

Clinical- and Cost-effectiveness of Telemedicine in Type 2 Diabetes Mellitus: A Systematic Review and Meta-analysis

Yun-kai Zhai, PhD, Wei-jun Zhu, MD, Yan-ling Cai, PhD, Dong-xu Sun, BS, and Jie Zhao, PhD

Abstract: Emerging telemedicine programs offer potential low-cost solutions to the management of chronic disease. We sought to evaluate the clinical effectiveness and cost effectiveness of telemedicine approaches on glycemic control in patients with type 2 diabetes mellitus.

Using terms related to type 2 diabetes and telemedicine, MEDLINE, Cochrane, EMBASE, and CINAHL Plus were searched to identify relevant studies published through February 28, 2014. Data from identified clinical trials were pooled according to telemedicine approach, and evaluated using conventional meta-analytical methods.

We identified 47 articles, from 35 randomized controlled trials, reporting quantitative outcomes for hemoglobin A1c (HbA_{1c}). Twelve of the 35 studies provided intervention via telephone, either in the form of a call or a text message; 19 studies tested internet-based programs, employing video-conferencing and/or informational websites; and four studies used interventions involving electronically transmitted recommendations made by clinicians in response to internet-based reporting by patients. Overall, pooled results from these studies revealed a small, but statistically significant, decrease in HbA_{1c} following intervention, compared to conventional treatment (pooled difference in means = -0.37, 95% CI = -0.49 to -0.25, Z = -6.08, P < 0.001). Only two of the 35 studies included assessment of cost-effectiveness. These studies were disparate, both in terms of overall expense and relative cost-effectiveness.

Optimization of telemedicine approaches could potentially allow for more effective self-management of disease in type 2 diabetes patients, though evidence to-date is unconvincing. Furthermore, significant publication bias was detected, suggesting that the literature should be interpreted cautiously.

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From the First Affiliated Hospital, Zhengzhou University, Zhengzhou, People's Republic of China (YKZ, WJZ, DXS, JZ); Henan Engineering Research Center of Digital Medicine, Zhengzhou, People's Republic of China (YKZ, YLC, DXS, JZ); Management Engineering School, Zhengzhou University, Zhengzhou, People's Republic of China (YKZ, YLC); and Henan Engineering Laboratory for Digital Telemedicine Service, Zhengzhou, People's Republic of China (WJZ, DXS, JZ)

Correspondence: Jie Zhao and Yun-kai Zhai, The first Affiliated Hospital, Zhengzhou University, Zhengzhou, No. 1, East Jianshe Road, Zhengzhou 450052, People's Republic of China (e-mail: zhaojie@zzu.edu.cn and zhayunkai@zzu.edu.cn).

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Abbreviations: CI = confidence interval, DM = diabetes mellitus, ICER = incremental cost-effectiveness ratio, WHO = World Health Organization.

INTRODUCTION

Telemedicine, as described by the World Health Organization (WHO) and the American Telemedicine Association, is characterized by the remote exchange of medical information and/or services between patient and clinician through electronic information communication technologies.^{1,2,3} Ideally, telemedicine improves healthcare outcomes by providing services and education, and overcoming geographic barriers to treatment.¹ Reflective of the rapidly evolving nature of technology, potential approaches to telemedicine are expanding exponentially. These electronic resources have included, but are not limited to, real-time video conferencing, email and websites, mobile phones, Bluetooth, and other telecommunications devices. In addition to increasing access for underserved populations, telemedicine has been reputed to lower healthcare costs while providing more effective management of chronic diseases.⁴ Despite optimism surrounding implementation of telemedicine in chronic disease management, little is known of the clinical efficacy and cost-effectiveness of such programs.

Roughly 312 million individuals worldwide are living with type 2 diabetes mellitus (DM), accounting for 90% of all diabetes cases.⁵ Diabetes self-management, combined with ongoing guidance from healthcare providers, is well established as an integral component of effective treatment plans.⁶ The complex nature of DM, however, frequently impedes optimal self-management, as efficacy relies upon adoption of major lifestyle changes – including those affecting diet and exercise, use of pharmaceuticals, and regular blood glucose monitoring – by patients.⁷ With rates of DM on the rise worldwide, the development and implementation of cost-effective programs that promote successful self-management of disease has become imperative.

With the goal of improving both glycemic control and outcomes through self-management, many telemedical devices that record, store, and/or transmit patient-monitored blood glucose levels to clinicians have been developed. Previously, strategies have included weekly transmission of blood glucose data by modem, with or without nurse follow-up, with moderate success.^{8,9} More recently, researchers have explored approaches utilizing the internet for reporting, education, and support; telemetry devices; and cell phone text messaging to improve type 2 DM self-management. While the potential clinical benefits of such therapies, and reputed advantages of monitoring and communicating with patients remotely, have been touted,^{10–12} there remains a dearth of convincing evidence regarding the efficacy and practicality of telemedicine in type

2 DM.^{13,14} Furthermore, while type 1 DM is first diagnosed in childhood, with patients acquiring self-management skills at a young age, type 2 DM is most frequently associated with an older population, more often unfamiliar with and averse to the technologies utilized in telemedicine.^{15,16}

To more clearly evaluate the potential of telemedicine in facilitating management of type 2 DM, we performed a meta-analysis and systematic review of randomized controlled trials of various telemedicine approaches. We determined changes in HbA_{1c} and cost, compared to usual care, to evaluate relative clinical- and cost-effectiveness of telemedicine in the establishment of glycemic control.

MATERIALS AND METHODS

Search Strategy

We conducted this meta-analysis with adherence to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.¹⁷ Medline, Embase, the Cochrane Library, and CINAHL (Cumulative Index to Nursing and Allied Health Literature) Plus were searched, through 28 February 2014, for various combinations of the following keywords diabetes/diabetes mellitus and telemedicine/telehealth/health information systems/internet/online program/mobile application/mobile phone/cellular phone. We further searched the reference lists of all relevant publications by hand, in order to identify any additional studies.

Criteria for Study Inclusion

Inclusion in this meta-analysis required that the study be: firstly, original – all review articles, meta-analyses, letters, comments, editorials, case reports, or technical reports were

excluded; secondly, a randomized, controlled trial involving telemedicine-based intervention, as per the WHO definition of telemedicine¹ (e.g. web-based systems, teleconferencing, mobile- and landline-based telephones), compared against a control group receiving standard care; thirdly, comprised of adult participants (>18 years old), with type 2 DM, receiving either insulin or oral diabetic drugs (e.g. metformin). Non-English publications, studies employing a single arm, trials lacking quantitative information for HbA_{1c}, and those involving either gestational or type 1 diabetes were excluded.

Study Selection and Data Extraction

Studies for use in this meta-analysis were identified by two independent reviewers, using the search strategy outlined above. Where there was uncertainty regarding eligibility, a third reviewer was consulted. The following information was extracted from studies that met the inclusion criteria: the name of the first author, year of publication, study design, demographics of study subjects, type and duration of telemedicine, pre- and post-intervention HbA_{1c}, and intervention-related costs. Data extraction was also performed by two independent reviewers, with a third consulted in instances of uncertainty.

Quality Assessment

The validity of each study was assessed using a risk-of-bias assessment tool, outlined in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0).¹⁸ Two reviewers subjectively reviewed all studies and assigned a value of “low risk,” “high risk,” or “unclear” to the following: firstly, random sequence generation; secondly, allocation concealment; thirdly, blinding (patients, personnel, and assessor); fourthly, adequate assessment of each outcome; fifthly, avoidance of

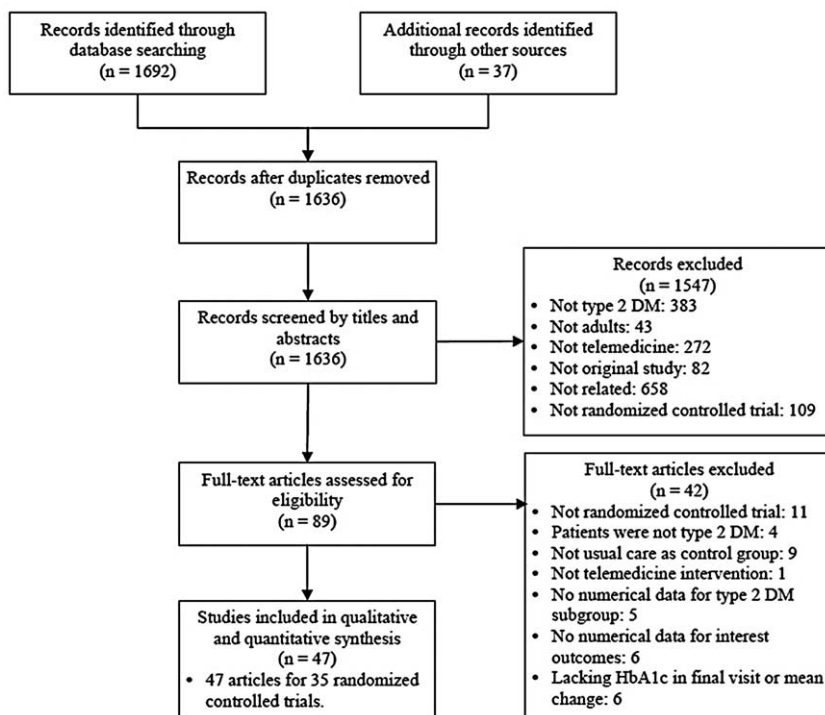


FIGURE 1. Flowchart of study selection.

selective-outcome reporting; and finally, inclusion of an intention-to-treat analysis.

Outcome Measures

The primary outcome, clinical effectiveness, was measured in terms of change in HbA_{1c}, pre- and post-intervention. The secondary outcome of cost effectiveness was measured by determination of the incremental cost-effectiveness ratio (ICER). Statistical analyses used to determine both the primary and secondary outcomes are detailed below.

Statistical Analysis

To determine the change in HbA_{1c}, the difference in means, with 95% confidence interval (CI), was calculated for the intervention group compared to the control group. Data from studies that expressed outcomes in terms of median and range, rather than means and standard deviations, were transformed to estimates of means and standard deviations using Hozo approach.¹⁹ Study heterogeneity was identified by χ^2 , using Cochran Q statistic, and quantified by I^2 , which determines the percent of the total variability that cannot be ascribed to chance. For analyses in which heterogeneity was present ($I^2 > 50\%$), a random-effects model (DerSimonian–Laird method) was applied. Alternately, a fixed-effects model (Mantel–Haenszel method) was employed in the absence of significant heterogeneity. Cochran Q was obtained by summing the square of the amount that each study's estimate deviates from the overall meta-analytic estimate, considering each study's respective weight contribution in the same manner as in the meta-analysis. *P*-values were determined by comparing the resulting statistic with a χ^2 distribution with $k - 1$ degrees of freedom, where k is the number of studies; *P*-values < 0.05 were considered statistically significant.

To determine the cost-effectiveness of the intervention, the incremental cost-effectiveness ratio (ICER) was employed. ICER is defined as the difference in costs between intervention and standard treatment effect (i.e. $(C_{\text{intervention}} - C_{\text{control}})/(E_{\text{intervention}} - E_{\text{control}})$, where *C* equals cost and *E* equals effect), was used to provide an evidence for economic evaluation regarding telemedicine intervention. The cost we collected was direction costs for intervention. The effectiveness we used was per unit reduction in HbA_{1c}. All statistical analyses were performed using Comprehensive Meta-Analysis, Version 2.0 (Biostat, Englewood, NJ) statistical software.

RESULTS

Literature Search and Evaluation for Study Inclusion

As illustrated in the flowchart depicted in Figure 1, an initial search of the literature yielded 1636 articles, 1547 of which were excluded; the remaining 91 studies were subjected to a full-text review. Following full-text review, an additional 42 articles [Supplemental Material (<http://links.lww.com/MD/A111>), excluded references 1–42] were excluded for the following reasons: firstly, not a randomized controlled trial ($n = 11$); secondly, patients did not have type 2 DM ($n = 4$); thirdly, lacked a usual care control group ($n = 9$); fourthly, not telemedicine-based intervention ($n = 1$); fifthly, no numerical data for type 2 DM subgroup ($n = 5$); sixthly, no numerical data for interest outcomes ($n = 6$); and finally, lacking data for HbA_{1c} in final visit or mean change ($n = 6$). The remaining 47 articles,^{20–66} reporting results from a total of 35 randomized

controlled trials, were included for examination in this meta-analysis.

Study Characteristics

The characteristics of the included 35 clinical trials are summarized in Table 1. Twelve of the 35 studies used telephone-based interventions that aimed at supporting and educating participant self-management, and were comprised of either periodic conversations with a healthcare advocate^{10,22,27,28,37,52,54,56} or automated text messaging.^{26,42} Most of the studies tailored these communications in response to data submitted by patients to their clinicians, though some contained more generalized information. Nineteen of the studies employed a web-based intervention.^{21,24,29,30,32,34–36,38,41,43–51,53,55,58,59} These trials typically involved uploading of blood glucose readings, either manually or electronically, to a web-accessible file, which was then to be monitored by both the patient and clinician. Additional follow-up with patients by a healthcare provider, either via videoconferencing or telephone, regarding the uploaded data was commonly included in web-based interventions. Additionally, these interventions frequently employed informational websites to further educate patients about optimal DM self-management. Four of the studies used internet-transmitted interventions, whereby participants' blood glucose readings were regularly transmitted directly to their nurses' or physicians' offices via the internet,³¹ telephone,^{23,31} Bluetooth,^{31,39} modem,³¹ cable,³¹ cellphone,³⁹ or a remote biometric devices that transmit data either wirelessly⁴² or via serial cable.²⁰

Across the 35 studies, the total number of participants ranged from 15 to 844 in the intervention group and 13 to 821 in the control group. Treatment duration ranged from 3 to 60 months, while mean age was 42.5 to 70.8 years in the intervention group and 42.3 to 70.9 years in the control group (Table 1). For the intervention group, HbA_{1c} ranged from 6.4% (46.5 mmol/mol) to 11.2% (98.9 mmol/mol) and 6.4% (46.5 mmol/mol) to 8.7% (71.6 mmol/mol) at baseline and final visit, respectively. For the usual care control group, HbA_{1c} ranged from 6.5% (47.5 mmol/mol) to 10.6% (92.4 mmol/mol) and 6.6% (48.6 mmol/mol) to 8.8% (72.7 mmol/mol) at baseline and final visit, respectively.

Effect of Telemedicine on HbA_{1c}

To determine the effect of the various telemedicine approaches on HbA_{1c}, data from the 35 studies were pooled and examined both in terms of each individual strategy (i.e. telephone, internet, and internet-transmitted), as well as overall. As shown in Figure 2, there was significant heterogeneity when data from all 35 studies were pooled (Heterogeneity test: $Q = 138.77$, $df = 34$, $P < 0.001$, $I^2 = 75.50\%$); therefore, a random-effects model of analysis was used. The overall analysis revealed a significant, albeit slight, decrease in HbA_{1c} in the intervention group, compared to that of control group (pooled difference in means = -0.37 , 95% CI = -0.49 to -0.25 , $Z = -6.08$, $P < 0.001$).

In subgroup analysis, pooling of the data from the 12 telephone-based intervention studies revealed considerable heterogeneity within this group (Heterogeneity test: $Q = 46.51$, $df = 11$, $P < 0.001$, $I^2 = 76.35\%$); therefore, a random-effects model of analysis was applied (Figure 2). Analysis of the pooled data from patients in the telephone-based subgroup demonstrated a significant decrease in HbA_{1c}, slightly greater than that observed overall, in the telemedicine group,

TABLE 1. Basic Characteristics of Studies Included in the Meta-Analysis

Authors (Year)	Comparison	Device	Duration of Intervention	Number of Subjects	Age [†]	Male (%)	HbA1c (%) [†]		
							Baseline	Final Visit	Change
Pressman (2014) ²⁰	Telemonitoring	Telephone + internet transmitted	6 months	107	54.8 ± 9.8	37	9.4 ± 1.7	NA	-2.0 ± 1.8
Tang (2013) ²¹	Usual care	Internet	12 months	91	56.4 ± 8.7	40	9.2 ± 1.5	NA	-1.8 ± 1.7
	Intervention			202	54.0 ± 10.7	58.9	9.24 ± 1.59	8.10 ± 1.68	NA
Bogner (2012) ²²	Usual care	Telephone	3 months	213	53.5 ± 10.2	61	9.28 ± 1.74	8.33 ± 1.81	NA
	Intervention			92	57.8 ± 9.4	NA	7.2 ± 1.8	NA	-0.70 ± 1.32
Del Prato (2012) ²³	Usual care	Internet	6 months	88	57.1 ± 9.6		7.0 ± 1.9	NA	0.50 ± 1.11
	Telecare			115	57.9 ± 8.7	52	8.83 ± 0.94	NA	-0.7 ± 0.06 [‡]
Glasgow (2012), ²⁴ Glasgow (2010) ²⁵	Conventional	Internet	12 months	126	58.7 ± 7.9	52	8.89 ± 0.95	NA	-0.7 ± 0.06 [‡]
	CASM			169	58.7 ± 9.3	55.4	8.14 ± 0.10 [‡]	8.16 ± 0.09 [‡]	NA
Goodarzi (2012) ²⁶	CASM+	Message	3 months	162	57.8 ± 9.3	46.3			
	Usual care			132	58.7 ± 9.1	48.5	8.16 ± 0.16 [‡]	8.04 ± 0.14 [‡]	NA
Jarab (2012) ²⁷	Examination	Telephone	6 months	43	50.98 ± 10.32	20.9	7.91 ± 1.24	7.02 ± 1.02	NA
	Control			38	56.71 ± 9.77	23.7	7.83 ± 1.12	7.48 ± 1.26	NA
Schechter (2012) ²⁸	Intervention	Telephone	12 months	85	63.4 ± 10.1	57.6	8.5 (6.9, 10.3) [#]	NA	-0.8 (-1.6, 0.1) ^{&}
	Usual care			86	65.3 ± 9.2	55.8	8.4 (6.6, 10.2) [#]	NA	0.1 (-0.4, 0.7) ^{&}
Bujnowska-Fedak (2011) ²⁹	Telephone	Internet	3 months	262	NA	NA	NA	NA	-0.36 (0.02, 0.69) ^{&}
	Paper material			264	NA	NA	NA	NA	
Lim (2011) ³⁰	Telehome	Internet	6 months	47	53.1 ± 25.2	55.3	7.63 ± 1.53	7.37 ± 1.27	NA
	Conventional			48	57.5 ± 27.4	52.1	7.61 ± 1.65	7.43 ± 1.49	NA
Luley (2011) ³¹	U-healthcare	Internet	6 months	51	67.2 ± 4.1	45.1	7.8 ± 1.0	7.4 ± 1.0	NA
	Control			52	68.1 ± 5.5	36.5	7.9 ± 0.8	7.8 ± 1.0	NA
Quinn (2011) ³²	Intervention	Internet	12 months	35	57 ± 9	43	7.5 ± 1.1	NA	-0.8 ± 0.8 [‡]
	Control			35	58 ± 7	54	7.6 ± 1.1	NA	0.2 ± 0.2 [‡]
Anderson (2010) ³³	Internet	Telephone	12 months	84	52.45 ± 8.05	48.9	9.66 ± 2.03	7.90 ± 1.63	NA
	Usual care			79	53.08 ± 8.29	50.6	9.23 ± 1.73	8.27 ± 1.61	NA
Lorig (2010) ³⁴	Intervention + usual care	Internet	6 months	146	NA	41.1	7.6 ± 1.75	7.66	0.08 (-0.25, 0.41) ^{&}
	Control			149	NA	43.0	8.4 ± 2.33	7.74	
Noh (2010) ³⁵	Treatment	Internet	6 months	491	NA	NA	NA	NA	-0.009 ± 0.852
	Control			270	NA	NA	NA	NA	0.126 ± 0.779
Tildesley (2010) ³⁶	eMOD	Internet	6 months	20	42.5 ± 10.6	80	9.0 ± 2.3	NA	-1.53 ± 1.42
	intervention			20	42.3 ± 7.6	75	8.6 ± 1.2	NA	-0.49 ± 1.07
Dale (2009) ³⁷	Intervention	Telephone	6 months	24	57 ± 10	58.3	8.8 ± 1.3	7.6 ± 0.74	NA
	Usual care			23	62 ± 7.2	65.2	8.5 ± 1.2	8.4 ± 1.4	NA
Holbrook (2009) ³⁸	Telecare	Internet	6 months	134	NA	54.6	8.6 (6.3, 16.1) [¶]	8.0 (5.2, 12.1) [¶]	-0.56 ± 1.73
	Routine care			97	NA	64.0	8.7 (5.6, 14.7) [¶]	7.9 (5.9, 12.1) [¶]	-0.8 ± 1.18
Istepanian (2009) ³⁹	Intervention	Internet	9 months	253	61.0 ± 13.1	51.4	7.0 ± 1.4	6.8 ± 1.2	-0.2 (-0.38, -0.02) ^{&}
	Control			258	60.5 ± 11.9	47.3	7.1 ± 1.6	7.3 ± 1.6	NA
Rodríguez-Idigoras (2009) ⁴⁰	Telemonitoring	Internet	12 months	72	NA	NA	7.9 ± 1.5	7.9	NA
	Control			65	NA	NA	8.1 ± 1.6	8.2	NA
IDEATel trial ⁵⁹⁻⁶⁶	Telemedicine	Internet	60 months	161	63.32 (61.60, 65.04) ^{&}	54.04	7.62 (7.38, 7.88) ^{&}	7.40 (7.17, 7.62) ^{&}	-0.22 (0.02, 0.41) ^{&}
	Control			167	64.52 (62.96, 66.09) ^{&}	49.10	7.41 (7.21, 7.61) ^{&}	7.35 (7.14, 7.56) ^{&}	-0.09 (0.08, 0.27) ^{&}
Yoo (2009) ⁴¹	Telemedicine	Internet	3 months	844	70.8 ± 6.5	36.5	7.43 ± 0.05 [‡]	7.09 ± 0.06 [‡]	-0.29 (0.12, 0.46) ^{&}
	Usual care			821	70.9 ± 6.8	37.9	7.45 ± 0.06 [‡]	7.38 ± 0.06 [‡]	
Faridi (2008) ⁴²	Intervention	Message + internet transmitted	3 months	57	57.0 ± 9.1	52.6	7.6 ± 0.9	7.1 ± 0.8	NA
	Control			54	59.4 ± 8.4	64.8	7.4 ± 0.9	7.6 ± 1.0	NA
Kim SI (2008), ⁴³ Kim HS (2008) ⁴⁴	Intervention	Internet	12 months	15	55.3 ± 8.7	40.0	6.4 ± 0.6	NA	-0.1 ± 0.3
	Control			15	56.7 ± 10.6	33.3	6.5 ± 0.7	NA	0.3 ± 1.0
Yoon (2008), ⁴⁵ Kim HS (2007), ⁴⁶ Kim HS (2007) ⁴⁷	Intervention	Internet	12 months	18	45.5 ± 9.1	50.0	8.16 ± 1.9	6.67 ± 0.77	NA
	Control			16	48.5 ± 8.0	43.8	7.66 ± 0.7	8.19 ± 0.54	NA
	Intervention			25	46.8 ± 8.8	44.0	8.09 ± 1.72	6.77 ± 0.77	NA

TABLE 1. (Continued)

Authors (Year)	Comparison	Device	Duration of Intervention	Number of Subjects	Age [†]	Male (%)	HbA _{1c} (%) [‡]		
							Baseline	Final Visit	Change
Bond (2007), ⁴⁸ Bond (2010) ⁴⁹	Control	Internet	6 months	26	47.5 ± 9.1	42.3	7.59 ± 1.09	8.40 ± 1.04	NA
	Treatment			31	66.2 ± 5.7	58	7.1 ± 0.18	6.4 ± 1.2	-0.62 ± 0.13
Cho (2006) ⁵⁰	Control	Internet	30 months	31	68.2 ± 6.2	52	7.1 ± 0.20	7.05 ± 0.99	-0.05 ± 0.14
	Intervention			40	51.3 ± 9.1	65	7.7 ± 1.5	6.7 ± 0.9	NA
Kim CJ (2006) ⁵¹	Control	Internet	3 months	40	54.6 ± 8.6	57.5	7.5 ± 1.3	7.4 ± 1.3	NA
	Intervention			28	55.1 ± 7.42	53.4	7.99 ± 1.22	7.40 ± 1.03	-0.59 ± 0.61
Maljanian (2005) ⁵²	Control	Telephone	3 months	45			7.69 ± 1.46	7.66 ± 1.63	-0.03 ± 1.08
	Intervention			176	56.98 ± 12.07	43.8	8.13 ± 1.89	6.9 ± 1.5	NA
McMahon (2005) ⁵³	Control	Internet	12 months	160	59.17 ± 13.38	50.0	7.65 ± 1.70	6.6 ± 1.1	NA
	Intervention			52	64 ± 7	99	10.0 ± 0.8	NA	-1.6 ± 1.4 [‡]
Wong (2005) ⁵⁴	Usual care	Telephone	6 months	52	63 ± 7	100	9.9 ± 0.8	NA	-1.2 ± 1.4 [‡]
	Case			49	61.3 ± 11.0	61.5	11.2 ± 2.7	7.6 ± 1.1	NA
Kwon (2004) ⁵⁵	Control	Internet	3 months	49	63.7 ± 11.1	51.0	10.6 ± 3.2	8.1 ± 1.5	NA
	Intervention			55	53.5 ± 8.8	63.6	7.59 ± 1.43	6.94 ± 0.13	NA
Kim HS (2003) ⁵⁶	Control	Telephone	3 months	55	54.7 ± 9.4	58.2	7.19 ± 1.17	7.62 ± 0.13	NA
	Intervention			20	59.7 ± 7.3	35.0	8.8 ± 1.2	7.6 ± 1.0	NA
Piette (2001) ⁵⁷	Control	Telephone	12 months	16	60.9 ± 5.8	25.0	8.2 ± 0.8	8.8 ± 0.9	NA
	Intervention			132	60 ± 10	95	8.2 ± 1.7	8.1 ± 0.1 [‡]	NA
Whitlock (2000) ⁵⁸	Control	Internet	3 months	140	61 ± 10	99	8.1 ± 1.7	8.2 ± 0.1 [‡]	NA
	Study			15	61.5 (41, 73) [¶]	40	9.5 (8.1, 12.6) [¶]	8.2 (5.7, 10.2) [¶]	NA
	Control			13	59 (32, 75) [¶]	38.5	9.5 (8.1, 11.9) [¶]	8.6 (7.1, 11.9) [¶]	NA

Abbreviations: NA, no data available; SMS, short message service; CASM, computer-assisted diabetes self-management; CASM+, computer-assisted diabetes self-management plus human support; TLC, telephone-linked care.

Data expressed as

[†] Mean ± standard deviation.

[‡] Mean ± standard error.

[§] Geometric means (95% CI).

[&] Mean (95% confidence interval).

[¶] Mean (range).

[#] Median (IQR).

when compared to the control group (pooled difference in means = -0.53, 95% CI = -0.81 to -0.26, Z = -3.80, P < 0.001). Significant heterogeneity was also observed when data from the 19 internet-based intervention studies was pooled (heterogeneity test: Q = 80.26, df = 18, P < 0.001, I² = 77.57%); therefore, a random-effects model of analysis was used. This analysis demonstrated a significant decrease in HbA_{1c} for patients receiving internet-based intervention, compared to the standard care groups (pooled difference in means = -0.62, 95% CI = -0.82 to -0.42, Z = -5.99, P < 0.001). The internet-transmitted intervention subgroup analysis demonstrated no significant heterogeneity when data from all four studies were pooled (Heterogeneity test: Q = 2.81, df = 3, P = 0.421, I² = 0.0%); therefore a fixed-effects model was applied. The overall analysis of the internet-transmitted studies revealed that no significant difference in HbA_{1c} between the intervention and control groups (pooled difference in means = -0.12, 95% CI = -0.29 to 0.06, Z = -1.28, P = 0.201).

Cost-Effectiveness of Telemedicine Intervention

Only two studies addressed the costs associated with telemedicine interventions.^{28,60} Schechter (2012) utilized a telephone-based intervention, comprised of 10 phone conversations per year between the patient and a healthcare practitioner. The IDEATel trial, examined by Moreno (2009), involved an internet-based intervention that consisted of live videoconferencing, automatic uploading of blood glucose levels, patient

monitoring of their own clinical data, and access to an educational website. Cost-effectiveness analysis revealed ICERs of \$491 and \$29,869 per capita for each unit reduction in HbA_{1c}, for the telephone- and internet-based interventions, respectively (Table 2).

Sensitivity Analysis

To evaluate the reliability of our meta-analytical data, we tested sensitivity using the “leave-one-out” approach. The sensitivities of both our fixed- and random-effects models are summarized in Figure 3. As shown, the direction and magnitude of the pooled estimates did not vary considerably, indicating that the meta-analysis had good reliability.

Publication Bias

In the funnel plot shown in Figure 4, the studies included in this meta-analysis are white circles, with the observed point estimate for the difference in means depicted as a white rhombus at -2.379 (95% CI: -3.527, -1.231). Egger test revealed significant evidence of publication bias, based on the preponderance of outcomes favoring intervention in the included studies (Figure 4). Specifically, the results showed bias with regard to the change in HbA_{1c} (t = 4.22, df = 33, P < 0.001). According to the “trim and fill” method, the 14 imputed studies are shown as black circles, while the imputed point estimate of the difference in the means is represented by a black rhombus at -0.534 (95% CI: -0.678, -0.389).

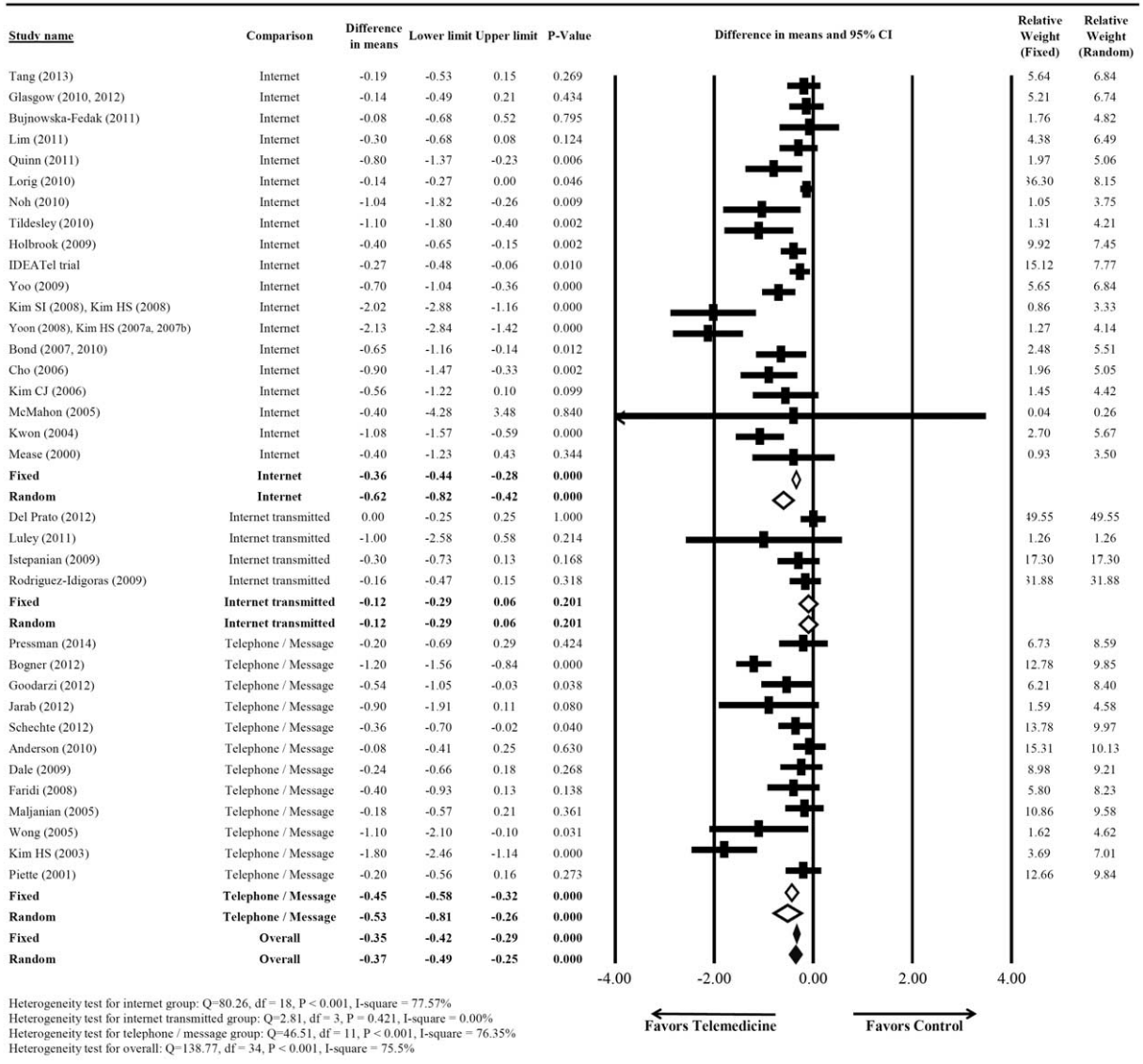


FIGURE 2. Effect of various telemedicine strategies on HbA_{1c} in type 2 DM patients. Forest plot showing results for the meta-analysis of HbA_{1c} change. *Abbreviation:* CI, confidence interval.

TABLE 2. Cost-Effectiveness of Intervention Relative to Change in HbA_{1c}

Authors (Year)	Comparison	Telemedicine Intervention Cost Per Capita	Difference Attributable to Telemedicine Per Capita	Change of HbA _{1c} (%)	ICER [†]
Schechter (2012) ²⁸	Telephone	\$180.61 [‡]	\$176.61	-0.36 (0.02, 0.69)	\$490.58
	Paper material	\$4.00 [§]			
IDEATel trial ⁵⁹⁻⁶⁶	Telemedicine	\$8662 [¶]	\$8662	-0.29 (0.12, 0.46)	\$29,869
	Usual care	\$0			

Abbreviation: ICER, incremental cost-effectiveness ratio.

[†] For each unit reduction in HbA_{1c}.

[‡] Included costs for (1) telephone charges averaged \$13.51 per person; (2) educator labor costs averaged \$146.49 per person; (3) supervisory labor costs averaged \$16.61 per person; and (4) paper material costs averaged \$4.00 per person of 1-year follow-up.

[§] Included costs for the educational materials, postage, and handling averaged \$4.00 per person of the 1-year follow-up.

[¶] Included costs for (1) a desktop model PC, connected to a regular telephone line, with a monitor, keyboard, and mouse; (2) video camera; (3) speakers; (4) microphone; and (5) glucose and blood pressure meters of 5-year follow-up.

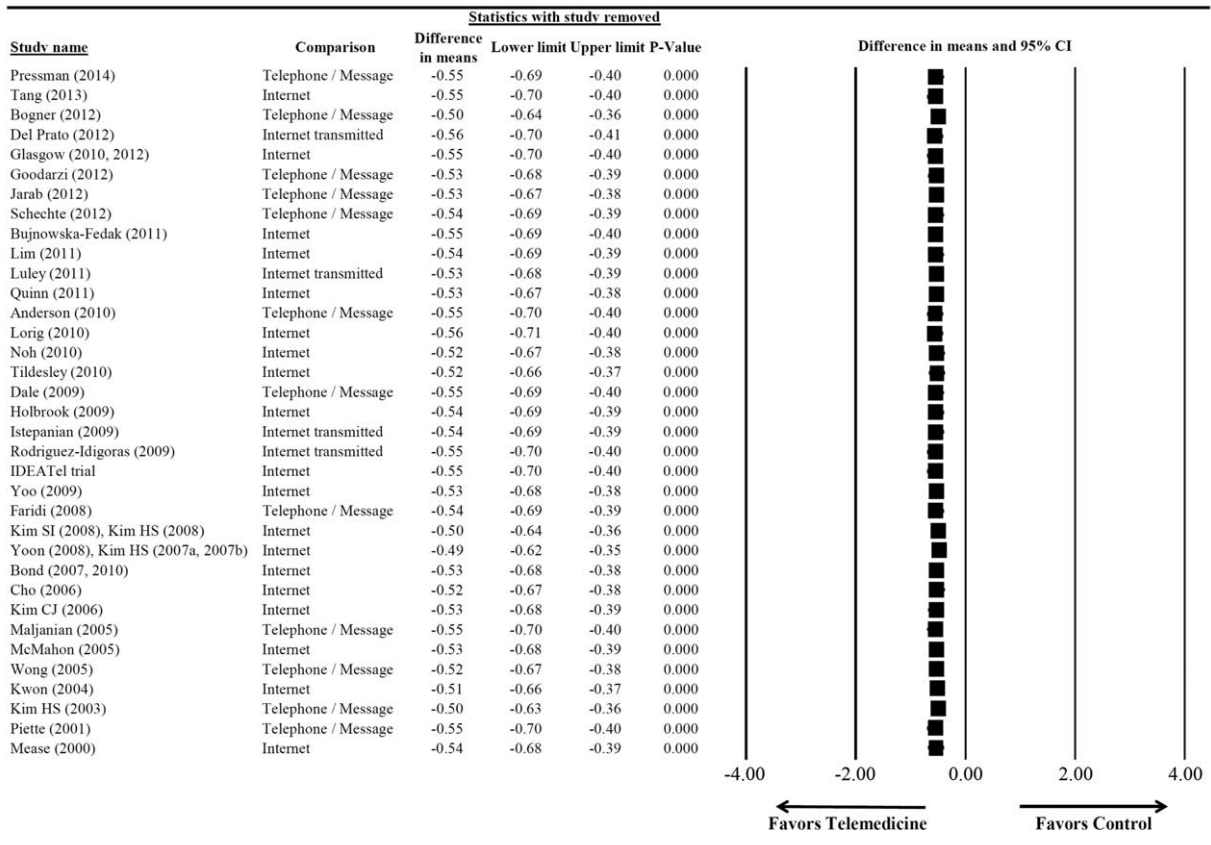


FIGURE 3. Evaluation of meta-analysis sensitivity by the “leave-one-out” approach. Abbreviation: CI, confidence interval.

Quality Assessment

Quality assessment of all included studies was carried out using a Delphi list (Figure 5).⁶⁷ This list employs eight conditions to evaluate quality: randomization; baseline characteristics; eligibility criteria; blinding of outcome assessor, physician, and patient; use of point estimates and variability; and intention-to-treat analysis. Figure 5A shows the quality of the individual trials included in this meta-analysis, while Figure 5B summarizes the quality of the entire study. Owing to the nature of the intervention, it was impossible for patients to

be blind with regard to their allocation. Some studies, however, were designed such that their outcome assessors were blind to the patient allocation.

DISCUSSION

Recent and continuing advances in areas of information and communication technology dramatically raise the potential for developing clinically impactful, low-cost telemedicine strategies. Indeed, we are presently seeing unprecedented opportunities to reach previously underserved communities through telemedicine, and much has been discussed in the literature about the utility of such approaches in the control of chronic diseases, like type 2 DM. Undoubtedly, telemedicine holds the potential to significantly affect glycemic control and self-management of disease in type 2 DM patients. The results of this meta-analysis, however, demonstrate only a nominal, albeit statistically significant, effect on HbA_{1c}, when telemedicine interventions are compared to standard care options. Additionally, significant publication bias was detected, suggesting that assumptions based on these results should be made with great caution.

Only two studies reported intervention-associated costs, making it impossible to draw a conclusion regarding this outcome measure. Additionally, these two studies employed highly disparate telemedicine approaches, resulting in wide-ranging costs following cost-effectiveness analysis. The aforementioned small number of studies, combined with this clinical heterogeneity, further confounded attempts to draw meaningful

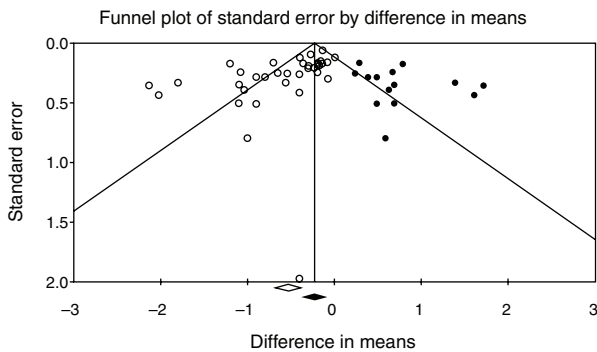


FIGURE 4. Funnel plot evaluating publication bias with regard to HbA_{1c} change for all studies. White circles represent observed studies; white rhombuses represent observed combined-effect size. Black circles represent imputed studies; black rhombuses represent imputed combined-effect size.

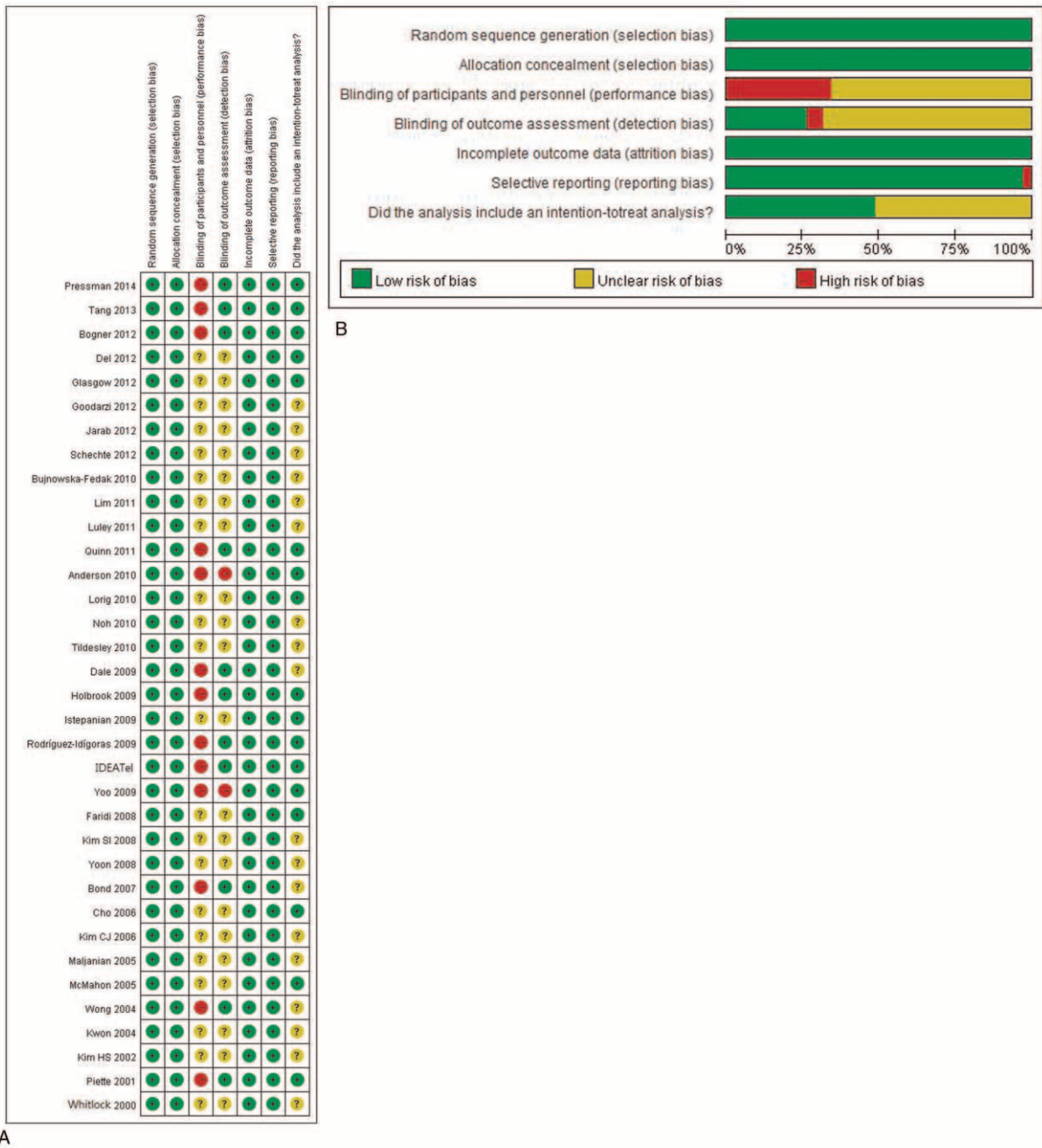


FIGURE 5. Quality assessment of included studies using the Delphi list. (A) