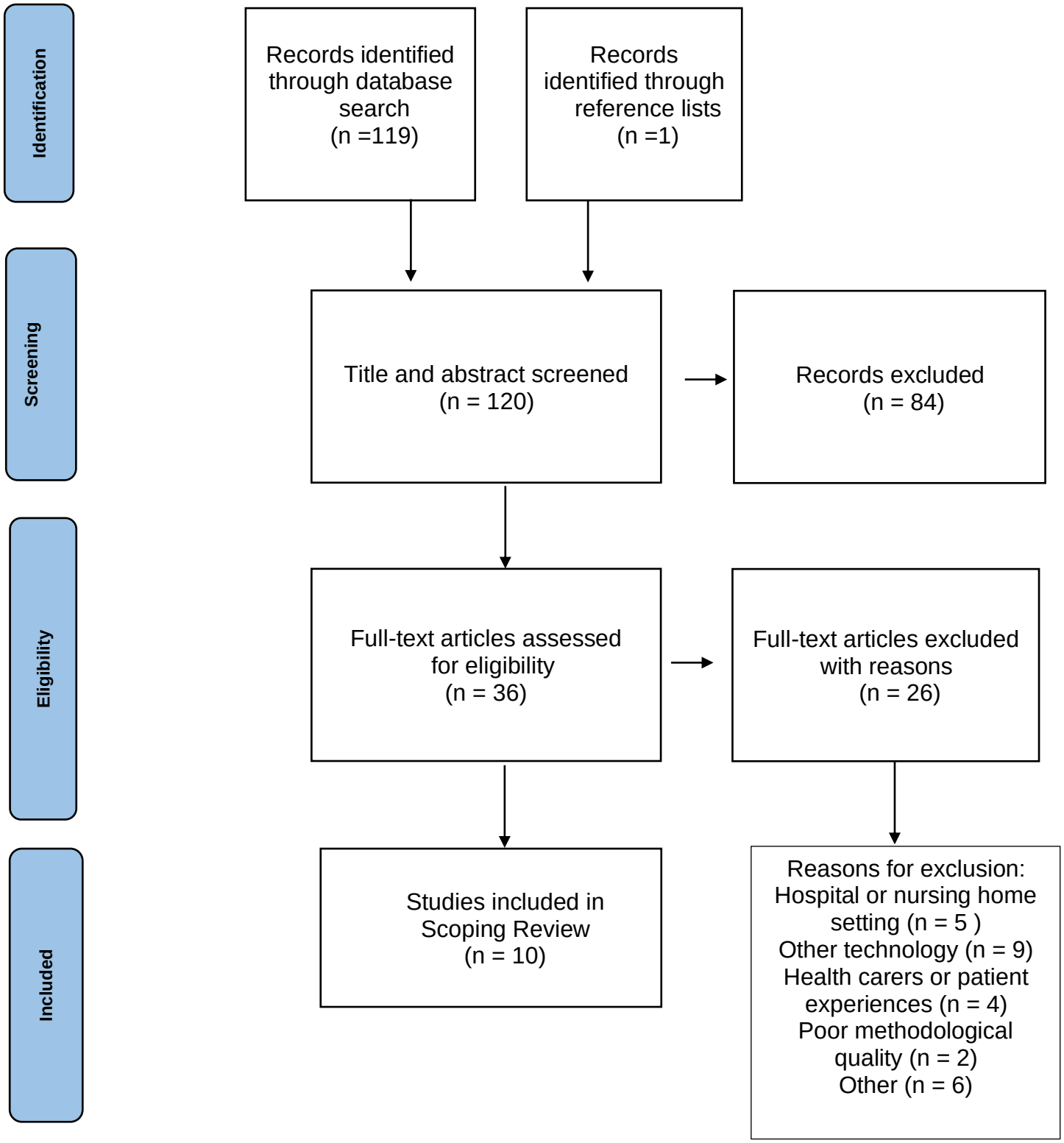
The search and inclusion criteria were revised post hoc from «multidose dispensers with bags» to «automatic/electronic medical dispensers» due to availability of studies. The search results were the same. Articles published before 2013 were excluded due to technology development of dispensers. Studies in hospital and nursing home settings were not included as they both have healthcare workers constantly present affecting the use of dispensers. Included studies had nurses, pharmacists or other health carers involved to various degrees but all participants lived in their home. Studies examining wrong type of technology, and qualitative studies focusing solely on subjective user experiences were not included. Studies that used a combination of interviews *and* collected quantitative data to measure adherence were included. See Figure 1 PRISMA Flow Chart below.

Inclusion criteria:

- Patient demographics: home dwelling adults ≥ 18 years of age
- Technology: Automated/electronic medical dispensers including these characteristics a) deliver multidose medication b) visual and/or audio reminder signals
- Time limit: Articles published from 2013
- Geographical limitation: None
- Study designs and attributes: Cohort and case control studies, randomized controlled trials (RCT´s), mixed-method
- Outcome: Quantitative measurements for medical adherence
- Written in English or Scandinavian language

The electronic search identified 119 articles, no duplicates. 84 records were excluded after reviewing title and abstract. After full-text review of the remaining 35, 26 did not meet inclusion criteria thus 9 studies were included. One study was included from a reference list resulting in a total of ten included studies.

