

Effect of telemedicine on glycated haemoglobin in people with type 2 diabetes in the MENA region: a systematic review and meta-analysis

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A – Study Design, B – Data Collection, C – Statistical Analysis, D – Data Interpretation, E – Manuscript Preparation, F – Literature Search, G – Funds Collection

Summary Background. Telemedicine has recently become a more important platform for the delivery of health interventions such as blood glucose monitoring and a range of other health concerns.

Objectives. The purpose of this systematic review and meta-analysis is to examine the effect of different types of telemedicine compared to standard care on glycated haemoglobin (HbA_{1c}) level and other glucose-related indicators for persons with diabetes in the Middle East and North Africa (MENA) region.

Material and methods. The following electronic databases were searched from 1990 to February 2022; MEDLINE, Embase, Scopus and the Cochrane Library. A total of six randomised controlled trials met the inclusion criteria and were included in the data for the meta-analysis.

Results. Six randomised controlled trials ($n = 461$ individuals) comparing telemedicine standard care in people with type 2 diabetes in the MENA region were included. The mean difference in HbA_{1c} between the control and telemedicine groups was -0.52 (95% CI, $-0.79, -0.25$) ($p < 0.001$), showing better HbA_{1c} scores in patients receiving telemedicine than those receiving standard care only. The study's heterogeneity was quite low, with an I² value of 1% ($p = 0.55$). The evidence surrounding the impacts of telemedicine on all categories of cholesterol was low and insignificant.

Conclusions. The evidence gathered in this systematic analysis shows that using telemedicine in comparison to standard care improves HbA_{1c} levels in persons with type 2 diabetes in the MENA region.

Key words: telemedicine, type 2 diabetes mellitus, meta-analysis.

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Background

Type 2 diabetes mellitus (T2DM) is a chronic disease that requires lifelong treatment and lifestyle changes, and throughout the past few decades, the prevalence of T2DM has been rising steadily [1]. In 2019, around 463 million people were estimated to be living with diabetes, representing 9.3% of the adult population (20–79 years of age) globally [2]. In the Middle East and North Africa region, one in six adults (73 million) are living with diabetes, with that number expected to reach 95 million by 2030 and 136 million by 2045 [3]. Middle Eastern countries with a high prevalence of T2DM among men include Bahrain (33.60%), Saudi Arabia (29.10%), United Arab Emirates (UAE; 25.83%) and Kuwait (25.40%), whereas a low prevalence was noted in Iran (9.90%) and Yemen (9.80%) [4]. The economic impact of diabetes in Saudi Arabia reached \$2.4 billion in 2015 and \$6.5 billion in 2020 [5]. In high-income countries, diabetes-related healthcare spending is on average \$5,063 per person with diabetes compared to \$271 in low- and middle-income countries [6]. Diabetes mellitus is currently the most common non-communicable disease (NCD) and the leading cause of mortality in the WHO Eastern Mediterranean Region, as well as the eighth leading cause of death globally [4, 7]. A diabetic defensive strategy must be incorporated into these states in the future, targeting the Middle East population to minimise the burden of the disease in the region [4].

Diabetes has a number of well-known complications. Microvascular complications of diabetes mellitus include nephropathy, neuropathy and retinopathy, as well as macrovascular complications including cardiovascular disease and cerebrovascular disease [8]. In T2DM, optimal glycaemic control requires a combination of pharmacological and non-pharmacological therapy [9]. Managing diabetes and its complications is expensive, though it can be avoided or minimised with effective hyperglycaemia control.

There has recently been renewed interest in the use of telemedicine solutions to reduce outpatient clinic appointments and visits to physicians' offices, thereby saving financial and personal resources, as well as time [10]. The newly developed telecommunications facility is a tool for improving the quality of care for type 2 diabetic patients [10]. Diabetes telemedicine solutions can range from simple text-messaging or phone calls to web interfaces or phone apps, where patients can input their recorded glucose levels and any home concerns, as well as other essential data, such as medications, food habits, exercise level. Recently, it was discovered that most patients in Saudi Arabia agreed or strongly agreed that telemedicine was important in keeping reasonable glycaemic control during the pandemic and that they recommend utilising the telemedicine clinic in the future [11]. Similarly, evidence from many studies implies that virtual clinics in Saudi Arabia were well-received during the



COVID-19 pandemic [12, 13]. To our knowledge, no systematic review or meta-analysis study has been conducted in the MENA region to assess the use of telemedicine and its impact on diabetic parameters.

