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Review Article

THE INFLUENCE OF MEDICATION THERAPY MANAGEMENT (MTM) ON CLINICAL OUTCOMES AND TREATMENT COMPLIANCE IN DIABETES MELLITUS PATIENTS: A SYSTEMATIC REVIEW

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ABSTRACT

This systematic review aims to determine the effect of MTM carried out by pharmacists on achieving medication adherence and clinical outcomes in diabetes mellitus patients. The journal search method was taken from PUBMED, Scopus, and Google Scholar using the keywords "diabetes mellitus", "DM", "medication therapy management", "MTM", "clinical outcome", "clinical results", "adherence", and " treatment compliance". The research identified came from Indonesia, the United States, Ethiopia, Brazil, New Zealand, Japan, Lebanon, and Malaysia. Out of the 169 studies identified, twenty-five met the inclusion and exclusion criteria, consisting of 5 RCTs, seven cohorts, and 13 quasi-experiments. MTM improves compliance and clinical outcomes of DM patients. Compliance increased from 80.5% to 87.5% ($p<0.05$). The average HbA1c value decreased from 10.5 to 8.2 ($p<0.05$), the average systolic blood pressure (SBP) decreased from 142.7 mmHg to 135.6 mmHg ($p<0.05$), mean diastolic blood pressure (DBP) decreased from 89.9 mmHg to 83.6 mmHg ($p<0.05$), and mean fasting plasma glucose (FPG) decreased from 218.5 mg/dl to 142.4 mg/dl ($p<0.05$). Overall, this study shows that pharmacist-provided MTM services can improve clinical outcomes and medication adherence in patients with diabetes.

Keywords: Pharmacist, Medication therapy management, Clinical outcomes, Medication adherence

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INTRODUCTION

Diabetes is a condition where insulin production is disrupted, which causes sugar to build up in the blood and has the potential for heart attacks, high blood pressure, kidney failure, and death [1]. Diabetes also causes ocular complications that remain a prominent factor in causing blindness [2]. Diabetes is a chronic disease that is a significant health concern with long-lasting impacts on clinical results and patient economics and requires meticulous management [3]. The International Diabetes Federation (IDF) data indicates that the direct expenses for diabetes treatment amount to about 727 billion United States Dollars (USD) annually, accounting for around 12% of worldwide health funding [4]. In 2014, around 422 million adults worldwide had diabetes mellitus (DM), with a prevalence of 8.5% in the adult population. This number is projected to rise to 641.8 million by 2040 [3]. Therefore, serious treatment, both prevention and effective and efficient management, is needed [4]. Numerous governmental and private groups have dedicated significant time, effort, and resources to address this global issue through treatment, prevention, and education [5]. There are numerous methods available for treating and managing diabetes mellitus. For example, niosomes, human embryonic stem cells (hESC), and human Induced pluripotent stem cells (hiPSC). Niosomes as drug delivery systems have improved in the treatment of diabetes because of the improvement in the bioavailability of antidiabetic drugs [6]. Also, with the advancement of diabetes mellitus treatment, hESC and hiPSC have become recognized as the potential future of diabetes treatment because the treatment could yield significant outcomes within a period of one to two months [7]. With all of the available treatments for diabetes mellitus, Medication Therapy Management (MTM) emerges as a crucial approach.

Medication Therapy Management (MTM) is pharmaceutical management through a patient-centric and comprehensive approach to optimize drug use, reduce the risk of side effects, and increase treatment compliance so that clinical outcome targets can be achieved [8]. The Medication Therapy Management (MTM) service model in pharmaceutical practice consists of five elements: Medication Therapy Review (MTR), Personal Medication Record (PMR), Medication-related Action Plan (MAP), Intervention and Referral, and Documentation and Follow-up. MTR is a systematic process for gathering patient-specific information, assessing therapy, identifying actual and potential drug-related problems, compiling a prioritized list of problems, and creating a plan to resolve them. PMR is a comprehensive record of independent patient therapy, such as buying medicine at a pharmacy without a recommendation from a doctor or consuming traditional medicine [9, 10].

