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SYSTEMATIC REVIEW

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The impact of pharmacy care and motivational interviewing on improving medication adherence in patients with cardiovascular diseases: A systematic review of randomised controlled trials

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Abstract

Background: Cardiovascular disease (CVD) is prevalent worldwide, and for many patients, non-adherence to medication remains a problem. Motivational interviewing is a behavioural, communication strategy used as an intervention aimed to improve health outcomes.

Aims: This systematic review sought to investigate the effect of motivational interviewing delivered as part of pharmacy care on medication adherence, and the effect this has on clinical outcomes. These included systolic and diastolic blood pressure, haemoglobin A1C, lipid profiles and cardiovascular risk scores.

Method: A systematic review was conducted in six databases: PubMed Central UK, Cochrane Library, CINAHL (EBSCO), PsycINFO, EMBASE and MEDLINE from the inception of motivational interviewing in 1983 to November 2020. Randomised controlled trials (RCTs) that assessed motivational interviewing as part of pharmacy care interventions were selected. The Cochrane risk of bias tool was used to assess the risk of bias for each included study. This review was registered with PROSPERO (registration number CRD42020222954).

Results: A total of eight RCTs met the inclusion criteria. Five out of eight studies demonstrated medication adherence significantly improved following motivational interviewing interventions. One study showed a significant improvement for systolic blood pressure change by 7.2 mmHg (95% CI 1.6-12.8 mmHg); this reduction was observed in patients whose baseline blood pressure was above their target blood pressure. No statistically significant effect was seen across other clinical outcomes.

Conclusion: Motivational interviewing could be an effective behavioural strategy to enhance medication adherence in patients with CVD. Although the evidence is promising thus far, further research is required to explore the impact of motivational interviewing on clinical outcomes as well as the feasibility of implementing motivational interviewing interventions within existing pharmacy care services.

1 | INTRODUCTION

Cardiovascular disease (CVD) affects approximately 7.4 million people in the UK[1] and is a leading cause of morbidity and mortality, contributing to 31% of deaths worldwide.[2] Evidence suggests that patients with good adherence to cardiovascular treatment therapies can lower their CVD risk by 20% and reduce mortality by 30%.[3] Such pharmacological therapy has been shown to be beneficial within the CVD population, including antihypertensive treatment (eg, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs] and calcium channel blockers[4]), dyslipidaemia therapies (eg, statins[5]) and antiplatelet therapies (eg, aspirin and clopidogrel[6]). However, research demonstrates that non-adherence to medications is prevalent in >60% cardiovascular patients,[7] despite the established benefits of prevention medication and recommendations made by the National Institute for Health and Care Excellence[8] and wider international guidelines.[9] As a consequence, non-adherence to these medications has been associated with up to a 40% relative increase in the risk of hospitalisation and up to 80% increased risk of mortality in cardiac patients.[10] Further factors can contribute to inconsistent use of medications and suboptimal adherence in patients with CVDs. These can include communication barriers between healthcare professionals (HCPs) and patients, lack of motivation of patients to take their medications as well as socio-economic factors.[11] Therefore, there is an urgent need to explore interventions which may improve adherence rates, enhance clinician–patient communication and maximise improvements in CVD.

Successful interventions are thought to be determined by patients taking an active role in their decision making, such that pharmacists should encourage participative behaviour rather than adopting authoritarian styles of communication.[12] Pharmacists in practice already play a key role in improving medication adherence through patient education, patient counselling and medication management across a variety of healthcare settings,[12] all factors central to effective CVD management. Indeed, several systematic reviews, meta-analyses and observational studies have shown that pharmacist-led interventions have been successful in improving medication adherence and subsequently enhancing disease outcomes in the CVD population.[13,14] Of particular promise in demonstrating a positive impact on pharmacy care in a community pharmacy setting is motivational interviewing. Motivational interviewing has been found to improve medication adherence across a number of major disease groups including diabetes and hypertension (HTN).[15] Thus far, the evidence centred around the use of motivational interviewing in pharmacy practice is encouraging but still limited.[14] The use of motivational interviewing as a behavioural intervention merits further exploration in pharmacy practice as it has potential for greater usage as a strategy to help improve medication adherence.[16]

Motivational interviewing is a "directive, collaborative, client-centred form of communication style used to elicit behavioural changes in the interests of their health".[17] Motivational interviewing works as an interventional technique to "activate patients' own motivation for change and adherence to treatment".[17] It is built upon a supportive, engaging and encouraging framework that incorporates a plethora of communication skills to help patients adopt a greater role in making decisions in regard to their own treatment. Such skills involve the HCP to use open-ended questions, reflective listening, affirmations and support self-efficacy to maintain patient optimism.[18] Motivational interviewing was initially developed as an intervention for problem drinking[17] and has since been established as an effective strategy for substance abuse for drug and alcohol use.[19] A meta-analysis of 119 studies has also demonstrated that motivational interviewing can be used as a technique to improve health-related behaviours (including gambling, smoking, diet, exercise and medication adherence) which found that motivational interviewing produces "statistically significant, durable results over a wide range of problem types".[20] Further systematic reviews show positive and encouraging results in regard to the management of conditions such as HIV[21] and diabetes.[22] Although motivational interviewing has proven significance in improving health behaviours in a variety of conditions, the evidence is still limited regarding a pharmacy role.[14] The aim of this review is therefore to assess the impact of pharmacy care and motivational interviewing as a behavioural intervention to improve medication adherence and clinical outcomes in patients with CVD.

