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Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in LMICs: A Systematic Review Protocol

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Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in LMICs: A Systematic Review

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Abstract

Introduction: There are a variety of mobile health applications available to monitor an individual's health or lifestyle to make it convenient and easy to access healthcare facilities at home. Despite the growing number of mobile applications, the evidence from research on normalising HbA1c levels with the use of these applications remains a mystery to many of them. As a result, the goal of this research is to see, how effective are the diabetic self-management applications on controlling type 2 diabetes? And To compare the evidence obtained among the LMICs

Methods and analysis: The electronic databases included for search will be PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials and additional sources of the search will be grey literature available on diabetes management websites, and reference lists of included studies. Studies published in the English language in indexed and peer-reviewed sources and additional sources will be considered. Studies reporting the effectiveness of mobile applications in the management of Type 2 diabetes in the LMICs will be eligible for inclusion. Editorials, letters, commentaries, conference and workshop reports, and articles in languages other than English, will be excluded.

The Population-Intervention-Comparison Outcomes (PICO) Framework and the PRISMA statement 2021, will be used for reporting this systematic review.

Data analysis will be done by narrative synthesis, and a meta-analysis may be conducted if we come across homogenous data for the outcome.

Ethics and dissemination: As this study is a systematic review, we will not be recruiting any participants for the study and hence will not require ethical approval. The dissemination of the summary of the study results will be done at the conferences.

Keywords: mobile health application, self-management applications, and type 2 diabetes mellitus

Prospero registration ID: CRD42021245517

Article summary:

Strengths of the study:

1. There are no systematic reviews published particularly focusing on self-managing type 2 diabetes with the help of mhealth technologies among the Low and Middle income countries.
2. The study findings are intended to support and generalize the factors obtained among the LMICs

Limitations of the study are:

1. The study isn't funded and hence will limit to only articles published in the English language

2. The geographical area under study will be limited to only low and middle-income countries specifically in the context of India since the trial is conducted representing the Indian population only.

Introduction

'Diabetes' is a term used to describe a group of diseases characterized by elevated blood glucose levels. It is caused by a lack of insulin production or function, or both, which may occur for various reasons and lead to protein and lipid metabolic disorders [1]. Various scientific studies have established that adequate blood glucose regulation minimizes the long-term effects of type 2 diabetes. Due to multiple circumstances, adolescents often fail to meet their blood glucose goals to the required level. But their deep inclination towards technology provides an opportunity for the delivery of innovative self-management interventions. A slew of issues plagues the delivery of healthcare in low and middle-income countries (LMICs). In 57 developing countries, the World Health Organization (WHO) estimates a 4.3 million healthcare worker shortage, resulting in understaffed hospitals, limited patient access to care, and a significant patient-physician contact gap, especially in rural areas [2]. To bridge this gap in terms of diabetes management, self-management app can play a pivotal role in India and the LMICs. The use of mobile health tools to help people manage chronic diseases is on the rise, but evidence of their effectiveness is mixed[3]. Patients with diabetes are increasingly using mobile technology for health (mHealth) interventions to help improve self-management; however, these interventions have not been implemented by a large number of patients, and dropout rates are common. In the management of diabetes, patient personality traits may play a key role in app adoption and active usage [4].

Diabetes has become so common in low- and middle-income countries (LMICs) that four out of every five people with diabetes now live in these countries, and the rate of diabetes is increasing in poorer communities [5]. Diabetes currently affects 336 million people in low- and middle-income countries (LMIC) [6&7]. Even in India, diabetes is rapidly growing and has reached the status of a potential epidemic, with more than 72.9 million diabetics currently diagnosed and projected to rise to 134.3 million by the year 2045, as reported by International Diabetes Federation (IDF) [8]. To manage diabetes and bridge the gap in terms of diabetes self-management among the LMICs, as well as to prioritise research agendas, public health interventions, and policies, a better understanding of the effect of mHealth in controlling and managing diabetes is indispensable. This review aims to assess the effectiveness of diabetic self-management applications on controlling type 2 diabetes in LMICs.

The global burden of type 2 diabetes mellitus (T2DM) continues to rise, with T2DM estimated to affect over 9% of the global population by 2035. The rising prevalence of T2DM will put pressure on healthcare systems to properly manage these individuals so that diabetes complications are avoided. Optimizing patient outcomes by combining medications with self-management of glycemic control and other risk variables could be a better approach. There is an increasing number of smartphone applications meant to help T2DM patients manage their condition, but only a few have been thoroughly tested[9]. mHealth applications are used in the self-management of type 2 diabetes mellitus along with standard care. The interventions may also include other forms of mHealth solutions like texting, emailing, video clips, and graphics. To find the evidence on how the use of mobile applications has impacted the health and self-management of type 2 diabetes among the individuals affected. Hence, our study objective is to understand- How effective are the diabetic self-management applications on controlling type 2 diabetes? And comparing the evidence obtained among the LMICs

Review Questions

1. Are diabetic self-management applications effective in controlling diabetes among the type 2 diabetic individuals?

2. To find out the impact on behavioral outcomes due to use of Diabetic self-management applications?

Methods

The PRISMA 2020 statement; an updated guideline for reporting systematic reviews[10] will be used for reporting the review and the population-intervention-comparison-outcomes (PICO) framework will be used for defining the methods of the review. (Refer; supplementary file 1- PRISMA checklist).

Criteria for considering studies for this review

Types of studies

Study design: The following study designs will be included: Randomized controlled trials (RCTs) to understand the effectiveness of the diabetic self-management app on the health of the app users, and Non Randomized controlled trials (NRCTs) like the Quasi-experimental studies, and controlled before after studies. We will exclude observational studies, conference papers, editorials, and other studies without any mobile app interventions in them.

Type of participants

Individuals with type 2 diabetes mellitus in the LMICs as listed in the World Bank Organization and individuals who fulfill the WHO criteria for being diagnosed with T2DM, with no age restrictions on the population.

Patient and public involvement: patients and the public were not involved in any way in this study.

Type of interventions

Digital health: The use of digital, mobile, and wireless technologies to support the achievement of health objectives. Digital health describes the general use of information and communications technologies (ICT) for health and is inclusive of both mHealth and eHealth[11].

EHealth: is the use of information and communication technologies (ICT) for health.

The unprecedented spread of mobile technologies as well as advancements in their innovative application to address health priorities have evolved into a new field of eHealth, known as mHealth.

mHealth: The Global Observatory for eHealth (GOe) defined mHealth or mobile health as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices[12].

From the context of our study, the term mHealth refers to the mobile applications used in the self-management of type 2 diabetes mellitus. The interventions may also include other simpler forms of mHealth solutions like texting, emailing, video clips, graphics, and web services.

Type of Comparison: the comparator groups would be the individuals who received standard hospital treatment or no hospital care and who received an intervention.

Type of outcome measures

Primary outcomes

- Clinical outcome (HbA1c at 3months, 6 months, and over 1 year)

  [A hemoglobin A1c (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin. An HbA1c test shows what the average amount of glucose attached to hemoglobin has been over the past three months. It's a three-month average because that's typically how long a red blood cell lives.[13]]

Secondary outcomes:

- Adherence to diabetic self-management applications and medication: The studies must have reported using any of the standard survey tools to record daily medication intake and app usage during the follow-up for a year.
- Self-efficacy with adherence to mHealth applications: Self-efficacy is defined as "the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations." - Albert Bandura [14, 15]. The studies must have done a subjective evaluation of the individual's willingness to use the self-management applications to manage t2dm and those who are confident to follow in their near future.
- Behavior change- If the study participants during their follow-up period adapted the positive change in behavior towards achieving better health, like opting for a healthy diet, regular moderate exercising, brisk walking, reducing/ managing their stress levels. Will be checked across the quality of life improvement index if any done in the studies[16].

Search methods for identification of studies

PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites, and reference lists of included studies. (Refer; supplementary file 2- Search strategies)

Data extraction and management

We will be using endnote library version X7 for screening and downloading the full-text articles and Microsoft Excel 2013 will be used for data extraction of the full-text articles. Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study then it will be excluded and if a disagreement arises between the two authors on inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart (Refer supplementary file 1) will be used to depict the screening process.

The rationale for exclusion will be provided for all the excluded studies throughout the process. Data extraction will be performed using a standardised pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. (Refer; supplementary file 3 - Data extraction format)

Any missing data in the studies included for review will be obtained through contacting the study authors of that particular study.

Assessment of risk of bias in included studies

Authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials[17]. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non Randomised studies[18]. The quality of the included studies will be assessed by using the Newcastle Ottawa Scale (NOS) for cross-sectional studies[19].

Data synthesis

Firstly, we will provide a detailed summary of all the included studies in a narrative format. A detailed summary of all the included studies will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications on controlling type 2 diabetes. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The results will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if needed. An attempt will be made to contact study authors if data is inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative

synthesis will be done if there are less than 10 included studies. All the analyses will be conducted in STATA 16.

Description of primary and secondary outcomes, whether adherence to diabetic self-management applications and medication has improved or not, Behavior change will be noted with the quality of life improvement index and self-efficacy will be checked following the improvement in managing T2DM. Listing out various measurement tools and devices used for judging the above-mentioned outcomes.

Subgroup analysis

Subgroup analysis will be performed for the following if appropriate

Table 1

1) Duration of the intervention	• 3 months • 6 months • 1 year
2) Across the regions (LMIC's)	Comparing study effectiveness within the LMICs
3) Age groups	The most effective rate of using the Diabetic self-management app in age groups as classified by UN
4) Gender	Male/ Females

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Ethics and dissemination: The study will be a systematic review of the published articles from different recognised and accessible databases and will not recruit any human participants directly, therefore, ethical clearance is not applicable. The dissemination of the final review findings will be done in a national or international conference and will be published in an indexed peer-reviewed journal.

Author Contributions: HB is the corresponding author, SMD, SS, JV, PP, PR and SMD conceptualized the study. SMD, SS, JV, PP, PR MGL and HB drafted the manuscript. All authors were involved in the development of the selection criteria and data extraction criteria. All authors will read, provide feedback and approve the final manuscript.

Acknowledgments: Not applicable.

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Conflicts of interest: There is no conflict of interest in this project.

Supplemental material: Supplementary materials are enclosed as 1, 2 and 3

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SUPPLEMENTARY FILE: 1

I. PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in LMICs: A Systematic Review (Refer; page no. 1)
Update	1b	N/A
Registration	2	The study has been registered in PROSPERO and the Registration ID is CRD42021245517. (Refer; page no. 1)
Authors:		
Contact	3a	Sherize Merlin Dsouza[1, 6], Sahana Shetty[2], Julien Venne[3], Prachi Pundir[4], Priyobrat Rajkhowa[1, 6], Melissa Glenda Lewis[5] and Helmut Brand[1, 6] 1. Department of Health Policy, Prasanna School of Public Health, Manipal Academy of Higher Education. 2. Department of Endocrinology, Kasturba Medical College Hospital, MAHE, Manipal, India. 3. Coordinator, Dept. of Digital Health and wellbeing, PSPH, MAHE, Manipal, India 4. Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Manipal Academy of Higher Education. 5. Indian Institute of Public Health Shillong, Lawmali, Pasteur Hill, Shillong, Meghalaya. 6. Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

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(Refer; page no. 8)

Contributions	3b	All authors were involved in development of the selection criteria, and data extraction criteria. All authors will read, provide feedback and approve the final manuscript. (Refer; page no. 8)
Amendments	4	As the review is being carried out amendments to the search strategy, selection criteria, and data extraction criteria may be amended to include the most pertinent information for this reviews objectives. If amendments to this protocol are made, the date of each amendment along with a description/rationale for the change will be noted.
Support:		
Sources	5a	Nil
Sponsor	5b	Nil
Role of sponsor or funder	5c	Not Applicable.