Objectives

We aim to assess the effect of different types of telemedicine compared to standard care on glycated haemoglobin (HbA_{1c}) and other glucose-related indicators in persons with diabetes in the MENA region.

Material and methods

Study design

This systematic review and further meta-analysis were performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [14]. This review was pre-registered as CRD42022302000 at the International Prospective Register of Systematic Reviews (PROSPERO). We searched the electronic databases of MEDLINE, Embase, Scopus and the Cochrane Library from 1990 to February 2022, with no language constraints. Proper key phrases and terminology, as well as different combinations, were used in the search technique (Appendix 1). All potentially qualifying studies were considered for evaluation after the searches were completed in all relevant databases.

Study eligibility & outcomes of interest

The inclusion criteria for this review include randomised placebo-controlled trials involving individuals over the age of 18 who have type 2 diabetes and are exploring the efficacy of telemedicine intervention on haemoglobin A_{1c} control in adults living in the MENA region. The outcomes of interest were haemoglobin A_{1c}, fasting plasma glucose, lipid profile, blood pressure, body mass index (BMI) and weight. Non-peer reviewed papers, abstracts, conference posters, government reports and unpublished studies were all excluded.

Study selection, data extraction & risk of bias assessment

All studies from the databases were uploaded to a reference using Rayyan, a free online bibliographic tool [15]. Duplicates were deleted, and the titles and abstracts were checked against the study eligibility criteria by two authors (AM and SA). Full-text analysis was performed on studies that met our inclusion criteria. Any disagreements that arose throughout the selection process were handled through mutual consultation with a third investigator (AA).

One author (ZA) extracted data from eligible studies using a specially developed data collection form, while a second author (JAT) independently compared the data to that in the original papers. In the event of any inconsistency, a consensus

was reached with the intervention of a third person (AA). Author names, publication year and type, country, study characteristics, mean age, gender distribution and sample size were extracted as overall data. The HbA_{1c} level and other diabetic parameters were also reported. For both intervention and placebo groups, outcome data was retrieved as mean change and standard deviation or standard error. Following data extraction, two authors (ZA & JAT) analysed and pre-piloted the RoB 2, an updated tool to assess risk of bias in randomised trials [16]. Any potential discrepancy was resolved by reaching an agreement.

Data analysis

Summary of findings' tables was used to summarise all of the papers included in this evaluation. Review Manager (RevMan) (Computer application) was used to do meta-analyses. The Cochrane Collaboration, Version 5.4, 2020, was used for outcomes where the mean and standard deviation (SD) for change values were provided or could be calculated [17]. To account for intra- and inter-study variability, the random-effects model was used for primary outcomes. The standardised mean difference (SMD) across groups is presented in order to combine possible heterogeneous outcomes. Data from all 6 studies was combined and analysed, with haemoglobin A_{1c} data being prioritised where available. The Higgins I² statistic test was used to interpret statistical heterogeneity [18]. A heterogeneity estimate of 25% for I² was judged low, > 25 to 75% moderate and 75% high. The acceptable criterion for statistical significance was a *p*-value of 0.05.

Results

Study selection

After removing duplicates, the electronic search resulted 394 articles. 6 studies met the criteria for inclusion and provided data for the meta-analysis (Figure 1). A total of 461 people were recruited from the studies, with an average age of 48.2 years. All of the trials in the study ranged from 12 to 24 weeks in length. 3 of the studies were conducted in Iran [19–21], 2 in Saudi Arabia [22, 23] and 1 in Egypt [24]. Text messages, phone calls and web applications were the most common ways of delivery of interventions in the telemedicine groups. 2 studies [22, 23] used more than 1 intervention mode. Text messages were mostly utilised in all of the studies [19–24]. The majority of the studies use telemedicine to give both lifestyle and drug treatment, while 1 study only used telemedicine to deliver lifestyle intervention [22]. Table 1 provides a detailed description of the studies included.