Review criteria

- Information was gathered systematically by searching relevant scientific databases.
- Studies to include in this systematic review were selected based on inclusion and exclusion criteria developed for this review.
- Relevant data were extracted and tabulated to answer the research question.

Message for the clinic

- Motivational interviewing could be utilised by pharmacists as a strategy to improve adherence to medication and clinical outcomes for patients with CVDs.

1.1 | Objectives

To conduct a systematic search of the databases to extract studies based on pharmacy care and motivational interviewing on improving medication adherence and clinical outcomes in patients with CVD.

2 | METHOD

This systematic review was conducted according to PRISMA guidelines[23] and was pre-registered with PROSPERO (registration number CRD42020222954). A completed PRISMA checklist can be found in Appendix A.

2.1 | Search strategy

A systematic search of literature was conducted in the following six databases: PubMed Central UK, Cochrane Library, CINAHL (EBSCO), PsycINFO, EMBASE and MEDLINE from the inception of motivational interviewing in 1983 to November 2020. The review utilised four main key words: 'pharmacy care', 'medication adherence', 'cardiovascular disease' and 'motivational interviewing'; with search restrictions to the English language and randomised controlled trials (RCTs) or cluster RCTs. Key words generated from MeSH terms were also used in relevant databases (see Appendix B for an example search strategy). Reference lists of included studies were hand-searched and reviewed to identify any relevant and additional studies.

2.2 | Study inclusion criteria

Studies that were RCTs or cluster RCTs that used motivational interviewing within pharmacy care to improve adherence to cardiovascular medication were included in this review. RCTs that incorporated motivational interviewing in combination with other interventions as part of a multifaceted intervention strategy as well as pharmacists working independently and/or alongside other HCPs in any care setting were also included. Studies in which interventions were focused on adult patients (≥18 years of age) with CVDs, following a major cardiac event (including myocardial infarction, heart failure, stroke and transient ischemic attack) or have had at least one CVD risk factor (including HTN, diabetes mellitus and dyslipidaemia). Furthermore, studies were included if they had patients taking at least one medication related to the management of their CVD, that compare interventions with an active control or usual, standard care were included in this review. Studies that investigated clinical outcomes alongside medication adherence were selected to be a part of this review. Studies that were not conducted in the English language and those that had no pharmacy involvement were excluded from this review.

2.3 | Outcomes assessed

2.3.1 | Primary outcomes

The primary outcome that was assessed was medication adherence to cardiovascular medication.

2.3.2 | Secondary outcomes

Secondary outcomes were the effect of the intervention on CVD outcomes. These included systolic and diastolic blood pressure, haemoglobin A1c (HbA1c), lipid profiles (eg, low-density lipoprotein cholesterol levels, LDL-Cs) and cardiovascular risk scores.

2.4 | Study selection and data extraction

The first author conducted initial screening of the titles (EA); this was checked by authors (KF and ZJ). The abstracts for inclusion of all identified studies were screened (EA), and full texts were retrieved. All researchers (EA, SA, KF, and ZJ) discussed the full text sources and identified the studies for inclusion. Any uncertainties were discussed amongst the authors to reach a consensus. Data extraction included the study design, the country of origin, sample size, control and intervention arms, the condition treated, the intervention used, the HCP who delivered the intervention, the length of intervention, the level of training the professionals received in motivational interviewing and the impact on assessed outcomes.

2.5 | Risk of bias assessment

The Cochrane Collaboration's Risk of Bias Tool was used to assess the risk of bias in each study.[24] The studies were assessed according to the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other bias. Each domain of the tool was allocated to one of these categories: low, high or unclear risk of bias.

3 | RESULTS

The study characteristics for each of the included RCTs, including the study design, healthcare setting, sample size, length of the intervention, the intervention(s) used, method of delivery and HCP responsible for delivering the intervention, are described in Table 1. The condition treated and level of motivational interviewing training the professionals received prior to delivering the intervention can be also be found in Table 1. The effect on medication adherence can be found in Table 2 and clinical outcomes in Table 3.

The initial search extracted a total number of 87 studies. Following the removal of duplicates, 71 records were screened at title and abstract level to determine their eligibility according to the inclusion criteria. Subsequently, 49 full-text articles were screened, where 41 studies were excluded for the reasons outlined in Figure 1. This review also included two studies that were found through other sources by searching reference lists of the included

TABLE 1 Study characteristics for the included studies

Study	Study design	Healthcare setting	Sample size	Control group
1. Abughosh et al (2017), USA[28]	RCT Prospective study	Electronic (telephone)	Intervention group: 248 Control group: 495 (n = 743)	Patients received usual care as part of Texas MAP enrolment
2. Stewart et al (2014), Australia[32]	Cluster RCT	Community Pharmacy	Intervention group: 207 Control group: 188 (n = 395)	Patients in the control group received routine care throughout
3. Hedegaard et al (2015), Denmark[31]	RCT	Hospital	Intervention group: 231 Control group: 285 (n = 532)	Patients received usual care (2-4 outpatient consultations per year)
Hedegaard et al (2014), Denmark	RCT	Hospital	Intervention group: 102 Control group: 101 (n = 203)	Patients received usual care with no pharmacist intervention
4. Pladevall et al (2014), USA	RCT	Primary care (general practice)	Control group: 567 Adherence information group (AI): 569 AI and motivational interviewing group: 556 (n = 1692)	Patients received usual care
5. Abughosh et al (2019), USA[27]	RCT	Electronic (telephone)	Intervention group: 152 Control group: 304 (n = 456)	Patients received usual care as part of Medicare Advantage prescription drug plan
6. Ostbring et al (2014), Sweden[25]	RCT Pilot study	Hospital	Intervention group: 11 Control group: 10 (n = 21)	Patients in the control group received usual care but received interventions following follow-up 1
7. Jalal et al (2016), UK[26]	Randomised Feasibility pilot-controlled study	Community pharmacy	Intervention group: 32 Control group: 39 (n = 71)	Patients received usual care by a hospital pharmacist

Abbreviations: ACS, acute coronary syndromes; CHD, coronary heart disease; DM, diabetes mellitus; HTN, hypertension; MINT, Motivational Interviewing Network of Trainers; MUR, Medication Usage Review; NMS, New Medicine Service; RCT, randomised controlled trial; Texas MAP, Texas Medicare Advantage Plan; TIA, transient ischemic attack.

studies.[25,26] Overall, eight studies were included in the systematic review (Figure 1), six of which were RCTs,[25,27-31] one study a randomised feasibility pilot controlled trial [26] and one cluster RCT.[32] The identification, selection and review of studies were undertaken by three independent authors. Review procedures, as well as any discrepancies, were discussed at regular meetings. A meta-analysis was considered, but it was not possible to conduct further analysis due to the heterogeneity amongst the included studies.

3.1 | Study characteristics

The eight studies that were included in this systematic review were conducted in the following different countries: Australia (1),[32] Denmark (2),[30,31] Sweden (1),[25] the United Kingdom (1) [26] and the United States (3).[27-29] The included studies involved a total of 4113 patients and the sample size ranged from 21 to 1692 patients[25-32] and the evaluation and follow-up period ranged from 1 to 36 months.[25-32] Further characteristics for each study are described in Table 1. Interventions were implemented monthly,[28] 2-monthly[27] or had 1-month and 6-month follow-up calls after the initial visit, and further intervention within this timeframe if necessary.[31] The included studies focused on patients with a range of cardiovascular conditions and risk factors including coronary heart disease, diabetes mellitus, dyslipidaemia, HTN and post-stroke/TIA patients as mentioned in Table 1. Of the eight studies that met the inclusion criteria, two were conducted in patients with HTN,[31,32] one in post stroke/TIA patients,[30] two in patients with CVD[26,27] (patients with acute coronary syndrome[26] and dyslipidaemia[27]) and one in patients with coronary heart disease.[25] One trial studied patients with both HTN and diabetes mellitus[28] and another studied patients with both dyslipidaemia and diabetes mellitus.[29]

Length of intervention	Intervention (s) used	Intervention(s) delivery method	Professional(s) who delivered the intervention	Condition treated	Level of motivational interviewing training
6 mo	Motivational Interviewing	Telephone	Pharmacy students undergraduates	DM and HTN	Pharmacy students trained over 3 d by a member of the MINT
6 mo	Motivational Interviewing, medication reviews, prescription refill reminders	Face-to-face	Pharmacists	HTN	Pharmacists received training modules and were subsequently assessed on skills and knowledge prior to the study
12 mo	Motivational Interviewing and medication reviews	Face-to-face and telephone	Pharmacists	HTN	Pharmacists attended a 3-d external training course in the aspects of motivational interviewing, including interactive practice sessions.
12 mo	Motivational Interviewing and medication reviews	Face-to-face and telephone	Pharmacists	Stroke/TIA	Total of 4-d motivational interviewing training
36 mo	Motivational Interviewing and adherence counselling	Telephone and face-to-face	Pharmacists and Nurses	DM and dyslipidaemias	Training involved simulated lessons with standardised patients
9 mo	Motivational Interviewing	Telephone	Pharmacy students (undergraduates)	Dyslipidaemias	Pharmacy students received motivational interviewing training by a trainer who is a verified member of the MINT
1 mo	Motivational Interviewing and medication review	Face-to-face and telephone	Pharmacists and cardiology specialists	CHD	No formal education or training in motivational interviewing
6 mo	Motivational Interviewing integrated within NMS and MURs service	Face-to-face and telephone	Pharmacists	ACS	2-day training session on Motivational interviewing, booster session

3.2 | Overview of goals of interventions and primary/secondary outcomes

In seven of the trials,[25-28,30-32] the primary outcome was medication adherence. Other secondary outcomes included reducing cardiovascular risk factors such as BP control[26,32] and LDL-C levels.[26] One trial measured medication adherence as a secondary outcome and HbA1C and LDL-C changes as a primary outcome.[29]

3.3 | Healthcare settings

The interventions were delivered in various healthcare settings, with three studies conducted in hospital settings,[25,30,31] two in community pharmacies,[26,32] one in primary care[29] and two studies conducted by telephone under the Texas Medicare Advantage Plan (MAP) scheme in the United States.[27,28] MAP is a health insurance programme in the United States that helps to cover healthcare expenses for certain patient groups (eg, over 65 years of age).[33] One RCT[26] involved patients in both the intervention and control group receiving usual care upon hospital discharge (medicines use and counselling, leaflets and referral to outpatient specialties if necessary) and community pharmacy consultations 2-week post discharge where motivational interviewing interventions were delivered. The same concept is used in other studies where following hospital discharge, patients were reviewed in outpatient clinics for further consultations and follow-up reviews.[25,30,31]

3.4 | Details of the intervention

As specified in the inclusion criteria, all interventions were pharmacy based. Five studies were conducted by pharmacists,[26,30-32]