INTRODUCTION

Rationale	6	Despite the growing number of mobile apps, the evidence from research on normalising HbA1c levels with the use of these apps remains a mystery to many of them. As a result, the goal of this research is to see, how effective are the diabetic self-management apps on controlling type 2 diabetes? And To compare the evidence obtained among the LMICs (Refer; page no. 2)

Objectives	7	Review question: how effective are the diabetic self-management apps on controlling type 2 diabetes? And To compare the evidence obtained among the LMICs (Refer; page no. 3)
METHODS		
Eligibility criteria	8	We followed PICOconcept/framework Population (P): Individuals with type 2 diabetes mellitus in the LMICs as listed in the World Bank organization and individuals who fulfill the WHO criteria for being diagnosed with T2DM, with no age restrictions on the population. Intervention (I): mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices. mHealth solutions like texting, emailing, video clips, graphics, and web services. Comparison (C): the comparator groups would be the individuals who received standard hospital treatment or no hospital care and who received an intervention. Country comparison: impact of using diabetes self-management app among the LMICs listed by the World Bank-India in particular. Outcomes(O): primary outcomes- clinical parameters like HbA1c Secondary outcomes- adherence to medications, self-efficacy and behavior changes. (Refer; page no. 3 onwards)
Information sources	9	Authors in collaboration developed search strategies using medical subject headings (MeSH) and text words related to the topic. We will search CINAHL complete, PubMed, Web of Science, and Scopus. Only studies with human subjects will be included. (Refer; page no. 5)
Search strategy	10	Refer supplementary file 2.
Study records: Data management	11a	The search results collected from the electronic databases will be exported to endnote version 20. Duplicate studies will be removed. Data will then be extracted, and relevant information will be extracted to Excel spreadsheet using a data extraction tool. (Refer; page no. 6)

Selection process	11b	Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study then it will be excluded and if a disagreement arises between the two authors on inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process. (Refer; page no. 6)
Data collection process	11c	Data extraction will be performed using a standardised pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. (Refer; supplementary file 3) Any missing data in the studies included for review will be obtained through contacting the study authors of that particular study.
Data items	12	Bibliometric information such as Author's name, Author's affiliations, Title, Journal name, publication year, country of conduct will be collected along with Characteristics of the included studies. Data will be extracted based on the type of study, study objectives, Inclusion criteria, participant's characteristics, Intervention details, comparator, and the study outcome. (Refer; supplementary file 3)
Outcomes and prioritization	13	A detailed summary of all the included studies will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country will be in a narrative format. An evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management apps on controlling type 2 diabetes. (Refer; page no. 5)

		Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. (Refer; page no. 6&7)
Risk of bias in individual studies	14	Authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials (Julian PT Higgins, et. al., 2019). Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non Randomised studies – case-control and cohort studies (Jonathan AC Sterne, et. al., 2016). The quality of the included studies will be assessed by using the Newcastle Ottawa Scale (NOS) for cross-sectional studies (Wells, G. A., et. al., 2011). (Refer; page no. 6)
Data synthesis	15a 15b	A detailed summary of all the included studies in a narrative format. The results will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if needed. (Refer; page no. 6&7)
	15c	
	15d	
Meta-bias(es)	16	Not applicable.
Confidence in cumulative evidence	17	Not applicable.

Supplementary file: 2

II. Search Strategy

Database	Search strategy	Hits
PubMed	(("diabetes mellitus, type 2"[MeSH Terms] OR "self-management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language]) AND ((fha[Filter]) AND (clinicaltrial[Filter] OR randomized controlled trial[Filter] OR review[Filter]) AND (humans[Filter]) AND (english[Filter]))	58
World Bank list of low and middle-income countries included in the study	"low and middle income countr*"[Title/Abstract] OR "LMIC"[Title/Abstract] OR "Afghanistan"[Title/Abstract] OR "Afghanistan"[MeSH Terms] OR "albania"[MeSH Terms] OR "albania"[Title/Abstract] OR "algeria"[Title/Abstract] OR "algeria"[MeSH Terms] OR "american samoa"[MeSH Terms] OR "american samoa"[Title/Abstract] OR "Angola"[Title/Abstract] OR "Angola"[MeSH Terms] OR "argentina"[MeSH Terms] OR "argentina"[Title/Abstract] OR "armenia"[Title/Abstract] OR "armenia"[MeSH Terms] OR "azerbaijan"[MeSH Terms] OR "azerbaijan"[Title/Abstract] OR "bangladesh"[MeSH Terms] OR "bangladesh"[Title/Abstract] OR "republic of belarus"[MeSH Terms] OR "belarus"[Title/Abstract] OR "belize"[MeSH Terms] OR "belize"[Title/Abstract] OR "BENIN"[MeSH Terms] OR "BENIN"[Title/Abstract] OR "bhutan"[MeSH Terms] OR "bhutan"[Title/Abstract] OR "bolivia"[MeSH Terms] OR "bolivia"[Title/Abstract] OR (("BOSNIA AND HERZEGOVINA"[MeSH Terms] OR ("bosnia"[All Fields] AND "herzegovina"[All Fields]) OR "BOSNIA AND HERZEGOVINA"[All Fields] OR "bosnia"[All Fields]) AND	1,476,962 1,529,015

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	africa"[MeSH Terms] OR "south africa"[Title/Abstract] OR "Sudan"[MeSH Terms] OR "Sudan"[Title/Abstract] OR "sri lanka"[MeSH Terms] OR "sri lanka"[Title/Abstract] OR "saint lucia"[MeSH Terms] OR "st lucia"[Title/Abstract] OR "saint vincent and the grenadines"[MeSH Terms] OR ("st vincent"[Title/Abstract] AND "the grenadines"[Title/Abstract]) OR "south sudan"[MeSH Terms] OR "south sudan"[Title/Abstract] OR "suriname"[MeSH Terms] OR "suriname"[Title/Abstract] OR ((("mesocricetus"[MeSH Terms] OR "mesocricetus"[All Fields] OR "syrian"[All Fields] OR "syrians"[All Fields]) AND "arb"[All Fields]) AND "republic"[Title/Abstract]) OR "tajikistan"[MeSH Terms] OR "tajikistan"[Title/Abstract] OR "tanzania"[MeSH Terms] OR "tanzania"[Title/Abstract] OR "thailand"[MeSH Terms] OR "thailand"[Title/Abstract] OR "timor leste"[MeSH Terms] OR "timor leste"[Title/Abstract] OR "togo"[MeSH Terms] OR "togo"[Title/Abstract] OR "Tonga"[MeSH Terms] OR "Tonga"[Title/Abstract] OR "Tunisia"[MeSH Terms] OR "Tunisia"[Title/Abstract] OR "turkey"[MeSH Terms] OR "turkey"[Title/Abstract] OR "turkmenistan"[MeSH Terms] OR "turkmenistan"[Title/Abstract] OR "micronesia"[MeSH Terms] OR "tuvalu"[Title/Abstract] OR "uganda"[MeSH Terms] OR "uganda"[Title/Abstract] OR "ukraine"[MeSH Terms] OR "ukraine"[Title/Abstract] OR "uzbekistan"[MeSH Terms] OR "uzbekistan"[Title/Abstract] OR "vanuatu"[MeSH Terms] OR "vanuatu"[Title/Abstract] OR "vietnam"[MeSH Terms] OR "vietnam"[Title/Abstract] OR ("west bank"[Title/Abstract] AND "gaza"[Title/Abstract]) OR "yemen"[MeSH Terms] OR "yemen"[Title/Abstract] OR "zambia"[MeSH Terms] OR "zambia"[MeSH Terms] OR "zimbabwe"[MeSH Terms] OR "zimbabwe"[Title/Abstract]	
Total	1AND 2	8

Supplementary file: 3

III. Data extraction from

Title of the study	
Authors	
Year of the study conducted	
Year of publication	
Doi & Journal	
Objectives of the study	
Participant characteristics	Number of participants Age Gender Ethnicity Socioeconomic group Educational status Duration of T2DM
Total number of participants	
Setting/ context/ country	Low-income country Lower Middle-income country Upper Middle-income country
World Bank Region	South Asia Sub-Saharan Africa East Asia and Pacific Europe and Central Asia Latin America and the Caribbean The Middle East and North Africa North America
Description of intervention for type 2 diabetes	M health application Infographics Video clips Text messages Others – to be specified
Search details	Year
Source	IndMED Medline Plus OpenMED

	Ovid Medline PubMed / MEDLINE Scopus Web of Science Other Bibliographical Databases
Range of years included	No limit
No of included studies	
Type of studies included	RCT Quasi-experimental study Case-control Cohort Controlled trial
Comparator	Duration of the intervention Across the regions (LMIC's) Age groups Gender
Analysis	
Method of analysis	
follow up sessions	
Outcome assessed	Primary secondary
Results/ findings	
Significance	
Heterogeneity if done	
Study Limitations	

BMJ Open

Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Diabetes and endocrinology, Health services research, Evidence based practice
Keywords:	PUBLIC HEALTH, Information management < BIOTECHNOLOGY & BIOINFORMATICS, DIABETES & ENDOCRINOLOGY, PREVENTIVE MEDICINE, NUTRITION & DIETETICS, Epidemiology < TROPICAL MEDICINE

EFFECTIVENESS OF SELF-MANAGEMENT APPLICATIONS IN IMPROVING CLINICAL HEALTH OUTCOMES AND ADHERENCE AMONG DIABETIC INDIVIDUALS IN LOW AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

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Total word count in main text – 3130 (excluding references and supplementary files/tables)

Total number of references: 25, **word count** - 705

Number of supplementary files - 3

Total word count of all three supplementary files -2136

Abstract

Introduction: There are a variety of mobile health applications available to monitor an individual's health or lifestyle to make it convenient and easy to access healthcare facilities at home. Despite the growing number of mobile applications, the evidence from research on normalising HbA1c levels (HbA1C is defined as “estimated average blood glucose”) with the use of these applications remains a mystery. The burden of type 2 diabetes mellitus (T2DM) is high in Low- and Middle-Income Countries (LMICs), with the highest-burden in the Indian population. The objective of the research is to identify how effective are the diabetic self-management applications (DSMA) in controlling the blood glucose levels of individuals with T2DM and to find the impact of DSMA in managing T2D in LMICs.

Methods and analysis: The electronic databases included for search are PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites, and reference lists of included studies. Studies published in the English language in indexed and peer-reviewed sources will be considered. Studies reporting the effectiveness of mobile applications in the management of T2D in the LMICs will be eligible for inclusion. The Population-Intervention-Comparison Outcomes (PICO) Framework and the PRISMA statement 2021, will be used for reporting this systematic review. Data analysis will be carried out using narrative synthesis, and a meta-analysis may be conducted if we come across homogenous data for the outcome.

Ethics and dissemination: As this study is a systematic review, we will not be recruiting any participants for the study and hence will not require ethical approval. The study summary will be disseminated at a conference.

Keywords: mobile health application, mHealth, self-management applications, type 2 diabetes mellitus

Prospero registration ID: CRD42021245517

Article summary:

Strengths of the study:

1. There are no similar systematic reviews published particularly focusing on self-managing type 2 diabetes with the help of mHealth technologies in the Low and Middle-income countries.
2. The study findings intend to support and generalize the factors obtained among the LMICs

Limitations of the study:

1. The exclusion of articles in languages other than English and articles behind a paywall may introduce a minor selection bias in the review, however, this could not be prevented because it is a non-funded study.
2. The geographical area under study will be limited to Low and Middle-Income Countries (LMICs) specifically in the context of India since India has the highest burden of diabetes among the LMICs and the systematic review findings may be used to inform future primary research in India

Introduction

'Diabetes' is a term used to describe a group of diseases characterized by elevated blood glucose levels. It is caused by a lack of insulin production or function, or both, which may occur for various reasons and lead to protein and lipid metabolic disorders[1]. Various scientific studies have established that adequate blood glucose regulation minimizes the long-term effects of type 2 diabetes. Increasing inclination towards technology provides an opportunity for the delivery of innovative self-management interventions. The global burden of type 2 diabetes mellitus (T2DM) continues to rise, with T2DM estimated to affect over 9% of the global population by 2035[2].

