Telemedicine in improving glycemic control among children and adolescents with type 1 diabetes mellitus: A systematic review and meta-analysis

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Abstract

Background: Type 1 diabetes mellitus (T1DM) is the most common chronic autoimmune disease among children and adolescents. Telemedicine is the use of medical information exchanged from one site to another via electronic communications to improve the health of patients. It has been widely used in the field of chronic disease management and brings the gospel to patients with T1DM.

Objective: This study aims to systematically review the evidence on the effectiveness of telemedicine intervention compared with usual care on glycemic control among children and adolescents with T1DM.

Methods: In this systematic review and meta-analysis, we searched PubMed, Cochrane Library, Embase, Web of Science (all databases), and CINAHL Complete from database inception to May 2023. We included randomized controlled trials that evaluated the effectiveness of a telemedicine intervention on glycemic control in children and adolescents with T1DM. Two independent reviewers performed the study selection and data extraction. Study quality was assessed using the Cochrane risk-of-bias tool 2.0. Our primary outcome was HbA1c levels. Secondary outcomes were quality of life (QOL), self-monitoring of blood glucose (SMBG), the incidence of hypoglycemia, and cost-effectiveness. The random effects model was used for this meta-analysis.

Results: In total, 20 randomized controlled trials (1704 participants from 12 countries) were included in the meta-analysis. Only one study was at high risk of bias. Compared to usual care, telemedicine was found to reduce HbA1c by 0.21% (95% CI –0.33 to –0.09; p<.001; I2=33.9%). There was an improvement in SMBG (MD 0.54; 95% CI –0.72 to 1.80; p=.045; I2=67.8%) and the incidence of hypoglycemia (MD –0.15; 95% CI –0.57 to 0.27; p=.017; I2=70.7%), although this was not statistically significant. Moreover, telemedicine also had no convincing effect on the DQOLY (Impact of diabetes p=59; Worries about diabetes: p=.71; Satisfaction with diabetes: p=.68) and the N-QOL (p=.054). Subgroup analyses revealed that the effect of telemedicine of on HbA1c appeared to be greater in studies involving children (MD –0.41; 95% CI –0.62 to –0.20; p<.001), in studies that lasted less than six months (MD –0.32; 95% CI –0.48 to –0.17; p<.001), in studies where providers used smartphone applications to communicate with patients (MD –0.36; 95% CI –0.52 to –0.21; p<.001), and in studies with medication dose adjustment (MD –0.25; 95% CI –0.37 to –0.12; p<.001).

Conclusions: This study has shown that telemedicine is an efficacious and safe treatment approach for children and adolescents with T1DM, leading to reduced HbA1c levels for children and adolescents with T1DM. Further research is needed to validate the effectiveness of telemedicine on the quality of life of children and adolescents and to measure the cost-effectiveness of telemedicine applications among children and adolescents with T1DM. Clinical Trial: PROSPERO International Prospective Register of Systematic Reviews CRD42023423882; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=423882

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Title page

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Conflict of interest

The authors declare no conflict of interest.

Authors' contributions

KZ and QW contributed to the study concept and design, KZ drafted the manuscript, QH helped to draft the manuscript, KZ, CL and QH assessed the risk of bias, QH and QW assessed the quality of each evidence, KZ and CL independently extracted the data for analysis, KZ, QZ, DX, CX, MZ and RL had been involved in discussing earlier versions of the text. All authors participated in its design, read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Abstract

Background: Type 1 diabetes mellitus (T1DM) is the most common chronic autoimmune disease among children and adolescents. Telemedicine has been widely used in the field of chronic disease management and brings the gospel to patients with T1DM. However, existing studies lack high-level evidence relating to the effectiveness of telemedicine for glycemic control in children and adolescents with T1DM.

Objective: This study aims to systematically review the evidence on the effectiveness of telemedicine intervention compared with usual care on glycemic control among children and adolescents with T1DM.

Methods: In this systematic review and meta-analysis, we searched PubMed, Cochrane Library, Embase, Web of Science (all databases), and CINAHL Complete from database inception to May 2023. We included randomized controlled trials that evaluated the effectiveness of a telemedicine intervention on glycemic control in children and adolescents with T1DM. Two independent reviewers performed the study selection and data extraction. Study quality was assessed using the Cochrane risk-of-bias tool 2.0. Our primary outcome was HbA1c levels. Secondary outcomes were quality of life (QOL), self-monitoring of blood glucose (SMBG), the incidence of hypoglycemia, and cost-effectiveness. The random effects model was used for this meta-analysis.

Results:

In total, 20 randomized controlled trials (1704 participants from 12 countries) were included in the meta-analysis. Only one study was at high risk of bias. Compared to usual care, telemedicine was found to reduce HbA1c by 0.22% (95% CI –0.33 to –0.10; p<.001; I^2=35.0%). There was an improvement in SMBG (MD 0.54; 95% CI –0.72 to 1.80; p=.403; I^2=67.8%) and the incidence of hypoglycemia (MD –0.15; 95% CI –0.57 to 0.27; p=.485; I^2=70.7%), although this was not statistically significant. Moreover, telemedicine also had no convincing effect on the DQOLY (Impact of diabetes p=.59; Worries about diabetes: p=.71; Satisfaction with diabetes: p=.68), but a statistically significant improvement in N-QOL((MD –0.24; 95% CI –0.45 to –0.02; p=.035; I^2=0%) occurred. Subgroup analyses revealed that the effect of telemedicine of on HbA1c appeared to be greater in studies involving children (MD –0.41; 95% CI –0.62 to –0.20; p<.001), in studies that lasted less than six months (MD –0.32; 95% CI –0.48 to –0.17; p<.001), in studies where providers used smartphone applications to communicate with patients (MD –0.37; 95% CI –0.53 to –0.21; p<.001), and in studies with medication dose adjustment (MD –0.25; 95% CI –0.37 to –0.12; p<.001).

Conclusions:

Telemedicine is an efficacious and safe approach of intervention. It can reduce HbA1c levels and improve quality of life in children and adolescents with T1DM. In accordance with the idea of providing health care from a distance, telemedicine should be regarded as a useful supplement to usual care to control HbA1c and a potentially cost-effective mode. Meanwhile, researchers should develop higher-quality RCTs using large samples that focus on hard clinical outcomes, cost-effectiveness, and quality of life.

Trial Registration:

PROSPERO International Prospective Register of Systematic Reviews CRD42023423882; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=423882

Key words: telemedicine; digital health; web-based; type 1 diabetes mellitus; children; adolescents; glycemic control; randomized controlled trials; systematic review; meta-analysis

Introduction

Type 1 diabetes mellitus (T1DM) is the most common chronic autoimmune disease among children and adolescents, characterized by hyperglycemia and caused by an absolute deficiency of insulin[1, 2]. More than 1.2 million children and adolescents worldwide currently have T1DM[3]. Adolescence is a period when glycemic control commonly deteriorates[4], and people with diabetes remain at high risk of serious complications, including diabetic cardiovascular disease and diabetic nephropathy[5-7]. T1DM has a serious impact on the life health of children and adolescents. It places a heavy medical burden on the families of those affected[8, 9]. Therefore, there is an imperative to explore effective treatment together with management strategies to help children and adolescents maintain normoglycemia and promote their long-term health as well as their well-being.

In recent years, telemedicine has been widely used in the field of chronic disease management. Telemedicine (a sub-component of eHealth) has been defined as “The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communications technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and the continuing education of health care workers, with the aim of advancing the health of individuals and communities”[10]. As a gospel for patients with chronic diseases, the advantages of telemedicine can be reflected in improving access to services, ensuring continuity of care, and mitigating the costs of care delivery[11, 12]. Although telemedicine may not be able to provide physicians with comprehensive diagnostic information about a patient in the same way that a physical examination can. However, it can assist physicians in monitoring and recording certain specific physiological indicators (e.g., Blood glucose, blood oxygen concentration, blood pressure, heart rate) to help them observe the trajectory of

a patient's health[13, 14]. The current studies on telemedicine interventions for glycemic control in patients with diabetes focus on (a) Tele-monitoring, for example, a web-based telemedicine system was used to monitor patients with type 1 diabetes by Ruiz et al[15]. (b) Tele-education, such as Molavynejad et al[16] delivered tele-education to patients with diabetes using remote video-based technology. (c) Tele-consultation and Virtual Group Appointments, for instance, Bisno et al[17] provided both individual telehealth provider visits and virtual group appointments (VGA) for patients with T1DM through the CoYoT1 clinic. Moreover, previous meta-analyses have shown that the effectiveness of telemedicine in controlling blood glucose levels in patients with T1DM has been well validated[18-20]. It can be seen that telemedicine plays a huge advantage in diabetes glycemic control.

However, existing studies lack high-level evidence relating to the effectiveness of telemedicine for glycemic control in children and adolescents with T1DM. Only a few studies have reported on the potential of telemedicine in the management of T1DM in children and adolescents. Moreover, the safety and applicability of telemedicine for children and adolescents with T1DM need to be further demonstrated. Therefore, we aim to conduct a systematic review and meta-analysis of current randomized controlled trials. To provide new evidence for clinical decision-making by comparing the effectiveness of telemedicine intervention with usual care in children and adolescents with T1DM.

Study question

How does telemedicine compare with usual care in improving glycemic control among children and adolescents with T1DM? Which form of telemedicine intervention is more effective in improving glycemic control among children and adolescents with T1DM?

Study objective

This meta-analysis aimed to comprehensively synthesize and evaluate evidence

on the effectiveness of telemedicine in glycemic control among children and adolescents with T1DM.

Methods

Search strategy

Five electronic databases covering the realms of biomedicine science, clinical medicine science, and general references were screened, including PubMed, Cochrane Library, Embase, Web of Science (all databases), and CINAHL Complete. The dates searched were from establishment of each database to May 1, 2023. Search was conducted using the following keywords: ("Diabetes Mellitus, Type 1") AND ("Telemedicine" OR "Telemetry" OR "Telenursing" OR "Internet-Based Intervention") AND ("Child" OR "Adolescent"). Medical Subject Headings terms and their related trems were used. Multimedia Appendix 1 shows the detailed search terms and search process. There were no restrictions in terms of participant age, year of publication or region of study at this stage. The review protocol was reported by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 Checklist for systematic review.

Inclusion and exclusion criteria

The inclusion criteria were defined by Population, Intervention, Comparison, Outcome and Study design (PICOS) as follows: (1) Population: The target participants were children (age≤10) and adolescents (10<age≤19)[21] with T1DM. (2) Intervention: Complete or partial telemedicine intervention. A complete telemedicine intervention was one in which there was no face-to-face contact between the participants and the healthcare providers throughout the trial period from baseline to the end of the intervention, and the only telemedicine interventions were via telephone, web-based videoconferencing, an online website, or a smartphone app (all treatments (including initial treatment) were delivered via telemedicine). Partial telemedicine intervention referred to treatments that combine telemedicine with non-telemedicine interventions (such as a follow-up visit in an outpatient clinic or a visit at home). These two

broad categories of telemedicine interventions were further subdivided by the number of intervention forms. “Single” refers to the inclusion of only one form of telemedicine intervention, while “mixed” refers to the inclusion of two or more forms of telemedicine intervention. Complete telemedicine interventions are categorised as single complete telemedicine interventions and mixed complete telemedicine interventions; partial telemedicine interventions are categorised as single partial telemedicine interventions and mixed partial telemedicine interventions. (3) Comparison: Containing comparison group with usual care, included non-telemedicine intervention and also health guidance only before discharge treated as a blank control. (4) Outcome: We included all studies that reported serum glycated hemoglobin (HbA1c) levels as either their primary or secondary outcomes. (5) Study design: Only randomized controlled trials (parallel or crossover)were included.

The exclusion criteria were: (1) Studies employing non-experimental designs and quasi-experimental designs. (2) Abstracts, brief reports, conference proceedings, conference papers, posters and letters to editors. (3) Studies on gestational diabetes patients. (4) Studies published in languages other than English because of our lack of high-quality translational resources.

Study screening

Throughout the screening processes, all studies included in the analysis were independently reviewed by two researchers (KZ, CL). Firstly, we screened the titles and abstracts of all bibliographic records against the inclusion and exclusion criteria, and a label was created on the serial numbered sheet to add the reason for exclusion as a note. Secondly, we thoroughly read the full text of the study without exclusion labels to ensure that all inclusion and exclusion criteria were met. Disagreements between the researchers were resolved by meeting with a third reviewer (QH). Studies judged to be eligible at this stage were then included in the quality assessment where applicable.

Quality assessment

We assessed the risk of bias using the Cochrane risk-of-bias tool 2.0[22] against the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Two researchers (KZ, CL) assessed the trials independently and resolved any disagreements by meeting with a third reviewer (QH). The quality of each evidence was assessed by two reviewers (QH, QW) using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach[23].

Outcome

The primary outcome was HbA1c levels. Secondary outcomes were quality of life as measured by a validated instrument, daily frequency of self-monitoring of blood glucose (SMBG), the incidence of hypoglycemia and cost-effectiveness.

Data extraction

For each included study, two reviewers (KZ, CL) independently extracted the data for analysis. When data were missing or unclear, we contacted the authors. If the authors did not respond, the study was reassessed and excluded.

We extracted the following information from selected studies: (1) study characteristics (study name, author, year of publication, country, study design, attrition rate and sample size). (2) characteristics of participants (age, gender, diabetes duration, baseline Hb1Ac, total cholesterol, triglyceride, blood pressure and body mass index). (3) intervention details (duration, types of the health care providers, frequency of feedback, characteristics of intervention content, communication forms between providers and patients, technology usage modes, and telemedicine intervention forms). Communication forms included modem, short message service (SMS), email, web conference, online website(websites where patients upload blood glucose levels or other clinical data and share it with their health care providers), computer software, smart wearable devices (smart wearable devices are consumer-grade connected electronic devices that can be worn on the body as an accessory or embedded into clothing[24]),

telephone, smartphone or its applications. (4) general information about outcomes (the mean and standard deviation [SD] at baseline and at the end of the intervention, number of participants analyzed at the end of the intervention, and tools used for measurement). When several analyses were performed on the same outcome at the same time point, we extracted the data from the intention-to-treat analysis.

Data Analysis

Stata 17 and Review Manager 5.4 were used for all statistical analysis. For quantitative synthesis, we collected the difference between baseline and endpoint values for both the intervention and control groups. In the absence of information, data were estimated from the mean and the SD of baseline and endpoint values using a correlation of 0.5[25]. To ensure accuracy, the different correlations such as 0.4 and 0.6 were used for estimation data and sensitivity analysis. The final results showed that the estimated results obtained using the different correlations remain stable after sensitivity analysis[25]. The data conversion tools were used to convert the median, maximum, and minimum values reported in the included studies into mean[26] and SD[27]. We reported the results of secondary outcomes when data from at least 2 studies could be merged. The magnitude of the overall effect size was calculated based on the pooled mean difference (MD) with 95% confidence interval (CI) when the same measures were used in studies. If outcomes were measured using different outcome measurement scales, pooled standard mean difference (SMD) with 95% CI was adopted. A p-value<.05 was considered statistically significant.

A random-effects or fixed-effects meta-analysis for continuous data was performed based on the results of the heterogeneity test. Study heterogeneity was determined using the Cochran Q test and Higgins I^2 test. I^2 of 25%, 50% and 75% indicates low, moderate and high heterogeneity, respectively[25]. If p>.1 and I^2<50% are identified, fixed-effects models were used, otherwise, random-effects models were applied. To ensure the robustness of our results, a sensitivity

analysis was performed by using leave-one-out analysis to assess the contribution of each study to the merged effect size.

The publication bias was assessed creating funnel plots, Begg test, and performing the Egger regression test (considered significant at $p<.05$) by two reviewers (QW, CL), and the agreement was reached by consensus[28, 29]. For the primary outcome, we performed a series of subgroup analyses to quantify specific differences in the size of effects of particular telemedicine interventions based on study characteristics and intervention characteristics[30]. Moreover, we performed a univariable meta-regression analysis to investigate whether there was heterogeneity due to differences in study characteristics or intervention characteristics.

Protocol deviation

First, The intervention group in the registration programme refers to web-based telemedicine interventions, which are expressed in a broader and simpler way. After further research, we decided to categorise the interventions into complete telemedicine interventions and partial telemedicine interventions. These two broad categories of telemedicine interventions were further subdivided by the number of intervention forms. “Single” refers to the inclusion of only one form of telemedicine intervention, while “mixed” refers to the inclusion of two or more forms of telemedicine intervention. Complete telemedicine interventions are categorised as single complete telemedicine interventions and mixed complete telemedicine interventions; partial telemedicine interventions are categorised as single partial telemedicine interventions and mixed partial telemedicine interventions. These changes and clarifications help to explain the impact of the “face-to-face contact between patient and healthcare provider” factor on telemedicine effectiveness during telemedicine interventions, which has important implications for the development of future telemedicine interventions.

Second, the definition of the control group is also an oversimplification, such as

“usual care”, so we illustrate two cases of “usual care” in this study, including a non-telemedicine intervention and also health guidance only before discharge treated as a blank control.

Third, regarding secondary outcomes, initially we identified secondary outcomes based on studies related to diabetes telemedicine in adults and other types of diabetes. However, during the literature reading, it was found that no studies analysed blood pressure, weight, and patient satisfaction as study outcomes in telemedicine interventions on children and adolescents with T1DM. Some studies used only weight and blood pressure as baseline indicators and lacked post-intervention data. Other studies only asked subjects how satisfied they were with the telemedicine intervention through interviews at the end of the intervention, which prevented us from quantitatively assessing it. Secondary outcomes such as blood pressure, weight, and patient satisfaction were therefore removed.

Finally, regarding the data synthesis strategy, we modified and improved the part of it for missing data estimation. Because data for the primary and secondary outcomes were partially missing, we first used the commonly used 0.5 as a correlation coefficient for data estimation according to the Cochrane Handbook for the Systematic Evaluation of Interventions. However, as there is currently no clear specification for the use of correlation coefficients for data estimation (only a broad range of choices), to ensure that the effect sizes synthesised using the 'estimated data' are sufficiently stable, we also used 0.4 and 0.6 as correlation coefficients for data estimation. (Our main purpose was to see if the new estimated effects with the new correlation coefficients would pass the sensitivity analyses after changing the correlation coefficient). The sensitivity analyses showed that the results synthesised after estimating the missing data using all three correlation coefficients were stable and reliable. But the data estimated

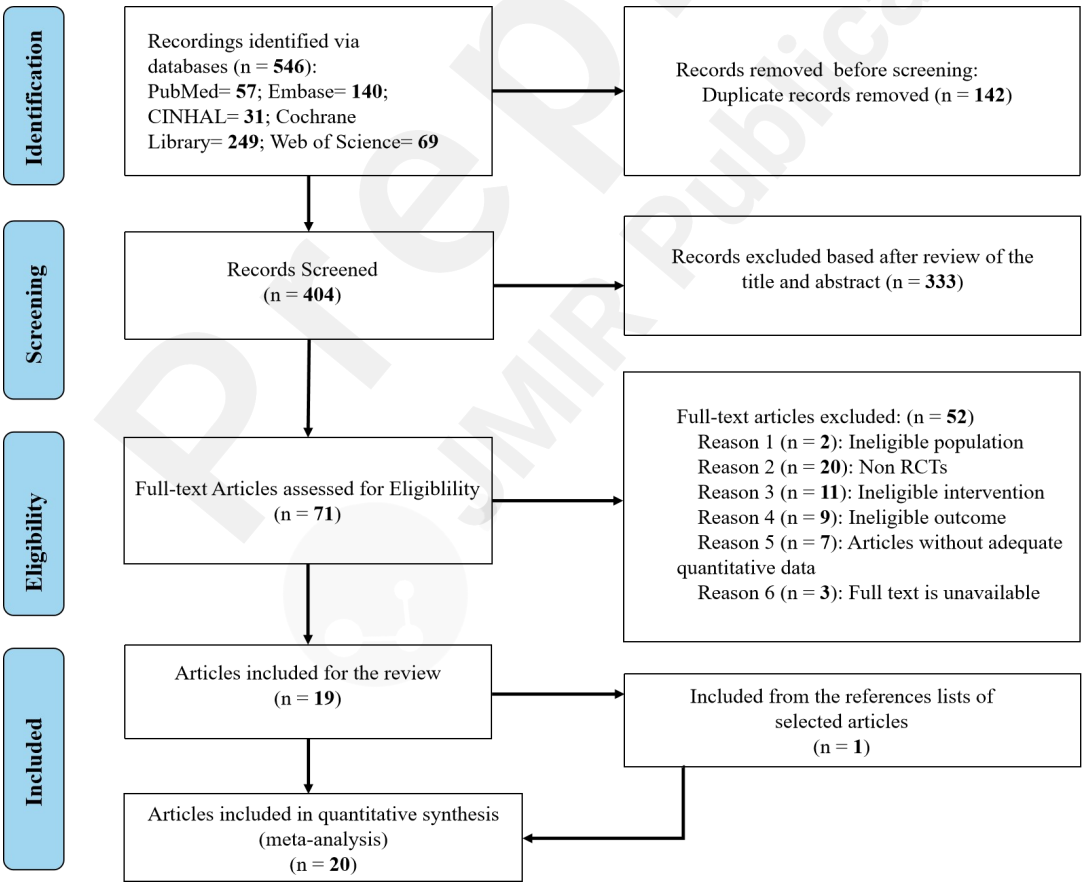
with the more common correlation coefficient of 0.5 was used as the result of this study.

Results

Search results

The phases of the electronic search, identification and screening for eligible studies are depicted in the PRISMA flowchart (Figure 1). A total of 546 studies were identified using the search strategy described above. After removing duplicates and screening titles and abstracts, studies were retained for full-text evaluation. Finally, a total of 20 studies with 1704 participants were included in this systematic review and meta-analysis.

Figure 1. PRISMA flowchart depicting the main stages of the systematic review process.



Study Characteristics

The characteristics of the studies are summarized in Supplementary Table S1. Eighteen studies were parallel group RCTs[31-48], and two were crossover studies[49, 50]. Of the 20 included studies, 12 were published after 2015. Eight studies were published in North America (40%)[31-34, 37, 39, 40, 44], seven studies were published in Europe (35%)[35, 36, 43, 45-47, 49], four studies were published in Asia (20%)[38, 42, 48, 50], one study was published in Oceania[41]. The sample size of studies ranged from 20 to 240, with the intervention periods ranging from 3 months to 60 months. All participants included in the studies were under the age of 20 and had T1DM. The median mean age at baseline was 13.5 years, and the median mean diabetes duration at baseline was 6.2 years. Eighteen studies were performed in adolescents (mean age: 13.6 years, range: 10.8-17.3 years) and two studies were performed in children (mean age: 5.8 years, range: 5.6-6.1 years). The proportion of female participants at baseline ranged from 42% to 62%. The floored threshold value of baseline HbA1c in 7 studies was 7.5% or greater.