TABLE 2 The effect of motivational interviewing on medication adherence

Study Country	Method of measuring medication adherence	Effect on adherence and mean change, 95% CI	*P* value
1. Abughosh et al (2017), USA[28]	PDC and refill data	Patients that received 2 or more follow-up phone calls had an improvement in adherence following the initial intervention and over the 6-mo follow-up period (95% CI = 1.53 [1.02-2.28])	*P* = .009
2. Abughosh et al (2019), USA[27]	PDC and refill data	Patients were more likely to adhere to medication after the initial intervention and over the 6-month follow-up period (95% CI = 1.87 [1.18-2.95])	*P* < .001
3. Hedegaard et al (2014), Denmark	MPR	No significant change in MPR (primary endpoint) over 12 mo (95% CI = 7 [−5 to 19])	*P* = .32
4. Hedegaard et al (2015), Denmark[31]	MPR	Statistically significant change in MPR (primary endpoint) over 12 mo (95% CI = −10 [−17 to 2])	*P* = .01
5. Jalal et al (2016), UK[26]	MMAS-8	Statistically significant improvement on medication adherence at 3 mo. MMAS score: At 3 mo (M = 7.7, SD = 0.56) and the control group (*M″* = 7.0, SD = 1.85), *P* = .026. At 6 mo: (M = 7.5 [93.75%], SD = 1.47) and the controls (M = 6.1 [76.25%], SD = 2.09), *P* = .004. Note: (M = mean).	*c*
6. Ostbring et al (2014), Sweden[25]	MMAS-8	No statistical difference in medication adherence. Sample size insufficient to draw conclusion following the 1-mo intervention period. MMAS score: At baseline: 3 patients with MMAS-8 score of low (<6), 3 with medium (6-8), 5 with high (8) in comparison to control group 1 patient with low (<6), 1 patient medium (6-8), 8 with high (8). After the first follow-up: 1 patient with low (<6), 4 with medium (6-8), 6 with high (8) in comparison to the control group with 1 patient with low (<6), 2 with medium (6-8), 7 with high (8) After the second follow-up, 1 patient with low (<6), 4 with medium (6-8), 6 with high (8) (n = 11)	Not reported
7. Pladevall et al (2015), USA[29]	Electronic prescription and refill data	No statistical difference on adherence to oral diabetes medication or lipid-lowering medication over the intervention period	*P* = .883 (oral diabetes medication) *P* = .633 (lipid lowering medication)
8. Stewart et al (2014), Australia[32]	MMAS-4 and prescription refill reminders	Medication adherence was significantly higher in PCG compared to UCG (61.8% vs. 39.2% - mean change of 22.6% 95% CI = 5.1%-40%) over the 6-mo follow-up period. MMAS score: UCG: 79% of patients had an MMAS-4 score > 0 compared to PCG with 85% Morisky score > 0 at baseline	*P* < .007

Abbreviations: MMAS-4, Morisky Medication Adherence Scale 4-item; MMAS-8, Morisky Medication Adherence Scale 8-item; MPR, medication possession ratio; PDC, proportion of days covered.

two studies were conducted by undergraduate pharmacy students under supervision,[27,28] one study[29] was conducted by pharmacists alongside nurses, and one study[25] had pharmacists working alongside cardiology specialists as part of collaborative care (Table 1). Follow-up consultations across the studies were relatively brief and ranged from five to 30 minutes on average with a range of two to six motivational interviewing consultations across all study intervention periods.[25-32]

3.5 | Delivery of the intervention and motivational interviewing training

Of the eight studies, six trials used motivational interviewing in combination with other interventions such as refill reminders, patient education and counselling through medication reviews. One study[26] integrated motivational interviewing within existing pharmacy-based services (New Medicine Service and Medication Use Reviews). Such

TABLE 3 The effect of motivational interviewing on clinical outcomes

Study Country	Clinical outcome measured	Effect of motivational interviewing on clinical outcome and mean change, 95% CI	*P* value
1. Hedegaard et al (2015), Denmark[31]	BP	No significant difference seen in both SBP and DBP. SBP change of −1.1 mmHg (95% CI = −5.0 to 2.8) and DBP change 0.4 mmHg (95% CI = −2.2 to 3.1) between intervention and UCG group over 12 mo.	Not reported
2. Jalal et al (2016), UK[26]	BP and LDL-C levels	No statistical difference seen in SBP or DBP or baseline LDL-C between intervention and UCG at 6 mo	*P* = .6 (BP) *P* = .9 (LDL-C)
3. Pladevall et al (2015), USA[29]	HbA1C and LDL-C levels	No statistical difference for HbA1C and LDL-C levels at 18 mo post randomisation between AI, AI + MI or UCG. AI vs UCG (95% CI = 0.76-1.27) and AI + MI vs UCG (95% CI = 0.76-1.28)	*P* = .763 (AI vs UCG) *P* = .285 (AI + MI vs UCG)
4. Stewart et al (2014), Australia[32]	BP	Significant difference of SBP between PCG and UCG for non-adherent patients at baseline by 9.4 mmHg (95% CI = 2.2-16.6). Significant difference of SBP between PCG and UCG for patients above target BP by 7.2 mmHg (95% CI = 1.6-12.8)	*P* =.01

Note: NB: Where clinical outcomes were not measured, these studies were not included in the table. NB: Usual care and control group are used as interchangeable terms.

Abbreviations: AI, adherence information; BP, blood pressure; DBP, diastolic blood pressure; haemoglobin A1c (HbA1c); LDL-C, low-density lipoprotein cholesterol; MI, motivational interviewing; PCG, pharmacy care group; SBP, systolic blood pressure; UCG, usual care group.

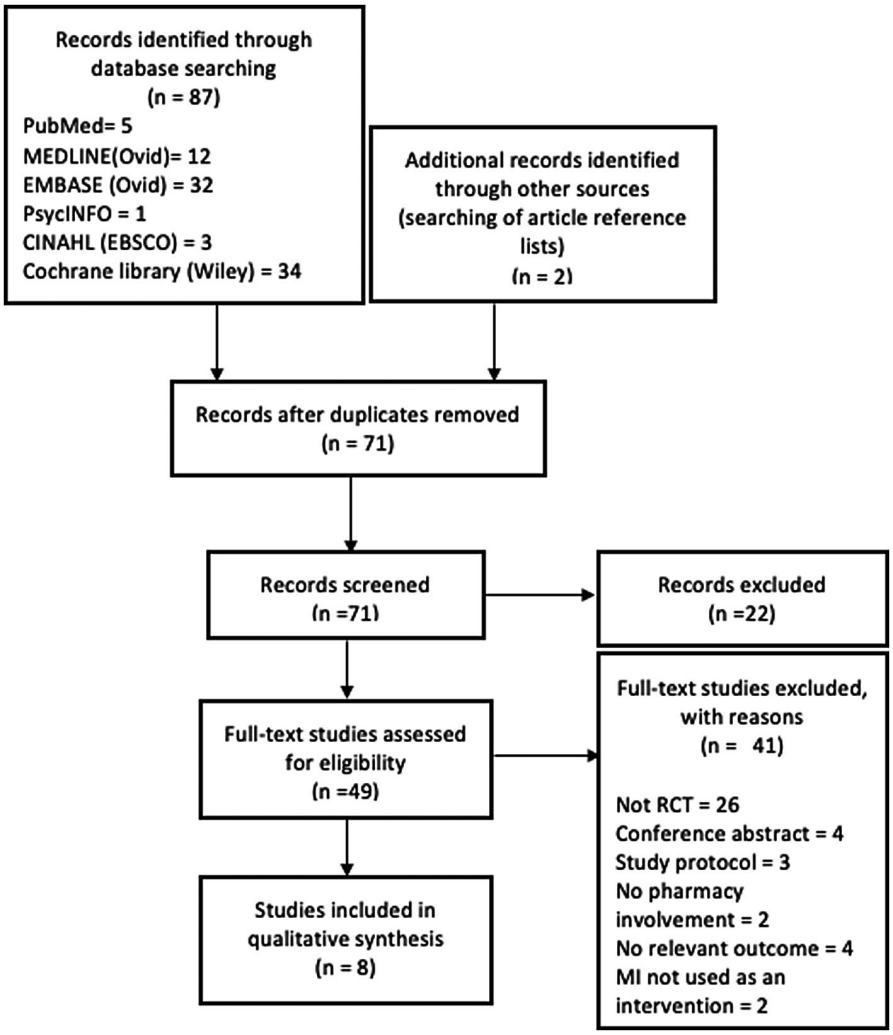

FIGURE 1 PRISMA flow chart of the study selection process

interventions were delivered as either face-to-face or by telephone, or a combination of both methods. Two studies[27,28] used motivational interviewing in isolation as a behavioural intervention to improve medication adherence and conducted the interventions by telephone only (Table 1).

All HCPs delivering the interventions were trained to various standards in motivational interviewing (Table 1). The level of training delivered to the HCPs differed in each study, including courses delivered by accredited members of the 'Motivational Interviewing Network of Trainers',[27,28] whilst others received either a 2-,[26] 3-[31] or 4-day[30] course or training modules[32] in the aspects of motivational interviewing. One study[29] trained HCPs via simulated lessons using standardised patients, whilst one study[25] had no formal training of professionals in motivational interviewing.

3.6 | Measurement of medication adherence

Medication adherence was measured in a variety of ways across the studies. Self-reported adherence questionnaires were used through Morisky Medication Adherence Scales (MMAS-8 and MMAS-4). The MMAS-8 scale is a commonly used screening tool to measure medication adherence, with non-adherence being defined as taking <80% of CVD medications.[34] Medication possession ratio and use of prescription refill data to calculate proportion of days covered (PDC) (a PDC <80% identified patients as non-adherent based on the patients' previous refill data) were common methods to measure adherence in the eight trials. Only one study used a combination of the MMAS-8 and prescription refill reminders to measure adherence[32] compared to the remaining seven studies[25-31] that only used one single medication adherence measurement.

3.7 | Impact of interventions on adherence

Five trials[26-28,31,32] demonstrated statistically significant ($P < .05$) improvement in adherence to cardiovascular medication following motivational interviewing interventions (Table 2). The remaining three studies[25,30,32] indicated no statistical difference on adherence improvement. The results also demonstrate that face-to-face, telephone or a combination of both were effective in delivering motivational interviewing interventions and thus improving medication adherence. The effect of medication adherence was assessed at the longest follow-up period for each included study; please see Table 1 for the length of the interventions.

3.8 | Impact of intervention on clinical outcomes

Clinical outcomes were assessed in five out of the eight trials,[26,29-32] including blood pressure (BP), HbA1c and LDL-Cs. Clinical outcomes were measured using home BP monitoring, 24-hour BP monitoring and blood sampling to determine LDL-C and HbA1C levels. Only one study[32] demonstrated statistical significance on the effect of BP levels following improvement of medication adherence after motivational interviewing interventions (Table 3). Patients in the intervention group with a baseline BP above their target range had a significant reduction of systolic BP by 7.2 mmHg (95% CI 1.6-12.8 mmHg; $P = .01$)[32] (Table 3).

