



Lay Health Worker Led Diabetes Task-Sharing Intervention in Middle-Income Countries: A Systematic Review and Meta-Analysis

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Abstract

Background: Task-sharing in diabetes management may be useful for health systems in staff- and resource-poor middle-income countries. The study evaluated the effectiveness of a task-sharing intervention for diabetes led by non-professional health workers in improving glycaemic indicators and blood pressure among adults in middle-income countries.

Methods: Embase, PubMed, MEDLINE and Cochrane Central Registry of Controlled Trials were searched for studies published from 2010-2022. Intervention studies involving task-sharing strategies for managing diabetes and other cardiovascular risk factors were included. Extracts were made on populations, interventions, and lay health worker training and supervision. The quality of studies was assessed using the Cochrane Risk of Bias tool. Performed a meta-analysis of randomised controlled trials. A random-effects model was used due to significant heterogeneity among the studies ($I^2 \geq 50\%$), otherwise, a fixed-effect model was used.

Results: Thirteen randomised controlled trials with 8183 patients were included in the meta-analysis. The population average pooled mean difference in HbA1c was -0.17% (95% CI -0.34 to -0.01) and in fasting blood glucose was -0.75 mmol/L (95% CI -1.14 to -0.35). The population average pooled mean difference in systolic blood pressure was -5.90 mmHg (95% CI -8.11 to -3.68) and in diastolic blood pressure was -2.25 mmHg (95% CI -3.10 to -1.40).

Conclusion: Task-sharing interventions for diabetes led by lay health workers in middle-income countries have shown potential for lowering blood glucose levels and reducing blood pressure.

Keywords: Diabetes; Task-sharing intervention; Non-professional health workers; Meta-analysis

Introduction

Four out of five individuals with undiagnosed diabetes reside in low- and middle-income countries (LMICs) due to inadequate diabetes detection and awareness (1). Moreover, LMICs exhibit notably lower rates of diabetes treatment and control. Studies have estimated that approximate-

ly 77% of the unmet need for diabetes care persists in LMICs as a result of inadequate detection, treatment, and control measures (2). To enhance diabetes care, the American Medical Association advocates for team-based, patient-centered care, long-term integrated treatment strategies for dia-



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betes and comorbidities, and collaborative communication among healthcare providers (3). However, middle-income countries face a significant scarcity of well-trained healthcare workers to meet the escalating demand for comprehensive diabetes care. Given the fragility of healthcare systems and the growing burden of cardiovascular disease in LMICs, innovative approaches to healthcare system management are imperative (4). Task shifting emerges as a potential solution to meet the burgeoning demand for integrated diabetes care. This approach involves delegating tasks to less specialized healthcare workers, thereby expanding healthcare coverage while reducing costs (5). Lay health workers, such as "patient peers" or community health workers (CHWs), are well-suited for task shifting. Research has demonstrated that interventions led by lay health workers are effective and cost-effective in assisting patients with managing chronic conditions (6). These workers can provide sustained behavioral, educational, and psychosocial support, thus improving access to comprehensive diabetes healthcare and mitigating the strain caused by healthcare workforce shortages (7).

However, the majority of diabetes interventions led by lay health workers have been implemented in high-income countries (8). Studies conducted in low- and middle-income settings have primarily focused on ethnic minorities and international migrants residing in high-income countries (9). Consequently, there is a dearth of research pertaining to LMICs. Existing systematic reviews have summarized diabetes task-shifting interventions in LMICs and diabetes self-management interventions led by lay health workers in LMICs (5, 7, 8, 10). Nevertheless, no review to date has specifically examined task-shifting interventions for diabetes led by lay health workers in middle-income countries or provided a comprehensive summary of the interventions' impact on other cardiovascular disease risk factors.

Thus, the objective of this systematic review is to comprehensively synthesize the content and outcomes of a lay health worker-led diabetes task-sharing intervention in a middle-income country setting. Specifically, this study aimed to address

two key research questions: 1) the intervention's content, encompassing the training and supervision of lay workers, as well as the modality of the intervention (e.g., health education); and 2) a comprehensive summary of the intervention's impact on glycemic outcomes and other cardiovascular disease risk factors.

Methods

Search Strategy

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive search strategy was developed based on previously published reviews in the relevant field and adapted to suit the search format of multiple databases. The databases searched included Embase, PubMed, and MEDLINE. Additionally, searches were conducted in the Cochrane Central Registry of Controlled Trials, and relevant reference lists were scrutinized. The search was restricted to articles published in English from 2010 to 31 Dec 2024.