MAP is a document that contains a list of actions that patients can take to determine the progress of therapy as self-management. Intervention and/or referral is the stage where pharmacists provide consultation and intervention services to overcome drug-related problems, as well as refer patients to doctors or other health professionals if needed. Documentation and Follow-up is recording and reviewing all activities or actions towards patients [9, 10].

MTM services focus on implementing preventative health tactics to enhance therapy outcomes. Pharmacists are knowledgeable in medication and play a crucial role in assisting patients in maximizing their treatment through MTM services. Pharmacists are trained to assess and determine drug suitability so that clinical outcomes are achieved, as well as reducing barriers to non-adherence. This program may be useful for patients with chronic diseases such as diabetes [3]. This systematic review aims to assess the impact of pharmacist-delivered MTM interventions on clinical outcomes and medication adherence in diabetes mellitus patients.

This systematic review has new information because it combines the benefits of MTM on clinical outcomes and treatment adherence in patients with diabetes. Clinical outcomes are more varied by adding fasting plasma glucose (FPG) as a measure of MTM success in diabetic patients, in addition to hemoglobin A1c (HbA1c) and general clinical outcomes such as blood pressure (BP), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), triglycerides (TD), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

Methods

Articles search strategy

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. The literature search strategy is systematic, focused, and carried out by researchers to identify relevant articles. The search technique included a combination of "medical subject headings" (MeSH), title, and abstract keywords. The search approach involves utilizing three

electronic databases: PUBMED, Scopus, and Google Scholar. Subsequently, the reference lists of the discovered papers were reviewed to find more studies. Keywords were utilized to explore databases and literature related to diabetes mellitus, medication adherence, and clinical outcomes. Keyword synonyms and alternative search phrases were utilized to enhance the comprehensiveness of the searches. Here are the results of the MeSH formulation and keywords used in the article search technique conducted by the researchers:

Keyword pubmed

((((("Diabetes mellitus"[Title]) OR (Diabetes[Title])) OR (DM[Title]) AND (fha[Filter])) AND ((("Medication therapy management"[Title]) OR ("Medication therapy review"[Title])) OR ("Personal medication record"[Title]) AND (fha[Filter]))) AND ((((((("quality of life"[Title]) OR (adherence[Title])) OR (compliance[Title])) OR (obedience[Title])) OR ("adverse drug reaction"[Title])) OR ("adverse event"[Title])) OR ("side effect"[Title])) OR ("clinical* outcome*"[Title]) AND (fha[Filter])) AND (fha[Filter])

Keyword scopus dan Google Scholar (GS)

("Diabetes mellitus" OR Diabetes OR DM) AND ("Medication therapy management" OR "Medication therapy review" OR "Personal medication record" OR "Medication-related action plan") AND ("quality of life" OR adherence OR compliance OR obedience OR "adverse drug reaction" OR "adverse event" OR "side effect" OR "clinical* outcome*").

Article criteria

Articles included in this systematic review must comply with the following criteria: research in the form of an experiment or intervention in the form of MTM either via face-to-face, telephone, Short Message Service (SMS) or booklet; research design can be cohort, Randomized Clinical Trial (RCT), and quasi-experimental; there is an analysis to determine significance; articles measuring clinical outcomes in the form of Hemoglobin A1c, instant blood sugar, fasting blood sugar, blood pressure, cholesterol, and treatment compliance, or one of them; The research year chosen was 2009-2023 [11].