Intervention Characteristics

The telemedicine systems used in most studies were relatively simple to operate, having clear processes and included data transmission of blood glucose data with feedback (75%; n=15)[31-34, 36, 38, 39, 41, 43-47, 49, 50] or blood glucose data only (25%; n=5)[35, 37, 40, 43, 48]. A specialist diabetes care team, including a diabetologist, nurse, dietician and psychologist, was reported in nine studies[32, 34, 39, 41, 43-45, 47, 50]. Feedback was provided monthly or less in 10 studies[33, 36, 41, 43-47, 49, 50], every two weeks or more in five studies[31, 32, 34, 38, 39], and the frequency of feedback was not specified in five studies(Table 1)[35, 37, 40, 42, 48].

The communication technologies used in the telemedicine interventions we included in the various studies took a variety of forms. Patients initiated

communication with healthcare providers through different forms of telemedicine: smart wearable device (30%; n=6)[33, 36, 42, 44, 45, 50], smartphone application (25%; n=5)[32, 34, 46-48], modem (15%; n=3)[31, 37, 39], online website (15%; n=3)[38, 40, 43], telephone (10%; n=2)[41, 49] and unclear (5%; n=1)[35]. Healthcare providers initiated communication with patients through different forms of telemedicine: smartphone application (25%; n=5)[33, 46-49], online website (15%; n=3)[37, 40, 50], web conference (15%; n=3)[43-45], telephone (15%; n=3)[31, 38, 41], SMS (15%; n=3)[32, 34, 35], computer software (10%; n=2)[36, 39] or smart wearable device (5%; n=1)[42]. Seventeen studies mainly used various types of software[32-40, 43-50], three studies used hardware[31, 41, 42].

Nine studies involved patients using telemedicine with parental assistance[36, 37, 41, 43-47, 50], six studies involved patients using telemedicine independently[33-35, 38, 42, 48]. The form of intervention was complete telemedicine intervention in twelve studies[31, 34, 37, 40-44, 46-48, 50] and partial telemedicine intervention in eight studies[32, 33, 35, 36, 38, 39, 45, 49]. The content of telemedicine interventions in different studies included a variety of features: interactive communication and follow-up (85%; n=17)[31-34, 36, 38, 39, 41-50], medication dose adjustment (70%; n=14)[32, 34, 36-39, 41, 42, 44-47, 49, 50], basic health education (45%; n=9)[31, 32, 34, 40, 41, 43, 45, 47, 48], diet guidance (45%; n=9)[36, 37, 39, 41-43, 47-49] and Physical exercise (30%; n=6)[32, 41-43, 45, 48]. 11 studies reported characteristics of the content of the intervention that included at least three features[32, 34, 36, 39, 41-43, 45, 47-49]. No features of the content of telemedicine interventions were reported in one study[35].

Table 1. Characteristics of telemedicine interventions.

First author,	Health care	Communication forms	Frequency	Intervention content	Technology	Te

year, country	provider	Provider to patient	Patient to provider	of feedback	Interactive follow-up	Medication adjustment	Diet guidance	Physical exercise	Basic health education	usage modes	y f
Chase et al., 2003, America	Nurse Doctor	Telephone	Modem	every 2 week	Y	N	N	N	Y	–	Ha
Gandrud et al., 2018, America	Diabetes educator Nurse Doctor	SMS E-mail	Smartphone application	weekly	Y	Y	N	Y	Y	–	So
Goyal et al., 2017, Canada	Human factors specialist Nurse Doctor	Smartphone application Telephone	Smart wearable device	every 3 month	Y	N	N	N	N	Independently	So
Han et al., 2015, America	Diabetes educator Nurse Doctor	SMS	Smartphone application SMS	every 2 day	Y	Y	N	N	Y	Independently	So
Ibrahim et al., 2021, European	Diabetologist	SMS	–	–	N	N	N	N	N	Independently	So
Klee et al., 2018, Switzerland	Nurse Diabetologist	Smartphone application Online website	Telephone E-mail	monthly	Y	Y	Y	N	N	–	So
Kowalska et al., 2017, Poland	Pediatrician Diabetologist	Computer software	Smart wearable device	every 13 week	Y	Y	Y	N	N	Parental assistance	So
Kumar et al., 2004, America	Trained research assistant	Online website	Modem Smart wearable device	–	N	Y	Y	N	N	Parental assistance	So

Landau et al., 2012, Israel	Dietitian Pediatric endocrinologist	Telephone	Online website Smart wearable device	every week		Y	Y	N	N	N	Independently	So
Marrero et al., 1995, America	Pediatric diabetologist Nurse social workers Dietitians	Computer software Telephone	Modem	every week	2	Y	Y	Y	N	N	–	So
Mulvaney et al., 2010, America	Diabetes professionals	Online website	Online website	–		N	N	N	N	Y	–	So
Nunn et al., 2006, Australia	Pediatric endocrinologists Nurse dietitian social worker	Telephone	Telephone	every month	2	Y	Y	Y	Y	Y	Parental assistance	Ha
Raviteja et al., 2019, India	Consultant Doctor	Smart wearable device	Smart wearable device Computer software	–		Y	Y	Y	Y	N	Independently	Ha
Schiaffini et al., 2016, Italy	Diabetologist Nurse Dietician Psychologist	Web conference	Online website Smart wearable device	every month		Y	N	Y	Y	Y	Parental assistance	So
Shalitin et al., 2014, Israel	Diabetes care team	Online website E-mail Telephone	Smart wearable device Online website	every month		Y	Y	N	N	N	Parental assistance	So

Stanger et al., 2018, America	Pediatric endocrinologist Diabetes care team	Web conference	Smart wearable device	every month(last period)	Y	Y	N	N	N	Parental assistance	So
von et al., 2020, Germany	Regular home diabetes team	Web conference	Smart wearable device Computer software	every month	Y	Y	N	Y	Y	Parental assistance	So
Ware(2) et al., 2022, UK	Nurse Doctor	Smartphone application Telephone email	Smartphone application Smart wearable device	every month	Y	Y	N	N	N	Parental assistance	So
Ware et al., 2022 UK	Research team Clinical team	Smartphone application Telephone E-mail	Smartphone application Smart wearable device	every month	Y	Y	Y	N	Y	Parental assistance	So
Xu et al., 2021, China	Nurse Third-party health manager	Smartphone application	Smartphone application Smart wearable device	–	Y	N	Y	Y	Y	Independently	So

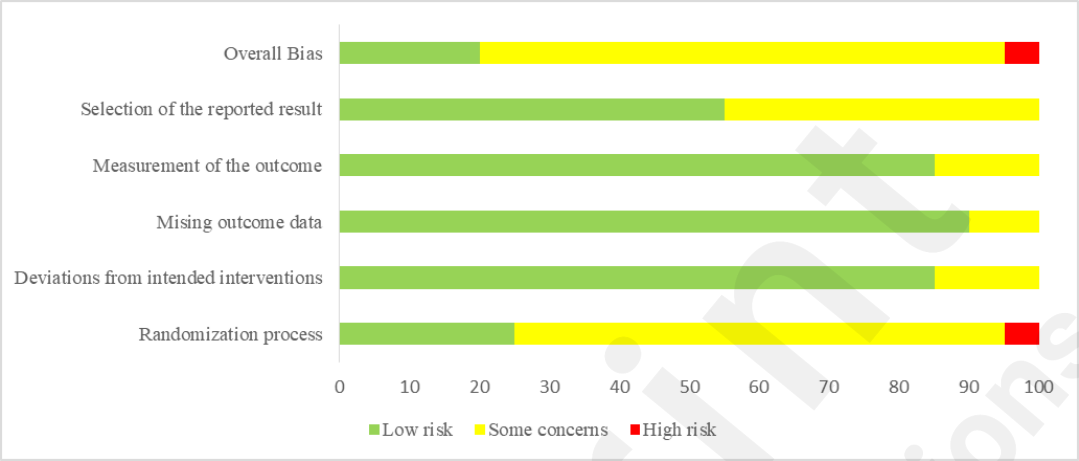
Note: SMS = Short Message Service; “–” = not reported.

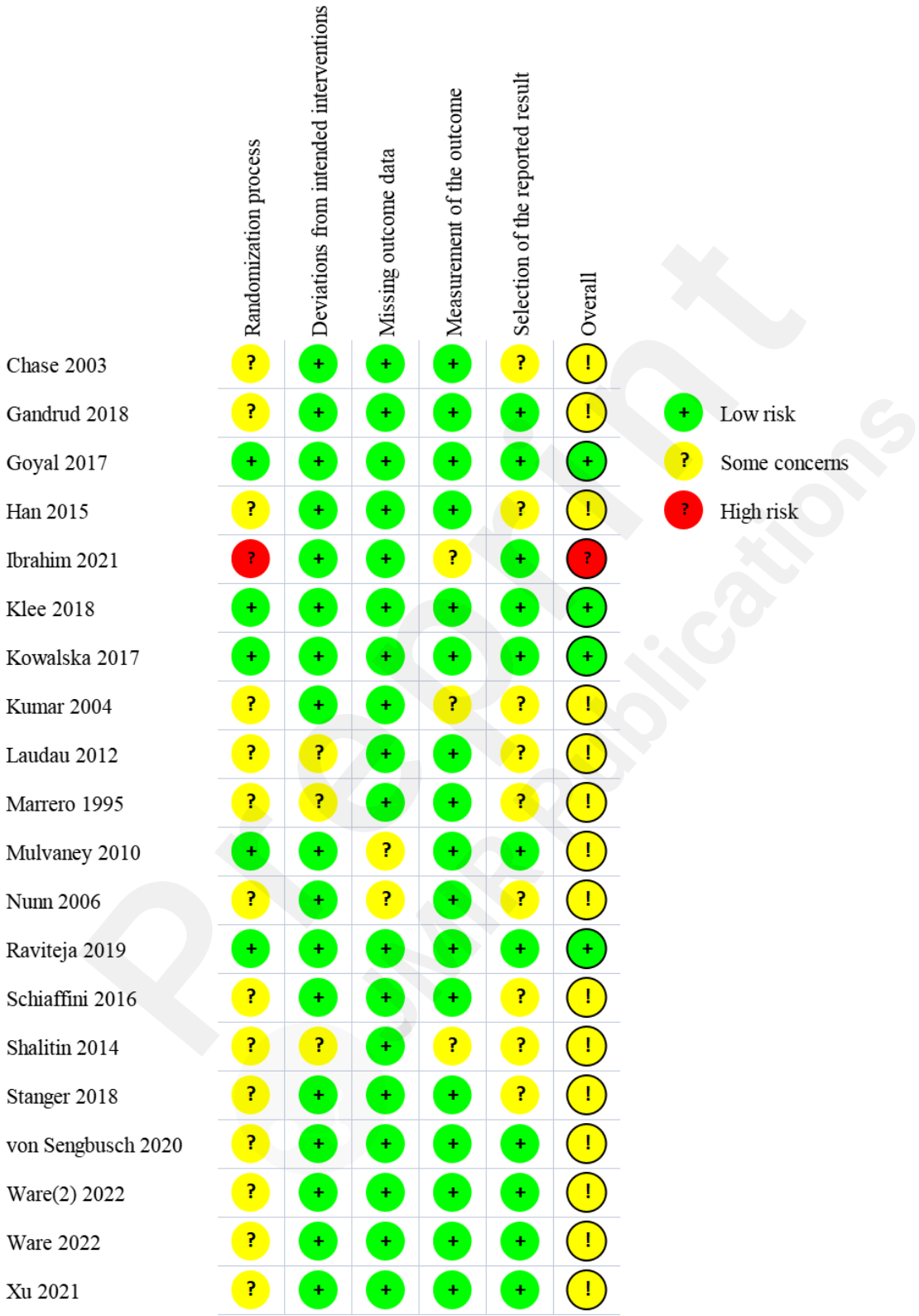
Risk of Bias

Based on the Cochrane Risk of Bias tool version 2.0, all studies, except for one with a high risk of bias[35] and four with a low risk of bias[33, 36, 42, 49], were found to have “some concerns” (Figure 2). The greatest bias was found in the Randomization process. Randomization was reported to be implemented in all studies, amongst which only 5 studies explicitly described the randomization strategies and properly applied the allocation concealment[33, 36, 40, 42, 49]. The other study was rated as high risk because of baseline differences between intervention groups. No pre-registration was reported in nine studies[31, 34, 37-39, 41, 43, 44, 50], and the risk of bias regarding the choice of reporting

outcomes was rated as “some concern”. One of the domains with the highest proportion of low risk of bias was “bias from mising outcome data”.