Type 2 Diabetes in LMICs: A slew of issues plagues the delivery of healthcare in low and middle-income countries (LMICs). Where four out of every five people with diabetes now live in these

countries, and the rate of diabetes is increasing in poorer communities [3]. In 57 developing countries, the World Health Organization (WHO) estimates a 4.3 million healthcare worker shortage, resulting in understaffed hospitals, limited patient access to care, and a significant patient-physician contact gap, especially in rural areas [4]. To bridge this gap in terms of diabetes management, self-management apps can play a pivotal role in India and the LMICs. The use of mobile health tools to help people manage chronic diseases is on the rise, but evidence of their effectiveness is mixed[5]. Patients with diabetes are increasingly using mobile technology for health (mHealth) interventions to help improve self-management; however, these interventions have not been implemented by many patients, and dropout rates are common.

Measures to control Type 2 Diabetes: The rising prevalence of T2DM has put pressure on healthcare systems to properly manage these individuals so that diabetes complications are avoided. Optimizing patient outcomes by combining medications with self-management of glycemic control and other risk variables could be a better approach. To help people keep blood sugar within the normal range (i.e., <= 5.7% of the HbA1c) the American Diabetes Association also recommends: engaging in weight management activities, eating a nutritious diet, getting regular exercise, smoking cessation, and stress reduction as the key factors to achieve normal glycemic levels.

Once diabetes has progressed to the extreme levels, dietary adjustments and lifestyle modifications alone are no longer sufficient to maintain appropriate blood sugar levels, and doctors may urge a person to take medications. However, for older adults diagnosed with diabetes and whose blood sugar is marginally high, drugs may or may not be required[6]. Along with dietary adherence, behavioral factors such as “Self-efficacy” have proved to be the most significant predictive factor of HbA1c, Physical activity for Body Mass Index (BMI), and glucose self-monitoring for Fasting Blood Glucose (FBG) in leading a healthy lifestyle[7]. In recent years, there are an increasing number of smartphone applications that are meant to help T2DM patients manage their condition, but only a few have been thoroughly evaluated among the general population globally[8].

eHealth: is the use of information and communication technologies (ICT) for health.

The unprecedented spread of mobile technologies as well as advancements in their innovative application to address health priorities have evolved into a new field of eHealth, known as mHealth.

mHealth: The Global Observatory for eHealth (GOe) defined mHealth or mobile health as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices[9].

A mHealth application used in the self-management of type 2 diabetes mellitus, along with standard care- a study conducted in India in the year 2017, has proved that the users of the study with "Gather m-Health app" as an intervention given to the participants of the study improved medication adherence and Blood glucose testing accuracy over 6 months of the study[10] Evidence generated by another Indian study using a mHealth application "DIAGURU" mainly focused on lifestyle modification and medication management over 6 months suggesting, that technological approaches can be used as a public health measure to improve the quality of life of patients with type 2 Diabetes Mellitus[11].

Non-exercise Activity Thermogenesis (NEAT) a smartphone intervention used to reduce the health consequences of sedentary behavior, provided an opportunity to intervene and improve the health of a large proportion of the population in Chicago[12]. Although there might be a few barriers to the use of remote mHealth technologies in self-managing type 2 diabetes with poor technology literacy[13,] desired elements such as blood sugar monitoring, instructional content, personalised feedback, reminders, and goal setting were thought to be beneficial[14]. The interventions may also include other forms of mHealth solutions like texting, emailing, video clips, and graphics. To find the evidence on how the use of mobile applications has impacted the health of type 2 diabetic individuals. Few of the proven interventions leading to more effective control of diabetes were reported[15].

Rationale: A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial to manage diabetes in terms of diabetic self-management in the LMICs, as well as to prioritize research agendas, and policies. Hence, this

review aims to assess the effectiveness of diabetic self-management applications in managing type 2 diabetes in LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs, and our systematic review findings may be used to inform future primary research related to the diabetes self-management in India.

Review Questions

1. Are diabetic self-management applications effective in controlling blood glucose levels among individuals with type 2 diabetes mellitus in LMICs?

2. What is the impact of using Diabetic self-management applications in managing type 2 diabetes in LMICs in the context of India?

Methods

The PRISMA 2020 statement; an updated guideline for reporting systematic reviews[16] will be used for reporting the review and the Population-Intervention-Comparison-Outcomes (PICO) framework will be used for defining the methods of the review. (Refer; to supplementary file 1-PRISMA checklist). The systematic review protocol was registered on the international prospective register of systematic reviews, PROSPERO, with the registration number CRD42021245517.

Criteria for considering studies for this review

Types of studies:

Study design: Randomized controlled trials (RCTs), Non-Randomized controlled trials (NRCTs) like the Quasi-experimental studies, and controlled before-after studies will be included. All observational studies, conference papers, editorials, reports, and other studies without any mobile app interventions in them will be excluded.

Year of publication: we will include publications matching our criteria from the year 2015 to 2022. As the search strategy yielded publications from the year 2015 onwards.

Type of participants: Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[17] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), an Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl.

FBG: Fasting means not having anything to eat or drink (except water) for at least 8 hours before the test. Diabetes is diagnosed at FBG of greater than or equal to 126 mg/dl.

RBS: This test is a blood check at any time of the day when an individual has severe diabetes symptoms (Diabetes is diagnosed at blood glucose of greater than or equal to 200 mg/dl.

OGTT: A two-hour test that checks your blood glucose levels before and two hours after you drink a special sweet drink. Diabetes is diagnosed at two-hour blood glucose ≥ 200 mg/dl[18].

Patient and public involvement: patients and the public will not be involved in any way in this study.

Type of interventions

Digital health: The use of digital, mobile, and wireless technologies to support the achievement of health objectives. Digital health describes the general use of information and communications technologies (ICT) for health and is inclusive of both mHealth and eHealth[19]. From the context of our study, the term mHealth refers to the mobile applications used in the self-management of T2DM. The interventions may also include other simpler forms of mHealth solutions like texting, emailing, video clips, graphics, and web services.

Type of Comparison: the comparator groups would be the individuals who received standard hospital treatment or no hospital care and who received an intervention.

Type of outcome measures: Primary outcomes include,

- *Clinical outcome* (HbA1c at 3 months interval): [A hemoglobin A1c (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin. An HbA1c test shows what the average amount of glucose attached to hemoglobin has been over the past three months. It's a three-month average because that's typically how long a red blood cell lives[20]]

Secondary outcomes include,

- *Adherence to diabetic self-management applications and medication:* The studies must have reported using any of the standard survey tools to record daily medication intake and app usage during the follow-up for a year.
- *Self-efficacy with adherence to mHealth applications:* Self-efficacy is defined as "the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations." - Albert Bandura [21, 22]. The studies must have done a subjective evaluation of the individual's willingness to use the self-management applications to manage t2dm and those who are confident to follow in their near future.
- *Behavior change:* If the study participants during their follow-up period adapted a positive change in behavior towards achieving better health, like opting for a healthy diet, regular moderate exercising, brisk walking, and reducing/ managing their stress levels. Will be checked across the quality of life improvement index if any done in the studies [23].

Search methods for identification of studies: PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites. Forward citation search will be undertaken for any key references identified and reference lists of included studies (Refer to supplementary file 2- 'Search strategies' for more search information).

We will be using Endnote library version X7 for screening and downloading the full-text articles and Microsoft Excel 2013 will be used for data extraction of the full-text articles. Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria.

Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study, then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart (Refer to supplementary file 1) will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.

Data extraction and management: Data extraction will be performed using a standardized pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. The data extraction form will include information on citation details, characteristics of the studies, location, region, population, intervention, the effectiveness of an intervention, and the information on outcome and the main findings (Refer to supplementary file 3 - Data extraction format)

Any missing data in the studies included for review will be obtained by contacting the study authors of that study with a minimum waiting period of two weeks for their reply. In the event of no response from the authors of the study, a decision will be taken by the team of authors of the systematic review.

Assessment of risk of bias in included studies: Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials[24]. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies[25].

Data synthesis: Firstly, we will provide a detailed summary of all the included studies in a narrative format. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation

will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies. All the analyses will be conducted in Review Manager 5.3 and STATA 16.

Description of primary and secondary outcomes, whether adherence to diabetic self-management applications and medication has improved or not, Behavior change will be noted with the quality of life improvement index and self-efficacy will be checked following the improvement in managing T2DM. Listing out various measurement tools and devices used for judging the above-mentioned outcomes.

Subgroup analysis: Subgroup analysis will be performed for the following if appropriate. Sensitivity analysis will be performed if we find out any uncertainties in one or more input variables that may lead to uncertainties among other output variables.

Subgroup analysis will be performed for the following:

- Duration of the given intervention (3 months intervals up to a year)
- Comparing study effectiveness within the LMICs
- The most effective rate of using the Diabetic self-management app in age groups as classified by the UN

- Gender

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Ethics and dissemination: The study will be a systematic review of the published articles from different recognised and accessible databases and will not recruit any human participants directly, therefore, ethical clearance is not applicable. The dissemination of the final review findings will be done at a national or international conference and will be published in an indexed peer-reviewed journal.

Author Contributions: HB is the corresponding author, SMD, SS, JV, PP, MGL, PR, and HB conceptualized the study. SMD, SS, JV, PP, MGL, PR, and HB drafted the manuscript. All authors were involved in the development of the selection criteria and data extraction criteria. All authors will read, provide feedback and approve the final manuscript.

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Conflicts of interest: There is no conflict of interest in this project.

Supplemental material: Supplementary materials are enclosed as 1, 2 and 3

Patient and public involvement: patients and the public were not involved in any way in this study

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SUPPLEMENTARY FILE: 1

I. **PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol***

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review
Update	1b	N/A
Registration	2	The study has been registered in PROSPERO and the Registration ID is CRD42021245517.
Authors:		
Contact	3a	Sherize Merlin Dsouza[1, 6], Sahana Shetty[2], Julien Venne[3], Prachi Pundir[4], Priyobrat Rajkhowa[1, 6], Melissa Glenda Lewis[5] and Helmut Brand[1, 6] 1. Department of Health Policy, Prasanna School of Public Health, Manipal Academy of Higher Education. 2. Department of Endocrinology, Kasturba Medical College Hospital, MAHE, Manipal, India. 3. Coordinator, Dept. of Digital Health and wellbeing, PSPH, MAHE, Manipal, India 4. Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Manipal Academy of Higher Education. 5. Indian Institute of Public Health Shillong, Lawmali, Pasteur Hill, Shillong, Meghalaya. 6. Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

Contributions	3b	All authors were involved in the development of the selection criteria, and data extraction criteria. All authors will read, provide feedback and approve the final manuscript.
Amendments	4	As the review is being carried out amendments to the search strategy, selection criteria, and data extraction criteria may be amended to include the most pertinent information for this review's objectives. If amendments to this protocol are made, the date of each amendment along with a description/rationale for the change will be noted.
Support:		
Sources	5a	Nil
Sponsor	5b	Nil
Role of sponsor or funder	5c	Not Applicable.

INTRODUCTION

Rationale	6	A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial to manage diabetes in terms of diabetic self-management in the LMICs, as well as to prioritize research agendas, and policies. Hence, this review aims to assess the effectiveness of diabetic self-management applications in managing type 2 diabetes in LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs, and our systematic review findings may be used to inform future primary research related to the diabetes self-management in India.
Objectives	7	1. To identify how effective are the diabetic self-management applications on controlling the blood glucose levels of individuals with type 2 diabetes mellitus and 2. To find the impact of diabetic self-management applications in managing type 2 diabetes in LMICs, specifically in the Indian context.

METHODS		
Eligibility criteria	8	We followed the PICO concept/framework Population (P): Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[17] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), an Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl. Intervention (I): mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices. mHealth solutions like applications or text messages, emails, video clips, graphics, and web services. Comparison (C): the comparator groups would be the individuals who received standard hospital treatment or no hospital care and those who received an intervention. Country comparison: impact of using diabetes self-management app among the LMICs listed by the World Bank-India in particular. Outcomes(O): primary outcomes- clinical parameter HbA1c Secondary outcomes- adherence to medications, self-efficacy, and behavior changes.
Information sources	9	Authors in collaboration developed search strategies using medical subject headings (MeSH) and text words related to the topic. We will search CINAHL, PubMed, Web of Science, and Scopus. Only studies with human subjects will be included.
Search strategy	10	Refer to supplementary file 2.
Study records:		
Data management	11a	The search results collected from the electronic databases will be exported to Endnote version X7. Duplicate studies will be removed.