Figure 1. PRISMA flow chart



Page MJ, et al. PRISMA flow chart (2020)

Charting the data

Data charting capture the following study characteristics: (1) author(s), year of publication, study location, journal of publication, (2) design, duration and time of data collection, (3) aim, (4) intervention/technology device, (5) sample size and characteristics.
See Table 1 Study Characteristics below

Collating, summarizing and reporting the results

The extracted results are reported narratively and summarized in a Diagram of Study Outcomes including (1) first author, year and country, (2) device/device features, (3) how adherence is measured, (4) key findings related to adherence.
See Table 2 Study Outcomes below

Quality assessment and reporting biases

According to Arksey and O´Malley´s (2005) framework for scoping reviews a quality assessment is not required. As this study is written as a master thesis it is included as an addition, and approved by my supervisors.
Included RCT studies were assessed using the Critical Appraisal Skills Programme Checklist (2021). The other five studies were assessed with the Mixed Methods Appraisal Tool (MMAT Checklist, 2018) by applying appropriate questions according to study design.
Two different checklists for quality appraisal and a variety of research methods in the studies included renders a comparison and justified overall assessment complicated (ie. low, medium, high). Descriptions of quality and bias is presented in Results and Discussion chapters and both checklists with comments are found in Appendix 2 Quality Appraisal

Table 1 Study Characteristics

Authors, year, country and journal	**Design, Duration& Data collection**	**Aim**	**Intervention / Technology device**	**Sample sizes and Characteristics**
Patel, Ivo, Pitre, Faisal et al. 2022. Canada JMIR Publications –Advancing Digital Health& Open Science	Prospective observational study 6 months Time for data collection not reported	Examine the use of a smart medication dispenser «spencer» as a medication adherence and self-management support tool, and pharmacists potential to address adherence- and medication related problems through AdhereNet.	«spencer»	N = 58 Mean age 66.36 years (range 48-90). Taking at least 1 chronic medication. Recruited from health care providers, outreach programs, independent living communities. Community medication management program or severe cognitive impairment excluded. Previously expressed interest in smart medication device.
Arain, Ahmad, et al. 2021. Canada BMC Geriatrics	Pilot RCT 6.5 months 2019/2020	Examine the effectiveness of an unnamed smart medication dispenser on improving medication adherence and health perception in older adults with chronic conditions	Medical dispenser unnamed.	N = 48 Intervention n = 23, mean age 63.96 Control group n = 25, mean age 59.52 Treatment as usual (TAU) Age range 51-82 years Taking five or more oral medications. Recruited from primary care clinic. Moderate to severe cognitive impairment excluded.

Vieira, Liliana Batista, et al. 2021. Brazil Einstein, Sao Paolo.	Mixed-method prospective study 7 months 2012-2013	To examine whether electronic medical device with alarm clock can improve medical adherence in older adults with hypertension	«Supermed»	N = 32 Adults >60 years, diagnosed with hypertension SBP >130mmHg. Mean age 71.4 years (range 62-84) Taking five or more oral medications. Recruited from a primary care unit. Cognitive impairment exluded.
Hoffmann, Charles, et al. 2018. USA Journal of Healthcare Quality	Prospective feasibility study 6 months Time for data collection not reported	Determine the use of a smart medical device on medical adherence	«MedaCube»	N = 21 patient-caregiver dyads Mean ages 75.1 years At least 2 medications in pill form. Known poor unintentional medication adherence, capacity to use dispenser, 13 with memory disorder. Recruited from clinical practices of authors or community collaborators.
Rantanen, Pekkari et al. 2017. Finland Clinical Therapeutics	Pilot Safety &usability study. Mean time 26.9 days with intervention 2013-2014	Phase II of safety and usability study of Evondos E300. Assess device performance to promote patient adherence	«Evondos E300»	N = 27 Average age 75.3 Long term daily medication. Recruited from home care setting. Assessed by a nurse to be committed to treatment and taking their medicine. 3 participants with early-stage dementia.

Henriksson, Jarmo, et al. 2016. Sweden. Transplantation	Prospective randomised study 1 year 2011-2013	To assess the effect of an electronic medication dispenser (EMD) on compliance with immunosuppressive medications in renal transplanted patients	Unnamed EMD	N = 80 n = 40 intervention EMD n = 40 control group TAU Renal transplanted >14 days ago. Average age 44.3 years. Recruited from surgery ward.
Marek, Karen, et al. 2013 USA Nursing Research	RCT 3-arm 12 months 2006-2010	To evaluate health status outcomes of frail older adults receiving a home-based support program that emphasized self-management of medications using both care coordination and technology	MD.2®	N = 456 Group 1 (n=152): MD.2+ nurse care co-ordination Group 2 (n=137): Medplanner (simple medication box) + nurse care coordination Group 3 (n=125): Usual care Average ages 78.2-79.6 years. Recruited from discharged home healthcare. Impaired ability to manage medication. Nurse care co-ordination: close follow-up, education&tools for participants to manage chronic conditions, enhanced communication with health professionals, plans for monitoring signs and symptoms of disease. Home visit at least every 2 weeks + additional visits if change in medication or if hospitalised.

Stip, Emmanuel, et al. 2013. Canada. Frontiers in Pharmacology	RCT 6 weeks 2008-2010	To test whether electronic pill dispenser can improve AAR (antipsychotic adherence ratio) in patients with schizofrenia AAR= number of pills taken x 100/number of pills prescribed, a quantification of implementation. <70% AAR = non-adherent.	DoPill®	N = 64 n = 26 intervention EMD n = 28 control group TAU Average age 43.3 years. Participants with moderate schizofrenia recruited from Institut universitaire en santé mentale de Montréal
Velligan, Dawn, et al. 2013. USA. Schizofrenia Bulletin	RCT 9 months Time for data collection not reported	To assess effect on medical adherence in psychiatric patients with the use of an EMD or PharmCAT therapy	Med eMonitor	N = 142 n = 48 intervention EMD n = 47 PharmCAT follow up n = 47 TAU Control groups also had EMD to register adherence. Ages 18-60, mean age 41.52. Missed at least 1 dose preceding week, able to understand and complete assessments. Recruited from a community mental health centre PharmCAT therapy: environmental support; pill containers, signs, alarms, checklists & weekly home visit from therapist

Simoni Jane M. et al. 2013. USA. AIDS and Behavior	Preliminary RCT 9 months 2009-2011	To test adherence using cognitive behavioural therapy (CBD) and an EMD in patients with HIV and depressive symptoms.	Pill box Developed by Medsignals ®	N = 40 n = 20 weekly intervention CBD* + pill box with alarms n = 20 TAU + pill box without alarm 24-63 years, various sub-optimal adherence. Excluded if signs of dementia. Recruited from community health clinic by referrals and advertising flyers *including Life Steps Adherence counceling

Table 2 Study Outcomes below

First author, year & country	Device/ Device features	How is adherence measured	Key findings related to adherence
Patel, et al. 2022. Canada	«spencer» Medication packed in labelled plastic pouches by pharmacy, filled every 1 or 2 weeks at home. Audiovisual reminders and touch screen to respond to reminder alerts and communication with pharmacist. Sends real time adherence data to clinician and pharmacist	1. Tracking of medicine bag removal through online AdhereNet platform Adherence defined as dose intake within 2 hours post scheduled time. Monthly adherence reports calculated from 24 hour periods, and total average adherence (SD) calculated by dividing individual adherence percentage by number of study participants (N).	Average monthly adherence over 6 months was 98% (n=56; SD 3.1%; range 76.5%-100%) Note: Baseline adherence not calculated.
Arain, et al. 2021. Canada	Device unnamed Medication packed in labelled plastic pouches by pharmacy. Audio signals at dosage time which amplified if pouch wasnt removed at dosage time. Notified pharmacy and caregivers of missed doses. Sends real time adherence data to pharmacist.	1. Tracking of medicine pouch removal through online AdhereNet platform 2. Monthly retrospect self reported adherence by questionnaire (scale 1 (non-adherent) -10 (adherent) and 6 questions with possible answers always, often, sometimes, rarely, never. Adherence defined as dose intake within 2 hours post scheduled time. Weekly adherence calculated by a 7-day average percent (o% (not taken) or 100% (taken) calculated using ITT (intention to treat) analysis Control group measured monthly by self-recording in dose-calender and questionnaire.	Average adherence in intervention group 98.35% +/-2.15%, control group 91.17%+/- 9.76% Self-rated adherence in intervention group significantly increased compared to control group and baseline.

Vieira, et al. 2021. Brazil	«Supermed» 1 compartment device filled with medication in plastic pouches for each dose, 1 month worth. Audio and visual alarm. 1 device for each dosing time (ie morning, noon, or bedtime) which resulted in several devices for some patients. Filled by pharmacist monthly along with dialog concerning medical treatment.	1. Baseline and post intervention questionnaire using Moriskey Medication Adherence Scale. *1. Do you ever forget to take your medicines? 2. Are you careless at times to take your medicines? 3.When you feel better do you sometimes stop taking your medicine? 4. Sometimes if you feel worse when you take your medicine do you stop taking it?* The answers were scored as yes (zero) and no (one); patients with final scores of zero to two and three to four were considered as "less adherent" and "more adherent", respectively 2. Adherence measured by patient turning off alarm and box opened/closed. Registered by a memory card in device, uploaded monthly. Time window unknown.	Self-assessments measured by Moriskey: 78.1% of patients changed from «less adherent» to «more adherent» with use of «Supermed» compared to baseline. 3.1% of participants report to forget to take medication during intervention vs 84.4% at baseline. 31.2% reported to be careless about the time they take medication vs 87.5% at baseline. Note: Registrations from device not presented.
Hoffmann, et al. 2018. USA	«MedaCube» Multi-compartment, holds up to 90 days supply of 16 medications. Dispenses small plastic cups with medication. Refill by non-formal caregiver. Audio and visual reminders. Caregiver notified of late or missed doses.	1. Medical adherence calculaled from dispenser recorded online dosing retrieval at 6 months 2. Pill counts performed at baseline and at 6 months Dispensing was considered incomplete if one or more medications were not available in the device or if the patient did not access the dispensed medications within the dispensing (not reported) time window. A paired t-test was used to compare previous and prospective adherence.	Improved mean adherence from 49.0% at baseline to 96.8% after 6 months of «MedaCube» use ($p < .001$). Note: Data from pill count at 6 months not presented.

Rantanen, et al. 2017. Finland	«Evondos E300» Medication packed in labelled plastic pouches by pharmacy, read by device. Audio and visual alarm. Spoken and written message (on LCD screen) to press a big dose button to release medicine pouch. Medicine is automatically retracted into a locked canister inside the device if not retracted within preset time and message is sent to caregiver (home care nurse).	1. on-time response to alarm by pressing button 2. retrieval of medicine and missed doses recorded by robotic system through Salo Evondos Telecare system. 2. Interviews of patients and nurses on perceived adherence Adherence registered if medicine pouch retrieved within an unknown time window.	98.7% of alerts resulted in on-time medicine sachet retrievals. At baseline 18% of patients reported missing doses at least 2 times a week. Post intervention not described.
Henriksson, et al. 2016. Sweden	Portable smart electronic medication dispenser with small chambers. Holds 1 week medication. Audio and visual alarm at dosing time. No signal to caregivers. Patient loaded device with medication.	1. Device recorded date and time for retrieved medicine doses via web based application. Adherence defined as dose intake within 1 hour before or 2 hours post scheduled time. Registrations obtained 10 times in 1 year.	Compliance in intervention group 97.8%. Control group not assessed. Baseline adherence not assessed. Note:indication of lower rejection rate in intervention group. Effect on hospital admission rates, p-creatinine levels and immunosuppressive drug concentrations were non-significant compared to control group.
Marek, et al. 2013 USA	«MD.2» Stores upto 60 reusable plastic cups with medication. Releases preloaded medication cups when user presses large red button. Audible and visual prompt for 45 minutes; sends notification to carer (family member or nurse) if not removed. Filled by nurse every 2 weeks.	1. Device recorded dispensing of medicine and missed doses online by robotic system. 2. Nurse counted medications left in planner	Average adherence Group 1 MD.2 + nurse care coordination: 98.8% (SD = 0.32%) Group 2 Medplanner + nurse care coordination: 97.4% (SD = 5.19%) Control group adherence not assessed. Note: Significant better clinical outcomes in group 1 & 2. Group 2 not better than 1.

		Unknown timewindow. Monthly average percentage of correct doses per month in 2 intervention groups.	
Stip, et al. 2013 Canada	«DoPill» Smart pill dispenser with 28 compartments in a blister covered with plastic lamina. Audiovisual signals. Device filled with medication and programmed by pharmacy weekly. Signal to pharmacist or caregiver when dose not removed	1.Recorded signals to pharmacist via Internet when plastic lamina is removed from blister (Time window unknown) 2. Home visit at 6 and 8 weeks measuring Brief Adherence Rating Scale (BARS) as reference measure BARS: 1.Self-assessment of missed medication by 3 questions + VAS rating 0-100% 2. Clinician evaluation AAR=Adherence ratio calculated by pills taken/pills given.	Mean AAR with use of EMD was 66.6% [secure digital (SD) 35.1]. 46% <70% AAR 54% >90% AAR BARS 86–99% across visits Note: PANSS (positive and negative syndrome scale for schizophrenia) only measured baseline. Baseline adherence unknown.
Velligan, et al. 2013 USA	«Med eMonitor» Semi-portable pill dispenser with 5 compartments. Sound alarm 30min after wakening, screen for written instructions. Warns when patient takes wrong medication, can record side effect complaints. +20 medications can be stored outside dispenser, managed by «Virtual Compartment» feature. Patient loaded device with medication. Signal to caregivers if	1. Recorded signals from compartment openings (Time window unknown) 2. Patient indication of ingested pill 3. Monthly pill count MM therapist checked recorded medication retrieval by Web every 3 days, possibility for telephone intervention. Supervision was conducted regularly to ensure adherence to the model. Aggregated adherence data measured at 3, 6 and 9 months	Adherence rates measured by EMD 91% for Med-eMonitor, 90% for PharmCAT, 72% for control group Adherence rates measured by pill count EMD 86%, PharmCAT 91%, TAU 80%. Baseline adherence assessed for 1 month using dispenser and pill-count for all groups Note: Did not improve clinical outcomes or decrease contact with

	dose not removed, checked every 3 days.		hospital or emergency psychiatric services
Simoni, et al. 2013. USA	Portable pillbox holding up to 4 medications. Prompted audiovisual signals at dosing times, voice and written instructions on LED-screen. Refill information not noted No signal to caregivers	1.Recorded web based data from compartment openings 2. Weekly visual analog scale self adherence report (0-100% visual scale) Adherence data measured at baseline, 6-months and 9-months. Past 2-week percentage calculated from compartment openings divided by total prescribed doses. Compartment openings recorded valid within 12h (daily dosing) or 6h (twice daily). Control group measured by EMD without alarm	Intervention group shows greater adherence with the electronic pillbox, nearly four-fold greater odds of 100 % adherence compared to baseline (OR = 3.78, SE = 1.31, 95% CI = 1.62 to 7.26, P = 0.001) Also greater adherence by self-report visual analogue scale, percentage adherence outcome: 93% at 9 months (baseline 87%). Note: Intervention group showed drop in depressive symptoms, improvement for CD4 count but not viral load (VL)

Results

Study selection summary

The ten included studies are from Canada (n=3), USA (n=4), Brazil (n=1), Finland (n=1) and Sweden (n=1) and were published between 2013 and 2022. Study designs included RCT´s (n=5), pilot safety & usability study (n=1), prospective feasibility, randomized or observational study (n=3) and mixed-method (n=1). Sample sizes ranged from 21- 456 participants. Mean ages ranged from 41- 80 years. Interventions lasted from mean 27 days upto one year. A majority of the study samples were female (52% - 70%) except for two studies where the samples included 69% and 73% males respectively (Stip et al.; Simoni et al.). Five studies included patients with specific illnesses; hypertension (Vieira et al.), recent renal transplant (Henriksson et al.), HIV&depression (Simoni et al.) and psychiatric illness (Stip et al.; Velligan et al.). The remining five included participants with non-specific chronic conditions. Three studies included participants with memory disorder or dementia (Hoffmann et al.; Rantanen et al.; Marek et al.). All EMD´s featured light and sound alarms at dosing times and registered medication removal. They varied in size, portability, medication packing and a few other additional features (see table 1 of Study Characteristics).

Medical adherence outcomes

Seven of the included studies were on the feasability level and information lacked on baseline or outcome measurements. Known non-adherence before study inclusion differ across the studies, so does baseline adherence measurements after inslusion. In one study participants were committed to treatment and taking their medicine (Rantanen et al.) and in another participants were recruited that previously had expressed interest in smart medication devices (Patel et al.). Participants´ medication regimens vary in complexity, from 1- 27 pills daily. See an overview of study results in table 2.

All included studies in this review found improved medical adherence outcomes with the use of an EMD. Six studies show an average adherence rate in the intervention group measured by the device of an exceptional 97-99% (Patel et al.; Arain et al.; Hoffmann et al.; Rantanen et al.; Marek et al.; Henriksson et al).

Use of EMD´s in patients with psychiatric illness

Two studies (Stip et al.; Velligan et al.) examined participants with psychiatric illness with inconsistent results. Stip et al. tested whether "DoPill" can be used for accurate adherence measurements of Antipshychotic Adherence Ratio (AAR) compared to Brief Adherence Rating Scale (BARS), and improve psychiatric symptoms in patients with moderate schizophrenia. They found mean 67% AAR measurements by EMD compared to self-assessment BARS scores of 86-99%. 54% of the intervention participants increased mean AAR >90% and the remaining <70%. Raw data suggests that more adherent patients at baseline have better adherence with the device compared to lesser adherent patients. Authors conclude that the EMD gives a more accurate measure of adherence for this patient group compared to BARS and that the EMD may help medication taking ability.Velligan et al. compared «Med-eMonitor», PharmCAT therapy and treatment as usual (TAU). Adherence rates measured by devices were 91% in EMD group, 90% for PharmCAT therapy group and 72% TAU group. Adherence rates measured by pill count were Med-eMonitor 86%, PharmCAT 91%, TAU 80% leaving both PharmCAT and Med-eMonitor more effective than TAU by both measurements.