Figure 2. Risk of bias graph of the included studies.





Meta-analysis and Descriptive Analysis results

A summary of the main results for the comparisons with GRADE ratings is presented in Table 2. Detailed meta-analytic forest plots on all outcomes and subgroups are shown in Figure 3, Supplementary Figure S2 and S3 in Multimedia Appendix 1.

Table 2. Summary of findings: Telemedicine compared to usual care for glycemic control in children and adolescents with T1DM.

Certainty assessment							Patients, N		Effect	Certainty
Studies, n	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemedicine	Usual care	Absolute (95% CI)	
HbA1c										
20	randomised trials	serious[a]	not serious[b]	not serious	serious[c]	none	822	822	MD[k] **-0.22** (−0.33 to −0.10)	⨁⨁◯◯ Low
DQOLY (Impact of diabetes)										
2	randomised trials	serious[d]	not serious	not serious	very serious[e]	none	30	23	MD **1.27** (−3.31 to 5.86)	⨁◯◯◯ Very low
DQOLY (Worries about diabetes)										
2	randomised trials	serious[d]	not serious	not serious	very serious[e]	none	30	23	MD **0.58** (−2.59 to 3.66)	⨁◯◯◯ Very low
DQOLY (Satisfaction with diabetes)										
2	randomised trials	serious[d]	serious[f]	not serious	very serious[e]	none	30	23	MD **3.27** (−12.53 to 19.08)	⨁◯◯◯ Very low
NQOL										
3	randomised trials	serious[g]	not serious	not serious	serious[h]	none	165	160	SMD[i] **-0.24** (−0.45 to −0.02)	⨁⨁◯◯ Low
SMBG										

Certainty assessment							Patients, N		Effect	Certainty
Studies, n	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Telemedicine	Usual care	Absolute (95% CI)	
3	randomised trials	serious[i]	serious[f]	not serious	very serious[e]	none	96	91	MD **0.54** (−0.72 to 1.8)	⊕●●● Very low

Incidence of hypoglycemia

4	randomised trials	serious[j]	serious[f]	not serious	serious[h]	none	153	156	MD **−0.22** (−0.66 to 0.23)	⊕●●● Very low

[a]Downgraded for unclear or inadequate randomization process(75% of included studies). A large number of studies were not adequately concealed due to the nature of the intervention.

[b]Although Cochran Q test and Higgins I^2 test suggested a low heterogeneity, we chose not to downgrade for inconsistency as this was fully explained by the inclusion of 1 study.

[c]65% of studies had sample sizes of less than 50 in both arms.

[d]One of the studies had some concerns(a moderate risk of bias).

[e]Sample sizes for each arm of the included studies were less than 50.

[f]Significant heterogeneity..

[g]All three studies had some concerns.

[h]There was at least one study with a sample size of less than 50 in both arms.

[i]Two studies had some concerns.

[j]One studies had some concerns.

[k]mean difference

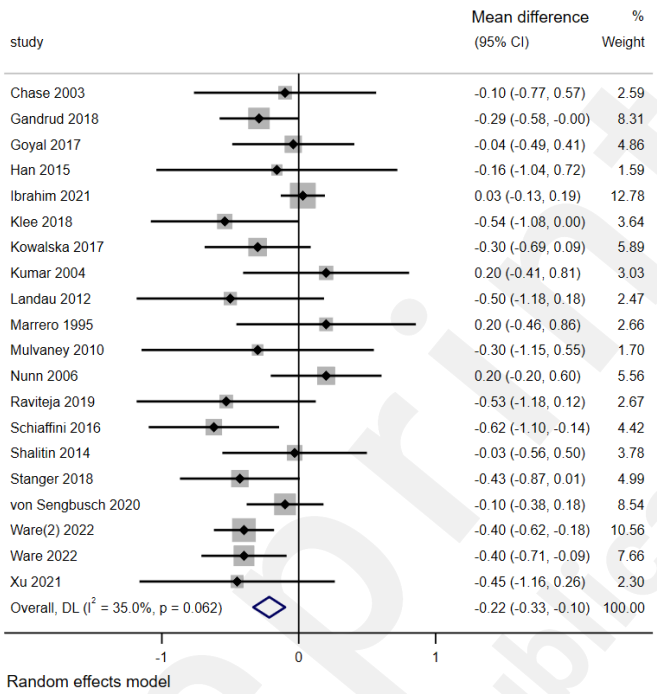
[l]standardised mean difference

Effect of Telemedicine Intervention on HbA1c

Twenty studies reported HbA1c at 3-50 months, examining 1704 participants were included in the meta-analysis. Overall, telemedicine was found to reduce HbA1c by 0.22% (95% CI –0.33 to –0.10; p<.001) at the end of the intervention. Further, the heterogeneity of the effect size was confirmed, as I^2 was 35.0% (Q= 29.23, Q-df=19, p<.1(P-value=.062)), suggesting heterogeneity of a low degree. Given the wide variety of technologies available for telemedicine, the heterogeneity of results is not surprising. No significant improvements were noted at the end of 3-month (MD –0.30; 95% CI –0.62 to 0.02; p=.07; n=4) or 12-month (MD –0.04; 95% CI –0.33 to 0.40; p=.85; n=2) follow-up; however, significant improvement was found at the end of the 6-month follow-up (MD –

0.21; 95% CI –0.37 to –0.05; *p*=.01; n=8).

Figure 3. Forest plot of the comparison: telemedicine interventions versus usual care. Outcome: HbA1c.



Effect of Telemedicine Intervention on Secondary Outcomes

We pooled the Diabetes Quality of Life for Youth (DQOLY)[51, 52] from 2 studies (n=53)[34, 49], Non-youth-specific quality of life (N-QOL) (using Diabetes Quality of Life[53] and Health-related Quality of Life[54]) from 3 studies (n=334) [45, 48, 50], daily frequency of SMBG from 3 studies (n=187)[33, 44, 50] and incidence of hypoglycemia from 4 studies (n=309)[33, 36, 42, 48].

There was no significant effect size in secondary outcomes except N-QOL, with MD for DQOLY (DQOLY-Impact of diabetes subscale: MD 1.27; 95% CI –3.31 to 5.86, n=53, I^2=32.2%; DQOLY-Worries about diabetes subscale: MD 0.58; 95% CI –2.49 to 3.66, n=53, I^2=23.8%; DQOLY-Satisfaction with diabetes subscale: MD 3.27; 95% CI –12.53 to 19.08, n=53, I^2=75.6%), with SMD of –0.24 for N-QOL (95% CI –0.45 to –0.02; n=334; I^2=0%), MD of 0.54 for daily frequency of SMBG

(95% CI –0.72 to 1.80; n=187; I^2=67.8%) and SMD of –0.22 for incidence of hypoglycemia (95% CI –0.66 to 0.23; n=309; I^2=73.7%).

Only one study[31] reported economic data. The difference in cost-effectiveness of care between the two groups was significant. The average cost per patient in the intervention group for the 6 months was $163.00. The control group spent an average of $246 to visit the clinic. If additional costs (average $59) such as mileage, parking, meals, hotel stays, and babysitting were included,the average cost of a clinic visit increasedto $305. This result shows that the telemedicine intervention was cost-effective, at least in America.

Subgroup analysis of HbA1c

Our subgroup analysis based on characteristics of study and intervention revealed that the subgroup differences that yielded statistical significance were publication date, communication forms (from patient to provider), and interactive follow-up (Table 3).

Regardless of age, intervention duration and health care provider, HbA1c significantly decreased in all studies after the telemedicine intervention.

Table 3. Summary of subgroup analysis based on HbA1c.

Characteristics	Subgroup	No. of trails (No. of participants)	Effect size MD, 95%CI	I^2	*p*-Value (Q test)	Heterogeneity between groups
Age						0.058
	Children	2(210)	−0.41(−0.62 to −0.20)	0	0.712	
	Adolescent	18(1434)	−0.18(−0.30 to −0.06)	28.1	0.129	
Publication date						0.010
	2010 and before	5(384)	0.11(−0.15 to 0.37)	0	0.804	
	After 2010	15(1260)	−0.27(−0.40 to −0.15)	36.8	0.075	
Intervention duration						0.199
	Less than 6 months	8(495)	−0.32(−0.48 to −0.17)	0	0.580	
	At least 6 months	12(1149)	−0.18(−0.33 to −0.03)	43.2	0.055	

Health care provider						0.884
	Professional diabetes care team	9(850)	−0.21(−0.38 to −0.04)	33.5	0.150	
	No professional diabetes care team	11(794)	−0.23(−0.40 to −0.06)	40.7	0.077	
Feedback frequency						0.426
	Greater than once a month	5(364)	−0.23(−0.449 to −0.002)	0	0.629	
	Less than or equal to once a month	10(983)	−0.27(−0.41 to −0.12)	35.6	0.123	
	Unclear	5(297)	−0.08(−0.32 to 0.16)	20.3	0.285	
Communication forms						
Provider-to-Patient						0.259
	Telephone	3(244)	−0.06(−0.46 to 0.35)	34.9	0.215	
	SMS	3(229)	−0.10(−0.35 to 0.15)	45.4	0.160	
	Smartphone application	5(440)	−0.37(−0.53 to −0.21)	0	0.620	
	Computer software	2(211)	−0.12(−0.59 to 0.35)	39.6	0.198	
	Online website	3(127)	0.00(−0.36 to 0.36)	0	0.634	
	Web conference	3(330)	−0.34(−0.65 to −0.02)	49.9	0.136	
	Smart wearable device	1(63)	−0.53(−1.18 to 0.12)	-	-	
Patient-to-Provider						0.002
	Modem	3(209)	0.11(−0.26 to 0.48)	0	0.764	
	Smartphone application	5(453)	−0.37(−0.51 to −0.22)	0	0.955	
	Smart wearable device	6(595)	−0.20(−0.37 to −0.03)	0	0.597	
	Telephone	2(156)	−0.15(−0.87 to 0.58)	78.3	0.032	
	Online website	3(139)	−0.53(−0.89 to −0.18)	0	0.808	
	Not reported	1(92)	0.03(−0.13 to 0.19)	-	-	
Technology forms						0.505
	Hardware	3(249)	−0.08(−0.51 to 0.35)	43.2	0.172	
	Software	17(1395)	−0.23(−0.36 to −0.11)	34.8	0.079	
Technology usage modes						0.534
	Independent use	6(374)	−0.11(−0.31 to 0.09)	0	0.526	
	Parental assistance	9(899)	−0.24(−0.41 to −0.07)	44.1	0.074	
	Unclear	5(371)	−0.26(−0.47 to −	0	0.526	

			0.04)			
Telemedicine intervention forms						0.206
	Complete telemedicine intervention	12(802)	−0.28(−0.43 to −0.13)	20.5	0.242	
	Partial telemedicine intervention	8(842)	−0.14(−0.29 to 0.01)	29.4	0.193	
Interactive follow-up						0.002
	With feature	17(1460)	−0.27(−0.38 to −0.17)	8.9	0.350	
	Without feature	3(184)	0.03(−0.12 to 0.18)	0	0.643	
Medication adjustment						0.577
	With feature	14(1267)	−0.25(−0.37 to −0.12)	20	0.236	
	Without feature	6(377)	−0.17(−0.41 to 0.07)	37.4	0.157	
Physical exercise						0.823
	With feature	6(691)	−0.24(−0.47 to 0.01)	44.6	0.108	
	Without feature	14(953)	−0.21(−0.35 to −0.07)	35.2	0.094	

Population of the study

No statistically significant subgroup differences were identified in the subgroup analysis by age. Statistically significant decrease in HbA1c was observed in subgroups of children (MD –0.41; 95% CI –0.62 to –0.20, p<.001), and adolescents (MD –0.18; 95% CI –0.30 to –0.06, p=.003). The children's group reported a higher mean difference compared to the adolescent group.

Publication date of studies

Subgroup analysis stratified by publication date demonstrated significant effectiveness of studies published after 2010 on glycemic control in children and adolescents with T1DM compared with those published before 2010. Moreover, decrease in heterogeneity and statistically significant subgroup differences was found in subgroup analysis based on publication date (p=.010), which can explain the heterogeneity in overall effect on HbA1c.

Duration of telemedicine interventions

We created two subgroups: interventions lasting less than six months, and interventions lasting at least six months. The result revealed that telemedicine interventions lasting less than six months demonstrated a more significant reduction in HbA1c level (MD –0.32; 95% CI –0.48 to –0.17; p<.001).

Health care provider of telemedicine interventions

Subgroup analysis based on health care provider demonstrated significant effectiveness with or without the professional diabetes care team, and similar mean differences were reported between the two groups (With MD –0.21; 95% CI –0.38 to –0.04; p=.016. Without MD –0.23; 95% CI –0.40 to –0.06; p=.010).

Feedback frequency of telemedicine interventions

Contrary to the non-significant overall effect of –0.01 on HbA1c in 5 studies with feedback (not reported), the overall effect in 5 studies with feedback (greater than once a month) was –0.23 (95% CI –0.449 to –0.002; p=.048) and the overall effect in 10 studies with feedback (less than or equal to once a month) was –0.27 (95% CI –0.41 to –0.12; p<.001); studies were of statistical significance.

Communication forms between patients and providers

The choice of provider-to-patient communication forms, smartphone application (MD –0.37; 95% CI –0.53 to –0.21; p<.001) and web conference (MD –0.34; 95% CI –0.65 to –0.02; p=.039), significantly influenced the effect of telemedicine on HbA1c. In addition, the choice of patient-to-provider communication in the form of a smartphone application (MD –0.37; 95% CI –0.51 to –0.22; p<.001), smart wearable devices (MD –0.20; 95% CI –0.37 to –0.03; p=.020) and an online website(MD –0.53; 95% CI –0.89 to –0.18; p=.003) had a significant impact on the effect of HbA1c. Statistically significant subgroup difference was found in subgroup analysis based on patient-to-provider communication forms(p=.002).

Forms of technology

Subgroup analysis by forms of technology showed that studies using software (MD –0.23; 95% CI –0.36 to –0.11; p<.001) had a significant effect on glycemic control in children and adolescents with T1DM compared with studies using only

hardware (MD –0.08; 95% CI –0.51 to 0.35; p=.708).

Modes of technology usage

The overall effect on HbA1c for the 6 studies with independent use of technology was –0.11(95% CI –0.31 to 0.09; p=.271), whereas the overall effect on HbA1c for the 9 studies with parental assistance was –0.24 (95% CI –0.41 to –0.07; p<.001).

Forms of telemedicine interventions

Subgroup analysis based on the form of telemedicine intervention showed that the complete telemedicine intervention (MD –0.28; 95% CI –0.43 to –0.13; p<.001) was better than the partial telemedicine intervention (MD –0.14; 95% CI –0.29 to 0.01; p=.062).

Content of telemedicine interventions

Interventions with interactive communication and follow-up (MD –0.27; 95% CI –0.38 to –0.17; p<.001) and Medication dose adjustment (MD –0.25; 95% CI –0.37 to –0.12; p<.001) were associated with the greater improvement in HbA1c. However, Interventions without physical exercise feature also significantly influenced the effect of telemedicine on HbA1c (MD –0.21; 95% CI –0.35 to –0.07; p=.004). Moreover, a decrease in heterogeneity and statistically significant subgroup differences was found in subgroup analysis based on interactive communication and follow-up (p=.002), which can also explain the heterogeneity in overall effect on HbA1c.

Sensitivity analysis

Leave-one-out analysis was performed by removing each study and there was no significant change in the effect size (Supplementary Figure S3 in Multimedia Appendix 1). Accordingly, no individual study had a statistically significant effect on the overall result. However, inspection of the effect size identified one outlier study[35] with an effect size larger than other studies. The exclusion of this study did not materially affect our results for the primary outcome, but it did reduce heterogeneity (I^2=9.0, Q=19.87, Q-df=18, p=.34, fixed effects model), and increased the impact of telemedicine (MD –0.26; 95% CI –0.36 to –0.17; p<.001).

Publication bias

The contour funnel plot of HbA1c was not obviously asymmetrical, consistent with publication bias (Supplementary Figure S1 in Multimedia Appendix 1). We used Egger's regression test and Begg's test to verify the publication bias. The regression analysis's bias estimate was insignificant (Egger's test: bias –1.02, p=.320; Begg's test: z=0.16, p=.871).

Meta-regression

The results of the meta-regression were presented in Supplementary Table S2 in Multimedia Appendix 1. Meta-regression analysis showed that publication date (p=.035), and "Interactive follow-up" of intervention characteristics (p=.015) were moderator factors to explain the heterogeneity of this study.

Discussion

Principal Results

In this systematic review and meta-analysis of randomized controlled trials comparing telemedicine with usual care, the difference in HbA1c in favor of telemedicine (MD –0.22, reduction, p<.001). Sensitivity analysis showed low heterogeneity (I^2=35.0%, p=.062) and stability of the outliers. Subgroup analyses revealed that the studies published after 2010, studies with less than six months of follow-up, studies in children with T1DM, studies in the form of smartphone applications (provider-to-patient) and online website (patient-to-provider) for communication, and studies with medication dose adjustment reported significantly larger effects of telemedicine. We were delighted to find that smartphone apps may be a particularly effective way of connecting providers and patients, and telemedicine improves quality of life for children and adolescents with T1DM (SMD –0.24; 95% CI –0.45 to –0.02; p=.035; I^2=0%). However, there was no direct evidence that telemedicine could reduce the risk of hypoglycemia and improve SMBG. Our findings may help guide future clinical decision-making about the use of telemedicine for T1DM in children and adolescents.

Comparison with Prior Work

Our results showed that the telemedicine intervention significantly reduced HbA1c in children and adolescents with T1DM, which is similar to the previous meta-analyses in adults[20, 55-57]. A recent study pointed out that the telemedicine intervention for HbA1c in adults had a significant treatment effect[18]. In addition, Shulman et al[58] found no evidence for the effectiveness of telemedicine on HbA1c in the 2010 meta-analysis specifically targeting T1DM in adolescents, which is consistent with the results of this study's time-of-publication subgroup analysis. This suggested that telemedicine has evolved and improved rapidly over the past decade or so, and is showing benefits for the treatment of children and adolescents with T1DM. And also the results of this study are contrary to the findings of Lee et al[20], Lee et al's study did not find that telemedicine improved glycemic control in children and adolescents with T1DM by subgroup analysis.

Although improvements in the secondary outcomes of hypoglycemia risk and SMBG were not confirmed, it is encouraging to find that telemedicine improves quality of life in children and adolescents withT1DM. This is in contrast to previous studies with adolescents and children, where Shulman et al[58] did not find differences in quality of life between the telemedicine and control groups. And it is also contrary to the results of previous studies[55, 57] that did not restrict the type of diabetes and studies of T1DM[20] that did not restrict the population, which did not find a benefit of telemedicine in terms of quality of life.

In terms of studying the effect of follow-up time on HbA1c. Previous studies (Not specifically for T1DM)[55, 57, 59] have shown that the effectiveness of telemedicine is higher when the study’s intervention duration is at least 6 months or longer. However, our findings are contrary to those presented above.

Our subgroup analysis showed a higher treatment effect in studies that lasted less than six months than in studies that lasted at least six months. This may be related to the “honeymoon” phase of T1DM. A “honeymoon” phase is a transient period of T1DM remission, characterized by a significant reduction in insulin requirements and good glycemic control due to a temporary restoration of pancreatic β-cell function, which usually lasts for several months. The exact mechanisms are still uncertain, but one of the generally recognized mechanisms is that correction of “glucotoxicity” by exogenous insulin therapy leads to “β-cell rest” and β-cell recovery[60]. The concept of “honeymoon” phase was first described by Jackson et al[61]. They observed a rapid decline in demand for exogenous insulin in diabetic children after regular insulin treatment. In general, patients enter the “honeymoon” period about 3 months after starting insulin therapy, which can last 6 to 9 months. Therefore, it is reasonable to speculate that in T1DM studies with shorter intervention durations, patients are more likely to be influenced by the “honeymoon” period, and thus show a better intervention effect. Future RCTs in this area should carefully consider the duration of telemedicine interventions in their design, which should be greater than six months or longer if possible, especially if it is not sufficiently known that the enrolled group is in or has passed the “honeymoon” period. This is to minimize the effects of the intervention being influenced by the “honeymoon” period, and to improve the realism and reliability of the effectiveness of telemedicine interventions. In addition, this may also be related to the fact that this study targeted children and adolescents with T1DM. Another alternative explanation might be that patients become less responsive to monitoring prompts as the potential novelty of telemedicine interventions diminishes. This explanation is well recognized in the related area of activity tracking by smart wearable device[62].

Our subgroup analysis results suggested differences between children and

adolescents. Telemedicine interventions had a greater effect in the children's study compared to the adolescent group. This contrasts with the findings of Shulman et al[58], who showed no difference in HbA1c between the adolescent and child subgroups at the end of the intervention. It may also be due to different criteria for defining children than those they studied. Regardless, according to the most recent age criteria for children and adolescents, we anticipate that more child-related studies in the future may make this difference more apparent. By conducting subgroup analysis, we have preliminarily excluded the influence of technology forms and usage modes on this result. Two studies were conducted in the children's group, one using a hardware device independently[42] and the other using software with parental assistance[46]. However, we found that the studies in the children's group were all complete telemedicine interventions. Subgroup analysis based on intervention form showed that the complete telemedicine intervention was better than the partial telemedicine intervention, which could explain the observed results. This finding is supported by Chen et al's study[63], which found that a mixed complete telemedicine intervention was superior to a partial telemedicine intervention in reducing the incidence of pressure injury in patients with spinal cord injury. Another plausible explanation is that children's blood glucose is more prone to fluctuations and a higher incidence of hypoglycemia compared to adolescents, which may lead to an exaggerated intervention effect. Although HbA1c is the gold standard for long-term glycemic control, the use of HbA1c alone to assess glycemic management in children can be misleading due to the magnitude of blood glucose fluctuations[64], and the pursuit of HbA1c compliance can be accompanied by an increase in the frequency of hypoglycemia[65, 66]. Hypoglycemia in children is a metabolic-endocrine emergency due to the potential for brain injury, permanent neurological sequelae and, in rare cases, death[67]. Therefore, when assessing glycemic control in children, special attention should be paid to the incidence of hypoglycemia. We also found that telemedicine interventions with medication

dose adjustment reported significant treatment effects in improving glycemic control in children and adolescents, consistent with the results of a study[55] on the effects of telemedicine on HbA1c in patients with diabetes. Consequently, future well-designed studies should consider further enhancing insulin adjustment and monitoring in the intervention.

Based on the subgroup analysis by communication forms, our results suggested that smartphone application may be a very effective vehicle for linking intervention providers and patients, which can provide an intelligent management pathway in the management of blood glucose in children and adolescents with T1DM. Nkhoma et al[68] also supported that smartphone applications improved glycemic control better than other tools. Moreover, the smartphone application studies included in this review all evaluated the safety of applications and reported the incidence of adverse events such as hypoglycemia and diabetic ketoacidosis (DKA). Overall, smartphone applications are safe and do not increase the number of episodes of hypoglycemia[69]. Future study could conduct an in-depth analysis of various types of smartphone applications in terms of core functionality (e.g., health monitoring, smart health interventions and guidance, community interactions and professional support), interface design and interaction experience, and dynamic sensing and self-adaptation (e.g., automatically recommending personalized health plans based on the user's basic information, such as age, gender, and body weight), in order to further improve the telemedicine intervention's usability and effectiveness. This will enable children or adolescents with T1DM to benefit more from telemedicine.

Concerning cost-effectiveness, evidence is still lacking. Few studies included in this meta-analysis discussed cost considerations, which is a common issue faced by telemedicine intervention studies. However, there are specific telemedicine cost analysis studies that may provide assistance with cost considerations. In a

recently published study on the cost-effectiveness of telemedicine interventions, smartphone application, short message, and online website interventions were confirmed to be cost-effective without substantial differences between the different delivery modes[70]. A study by Elliott et al[71] showed that smart wearable device will increase short-term costs, but its HbA1c lowering benefits will provide sufficient long-term health benefits and cost savings to justify the costs as long as the effects last into the medium term. The implementation of telemedicine services continues to be limited by cost and reimbursement barriers, future studies should increase transparency conduct rigorous and in-depth cost-effective analyses of the various types of telemedicine strategies to support T1DM management.

Practice, policy and future study

Our findings have potential ramifications for practice and policy. First, in studies evaluating the use of telemedicine interventions to improve care for children and adolescents with T1DM, we found that the majority of studies focused on HbA1c, with only a small proportion of studies reporting other outcomes such as quality of life and incidence of hypoglycemia. This prevents policy makers from considering the impact of interventions on outcomes other than glycated haemoglobin when developing and implementing telemedicine interventions for this population. This situation may result in the healthcare system failing to respond to the needs of children and adolescents with T1DM and creates difficulties in tailoring telemedicine interventions to this population[72]. Focusing only on HbA1c may, in turn, compromise the continuity of managed care for patients with T1DM. We therefore suggest that future studies need to add assessment of other important outcomes such as quality of life, incidence of hypoglycemia, SMBG, and cost-effectiveness.

However, the importance of HbA1c is undisputed, with findings published by the

UKPDS (United Kingdom Prospective Diabetes Study) as early as 2000 showing that a 1% reduction in mean HbA1c was associated with a 21% reduction in diabetes-related deaths, a 14% reduction in the risk of myocardial infarction, and a 37% reduction in microvascular complications in patients with T2DM (Type 2 diabetes mellitus)[73]. Results of a recent cross-sectional study of 156,090 children and adolescents with T1DM showed that the probability of diabetic retinopathy increased with increasing HbA1c ($aOR_{per\text{-}1\text{-}mmol/mol\text{-}increase\text{-}in\text{-}HbA1c}$ = 1.03; 95% CI: 1.03 to 1.03; p<.0001)[74]. Therefore if telemedicine could be implemented in all children and adolescents with T1DM, it would help to reduce the risk of macrovascular and microvascular complications, improve glycemic control and enhance quality of life.

In light of the above, our findings suggest a promising application of telemedicine in the management of the disease in children and adolescents with T1DM, especially after several decades of development, when telemedicine has revealed many benefits for children and adolescents with T1DM. Future studies should carefully consider the various forms of interventions as well as the age group of the target population when tailoring telemedicine interventions for T1DM in adolescents and children, particularly with regard to the need for self-monitoring and recognition of hypoglycemia. Although the results of this study suggest that smartphone apps may be the best way to improve patients' glycemic control, they may not be applicable to children under 10 years of age. Taking China as an example, in addition to Chinese education policy discouraging the use of electronic devices in schools to minimise disruption and promote traditional teaching methods, children's weaker self-control and potential addiction to gaming and entertainment, difficulties in parental supervision, and adverse effects on children's face-to-face interactions and social skills development are also important factors that make it difficult to apply this form of telemedicine.

Finally, this study also identified the lowest threshold of intervention duration intervals that may be able to safeguard the effectiveness of telemedicine interventions in children and adolescents with T1DM, making it necessary to continue further studies with longer durations and larger cohort sizes in the future to determine the optimal intervals of intervention durations. Although this may be difficult, and patients' ability to improve their self-management of glycemia through telemedicine is a gradual process involving multiple factors, including patients' learning ability, adaptability, acceptance of the technology, and the level of support from the healthcare team, and the time to achieve independent glycemic management may vary due to individual differences, the conduct of studies of longer durations is still very much appreciated.

Strengths and limitations

This systematic review and meta-analysis has several strengths. To our knowledge, this paper is the first meta-analysis on telemedicine aimed at improving HbA1c in children and adolescents. The substantial number of included randomized controlled trials and participants provided strong evidence for the clinical application of telemedicine improving glycemic control in children and adolescents with T1DM. Secondly, we performed a relatively comprehensive subgroup analysis and confirmed that telemedicine may have the opposite effect in children and adolescents than in adults in terms of intervention duration. Meanwhile, we undertook a comprehensive search of multiple databases and strictly adhered to methodological tools to report our research. Finally, we performed a leave-one-out sensitivity analysis, which allowed us to assess whether high-risk studies influenced the final results; however, excluding the high-risk study did not change the final results.

We also acknowledge this meta-analysis has several limitations. First and foremost, statistical assumptions, such as deriving the mean and standard deviation from the sample size, baseline, endpoint and median, although these

assumptions were robust in several sensitivity analyses. Second, data extraction could include more baseline data from the study, such as medication use since diagnosis (total daily insulin dose, number of insulin injections per day, insulin pump use), ethnicity and nationality. Third, there was a certain degree of heterogeneity in the different types of telemedicine interventions. However, subgroup analysis should overcome this flaw. Fourth, only RCTs were included in this research, observational studies may yield pertinent insights for the correlation between telemedicine and HbA1c. Fifth, most RCTs did not explicitly report blinding or allocation concealment procedures because of intervention characteristic limitations, which would lead to performance and detection biases. Sixth, the precision of some secondary outcomes was relatively low because of the small number of relevant trials. More RCTs with high quality and large samples are needed for further validation. Lastly, only articles published in English were reviewed, which would lead to potential selection bias and, therefore, the results' generalizability may be limited.

Conclusions

Our systematic review and meta-analysis has shown that telemedicine is an efficacious and safe approach of intervention. It can reduce HbA1c levels and improve quality of life in children and adolescents with T1DM. Complete telemedicine intervention is better than partial telemedicine intervention. However, in accordance with the idea of providing health care from a distance, telemedicine should not be regarded as a uniform approach to medication or as an alternative to usual care, but rather as a useful supplement to usual care to control HbA1c and a potentially cost-effective mode. Given the potential benefits of telemedicine, such as greater access to remote populations or people with ambulatory restrictions, these findings may encourage further implementation of eHealth strategies for T1DM management, particularly as part of multifaceted interventions for integrated care of chronic diseases. These above conclusions

need to be further verified in future studies. Meanwhile, researchers should develop higher-quality RCTs using large samples that focus on hard clinical outcomes, cost-effectiveness, and quality of life.

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Conflicts of Interest

None declared.

Authors' contributions

KZ and QW contributed to the study concept and design, KZ drafted the manuscript, QH helped to draft the manuscript, KZ, CL and QH assessed the risk of bias, QH and QW assessed the quality of each evidence, KZ and CL independently extracted the data for analysis, KZ, QZ, DX, CX, MZ and RL had been involved in discussing earlier versions of the text. All authors participated in its design, read and approved the final manuscript.

Reference

1. Sperling MA, Laffel LM. Current Management of Glycemia in Children with Type 1 Diabetes Mellitus. The New England journal of medicine. 2022 Mar 24;386(12):1155-64. PMID: 35320645. doi: 10.1056/NEJMcp2112175.
2. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. Lancet (London, England). 2018 Jun 16;391(10138):2449-62. PMID: 29916386. doi: 10.1016/s0140-6736(18)31320-5.
3. Magliano DJ, Boyko EJ, committee IDFDAtes. IDF Diabetes Atlas. Idf diabetes atlas. Brussels: International Diabetes Federation
© International Diabetes Federation, 2021.; 2021.
4. Gregory JW, Cameron FJ, Joshi K, Eiswirth M, Garrett C, Garvey K, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetes in adolescence. Pediatric diabetes. 2022 Nov;23(7):857-71. PMID: 36250644. doi: 10.1111/pedi.13408.
5. von Scholten BJ, Kreiner FF, Gough SCL, von Herrath M. Current and future therapies for type 1 diabetes. Diabetologia. 2021 May;64(5):1037-48. PMID: 33595677. doi: 10.1007/s00125-021-05398-3.
6. Bjornstad P, Donaghue KC, Maahs DM. Macrovascular disease and risk factors in youth with type 1 diabetes: time to be more attentive to treatment? The lancet Diabetes & endocrinology. 2018 Oct;6(10):809-20. PMID: 29475800. doi: 10.1016/s2213-8587(18)30035-4.
7. Marcovecchio ML, Dalton RN, Daneman D, Deanfield J, Jones TW, Neil HAW, et al. A new strategy for vascular complications in young people with type 1 diabetes mellitus. Nature reviews Endocrinology. 2019 Jul;15(7):429-35. PMID: 30996294. doi: 10.1038/s41574-019-0198-2.
8. Katsarou A, Gudbjörnsdottir S, Rawshani A, Dabelea D, Bonifacio E, Anderson BJ, et al. Type 1 diabetes mellitus. Nature reviews Disease primers. 2017 Mar 30;3:17016. PMID: 28358037. doi: 10.1038/nrdp.2017.16.
9. Teo E, Hassan N, Tam W, Koh S. Effectiveness of continuous glucose monitoring in maintaining glycaemic control among people with type 1 diabetes mellitus: a systematic review of randomised controlled trials and meta-analysis. Diabetologia. 2022 Apr;65(4):604-19. PMID: 35141761. doi: 10.1007/s00125-021-05648-4.
10. Organization WH. Global Strategy on Digital Health 2020–2025. Geneva, Switzerland2021; Available from: https://www.who.int/publications/i/item/9789240020924.
11. Chan RJ, Crichton M, Crawford-Williams F, Agbejule OA, Yu K, Hart NH, et al. The efficacy, challenges, and facilitators of telemedicine in post-treatment cancer survivorship care: an overview of systematic reviews. Annals of oncology : official journal of the European Society for Medical Oncology. 2021 Dec;32(12):1552-70. PMID: 34509615. doi: 10.1016/j.annonc.2021.09.001.