Study selection process

Two independent reviewers screened the titles and abstracts of the identified articles to determine eligibility through screening. Screening is carried out by assessing the title of the research. The next step is data extraction using Microsoft Excel. The extracted data encompassed details such as study design, analysis methods, number of patients in MTM intervention, presence or absence of MTM control group, duration of MTM intervention, disease type, delivery of MTM services, characteristics of standard care, and outcomes reported in studies for MTM services or non-MTM groups. Discussions were conducted with fellow members of the study team until a consensus was achieved. Google Drive is utilized for managing quotes. Data were gathered utilizing Microsoft Excel (Version 16.48).

Articles quality assessment

Journal quality assessment uses the Joanna Briggs Institute (JBI) Critical Appraisal. The JBI critical appraisal questionnaire was used in accordance with the research methods carried out in the form of a Checklist for Randomized Controlled Trials, Checklist for Cohort Studies, and Checklist for Quasi-Experimental Studies (non-randomized experimental studies) [12]. *Critical appraisal (CA) is essentially a process for assessing whether a paper/manuscript/study is valid, important, and applicable.* To determine validity, importance, and application, several questions can be confirmed directly in the manuscript/paper/study to assess whether it is valid, important, and applicable [13]. Article quality assessment using JBI is depicted in table 1.

Table 1: Assessment of the quality of articles included in the systematic review

Study	Design	Questions													Σ
		1	2	3	4	5	6	7	8	9	10	11	12	13	
Planas *et al.* [14]	RCT	y	y	y	y	y	y	y	y	y	y	n	y	n	11/13
Skinner *et al.* [15]	Cohort	y	y	y	y	y	y	y	y	y	y	y	-	-	11/11
Morelo *et al.* [37]	Cohort	y	y	y	y	y	y	y	y	y	n	y	-	-	10/11
Leticia *et al.* [39]	Quasi experiment	y	y	y	y	y	y	y	y	y	-	-	-	-	9/9
Reininger *et al.* [17]	RCT	y	n	y	n	n	y	n	y	y	y	y	y	y	9/13
Daniel *et al.* [40]	RCT	y	n	y	n	n	y	n	y	y	n	y	y	y	7/13
Zillich *et al.* [22]	Cohort	y	y	y	y	y	y	y	y	n	y	y	-	-	10/11
Maiguma *et al.* [23]	Cohort	y	y	y	n	n	y	y	y	n	n	y	-	-	7/11
McFarland *et al.* [29]	Quasi experiment	y	y	y	y	y	n	y	y	y	-	-	-	-	8/9
Brummel *et al.* [30]	Quasi experiment	y	y	y	y	y	y	y	y	y	-	-	-	-	9/9
Negash *et al.* [3]	Quasi experiment	y	y	y	n	n	y	y	y	y	-	-	-	-	7/9
Ndefo *et al.* [16]	Quasi experiment	y	n	n	n	y	y	y	y	y	-	-	-	-	6/9
Malina *et al.* [10]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Ross *et al.* [31]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Rocha *et al.* [32]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Murali [41]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Yasin *et al.* [26]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Rosli *et al.* [19]	RCT	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
Chong [27]	Quasi experiment	y	y	y	n	y	n	y	y	y	-	-	-	-	7/9
Pinto *et al.* [38]	Quasi experiment	y	y	y	n	y	n	y	y	y	-	-	-	-	7/9
Ferries *et al.* [24]	Cohort	n	n	y	y	n	y	y	y	y	y	y	-	-	9/11
Mathis [20]	RCT	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
Ross *et al.* [31]	Quasi experiment	y	y	y	n	y	y	y	y	y	-	-	-	-	8/9
Pinto *et al.* [25]	Cohort	n	n	y	y	y	y	y	y	n	n	y	-	-	7/11

Note: RCT (13 questions), Cohort (11 questions), Quasi experiment (9 questions). y= yes, no

RESULTS

Study selection

As a result of the literature search that met the criteria, 271 articles were found. After duplicates were removed, 169 articles were completely assessed. A total of 25 articles were finally included in this systematic review. The study selection process is described in fig. 1.