Use of EMD´s in patients with specific chronic illnesses

Three studies (Simoni et al.; Henriksson et al.; Vieira et al.) explored the use of EMD´s in patients with specific chronic illnesses. Simoni et al. examined HIV patients with depressive symptoms comparing cognitive behavioral therapy including Life Steps Adherence counceling and an EMD to TAU. The intervention group showed nearly four-fold greater odds of 100 % adherence measured by device. Measures by self-report showed 93% adherence compared to 87% at baseline. Two simultaneous interventions renders EMD-effect unclear.

Henriksson et al. examined the effect of a small portable EMD in renal transplanted patients and found 97.8% adherence in the intervention group. Baseline and contol group adherence were not measured.

Vieira et al. examined older adults with hypertension using «Supermed». 78% of patients changed from «less adherent» to «more adherent» and 3% of participants reported to forget to take medication during intervention compared to 84% at baseline. Outcomes documented were measured by self-assessment Moriskey Medication Adherence Scale.

Use of EMD´s in other, non-specific conditions

The five remaining studies (Arain et al.; Marek et al.; Hoffmann et al.; Rantanen et al.; Patel et al.) examined non-specific chronic ill samples of adults or older adults. In summary, all found that use of an EMD resulted in increased medical adherence.

Arain et al. found an average adherence rate of 98% with use an unnamed EMD compared to 91% in a control group which received TAU, suggesting samples with small adherence problems became more adherent. The EMD sends real time adherence data to pharmacist but interventions upon missed doses remains undescribed.

Marek et al. evaluated effect on adherence by nurse care coordination and «MD.2» or nurse care coordination with a medplanner (dosette) compared to TAU control group. The «MD.2» group had an average adherence of 98.8% versus medplanner group 97.4%. «MD.2» can send a signal to family or research nurse when a dose is not removed, there is documentation about the function used but not to what extent.

Hoffmann et al. examined 21 patient/caregiver dyads using «MedaCube». Measurements showed that mean adherence improved from 49% at baseline to 97%. Pill counts were used for baseline adherence measurements and at six months, the latter remains unkown. «MedaCube» can be locked to prevent inappropriate access to medication and can send a notification to a caregiver when a dose is missed. Use of the features remain undescribed.

The two remaining studies examined similar EMD´s holding multidose plastic pouches labelled with patient name, date and time for dose and medication contents, prepacked from pharmacy. Rantanen et al. examined «Evondos300» performance to promote adherence in participants in a home care setting. Results showed that 98.7% of alerts resulted in on-time medicine sachet retrievals. Medication was not retrieved 12 times (of 2090 doses). The sachet was then retracted automatically by the device and placed in a separate compartment, unreachable for the patient. A message was sent to a home care nurse who intervened and gave medication. At baseline 18% of patients reported missing doses at least two times a week, post intervention is not described.

In the last included study Patel et al. examined the use of «spencer» as a medication adherence and self-management tool. Pharmacist interacted with participants to detect and address drug therapy problems during the study period. Average monthly adherence was 98%.

Methods used for adherence measurements

All 10 included studies measured adherence with registrations from the EMD. Two EMD´s saved information on a memory card in the device (Simoni et al.; Vieira et al.) to be uploaded at a clinical visit, while the rest of the devices sent real time adherence data to a web-based platform. «Dose intake» was registered electronically by the device upon opening or by removal of plastic lamina, pouch or cup from the device and/or a pressed button. See Table 1 for description of adherence calculations based on EMD for each study. Adherence definitions differed: six studies did not report a valid time window for registered adherence. Two studies defined adherence as dose intake within two hours post scheduled time (Patel et al.; Arain et al.) Henriksson et al. defined adherence as dose intake within one hour before or two hours post scheduled dosing time whereas Simoni et al. defined adherence as dose intake within 12 hours for daily dosing or within six hours at twice daily dosing schedule. Two studies measured intervention adherence only electronically from EMD (Henriksson et al.; Patel et al.). Three studies also performed pill counts for adherence measurements (Marek et al.; Hoffmann et al.; Velligan et al.). Three studies did additional adherence self-assessments which supported the positive outcomes from the EMD measurements: monthly retrospect questionnaire and calender (Arain et al.), baseline and post-intervention questionnaire with Moriskey Medication Adherence Scale (Vieira et al.) and visual analog rating scale (VAS 0-100%) weekly (Simoni et al.). Stip et al., measured BARS scores. Rantanen et al. also interviewed patients and involved home care nurses on their perceived adherence and noted 89% of patients and 88% nurses recommended or probably recommended the device for further use. Data collection of interviews was undocumented making analysis and interpretation impossible. A great variety of statistical analysis was used for adherence calculations across the studies.

Discussion

The aim of this review is to present an updated scope of quantitative research literature on the influence of automatic medical dispenser´s on medical adherence in adult home dwellers and to present the measurements of adherence used. Heterogeneity between studies, study design and possible bias restricts the quality of evidence and the possibility to draw conclusions. A key finding is that rates varied depending on the definitions of adherence and the

methodological approaches employed. There are only two studies (Hoffmann et al.; Henriksson et al.) where participants are *not* given information and follow up on medication use during the intervention, and in two studies simultaneous treatment is part of the method (Marek et al.; Simoni et al.,) making it difficult to measure EMD effect exclusively. All EMD´s feature audiovisual alarms and some a LCD-screen with written instructions. Nine examined EMD´s holds the additional technological feature of real time monitoring and seven can send a message to a carer when a dose is not retrieved, but studies lack documentation on it´s use making it difficult to assess impact on adherence. High quality evidence from these modern technical feature´s usefulness and effect on adherence lack, and larger well conducted research is warranted. All studies exclude persons with moderate to severe cognitive impairment and only three studies (Hoffmann et al.; Marek et al.; Rantanen et al.) include participants with old age from a communal or home health care setting where small or moderate numbers have early dementia or a memory disorder, raising questions of generalizability.