		Data will then be extracted, and relevant information will be extracted to an Excel spreadsheet using a data extraction tool.
Selection process	11b	Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.
Data collection process	11c	Data extraction will be performed using a standardised pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. (Refer; supplementary file-3 Data extraction format) Any missing data in the studies included for review will be obtained by contacting the study authors of that study.
Data items	12	Bibliometric information such as Author's name, Author's affiliations, Title, Journal name, publication year, and country of conduct will be collected along with Characteristics of the included studies. Data will be extracted based on the type of study, study objectives, Inclusion criteria, participant's characteristics, Intervention details, comparator, and the study outcome.
Outcomes and prioritization	13	A detailed summary of all the included studies will include information on authors, study objectives, Inclusion criteria,

		Intervention details, comparator, outcome measures, and the country will be in a narrative format. An evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management apps in controlling type 2 diabetes. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes.
Risk of bias in individual studies	14	Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies.
Data synthesis	15a 15b	A detailed summary of all the included studies in a narrative format will be given. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is

inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies.

	15c 15d	
Meta-bias(es)	16	Not applicable.
Confidence in cumulative evidence	17	Not applicable.

Supplementary file: 2

II. Search Strategy

Database	Search strategy	Hits
PubMed	(("diabetes mellitus, type 2"[MeSH Terms] OR "self-management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language]) AND ((fha[Filter]) AND (clinicaltrial[Filter] OR randomized controlled trial[Filter] OR review[Filter]) AND (humans[Filter]) AND (english[Filter]))	65
World Bank list of low and middle-income countries included in the study (OR)	Afghanistan, Albania, Algeria, American Samoa, Angola, Argentina, Armenia, Azerbaijan, Bangladesh, Belarus, Belize, Benin, Bhutan, Bolivia, Bosnia and Herzegovina, Botswana, Brazil, Bulgaria, Burkina Faso, Burundi, Cabo Verde, Cambodia, Cameroon, Central African Republic, Chad, China, Colombia, Comoros, Congo, dem. Rep., Congo, rep., Costa Rica, Cote d'Ivoire, Cuba, Djibouti, Dominica, Dominican Republic, Ecuador, Egypt, Arab Rep., El Salvador, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Fiji, Gabon, Gambia, the Georgia, Ghana, Grenada, Guatemala, Guinea, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Iran, Islamic Rep. Iraq, Jamaica, Jordan, Kazakhstan, Kenya, Kiribati, Korea, dem. People's rep. Kosovo, Kyrgyz, republic, Lao pdr, Lebanon, Lesotho, Liberia, Libya, Madagascar, Malawi, Malaysia, Maldives, Mali, Marshall Islands, Mauritania, Mauritius, Mexico, Micronesia, fed. Sts., Moldova, Mongolia, Montenegro, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, North Macedonia, Pakistan, Panama, Papua new guinea, Paraguay, Peru, Philippines, Romania, Russian Federation, Rwanda, Samoa, Sao tome and Principe,	7,361,793

	Senegal, Serbia, Sierra Leone, Solomon Islands, Somalia, South Africa, South Sudan, Sri Lanka, St. Lucia, St. Vincent, and the Grenadines, Sudan, Suriname, Syrian Arab Republic, Tajikistan, Tanzania, Thailand, Timor-Leste, Togo, Tonga, Tunisia, Turkey, Turkmenistan, Tuvalu, Uganda, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Yemen, rep., Zambia and Zimbabwe	
Total 1AND 2 (2015-2022)	("diabetes mellitus, type 2"[MeSH Terms] OR "self management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language] AND ("hasabstract"[All Fields] AND ("clinical trial"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "review"[Publication Type]) AND "humans"[MeSH Terms] AND "english"[Language]) AND ("afghanistan"[All Fields] OR "Albania"[All Fields] OR "Algeria"[All Fields] OR "American"[All Fields] OR "Samoa"[All Fields] OR "Angola"[All Fields] OR "Argentina"[All Fields] OR "Armenia"[All Fields] OR "Azerbaijan"[All Fields] OR "Bangladesh"[All Fields] OR "Belarus"[All Fields] OR "Belize"[All Fields] OR "Benin"[All Fields] OR "Bhutan"[All Fields] OR "Bolivia"[All Fields] OR "Bosnia"[All Fields] OR "Herzegovina"[All Fields] OR "Botswana"[All Fields] OR "Brazil"[All Fields] OR "Bulgaria"[All Fields] OR "Burkina"[All Fields] OR "Faso"[All Fields] OR "Burundi"[All Fields] OR "Cabo"[All Fields] OR "Verde"[All Fields] OR "Cambodia"[All Fields] OR "Cameroon"[All Fields] OR "Central"[All Fields] OR "African"[All Fields] OR "Republic"[All Fields] OR "Chad"[All Fields] OR "China"[All Fields] OR "Colombia"[All Fields] OR "Comoros"[All Fields] OR "Congo"[All Fields] OR "dem"[All Fields] OR "rep"[All Fields] OR "Congo"[All Fields] OR "rep"[All Fields] OR "Costa"[All Fields] OR "Rica"[All Fields] OR "Cote"[All Fields] OR "d'Ivoire"[All Fields] OR "Cuba"[All Fields] OR "Djibouti"[All Fields] OR "Dominica"[All Fields] OR "Dominican"[All Fields] OR "Republic"[All Fields] OR "Ecuador"[All Fields] OR "Egypt"[All Fields] OR "Arab"[All Fields] OR "rep"[All Fields] OR "El"[All Fields] OR "Salvador"[All Fields] OR "Equatorial"[All Fields] OR	19

	"Guinea"[All Fields] OR "Eritrea"[All Fields] OR "Eswatini"[All Fields] OR "Ethiopia"[All Fields] OR "Fiji"[All Fields] OR "Gabon"[All Fields] OR "Gambia"[All Fields] OR "Georgia"[All Fields] OR "Ghana"[All Fields] OR "Grenada"[All Fields] OR "Guatemala"[All Fields] OR "Guinea"[All Fields] OR "Guinea-Bissau"[All Fields] OR "Guyana"[All Fields] OR "Haiti"[All Fields] OR "Honduras"[All Fields] OR "India"[All Fields] OR "Indonesia"[All Fields] OR "Iran"[All Fields] OR "Islamic"[All Fields] OR "rep"[All Fields] OR "Iraq"[All Fields] OR "Jamaica"[All Fields] OR "Jordan"[All Fields] OR "Kazakhstan"[All Fields] OR "Kenya"[All Fields] OR "Kiribati"[All Fields] OR "Korea"[All Fields] OR "dem"[All Fields] OR "People's"[All Fields] OR "rep"[All Fields] OR "Kosovo"[All Fields] OR "Kyrgyz"[All Fields] OR "Republic"[All Fields] OR "Lao"[All Fields] OR "pdr"[All Fields] OR "Lebanon"[All Fields] OR "Lesotho"[All Fields] OR "Liberia"[All Fields] OR "Libya"[All Fields] OR "Madagascar"[All Fields] OR "Malawi"[All Fields] OR "Malaysia"[All Fields]) **Translations** **fha[Filter]:** hasabstract **clinicaltrial[Filter]:** clinical trial [PT] **randomized controlled trial[Filter]:** randomized controlled trial [PT] **review[Filter]:** review [PT] **humans[Filter]:** humans[MH] **english[Filter]:** english [LA]	

Supplementary file: 3

III. Data extraction from

Title of the study	
Authors	
The Year of the study conducted	
Year of publication	
Doi & Journal	
Objectives of the study	
Participant characteristics	Number of participants Age Gender Ethnicity Socioeconomic group Educational status Duration of T2DM
Total number of participants	
Setting/ context/ country	Low-income country Lower Middle-income country Upper Middle-income country
World Bank Region	South Asia Sub-Saharan Africa East Asia and the Pacific Europe and Central Asia Latin America and the Caribbean The Middle East and North Africa North America
Description of intervention for type 2 diabetes	M health application Infographics Video clips Text messages Others – to be specified
Search details	Year
Source	IndMED Medline Plus OpenMED

	Ovid Medline PubMed / MEDLINE Scopus Web of Science Other Bibliographical Databases
The range of years included	No limit
No of included studies	
Type of studies included	RCT Quasi-experimental study Case-control Cohort Controlled trial
Comparator	Duration of the intervention Across the regions (LMICs) Age groups Gender
Analysis	
Method of analysis	
follow up sessions	
Outcome assessed	Primary secondary
Results/ findings	
Significance	
Heterogeneity if done	
Study Limitations	

BMJ Open

Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-060108.R2
Article Type:	Protocol
Date Submitted by the Author:	01-Aug-2022
Complete List of Authors:	dsouza, sherize; Manipal Academy of Higher Education, Health Policy, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands Shetty, Sahana; Manipal Academy of Higher Education, Dept. Endocrinology, Kasturba Medical College Hospital, MAHE venne, Julien; Manipal Academy of Higher Education, Digital Health and wellbeing, Prasanna School of Public Health Pundir , Prachi ; Manipal Academy of Higher Education, Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Rajkhowa, Priyobrat; Manipal Academy of Higher Education, Health Policy, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Department of International Health, CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands Lewis, Melissa; Indian Institutes of Public Health Brand, Helmut; Manipal Academy of Higher Education, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Jean Monnet Chair in European Public Health, Department of International Health
Primary Subject Heading:	Public health
Secondary Subject Heading:	Diabetes and endocrinology, Health services research, Evidence based practice
Keywords:	PUBLIC HEALTH, Information management < BIOTECHNOLOGY & BIOINFORMATICS, DIABETES & ENDOCRINOLOGY, PREVENTIVE MEDICINE, NUTRITION & DIETETICS, Epidemiology < TROPICAL MEDICINE

EFFECTIVENESS OF SELF-MANAGEMENT APPLICATIONS IN IMPROVING CLINICAL HEALTH OUTCOMES AND ADHERENCE AMONG DIABETIC INDIVIDUALS IN LOW AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

Sherize Merlin Dsouza[1, 6], Sahana Shetty[2], Julien Venne[3], Prachi Pundir[4], Priyobrat Rajkhowa[1, 6], Melissa Glenda Lewis[5] and Helmut Brand[1, 6]

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Total word count in main text – 2731 (excluding references and supplementary files/tables)

Total number of references: 28, **word count** - 820

Number of supplementary files - 3

Total word count of all three supplementary files -2099

Abstract

Introduction: A variety of mobile health applications are available to monitor an individual's health or lifestyle to make it convenient to access healthcare facilities at home. Despite the growing number of mobile applications, the evidence from research on normalizing HbA1c levels (HbA1C is defined as “estimated average blood glucose”) but the use of these applications remains a mystery. The burden of Type 2 diabetes mellitus (T2DM) is high in Low- and Middle-Income Countries (LMICs), with the highest burden in the Indian population. Our objective is to identify the effectiveness of mHealth applications in managing blood glucose levels of individuals with T2DM and to assess the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India

Methods and analysis: The electronic databases included for search are PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites, and reference lists of included studies. Studies published in the English language in indexed and peer-reviewed sources will be considered. Studies reporting the effectiveness of mobile applications in the management of T2D in LMICs will be eligible for inclusion. The Population-Intervention-Comparison Outcomes (PICO) Framework and the PRISMA statement 2021, will be used for reporting. Data analysis will be carried out using narrative synthesis, and a meta-analysis may be conducted if we come across homogenous data for the outcome.

Ethics and dissemination: As this study is a systematic review, we will not be recruiting any participants for the study and hence will not require ethical approval. The study summary will be disseminated at a conference.