We used MeSH terms to ensure the comprehensiveness and accuracy of our search strategy. The search terms included "diabetes mellitus", "task shifting", "non physician health care workers", "community health workers", "lay health workers", and "peer education". The search was conducted in PubMed, EMBASE, and MEDLINE, with additional searches in the Cochrane Central Register of Controlled Trials.

Diabetes

("diabetes mellitus"[MeSH Terms] OR "blood sugar"[MeSH Terms] OR "glycemic control"[MeSH Terms])

Intervention:

("task shifting"[MeSH Terms] OR "non physician health care workers"[MeSH Terms] OR "community health workers"[MeSH Terms] OR "lay health workers"[MeSH Terms] OR "peer education"[MeSH Terms])

Country

("developing countries"[MeSH Terms] OR "low-income countries"[MeSH Terms] OR "middle income countries"[MeSH Terms] OR "resource poor"[MeSH Terms])

By using MeSH terminology, you can improve the efficiency and accuracy of your searches. For some non-MeSH terms, it is advisable to conduct a supplementary search after the initial search to ensure that no important documents have been missed.

Inclusion and Exclusion Criteria

The inclusion criteria for study selection were determined using the PICOS strategy. 1) Participants: Patients aged 18 yr or older with type 1 or type 2 diabetes or those with risk factors for diabetes (e.g., high blood pressure, obesity). The study focused on middle-income countries based on the World Bank country classification, while excluding children and mothers with gestational diabetes. 2) Interventions: Interventions aimed at improving glycemic control delivered by trained non-medical professional workers (e.g., community health workers, peer health educators, or peer leaders). 3) Control: Routine care or diabetes education only. 4) Outcome: Glycated hemoglobin or fasting blood glucose. 5) Study Design: Randomized controlled trials or cluster randomized trials.

Quality Assessment of Literature

The quality of studies that met the inclusion criteria after full-text review was evaluated using the Cochrane Risk of Bias tool. This assessment included aspects such as the method of randomization, concealment of the allocation scheme, blinding of participants and investigators, blinding of outcomes assessors, completeness of outcome data, selective reporting of study results, and other potential sources of bias. Two independent authors assessed the quality of the literature, with a third investigator resolving any disagreements.

Data Extraction

Data extraction was performed using pre-developed Excel sheets, which included details of

the patients, interventions provided, components of the interventions, and relevant outcomes of the study. Outcome measures of glycated hemoglobin (HbA1c), fasting blood glucose (FBG), and blood pressure before and after the intervention were extracted for both the intervention and control groups. Information regarding the country in which the study was conducted, as well as the type and size of the study population, was also recorded. Two independent authors conducted the data extraction, with a third investigator resolving any discrepancies.

Statistical Analysis

A qualitative synthesis of the interventions included in the trials was conducted. For quantitative synthesis, eligible randomized controlled trials were included in the meta-analysis. In the case of cluster-randomized trials, effective study sample sizes were estimated using reported design effects or calculated design effects based on within-group correlation coefficients and mean group sizes. Changes in blood glucose levels were estimated by calculating the difference between the mean HbA1c or FBG in the intervention group and the control group.

Pooled mean differences of outcome measures and their corresponding 95% confidence intervals (CIs) were calculated. Heterogeneity among the studies was assessed using the I² statistic. If $I^2 < 50\%$ or the heterogeneity P-value was greater than 0.10, indicating low heterogeneity, a fixed-effect model was employed. Conversely, if $I^2 \geq 50\%$ or the heterogeneity P-value was less than 0.10, indicating significant heterogeneity, a random-effects model was utilized. A statistically significant result was determined when the 95% confidence interval did not include zero. All statistical analyses and figures were performed using Revman software (ver. 5.3).

Consent for publication

This meta-analysis was approved by the institutional review board, the need for informed patient consent for inclusion was waived.

Ethical Statement

This study was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki.

Results

Literature screening

The initial database searches and examination of reference lists yielded 1188 records. After removing duplicates, 847 unique records remained for review. Among these, 596 records were excluded based on the information provided in the title and abstract, as they did not meet the predetermined inclusion criteria. This left 251 studies that

were potentially eligible for full-text review. Of these, 243 studies were subsequently excluded for various reasons, with some studies meeting multiple exclusion criteria. The reasons for exclusion included not being a lay health worker intervention study ($n=17$), not being a randomized controlled trial ($n=78$), not being conducted in a low-income country ($n=43$), being part of a research protocol or secondary study ($n=54$), having a study population of gestational diabetic mothers ($n=5$), and not reporting blood glucose as an outcome ($n=39$). Ultimately, 13 randomized controlled trials were included in this review (11-23). The PRISMA flow chart is shown in Fig. 1.

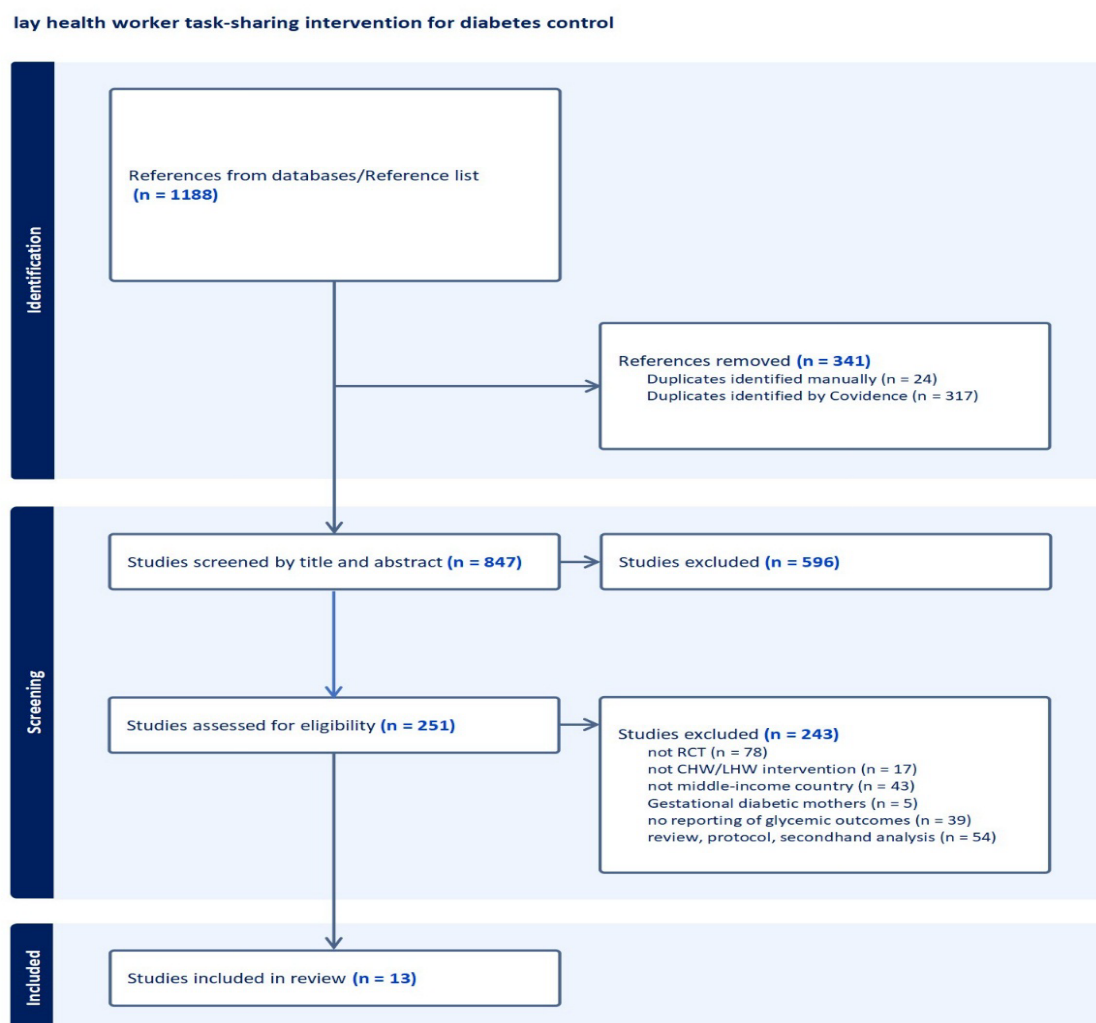


Fig. 1: PRISMA flow chart of study selection

Literature information and quality evaluation

Among 13 studies enrolled, 10 were conducted in patients with diabetes, and three were conducted in patients with at least one cardiovascular disease risk factor or diabetes risk factor. Geographically, six studies were conducted in China, two in Africa, three in Southeast Asia, one in South America, and one in a Pacific Island country. The study design consisted of five randomized controlled trials and eight whole-cluster randomized controlled trials. The sample sizes in the included

studies ranged from 100 to 3539, with a total sample size of 8183 participants. All of the studies enrolled adult participants, except for one study that recruited individuals between the ages of 5 and 40 yr (21). Among the included studies, six investigated the provision of peer support, while the remaining seven explored the support provided by community health workers (CHWs). Table 1 provides a summary of the key characteristics of the included studies.

Table 1: Summary of literature information

Author year Country	Sample size	Study design	Delivered by	Intervention	Follow up duration	Outcome assessed
Chao 2015 (China) (11)	100, Patients with diabetes mellitus	RCT	Community health worker based integrated health management	1) Health profile creation 2) Health evaluation, done by the researcher 3) Non pharmacologic education	18 months	1) BMI 2) blood pressure 3) FBG 4) Waist-hip ratio
Mash 2014 (South Africa) (12)	866, Patients with diabetes mellitus	Cluster RCT	Community health workers (Health promoters)	Group education session and CHW-led group discussion	12 months	1) 5% weight loss, and a 1% reduction in HbA1c level 2) Mean Blood pressure 3) Mean weight loss 4) Mean HbA1c 5) Mean total cholesterol levels 6) Mean waist circumference
Ju 2018 (China) (13)	343, Patients with diabetes mellitus	Cluster RCT	Peer leaders + professional diabetes educator support	1) Non pharmacologic education, counselling. 2) telephone education and reminds. 3) home visits	12 months	1) HbA1c level 2) FPG 3) 2-h PPG
Debussche 2018 (Mali) (14)	151, Patients with diabetes mellitus	RCT	Peer educators	1) Non pharmacologic education, counselling.	12 months	1) HbA1c level 2) Mean blood pressure 3) Mean BMI 4) Mean waist circumference
Browning 2016 (China) (15)	780, Patients with diabetes mellitus	Cluster RCT	Community health workers, nurses and psychologists	1) Non pharmacologic education, counselling. 2) telephone education and reminds	12 months	1) HbA1c level 2) Mean blood pressure 3) Mean weight loss 4) Mean BMI 5) Cholesterol levels 6) Mean waist circumference 7) Triglycerides 8) FPG

Table 1: Continued...

de Souza 2017 (Brazil) (16)	118, Patients with diabetes mellitus	RCT	Community health worker	1)Non pharmacologic education 2) Home visits	3 months	1)HbA1c 2) BMI 3) Blood Pressure 4) FPG 5)HDL 6)Creatinine, TG 7)Albuminuria
Depue 2013 (American Samoa) (17)	268, Patients with diabetes mellitus	Cluster RCT	Nurse care manager trained Community Health Worker (CHW)	1)Non pharmacologic education 2)Maintain appointments 3)Feedback to physicians about patient care needs	12 months	1)HbA1c 2) BMI 3) Waist circumference 4)Blood pressure
Zhong 2015 (China) (18)	229, Patients with diabetes mellitus	Cluster RCT	Peer educators + workers in community health centers	1)Non pharmacologic education 2)Physical activity 3)Feedback to physicians about patient care needs	6 months	1)BMI 2) blood pressure 3) FBG 4)2h-PG
Yin 2018 (China) (19)	184, Females with prediabetes, overweight or obese, not physically active and expressed interest on lifestyle changes.	RCT	Community health educator	1)Non pharmacologic education, counselling. 2)Group physical activity training	12 months	1)Weight 2) Waist circumference 3)HbA1c 4) FBG 5)Heart rate
Deng 2016 (China) (20)	208, Patients with diabetes mellitus	RCT	Peer educators	1)Non pharmacologic education, counselling. 2) telephone education and reminds. 3) specific education on insulin use	7 months	1)HbA1c level 2)FPG 3) 2h-PG 4) Incidence of hypoglycemia 5) BMI 6) TG
Wijesuriya 2017 (Sri Lanka) (21)	3539, Population with any 2 risk factors: Family history of T2DM, physical inactivity, increased body mass index (BMI) and increased waist circumference	Cluster RCT	Peer educators	1)Non pharmacologic education, counselling 2) telephone education and reminds.	3 yr	New onset dysglycaemia (defined as a composite of T2DM, IFG and IGT)
Paz-Pacheco 2017 (Philippine) (22)	155, Patients with diabetes mellitus	Cluster RCT	Peer educators	1)Non pharmacologic education 2)Encourage visits to physicians about patient care needs	6 months	1)Weight 2) BMI 3)HbA1c
Khetan 2019 (India) (23)	1242 Participants who had at least 1 risk factor (hypertension, diabetes, smoking)	Cluster RCT	Community Health Workers recruited by research group	1)Non-pharmacologic Home based counselling, Flipbooks 2)Follow-up visits	24 months	1) SBP 2) FBG 3)Change in selfreported mean number of daily cigarettes/bidis smoked from visit 1 to postintervention

