Effect of mHealth Interventions on Glycemic Control and HbA1c Improvement among Type II Diabetes Patients in Asian Population: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Due to the high prevalence of diabetes mellitus, it is pertinent to educate and inform diabetes patients about their self-management. It can be done effectively using innovative methods like mobile health (mHealth), which includes mobile applications, phone calls, and text messages. Thus, this meta-analysis was conducted to summarize the effectiveness of mHealth interventions for the management of diabetes compared with usual care in the Asian population. **Materials and Methods:** Searches were performed in electronic databases, namely PubMed, Scopus, Embase, and Cochrane Library, in August and September 2020. Search terms used were "Diabetes Mellitus," "mHealth," "glycemic control", "HbA1c levels," and "Blood glucose levels." The primary outcome was glycated hemoglobin and blood glucose levels. Trials were pooled, and heterogeneity was quantified using the I^2 statistic. **Results:** The search yielded 3980 abstracts, of which 18 trials met the inclusion criteria. Lowering of Hba1c levels was reported in the majority of trials, which aided in Glycemic control. For post prandial blood glucose (PPBG) levels, a statistically significant reduction of value –20.13 (95%CI –35.16 to –5.10, $P = 0.009$, $I^2 = 59\%$) was seen in the mean in the intervention group, whereas for HbA1c levels the mean reduction in the intervention group was –0.44 (95%CI, –0.79 to 0.10, $P = 0.01$, $I^2 = 87\%$). Although these interventions proved beneficial for these outcomes, there was a difference in the amount of effects caused by different mHealth interventions. **Conclusion:** This study acknowledged the effects of different mHealth interventions as per their accessibility and availability in recent years. There is a need to include more studies in future reviews to generate a larger body of evidence for the reported outcomes. The researchers should give the utmost priority to the transparency while reporting the interventions for effective interpretation of the retrieved data.

Keywords: Diabetes mellitus, glycemic control, HbA1c, meta-analysis, mHealth

Introduction

Diabetes mellitus is a component of "Metabolic Syndrome" usually characterized by hyperglycemia. For a few decades, documented cases of diabetes mellitus have shown an incremental trend.[1,2] "The Global Diabetes Report" by World Health Organization (WHO) states that about 422 million patients suffered from diabetes mellitus in 2014. An incremental trend is seen in the South-Eastern Asian Region of WHO, with approximately 96 million diabetes patients.[1]

Thus, the hour's need is to educate and aware patients with diabetes about their self-management and self-care to improve their clinical and health outcomes.[1] Glycemic control is associated with complications resulting from diabetes. Hence, a balanced glycemic control is required to avoid chronic complications in T2DM patients.[3-5]

mHealth is an essential component of electronic health (eHealth). As stated by the "Global Observatory for eHealth (GOe)," mobile health or mHealth can be defined as "a medical and

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public health practice promoted and supported by mobile devices like mobile phones, personal digital assistants (PDAs), patient monitoring devices and other wireless devices."[6]

The "International Telecommunication Union (ITU)" reported that the number of wireless subscribers has risen to over 5 billion, and nearly 70% of these users belong to LMIC.[7] With this extensive market penetration of mobile and wireless technologies, it serves as an essential means to enhance the education and support for the patients and prove beneficial for health care professionals.[8] Various components of mHealth include mobile apps, phone calls, and text messages, which help in the fast and instant transmission of the information at a low cost to users and could become an ideal technique for diabetes self-management.[8,9]

Diabetes Mellitus exhibits disparities in Asia compared to Western countries. The disease biology, etiology, and genetic predilection are different for Asians.[10,11] Hence, it became pertinent for a systematic review and meta-analysis of the trials specifically confined to the Asian population to evaluate and assess the effects of mHealth interventions on glycemic control and HbA1c among type II diabetes patients. The review aimed to estimate the mean difference in blood glucose levels measured in mg/dL and mean the difference in glycosylated hemoglobin (HbA1c) measured in % (mmol/mol) levels intervention and control group.

Materials and Methods

This Systematic Review with Meta-Analysis was conducted and reported according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" guidelines.[12]

The protocol was duly submitted to the Institutional Research Review Board and PROSPERO. It has been registered in PROSPERO under the registration ID- CRD42020194063. Ethical approval for the same was also obtained from the Institutional Ethics Committee as letter no- AIIMS/IEC/20/710 dated 19th October 2020.

Database and search strategies

A comprehensive and thorough search strategy was conducted in August and September 2020 on electronic database searches, namely PubMed, Scopus, Embase, and Cochrane Library. Google Scholar was used to browsing gray literature, and the Trial registry - clinicaltrials.org was searched to track publications not indexed in other databases.

A standard and accepted search strategy was designed for PubMed and other databases to broadly search the publications starting from the month of January in 1990 to the month of August in 2020. It was later modified as per the requirement of other databases.

Various search strategies, according to database scanned, are given in the table below [Table 1]:

Criteria for study inclusion and exclusion

Randomized controlled trials (RCTs) or clinical trials that reported the clinical outcomes of the mHealth interventions in T2DM adults compared with conventional care or usual care were included. The mHealth intervention arm was needed to have one or more of the following categories:

1. Mobile Health applications targeting patients with type II DM
2. Text messages- SMS (Short Message Service) used to manage type II DM.
3. Phone calls used for management of type II DM.

The studies which were conducted in the Asian population and published in English were included.

The studies where diabetes patients reported severe diabetic complications such as diabetic foot, diabetic heart disease, etc., were excluded. Also, the studies with mixed population of patients such as type 1 and type 2 diabetics were excluded, along with the studies on pregnant women with type 2 diabetes.

Study selection

After the literature search, the titles and abstracts of the obtained studies were individually scanned by authors, and potentially eligible studies were identified. Consensus was obtained between the two reviewers in case of disagreement and the exclusion reasons were recorded. **[Annexure I].**

Data extraction

All the obtained records were then collected into the Zotero library for deletion of duplicate studies. The remaining references were then transported to an excel file that contained all the essential information required for screening.

Outcome measures

The primary outcomes assessed were the change in glycated hemoglobinA1c (HbA1c) and blood glucose levels post-intervention in both the arms.

Assessment of risk of bias

The "risk of bias" was assessed in the included studies as per "Cochrane Handbook for Systematic Reviews of Interventions."[13] Two reviewers independently evaluated the studies and the risk of bias was noted. The risk had a judgment as high risk, low risk, unclear risk, and the reason for every decision was further recorded. **[Annexure II].**

Data analysis methods

A quantitative synthesis of data was further done to have a pooled estimate of the included studies to estimate mHealth interventions' effect in glycemic control outcomes and HbA1c Improvement on type 2 diabetes patients.

"Review Manager Software (version 5.3)" was used for statistical analysis. Cochrane's Q statistic and inconsistency index (I^2) was used to compute the statistical heterogeneity. Pooled effect size estimates along with a 95% confidence interval were calculated. The mean, standard deviation (SD), and the participant number given in both the groups (intervention and control) for each outcome at last follow-up were collected from each study. Funnel plots were used to assess publication bias.

Subgroup analysis was done based on the type of mHealth intervention used among the RCTs participants.

Result

After the combined database search, it resulted in a total number of 3980 records. Out of these, 72 articles were shortlisted based on their eligibility, and after the full-text screening, it resulted in 18 eligible trials for qualitative synthesis and 14 trials for quantitative synthesis (Meta-Analysis). Details of the screening process and results are presented in Supplementary Figure 1.

Characteristics of the studies

The studies included in the systematic review are listed in Table 2.