Keywords: mobile health application, mHealth, self-management applications, type 2 diabetes mellitus

Prospero registration ID: CRD42021245517

Article summary:

Strengths of the study:

1. Novelty of the systematic review topic
2. Adherence to mHealth applications and Positive behavioral outcomes will be evaluated

Limitations of the study:

1. The exclusion of articles in languages other than English and articles behind a paywall
2. The geographical area of the study will be limited to Low and Middle-Income Countries (LMICs)

Introduction

'Diabetes' is a term used to describe a group of diseases characterized by elevated blood glucose levels. It is caused by a lack of insulin production or function, or both, which may occur for various reasons and lead to protein and lipid metabolic disorders[1]. Various scientific studies have established that adequate blood glucose regulation minimizes the long-term effects of type 2 diabetes. Increasing inclination towards technology provides an opportunity for the delivery of innovative self-management interventions. The global burden of type 2 diabetes mellitus (T2DM) continues to rise, with T2DM estimated to affect over 9% of the global population by 2035[2]. The use of mobile health tools to help people manage chronic diseases is on the rise, but evidence of their effectiveness is mixed[3]. An overview and a scoping review were conducted to understand the Impact of mobile health (mHealth) Interventions among chronic diabetic patients showed improving glycemic control using diverse mHealth interventions[4&5]. Another trial proved to have improved behavioral outcomes among diabetic individuals[6]. People with diabetes are increasingly using mobile technology for health (mHealth) interventions to help improve self-management; however, these interventions have not been implemented by many patients, and dropout rates are common.

Type 2 Diabetes in LMICs: A slew of issues plagues the delivery of healthcare in low and middle-income countries (LMICs). Where four out of every five people with diabetes now live in these countries, and the rate of diabetes is increasing in poorer communities[7]. In 57 developing countries, the World Health Organization (WHO) estimates a 4.3 million healthcare worker shortage, resulting in understaffed hospitals, limited patient access to care, and a significant patient-physician contact gap, especially in rural areas [8]. To bridge this gap in terms of diabetes management, self-management apps can play a pivotal role in India and the LMICs. To understand how mHealth apps aid in diabetes management, knowing what is meant by eHealth is important.

eHealth: is the use of information and communication technologies (ICT) for health.

The unprecedented spread of mobile technologies as well as advancements in their innovative application to address health priorities have evolved into a new field of eHealth, known as mHealth.

mHealth: The Global Observatory for eHealth (GOe) defined mHealth or mobile health as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices[9].

A mHealth application used in the self-management of T2DM, along with standard care- a study conducted in India in the year 2017, has proved that the users of the study with "Gather m-Health app" as an intervention given to the participants of the study improved medication adherence and Blood glucose testing accuracy over 6 months of the study[10] Evidence generated by another Indian study using a mHealth application "DIAGURU" mainly focused on lifestyle modification and medication management over 6 months suggesting, that technological approaches can be used as a public health measure to improve the quality of life of patients with type 2 Diabetes Mellitus[11].

Non-exercise Activity Thermogenesis (NEAT) a smartphone intervention used to reduce the health consequences of sedentary behavior, provided an opportunity to intervene and improve

the health of a large proportion of the population in Chicago[12]. Although there might be a few barriers to the use of remote mHealth technologies in self-managing type 2 diabetes with poor technology literacy[13,] desired elements such as blood sugar monitoring, instructional content, personalized feedback, reminders, and goal setting were thought to be beneficial[14]. The interventions may also include other forms of mHealth solutions like texting, emailing, video clips, and graphics. To find evidence on how the use of mobile applications has impacted the health of type 2 diabetic individuals. Few of the proven interventions leading to more effective control of diabetes were reported[15].

Measures to control T2DM: The rising prevalence of T2DM has put pressure on healthcare systems to properly manage diabetic individuals so that diabetes complications are avoided. Optimizing patient outcomes by combining medications with self-management of glycemic control and other risk variables could be a better approach. To help people keep blood sugar within the normal range (i.e., <= 5.7% of the HbA1c) the American Diabetes Association also recommends: engaging in weight management activities, eating a nutritious diet, getting regular exercise, smoking cessation, and stress reduction as the key factors to achieve normal glycemic levels.

Once diabetes has progressed to extreme levels, dietary adjustments and lifestyle modifications alone are no longer sufficient to maintain appropriate blood sugar levels, and doctors may urge a person to take medications. However, for older adults diagnosed with diabetes and whose blood sugar is marginally high, drugs may or may not be required[16]. Along with dietary adherence, behavioral factors such as “Self-efficacy” have proved to be the most significant predictive factor of HbA1c, Physical activity for Body Mass Index (BMI), and glucose self-monitoring for Fasting Blood Glucose (FBG) in leading a healthy lifestyle[17]. In recent years, there are an increasing number of smartphone applications that are meant to help T2DM patients manage their condition, but only a few have been thoroughly evaluated among the general population globally[18].

Review Questions

1. Are mHealth applications effective in managing blood glucose levels among individuals with type 2 diabetes mellitus in LMICs?

2. What is the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India?

Rationale: A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial for diabetes self-management, especially in the LMICs. Hence, this review aims to assess the effectiveness of mHealth applications in managing T2DM among the LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs.

Methods

The PRISMA 2020 statement; an updated guideline for reporting systematic reviews[19] will be used for reporting the review and the Population-Intervention-Comparison-Outcomes (PICO) framework will be used for defining the methods of the review. (Refer; to supplementary file 1-PRISMA checklist). The systematic review protocol was registered on the international prospective register of systematic reviews, PROSPERO, with the registration number CRD42021245517.

Criteria for considering studies for this review

Types of studies:

Study design: Randomized controlled trials (RCTs), Non-Randomized controlled trials (NRCTs) like the Quasi-experimental studies, and controlled before-after studies will be included. Observational studies, conference papers, editorials, reports, and other studies without any mobile app interventions in them will be excluded.

Year of publication: we will include publications matching our criteria from the year 2015 to 2022. As the search strategy yielded publications from the year 2015 onwards.

Type of participants: Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[20] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl.

FBG: Fasting means not having anything to eat or drink (except water) for at least 8 hours before the test. Diabetes is diagnosed at FBG of greater than or equal to 126 mg/dl.

RBS: This test is a blood check at any time of the day when an individual has severe diabetes symptoms (Diabetes is diagnosed at blood glucose of greater than or equal to 200 mg/dl.

OGTT: A two-hour test that checks your blood glucose levels before and two hours after you drink a special sweet drink. Diabetes is diagnosed at two-hour blood glucose ≥ 200 mg/dl [21].

Patient and public involvement: patients and the public will not be involved in any way in this study.

Type of interventions

Digital health: The use of digital, mobile, and wireless technologies to support the achievement of health objectives. Digital health describes the general use of information and communications technologies (ICT) for health and is inclusive of both mHealth and eHealth[22]. From the context of our study, the term mHealth refers to the mobile applications used in the self-management of T2DM. The interventions may also include other simpler forms of mHealth solutions like texting, emailing, video clips, graphics, and web services.

Type of Comparison: the comparator groups would be the individuals who received standard hospital treatment or no hospital care and who received an intervention.

Type of outcome measures: Primary outcomes include,

- *Clinical outcome* (HbA1c at 3 months interval): [A hemoglobin A1c (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin. An HbA1c test shows what the average amount of glucose attached to hemoglobin has been over the past three months. It's a three-month average because that's typically how long a red blood cell lives[23]]

Secondary outcomes include,

- *Adherence to diabetic self-management applications and medication:* The studies must have reported using any of the standard survey tools to record daily medication intake and app usage during the follow-up for a year.
- *Self-efficacy with adherence to mHealth applications:* Self-efficacy is defined as "the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations." - Albert Bandura [24, 25]. The studies must have done a subjective evaluation of the individual's willingness to use the self-management applications to manage T2DM and those who are confident to follow in their near future.
- *Health promoting behavior:* If the study participants during their follow-up period adapted a positive change in behavior towards achieving better health, like opting for a healthy diet, regular moderate exercising, brisk walking, and reducing/ managing their stress levels. Will be checked across the quality of life improvement index if any done in the studies [26]. Health-promoting behavior changes will not be limited to nutrition, physical exercise/ activity, or regular/ frequency of blood glucose monitoring.

Search methods for identification of studies: PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites. Forward citation search will be undertaken for any key references identified and reference lists of included studies (Refer to supplementary file 2- 'Search strategies' for more search information).

We will be using Endnote library version X7 for screening and downloading the full-text articles and Microsoft Excel 2013 will be used for data extraction of the full-text articles. Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study, then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart (Refer to supplementary file 1) will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.

Data extraction and management: Data extraction will be performed using a standardized pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. The data extraction form will include information on citation details, characteristics of the studies, location, region, population, intervention, the effectiveness of an intervention, and the information on outcome and the main findings (Refer to supplementary file 3 - Data extraction format)

Any missing data in the studies included for review will be obtained by contacting the study authors of that study with a minimum waiting period of two weeks for their reply. In the event of no response from the authors of the study, a decision will be taken by the team of authors of the systematic review.

Assessment of risk of bias in included studies: Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials[27]. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies[28].

Data synthesis: Firstly, we will provide a detailed summary of all the included studies in a narrative format. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies. All the analyses will be conducted in Review Manager 5.3 and STATA 16.

Description of primary and secondary outcomes, whether adherence to diabetic self-management applications and medication has improved or not, Behavior change will be noted with the quality of life improvement index and self-efficacy will be checked following the improvement in managing T2DM. Listing out various measurement tools and devices used for judging the above-mentioned outcomes.

Subgroup analysis: Subgroup analysis will be performed for the following if appropriate. Sensitivity analysis will be performed if we find out any uncertainties in one or more input variables that may lead to uncertainties among other output variables.

Subgroup analysis will be performed for the following:

- Duration of the given intervention (3 months intervals up to a year)

- Comparing study effectiveness within the LMICs
- The most effective rate of using the Diabetic self-management app in age groups as classified by the UN
- Gender

Author affiliations:

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6. Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

Ethics and dissemination: The study will be a systematic review of the published articles from different recognised and accessible databases and will not recruit any human participants directly, therefore, ethical clearance is not applicable. The dissemination of the final review findings will be done at a national or international conference and will be published in an indexed peer-reviewed journal.

Author Contributions: HB is the corresponding author, SMD, SS, JV, PP, MGL, PR, and HB conceptualized the study. SMD, SS, JV, PP, MGL, PR, and HB drafted the manuscript. All authors

were involved in the development of the selection criteria and data extraction criteria. All authors will read, provide feedback, and approve the final manuscript.

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Conflicts of interest: There is no conflict of interest in this project.

Supplemental material: Supplementary materials are enclosed as 1, 2 and 3

Patient and public involvement: patients and the public were not involved in any way in this study

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SUPPLEMENTARY FILE: 1

I. **PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol***

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review
Update	1b	N/A
Registration	2	The study has been registered in PROSPERO and the Registration ID is CRD42021245517.
Authors:		
Contact	3a	Sherize Merlin Dsouza[1, 6], Sahana Shetty[2], Julien Venne[3], Prachi Pundir[4], Priyobrat Rajkhowa[1, 6], Melissa Glenda Lewis[5] and Helmut Brand[1, 6] 1. Department of Health Policy, Prasanna School of Public Health, Manipal Academy of Higher Education. 2. Department of Endocrinology, Kasturba Medical College Hospital, MAHE, Manipal, India. 3. Coordinator, Dept. of Digital Health and wellbeing, PSPH, MAHE, Manipal, India 4. Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Manipal Academy of Higher Education. 5. Indian Institute of Public Health Shillong, Lawmali, Pasteur Hill, Shillong, Meghalaya. 6. Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

Contributions	3b	All authors were involved in the development of the selection criteria, and data extraction criteria. All authors will read, provide feedback and approve the final manuscript.
Amendments	4	As the review is being carried out amendments to the search strategy, selection criteria, and data extraction criteria may be amended to include the most pertinent information for this review's objectives. If amendments to this protocol are made, the date of each amendment along with a description/rationale for the change will be noted.
Support:		
Sources	5a	Nil
Sponsor	5b	Nil
Role of sponsor or funder	5c	Not Applicable.
INTRODUCTION		
Rationale	6	**Rationale:** A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial for diabetes self-management, especially in the LMICs. Hence, this review aims to assess the effectiveness of mHealth applications in managing T2DM among the LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs.
Objectives	7	1. To identify the effectiveness of mHealth applications in managing blood glucose levels of individuals with T2DM and 2. To assess the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India

	1.	
METHODS		
Eligibility criteria	8	We followed the PICO concept/framework Population (P): Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[17] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), an Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl. Intervention (I): mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices. mHealth solutions like applications or text messages, emails, video clips, graphics, and web services. Comparison (C): the comparator groups would be the individuals who received standard hospital treatment or no hospital care and those who received an intervention. Country comparison: impact of using diabetes self-management app among the LMICs listed by the World Bank-India in particular. Outcomes(O): primary outcomes- clinical parameter HbA1c Secondary outcomes- adherence to medications, self-efficacy, and Health-promoting behaviour.
Information sources	9	Authors in collaboration developed search strategies using medical subject headings (MeSH) and text words related to the topic. We will search CINAHL, PubMed, Web of Science, and Scopus. Only studies with human subjects will be included.
Search strategy	10	Refer to supplementary file 2.
Study records:		
Data management	11a	The search results collected from the electronic databases will be exported to Endnote version X7. Duplicate studies will be removed.

		Data will then be extracted, and relevant information will be extracted to an Excel spreadsheet using a data extraction tool.
Selection process	11b	Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.
Data collection process	11c	Data extraction will be performed using a standardised pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. (Refer; supplementary file-3 Data extraction format) Any missing data in the studies included for review will be obtained by contacting the study authors of that study.
Data items	12	Bibliometric information such as Author's name, Author's affiliations, Title, Journal name, publication year, and country of conduct will be collected along with Characteristics of the included studies. Data will be extracted based on the type of study, study objectives, Inclusion criteria, participant's characteristics, Intervention details, comparator, and the study outcome.
Outcomes and prioritization	13	A detailed summary of all the included studies will include information on authors, study objectives, Inclusion criteria,

		Intervention details, comparator, outcome measures, and the country will be in a narrative format. An evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management apps in controlling type 2 diabetes. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes.
Risk of bias in individual studies	14	Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies.
Data synthesis	15a 15b	A detailed summary of all the included studies in a narrative format will be given. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is

inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies.

	15c 15d	
Meta-bias(es)	16	Not applicable.
Confidence in cumulative evidence	17	Not applicable.

Supplementary file: 2

II. Search Strategy

Database	Search strategy	Hits
PubMed	(("diabetes mellitus, type 2"[MeSH Terms] OR "self-management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language]) AND ((fha[Filter]) AND (clinicaltrial[Filter] OR randomized controlled trial[Filter] OR review[Filter]) AND (humans[Filter]) AND (english[Filter]))	65
World Bank list of low and middle-income countries included in the study (OR)	Afghanistan, Albania, Algeria, American Samoa, Angola, Argentina, Armenia, Azerbaijan, Bangladesh, Belarus, Belize, Benin, Bhutan, Bolivia, Bosnia and Herzegovina, Botswana, Brazil, Bulgaria, Burkina Faso, Burundi, Cabo Verde, Cambodia, Cameroon, Central African Republic, Chad, China, Colombia, Comoros, Congo, dem. Rep., Congo, rep., Costa Rica, Cote d'Ivoire, Cuba, Djibouti, Dominica, Dominican Republic, Ecuador, Egypt, Arab Rep., El Salvador, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Fiji, Gabon, Gambia, the Georgia, Ghana, Grenada, Guatemala, Guinea, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Iran, Islamic Rep. Iraq, Jamaica, Jordan, Kazakhstan, Kenya, Kiribati, Korea, dem. People's rep. Kosovo, Kyrgyz, republic, Lao pdr, Lebanon, Lesotho, Liberia, Libya, Madagascar, Malawi, Malaysia, Maldives, Mali, Marshall Islands, Mauritania, Mauritius, Mexico, Micronesia, fed. Sts., Moldova, Mongolia, Montenegro, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, North Macedonia, Pakistan, Panama, Papua new guinea, Paraguay, Peru, Philippines, Romania, Russian Federation, Rwanda, Samoa, Sao tome and Principe,	7,361,793

	Senegal, Serbia, Sierra Leone, Solomon Islands, Somalia, South Africa, South Sudan, Sri Lanka, St. Lucia, St. Vincent, and the Grenadines, Sudan, Suriname, Syrian Arab Republic, Tajikistan, Tanzania, Thailand, Timor-Leste, Togo, Tonga, Tunisia, Turkey, Turkmenistan, Tuvalu, Uganda, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Yemen, rep., Zambia and Zimbabwe	
Total 1AND 2 (2015-2022)	("diabetes mellitus, type 2"[MeSH Terms] OR "self management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language] AND ("hasabstract"[All Fields] AND ("clinical trial"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "review"[Publication Type]) AND "humans"[MeSH Terms] AND "english"[Language]) AND ("afghanistan"[All Fields] OR "Albania"[All Fields] OR "Algeria"[All Fields] OR "American"[All Fields] OR "Samoa"[All Fields] OR "Angola"[All Fields] OR "Argentina"[All Fields] OR "Armenia"[All Fields] OR "Azerbaijan"[All Fields] OR "Bangladesh"[All Fields] OR "Belarus"[All Fields] OR "Belize"[All Fields] OR "Benin"[All Fields] OR "Bhutan"[All Fields] OR "Bolivia"[All Fields] OR "Bosnia"[All Fields] OR "Herzegovina"[All Fields] OR "Botswana"[All Fields] OR "Brazil"[All Fields] OR "Bulgaria"[All Fields] OR "Burkina"[All Fields] OR "Faso"[All Fields] OR "Burundi"[All Fields] OR "Cabo"[All Fields] OR "Verde"[All Fields] OR "Cambodia"[All Fields] OR "Cameroon"[All Fields] OR "Central"[All Fields] OR "African"[All Fields] OR "Republic"[All Fields] OR "Chad"[All Fields] OR "China"[All Fields] OR "Colombia"[All Fields] OR "Comoros"[All Fields] OR "Congo"[All Fields] OR "dem"[All Fields] OR "rep"[All Fields] OR "Congo"[All Fields] OR "rep"[All Fields] OR "Costa"[All Fields] OR "Rica"[All Fields] OR "Cote"[All Fields] OR "d'Ivoire"[All Fields] OR "Cuba"[All Fields] OR "Djibouti"[All Fields] OR "Dominica"[All Fields] OR "Dominican"[All Fields] OR "Republic"[All Fields] OR "Ecuador"[All Fields] OR "Egypt"[All Fields] OR "Arab"[All Fields] OR "rep"[All Fields] OR "El"[All Fields] OR "Salvador"[All Fields] OR "Equatorial"[All Fields] OR	19

	"Guinea"[All Fields] OR "Eritrea"[All Fields] OR "Eswatini"[All Fields] OR "Ethiopia"[All Fields] OR "Fiji"[All Fields] OR "Gabon"[All Fields] OR "Gambia"[All Fields] OR "Georgia"[All Fields] OR "Ghana"[All Fields] OR "Grenada"[All Fields] OR "Guatemala"[All Fields] OR "Guinea"[All Fields] OR "Guinea-Bissau"[All Fields] OR "Guyana"[All Fields] OR "Haiti"[All Fields] OR "Honduras"[All Fields] OR "India"[All Fields] OR "Indonesia"[All Fields] OR "Iran"[All Fields] OR "Islamic"[All Fields] OR "rep"[All Fields] OR "Iraq"[All Fields] OR "Jamaica"[All Fields] OR "Jordan"[All Fields] OR "Kazakhstan"[All Fields] OR "Kenya"[All Fields] OR "Kiribati"[All Fields] OR "Korea"[All Fields] OR "dem"[All Fields] OR "People's"[All Fields] OR "rep"[All Fields] OR "Kosovo"[All Fields] OR "Kyrgyz"[All Fields] OR "Republic"[All Fields] OR "Lao"[All Fields] OR "pdr"[All Fields] OR "Lebanon"[All Fields] OR "Lesotho"[All Fields] OR "Liberia"[All Fields] OR "Libya"[All Fields] OR "Madagascar"[All Fields] OR "Malawi"[All Fields] OR "Malaysia"[All Fields]) **Translations** **fha[Filter]:** hasabstract **clinicaltrial[Filter]:** clinical trial [PT] **randomized controlled trial[Filter]:** randomized controlled trial [PT] **review[Filter]:** review [PT] **humans[Filter]:** humans[MH] **english[Filter]:** english [LA]	

Supplementary file: 3

III. Data extraction from

Title of the study	
Authors	
The Year of the study conducted	
Year of publication	
Doi & Journal	
Objectives of the study	
Participant characteristics	Number of participants Age Gender Ethnicity Socioeconomic group Educational status Duration of T2DM
Total number of participants	
Setting/ context/ country	Low-income country Lower Middle-income country Upper Middle-income country
World Bank Region	South Asia Sub-Saharan Africa East Asia and the Pacific Europe and Central Asia Latin America and the Caribbean The Middle East and North Africa North America
Description of intervention for type 2 diabetes	M health application Infographics Video clips Text messages Others – to be specified
Search details	Year
Source	IndMED Medline Plus OpenMED

	Ovid Medline PubMed / MEDLINE Scopus Web of Science Other Bibliographical Databases
The range of years included	No limit
No of included studies	
Type of studies included	RCT Quasi-experimental study Case-control Cohort Controlled trial
Comparator	Duration of the intervention Across the regions (LMICs) Age groups Gender
Analysis	
Method of analysis	
follow up sessions	
Outcome assessed	Primary secondary
Results/ findings	
Significance	
Heterogeneity if done	
Study Limitations	

BMJ Open

Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review

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Complete List of Authors:	dsouza, sherize; Manipal Academy of Higher Education, Health Policy, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands Shetty, Sahana; Manipal Academy of Higher Education, Dept. Endocrinology, Kasturba Medical College Hospital, MAHE venne, Julien; Manipal Academy of Higher Education, Digital Health and wellbeing, Prasanna School of Public Health Pundir , Prachi ; Manipal Academy of Higher Education, Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Rajkhowa, Priyobrat; Manipal Academy of Higher Education, Health Policy, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Department of International Health, CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands Lewis, Melissa; Indian Institutes of Public Health Brand, Helmut; Manipal Academy of Higher Education, Prasanna School of Public Health; Maastricht University Care and Public Health Research Institute, Jean Monnet Chair in European Public Health, Department of International Health
Primary Subject Heading:	Public health
Secondary Subject Heading:	Diabetes and endocrinology, Health services research, Evidence based practice
Keywords:	PUBLIC HEALTH, Information management < BIOTECHNOLOGY & BIOINFORMATICS, DIABETES & ENDOCRINOLOGY, PREVENTIVE MEDICINE, NUTRITION & DIETETICS, Epidemiology < TROPICAL MEDICINE

EFFECTIVENESS OF SELF-MANAGEMENT APPLICATIONS IN IMPROVING CLINICAL HEALTH OUTCOMES AND ADHERENCE AMONG DIABETIC INDIVIDUALS IN LOW AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

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Total number of references: 28, **word count** – 820

Number of supplementary files - 3

Total word count of all three supplementary files -1925

Abstract

Introduction: A variety of mobile health applications are available to monitor an individual's health or lifestyle to make it convenient to access healthcare facilities at home. Despite the growing number of mobile applications, the evidence from research on normalizing HbA1c levels (HbA1C is defined as “estimated average blood glucose”) but the use of these applications remains a mystery. The burden of Type 2 diabetes mellitus (T2DM) is high in Low- and Middle-Income Countries (LMICs), with the highest burden in the Indian population. Our objective is to identify the effectiveness of mHealth applications in managing blood glucose levels of individuals with T2DM and to assess the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India

Methods and analysis: The electronic databases included for search are PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites, and reference lists of included studies. Studies published in the English language in indexed and peer-reviewed sources will be considered. Studies reporting the effectiveness of mobile applications in the management of T2D in LMICs will be eligible for inclusion. The Population-Intervention-Comparison Outcomes (PICO) Framework and the PRISMA statement 2021, will be used for reporting. Data analysis will be carried out using narrative synthesis, and a meta-analysis may be conducted if we come across homogenous data for the outcome.

Ethics and dissemination: As this study is a systematic review, we will not be recruiting any participants for the study and hence will not require ethical approval. The study summary will be disseminated at a conference.

Keywords: mobile health application, mHealth, self-management applications, type 2 diabetes mellitus

Prospero registration ID: CRD42021245517

Article Summary:

Strengths of the study:

1. Effectiveness of using mHealth apps on HbA1c levels
2. Adherence to mHealth applications and Positive behavioral outcomes will be evaluated

Limitations of the study:

1. The exclusion of articles in languages other than English and articles behind a paywall
2. The geographical area of the study will be limited to Low and Middle-Income Countries (LMICs)

Introduction

'Diabetes' is a term used to describe a group of diseases characterized by elevated blood glucose levels. It is caused by a lack of insulin production or function, or both, which may occur for various reasons and lead to protein and lipid metabolic disorders[1]. Various scientific studies have established that adequate blood glucose regulation minimizes the long-term effects of type 2 diabetes. Increasing inclination towards technology provides an opportunity for the delivery of innovative self-management interventions. The global burden of type 2 diabetes mellitus (T2DM) continues to rise, with T2DM estimated to affect over 9% of the global population by 2035[2]. The use of mobile health tools to help people manage chronic diseases is on the rise, but evidence of their effectiveness is mixed[3]. An overview and a scoping review were conducted to understand the Impact of mobile health (mHealth) Interventions among chronic diabetic patients showed improving glycemic control using diverse mHealth interventions[4&5]. Another trial proved to have improved behavioral outcomes among diabetic individuals[6]. People with diabetes are increasingly using mobile technology for health (mHealth) interventions to help improve self-management; however, these interventions have not been implemented by many patients, and dropout rates are common.

Type 2 Diabetes in LMICs: A slew of issues plagues the delivery of healthcare in low and middle-income countries (LMICs). Where four out of every five people with diabetes now live in these

countries, and the rate of diabetes is increasing in poorer communities[7]. In 57 developing countries, the World Health Organization (WHO) estimates a 4.3 million healthcare worker shortage, resulting in understaffed hospitals, limited patient access to care, and a significant patient-physician contact gap, especially in rural areas [8]. To bridge this gap in terms of diabetes management, self-management apps can play a pivotal role in India and the LMICs. To understand how mHealth apps aid in diabetes management, knowing what is meant by eHealth is important.

eHealth: the use of information and communication technologies (ICT) for health.

The unprecedented spread of mobile technologies as well as advancements in their innovative application to address health priorities have evolved into a new field of eHealth, known as mHealth.

mHealth: The Global Observatory for eHealth (GOe) defined mHealth or mobile health as medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices[9].

A mHealth application used in the self-management of T2DM, along with standard care- a study conducted in India in the year 2017, has proved that the users of the study with "Gather m-Health app" as an intervention given to the participants of the study improved medication adherence and Blood glucose testing accuracy over 6 months of the study[10] Evidence generated by another Indian study using a mHealth application "DIAGURU" mainly focused on lifestyle modification and medication management over 6 months suggesting, that technological approaches can be used as a public health measure to improve the quality of life of patients with type 2 Diabetes Mellitus[11].

Non-exercise Activity Thermogenesis (NEAT) a smartphone intervention used to reduce the health consequences of sedentary behavior, provided an opportunity to intervene and improve the health of a large proportion of the population in Chicago[12]. Although there might be a few barriers to the use of remote mHealth technologies in self-managing type 2 diabetes with poor

technology literacy[13,] desired elements such as blood sugar monitoring, instructional content, personalized feedback, reminders, and goal setting were thought to be beneficial[14]. The interventions may also include other forms of mHealth solutions like texting, emailing, video clips, and graphics. To find evidence on how the use of mobile applications has impacted the health of type 2 diabetic individuals. Few of the proven interventions leading to more effective control of diabetes were reported[15].

Measures to control T2DM: The rising prevalence of T2DM has put pressure on healthcare systems to properly manage diabetic individuals so that diabetes complications are avoided. Optimizing patient outcomes by combining medications with self-management of glycemic control and other risk variables could be a better approach. To help people keep blood sugar within the normal range (i.e., <= 5.7% of the HbA1c) the American Diabetes Association also recommends: engaging in weight management activities, eating a nutritious diet, getting regular exercise, smoking cessation, and stress reduction as the key factors to achieve normal glycemic levels.

Once diabetes has progressed to extreme levels, dietary adjustments and lifestyle modifications alone are no longer sufficient to maintain appropriate blood sugar levels, and doctors may urge a person to take medications. However, for older adults diagnosed with diabetes and whose blood sugar is marginally high, drugs may or may not be required[16]. Along with dietary adherence, behavioral factors such as “Self-efficacy” have proved to be the most significant predictive factor of HbA1c, Physical activity for Body Mass Index (BMI), and glucose self-monitoring for Fasting Blood Glucose (FBG) in leading a healthy lifestyle[17]. In recent years, there are an increasing number of smartphone applications that are meant to help T2DM patients manage their condition, but only a few have been thoroughly evaluated among the general population globally[18].

Review Questions

1. Are mHealth applications effective in managing blood glucose levels among individuals with type 2 diabetes mellitus in LMICs?

2. What is the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India?

Rationale: A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial for diabetes self-management, especially in LMICs. Hence, this review aims to assess the effectiveness of mHealth applications in managing T2DM among the LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs.

Methods

The PRISMA 2020 statement; an updated guideline for reporting systematic reviews[19] will be used for reporting the review and the Population-Intervention-Comparison-Outcomes (PICO) framework will be used for defining the methods of the review. (Refer; to supplementary file 1-PRISMA checklist). The systematic review protocol was registered on the international prospective register of systematic reviews, PROSPERO, with the registration number CRD42021245517.

Criteria for considering studies for this review

Types of studies:

Study design: Randomized controlled trials (RCTs), Non-Randomized controlled trials (NRCTs) like the Quasi-experimental studies, and controlled before-after studies will be included. Observational studies, conference papers, editorials, reports, and other studies without any mobile app interventions in them will be excluded.

Year of publication: we will include publications matching our criteria from the year 2016 to 2022. As the search strategy yielded publications from the year 2016 onwards.

Type of participants: Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[20] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl.

FBG: Fasting means not having anything to eat or drink (except water) for at least 8 hours before the test. Diabetes is diagnosed at FBG of greater than or equal to 126 mg/dl.

RBS: This test is a blood check at any time of the day when an individual has severe diabetes symptoms (Diabetes is diagnosed at blood glucose of greater than or equal to 200 mg/dl.

OGTT: A two-hour test that checks your blood glucose levels before and two hours after you drink a special sweet drink. Diabetes is diagnosed at two-hour blood glucose ≥ 200 mg/dl [21].

Patient and public involvement: patients and the public will not be involved in any way in this study.

Type of interventions

Digital health: The use of digital, mobile, and wireless technologies to support the achievement of health objectives. Digital health describes the general use of information and communications technologies (ICT) for health and is inclusive of both mHealth and eHealth[22]. From the context of our study, the term mHealth refers to the mobile applications used in the self-management of T2DM. The interventions may also include other simpler forms of mHealth solutions like texting, emailing, video clips, graphics, and web services.

Type of Comparison: the comparator groups would be the individuals who received standard hospital treatment or no hospital care and who received an intervention.

Type of outcome measures: Primary outcomes include,

- *Clinical outcome* (HbA1c at 3 months interval): [A hemoglobin A1c (HbA1c) test measures the amount of blood sugar (glucose) attached to hemoglobin. An HbA1c test shows what the average amount of glucose attached to hemoglobin has been over the past three months. It's a three-month average because that's typically how long a red blood cell lives[23]]

Secondary outcomes include,

- *Adherence to diabetic self-management applications and medication:* The studies must have reported using any of the standard survey tools to record daily medication intake and app usage during the follow-up for a year.
- *Self-efficacy with adherence to mHealth applications:* Self-efficacy is defined as "the belief in one's capabilities to organize and execute the courses of action required to manage prospective situations." - Albert Bandura [24, 25]. The studies must have done a subjective evaluation of the individual's willingness to use the self-management applications to manage T2DM and those who are confident to follow in their near future.
- *Health promoting behavior:* If the study participants during their follow-up period adapted a positive change in behavior towards achieving better health, like opting for a healthy diet, regular moderate exercising, brisk walking, and reducing/ managing their stress levels. Will be checked across the quality of life improvement index if any done in the studies [26]. Health-promoting behavior changes will not be limited to nutrition, physical exercise/ activity, or regular/frequent blood glucose monitoring.

Search methods for identification of studies: PubMed, Ovid Medline, EBSCO, CINAHL, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials, and additional sources of the search will be grey literature available on diabetes management websites. Forward citation search will be undertaken for any key references identified and reference lists of included studies (Refer to supplementary file 2- 'Search strategies' for more search information).

We will be using Endnote library version X7 for screening and downloading the full-text articles and Microsoft Excel 2013 will be used for data extraction of the full-text articles. Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study, then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart (Refer to supplementary file 1) will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.

Data extraction and management: Data extraction will be performed using a standardized pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. The data extraction form will include information on citation details, characteristics of the studies, location, region, population, intervention, the effectiveness of an intervention, and the information on outcome and the main findings (Refer to supplementary file 3 - Data extraction format)

Any missing data in the studies included for review will be obtained by contacting the study authors of that study with a minimum waiting period of two weeks for their reply. In the event of no response from the authors of the study, a decision will be taken by the team of authors of the systematic review.

Assessment of risk of bias in included studies: Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials[27]. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies[28].

Data synthesis: Firstly, we will provide a detailed summary of all the included studies in a narrative format. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies. All the analyses will be conducted in Review Manager 5.3 and STATA 16.

Description of primary and secondary outcomes, whether adherence to diabetic self-management applications and medication has improved or not, Behavior change will be noted with the quality of life improvement index and self-efficacy will be checked following the improvement in managing T2DM. Listing out various measurement tools and devices used for judging the above-mentioned outcomes.

Subgroup analysis: Subgroup analysis will be performed for the following if appropriate. Sensitivity analysis will be performed if we find out any uncertainties in one or more input variables that may lead to uncertainties among other output variables.

Subgroup analysis will be performed for the following:

- Duration of the given intervention (3 months intervals up to a year)

- Comparing study effectiveness within the LMICs
- The most effective rate of using the Diabetic self-management app in age groups as classified by the UN
- Gender

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Ethics and dissemination: The study will be a systematic review of the published articles from different recognised and accessible databases and will not recruit any human participants directly, therefore, ethical clearance is not applicable. The dissemination of the final review findings will be done at a national or international conference and will be published in an indexed peer-reviewed journal.

Author Contributions: HB is the corresponding author, SMD, SS, JV, PP, MGL, PR, and HB conceptualized the study. SMD, SS, JV, PP, MGL, PR, and HB drafted the manuscript. All authors

were involved in the development of the selection criteria and data extraction criteria. All authors will read, provide feedback, and approve the final manuscript.

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Conflicts of interest: There is no conflict of interest in this project.

Supplemental material: Supplementary materials are enclosed as 1, 2 and 3

Patient and public involvement: patients and the public were not involved in any way in this study

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SUPPLEMENTARY FILE: 1

I. **PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol***

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Effectiveness of self-management applications in improving clinical health outcomes and adherence among diabetic individuals in Low and Middle-Income Countries: A Systematic Review
Update	1b	N/A
Registration	2	The study has been registered in PROSPERO and the Registration ID is CRD42021245517.
Authors:		
Contact	3a	Sherize Merlin Dsouza[1, 6], Sahana Shetty[2], Julien Venne[3], Prachi Pundir[4], Priyobrat Rajkhowa[1, 6], Melissa Glenda Lewis[5] and Helmut Brand[1, 6] 1. Department of Health Policy, Prasanna School of Public Health, Manipal Academy of Higher Education. 2. Department of Endocrinology, Kasturba Medical College Hospital, MAHE, Manipal, India. 3. Coordinator, Dept. of Digital Health and wellbeing, PSPH, MAHE, Manipal, India 4. Public Health Evidence South Asia (PHESA), Prasanna School of Public Health, Manipal Academy of Higher Education. 5. Indian Institute of Public Health Shillong, Lawmali, Pasteur Hill, Shillong, Meghalaya. 6. Department of International Health, Care and Public Health Research Institute – CAPHRI, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands.