Tables 2 and 3 describe the characteristics of each study that assessed the effect of MTM interventions on clinical outcomes and compliance in DM patients.

Table 2: Clinical outcomes reported in the included studies

No	Study	Study design	Delivery	Followup (mo)	Sample	Mean age	Outcomes	Intervention	Control	p-value
1	Planas *et al.* [14]	RCT	Face to face	12	I =32; C=20	64.7	BP	Pre = 141.76;Post = 124.44	Pre = 145.40; Post= 148.13	0.021
2	Skinner *et al.* [15]	Cohort	Face to face	12	I = 50; C = 50	53.7	HbA1c LDL HDL SBP DBP	7.5±0.38 92.7 ±36.4 48.2 ±10.3 136.5 ±19.8 72.7 ±10.3	10.8 ±2.0 110.8±65.7 45.2 ±12.9 145.4 ±17.8 73.8±14.7	0.001 0.17 0.16 0.12 0.63
3	Morelo *et al.* [37]	Cohort	Face to face	6	I = 99; C= 56	62.2	A1c FPG LDL HDL TG SBP DBP	Pre=10.5, post=8.2 Pre=222.7, post=159 Pre=90.1, post=84.0 Pre=40.0, post=40.7 Pre=266.3, post=185.9 Pre=130.5, post=127.0 Pre=75.5, post=71.8	Pre=9.7, post=9.0 Pre=225.1, post=179.4 Pre=94.4, post=82.8 Pre=42.1, post=42.9 Pre=214.0, post=189.2 Pre=135,0, post=136.7 Pre=77.0, post=74.5	<0.001 0.08 0.58 0.57 0.33 0.11 0.59
4	Reininger *et al.* [17]	RCT	Face to face and telepon	12	I = 147; C = 145	I=51;C= 52	HbA1c	0.35	0.26	0.7604
5	Maiguma *et al.* [23]	Cohort	Face to face	2	I = 26; C = 89	I=64;C= 66	HbA1c	8.9	15.1	0.0195
6	McFarland *et al.* [29]	Quasi experiment	Telepon	6	I = 36; C = 67	I=66;C= 53	HbA1c	Pre=9.0;Post=6.9	Pre=9.1;Post=7.6	0.006
7	Morello *et al.* [42]	Cohort	Face to face and telephone	6	I = 99; C = 56	62	HbA1c FPG BMI LDL HDL TG SBP DBP	Pre=10.5, post=8.2 Pre=222.7, post=159 Pre=32.9, post=33.3 Pre=90.1, post=84.0 Pre=40.0, post=40.7 Pre=266.3, post=185.9 Pre=130.5,post=127 Pre=75.5, post=71.8	Pre=9.7, post=9.0 Pre=225.1, post=194.3 Pre=31.6, post=31.9 Pre=94.4, post=82.8 Pre=42.1, post=42.9 Pre=214.0, post=189.2 Pre=135.0, post=136.7 Pre=77.0, post=74.5	<0.001 0.08 0.99 0.58 0.57 0.33 0.11 0.59
8	Brummel *et al.* [30]	Quasi experiment	Face to face	12	I = 212; C = 103	I=58 C=58	HbA1c LDL BP	Pre=43.80, post=42.15 Pre=63.64, post=79.34 Pre=66.12, post=76.03	Pre=63.11, post=59.22 Pre=65.05, post=73.7 Pre=61.17, post=73.79	0.01 0.32 0.30
9	Negash *et al.* [3]	Quasi experiment	Face to face	4	423	52.3	BMI SBP HbA1c FPG	Pre= 25, Post= 24.7 Pre= 141.2, post= 134.5 Pre= 9.3, post= 8.2 Pre= 167, post= 141.7	N/A	0.108 0.000 0.001 0.000
10	Ndefo *et al.* [16]	Quasi experiment	Face to face	4	I= 25; C=26	53	HbA_1C	Pre=10.06;Post=8.53	Pre=10.32;Post=10.06	<0.05
11	Ross *et al.* [31]	Quasi experiment	Face to face	12	N=749	-	SBP DBP LDL TD HbA1c 6 mo HbA1c 9 mo	Pre=142.7, post= 135.6 Pre=89.9, post=83.6 Pre=140.9, post=116 Pre=249.9, post=204.4 Pre=10.7, post=9.1 Pre=11.2, post=9.3	N/A	<0.001 <0.001 <0.001 <0.001 <0.001 <0.001
12	Rocha *et al.* [32]	Quasi experiment	Face to face	9	N= 34	65,9	SBP DBP BMI	Pre=148.5, post=128.9 Pre=83.1, post=76.1 Pre=27.9, post=28.1	N/A	<0.001 <0.001 0.089
13	Yasin *et al.* [26]	Quasi experiment	Face to face	1	N=20	69,5	FPG	Pre = 128.55;Post = 129.95	N/A	>0.05
14	Rosli *et al.* [19]	RCT		3 and 6	N=166	-	HbA1c FPG BMI DBP	Pre=10.29;post1=10.6;post2 =9.32 Pre=10.93; post1=9.60; post2=9.31 Pre=28.02; post1=27.8; post2=27.93 Pre=75.30;post1=76.52; post2=76.3	Pre=9.6;post1=9.9;post2=9.6 Pre=9.5;post1=10.6;post2=9.8 Pre=27.6;post1=27.4; post2=27 Pre=75.7;post1=78.5; post2=78	0.004 0.015 0.409 0.575
15	Chong [27]	Quasi experiment	Face to face	12	N= 47	54	HbA1c FPG TG LDL HDL SBP DBP	Pre=9.85; post=7.55 Pre=218.50; Post=142.40 Pre=203.40; post=147.90 Pre=138.90, post=95.86 Pre=48.57, post=46.00 Pre=144.50, post=130.80 Pre=79.00, post=71.25	N/A	<0.05 <0.05 <0.05 NS NS NS <0.05
16	Pinto *et al.* [38]	Quasi experiment	Face to face	12	N= 172	NA	HbA1c SBP DBP	Pre=8.41, post=7.22 Pre=134.15, post=129.68 Pre=88.10, post=84.92	N/A	0.000 0.039 0.053
17	Mathis [20]	RCT	Face to	6	I=176	59	HbA1c	Pre=7.8, post=7.37	Pre=7.6, post=7.44	0.763

			face		C=168		SBP DBP BMI	Pre=132.4, post=128.53 Pre=78, post=76.20 Pre=35.6, post=34.15	Pre=130.6, post=126.12 Pre=78.9, post=77.88 Pre=35.7,post=34.88	0.270 0.272 0.542
18	Ross *et al.* [31]	Quasi experiment	Face to face	6	N= 468	67	A1c SBP DBP HDL LDL TD	Pre=7.72, post=7.68 Pre=138.76, post=132.22 Pre=77.95, post=75.29 Pre=46.91, post=46.84 Pre=93.06, post=91.87 Pre=200.54, post=184.13	N/A	<0.05 <0.05 <0.05 <0.05 <0.05 <0.05
19	Pinto (2013)	Cohort	Face to face	12	N= 101	N/A	A1c A1c SBP SBP DBP DBP BMI	Pre=7.77, post=7.50 Pre=8.87, post=8.18 Pre=136.17, post=130.57 Pre=155.36, post=139.14 Pre=84.40, post=80.20 Pre=98.80, post=86.50 Pre=37.33, post=37.37	N/A	0.866 0.247 0.189 0.001 0.252 0.000 0.837

Note: BP (blood pressure), SBP (systolic blood pressure), DBP (diastolic blood pressure), HbA1c (Hemoglobin A1c), BMI (Body Mass Index), TD (Triglycerides), LDL (low-density lipoprotein), HDL (high-density lipoprotein), FPG (fasting plasma glucose), N/A (not available), NS (no statistic)

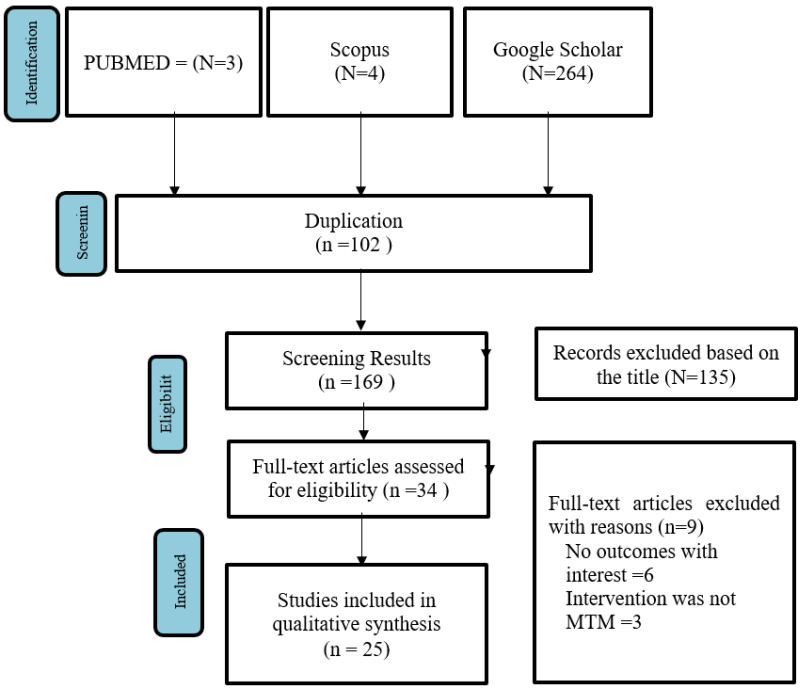

Fig. 1: PRISMA flowchart of the research article selection process

Table 3: Effect of MTM on adherence

No	Study	Study design	Delivery	Follow-up (mo)	Sample	Mean age	Intervention	Control	p-value
1	Planas *et al.* [14]	RCT	Face to face	12	I =32; C=20	64.7	Pre= 80.5%; Post= 87.5%	Pre= 79.5%; Post= 78.8%	0.012
2	Skinner *et al.* [15]	Cohort	Face to face	12	I = 50; C = 50	53.7	62.1%	6.9%	0.001
3	Leticia *et al.* [39]	Quasi experiment	Telephone	6	I = 60; C = 60	71.2	Pre=0.67; post=0.67	Pre=0.70; post=68	0.79
4	Daniel *et al.* [40]	RCT	Face to face	6	I = 62; C = 65	I=61.3C=59.8	Pre=9.2%; post=61%	Pre=13.2, post=30.2	<0.001
5	Zillich *et al.* [22]	Cohort	Face to face	12	I = 1007; C=13614	I=49;C=48	80.8%	36.4%	<0.001
6	Ndefo *et al.* [16]	Quasi experiment	Face to face	4	I= 25;C=26	53	Pre=28.33;Post=29.22	N/A	<0.05
7	Malina *et al.* [10]	Quasi experiment	Face to face	1	N= 20	59.5	Pre = 0; Post= 30	N/A	0.005
8	Murali [41]	Quasi experiment	Face-to-face and telephone	12	N= 104	75.5	Pre= 39;Post=54	N/A	0.000
9	Ferries *et al.* [24]	Cohort	Face to face	6	N= 80369	71	Pre=50%;Post=87%	NA	<0.001