12. Cunha AS, Pedro AR, Cordeiro JV. Facilitators of and Barriers to Accessing Hospital Medical Specialty Telemedicine Consultations During the COVID-19 Pandemic: Systematic Review. Journal of medical Internet research. 2023 Jul 10;25:e44188. PMID: 37262124. doi: 10.2196/44188.
13. Anderson K, Francis T, Ibanez-Carrasco F, Globerman J. Physician's Perceptions of Telemedicine in HIV Care Provision: A Cross-Sectional Web-Based Survey. JMIR public health and surveillance. 2017 May 30;3(2):e31. PMID: 28559226. doi: 10.2196/publichealth.6896.
14. Sengupta A, Pettigrew S, Jenkins CR. Telemedicine in specialist outpatient care during COVID-19: a qualitative study. Internal medicine journal. 2024 Jan;54(1):54-61. PMID: 37926924. doi: 10.1111/imj.16288.
15. Ruiz de Adana MS, Alhambra-Expósito MR, Muñoz-Garach A, Gonzalez-Molero I, Colomo N, Torres-Barea I, et al. Randomized Study to Evaluate the Impact of Telemedicine Care in Patients With Type 1 Diabetes With Multiple Doses of Insulin and Suboptimal HbA(1c) in Andalusia (Spain): PLATEDIAN Study. Diabetes care. 2020 Feb;43(2):337-42. PMID: 31831473. doi: 10.2337/dc19-0739.
16. Molavynejad S, Miladinia M, Jahangiri M. A randomized trial of comparing video telecare education vs. in-person education on dietary regimen compliance in patients with type 2 diabetes mellitus: a support for clinical telehealth Providers. BMC endocrine disorders. 2022 May 2;22(1):116. PMID: 35501846. doi: 10.1186/s12902-022-01032-4.
17. Bisno DI, Reid MW, Fogel JL, Pyatak EA, Majidi S, Raymond JK. Virtual Group Appointments Reduce Distress and Improve Care Management in Young Adults with Type 1 Diabetes. Journal of diabetes science and technology. 2022 Nov;16(6):1419-27. PMID: 34328029. doi: 10.1177/19322968211035768.
18. Udsen FW, Hangaard S, Bender C, Andersen J, Kronborg T, Vestergaard P, et al. The Effectiveness of Telemedicine Solutions in Type 1 Diabetes Management: A Systematic Review and Meta-analysis. Journal of diabetes science and technology. 2023 May;17(3):782-93. PMID: 35135365. doi: 10.1177/19322968221076874.
19. Eberle C, Stichling S. Clinical Improvements by Telemedicine Interventions Managing Type 1 and Type 2 Diabetes: Systematic Meta-review. Journal of medical Internet research. 2021 Feb 19;23(2):e23244. PMID: 33605889. doi: 10.2196/23244.
20. Lee SWH, Ooi L, Lai YK. Telemedicine for the Management of Glycemic Control and Clinical Outcomes of Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Studies. Front Pharmacol. 2017;8:330. PMID: 28611672. doi: 10.3389/fphar.2017.00330.
21. Campbell F, Biggs K, Aldiss SK, O'Neill PM, Clowes M, McDonagh J, et al. Transition of care for adolescents from paediatric services to adult health services. The Cochrane database of systematic reviews. 2016 Apr 29;4:Cd009794. PMID: 27128768. doi: 10.1002/14651858.CD009794.pub2.

22. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ (Clinical research ed). 2019 Aug 28;366:l4898. PMID: 31462531. doi: 10.1136/bmj.l4898.
23. Schünemann HJ, Mustafa RA, Brozek J, Steingart KR, Leeflang M, Murad MH, et al. GRADE guidelines: 21 part 2. Test accuracy: inconsistency, imprecision, publication bias, and other domains for rating the certainty of evidence and presenting it in evidence profiles and summary of findings tables. Journal of clinical epidemiology. 2020 Jun;122:142-52. PMID: 32058069. doi: 10.1016/j.jclinepi.2019.12.021.
24. Bayoumy K, Gaber M, Elshafeey A, Mhaimeed O, Dineen EH, Marvel FA, et al. Smart wearable devices in cardiovascular care: where we are and how to move forward. Nature reviews Cardiology. 2021 Aug;18(8):581-99. PMID: 33664502. doi: 10.1038/s41569-021-00522-7.
25. J.P. Higgins JT, J. Chandler, M. Cumpston, M.J. Page, V.A. Welch Cochrane Handbook for Systematic Reviews of Interventions Version 6.3 (Updated February 2022). 2022; Available from: www.training.cochrane.org/handbook.
26. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Statistical methods in medical research. 2018 Jun;27(6):1785-805. PMID: 27683581. doi: 10.1177/0962280216669183.
27. Shi J, Luo D, Weng H, Zeng XT, Lin L, Chu H, et al. Optimally estimating the sample standard deviation from the five-number summary. Research synthesis methods. 2020 Sep;11(5):641-54. PMID: 32562361. doi: 10.1002/jrsm.1429.
28. Littell J.H. CJ, Pillai V. . Systematic Reviews and Meta-Analysis. New York, NY, USA: Oxford University Press; 2008.
29. Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method and selection models. Evidence-based mental health. 2014 Feb;17(1):30. PMID: 24477535. doi: 10.1136/eb-2013-101699.
30. Fu R, Gartlehner G, Grant M, Shamliyan T, Sedrakyan A, Wilt TJ, et al. Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. Journal of clinical epidemiology. 2011 Nov;64(11):1187-97. PMID: 21477993. doi: 10.1016/j.jclinepi.2010.08.010.
31. Chase HP, Pearson JA, Wightman C, Roberts MD, Oderberg AD, Garg SK. Modem transmission of glucose values reduces the costs and need for clinic visits. Diabetes care. 2003 May;26(5):1475-9. PMID: 12716807. doi: 10.2337/diacare.26.5.1475.
32. Gandrud L, Altan A, Buzinec P, Hemphill J, Chatterton J, Kelley T, et al. Intensive remote monitoring versus conventional care in type 1 diabetes: A randomized controlled trial. Pediatric diabetes. 2018 Feb 21. PMID: 29464831. doi: 10.1111/pedi.12654.
33. Goyal S, Nunn CA, Rotondi M, Couperthwaite AB, Reiser S, Simone A, et al. A Mobile App for the Self-Management of Type 1 Diabetes Among Adolescents: A

Randomized Controlled Trial. JMIR mHealth and uHealth. 2017 Jun 19;5(6):e82. PMID: 28630037. doi: 10.2196/mhealth.7336.

34. Han Y, Faulkner MS, Fritz H, Fadoju D, Muir A, Abowd GD, et al. A Pilot Randomized Trial of Text-Messaging for Symptom Awareness and Diabetes Knowledge in Adolescents With Type 1 Diabetes. Journal of pediatric nursing. 2015 Nov-Dec;30(6):850-61. PMID: 25720675. doi: 10.1016/j.pedn.2015.02.002.
35. Ibrahim N, Treluyer JM, Briand N, Godot C, Polak M, Beltrand J. Text message reminders for adolescents with poorly controlled type 1 diabetes: A randomized controlled trial. PloS one. 2021;16(3):e0248549. PMID: 33720997. doi: 10.1371/journal.pone.0248549.
36. Kowalska A, Piechowiak K, Ramotowska A, Szypowska A. Impact of ELKa, the Electronic Device for Prandial Insulin Dose Calculation, on Metabolic Control in Children and Adolescents with Type 1 Diabetes Mellitus: A Randomized Controlled Trial. Journal of diabetes research. 2017;2017:1708148. PMID: 28232949. doi: 10.1155/2017/1708148.
37. Kumar VS, Wentzell KJ, Mikkelsen T, Pentland A, Laffel LM. The DAILY (Daily Automated Intensive Log for Youth) trial: a wireless, portable system to improve adherence and glycemic control in youth with diabetes. Diabetes technology & therapeutics. 2004 Aug;6(4):445-53. PMID: 15320998. doi: 10.1089/1520915041705893.
38. Landau Z, Mazor-Aronovitch K, Boaz M, Blaychfeld-Magnazi M, Graph-Barel C, Levek-Motola N, et al. The effectiveness of Internet-based blood glucose monitoring system on improving diabetes control in adolescents with type 1 diabetes. Pediatric diabetes. 2012 Mar;13(2):203-7. PMID: 21848925. doi: 10.1111/j.1399-5448.2011.00800.x.
39. Marrero DG, Vandagriff JL, Kronz K, Fineberg NS, Golden MP, Gray D, et al. Using telecommunication technology to manage children with diabetes: the Computer-Linked Outpatient Clinic (CLOC) Study. The Diabetes educator. 1995 Jul-Aug;21(4):313-9. PMID: 7621734. doi: 10.1177/014572179502100409.
40. Mulvaney SA, Rothman RL, Wallston KA, Lybarger C, Dietrich MS. An internet-based program to improve self-management in adolescents with type 1 diabetes. Diabetes care. 2010 Mar;33(3):602-4. PMID: 20032275. doi: 10.2337/dc09-1881.
41. Nunn E, King B, Smart C, Anderson D. A randomized controlled trial of telephone calls to young patients with poorly controlled type 1 diabetes. Pediatric diabetes. 2006 Oct;7(5):254-9. PMID: 17054446. doi: 10.1111/j.1399-5448.2006.00200.x.
42. Raviteja KV, Kumar R, Dayal D, Sachdeva N. Clinical efficacy of Professional Continuous Glucose Monitoring in improving glycemic control among children with Type 1 Diabetes Mellitus: An Open-label Randomized Control Trial. Sci Rep. 2019 Apr 16;9(1):6120. PMID: 30992480. doi: 10.1038/s41598-019-42555-6.

