

ORIGINAL ARTICLE

Effectiveness of a targeted and tailored pharmacist-led intervention to improve adherence to antihypertensive drugs among patients with type 2 diabetes in Indonesia: A cluster randomised controlled trial

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Funding information

Indonesia Endowment Fund for Education (LPDP), Grant/Award Number: (LPDP No: PRJ-2361/LPDP/2015).

Aim: To assess the effects of a targeted and tailored pharmacist-led intervention among patients with type 2 diabetes (T2DM) who are nonadherent to antihypertensive drugs.

Methods: A cluster-randomised controlled trial was conducted in 10 community health centres (CHCs) in Indonesia among T2DM patients aged ≥ 18 years who reported nonadherence to antihypertensive drugs according to the Medication Adherence Report Scale (MARS-5). Patients in CHCs randomised to the intervention group received a tailored intervention based on their adherence barriers (eg, forgetfulness, lack of knowledge, lack of motivation and/or other drug-related problems) using a simple question-based flowchart at baseline and 1-month follow-up. Patients in control CHCs received usual care. Primary outcome was the between-group difference in change in MARS-5 score from baseline to 3-month follow-up. Secondary outcomes included changes in patients' blood pressure and their medication beliefs. Differences in difference in primary and secondary outcomes between groups were assessed using general linear models.

Results: In total, 201 patients were screened for eligibility, 113 met the inclusion criteria and participated, and 89 (79%) patients had complete follow-up. Forgetfulness (42%) and lack of knowledge (18%) were the most common adherence barriers identified at baseline. The intervention improved medication adherence by 4.62 points on the MARS-5 scale (95% CI 0.93 to 8.34, P value = 0.008). There were no significant changes in blood pressure levels and beliefs about antihypertensive drugs.

Conclusion: A tailored low-cost pharmacist-led intervention aimed at nonadherent T2DM patients resulted in an improvement in medication adherence to antihypertensive drugs. There were no significant changes in secondary outcomes.

The authors confirm that the principal investigator for this paper is S.D.A. and that she had direct clinical responsibility for patients.

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KEYWORDS

adherence intervention wheel, antihypertensive drugs, cluster randomised controlled trial, community pharmacist, diabetes, low- and middle-income countries, medication adherence

1 | INTRODUCTION

Hypertension is common in patients with type 2 diabetes (T2DM) and contributes significantly to an increased risk of cardiovascular complications,¹ therefore antihypertensive medication is often necessary in patients with T2DM.¹ However, patients may have particular problems with adherence to their antihypertensive co-medication. Indeed, previous studies showed that adherence to antihypertensive drugs is suboptimal in high- and low- and middle-income countries.²⁻⁵ While intervention programs have been conducted among patients with diabetes to improve adherence to their antidiabetic drugs,^{6,7} there is limited knowledge regarding the effect of adherence interventions to cardiovascular co-medications among these patients, particularly in low- and middle-income countries.

Numerous interventions to improve medication adherence have been studied in high-income countries,^{8,9} yet the majority of interventions are too complex and have limited efficacy.⁸ This limited efficacy may reflect that many interventions do not adequately address each individual's barriers to adherence and are delivered to the general population rather than to those who actually need it.^{10,11} In addition, many interventions showing promising results have not been widely adopted given the substantial human resources required to maintain them.⁸ Nonadherence may be more efficiently improved if only patients who need it are targeted and interventions are tailored to patients' individual adherence barriers.^{10,11} Furthermore, interventions led by a pharmacist and delivered face-to-face to patients have been shown to effectively improve adherence.¹² With the Behavior Change Wheel¹³ and previous interventions as a basis,¹⁴⁻¹⁶ we have designed a medication adherence intervention wheel to support pharmacists in selecting a personalized, low-cost intervention for each individual nonadherent patient barrier.¹⁷

The primary objective of this study was to assess the effect of this innovative low-cost, targeted and tailored pharmacist-led intervention on medication adherence to antihypertensive drugs among nonadherent patients with T2DM. The secondary objectives were (a) to assess the effect of the intervention on medication beliefs and blood pressure, and (b) to explore the effects of the intervention across different subgroups of patients.