Risk-of-bias assessment

The RoB-2 for RCTs was used to assess the risk of bias in the included studies. The risk of bias in each domain and the overall risk of bias are shown in Appendix 2. Overall, three studies showed a high risk of bias [19, 20, 24], two had some concerns [22, 23], and one had a low risk of bias [21].

Table 1. Common characteristics of the included studies

Author/Year of publication	Country of study	Sample size	Type of study	Study duration	Method of delivery/ Mode of intervention	Type of intervention	Type of management
Mandana Goodarzi, 2012	Iran	81	RCT	12 weeks	SMS/4 message per week	Text message	Lifestyle + Drug
Amir Sarayani, 2018	Iran	100	RCT	12 weeks	Phone calls/1 st month 2 calls	Telephone	Lifestyle + Drug
Maryam Peimani, 2016	Iran	150	RCT	12 weeks	SMS	Text message	Lifestyle + Drug
Haitham Abaza, 2017	Egypt	90	RCT	12 weeks	SMS/1 message per week	Text message	Lifestyle + Drug

Author/Year of publication	Country of study	Sample size	Type of study	Study duration	Method of delivery/ Mode of intervention	Type of intervention	Type of management
Turki Alanzi, 2018,	Saudi Arabia	20	RCT	24 weeks	SMS/SANAD system (Saudi Arabia Networking for Aiding Diabetes)	Text message and application	Lifestyle
Mohammed M. Alotaibi, 2016	Saudi Arabia	20	RCT	24 weeks	SMS, SAED (Educational system for type 2 diabetics in Saudi Arabia)/Weekly message	Text message and mobile diabetes management and educational system	Lifestyle + Drug