During the search, a total of 25 articles were found that met the inclusion and exclusion criteria, of which 19 articles examined the impact of MTM on clinical outcomes (table 2), nine studies examined the impact of MTM on adherence (table 3), and three studies examined the impact of MTM on clinical outcomes and compliance [14–16]. The study design consists of 5 RCTs [14, 17–20], seven cohorts [15, 21–25], and 13 quasi-experiments [1, 3, 10, 16, 25–32]. Delivery of intervention 20 via face-to-face [3, 10, 14–16, 18–27, 30–32], two by telephone [28-29], as well as three face-to-face and telephone [1, 17, 21]. Pharmacists carry out all MTM interventions except for research carried out by Negash *et al.*, 2021 carried out by pharmacists, doctors, and nurses. Follow up from 1 mo [26] up to 2 years [23]. The minimum number of intervention samples is 20 people [10], and a maximum of 212 people [30]. Age between 52.3 years [3] up to 75.5 years [1]. The percentage of male gender is between 25% [10], up to 100% [29]. Clinical results of HbA1c in 16 of 25 studies (64%) were 12 significantly (75%) influenced by MTM ($p<0,05$) [3, 15, 16, 19, 21, 23, 25, 27, 29–31]. Of the 25 studies reporting treatment compliance results (35%), there were seven studies (77.78%) significantly influenced by MTM services [1, 10, 13–14, 17, 21, 23].

DISCUSSION

This systematic study contributes to the existing research by outlining the advantages of pharmacist-delivered MTM treatments for prevalent clinical problems in diabetic patients. The systematic study determined that pharmacist-provided Medication Therapy Management (MTM) services have statistically significant effects on improving clinical outcomes, particularly in reducing HbA1c levels. Across various studies, a higher percentage of patients achieved a HbA1C level below 7% and experienced a decrease in mean HbA1c values after receiving pharmacist-led Medication Therapy Management (MTM) services compared to standard care without MTM services.

Assessing HbA1c is crucial for diabetic individuals as it can forecast diabetes complications. It shows the consequences of glycation, like retinopathy and nephropathy, caused by the reproduction of hazardous end products. HbA1c is a biomarker of overall glucose exposure since it measures the average glycemic value over the past 2-3 mo, integrating fasting blood glucose and postprandial blood glucose [33]. The most common complication suffered by diabetic patients at RSUD Dr. Moewardi was hypertension in 46 patients (41%), and the most common therapeutic regimen received by patients was oral hypoglycemia in 50 patients (52%) [34]. The antibiotics used for diabetic foot ulcers inpatient at Hospital in Surakarta are metronidazole (4.8%), vancomycin (4.8%) and antibiotics combination are ceftriaxone-metronidazole (47.6%), ceftriaxone-metronidazole-clindamycin (4,8%), levofloxacin-azithromycin-ceftriaxone (4.8%), cotrimoxazole-ciprofloxacin (4.8%), metronidazole-meropenem (4.8%), ceftriaxone-metronidazole-gentamicin (4.8%), metronidazole-clindamycin-ciprofloxacin (4.8%), ceftriaxone-levofloxacin (4.8%), and ceftriaxone-metronidazole-ciprofloxacin (9.5%). The evaluation results according to criteria appropriate usage of antibiotics that is 100% appropriate indication, 100% for appropriate of patients, 42.3% for appropriate drug, and 61.9% for the appropriate dose [35].

The final results of the average SBP and DBP have improved compared to the baseline, which means that MTM services are effectively able to reduce SBP and DBP. Hypertension and DM that occur simultaneously can increase the risk of microvascular and macrovascular complications. Managing blood pressure is equally crucial to regulating glucose levels. A 10 mm Hg drop in systolic blood pressure (SBP) reduces the risk of complications for individuals with diabetes by 12% [14]. Therefore, efforts are needed to appropriately manage antihypertension in DM patients as a strategic and very important treatment step, with the hope that these efforts can delay the development of complications or inhibit the progression of complications that have occurred [36].