2 | METHODS

This study was reported according to the CONSORT 2010 statement for cluster randomised trials¹⁸ (Supporting Information Table S1) and the ESPACOMP Medication Adherence Reporting Guideline (EMERGE)¹⁹ (Supporting Information Table S2). The protocol for this study has been described elsewhere.¹⁷ The study was approved by

What is already known about this subject

- Adherence to chronic preventive medications remains poor despite the development of many interventions to address nonadherence.
- Interventions to improve medication adherence are often too complex or costly to implement in low- and middle-income countries.
- Nonadherence is the result of a multifactorial behavioural process that requires a patient-tailored approach.

What this study adds

- An innovative, low-cost, pharmacist-led intervention that is targeted to nonadherent patients with type 2 diabetes and tailored to a patient's personal adherence barriers can improve adherence to antihypertensive drugs.
- The most important barriers that need to be addressed in patients with type 2 diabetes in Indonesia are forgetfulness and lack of knowledge regarding antihypertensive drugs.

the Health Research Ethics Committee of Universitas Padjadjaran No. 859/UN6.KEP/EC/2019 and all participants gave written informed consent. The study was registered at clinicaltrials.gov under the identifier NCT04023734.

2.1 | Study design and setting

We conducted a cluster randomised controlled trial with two parallel arms in community health centres (CHCs) in Bandung City, Indonesia from August to December 2019. Clusters of randomisation were CHCs. In Indonesia, the prescription length for medication used for chronic diseases is 30 days, therefore patients need to return to the CHCs to collect their medication every month. The principal investigator randomised the CHCs into the control or intervention group in a 1:1 ratio using a computer-generated random number sequence.

2.2 | Study population

A total of 10 CHCs were purposively selected based on a sufficient number of T2DM patients with hypertension from 78 CHCs in Bandung

City, Indonesia. Screening for patients' eligibility was conducted by the pharmacist during regular outpatient visits. Patients were eligible if they met the following inclusion criteria: at least 18 years old, diagnosed with T2DM for at least 1 year based on the patient's medical record, using at least one antihypertensive drug in the last 3 months, have signed informed consent and have suboptimal medication adherence to antihypertensive drugs according to the Medication Adherence Report Scale (MARS-5 score <20; MARS-5 scores range from 5 to 25). Patients with severe mental or physical constraints, pregnancy or in the lactation period, illiterate in the Indonesian language, enrolled in another intervention study and those not responsible for taking their own medication were excluded. This study focused on medication adherence in the implementation phase of treatment.²⁰

2.3 | Intervention

Patients in the five CHCs randomised to the intervention group who were screened as nonadherent to their antihypertensive drugs received a tailored pharmacist-led intervention during two sessions in addition to usual care. Both were regular outpatient visits, when patients collect their medication. Pharmacists were supported by a paper-based medication adherence intervention wheel.¹⁷ All interventions were conducted by the same pharmacist to ensure consistency. Intervention fidelity was addressed by providing a checklist of items that pharmacists needed to do at each patient visit and a counselling protocol for the intervention group. The completed checklists were collected on a weekly basis and minor suggestions to the pharmacists were made by the researcher when needed. The checklist and counselling protocol have been published elsewhere, together with the study protocol.¹⁷

2.3.1 | Training for pharmacists

Pharmacists received a 3-hour obligatory communication training conducted by a senior pharmacist focusing on how to elicit and classify barriers to adherence, the teach-back method and motivational interviewing (MI). The main elements of MI were explained and shown, such as collaboration (engaging with the patient), evocation (exploring patient ambivalence to adhere and evoking rather than instilling motivation for change) and autonomy (emphasizing the patient's ability for making the decision to change).²¹ The use of open questions, and patient-centred and respectful communication techniques were explained and illustrated by the senior pharmacist.

2.3.2 | Intervention at baseline (first session)

Before dispensing antihypertensive drugs during the first session, the pharmacist discussed patient-specific barrier(s) for medication adherence. The intervention strategy was tailored to the identified adherence barrier(s). Based on literature,²²⁻²⁴ we defined four main adherence barriers that could be addressed by the community

pharmacists: (1) forgetfulness; (2) lack of knowledge; (3) lack of motivation; and/or (4) other drug-related problems. Of note, patients might need a combined intervention strategy to address all experienced barrier(s). Simple question-based flowcharts and the adherence intervention wheel were provided to support the pharmacy staff in identifying the patient's personal adherence barriers and tailoring the intervention to these barriers.¹⁷ The session was ended with involving patients in goal setting and writing the agreed goal(s) at the top of a personalized leaflet.

2.3.3 | Interventions at follow-up (second session)

The follow-up session was conducted 1 month after the baseline session, when patients refill their medication at the next regular outpatient visit. The purpose of the follow-up session was to evaluate the short-term effect of the intervention and discuss the patient's implementation of, and experiences with, the offered information and recommendations, and to address nonadherence problems that had not been addressed during the first session. Based on patients' responses to the MARS-5, those who had already become adherent (MARS-5 score ≥ 20) in the follow-up session were complimented and asked about their experience and expectations to maintain good adherence. In patients that still showed nonadherence, the pharmacist, together with patients, made changes to the action plan and discussed additional interventions. This session was again ended with involving patients in goal setting and writing the agreed goal(s) at the top of a personalized leaflet.

2.4 | Control group

Patients in the five CHCs randomised to the control group received pharmacist counselling based on the Indonesian guideline of pharmacy practice (PMK No.74/2016).²⁵ At each visit, they received information about the quantity and dose of the dispensed drugs, when and how to use and store the drugs, side effects and how to deal with them, the importance of medication adherence, and confirming if the patient understands how to take medications correctly. Patients in the control group who were screened as nonadherent to their antihypertensive drugs at baseline completed the assessments at the same time points as those in the intervention group.

2.5 | Outcomes

The primary outcome was the difference between the intervention and control groups in change in MARS-5 score from baseline (T0) to 3-month follow-up (T2). The MARS-5 has been shown to correlate well with indirect measures of adherence, including pill counts among patients with hypertension and refill rates (using medication possession ratio) among patients with stroke.^{26,27} Secondary outcomes were medication beliefs (necessity, concerns, side effects and necessity-

concern differential) assessed using the Beliefs about Medicines Questionnaire (BMQ) specific at baseline (T0), 1-month (T1) and 3-month follow-up (T2), MARS-5 score from baseline (T0) to 1-month follow-up (T1), and blood pressure level (systolic and diastolic blood pressure). Details on study outcomes have been published elsewhere.¹⁷

2.6 | Baseline participant and CHC characteristics

Participants' baseline characteristics, including sociodemographic and clinical-related factors, were obtained. Sociodemographic factors were self-reported and included age at the completion of the questionnaire, gender, highest level of education completed and type of health insurance. Clinical-related factors included time since diagnosis of T2DM and hypertension (years), T2DM complications that developed after the diagnosis of T2DM, and types and number of concomitant drugs. Clinical-related factors, organizational information of each CHC and pharmacist characteristics were collected using a predefined data collection form.

2.7 | Sample size calculation

A sample size calculation for cluster randomised controlled trials as described in the study protocol¹⁷ was performed to detect a difference between the intervention and control groups in change in adherence score of at least 2.5 points on the self-reported MARS-5 (range 5-25 points). Given an expected standard deviation of 3.8 for this difference in difference score, based on data collected in a similar population,²⁸ this would represent a medium to large effect size. With an estimated intracluster correlation coefficient (ICC) of 0.014²⁸ and assumed equal cluster sizes, we required 41 nonadherent patients with completed follow-up in each study arm to achieve 80% power to detect this difference using a two-sided test at the 5% level of significance.

2.8 | Statistical analysis

Data analysis was performed based on the intention-to-treat principle. Descriptive statistics was used to summarize the baseline characteristics. Analyses of intervention effects were performed by a biostatistician (HS) blinded to the group allocation. Differences in difference in primary and secondary outcomes between groups were assessed using a general linear model accounted for the clustering of patients within CHCs, with individual CHCs treated as a random effect. Missing values on the 3-month adherence score, systolic and diastolic blood pressure levels, and medication beliefs were dealt with multiple imputation.²⁹ Five imputed datasets were obtained for each measurement. In addition, a per-protocol analysis was conducted including only those patients who completed both the baseline and 3-month follow-up assessments. Finally, subgroup per protocol analyses regarding the effect of the intervention on the MARS-5 score were conducted using stratification by diabetes complications

(yes/no) and number of concomitant drugs (1, 2 or ≥ 3 drugs). All tests were two-tailed and P value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 25.0; IBM, Armonk, NY, USA).

3 | RESULTS

3.1 | Baseline characteristics

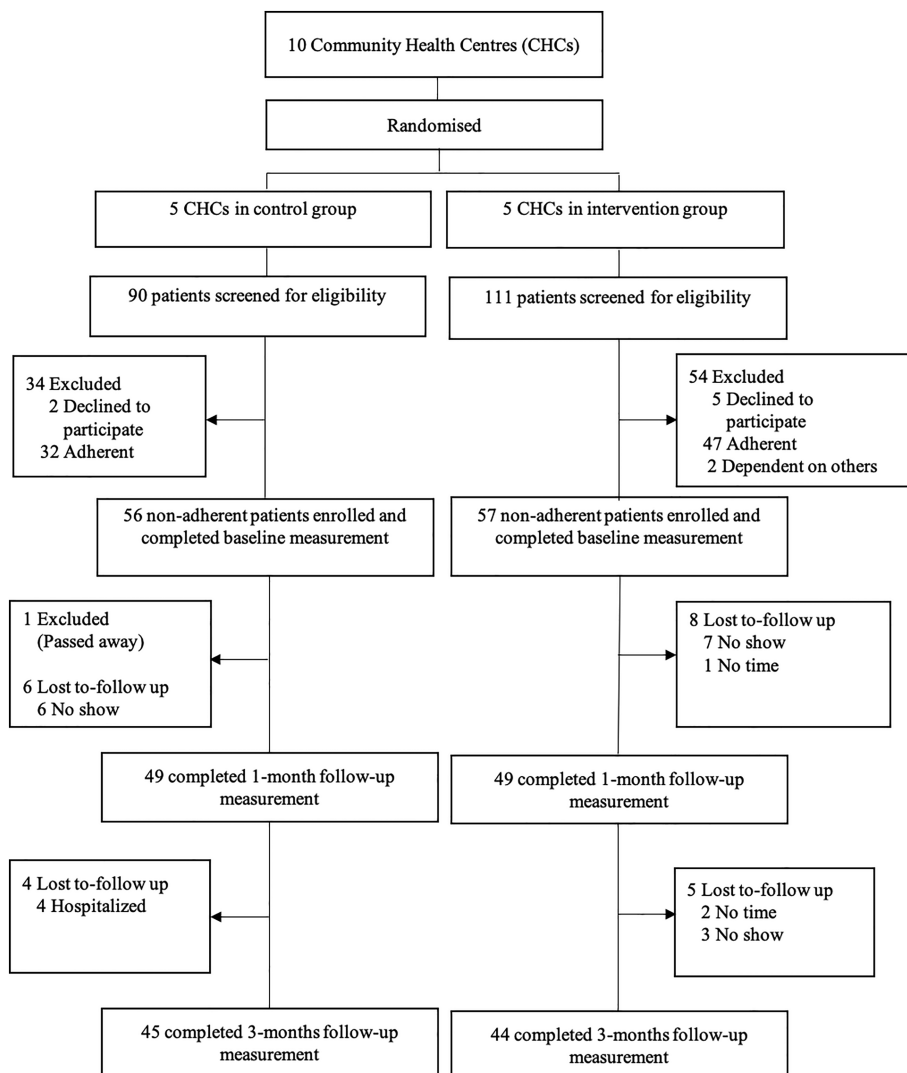
In total, 201 patients from 10 CHCs were screened for eligibility to participate. Of these, 113 patients (56 in the control group [five CHCs] and 57 in the intervention group [five CHCs]) met the inclusion criteria (Figure 1). The intended number of screening at least 20 patients per CHC for eligibility was achieved in six CHCs. The number of patients screened in the other four CHCs ranged from 14 to 17 patients depending on the size of the CHC. Overall, most patients were female, aged between 60 and 69 years, and graduated from elementary school (Table 1). Patients in the control group had a higher mean systolic blood pressure compared with those in the intervention group (Table 1). Mean adherence scores of patients were 16.8 and 16.3 among patients in the control and intervention groups, respectively. There were no significant differences with respect to baseline characteristics between control and intervention groups (Table 1). Organizational information and pharmacist characteristics of each CHC are shown in Supporting Information Table S3.

3.2 | Intervention programme

In total, all 57 nonadherent patients completed a first counselling session at baseline that on average lasted for 14.2 minutes (range 5.0-20.0 minutes). Among these 57 nonadherent patients, 41 (71.9%) patients had one barrier for adherence identified and 14 (24.6%) patients had two or more barriers identified (Figure 2). The most common barriers were forgetfulness (23 [41.8%]), lack of knowledge (10 [18.2%]) and lack of motivation (8 [14.5%]). Knowledge problems included patients who did not know the purpose of the medication, only took the medication when they had symptoms or did not know the importance of taking the medication daily. Motivation problems included concerns about side effects and not feeling better when taking the medication. Among those who completed the first counselling session, 49 (86.0%) patients received a second session that on average lasted for 10.6 minutes (range 3.2-18.3). Of these 49 patients, 31 (63.3%) patients had already become adherent (MARS-5 score ≥ 20) according to their response on the MARS-5 at the second session.

3.3 | Primary and secondary outcomes

A statistically significant intervention effect was observed in self-reported medication adherence (pooled estimate of mean difference



4.62 on the MARS-5 score [95% CI 0.93 to 8.32, P value = 0.008]) after 3 months (Table 2). For the per-protocol-analysis, complete follow-up was available for 45 (80.4%) control and 44 (77.2%) intervention patients. The intervention effects were similar to those observed in the intention-to-treat analysis (mean difference 4.86 on the MARS-5 score [95% CI 1.57 to 8.16, P value = 0.004]) after 3 months (Supporting Information Table S4). Subgroup analyses showed similar significant intervention effects among those with or without diabetes complications and those with different numbers of concomitant drugs (Supporting Information Table S5).

Increases in necessity beliefs and decreases in concern beliefs showed statistically nonsignificant differences between the intervention and control groups (Table 2). The difference in the necessity-concern differential was 2.42 points higher in the intervention group as compared to the control group (95% CI -5.05 to 9.89 , P value = 0.238). No significant intervention effects were observed in systolic blood pressure (mean difference 5.98 mmHg [95% CI -10.80 to 22.76], P value = 0.241) and diastolic blood pressure (mean difference -8.61 mmHg [95% CI -20.01 to 2.78], P value = 0.931). Per-protocol analysis did not show different results for secondary outcomes (Supporting Information Table S4).

4 | DISCUSSION

In this cluster randomised controlled trial of patients with T2DM who were nonadherent to antihypertensive drugs we observed that an innovative, low-cost, tailored pharmacist-led intervention resulted in a significant improvement in self-reported adherence after 3-month follow-up. The results were similar for subgroups according to the presence of comorbidities and number of medications. There were positive, though nonsignificant, differences in medication necessity and concern beliefs.

The tailored pharmacist-led intervention, supported by a practical adherence intervention wheel, resulted in identifying individual adherence barriers among patients with T2DM. The most commonly identified barriers were forgetfulness and lack of knowledge, whereas lack of motivation and other drug-related problems were less common. This is partly in line with previous studies conducted in the United States among patients with diabetes and/or hypertension,^{14,30} where forgetfulness was also the most common barrier to adherence during pharmacist telephone consultations. Other frequent barriers identified in those studies were health beliefs (eg, lack of perceived need of therapy)³⁰ or doctor-related issues

TABLE 1 Baseline characteristics of participants

Characteristic	Control group (n = 56)	Intervention group (n = 57)	Pvalue ^a
	n (%) or mean ± SD	n (%) or mean ± SD	
Gender			0.054
Male	6 (10.7)	14 (24.6)	
Female	50 (89.3)	43 (75.4)	
Age (years)			0.509
≤49	7 (12.5)	3 (5.3)	
50-59	15 (26.8)	14 (24.6)	
60-69	23 (41.1)	29 (50.9)	
≥70	11 (19.6)	11 (19.3)	
Type of insurance			0.642
BPJS-non-PBI	21 (37.5)	23 (40.4)	
BPJS-PBI	35 (62.5)	32 (56.1)	
Missing	...	2 (3.5)	
Education			0.990
No formal education/elementary school	19 (33.9)	19 (33.3)	
Junior high school	14 (25.0)	13 (22.8)	
Senior high school	17 (30.4)	17 (29.8)	
University	6 (10.7)	7 (12.3)	
Missing	...	1 (1.8)	
Time from diagnosis (years)			
Diabetes	5.2 ± 4.4	5.4 ± 3.6	0.846
Missing	1	...	
Hypertension	5.6 ± 5.0	5.5 ± 3.5	0.878
Missing	1	...	
Clinical data (mmHg)			
SBP	136.6 ± 20.1	132.7 ± 15.1	0.243
DBP	80.4 ± 6.0	81.9 ± 8.2	0.262
Type of antihypertensive drugs ^b			0.583
Diuretics	4 (6.0)	1 (1.5)	
Beta-blocking agents	1 (1.5)	3 (4.6)	
Calcium channel blockers	48 (71.6)	49 (75.4)	
Agents acting on the renin-angiotensin system	14 (20.9)	11 (16.9)	
Missing	...	1 (1.5)	
Number of antihypertensive drugs			0.799
1	48 (85.7)	49 (86.0)	
2	6 (10.7)	6 (10.5)	
3	1 (1.8)	1 (1.8)	
4	1 (1.8)	...	
Missing	...	1 (1.8)	
Number of concomitant drugs			0.936
1	20 (35.7)	21 (36.8)	
2	25 (44.6)	20 (35.1)	
≥3	11 (19.6)	15 (26.3)	
Missing	...	1 (1.8)	

(Continues)

TABLE 1 (Continued)

Characteristic	Control group (n = 56)	Intervention group (n = 57)	Pvalue ^a
Diabetes complications			0.465
No	42 (75.0)	46 (80.7)	
Yes	14 (25.0)	11 (19.3)	
Medication adherence (MARS-5)	16.8 ± 3.0	16.3 ± 3.2	0.390
Sum score (5-20)			
Medication beliefs (BMQ)			
Necessity (5-25)	14.5 ± 4.1	15.0 ± 3.6	0.490
Concern (5-25)	16.1 ± 3.4	16.3 ± 2.4	0.780
Side effects (1-5)	2.4 ± 1.0	2.6 ± 1.1	0.272
Necessity-concern differential (-20-20)	-1.7 ± 4.9	-1.3 ± 4.0	0.683

^aIndependent sample t-tests and chi-square tests were used to test for differences between the control and intervention groups.

^bPatients may use more than one type of antihypertensive drug.

Abbreviations: BMQ, Beliefs about Medicines Questionnaire; BPJS-PBI, insurance premium was paid by the government; BPJS-non PBI, insurance premium was paid by the patients themselves; DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; MARS, Medication Adherence Report Scale.

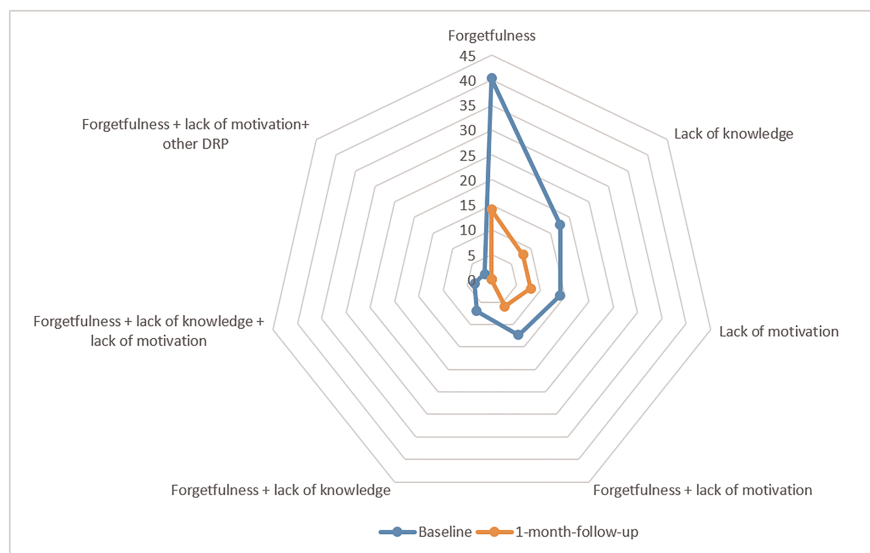


FIGURE 2 Percentage of patients with different identified barriers to optimal adherence at baseline (n = 55) and 1-month follow-up (n = 18). Note: Data from two and eight patients at baseline and at 1-month follow-up are missing

(eg, having difficulty in scheduling appointments).¹⁴ Our study showed that in a low- and middle-income country such as Indonesia, lack of knowledge about hypertension and its treatment was also an important barrier to adherence.

Our study indicates that simple, low-cost measures, such as encouraging patients to include medication-taking routines into their daily activities, implementing action plans with agreed goals and/or involving family members, could potentially help patients take their medication appropriately and may improve their adherence. Pharmacist educational counselling to cope with patients' lack of knowledge may help T2DM patients to better understand how and why they need to take antihypertensive drugs. We observed a nonsignificant improvement of more than 2.42 points in the necessity-concern differential in the intervention as compared to the control group. As reported in previous studies,^{31,32} an increase in knowledge about hypertension and its treatment may decrease misconceptions

about the benefit and risk of the treatment, leading to a positive change in the patient's beliefs about antihypertensive drugs. In our study, concerns about medicines were relatively low at baseline, showing little need and potential room for improvement. As a result, lack of motivation was not identified as a main barrier, and pharmacists have focused less on this barrier.

The observed improvement of 4.62 on the MARS-5 scale reflects a substantial effect size. Whether this is a clinically relevant difference is difficult to say, since there are no studies showing which difference on the MARS-5 scale is clinically relevant. This may be due to the fact that adherence does not correlate well with single blood pressure measurements, and the premises to validate a questionnaire measuring adherence to antihypertensive treatment are difficult to fulfil.³³ Recently, the reliability and validity of the MARS-5 were tested in patients with hypertension, showing that it can discriminate on clinically relevant targets based on three blood pressure measurements.³⁴

TABLE 2 Intervention effects of the primary and secondary outcomes in the intention-to-treat analysis

Outcomes	Baseline (T0)		T1		T2		Intervention effect (T2-T0) ^a			
	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean difference (95% CI)	P value	ICC	
MARS-5 sum score (5-25)	Control	16.8 ± 3.0	56	18.8 ± 3.8	56	18.1 ± 4.7	56	4.62 (0.93; 8.32)	0.008	0.064
	Intervention	16.3 ± 3.2	57	21.5 ± 4.3	57	22.3 ± 3.7	57			
Systolic blood pressure (mmHg)	Control	136.6 ± 20.1	56	135.1 ± 20.1	56	132.2 ± 16.6	56	5.98 (-10.80; 22.76)	0.241	0.038
	Intervention	132.7 ± 15.1	57	136.3 ± 20.5	57	130.3 ± 17.4	57			
Diastolic blood pressure (mmHg)	Control	80.4 ± 6.0	56	79.6 ± 5.9	56	84.5 ± 16.5	56	-8.61 (-20.01; 2.78)	0.931	0.012
	Intervention	81.9 ± 8.2	57	80.5 ± 10.0	57	80.7 ± 11.8	57			
Necessity (5-25)	Control	14.5 ± 4.1	56	14.7 ± 3.3	56	15.3 ± 2.9	56	1.94 (-0.78; 4.66)	0.080	0.003
	Intervention	15.0 ± 3.6	57	15.5 ± 3.1	57	15.7 ± 2.9	57			
Concern (5-25)	Control	16.1 ± 3.4	56	15.6 ± 3.3	56	15.6 ± 3.3	56	-0.48 (-3.44; 2.47)	0.627	0.002
	Intervention	16.3 ± 2.4	57	15.1 ± 3.3	56	14.6 ± 3.1	57			
Side effects (1-5)	Control	2.4 ± 1.0	56	2.8 ± 1.1	57	2.7 ± 1.3	56	-0.24 (-1.25; 0.78)	0.679	0.106
	Intervention	2.3 ± 1.1	56	2.5 ± 1.2	56	2.6 ± 1.3	57			
Necessity-concern differential (-20-20)	Control	-1.7 ± 4.9	56	-0.9 ± 4.7	57	-0.4 ± 3.9	56	2.42 (-5.05; 9.89)	0.238	0.795
	Intervention	-1.3 ± 4.1	57	0.4 ± 4.6	56	1.1 ± 4.0	57			

^aIntervention effects were adjusted for clustering effects.

Abbreviations: T1, 1-month follow-up measurement; T2, 3-month follow-up measurement; SD, standard deviation; CI, confidence interval; ICC, intraclass correlation coefficient; MARS, Medication Adherence Report Scale.