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Browning 2016	+	-	-	+	?	+
Chao 2015	+	?	?	+	+	?
Debussche 2018	+	+	-	+	+	?
Deng 2016	+	?	-	+	+	?
DePue 2013	+	?	-	+	+	+
DeSouza 2017	+	+	-	+	+	?
Ju 2018	+	-	-	+	-	+
Khetan 2019	+	+	-	+	-	+
Mash 2014	+	+	-	+	-	+
Paz-Pacheco 2017	?	-	-	+	-	?
Wijesuriya 2017	+	?	-	+	?	+
Yin 2018	+	?	-	?	+	+
Zhong 2015	+	-	-	+	?	?

Fig. 2: Risk of bias assessment for included studies

The assessment of risk of bias for the included studies is presented in Fig. 2. There was considerable variation in the risk of bias across the individual studies. Specifically, the risk of selection

bias resulting from random sequence generation was deemed low in 12 studies but high in 1 study. Additionally, only 4 trials reported adequate allocation concealment during randomization. Due

to the nature of the intervention, achieving blinding of participants and personnel was not feasible in any of the trials. However, since the blood glucose indicator is an objective outcome measure, a low risk of bias for blinding of outcome assessment is anticipated. One study did not specify the measurement standard for the blood glucose indicator (19). Furthermore, in 4 studies (12, 13, 22, 23), the rate of participants lost to follow-up was high and imbalanced between the intervention and control groups.

Meta-analysis of HbA1c and FBG

The analysis included 7 long-term (>6 months) studies reporting HbA1c results and 6 long-term studies reporting FBG results. A random-effects model was employed to pool the unadjusted within-group mean reduction in the LHW intervention groups compared to the usual care groups.

The results of the heterogeneity analysis indicated significant heterogeneity among the studies, warranting the use of a random-effects model for the analysis ($I^2 = 65\%$, $P=0.009$). Overall, the population average pooled mean difference in HbA1c was -0.17% (95% CI -0.34 to -0.01). The forest plot of HbA1c is presented in Fig. 3.

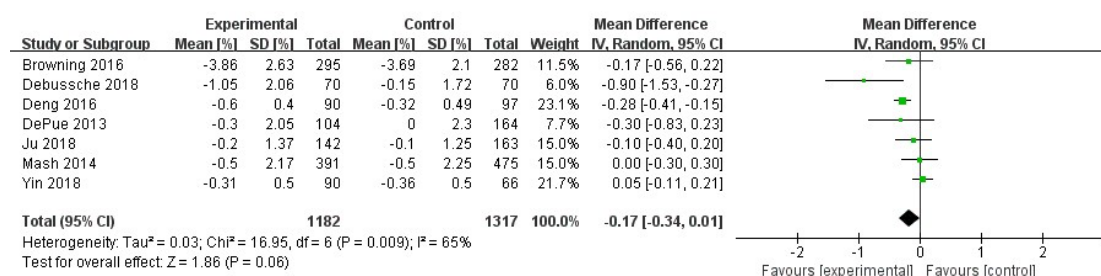


Fig. 3: Forest plot of HbA1c levels

Similarly, the results of the heterogeneity analysis demonstrated significant heterogeneity between the studies ($I^2=59\%$, $P=0.03$), necessitating the use of a random-effects model for the analysis of

FBG. The overall population average pooled mean difference in fasting blood glucose was -0.75 mmol/L (95% CI -1.14 to -0.35). The forest plot of FBG is displayed in Fig. 4.