The average FPG experienced a significant decrease in the final results compared to the baseline. This means that MTM services are effective in controlling blood pressure in diabetes patients. Fasting plasma glucose (FPG), which measures blood sugar levels after fasting for 8 h. This test is usually done first to check whether you have prediabetes or diabetes. According to Murad's research, an FPG assessment is also carried out to determine the effectiveness of therapy and treatment in diabetes patients. The limitation of FPG measurement in diabetics is that this examination can only measure the state of blood sugar at a certain time after the patient has fasted for 8 h. This examination cannot describe the patient's blood sugar state over a longer period. Therefore, multiple examinations are needed to get an impression of the patient's blood sugar. Patients can take the HbA1c test, which is a value that represents the patient's average blood sugar over the past three months [36].

The findings from this systematic review indicate that MTM services are able to improve medication adherence in diabetes mellitus patients. Comprehensive, intensive assistance from MTM services can increase patient motivation to comply with treatment. It is proven that the overall study shows an increase in the percentage of medication adherence after receiving MTM services compared to baseline.

Research conducted by Planas shows that one of the things that worsens the condition of type 2 diabetes patients is non-compliance with treatment [14]. The success of a therapy does not only depend on the accuracy of diagnosis, selection, and administration of the right drug, but treatment compliance is a determinant of success. Compliance is very important in carrying out treatment because it affects the results of therapy. Non-compliance with therapy can cause negative effects. The problem of non-compliance with medication use causes therapy to fail and hospitalization rates to increase

Pharmacist-provided MTM services offer a chance to assist patients, particularly those in high-risk and disadvantaged groups. MTM services employ a proactive approach to patient healthcare and are widely applicable in community-based settings. MTM services tailored for individuals with diabetes are certain to enhance health outcomes by lowering HbA1c levels through improved treatment adherence, considering diabetes is a prevalent chronic condition globally. Differences in the delivery of MTM services, both face-to-face and via telephone, must be considered carefully because they can influence the results of the MTM service to a greater or lesser extent.

LIMITATION AND STRENGTH

This journal review presents research from a total of 25 journals on MTM services on clinical outcomes and medication adherence in patients with diabetes. Clinical outcomes are more varied by adding fasting plasma glucose (FPG) as a measure of MTM success in diabetic patients, in addition to Hemoglobin A1c (HbA1c) and general clinical outcomes such as blood pressure (BP), systolic blood pressure (SBP), diastolic blood pressure (DBP), Body Mass Index (BMI), Triglycerides (TD), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). MTM interventions are more varied in terms of delivery, namely face-to-face, telephone, and face-to-face combined with telephone and service follow-up time, from 4 mo to 12 mo.

The limitation of this study is that the effectiveness of MTM on clinical outcomes and medication adherence in shorter periods below four months or longer periods above 12 mo is unknown. This study also did not know the difference in MTM delivery between face-to-face and telephone and the combination of the two.

Recommendations for future research could examine the benefits of MTM on clinical outcomes with a shorter duration of under four months or a longer duration of over 12 mo. This is to determine the best duration of MTM services in diabetic patients. Future researchers can also research differences in the effectiveness of MTM services in diabetic patients in terms of delivery between face-to-face, telephone, and telephone.

CONCLUSION

The systematic evaluation indicates that pharmacist-provided MTM services can enhance clinical outcomes and medication adherence in diabetic patients compared to those not receiving MTM services.

This research offers more proof of the involvement of pharmacists in delivering Medication Therapy Management (MTM) services to diabetic patients. Future studies could be undertaken to offer more precise and conclusive data regarding the benefit of this service.

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AUTHORS CONTRIBUTIONS

Conceptualization: HK, ZC, MTKS; methodology: HK, MTKS; data curation: MTKS; analysis: HK, MTKS; writing-original draft preparation: MTKS, ZC; writing-review and editing: HK, ZC, MTKS; supervision: HK, ZC; project administration: MTKS; all authors have read and agreed to the published version of the manuscript.

CONFLICT OF INTERESTS

Declared none

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