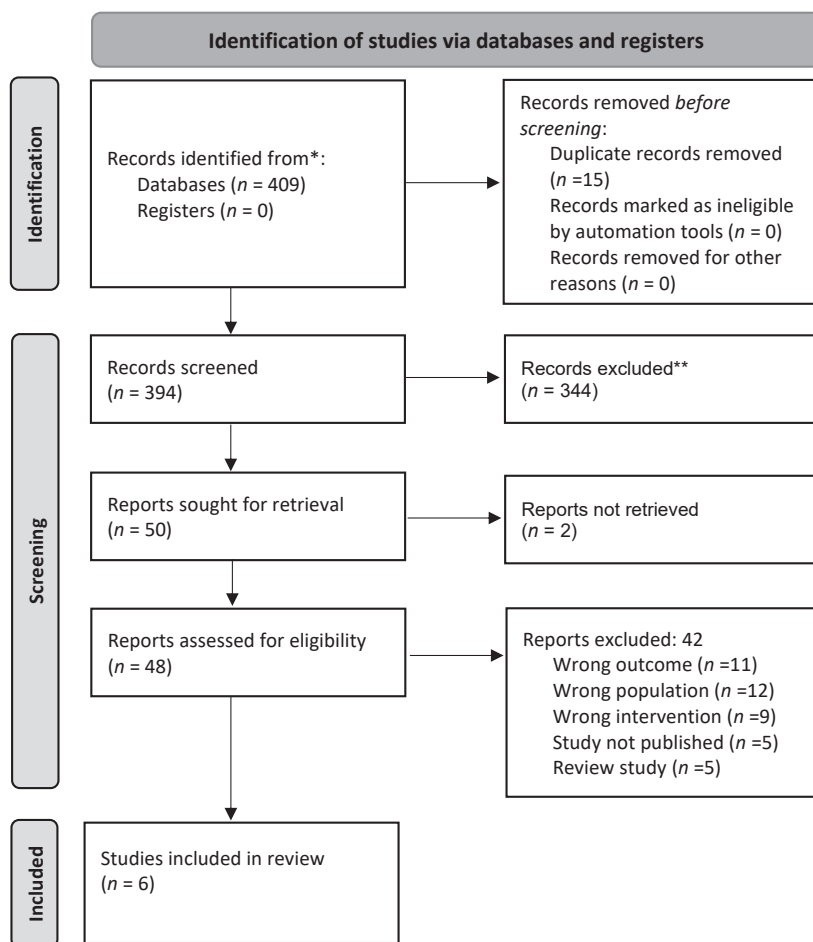


Figure 1. Systematic review of the search process

Effects of intervention

The results of the meta-analysis are presented in Figures 2, 3 and 4. In most of the outcomes, the heterogeneity was very low. The pooled effect and 95% CI were significant in the case of HbA_{1c}; however, on the forest plots of the outcomes, the pooled effect for total cholesterol, LDL, HDL and triglycerides went over the line of no effect, indicating that the results for these outcomes were not significant. The meta-analysis could not be performed for the FBG, SBP or DBP outcomes.

The mean difference in HbA_{1c} change (pooled effect size) between the control and telemedicine was -0.52 (95% CI, -0.79, -0.25) and was significant ($p = 0.0002$), showing that patients receiving telemedicine improved their HbA_{1c} more than patients receiving conventional care. The study's heterogeneity was very low, with a value of $I^2 = 1\%$ ($p = 0.55$) (Figure 2). Similarly, the study heterogeneity remains the same at $I^2 = 1\%$ ($p = 0.37$) and

the mean difference in HbA_{1c} change was -0.70 (95% CI, -1.10, -0.30) and significant ($p = 0.0005$) based on subgroup analysis, as shown in Figure 2.

The findings obtained in all cholesterol categories (total cholesterol, LDL, HDL and triglycerides) were not statistically significant. Total cholesterol, LDL, HDL and triglycerides had mean differences of 0.34 (95% CI, -8.75, 9.43; $p = 0.94$), 1.04 (95% CI, -5.59, 7.67; $p = 0.76$), -1.38 (95% CI, -4.07, 1.30; $p = 0.31$) and 12.16 (95% CI, -7.66, 31.99; $p = 0.23$) (Figure 3). The study heterogeneities for LDL, HDL and triglycerides were all non-significant, with p -values of $I^2 = 57\%$ ($p = 0.10$), $I^2 = 17\%$ ($p = 0.30$) and $I^2 = 42\%$ ($p = 0.18$), respectively. It was significant for total cholesterol, with a value of $I^2 = 78\%$ ($p = 0.01$), indicating high heterogeneity. There was no statistical significance between the lipid subgroups according to the test for subgroup analysis for the lipid profile ($p = 0.54$).