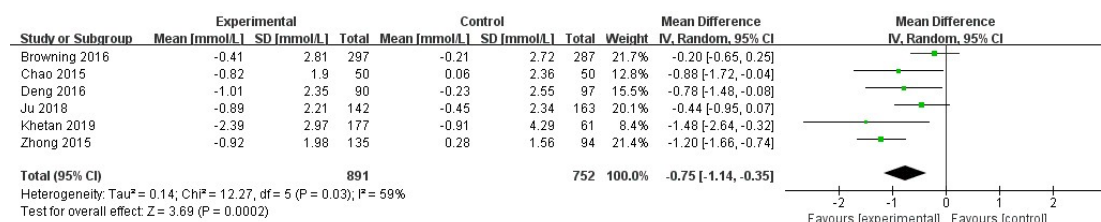


Fig. 4: Forest plot of fasting blood glucose levels

Given the limited number of studies ($n<10$), the assessment of publication bias using funnel plots

and Egger's test was inconclusive. The funnel plots are presented in Fig. 5.

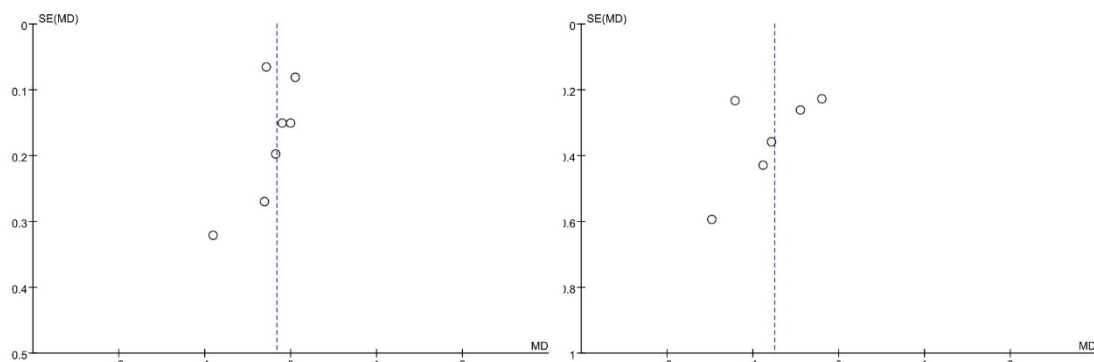


Fig. 5: Funnel plot for publication bias assessment of HbA1c (left) and fasting blood glucose (right)

Meta-analysis of blood pressure

Six out of the 13 included studies reported baseline and intervention endpoint measurements of participants' systolic and diastolic blood pressure. Additionally, one study reported a significant reduction in the incidence rate of new-onset hypertension (Incident rate ratio: 0.79, 95% CI: 0.68-0.9, $P=0.01$).

The results of the heterogeneity analysis revealed significant heterogeneity among the studies, thus necessitating the use of a random-effects model for the analysis of systolic blood pressure ($I^2=50\%$, $P=0.08$). Overall, the population average pooled mean difference in systolic blood pressure was -5.90 mmHg (95% CI -8.11 to -3.68). The forest plot of systolic blood pressure can be found in Fig. 6.

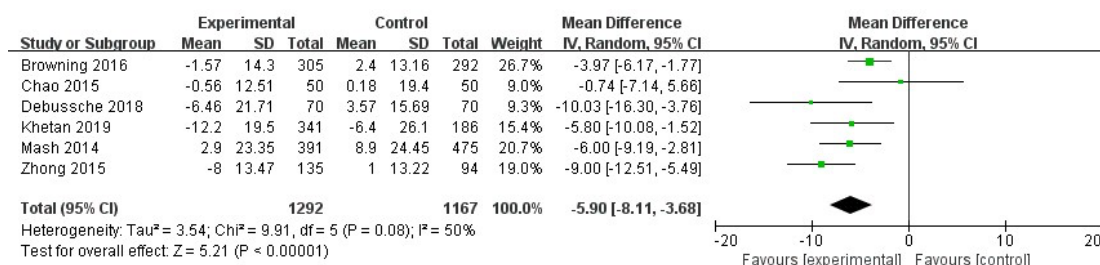


Fig. 6: Forest plot of systolic blood pressure

Conversely, the results of the heterogeneity analysis indicated no significant heterogeneity among the studies for diastolic blood pressure ($I^2=41\%$, $P=0.08$). Therefore, a fixed-effects model was employed for the analysis. The overall population

average pooled mean difference in diastolic blood pressure was -2.25 mmHg (95% CI -3.10 to -1.40). The forest plot of diastolic blood pressure is presented in Fig. 7.

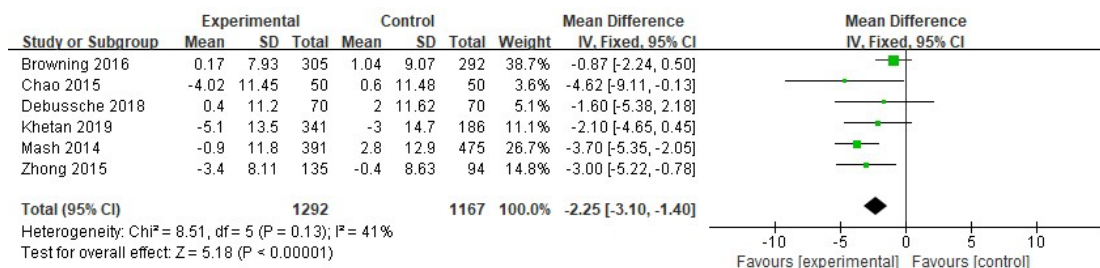


Fig. 7: Forest plot of diastolic blood pressure

Given the limited number of studies ($n < 10$), the evaluation of publication bias using funnel plots

and Egger's test did not yield conclusive results. The funnel plots are displayed in Fig. 8.

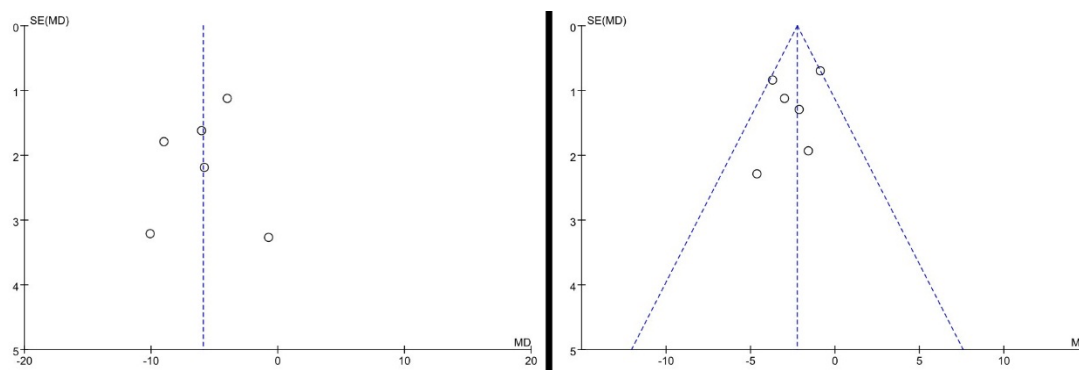


Fig. 8: Forest plot of diastolic blood pressure

Mental health and behavioural health outcomes Self-efficacy and behavioral improvement:

Three studies (11, 13, 18) reported improvements in self-efficacy, although they utilized different measurement scales. The intervention did not lead to improvements in mental health outcomes, including self-efficacy. Wijesuriya et al. reported significant effects on behavioral change, specifically increased physical activity. Patients who received peer support training had greater knowledge about insulin use compared to those who received traditional educational training.

Psychological distress related to diabetes and quality of life:

Increased peer support led to a reduction in concerns about medication and emotional burden, both of linked to poorer adherence to diabetes management. One potential benefit of peer support is the provision of emotional support for older individuals. Peer support creates a supportive environment where individuals can openly discuss their feelings without fear of burdening their families. Browning et al. observed greater psychological distress in the control group, with mean psychological scores shifting from "low risk of psychological distress" to "moderate risk of psychological distress" (24).

Discussion

This review of the existing literature on lay health worker-led task-sharing interventions for diabetes in middle-income countries provides a quantitative synthesis of population-averaged pooled mean differences in blood glucose levels (HbA1c and FBG) and blood pressure levels. Our findings support the use of lay health worker-led task-sharing interventions for diabetes management in middle-income countries, with overall reductions in HbA1c and FBG.

Our meta-analysis revealed that task-sharing interventions led by lay health workers resulted in a statistically significant reduction in HbA1c (-0.17%) and fasting blood glucose (-0.75 mmol/L) among patients with diabetes in middle-income countries. These findings are consistent with previous studies that have demonstrated the effectiveness of lay health worker interventions in improving glycemic control. For instance, a systematic review by Palmas et al. (8) reported that community health worker interventions significantly improved glycemic control in patients with diabetes in various settings. Similarly, peer and community health worker-led self-management support programs were effective in improving diabetes-related health outcomes in low- and middle-income countries (10).