3.9 | Risk of bias of included studies

The risk of bias summary was generated using RevMan software version 5.3.[35] Only five studies adequately reported allocation sequence generation,[28-32] and five reported a low risk of bias for allocation concealment,[25,26,30-32] whilst the remaining studies allocation concealment process remains unclear.[27-29] The blinding of participants and personnel had either a high or unclear risk of bias due to the nature of the intervention where it is not possible to blind the HCPs or patients. Not all studies involved the blinding of outcome assessors (the researcher responsible for data analysis) therefore leading to a high or unclear risk of bias (Figure 2). However, seven

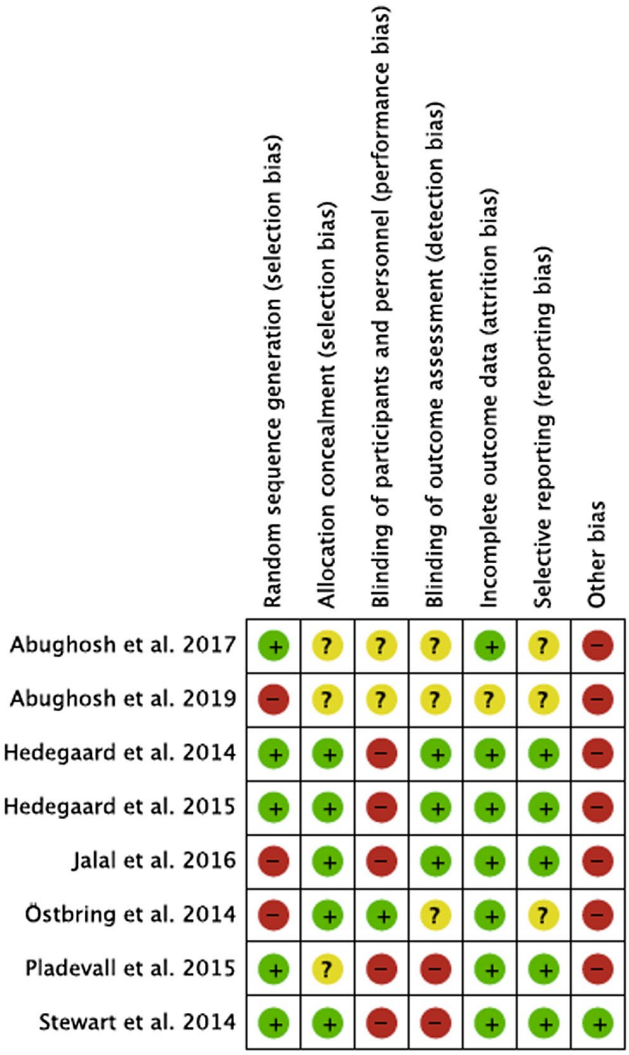

FIGURE 2 Risk of bias summary graph and the outcome of each domain for included studies

out of the eight studies[25,26,28-32] reported a low risk of bias for incomplete outcome data where reasons were given for patient drop-outs. The risk of bias for selective reporting was also generally low given that most studies reported their outcomes as intended in their published protocols.[26,29-32] The risk of bias for other sources of bias was high overall given that most studies[25-31] only used one method to measure medication adherence (Figure 3).

4 | DISCUSSION

The aim of this systematic review was to assess the impact of pharmacy care and motivational interviewing on adherence to cardiovascular medication in the CVD population. This review demonstrated that pharmacy care and motivational interviewing as a behavioural intervention were effective in improving medication adherence in the CVD population. Five out of eight studies[26-28,31,32] showed statistically significant results on improving medication adherence. In addition, one RCT[32] showed statistically significant results for improved medication adherence as well as clinical outcomes for BP reduction. The same study[32] concluded that motivational interviewing had a greater effect in patients who were both non-adherent to antihypertensives and above their baseline BP target. Such findings are synonymous with the view from the Accreditation Council for Pharmacy Education and American Association of Colleges of Pharmacy, who emphasise the importance of motivational interviewing as an integral skill for delivering high-quality pharmaceutical care, and that the incorporation of such skills will ensure direct patient care and could potentially lead to better health outcomes.[36] This confirms recent research further exploring the use of motivational interviewing in the CVD population, which concluded there was a positive impact of motivational interviewing in a variety of health settings. Additionally, a review by Dalem et al[37] deduced that behavioural interventions such as motivational interviewing were the most successful in improving adherence and persistence to medication in CVD.

The current findings showed that motivational interviewing interventions could be delivered as effectively by both face-to-face and telephone consultations or through a combination of both methods. A review by Hervé et al[38] suggested that face-to-face consultations are more effective than telephone interventions. However, the findings of this study suggest that this pattern may not be universal. Indeed, a wide range of studies have demonstrated that motivational interviewing can be effectively delivered remotely: a nurse-led RCT[39] found that telephone-based motivational interviewing interventions increased adherence to antiplatelet medication by 14% ($P < .01$). Similarly, a study conducted by Young et al[40] also concluded that motivational interviewing delivered by telephone increased adherence to antidiabetic medication. Moreover, the studies conducted solely by telephone[27,28] showed statistically significant results in improving medication adherence, thus demonstrating that motivational interviewing interventions delivered by telephone could also be both feasible, effective and efficient way to deliver motivational interviewing interventions,[41] across a range of healthcare settings, as demonstrated in this review.

The improvements in medication adherence were consistent with the findings of a systematic review and meta-analysis showing that motivational interviewing can be effective in 'brief encounters' and that multiple motivational interviewing sessions can increase the probability of this effect.[42] In confirmation, the study that delivered brief and frequent motivational interviewing interventions over the intervention period[28] demonstrated significant improvement for medication adherence. Such findings suggest that motivational interviewing interventions with a shorter duration over multiple sessions could be preferable and more effective in patients to help improve medication adherence.

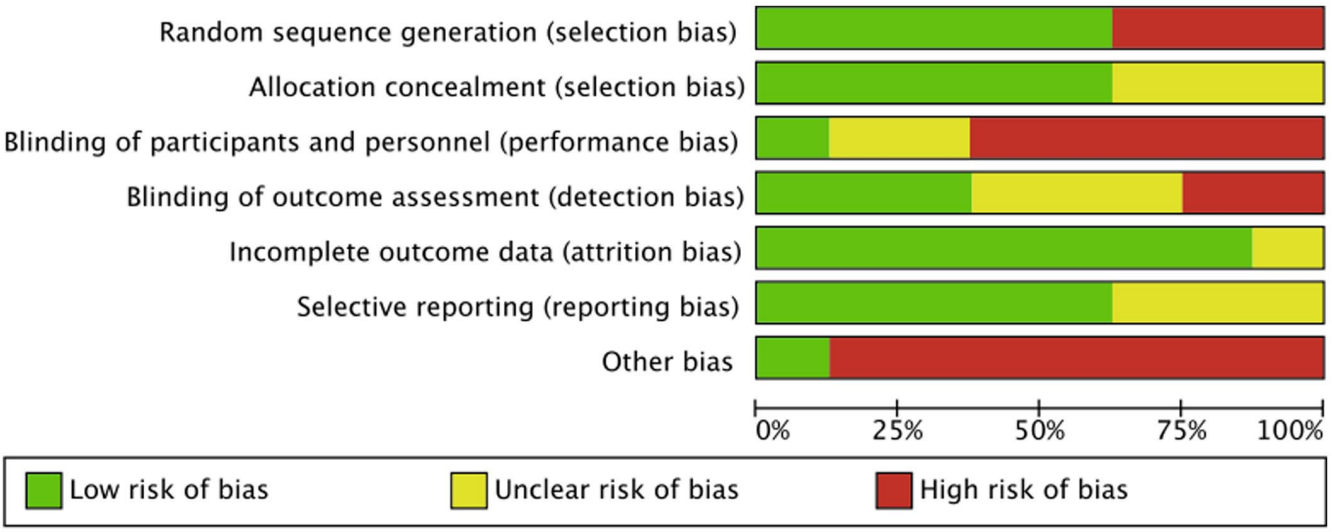

FIGURE 3 Risk of bias graph of the included studies presented as percentages for each risk of bias domain

It is notable that the standard of motivational interviewing training for intervention delivery was inconsistent across the studies. The HCPs in one RCT[25] received no formal training in motivational interviewing prior to the study and did not show any statistical improvement in medication adherence overall. It has been suggested that learning motivational interviewing is a difficult process consisting of eight phases, where one must also understand the philosophical nature behind the intervention before becoming competent in motivational interviewing.[43] Thus, the inconsistency and lack of motivational interviewing training may have limited the effectiveness of motivational interviewing delivery to patients, impacting on medication adherence and clinical outcomes overall.

Poor participation rates in some of the studies[29,31] also limit the confidence in the results. Although the RCT conducted by Pladevall et al[29] had the largest sample size and conducted interventions over the longest time period, poor participation rates were an issue. The same study[29] concluded that the lack of statistical improvement in medication adherence could be down to the reluctancy of the least adherent patients to make change and that a multimethod approach including further behavioural interventions or 'patient incentives'[29] may be needed to further boost their motivation for change. This study[29] also offered the service in the United States free of charge, increasing the likelihood of patients to not participate to their fullest potential.[25,29] Another study[30] in this review conducted in post-stroke/TIA patients had no significant improvement of adherence rates for the fact that adherence rates were already high, leaving a small margin for improvement. This suggests that motivational interviewing may only be effective in patients with poor adherence rates over a longer term.

4.1 | Strengths and limitations

The majority of the studies[27-32] focused on the use of pharmacy-led motivational interviewing within a range of healthcare settings. Thus, this review demonstrated encouraging evidence for implementing motivational interviewing into everyday pharmacy practice, whether by face-to-face or by telephone. However, there are some limitations to this review: motivational interviewing was delivered in combination with other interventions in six out of the eight trials[25,26,29-32]; meaning, it is difficult to definitely determine the extent to which motivational interviewing caused a significant effect on medication adherence improvement. Additionally, there are very few studies available that explore the role of pharmacy care and motivational interviewing in isolation, and this can limit the overall 'statistical power'[44] for medication adherence improvement rates. Furthermore, the level of motivational interviewing training received by the HCPs varied greatly between each study, and the lack of standardised training could have impacted the quality and effectiveness of motivational interviewing interventions overall. Regarding measurement of adherence, the use of refill data as a way of measuring medication adherence can be an unreliable method given that it does not guarantee that the patient took the medication, although it has been validated as an acceptable measure of adherence rates.[45] Similarly, the use of self-reported questionnaires, ie, MMAS-8, can also overestimate the degree of medication adherence if patients answer the questions untruthfully. This can be explained from a psychological point of view by the Hawthorne effect, defined as an artefact for the impact of research upon behaviour.[46] Furthermore, studies that were non-RCTs and not conducted in the English language were excluded, and this may have limited the scope of the studies that could have been included in this review. Finally, most of the included studies had an uncertain potential for bias, including blinding and allocation methods and publication bias. The positive results from the studies included in this review, thus, should be interpreted with caution.