18 trials were obtained for the qualitative synthesis (Systematic Review), whereas only 14 trials were finalized for Quantitative synthesis (Meta-Analysis). A total of 3368 participants were recruited in these trials, whereas only 2931 participants could complete the trials. The majority of trials were conducted in the Southern Asian region, followed by the eastern region, western region, and the southeastern region. The region-wise distribution of included studies is given in Table 3.

Supplementary Figure 2 demonstrates the distribution of included trials based on the Asian region in which they are conducted.

The intervention duration was 7 months on average and ranged from 3 months to 24 months. Most of the trials were published in the current decade (2011–2020). In 6 trials, the mobile application was used as an intervention. Phone calls were used in 4 trials, and text messages were used in 7 trials. One trial involved both the use of text messages and phone calls in the intervention arm.

In most trials, the number of participants recruited ranged from 100 to 500. Seven trials reported only about HbA1c as an outcome measure. Seven trials reported fasting blood glucose (FBG) levels along with HbA1c levels, whereas one trial reported HbA1c and Post Prandial Blood glucose (PPBG) levels. Four trials reported all the three outcome measures i.e., HbA1c, FBG and PPBG. One trial reported only about FBG levels, whereas another reported only blood glucose levels, including FBG and PPBG levels.

Risk of bias

The risk of bias observed commonly was unclear bias, reported in all the studies due to insufficient evidence as no information was given regarding their protocol registration or publication. High risk of bias was also reported in maximum studies as no blinding of participants and researcher was possible due to the nature and requirement of these trials and thus, the majority of trials were open labeled. Figure 1 (a) demonstrates the risk of bias graph where each risk is given as low risk, unclear risk and high risk and Figure 1 (b) summarizes the risk of bias summary and assessment for every included study.

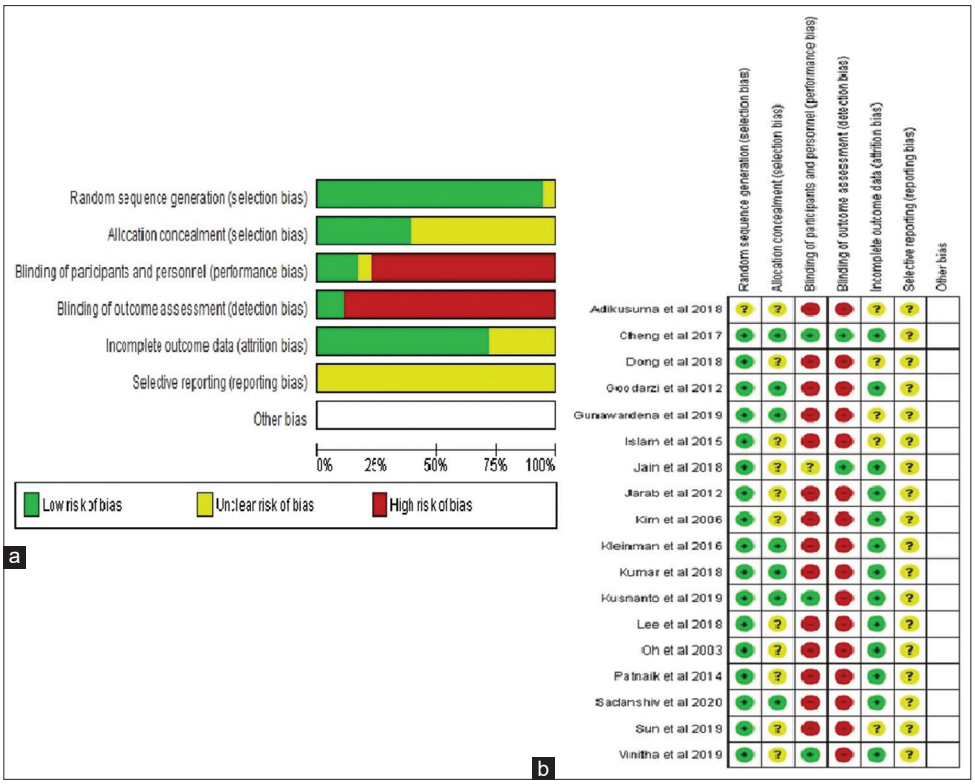

Figure 1: (a) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies (b) Risk of bias summary: review authors' judgements about each risk of bias item for each selected study

Table 1: Various search strategies according to databases scanned

Database	Search Strategy	No. of studies
Pubmed	((("diabetes mellitus" OR "diabetes type 2" OR "type 2 diabetes" OR "DM type 2" OR "type 2 DM" OR "Diabetes Mellitus Type II" OR "type II Diabetes mellitus" OR "adult diabetes" OR "Type 2 diabetes patients" OR "Diabetes mellitus patients" OR "patients with type 2 diabetes" OR "Diabetes type 2 patients" OR "Diabetes in older age" OR "Maturity Onset Diabetes Mellitus" OR "Adult-Onset Diabetes Mellitus") AND ("mhealth" OR "mobile health" OR "m-health" OR "e-health" OR "electronic health" OR "ehealth" OR "phone calls" OR "phone call management" OR "text messaging" OR "text messages" OR "mobile texts" OR "SMS text" OR "mobile applications" OR "mobile apps" OR "mobile health applications" OR "mobile health apps")) AND ("Glycemic control" OR "HbA1c" OR "HbA1c levels" OR "Haemoglobin A, Glycated" OR "Glycosylated Haemoglobin A" OR "blood glucose levels" OR "blood sugar levels" OR "Blood Glucose Self-Monitoring" OR "Blood Sugar Self-Monitoring" OR "Home Blood Glucose Monitoring")).	908
Embase	#1- 'glycemic control'/exp OR 'hemoglobin a1c'/exp OR 'glucose blood level'/exp OR 'blood glucose monitoring'/exp #2- 'telehealth'/exp OR 'mhealth'/exp OR 'mobile application'/exp OR 'text messaging'/exp OR 'phone call'/exp #3- 'diabetes mellitus'/exp OR 'diabetic patient'/exp OR 'non-insulin dependent diabetes mellitus'/exp-305 #1 AND #2 AND #3 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim) AND [embase]/lim AND [1-1-1990]/sd NOT [1-9-2020]/sd AND [1990-2020]/py #5 AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim OR [young adult]/lim)	1624
Scopus	(TITLE-ABS-KEY ("Diabetes Mellitus" OR "Non-Insulin Dependent Diabetes Mellitus" OR "diabetic patient") AND TITLE-ABS-KEY ("telehealth" OR "mhealth" OR "mobile application" OR "text messaging" OR "SMS" OR "phone call") AND TITLE-ABS-KEY ("glycemic control" OR "hemoglobin a1c" OR "glucose blood level" OR "blood glucose monitoring") AND TITLE-ABS-KEY ("randomised controlled trial" OR "RCT" OR "clinical trial")) AND (EXCLUDE (PUBYEAR , 1987) OR EXCLUDE (PUBYEAR , 1986)) AND (LIMIT-TO (DOCTYPE , "ar"))	417
Cochrane Library	#1- MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees #2- MeSH descriptor: [Telemedicine] explode all trees #3- MeSH descriptor: [Glycated Hemoglobin A] explode all trees #4- MeSH descriptor: [Blood Glucose Self-Monitoring] explode all trees #5= #1 AND #2 AND #3 OR #4	815
Google Scholar	"mhealth" AND "Diabetes mellitus type 2" AND "HbA1c" AND "Blood glucose"	192
Clinicaltrials.gov	Telemedicine, glycemic control | Available, Completed Studies | Interventional Studies|Diabetes Mellitus	24

Table 2: Characteristics of Included Studies in the Systematic Review

Author	Year of study	Year of publication	Country	Sample size (Recruited/ Completed)	mhealth intervention Group	Control Group	Follow-up duration (months)	Outcome Measure Reported		
								HbA1c	FBG	PPBG
Cheng *et al*.[14]	2014-15	2017	China	242/201	Phone calls	usual care	5	Yes	-	-
Vinitha *et al*.[15]	2014-15	2019	India	248/218	SMS	usual care	24	Yes	Yes	Yes
Kusnanto *et al*.[16]	2018	2019	Indonesia	30/30	Mobile application	usual care	3	Yes	-	-
Adikusuma *et al*.[17]	2017	2018	Indonesia	40/40	SMS	usual care	6	Yes	-	-
Dong *et al*.[18]	2016	2018	China	120/119	Mobile application	usual care	12	Yes	Yes	Yes
Goodarzi *et al*.[19]	2011	2012	Iran	100/81	SMS	usual care	3	Yes	Yes	-
Gunawardena *et al*.[20]	2017-18	2019	Sri Lanka	67/52	Mobile application	usual care	6	Yes	-	-
Kumar *et al*.[21]	2015-16	2018	India	955/852	SMS	usual care	12	-	Yes	-
Kim *et al*.[22]	2005	2006	South Korea	60/51	SMS	usual care	6	Yes	Yes	Yes
Jarab *et al*.[23]	2011-12	2012	Jordan	171/156	Phone calls	usual care	6	Yes	Yes	-
Jain *et al*.[24]	-	2018	India	299/290	Phone calls	usual care	6	Yes	Yes	Yes
Kleinman *et al*.[25]	2015	2016	India	91/80	Mobile application	usual care	6	Yes	Yes	-
Lee *et al*.[26]	2014-15	2018	South Korea	148/105	Mobile application	usual care	12	Yes	Yes	-
Sun *et al*.[27]	2016	2019	China	91/91	Mobile application	usual care	6	Yes	-	Yes
Oh at al.[28]	2000-01	2003	South Korea	50/38	Phone calls	usual care	3	Yes	Yes	Yes
Patnaik *et al*.[29]	2012-13	2014	India	100/55	SMS+Phone calls	usual care	3	-	Yes	Yes
Sadanshiv *et al*.[30]	2015-16	2020	India	320/302	SMS	usual care	6	Yes	-	-
Islam *et al*.[31]	2013-14	2015	Bangladesh	236/230	SMS	usual care	6	Yes	-	-

Table 3: Region wise distribution of included studies from Asia

Asian region (23)	Country of published study	No of studies
Eastern Asia *n*=6	Korea	3
	China	3
Western Asia *n*=2	Jordan	1
	Iran	1
Southern Asia *n*=8	India	6
	Bangladesh	1
	Sri Lanka	1
South Eastern Asia *n*=2	Indonesia	2
Central Asia *n*=0	No study published	0
Total	18	

Meta-Analysis

Part A: Primary objective

A meta-analysis of the effect of mHealth interventions on

(i) Glycosylated Hemoglobin (HbA1c)
The data from 13 eligible studies, included a total of 1713 type 2 diabetes patients, were pooled to find the effects of diverse mHealth interventions on HbA1c. The impact of mHealth intervention was favoring the intervention group as a statistically significant reduction was seen in the mean in the intervention group as –0.44 (95%CI, –0.79 to 0.10, $P = 0.01$, $I^2 = 87\%$), suggesting that HbA1c levels in the mHealth group were significantly lower than those in the usual care group [Figure 2a].

(ii) Fasting Blood Glucose (FBG) levels
8 studies which included a total of 1893 type 2 diabetes patients, were found eligible while reporting the effect of mHealth interventions on FBG levels. The result suggested that the effect of mHealth intervention was inconclusive and doesn't affect FBG in T2DM patients in the intervention group. The studies sample showed no heterogeneity ($I^2 = 0\%$) with fixed-effects model [Figure 3a].

(iii) Post-Prandial Blood Glucose (PPBG) Levels
While reporting about the effect of mHealth interventions on PPBG levels, 6 studies were found eligible which included a total of 858 type 2 diabetes patients. The forest plot of these studies concluded the results as -20.13 (95%CI –35.16 to –5.10, $P = 0.009$, $I^2 = 59\%$). There was a reduction in PPBG levels in mHealth group as compared to the usual care group. A moderate heterogeneity was seen with random-effects model [Figure 4a].

Part B: Subgroup analysis

Subgroup analyses were done for the different mHealth interventions on all the primary outcome measures- glycated hemoglobin (HbA1c), FBG, and PPBG levels.

The subgroup analysis done to assess the effect of different mHealth intervention on Glycosylated Hemoglobin (HbA1c) showed that when SMSs were used as an intervention, the result showed –0.58 (95%CI, –1.03 to –0.13, $P = 0.01$, $I^2 = 84\%$) suggesting that there was a reduction in HbA1c levels in T2DM patients of SMS group compared to a usual care group. Other interventions didn't have any effect on HbA1c levels [Figure 2b-d].

To report the effect of different mHealth interventions on FBG levels, the result of subgroup analysis suggested that all three interventions showed an inconclusive result and no effect can be seen in FBG levels in any intervention group than usual care groups [Figure 3b-d].

The result of subgroup analysis on PPBG levels showed that mobile applications were the most effective intervention used to reduce PPBG levels in the intervention group compared with the usual care group. The result showed a reduction in mean of mHealth group as –21.70 (95%CI –35.28 to –8.12, $P = 0.002$, $I^2 = 42\%$). No conclusive result was seen in the use of other interventions. [Figure 4b-d].

Another Subgroup analyses were done based on duration of follow-up on all the primary outcome measures- glycated hemoglobin (HbA1c), FBG, and PPBG levels. There are two subgroups on the basis of follow-up period. One subgroup consists of studies whose follow-up duration was from 3 to 6 months. Second subgroup included the studies with a follow-up duration of 7–24 months.

The subgroup analysis done to assess the effect of follow-up duration on Glycosylated Hemoglobin (HbA1c) showed the result as –0.20 (95%CI, –0.33 to –0.07, $P = 0.002$, $I^2 = 85\%$) in studies with the duration of 3–6 months while in studies with follow-up period of 7–24 months, the result was as –0.85 (95%CI, –1.15 to –0.55, $P < 0.00001$, $I^2 = 94\%$). It suggested that there was a reduction in HbA1c levels in T2DM patients of mHealth group compared to a usual care group in both the subgroups [Supplementary Figure 3a-b].

To report the effect of different follow-up duration on FBG levels, the result of subgroup analysis of follow-up duration of 3–6 months was –4.72 (95%CI, –13.52 to 4.08, $P = 0.29$, $I^2 = 0\%$). The studies with duration of 7–24 months showed 2.72 (95%CI, –3.62 to 9.06, $P = 0.40$, $I^2 = 0\%$). No conclusive result was seen in the FBG levels on the basis of follow-up duration [Supplementary Figure 4a-b].

The result of subgroup analysis on PPBG levels showed that the result was -27.15 (95%CI, -39.33 to -14.08, $P < 0.0001$, $I^2 = 50\%$) in subgroup of 3–6 months follow-up period, whereas the subgroup with 7–24 months showed –5.09 (95%CI, –17.99 to 7.81, $P = 0.44$, $I^2 = 0\%$). The result showed a reduction in mean of mHealth group when follow-up continued for 3–6 months and no conclusive result was seen in the other subgroup [Supplementary Figure 5a-b].

Funnel plots

Publication bias was assessed by a funnel plot for each outcome measure [Figure 5 (a), (b) and (c)]. The symmetrical presentation of the funnel plot for HbA1c and PPBG levels indicated slight

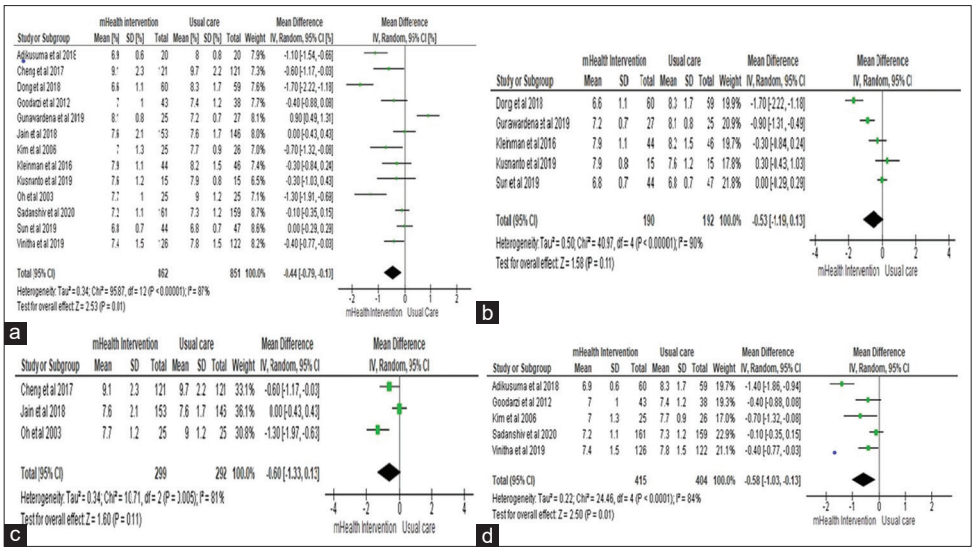

Figure 2: (a) Effect of mHealth interventions on HbA1c (b) Effect of mobile applications as an intervention on HbA1c (c) Effect of phone calls as an intervention on HbA1c (d) Effect of SMS as an intervention on HbA1c

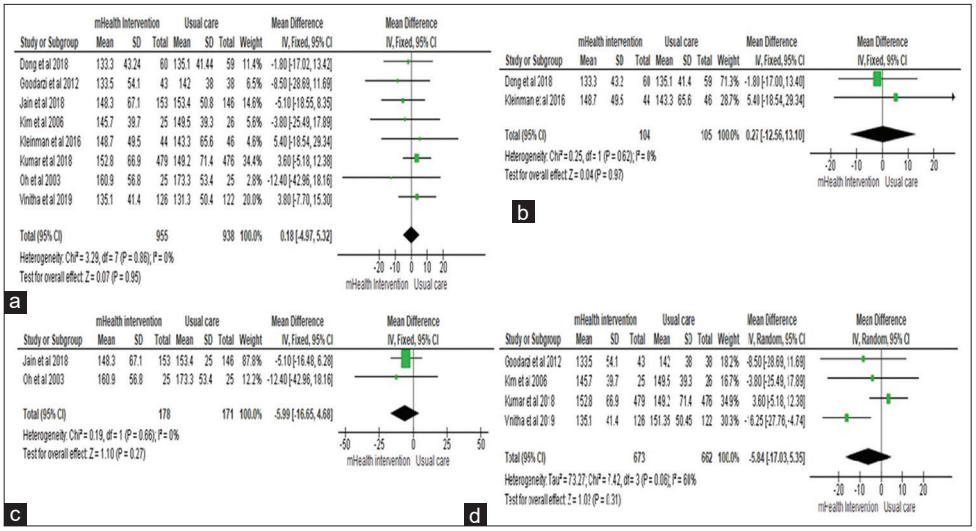

Figure 3: (a) Effect of mHealth interventions on FBG (b) Effect of mobile applications as an intervention on FBG (c) Effect of phone calls as an intervention on FBG (d) Effect of SMS as an intervention on FBG

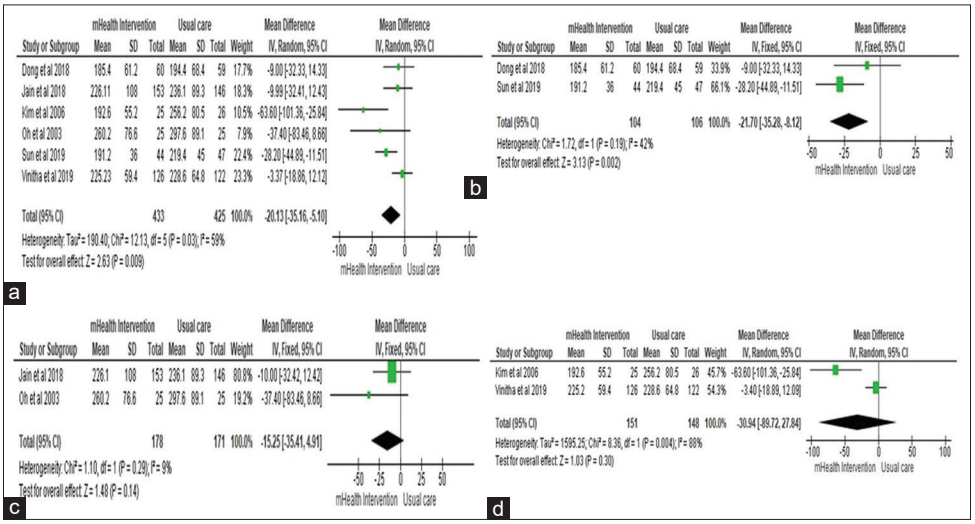

Figure 4: (a) Effect of mHealth interventions on PPBG (b) Effect of mobile applications as an intervention on PPBG (c) Effect of phone calls as an intervention on PPBG (d) Effect of SMS as an intervention on PPBG

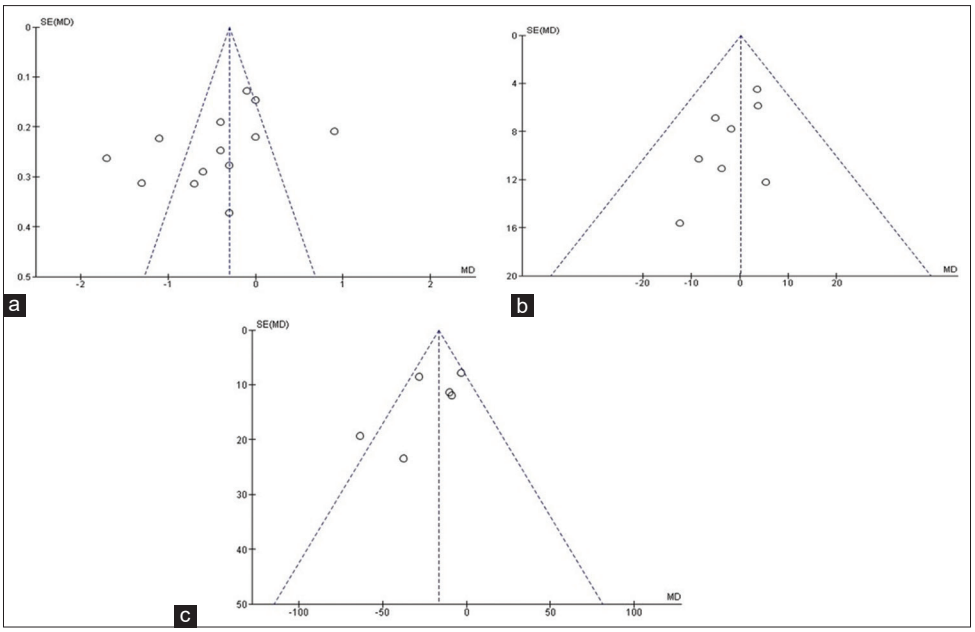

Figure 5: (a) Funnel plot of comparison: 1 mHealth intervention v/s usual care, outcome: 1.1 HbA1c Outcome (b) Funnel plot of comparison: 1 mHealth intervention v/s usual care, outcome: 1.5 Fasting Blood Glucose levels (c) Funnel plot of comparison: 1 mHealth intervention v/s usual care, outcome: 1.9 Post prandial blood glucose levels

publication bias. For FBG levels, no significant publication bias was observed. Each study was symmetrically distributed on both sides [Figure 5a-c].

Discussion

This systematic review and meta-analysis gave a vast horizon on the effects of mHealth interventions on managing type 2 diabetes patients in the Asian population. This study acknowledged the effects of different mHealth interventions as per their accessibility and availability in recent years. The effects of various mHealth interventions are very well reported in the Asian population. It is also evident that these interventions can also be utilized to increase the quality of diabetes self-management and serve to collect patients' clinical data.

In most of the studies, there was an improvement in HbA1c levels and glycemic control. Although these interventions proved beneficial for these outcomes, there was a difference in the effects it caused in specific trials.

When meta-analysis was done based on any mHealth interventions,' it reduced HbA1c and PPBG levels. No effect can be seen in FBG levels.

After the subgroup analysis, the most effective mHealth intervention was the use of SMSs while reporting their effect on HbA1c levels. No remarkable change in HbA1c levels was reported in mobile applications and phone calls as mHealth intervention. When subgroup analysis was done for FBG levels, no specific mHealth intervention proved to be conclusive about their effect in reducing FBG levels. While reporting about PPBG levels, the most effective intervention was seen in the form of mobile applications. They help reduce the PPBG levels while given in the intervention arm compared to the usual care arm. The other two interventions produce no conclusive result on PPBG levels.

Among the included trials, there is vast difference in sample size and intervention duration. Also, there was a considerable variability in the types of mHealth technology used. This wide variation may have caused the observed heterogeneity. Compared with usual care, the addition of mHealth intervention appeared to have a significant effect on people with type 2 diabetes. Although there was substantial heterogeneity, the pooled analyses showed that mHealth intervention lowered HbA1C levels and Post Prandial blood glucose levels. The effect of intervention on Fasting Blood Glucose levels remains inconclusive.

The difference in effects can be attributed to the different technology which was incorporated for various mHealth interventions. The mixed results can be attributed to having different lengths of intervention periods and a large difference in the number of participants included in separate trials.

Most mobile applications were linked with a glucometer to record the patients' values of different clinical outcomes, which was later used for person-specific recommendations to all the patients as per their needs. Although these mobile apps are very beneficial, they might have posed difficulty using their technical advancement, specifically in the elderly population. Compared to mobile apps, phone calls and SMSs are considered an easy option to transmit information quickly. But due to various additional features available in mobile applications, we can still consider them as one of

the most promising platforms compared to phone calls and SMSs.

These interventions were strong evidence that their effectiveness was based on the users' awareness and education, and the type of behavior change communication methods used. Hence, these interventions must be designed in a user-friendly manner and should be able to produce similar effects in all the patients. The health care professionals should also take the patients' economic condition into account while developing a mHealth intervention to obtain full use and services. Also, patients' needs should be prioritized, and their present situation and complexities should be assessed before any intervention is administered. Our findings suggest that all three mHealth interventions can be a highly effective mechanism for linking providers to patients with diabetes.

Limitations

This review was confined to the Asian population, so it included the studies conducted only in the Asian population. Since there is a remarkable difference in terms of income and education compared to Asians and non-Asians, this review's results may not apply to global studies. As our systematic review included fewer studies, there was a limitation of the inclusion of constituent trials. There is a need to include more studies in future reviews to generate a larger body of evidence and establish their integration with already published research. Some of the trials reported a smaller sample size, insufficient blinding, and shorter trial duration, which is inadequate to determine the effects of mHealth interventions on this population over a long period. We did not report the data regarding the effects of mHealth on cost-effectiveness or amount of care satisfaction. The effectiveness of these interventions on various self-management aspects such as dietary management, more physical activity, or increased medication adherence was not considered in this review.

Implications

Further exploration of the relationships between different intervention strategies and their components is recommended. Patients' beliefs and attitudes focused on the design aspects and physical features of various interventions- mobile applications, text messages, and phone calls need to be explored further. After exploring the patients' belief regarding the mHealth usage, the factors regarding its acceptability and utility need to be put forward in future research. The evaluation of these interventions based on their cost-effectiveness aspect should also be assessed, as it is crucial for their impact and applicability in clinical practice. The use of these mHealth interventions can be prioritized in National Health Programs, and their cost-effectiveness can be assessed at larger levels.

Conclusion

In conclusion, the current research has assessed mHealth interventions on glycemic control and HbA1c improvement in T2DM patients in the Asian population. Although the evidence that is generated by this review shows a mixed result, mHealth interventions can be seen as a suitable medium to improve the glycemic index among diabetic patients. The available literature about assessing the use of mHealth is limited and inconsistent to draw any robust conclusions.

This review recommends that mHealth researchers give the utmost priority to the transparency in the reporting of interventions based on their contexts, aims, delivery pathway and mechanisms of impact for effective interpretation of the retrieved data. These interventions work on the following aspects: easy transmission of health-related information and timely notifications for various health-related behaviors, including medication adherence, proper dietary intake, and regular exercise and also give the patients a chance to provide their feedback, which can enhance the further development of these interventions. More innovative and robust research work concerning various mHealth intervention strategies is needed in the near future.

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Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY FILE

Annexure I: Characteristics of Excluded studies

Title	Author	Reason for Exclusion
SMS education for the promotion of diabetes self-management in low & middle income countries: a pilot randomized controlled trial in Egypt	Abaza *et al*	Not Asian
Diabetes and TelecommunicationS (DATES) study to support self-management for people with type 2 diabetes: a randomized controlled trial	Al-Ozairi *et al*	Only protocol reported
DialBetics: A Novel Smartphone-based Self-management Support System for Type 2 Diabetes Patients	Waki *et al*	Website based intervention used
Effects of mobile phone application combined with or without self-monitoring of blood glucose on glycemic control in patients with diabetes: A randomized controlled trial	Yu *et al*	4 intervention arms are used in the study
Effect of case management on glycemic control and behavioral outcomes for chinese people with type 2 diabetes: A 2-year study	Yuan *et al*	Patient centered case management intervention used
Electronic messaging intervention for management of cardiovascular risk factors in type 2 diabetes mellitus: A randomised controlled trial	Fang *et al*	No usual care intervention
Impact of web-based nurse's education on glycosylated haemoglobin in type 2 diabetic patients	Kim *et al*	Sub study reported
Effects of Mobile Text Messaging on Glycemic Control in Patients With Coronary Heart Disease and Diabetes Mellitus: A Randomized Clinical Trial	Huo *et al*	Coronary heart disease patients also included
Effectiveness of mobile and internet intervention in patients with obese type 2 diabetes	Kim *et al*	Internet based intervention used
Automated Feedback Messages With Shichifukujin Characters Using IoT System-Improved Glycemic Control in People With Diabetes: A Prospective, Multicenter Randomized Controlled Trial	Kobayashi *et al*	No full text available
Effectiveness of short message service-based intervention (SMS) on self-care in type 2 diabetes: A feasibility study	Peimani *et al*	No full text available
Feasibility study of automated interactive voice response telephone calls with community health nurse follow-up to improve glycaemic control in patients with type 2 diabetes	Pichayapinyo *et al*	No full text available
Efficacy of a telephone-based intervention among patients with type-2 diabetes; a randomized controlled trial in pharmacy practice	Sarayani *et al*	No full text available
Effects of a patient oriented decision aid for prioritising treatment goals in diabetes: pragmatic randomised controlled trial	Denig *et al*	Not Asian
The development and feasibility of a web-based intervention with diaries and situational feedback via smartphone to support self-management in patients with diabetes type 2	Nes *et al*	Not Asian
Reduced HbA1c levels in type 2 diabetes patients: An interaction between a pedagogical format for students and psycho-educational intervention for patients	Sarid *et al*	No full text available
Mobile phone intervention to improve diabetes care in rural areas of Pakistan: a randomized controlled trial	Shahid *et al*	No full text available
Reinforcement of adherence to prescription recommendations in Asian Indian diabetes patients using short message service (SMS)--a pilot study	Shetty *et al*	Different outcome reported
Effects of continuous care for patients with type 2 diabetes using mobile health application: A randomised controlled trial	Wang *et al*	No full text available
Effectiveness of Smartphone App–Based Interactive Management on Glycemic Control in Chinese Patients With Poorly Controlled Diabetes: Randomized Controlled Trial	Zhang *et al*	3 intervention arms used
Welltang – A smart phone-based diabetes management application – Improves blood glucose control in Chinese people with diabetes	Zhou *et al*	Type 1 and type 2 Diabetes patients included
Web-Based Care Management in Patients With Poorly Controlled Diabetes	McMohan *et al*	Not Asian
Remote Lifestyle Coaching Plus a Connected Glucose Meter with Certified Diabetes Educator Support Improves Glucose and Weight Loss for People with Type 2 Diabetes	Bollyky *et al*	Not Asian
Design and patient characteristics of the randomized controlled trial TExT-MED+FANS A test of mHealth augmented social support added to a patient-focused text-messaging intervention for emergency department patients with poorly controlled diabetes	Burner *et al*	Not Asian

Contd...

Annexure I: Contd...

Title	Author	Reason for Exclusion
Effectiveness and safety of a glucose data-filtering system with automatic response software to reduce the physician workload in managing type 2 diabetes	Cho *et al*	Different intervention used
Mobile communication using a mobile phone with a glucometer for glucose control in Type 2 patients with diabetes: as effective as an Internet-based glucose monitoring system	Cho *et al*	Different intervention used
Impact of web-based nurse's education on glycosylated haemoglobin in type 2 diabetic patients	Kim *et al*	Sub study reported
Design and rationale of the Cardiovascular Health and Text Messaging (CHAT) Study and the CHAT-Diabetes Mellitus (CHATDM) Study: two randomised controlled trials of text messaging to improve secondary prevention for coronary heart disease and diabetes	Huo *et al*	CHD patients included
The Effect of a Smartphone-Based, Patient-Centered sDiabetes Care System in Patients With Type 2 Diabetes: A Randomized, Controlled Trial for 24 Weeks	Kim *et al*	Control group is logbook user
A randomized controlled trial of a nurse short-message service by cellular phone for people with diabetes	kim *et al*	Substudy
A randomised, controlled trial of the effects of a mobile telehealth intervention on clinical and patientreported outcomes in people with poorly controlled diabetes	Baron *et al*	Not Asian
Mobile Phone-Based Video Messages for Diabetes Self-Care Support	Bell *et al*	Not Asian
Feasibility study of portable technology for weight loss and HbA1c control in type 2 diabetes	Bentley *et al*	Not Asian
Automated Insulin Dosing Guidance to Optimize Insulin Management in Patients with Type 2 Diabetes; A Multi-Center Randomized-Controlled Trial	Bergenstal *et al*	Not Asian
Effectiveness of diabetes self-management education via a smartphone application in insulin treated type 2 diabetes patients – design of a randomised controlled trial ('TRIGGER study')	Boels *et al*	Not Asian
Efficacy of an Electronic Health Management Program for Patients With Cardiovascular Risk: Randomized Controlled Trial	Yun *et al*	Other diseases also included
Effectiveness and cost effectiveness of a mobile phone text messaging intervention for prevention of cardiovascular risk factors among patients with type 2 diabetes: A randomized controlled trial	Islam *et al*	Substudy
Effects of Face-to-Face and Telephone-Based Family-Oriented Education on Self-Care Behavior and Patient Outcomes in Type 2 Diabetes: A Randomized Controlled Trial	Maslakpak *et al*	3 intervention arms used
The long-term effect of community-based health management on the elderly with type 2 diabetes by the Markov modeling	Chao *et al*	Different intervention (Markov modeling) used
Mobile phone text messaging and Telephone follow-up in type 2 diabetic patients for 3 months: A comparative study	Zolfaghari *et al*	Both arms used intervention
Effectiveness of a Video-Based Lifestyle Education Program Compared to Usual Care in Improving HbA1c and Other Metabolic Parameters in Individuals with Type 2 Diabetes: An Open-Label Parallel Arm Randomized Control Trial (RCT)	gupta *et al*	Different intervention used
A smartphone app to improve medication adherence in patients with type 2 diabetes in Asia: Feasibility randomized controlled trial	Huang *et al*	Different outcome reported
A nurse short message service by cellular phone in type-2 diabetic patients for six months	kim *et al*	Substudy
The effectiveness, reproducibility, and durability of tailored mobile coaching on diabetes management in policyholders: A randomized, controlled, open-label study	lee *et al*	Different intervention used
Effectiveness of an mHealth-Based Electronic Decision Support System for Integrated Management of Chronic Conditions in Primary Care The mWellcare Cluster-Randomized Controlled Trial	Prabhakarn *et al*	Hypertensive patients also included
Effects of telephone-delivered lifestyle support on the development of diabetes in participants at high risk of type 2 diabetes: J-DOIT1, a pragmatic cluster randomised trial	Sakane *et al*	no diabetes patients are included (only the risky patients)
Effect of a mobile phone-based glucose-monitoring and feedback system for type 2 diabetes management in multiple primary care clinic settings: Cluster randomized controlled trial	Yang *et al*	no full text available

Contd...

Annexure I: Contd...

Title	Author	Reason for Exclusion
Use of a Novel, Remotely Connected Diabetes Management System Is Associated with Increased Treatment Satisfaction, Reduced Diabetes Distress, and Improved Glycemic Control in Individuals with Insulin-Treated Diabetes: First Results from the Personal Diabetes Management Study	Mora *et al*	Not Asian
The impact of a structured education and treatment programme (FLASH) for people with diabetes using a flash sensor-based glucose monitoring system: Results of a randomized controlled trial	Hermanns *et al*	Not Asian
Effect of structured self-monitoring of blood glucose, with and without additional TeleCare support, on overall glycaemic control in non-insulin treated Type 2 diabetes: the SMBG Study, a 12-month randomized controlled trial	Parsons *et al*	Not Asian

Annexure II: Risk of bias of included studies

Adikusuma *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient evidence to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Cheng *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	a computer generated block randomization list using a block size of 4 at 1:1 ratio
Allocation concealment (selection bias)	Low risk	the enrolling investigators opened the sealed envelope after participant's name was written on next available envelopes;
Blinding of participants and personnel (performance bias)	Low risk	the enrolling investigators were blinded to the trial design and study hypotheses
Blinding of outcome assessment (detection bias)	Low risk	the trained outcome assessors were blinded to trial hypotheses and group allocation throughout the study period
Incomplete outcome data (attrition bias)	Low risk	no group differences in attrition rate was observed
Selective reporting (reporting bias)	Unclear risk	insufficient evidence to permit judgement
Other bias	Unclear risk	

Dong *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Diabetes patients were randomly classified into control (n=60) and intervention (n=60) group
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient evidence to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Goodarzi *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Finally 100 patients were selected on a random sampling scheme where in a list of random numbers was provided before data collection using the software.
Allocation concealment (selection bias)	Low risk	For allocation to exp. and cont. groups, the researchers use RAS software and randomized by random permuted block design by a size of 2.
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Therefore, we report data from the 81 subjects who remained to complete the study protocol.
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Gunawardena *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomized, using a computer-generated random sequence method created by Sealed Envelope Ltd
Allocation concealment (selection bias)	Low risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient evidence to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Islam *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomly assigned 1:1 to SMS intervention and standard care groups.
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	no blind
Blinding of outcome assessment (detection bias)	High risk	no blind
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient evidence to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Jain *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The study participants were randomized into 2 groups
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of outcome assessment (detection bias)	Low risk	by a blinded investigator
Incomplete outcome data (attrition bias)	Low risk	We were able to include 299 patients out of estimated 322 patients in our study (92.8%)
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Jarab *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Study participants were randomly assigned to intervention and control groups via a minimization technique using Minim software
Allocation concealment (selection bias)	Unclear risk	insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Therefore, a total of 156 patients (77 intervention; 79 usual care) completed the 6-month study period
Selective reporting (reporting bias)	Unclear risk	insufficient evidence to permit judgement
Other bias	Unclear risk	

Kim *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	They were randomized by random permuted block design using a random number table and assigned to one of two groups, either intervention (n=30) or control (n=30)
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	Only 51 subjects completed the entire study, 25 interventions and 26 controls.
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Klienman *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomization sequence was investigator generated, stratified by site, with a 1:1 allocation
Allocation concealment (selection bias)	Low risk	The allocation sequence was concealed from implementing staff through sequentially numbered, opaque, sealed, and stamped envelopes
Blinding of participants and personnel (performance bias)	High risk	open-label
Blinding of outcome assessment (detection bias)	High risk	open-label
Incomplete outcome data (attrition bias)	Low risk	80 returning participants
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Kumar *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	955 study individuals were randomized
Allocation concealment (selection bias)	Low risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	The endline assessment for 6 months was done in 852 patients (intervention: 441 and control: 411) with 11.0% drop out rate
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Kusnanto *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization
Allocation concealment (selection bias)	Low risk	Determination of research samples using random allocation.
Blinding of participants and personnel (performance bias)	Low risk	Respondents in both groups did not know whether they belonged to the experimental group or the control group
Blinding of outcome assessment (detection bias)	High risk	single blind
Incomplete outcome data (attrition bias)	Low risk	In the third month there are 30 respondents who are able to follow the program to completion
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Lee *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomly assigned into 2 groups
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	open label
Blinding of outcome assessment (detection bias)	High risk	open label
Incomplete outcome data (attrition bias)	Low risk	Among 148 participants, 136 completed phase 1 of the study
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Oh *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomized by a toss of a coin
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	no blinding
Blinding of outcome assessment (detection bias)	High risk	no blinding
Incomplete outcome data (attrition bias)	Low risk	only 38 subjects completed the entire study
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Patnaik *et al*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Starting at random, the patients were allocated to control group and test group
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	no blinding
Blinding of outcome assessment (detection bias)	High risk	no blinding
Incomplete outcome data (attrition bias)	Low risk	Out of 100 participants, total 55 patients (control-21, Intervention-34) came for follow up
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Sadanshiv *et al*

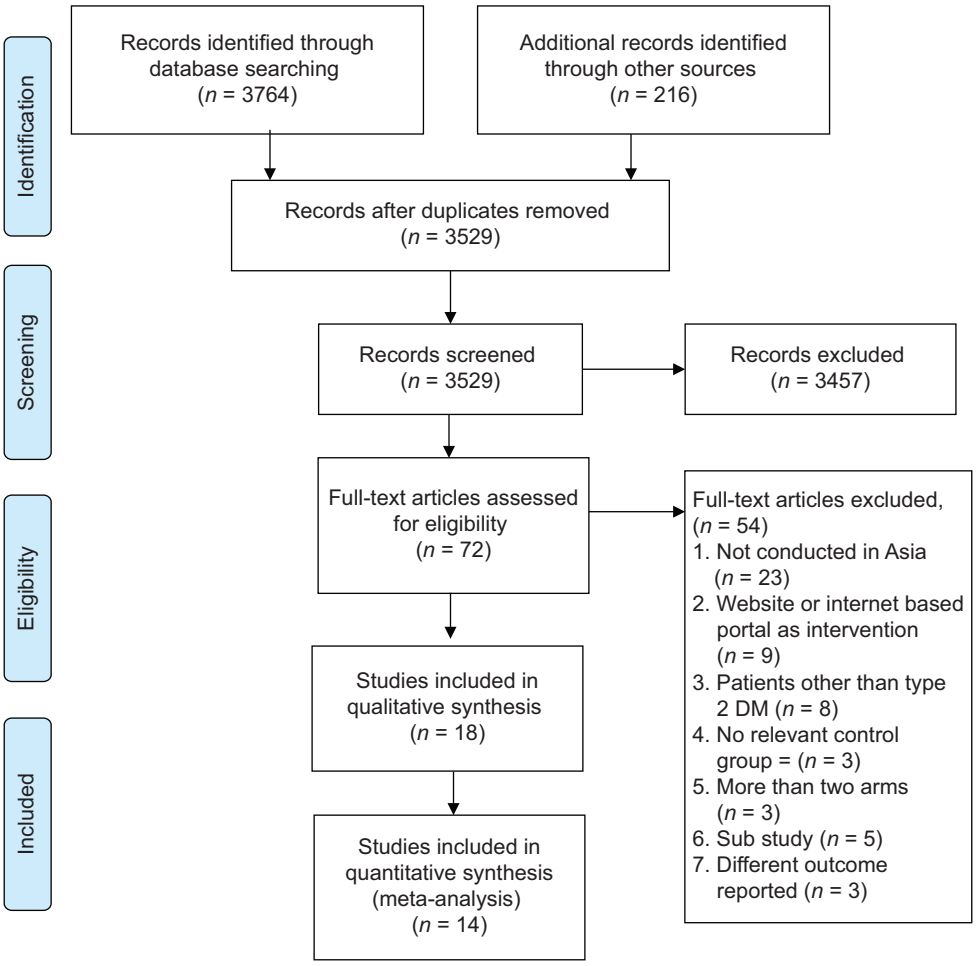
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomization was done
Allocation concealment (selection bias)	Low risk	The codes were given to the principal investigator in sequentially labeled sealed opaque envelopes to randomly allocate patients
Blinding of participants and personnel (performance bias)	High risk	Openlabeled
Blinding of outcome assessment (detection bias)	High risk	Openlabeled
Incomplete outcome data (attrition bias)	Low risk	A total of 18 people failed to follow-up
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Sun *et al*