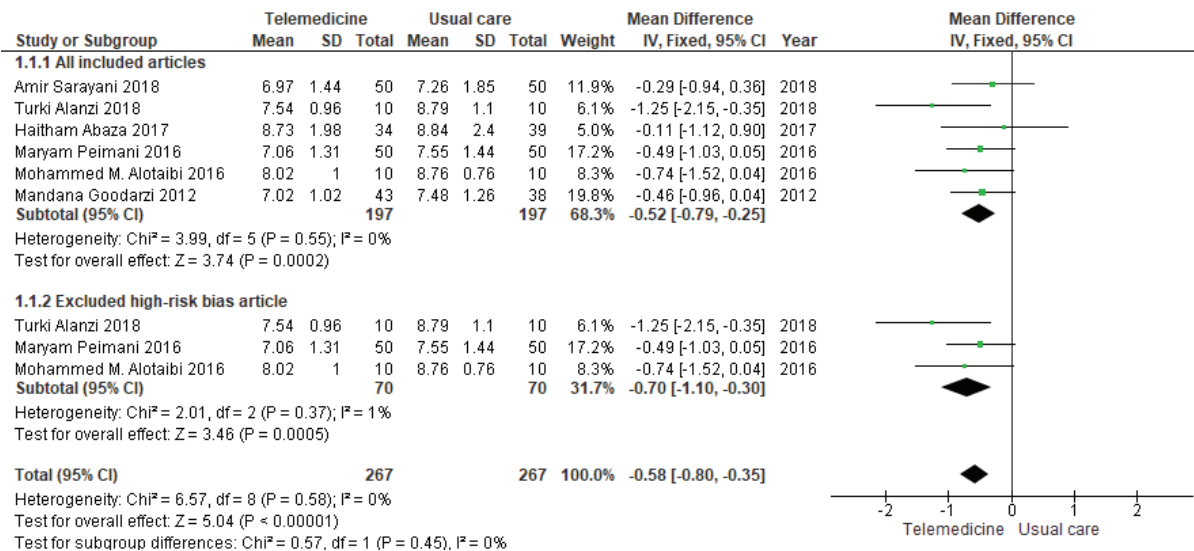


Figure 2. Meta-analyses and sub-group analysis of HgA_{1c} outcomes

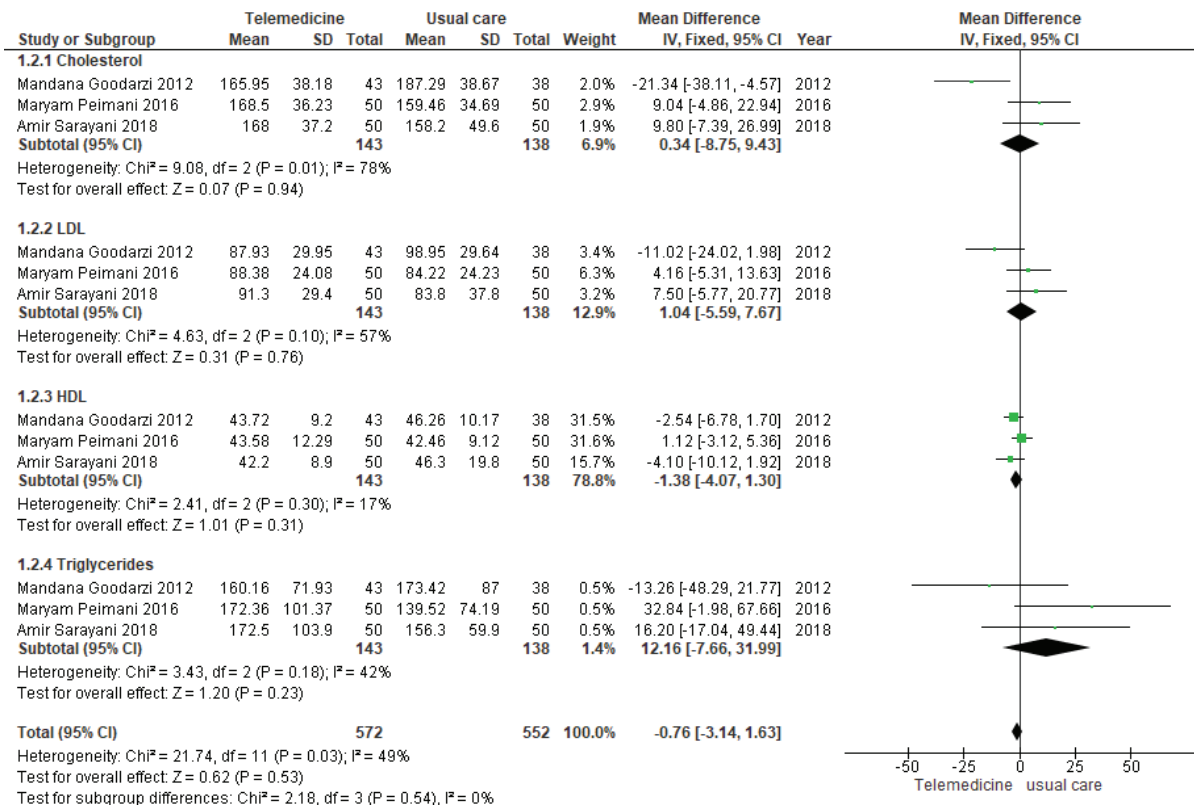


Figure 3. Meta-analyses and sub-group analysis of lipid profile outcomes

Discussion

The findings of this systematic review and meta-analysis of six studies suggest that patients receiving telemedicine have lower HgA_{1c} levels than patients receiving standard care. These findings show that close and continuous patient monitoring may have significant clinical benefits. Previous research has shown that a 1% decrease in HbA_{1c} lowers the risk of diabetes-related death by 21%, MI by 14%, and microvascular complications by 31% [25]. Several lines of evidence suggest that longer telemedicine use with a larger sample size is suggested, indicating that telemedicine is effective in improving HbA_{1c} and that telemedicine care could be adopted in treatment of diabetes [26, 27].

In the MENA region, the evidence for the influence of telemedicine on FBG, BMI, SBP, DPB and all forms of cholesterol was limited, precluding meaningful interpretation and emphasising an important evidence gap in literature. Although there was an improvement in HbA_{1c} levels in patients receiving telemedicine, the small number of included studies makes drawing significant inferences on the relative effectiveness of telemedicine versus standard treatment within the analysis challenging.

It has been suggested to evaluate the impact of telemedicine on outcomes related to diabetes such as BMI, cholesterol and blood pressure, as T2DM is commonly associated with obesity, dyslipidaemia, and/or hypertension [28]. Furthermore, the majority of the studies considered did not provide a wide range of outcomes, such as BMI, FBG, SBP and DBP.

The results of the meta-analysis indicate that in the telemedicine group, all categories of cholesterol (total cholesterol, LDL, HDL, and triglycerides) were not statistically significant; however, this cannot be inferred as the study's results were not significant. Even while cholesterol and LDL appeared to favour telemedicine over traditional care, the results were not statistically significant. A recent umbrella review showed that telemedicine only improves HbA_{1c} levels in a large number of systematic reviews and meta-analyses. Furthermore, the evidence to support the use of telemedicine for other outcomes, including as blood pressure, lipids and patient reported outcomes, was insufficient [29]. Taken together, these findings indicate that the use of telemedicine in community care will have a significant influence on health care, particularly type 2 diabetes.

This study is the first systematic review to date that looks at the effects of telemedicine in the MENA region. Limitations include the limited trials included, the lack of current trials ad-

ressing this issue, the brief follow-up period and the small number of participants.

Conclusions

Overall, the evidence collected in this systematic review demonstrates an improvement in the level of HbA_{1c} with the use of telemedicine compared to usual care among people with type 2 diabetes in the region. The evidence surrounding the effects of cholesterol parameters with telemedicine was minimal and insignificant, therefore signifying the need for further research to investigate the effect of telemedicine on lipid, weight loss and blood pressure. A future systemic review is also required to determine the effect of various digital modalities on diabetes. The findings of this study provide insights for health policymakers in the MENA region to consider adopting and for implementing comprehensive standards for telemedicine care in order to assure better quality of care.

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Conflicts of interest: The authors declare no conflicts of interest.

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Tables: 1

Figures: 3

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Supplementary material

Appendix 1. MEDLINE literature search strategy

Database: Ovid MEDLINE(R) <1946 to present>

Search Strategy:

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1      Diabetes Mellitus.mp. or exp Diabetes Mellitus/ 544921
2      Diabetes Mellitus, Type 2/ or diagnosis type 2 diabetes.mp. 149499
3      glucose intolerance.mp. 17315
4      type 2 diabetes/ 149497
5      Diabetes Mellitus, Type 2.mp. 151226
6      type 2 diabetes mellitus.mp. 52735
7      NIDDM.mp. 6968
8      non-insulin depend* diabetes.mp. 8709
9      diabetes type two.mp. 4
10     diabetes mellitus type II.mp. 632
11     diabetes type II.mp. 373
12     type two diabetes.mp. 215
13     type two diabetes mellitus.mp. 101
14     type two DM.mp. 3
15     type II diabetes.mp. 9145
16     type II diabetes mellitus.mp. 3066
17     T2DM.mp. 25930
18     T2D.mp. 12893
19     diagnosis type 1 diabetes.mp. 4
20     exp type 1 diabetes/ 80723
21     Diabetes Mellitus, Type 1.mp. 80909
22     type 1 diabetes mellitus.mp. 12001
23     diabetes mellitus type I.mp. 426
24     diabetes type I.mp. 223
25     type one diabetes.mp. 66
26     type one diabetes mellitus.mp. 35
27     type one DM.mp. 3
28     type I diabetes.mp. 5336
29     type I diabetes mellitus.mp. 1845
30     T1DM.mp. 5445
31     T1D.mp. 8267
32     1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
or 25 or 26 or 27 or 28 or 29 or 30 or 31 562877
33     glycemic control.mp. or Glycemic Control/ 27791
34     Glycated Hemoglobin A/ or glycaemic control.mp. 45011
35     Hba1c.mp. 39586
36     Blood Glucose/ or glycemia.mp. 178823
37     Glycaemia.mp. 4258
38     blood sugar.mp. 15130
39     blood glucose.mp. or Blood Glucose/ 214164
40     Glucose/ or glucose level.mp. 176242
41     blood glucose level.mp. 8037
42     33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 411882
43     Telemedicine/ or Remote Consultation/ 35748
44     Telecare.mp. 838
45     Telehealth.mp. 9045
46     exp Telemedicine/ 38081
47     Tele-education.mp. 204
48     e-health.mp. 3471
49     Tele-medicine.mp. 162
50     Teleconsultation.mp. 1262
51     Tele-consultation.mp. 103
52     ehealth.mp. 5318
53     Telemedical.mp. 904
54     Tele-medical.mp. 30
55     mHealth.mp. 6767
56     exp Cell Phone/ or m-Health.mp. or Mobile Applications/ or exp Computer Communication Networks/ 125667
57     Mobile Health.mp. 9826
58     mobile-health.mp. or exp Telemedicine/ 45316
59     Telemanagement.mp. or exp Internet/ 89429
60     Telecare.mp. 838
61     Tele-care.mp. 35

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- 62 Telematic.mp. 298
 63 Telepharmacy.mp. 128
 64 User-Computer Interface/ or virtual health.mp. 39363
 65 Virtual-health.mp. 672
 66 SMS.mp. 6917
 67 exp Text Messaging/ 3884
 68 smartphone.mp. or exp Smartphone/ 15846
 69 iphone.mp. or exp Cell Phone/ or i-phone.mp. 19688
 70 skype.mp. or exp Videoconferencing/ 2939
 71 zoom.mp. 2312
 72 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 213488
 73 Algeria.mp. 4752
 74 Bahrain.mp. 1231
 75 Djibouti.mp. 468
 76 Egypt.mp. 24180
 77 Iraq.mp. 11084
 78 Jordan.mp. 8612
 79 Kuwait.mp. 4817
 80 Lebanon.mp. 7028
 81 Libya.mp. 1865
 82 Jamahiriya.mp. 49
 83 Mauritania.mp. 793
 84 Djibouti.mp. 468
 85 Morocco.mp. 8929
 86 Oman.mp. 3753
 87 Palestine.mp. 1708
 88 Qatar.mp. 2791
 89 Saudi Arabia.mp. or exp Saudi Arabia/ 25244
 90 Somalia.mp. 2516
 91 Sudan.mp. 10158
 92 Gaza.mp. 1396
 93 middle east.mp. or exp Middle East/ 161199
 94 Syria.mp. 3645
 95 Tunisia.mp. 11224
 96 exp United Arab Emirates/ or The United Arab Emirates.mp. 3687
 97 Yemen.mp. 2452
 98 Iran.mp. or exp Iran/ 56961
 99 Islamic Republic.mp. 870
 100 Coronavirus, Turkey/ or exp Turkey/ or Turkey.mp. 58883
 101 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 286656
 102 32 and 42 and 72 and 101 44
 103 32 or 42 813257
 104 72 and 101 and 103 96

Each part was specifically translated for searching alternative databases.

Appendix 2. Assessment of risk of bias

	Mandana Goodarzi, 2012	Amir Sarayani, 2018	Haitham Abaza, 2017	Maryam Peimani, 2016	Turki Alanzi, 2018	Mohammed M. Alotaibi, 2016
Random sequence generation	+	+	+	+	?	?
Deviations from the intended interventions (effect of assignment to intervention)	?	-	-	?	?	?
Deviations from the intended interventions (effect of adhering to intervention)	-	+	+	+	?	+
Missing outcome data	+	+	+	+	+	+
Measurement of the outcome	?	+	+	+	+	+
Selection of the reported result	+	+	+	+	+	+
Overall risk of bias	-	-	-	+	?	?

+	Some concerns
?	Low risk
-	High risk