However, findings from this review indicate that patients with a smaller non-adherence problems seem to benefit from an EMD to organize pills and give audiovisual alarms to become more adherent with medication. In populations with more complex chronic illness such as schizofrenic disease and older adults with cognitive impairment findings imply there may also be a benefit for EMD´s to serve as a tool to increase their adherence. Yet these populations appear to profit from a combination with other supplementary interventions and follow up addressing non-adherence and medication use (including pharmacy screens), and health issues.

Use of EMD´s in patients with psychiatric illness

Two studies (Stip et al.; Velligan et al.) examined EMD-effectiveness in patients on antipsychotic polypharmacy and their adherence outcomes differ; in the Stip et al. the intervention participants had either >90% or <70% AAR. Velligan et al., notes that 80% of participants in their study use concominant medication for side effects, anxiety, sleep and mood problems indicating a patient group with complex needs and changing medication treatment. Their EMD group was given regular follow up where pratical issues, episodes of missed doses and motivation for adherence were addressed which may have influenced adherence positively achieving 91% adherence measured by EMD, indicating that lesser adherent patients need supplementary or other initiatives to become more adherent to

medication. This is similarly suggested by Paterson et al., (2016); electronic reminder aids may have a limit for increasing adherence for those not simply forgetful.
Examples from included studies demonstrate that not all patients benefit from new EMD technology reminding us they must be used with caution. Drop out reasons from participants using EMD´s, across the studies, were such as «extremely stressful», «psychiatric patient didn´t like the sound alarm» and «fear of technology». A 30% drop out rate was recorded from the intervention group of patients with schizofrenia using EMD´s (Velligan et al.). Outcomes from two previous studies on monitoring and feedback on adherence concluded that patients with psychiatric disease may have difficulty adjusting to EMD´s (Elixhauser et al. 1990; Kozuki et al. 2005).

Use of EMD´s in non-specific chronic ill older adults

Among the studies of EMD´s in patients with non-specific chronic illnesses, all include mean aged older adults, and all found high rates of adherence (>97%) (Patel et al.; Arain et al.; Hoffmann et al.; Rantanen et al.; Marek et al.). This suggests that EMD´s may also serve as a positive stimulant to improve medical adherence in this population. Ages did however vary across the studies; Patel et al. included adults from 48 years and Arain et al. from 50 years. Hoffmann et al., does not intervene (other than monthly by telephone to ensure EMD operates correctly) during the six months of intervention for the purpose of measuring the effect of «MedaCube» alone. Their study examined use of the EMD in patient and caregiver dyads where a caregiver was given the role of filling the device with medication. Half (10 of 21) of caregivers lived with the patient. According to DiMatteo (2004) there are higher odds of adherence for people living with someone than alone. Adherence measurements in participants living alone were almost equal (96%) demonstrating a positive effect also in these. One can question whether giving the caregivers the responsability for the EMD set up and filling compensates for other adherence-related interventions the authors claim to leave out. And it does not exclude the possibility of medication errors.
Three of the studies (Patel et al.; Rantanen et al.; Marek et al.) have in common that they performed a pharmacy screen for all included patients at the beginning of the study and an intervention is presented when medication is not retracted from the EMD, yet in different manners. Patel et al., identified 117 drug problems in the 39 (of 58) participants including 23

occasions of dangerously high dose and 19 adverse drug reactions. This was addressed through telephone calls, possibly influencing adherence rates positively.
Rantanen et al. documented that home care nurse interviened and gave medication to patients a total of 12 times when it was not retrieved from «Evondos300». The role and participation of home care nurses other than the mentioned remains largely unknown. They might possibly have acted to influence patients´ adherence also in other ways. In both intervention arms in Marek et al., study patients received enhanced nurse care co-ordination by nurse practitioners (resembles AKS-nurse in Norway) in the form of close follow-up on medication and health related issues during the year of intervention which along with «MD.2» or a simple medplanner increased adherence compared to baseline. This is also the only study which showed decreased hospital admission numbers, yet the «MD.2» device did not give additional benefit over the medplanner when comparing the two on health outcome measures. Higher odds of better adherence when EMD is part of a complex intervention corresponds with the findings of Checchi et al. and their systematic review from 2014. Equally Paterson et al., (2016) found EMD´s may have potential to increase patient medication adherence, influenced by medical condition, context and usability.

Measurements of adherence

Although digital measurements of adherence by EMD´s have currently been seen as the «gold standard» (Vrijens & Urquhart, 2014), one very important aspect regarding their use is that they all rely on presumptive dosing; adherence is measured by removal of medication from device regarding it equal to ingested medication. Confirmation of ingested medication is only partly sought through other adherence measurements, and is problematized inconsistently in the included studies. The patient may retrieve the medication but loose a pill on the floor, unknowingly or not being able to find it, put it aside on purpose or simply mislay it being distracted or forgetful. Rates of adherence will be influenced by methods of measurements; windows of valid «dose intake» and statistical methods calculating these, at baseline, during intervention and post intervention. All 10 included studies used different methods. Missing data was also calculated and reported differently. Evaluating these methods is not the scope of this review, but a short approach is presented.
According to Lam et al., (2015) a multi-measure approach to measuring medication adherence is the recommended practice to increase the accuracy of adherence measurements.

2 studies measure intervention adherence only from EMD (Henriksson et al.; Patel et al.). Three studies measured pill count (Velligan et al; Marek et al.; Hoffmann et al) yet only Velligan et al., measured it monthly and reported correlations to EMD measurements. Marek et al. do pill counts only in the medplanner group, not EMD, and Hoffmann et al., measure pill count for baseline adherence measurements only. The most common adherence calculation was pills taken divided by pills prescribed.

4 studies did adherence self-assessments for a subjective measure, they differed across the studies. In three of these adherence significantly increased (Arain et al.; Simoni et al.; Vieira et al.,) in accordance with EMD measurements. In Stip et al. study BARS scores were 86-99% which are explained to be overly optimistic, a pill found in the device cannot have been taken. BARS includes both a self-assessment and a clinician assessment based on the patient response, demonstrating the unspecificity and vulnerability of both in this study.

Medication use and influence of the EMD-intervention on medical outcomes

A total of six included studies reported effectiveness of EMD use on medical outcomes showing mixed results for the correlation between improved adherence and improved health. Three found improvement (Vieira et al.; Arain et al.; Marek et al.), two found a partial improvement (Simoni et al.; Henriksson et al.) and 1 did not (Velligan et al.).

There are examples from the included studies of older adult patients with polypharmacy; in Vieira et al., study participants use mean 8 medicines a day (range 6-24 tablets a day) and in Hoffmann et al., the average number of medications at baseline is 7, and it increased to 9 (range 5-27). Polypharmacy indicates more than 4-5 medications daily and/or the use of more drugs than medically necessary (Patterson, 2014). It is common in the older population with multimorbidity (2 or more chronic diseases), as one or more medications may be used to treat one single condition or to treat drug related problems (Maher et al. 2004). Polypharmacy is associated with non-adherence, adverse drug reactions, falls, increased length of stay in hospital, readmissions, death and increased healthcare costs, and these risks increase with increasing number of medications due to a multitude of factors including drug-drug interactions and drug-disease interactions (Maher et al, 2014; Milton et al, 2004).

A Norwegian cohort study from 2022 investigated 402 patients in a hospital emergency department and found that 19.7% of the admissions were drug related. Adverse effects (72%) and non-adherence (16,5%) were the most common causes, and risk factors were increasing age, increasing number of medications and medical referral reason (Nymoen et al., 2022).

Patel et al. demonstrate that use of an EMD offers the opportunity to identify drug related problems (DRP´s) in patients using EMD´s. The EMD examined in their study use multidose drug sachets (MMD). Earlier studies investigating MDD´s showed that patients with MDD use more inappropriate drugs, have higher risk of DRPs (drug related problems) and less knowledge about the medications they take compared to non-MDD users, leading to non-adherence and medication errors (Johnell et al, 2008; Kwint et al, 2011; Sinnemaki, 2011) demonstating the importance of simultaneously addressing the medication contents of MDD´s and EMD´s to reach the goal of dherent medication users and reduced healthcare costs. Studies on ADD users in Finland and the Netherlands show that medication reviews reduce the number of medications and DRP´s (Kwint et al. 2011; Sinnemaki et al. 2017) offering a broader solution to the problem of non-adherence.

Strengths and weaknesses

This study has several strengths. Assisted by a professional librarian, a comprehensive search was done in the largest databases for international medical research. The scoping review design and use of the Arksey and O´Malley framework (2005) allowed to map international research literature for extensive evidence. The first author has clinical nursing experience with EMD´s in home health care, which gave the advantage of clinically relevant perspectives regarding the topic.

The selection of articles, data extraction and narrative synthesis was done by the first author alone, which is a limitation. The included studies were characterized by heterogeneity in study populations and variations in definitions and measurements of adherence, which has limited the ability to compare findings across studies. Methodological problems were noted in numerous studies and the study designs were weak. More than half were feasability studies (lacking information on baseline, control groups and outcome measurements) which limits the ability to draw sound conclusions on EMD´s effectiveness on adherence.

In all studies EMD-technology was impossible to blind, and used both as intervention and measurement tool, which may introduce bias. Three of the included studies were funded by the EMD firms, which means that a conflict of interest may have influenced their results. The search was restricted to a specific type of EMD, which may reduce generalizability to other technologies. The samples of patients included relatively few older adults, and patients with moderate to severe dementia are excluded, thus the results may not be generalized to these patients. All available research may not have been identified because of language restrictions.

Conclusion

The ten included studies indicate overall positive outcomes from various types of automatic medical dispensers on medical adherence in adult home dwellers. Patients with smaller non-adherence problems seem to benefit from an EMD to organize pills and give audiovisual alarms to become more adherent with medication, whereas patients with more complex chronic illness such as schizofrenic disease and older adults with cognitive impairment also may benefit from EMD´s as a tool to increase adherence, yet along with a combination of other supplementary interventions and regular follow ups addressing non-adherence and medication use (including pharmacy screens), and health issues. Most included studies were small, characterized by large heterogeneity and weak designs, which affected the ability to draw conclusions. Adherence was defined and measured differently between the studies which leaves it challenging to compare adherence outcomes across the studies.
High quality evidence from EMD´s modern technical features usefulness and effect on adherence is lacking, especially in the elderly. Thus, larger well conducted research studies are warranted.

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Appendix 1

Boolean search strip used in PubMed:

Medication Systems"[Mesh:NoExp] OR ((drug*[Title] OR multidrug*[Title] OR pill*[Title] OR medicat*[Title] OR medicin*[Title] OR multidos*[Title] OR dose*[Title] OR pharm*[Title] OR polypharm*[Title]) AND (dispens*[Title] OR distribut*[Title] OR device*[Title] OR machine*[Title] OR alarm*[Title]))) AND (automat*[Title] OR electronic*[Title] OR digital*[Title] OR technol*[Title] OR robot*[Title] OR smart[Title]) AND ("Treatment Adherence and Compliance"[Mesh] OR adher*[Title] OR nonadher*[Title] OR comply[Title] OR complian*[Title] OR noncompl*[Title] OR elder*[Title] OR geriat*[Title] OR aged[Title] OR ageing[Title] OR aging[Title] OR older[Title] OR oldest[Title] OR old adult[Title] OR old adults[Title] OR alzheimer*[Title] OR dement*[Title] OR home*[Title/Abstract] OR dwell*[Title/Abstract] OR "community living" [Title/Abstract] OR domest*[Title/Abstract] OR "independent living"[title/abstract] OR Independent Living[Mesh] OR Community Health Services[Mesh:NoExp] OR Community Health Nursing[Mesh] OR Home Health Nursing[Mesh] OR Home Care Services[Mesh:NoExp] OR Home Nursing[Mesh] OR primary care*[Title] OR primary health*[Title] OR community health*[Title])

PICO:

PATIENT	**INTERVENTION**	**COMPARISON**	**OUTCOME**
Adult home dweller	EMD Electronic medication dispenser [1]	**AND**	Medical adherence
OR			**OR**
Adult living at home			Medical Compliance

[1] Also called: ADD (automated pill / dose / medicine dispenser system), eMMD electronic multi-compartment device, e-MMA (electronic medication management aid / system / device), MDS Medication reminder system / device (Canada), AHMD; Automated Home Medication Dispenser (USA), MDU; Automated integrated medication delivery unit (USA).

Appendix 2
Quality Appraisal

Quality Appraisal of included RCT studies based on CASP/Critical Appraisal Skills Program (2021). Responses: Yes, no, can´t tell.

	Arain, et al. 2021.	Marek, et al. 2013.	Simoni, et al. 2013.	Stip, et al. 2013.	Velligan, et al. 2013.
1. Did the study address a clearly focused research question?	Yes	Yes	No	Yes	Yes
2. Was the assignment of participants to interventions randomised?	Yes	Yes	Yes	Yes but no explanation of how	Yes
3.Were all participants who entered the study accounted for at its conclusion?	Yes	Yes	No	No	Yes
4.Were the participants 'blind' to intervention they were given? Were the investigators 'blind' to the intervention they were giving to participants? Were the people assessing/analysing outcome/s 'blinded'?	No No No	No No Partly	No No Partly	Can´t tell Can´t tell Can´t tell	No No Can´t tell
5.Were the study groups similar at the start of the randomised controlled trial?	Yes	No	Yes	Yes	Yes
6.Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?	No (monthly pharmacist follow up)	Yes	Yes	Yes	Yes

	Arain, Ahmad, et al. 2021.	Marek, Karen, et al. 2013.	Simoni Jane M. et al. 2013.	Stip, Emmanuel, et al. 2013.	Velligan, Dawn, et al. 2013.
7.Were the effects of intervention reported comprehensively?	Yes	Yes	Yes	No	Yes
8.Was the precision of the estimate of the intervention or treatment effect reported?	Yes	Yes	No	No	Yes
9.Do the benefits of the experimental intervention outweigh the harms and costs?	Can´t tell	Can´t tell	Can´t tell	Can´t tell	Can´t tell
10.Can the results be applied to your local population/in your context?	Yes	Yes	Yes	Yes	Yes
11.Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?	No	Yes	No	No	Maybe

CASP/Critical Appraisal Skills Program (2021)

Quality appraisal of included mixed-method and non-RCT studies based on Mixed Methods Appraisal Tool (MMAT), version 2018 (layout slightly altered to fit all studies).
Responses: Yes, no, can´t tell.

Category of study designs	**Methodological quality criteria**	Patel, 2022.	Vieira, 2021.	Hoff-mann, 2018.	Ranta-nen, 2017	Henri ksson, 2016
Screening questions (for all types)	S1. Are there clear research questions?	Yes	Yes	Yes	Yes	
	S2. Do the collected data allow to address the research questions?	Yes	Yes	Yes	Can´t tell	
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.					
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?	Yes	Yes		Yes	
	1.2. Are the qualitative data collection methods adequate to address the research question?	Yes	Yes		Can´t tell	
	1.3. Are the findings adequately derived from the data?	Yes	Yes		Can´t tell	
	1.4. Is the interpretation of results sufficiently substantiated by data?	Yes	Yes		No	
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?	Yes	Can´t tell		Can´t tell	
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?					
	2.2. Are the groups comparable at baseline?					
	2.3. Are there complete outcome data?					
	2.4. Are outcome assessors blinded to the intervention provided?					
	2.5 Did the participants adhere to the assigned intervention?					
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?					
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?					
	3.3. Are there complete outcome data?					
	3.4. Are the confounders accounted for in the design and analysis?					
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?					

4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?	Yes	Yes	Yes	Yes	Yes
	4.2. Is the sample representative of the target population?	Yes	Yes	Yes	Yes	Yes
	4.3. Are the measurements appropriate?	Yes	Can´t tell	Yes	Yes	Yes
	4.4. Is the risk of nonresponse bias low?	Yes	Can´t tell	Yes	Yes	Yes
	4.5. Is the statistical analysis appropriate to answer the research question?	Yes	Can´t tell	Yes	Yes	Yes
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	Yes	Yes		Yes	
	5.2. Are the different components of the study effectively integrated to answer the research question?	Yes	No		No	
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?	Yes	No		No	
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?	Yes	No		No	
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	Yes	No		No	

Hong et al. (2018). Mixed Methods Appraisal Tool (MMAT)

Comments:

Patel, 2022: 2 authors are stock holders in «spencer».

Rantanen, 2017: Study funded by Evondos, the EMD examined in the study

Vieira, 2021: Author prototyping the EMD device examined in the study (Vieira, et al. 2016)

Stip, 2013: Study lacks information on power calculations, drop outs, randomizations and detailed results

Appendix 3

Tidsskrift for Omsorgsforskning. Mai, 2023.
https://www.idunn.no/page/tfo/author
Artikkelmanuskriptet skal normalt ikke overskride 5 000 ord, eksklusive sammendrag, nøkkelord, referanser, tabeller, figurer, takksigelser, finansiering, interessekonflikter, noter og litteraturreferanser.
Sitat fra litteratur eller tekst over tre linjer skilles ut i eget avsnitt. Kortere sitater integreres i løpende tekst med anførselstegn. Sitater skal ikke kursiveres. Boktitler og begreper brukt i løpende tekst kan enten kursiveres eller markeres med anførselstegn.
Dersom manuskriptet bygger på resultater presentert i **masteroppgave** eller annen oppgave, må forfatter opplyse om dette og om oppgaven er klausulert.