The reductions in systolic (-5.90 mmHg) and diastolic blood pressure (-2.25 mmHg) observed in our study also align with findings from other reviews that have assessed the impact of task-sharing interventions on blood pressure control. Anand et al. (4) conducted a systematic review and meta-analysis on task sharing with non-physician health-care workers for blood pressure management in low- and middle-income countries and reported significant reductions in both systolic and diastolic blood pressure. This suggests that lay health worker-led interventions may have a dual benefit in managing both diabetes and hypertension, which are often comorbid conditions.

From the results of this study, task-sharing interventions for lay health worker-led diabetes management were primarily non-pharmacological lifestyle interventions, including health education, lifestyle modifications focusing on diet and physical activity, experience sharing with other patients, active communication with medical professionals for diabetes diagnosis, and support for self-management behaviors. No standardized training standards for lay health workers (LHWs) were identified in this review. Training requirements varied between studies depending on the specific focus of the intervention. In high-income areas, diabetes self-management education programs are organized by healthcare professionals such as nurses, pharmacists and certified diabetes educators (25). Therefore, it is necessary to adapt and organize the roles of LHWs and provide appropriate training and supervision to effectively manage diabetes and other chronic non-communicable diseases in an integrated team-based care model. The heterogeneity of interventions found in randomized trials may be indicative of the heterogeneity observed in diabetes self-management programs implemented by lay health workers in middle-income countries worldwide. We need evidence-based approaches to standardize the training of lay health workers and validate the programs and tools they implement in their work, while maintaining flexibility to adapt to the specific needs of the communities they serve.

In addition, lay health worker-led task-sharing interventions for diabetes reduced mean blood pressure levels, possibly due to similarities between lay health worker-led task-sharing interventions for diabetes and blood pressure interventions. Related reviews have shown that blood pressure interventions led by lay health workers also focus on healthy lifestyle education, with similar components of healthy diet education and physical activity education (4, 26). This result suggests the potential utility of lay health worker-led task-sharing for diabetes and blood pressure management, and the possibility of training lay health workers to implement diabetes and blood pressure co-interventions in middle-income countries with insufficient medical manpower. Our results are particularly relevant in the context of the global diabetes epidemic, where resource constraints in middle-income countries pose significant challenges to effective diabetes management. The American Medical Association's recommendation for team-based, patient-centered care is supported by our findings, highlighting the potential of lay health workers to contribute to this model (27). This is especially important in settings where there is a scarcity of well-trained healthcare professionals.

However, there were still some limitations in this study. Most of the included studies were low-quality designs with a significant risk of bias. In addition, most randomised controlled trials did not address the issue of selection bias or did not provide sufficient information about the selection process, the intervention strategies used were often not described in detail and were poorly assessed or not assessed in terms of implementation fidelity. Finally, most studies reporting clinical outcomes assessed outcomes only in terms of statistical significance. It is important to consider the limitations of the available evidence for meta-analyses. First, the small number of eligible randomised controlled trials results in wide confidence intervals for the combined estimates, limiting the ability to exclude publication bias and reducing the reliability of the meta-results. Second, there was considerable variability in trial designs, including target populations, intervention com-

ponents, control groups, trial lengths, and baseline values of study participants. However, it is reassuring that outcome heterogeneity between studies, such as the I^2 statistic, was moderate, suggesting that despite methodological differences, efficacy estimates, i.e., the observed effects of LHW interventions, were not overly heterogeneous.

Conclusion

Task-sharing interventions for diabetes led by lay health workers in middle-income countries have shown potential for lowering blood glucose levels and reducing blood pressure. However, further research on implementation is needed to understand its impact on health systems and patient-oriented outcomes. Future research should focus on determining the effectiveness of interventions in community settings. Research should be conducted on how healthcare teams and systems ensure the continuity of task-sharing interventions. Future research should also include information about the existing healthcare workforce. Evaluating the cost-effectiveness of task-sharing interventions will aid in decision-making. Barriers and facilitators to scaling up interventions in various settings should be examined. Policies are needed to facilitate the broader implementation of task-sharing interventions aimed at controlling blood pressure and other risk factors associated with non-communicable diseases.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Data Availability

The simulation experiment data used to support the findings of this study are available from the corresponding author upon request.

Conflict of interest

The authors declare that there is no conflict of interests.

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