Contributions	3b	All authors were involved in the development of the selection criteria, and data extraction criteria. All authors will read, provide feedback and approve the final manuscript.
Amendments	4	As the review is being carried out amendments to the search strategy, selection criteria, and data extraction criteria may be amended to include the most pertinent information for this review's objectives. If amendments to this protocol are made, the date of each amendment along with a description/rationale for the change will be noted.
Support:		
Sources	5a	Nil
Sponsor	5b	Nil
Role of sponsor or funder	5c	Not Applicable.
INTRODUCTION		
Rationale	6	**Rationale:** A deeper knowledge of the influence of mHealth applications in controlling blood sugar levels and managing diabetes is crucial for diabetes self-management, especially in the LMICs. Hence, this review aims to assess the effectiveness of mHealth applications in managing T2DM among the LMICs, with a focus on Indian studies because India has the highest burden of diabetes among the LMICs.
Objectives	7	1. To identify the effectiveness of mHealth applications in managing blood glucose levels of individuals with T2DM and 2. To assess the impact of using mHealth applications in managing T2DM concerning health-promoting behavior among the LMICs in the context of India

	1.	
METHODS		
Eligibility criteria	8	We followed the PICO concept/framework Population (P): Adults over 18 years of age, technology literate, using a smartphone or personal computer diagnosed with type 2 diabetes mellitus based on any one of the WHO 2020 criteria for diagnosis[17] i.e., HbA1c values ≥6.5% (48 mmol/mol), Fasting Blood Glucose (FBG) ≥7.0 mmol/L (126 mg/dL), Random plasma/Blood Glucose (RBS) ≥11.1 mmol/L (200 mg/dL), an Oral Glucose Tolerance Test (OGTT) ≥200 mg/dl. Intervention (I): mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices. mHealth solutions like applications or text messages, emails, video clips, graphics, and web services. Comparison (C): the comparator groups would be the individuals who received standard hospital treatment or no hospital care and those who received an intervention. Country comparison: impact of using diabetes self-management app among the LMICs listed by the World Bank-India in particular. Outcomes(O): primary outcomes- clinical parameter HbA1c Secondary outcomes- adherence to medications, self-efficacy, and Health-promoting behaviour.
Information sources	9	Authors in collaboration developed search strategies using medical subject headings (MeSH) and text words related to the topic. We will search CINAHL, PubMed, Web of Science, and Scopus. Only studies with human subjects will be included.
Search strategy	10	Refer to supplementary file 2.
Study records:		
Data management	11a	The search results collected from the electronic databases will be exported to Endnote version X7. Duplicate studies will be removed.

		Data will then be extracted, and relevant information will be extracted to an Excel spreadsheet using a data extraction tool.
Selection process	11b	Two authors will independently screen each title for inclusion in the systematic review using the eligibility criteria. Abstracts of studies included in the first stage of screening will be independently evaluated by two authors. Exclusion of the studies in this stage will be done only after expert advice and the included studies will be screened further for full text by the authors. At the full-text screening stage, if both the authors reject a study then it will be excluded and if a disagreement arises between the two authors on the inclusion or exclusion of the paper, then the disagreement will be resolved by the third reviewer or an expert and then will arrive at conclusion on including or excluding a paper based on predetermined criteria. Reasons for exclusion will be given at the full-text screening stage and the PRISMA flowchart will be used to depict the screening process. The rationale for exclusion will be provided for all the excluded studies throughout the process.
Data collection process	11c	Data extraction will be performed using a standardised pre-tested data extraction format by the authors. The data extraction form will be pilot tested by each author and will be edited based on discussion among the authors. (Refer; supplementary file-3 Data extraction format) Any missing data in the studies included for review will be obtained by contacting the study authors of that study.
Data items	12	Bibliometric information such as Author's name, Author's affiliations, Title, Journal name, publication year, and country of conduct will be collected along with Characteristics of the included studies. Data will be extracted based on the type of study, study objectives, Inclusion criteria, participant's characteristics, Intervention details, comparator, and the study outcome.
Outcomes and prioritization	13	A detailed summary of all the included studies will include information on authors, study objectives, Inclusion criteria,

		Intervention details, comparator, outcome measures, and the country will be in a narrative format. An evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management apps in controlling type 2 diabetes. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes.
Risk of bias in individual studies	14	Two authors will independently assess the risk of bias in included studies. The Cochrane Risk of Bias (RoB 2) tool will be used to evaluate Randomised controlled trials. Risk of bias in Non-randomized Studies of Interventions assessment tool (ROBINS-I) for Non-Randomised studies.
Data synthesis	15a 15b	A detailed summary of all the included studies in a narrative format will be given. It will include information on authors, study objectives, Inclusion criteria, Intervention details, comparator, outcome measures, and the country. Secondly, an evaluation will be done if it is appropriate to perform a meta-analysis to assess the effectiveness of diabetic self-management applications in controlling blood sugar levels. Meta-analysis with a random-effects model will be performed if there is a similarity in terms of the participants, study design, comparator, and outcomes. The pooled estimates will be obtained separately for RCTs, and Non-RCTs (Quasi-experimental and controlled before-after studies). The summary estimates will be expressed in mean difference, standardized mean difference for continuous outcomes, and relative risk & odds ratio for categorical outcomes with 95% confidence intervals. Forest plots, I^2 statistic, Chi^2 test, and Tau^2 will be used to measure and assess heterogeneity among the included studies in each analysis. Meta-regression will be used to investigate heterogeneity if appropriate data is obtained. An attempt will be made to contact the study authors if data is

inadequate or missing and the record will be maintained on the amount of missing data with reasons. An assessment for publication bias will be made by creating a funnel plot only if there are at least 10 studies in the meta-analysis. A narrative synthesis will be done if there are less than 10 included studies.

	15c 15d	
Meta-bias(es)	16	Not applicable.
Confidence in cumulative evidence	17	Not applicable.

Supplementary file: 2		
Database	**Search strategy**	**Hits**
1 PubMed	Search: (("diabetes mellitus, type 2"[MeSH Terms] OR "self-management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language]) AND ((fha[Filter]) AND (clinicaltrial[Filter] OR randomized controlled trial[Filter] OR review[Filter]) AND (humans[Filter]) AND (english[Filter]))	68
2 World Bank list of low and middleincome countries included in the study	Search: ("Afghanistan"[All Fields] OR "Albania"[All Fields] OR "Algeria"[All Fields] OR "American"[All Fields] OR "Samoa"[All Fields] OR "Angola"[All Fields] OR "Argentina"[All Fields] OR "Armenia"[All Fields] OR "Azerbaijan"[All Fields] OR "Bangladesh"[All Fields] OR "Belarus"[All Fields] OR "Belize"[All Fields] OR "Benin"[All Fields] OR "Bhutan"[All Fields] OR "Bolivia"[All Fields] OR "Bosnia"[All Fields] OR "Herzegovina"[All Fields] OR "Botswana"[All Fields] OR "Brazil"[All Fields] OR "Bulgaria"[All Fields] OR "Burkina"[All Fields] OR "Faso"[All Fields] OR "Burundi"[All Fields] OR "Cabo"[All Fields] OR "Verde"[All Fields] OR "Cambodia"[All Fields] OR "Cameroon"[All Fields] OR "Central"[All Fields] OR "African"[All Fields] OR "Republic"[All Fields] OR "Chad"[All Fields] OR "China"[All Fields] OR "Colombia"[All Fields] OR "Comoros"[All Fields] OR "Congo"[All Fields] OR "dem"[All Fields] OR "rep"[All Fields] OR "Congo"[All Fields] OR "rep"[All Fields] OR "Costa"[All Fields] OR "Rica"[All Fields] OR "Cote"[All Fields] OR "d'Ivoire"[All Fields] OR "Cuba"[All Fields] OR "Djibouti"[All Fields] OR "Dominica"[All Fields] OR "Dominican"[All Fields] OR "Republic"[All Fields] OR "Ecuador"[All Fields] OR "Egypt"[All Fields] OR "Arab"[All Fields] OR "rep"[All Fields] OR "El"[All Fields] OR "Salvador"[All Fields] OR "Equatorial"[All Fields]	5,860,984
1 & 2 (2016-2022)	Search: ((("diabetes mellitus, type 2"[MeSH Terms] OR "self-management/education"[MeSH Major Topic]) AND "Mobile Applications"[MeSH Major Topic] AND "english"[Language] AND "english"[Language]) AND ((fha[Filter]) AND (clinicaltrial[Filter] OR randomized controlled trial[Filter] OR review[Filter]) AND (humans[Filter]) AND (english[Filter]))) AND (("Afghanistan"[All Fields] OR "Albania"[All Fields] OR "Algeria"[All Fields] OR "American"[All Fields] OR "Samoa"[All Fields] OR "Angola"[All	15

	Fields] OR "Argentina"[All Fields] OR "Armenia"[All Fields] OR "Azerbaijan"[All Fields] OR "Bangladesh"[All Fields] OR "Belarus"[All Fields] OR "Belize"[All Fields] OR "Benin"[All Fields] OR "Bhutan"[All Fields] OR "Bolivia"[All Fields] OR "Bosnia"[All Fields] OR "Herzegovina"[All Fields] OR "Botswana"[All Fields] OR "Brazil"[All Fields] OR "Bulgaria"[All Fields] OR "Burkina"[All Fields] OR "Faso"[All Fields] OR "Burundi"[All Fields] OR "Cabo"[All Fields] OR "Verde"[All Fields] OR "Cambodia"[All Fields] OR "Cameroon"[All Fields] OR "Central"[All Fields] OR "African"[All Fields] OR "Republic"[All Fields] OR "Chad"[All Fields] OR "China"[All Fields] OR "Colombia"[All Fields] OR "Comoros"[All Fields] OR "Congo"[All Fields] OR "dem"[All Fields] OR "rep"[All Fields] OR "Congo"[All Fields] OR "rep"[All Fields] OR "Costa"[All Fields] OR "Rica"[All Fields] OR "Cote"[All Fields] OR "d'Ivoire"[All Fields] OR "Cuba"[All Fields] OR "Djibouti"[All Fields] OR "Dominica"[All Fields] OR "Dominican"[All Fields] OR "Republic"[All Fields] OR "Ecuador"[All Fields] OR "Egypt"[All Fields] OR "Arab"[All Fields] OR "rep"[All Fields] OR "El"[All Fields] OR "Salvador"[All Fields] OR "Equatorial"[All Fields]) Filters: Abstract, Clinical Trial, Randomized Controlled Trial, Review	

Supplementary file: 3

III. Data extraction from

Title of the study	
Authors	
The Year of the study conducted	
Year of publication	
Doi & Journal	
Objectives of the study	
Participant characteristics	Number of participants Age Gender Ethnicity Socioeconomic group Educational status Duration of T2DM
Total number of participants	
Setting/ context/ country	Low-income country Lower Middle-income country Upper Middle-income country
World Bank Region	South Asia Sub-Saharan Africa East Asia and the Pacific Europe and Central Asia Latin America and the Caribbean The Middle East and North Africa North America
Description of intervention for type 2 diabetes	M health application Infographics Video clips Text messages Others – to be specified
Search details	Year
Source	IndMED Medline Plus OpenMED

	Ovid Medline PubMed / MEDLINE Scopus Web of Science Other Bibliographical Databases
The range of years included	No limit
No of included studies	
Type of studies included	RCT Quasi-experimental study Case-control Cohort Controlled trial
Comparator	Duration of the intervention Across the regions (LMICs) Age groups Gender
Analysis	
Method of analysis	
follow up sessions	
Outcome assessed	Primary secondary
Results/ findings	
Significance	
Heterogeneity if done	
Study Limitations	