In our study, the reported improvement in adherence to antihypertensive drugs did not translate into a measurable significant improvement in blood pressure at 3-month follow-up. First, we should note that this study was not powered on this secondary endpoint. Additionally, a systematic review reported that only 24 out of 47 of intervention studies to improve adherence in patients with hypertension did significantly improve systolic and/or diastolic blood pressure.³⁵ This can be partly explained by the wide intra-individual variability in blood pressure levels.^{36,37} Therefore, the relationship between drug adherence and blood pressure control is difficult to demonstrate.^{33,38} Also, some patients may have been prescribed their medication for cardiovascular diseases other than hypertension. Thus, blood pressure is not a robust outcome among these patients. At baseline, patients included in our study had generally well-controlled blood pressure levels despite suboptimal adherence. This could in part be due to 'white coat adherence', that is, more punctual dosing in the days before their blood pressure was measured.³⁹

The strength of this study is that we used cluster randomisation at CHC level to reduce risk of contamination across study groups. Also, we had a very high participation rate among the patients eligible for the intervention, limiting potential inclusion bias, but some limitations also need to be mentioned. As is common with many behavioural intervention studies, it was not possible to blind the researchers and pharmacists to the group allocation of patients. The assessments of medication adherence at baseline and 1-month follow-up could have created a Hawthorne effect, which might have influenced patient behaviour in both the intervention and control groups. Some improvements in MARS-5 scores were indeed also seen in the control group and may have led to an underestimated intervention effect. Some patients did not visit the CHCs at 1-month and/or 3-month follow-up. These patients could have more adherence problems. By using multiple imputation, they were included in our estimated intervention effects. Furthermore, using a self-reported questionnaire is prone to socially desirable answers and as such leads to underestimating the true rate of nonadherence. Although pharmacy databases also come with limitations, such registries would allow for a more objective assessment of adherence, but these sources were unavailable in our study setting in Indonesia. Our finding that the changes in the patient's necessity and concerns beliefs were not significant could be due to a lack of power for assessing relatively small differences. It could also be that the duration of outcome assessment was too short to observe a significant impact on necessity and concern beliefs. Previous studies among patients with hypertension showed a significant effect of repeated counselling on necessity beliefs after 9 months¹⁶ and on necessity and concern beliefs after 12 months.³² Furthermore, our blood pressure data were obtained from routine practice and may be influenced by inconsistent measurement procedures.

The pharmacist-led intervention programme used principles of targeting by screening for nonadherence and tailoring interventions to patients' personal adherence problems to enhance its potential effect. We therefore cannot say which elements were responsible

for the observed effects. The key aspects included identifying the individual, patient-specific problems for nonadherence, and subsequently delivering and implementing personalised adherence support strategies supported by practical decision support tools. Whether this works similarly in other settings should be evaluated in future studies. The intervention aligns with the current workflow and resources in the daily clinical practice of a low- and middle-income country, and does not require a substantial logistical change to the current care system. The pharmacists in our study received 3 hours of training conducted by a senior pharmacist. The effects might have been smaller without this training. Our findings are encouraging, since nonadherence can be reduced with a relatively simple and low-cost intervention. Incorporating the use of our intervention tools in regular counselling by pharmacists may lead to sustainable effects. For this, a longer follow-up study focusing on how patients' adherence and beliefs about their antihypertensive drugs change over time is needed.

5 | CONCLUSIONS

A tailored low-cost pharmacist-led intervention aimed at nonadherent T2DM patients resulted in an improvement in medication adherence to antihypertensive drugs. There were no significant changes in beliefs about antihypertensive drugs or blood pressure levels.

TRIAL REGISTRATION

clinicaltrials.gov identifier: NCT04023734.

ACKNOWLEDGEMENTS

We thank all study participants and research assistants for their effort and contributions. Furthermore, we would like to thank Stijn de Vos (University of Groningen, the Netherlands) for helping us with the multiple imputation. S.D.A. is supported by a scholarship from the Indonesia Endowment Fund for Education (LPDP No: PRJ-2361/LPDP/2015). This funding body did not have any role in designing the study, writing this article and deciding to submit it for publication.

COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

S.D.A., J.F.M.vB., R.A., P.D. and E.H. contributed to conception and study design. S.D.A. and R.A. contributed to data collection. S.D.A. and H.S. contributed to statistical analysis. S.D.A., J.F.M.vB., R.A., H.S., P.D. and E.H. contributed to data interpretation. S.D.A., J.F.M.vB., P.D. and E.H. contributed to drafting the manuscript. All authors approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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How to cite this article: Alfian SD, van Boven JFM, Abdulah R, Sukandar H, Denig P, Hak E. Effectiveness of a targeted and tailored pharmacist-led intervention to improve adherence to antihypertensive drugs among patients with type 2 diabetes in Indonesia: A cluster randomised controlled trial. *Br J Clin Pharmacol*. 2021;87:2032–2042. <https://doi.org/10.1111/bcp.14610>