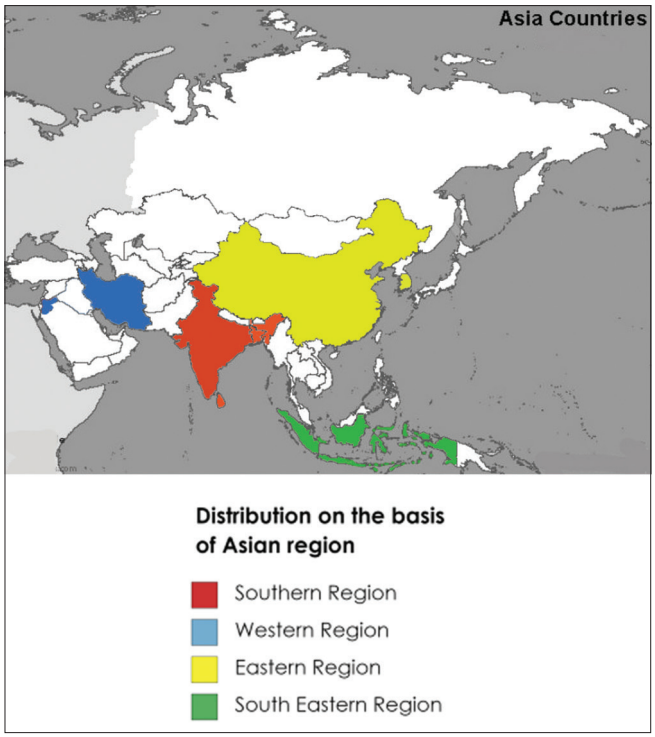
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned to the intervention and control groups using the random number sequence
Allocation concealment (selection bias)	Unclear risk	Insufficient evidence to permit judgement
Blinding of participants and personnel (performance bias)	High risk	no blinding
Blinding of outcome assessment (detection bias)	High risk	no blinding
Incomplete outcome data (attrition bias)	Unclear risk	Insufficient evidence to permit judgement
Selective reporting (reporting bias)	Unclear risk	Insufficient evidence to permit judgement
Other bias	Unclear risk	

Vinitha *et al*

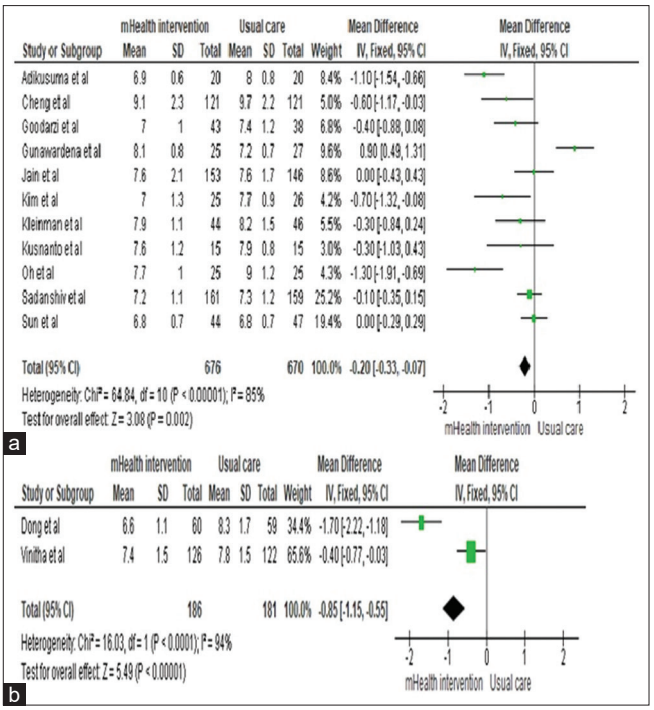
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Diabetes patients were randomly classified into control (n=60) and intervention (n=60) group by using a set of 120 random numbers, according to 1:1 ratio
Allocation concealment (selection bias)	Unclear risk	No random allocation reported
Blinding of participants and personnel (performance bias)	Low risk	Respondents in both groups did not know whether they belonged to the experimental group or the control group.
Blinding of outcome assessment (detection bias)	High risk	single blind
Incomplete outcome data (attrition bias)	Low risk	In the third month there are 30 respondents who are able to follow the program to completion
Selective reporting (reporting bias)	Unclear risk	insufficient evidence to permit judgement
Other bias	Unclear risk	



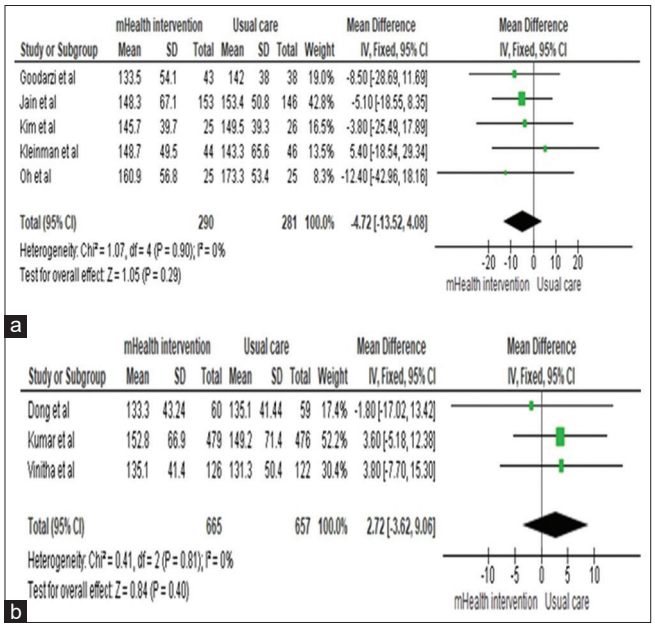
Supplementary Figure 1: PRISMA flow Diagram



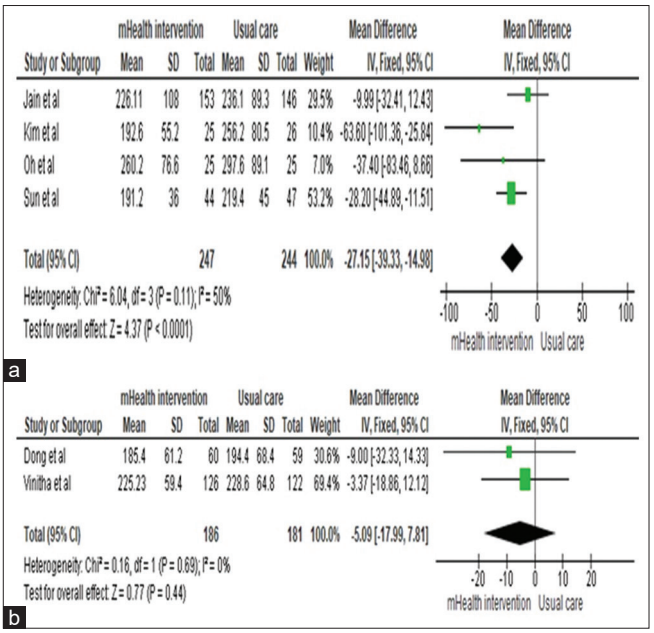
Supplementary Figure 2: Graph showing the distribution of included trials on the basis of Asian region in which they are conducted. Source: emapsworld.com



Supplementary Figure 3: (a) Effect of follow up duration (3-6 months) on HbA1c (b) Effect of follow up duration (7-24 months) on HbA1c



Supplementary Figure 4: (a) Effect of follow up duration (3-6 months) on FBG (b) Effect of follow up duration (7-24 months) on FBG



Supplementary Figure 5: (a) Effect of follow up duration (3-6 months) on PPBG (b) Effect of follow up duration (7-24 months) on PPBG