4.2 | Recommendations for policy and practice

Overall, this review suggests that motivational interviewing can be effective in improving medication adherence by both face to face and telephonically when applied in pharmacy practice. Research conducted to date also indicates that motivational interviewing can help to drive patients' own motivation for change and, in turn, enhance their health behaviours. However, further research is required to assess the impact of motivational interviewing on adherence rates in larger study cohorts over a longer period of time. Moreover, motivational interviewing as a behavioural intervention in isolation could be explored further to determine its impact on medication adherence as well as on clinical outcomes in a variety of disease states, although causes of non-adherence are multifactorial and thus one strategy might not be effective. More in-depth research could also be conducted to further explore the feasibility of incorporating motivational interviewing into everyday pharmacy practice.

The results of this review conclude the need for further research which implements motivational interviewing within larger sample sizes over longer intervention periods to determine the statistical impact of motivational interviewing on medication adherence and clinical outcomes. Furthermore, multiple methods to measure medication adherence in addition to self-reported adherence would also be recommended to assess adherence rates such as electronic monitoring systems.[47] The use of standardised or consistent motivational interviewing training amongst HCPs is also needed.

5 | CONCLUSION

The evidence from this review shows that incorporating motivational interviewing within pharmacy care can improve medication adherence. It also shows that motivational interviewing has the potential to be incorporated into existing pharmacy services, across of a range of different healthcare settings and be delivered both face to face and telephonically. There is also encouraging evidence to support the positive impact of motivational interviewing on improving clinical outcomes. However, given the limited number further

research required to further explore the impact of motivational interviewing on both medication adherence and clinical outcomes in pharmacy practice, preferably as larger scale trials conducted over longer durations. More research could also examine the feasibility of including motivational interviewing interventions alongside standard pharmacy care.

DISCLOSURE

Authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Study design (EA, ZJ, SA, and KF); methodology (EA, ZJ, SA, and KF), database searches (EA) and study selection (EA, ZJ, SA, and KF), data extraction (EA), manuscript writing and revising (EA, KF, and ZJ), selection of bias (EA and SA), manuscript drafting and editing (EA, ZJ, SA, and KF), and supervision (ZJ, SA, and KF).

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APPENDIX A

PRISMA CHECKLIST (2009)

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1, 2
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2, 5, 6, 7, 8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 23, 25
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3, 4, 5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6, 7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (eg, Web address), and, if available, provide registration information including registration number.	5 Access here: https://www.crd.york.ac.uk/prospero/ Registration number: CRD42020222954
Eligibility criteria	6	Specify study characteristics (eg, PICOS, length of follow-up) and report characteristics (eg, years considered, language, publication status) used as criteria for eligibility, giving rationale.	6, 7, 12, 13, 14
Information sources	7	Describe all information sources (eg, databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5, 6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	30
Study selection	9	State the process for selecting studies (ie, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6, 7, 11
Data collection process	10	Describe method of data extraction from reports (eg, piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (eg, PICOS, funding sources) and any assumptions and simplifications made.	5, 6, 7, 8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7, 19, 20, 21
Summary measures	13	State the principal summary measures (eg, risk ratio, difference in means).	16, 17,18
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg, I^2) for each meta-analysis.	—
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (eg, publication bias, selective reporting within studies).	19, 20, 21
Additional analyses	16	Describe methods of additional analyses (eg, sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	—

Section/topic	#	Checklist item	Reported on page #
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11
Study characteristics	18	For each study, present characteristics for which data were extracted (eg, study size, PICOS, follow-up period) and provide the citations.	12, 13, 14,
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	19, 20, 21
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	16, 17,18
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	—
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	19, 20, 21
Additional analysis	23	Give results of additional analyses, if done (eg, sensitivity or subgroup analyses, meta-regression [see Item 16]).	—
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg, healthcare providers, users, and policy makers).	17, 18, 20, 21, 22
Limitations	25	Discuss limitations at study and outcome level (eg, risk of bias), and at review-level (eg, incomplete retrieval of identified research, reporting bias).	18, 22, 23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21, 22, 23, 24, 25
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (eg, supply of data); role of funders for the systematic review.	26

APPENDIX B

A database search conducted in Ovid Medline (1946 to October 2020)

Results (n = 12). By applying a filter of clinical trials (n = 6).

1. exp Pharmacy/
2. Pharmacy care.mp.
3. Pharmacy service*.mp.
4. exp Pharmaceutical Services/
5. (pharmacy adj3 counsel$).mp.
6. (pharmacy adj3 follow-up).mp.
7. Pharmacist*.mp.
8. Pharmacist intervention.mp.
9. (intervention$ adj3 pharmacist$).mp.
10. Medication therapy management.mp.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp Motivational Interviewing/
13. (motivational adj3 interviewing).mp.
14. Motivational technique*.mp.
15. Motivational behavio*.mp.
16. Motivational change*.mp.
17. (motivat$ adj3 behavio$).mp.
18. (behavio$ change adj3 motivational interviewing).mp.
19. (behavio$ adj3 motivational interviewing).mp.
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp Medication Adherence/
22. exp Patient Compliance/
23. exp "Treatment Adherence and Compliance"/
24. (treatment adherence and compliance).mp.
25. 21 or 22 or 23 or 24
26. exp Cardiovascular Diseases/
27. Cardiovascular disease*.mp.
28. Cardiovascular disease$.tw.
29. 26 or 27 or 28
30. 11 and 20 and 25 and 29