43. Schiaffini R, Tagliente I, Carducci C, Ullmann N, Ciampalini P, Lorubbio A, et al. Impact of long-term use of eHealth systems in adolescents with type 1 diabetes treated with sensor-augmented pump therapy. Journal of telemedicine and telecare. 2016 Jul;22(5):277-81. PMID: 26289613. doi: 10.1177/1357633x15598425.
44. Stanger C, Lansing AH, Scherer E, Budney A, Christiano AS, Casella SJ. A Web-Delivered Multicomponent Intervention for Adolescents with Poorly Controlled Type 1 Diabetes: A Pilot Randomized Controlled Trial. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2018 Nov 12;52(12):1010-22. PMID: 30418521. doi: 10.1093/abm/kay005.
45. von Sengbusch S, Eisemann N, Mueller-Godeffroy E, Lange K, Doerdelmann J, Erdem A, et al. Outcomes of monthly video consultations as an add-on to regular care for children with type 1 diabetes: A 6-month quasi-randomized clinical trial followed by an extension phase. Pediatric diabetes. 2020 Dec;21(8):1502-15. PMID: 33009690. doi: 10.1111/pedi.13133.
46. Ware J, Allen JM, Boughton CK, Wilinska ME, Hartnell S, Thankamony A, et al. Randomized Trial of Closed-Loop Control in Very Young Children with Type 1 Diabetes. N Engl J Med. 2022 Jan 20;386(3):209-19. PMID: 35045227. doi: 10.1056/NEJMoa2111673.
47. Ware J, Boughton CK, Allen JM, Wilinska ME, Tauschmann M, Denvir L, et al. Cambridge hybrid closed-loop algorithm in children and adolescents with type 1 diabetes: a multicentre 6-month randomised controlled trial. The Lancet Digital health. 2022 Apr;4(4):e245-e55. PMID: 35272971. doi: 10.1016/s2589-7500(22)00020-6.
48. Xu Y, Xu L, Zhao W, Li Q, Li M, Lu W, et al. Effectiveness of a WeChat Combined Continuous Flash Glucose Monitoring System on Glycemic Control in Juvenile Type 1 Diabetes Mellitus Management: Randomized Controlled Trial. Diabetes, metabolic syndrome and obesity : targets and therapy. 2021;14:1085-94. PMID: 33727842. doi: 10.2147/dmso.S299070.
49. Klee P, Bussien C, Castellsague M, Combescure C, Dirlewanger M, Girardin C, et al. An Intervention by a Patient-Designed Do-It-Yourself Mobile Device App Reduces HbA1c in Children and Adolescents with Type 1 Diabetes: A Randomized Double-Crossover Study. Diabetes technology & therapeutics. 2018 Dec;20(12):797-805. PMID: 30403495. doi: 10.1089/dia.2018.0255.
50. Shalitin S, Ben-Ari T, Yackobovitch-Gavan M, Tenenbaum A, Lebenthal Y, de Vries L, et al. Using the Internet-based upload blood glucose monitoring and therapy management system in patients with type 1 diabetes. Acta diabetologica. 2014 Apr;51(2):247-56. PMID: 23982170. doi: 10.1007/s00592-013-0510-x.
51. Ingersoll GM, Marrero DG. A modified quality-of-life measure for youths: psychometric properties. The Diabetes educator. 1991 Mar-Apr;17(2):114-8. PMID: 1995281. doi: 10.1177/014572179101700219.
52. Skinner TC, Hoey H, McGee HM, Skovlund SE. A short form of the Diabetes Quality of Life for Youth questionnaire: exploratory and confirmatory analysis in

a sample of 2,077 young people with type 1 diabetes mellitus. Diabetologia. 2006 Apr;49(4):621-8. PMID: 16525844. doi: 10.1007/s00125-005-0124-0.

53. Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT). The DCCT Research Group. Diabetes care. 1988 Oct;11(9):725-32. PMID: 3066604. doi: 10.2337/diacare.11.9.725.
54. Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 1998 Jul;7(5):399-407. PMID: 9691720. doi: 10.1023/a:1008853819715.
55. Faruque LI, Wiebe N, Ehteshami-Afshar A, Liu Y, Dianati-Maleki N, Hemmelgarn BR, et al. Effect of telemedicine on glycated hemoglobin in diabetes: a systematic review and meta-analysis of randomized trials. Cmaj. 2017 Mar 6;189(9):E341-e64. PMID: 27799615. doi: 10.1503/cmaj.150885.
56. Wang X, Shu W, Du J, Du M, Wang P, Xue M, et al. Mobile health in the management of type 1 diabetes: a systematic review and meta-analysis. BMC endocrine disorders. 2019 Feb 13;19(1):21. PMID: 30760280. doi: 10.1186/s12902-019-0347-6.
57. Correia JC, Meraj H, Teoh SH, Waqas A, Ahmad M, Lapão LV, et al. Telemedicine to deliver diabetes care in low- and middle-income countries: a systematic review and meta-analysis. Bull World Health Organ. 2021 Mar 1;99(3):209-19b. PMID: 33716343. doi: 10.2471/blt.19.250068.
58. Shulman RM, O'Gorman CS, Palmert MR. The impact of telemedicine interventions involving routine transmission of blood glucose data with clinician feedback on metabolic control in youth with type 1 diabetes: a systematic review and meta-analysis. Int J Pediatr Endocrinol. 2010;2010. PMID: 20886054. doi: 10.1155/2010/536957.
59. Tchero H, Kangambega P, Briatte C, Brunet-Houdard S, Retali GR, Rusch E. Clinical Effectiveness of Telemedicine in Diabetes Mellitus: A Meta-Analysis of 42 Randomized Controlled Trials. Telemedicine journal and e-health : the official journal of the American Telemedicine Association. 2019 Jul;25(7):569-83. PMID: 30124394. doi: 10.1089/tmj.2018.0128.
60. Zhong T, Tang R, Gong S, Li J, Li X, Zhou Z. The remission phase in type 1 diabetes: Changing epidemiology, definitions, and emerging immuno-metabolic mechanisms. Diabetes/metabolism research and reviews. 2020 Feb;36(2):e3207. PMID: 31343814. doi: 10.1002/dmrr.3207.
61. Jackson RL BJ, Smith TE. Stabilization of the diabetic child. Am J Dis Child. 1940;59:332–337.
62. Shin G, Feng Y, Jarrahi MH, Gafinowitz N. Beyond novelty effect: a mixed-methods exploration into the motivation for long-term activity tracker use. JAMIA open. 2019 Apr;2(1):62-72. PMID: 31984346. doi: 10.1093/jamiaopen/ooy048.
63. Chen G, Wang T, Zhong L, He X, Huang C, Wang Y, et al. Telemedicine for Preventing and Treating Pressure Injury After Spinal Cord Injury: Systematic

Review and Meta-analysis. J Med Internet Res. 2022 Sep 7;24(9):e37618. PMID: 36069842. doi: 10.2196/37618.

64. Beck RW, Connor CG, Mullen DM, Wesley DM, Bergenstal RM. The Fallacy of Average: How Using HbA(1c) Alone to Assess Glycemic Control Can Be Misleading. Diabetes care. 2017 Aug;40(8):994-9. PMID: 28733374. doi: 10.2337/dc17-0636.
65. Gimenez M, Tannen AJ, Reddy M, Moscardo V, Conget I, Oliver N. Revisiting the Relationships Between Measures of Glycemic Control and Hypoglycemia in Continuous Glucose Monitoring Data Sets. Diabetes care. 2018 Feb;41(2):326-32. PMID: 29191845. doi: 10.2337/dc17-1597.
66. Seyed Ahmadi S, Westman K, Pivodic A, Ólafsdóttir AF, Dahlqvist S, Hirsch IB, et al. The Association Between HbA(1c) and Time in Hypoglycemia During CGM and Self-Monitoring of Blood Glucose in People With Type 1 Diabetes and Multiple Daily Insulin Injections: A Randomized Clinical Trial (GOLD-4). Diabetes care. 2020 Sep;43(9):2017-24. PMID: 32641374. doi: 10.2337/dc19-2606.
67. Quarta A, Iannucci D, Guarino M, Blasetti A, Chiarelli F. Hypoglycemia in Children: Major Endocrine-Metabolic Causes and Novel Therapeutic Perspectives. Nutrients. 2023 Aug 11;15(16). PMID: 37630734. doi: 10.3390/nu15163544.
68. Nkhoma DE, Soko CJ, Bowrin P, Manga YB, Greenfield D, Househ M, et al. Digital interventions self-management education for type 1 and 2 diabetes: A systematic review and meta-analysis. Computer methods and programs in biomedicine. 2021 Oct;210:106370. PMID: 34492544. doi: 10.1016/j.cmpb.2021.106370.
69. Pi L, Shi X, Wang Z, Zhou Z. Effect of smartphone apps on glycemic control in young patients with type 1 diabetes: A meta-analysis. Frontiers in public health. 2023;11:1074946. PMID: 37064701. doi: 10.3389/fpubh.2023.1074946.
70. Willems R, Annemans L, Siopis G, Moschonis G, Vedanthan R, Jung J, et al. Cost effectiveness review of text messaging, smartphone application, and website interventions targeting T2DM or hypertension. NPJ digital medicine. 2023 Aug 18;6(1):150. PMID: 37596488. doi: 10.1038/s41746-023-00876-x.
71. Elliott RA, Rogers G, Evans ML, Neupane S, Rayman G, Lumley S, et al. Estimating the cost-effectiveness of intermittently scanned continuous glucose monitoring in adults with type 1 diabetes in England. Diabetic medicine : a journal of the British Diabetic Association. 2024 Mar;41(3):e15232. PMID: 37750427. doi: 10.1111/dme.15232.
72. Zafra-Tanaka JH, Beran D, Bernabe-Ortiz A. Health system responses for type 1 diabetes: A scoping review. Diabet Med. 2022 Jul;39(7):e14805. PMID: 35124856. doi: 10.1111/dme.14805.
73. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. Bmj. 2000 Aug 12;321(7258):405-12. PMID: 10938048. doi: 10.1136/bmj.321.7258.405.

74. Bratina N, Auzanneau M, Birkebaek N, de Beaufort C, Cherubini V, Craig ME, et al. Differences in retinopathy prevalence and associated risk factors across 11 countries in three continents: A cross-sectional study of 156,090 children and adolescents with type 1 diabetes. Pediatr Diabetes. 2022 Dec;23(8):1656-64. PMID: 36097824. doi: 10.1111/pedi.13416.

Abbreviations

CI: confidence interval
DKA: diabetic ketoacidosis
DQOL: diabetes quality of life
DQOLY: diabetes quality of life for youth
GRADE: Grading of Recommendations, Assessment, Development and Evaluations
HRQOL: health-related quality of life
MD: mean difference
N-QOL: non-youth-specific quality of life
PICOS: Population, Intervention, Comparison, Outcome and Study design
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QOL: quality of life
RCT: randomized controlled trial
SD: standard deviation
SMD: standard mean difference
SMS: short message service
SMBG: self-monitoring of blood glucose
T1DM: type 1 diabetes mellitus
T2DM: type 2 diabetes mellitus
UKPDS: United Kingdom Prospective Diabetes Study
VGA: virtual group appointments

Supplementary Files

Untitled.
URL: http://asset.jmir.pub/assets/6a3919ed3ffb77453a522c4772eb9ae6.docx

Multimedia Appendixes

Search strategy, funnel plot for primary outcome, forest plots of the subgroups and the secondary outcomes, summary of meta-regression results, and sensitivity analysis.
URL: http://asset.jmir.pub/assets/4a3dfa4f834dc5f2072361e645920b1c.docx

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 checklist.
URL: http://asset.jmir.pub/assets/19bf6d9245ce20c0adf98f99bd8add80.docx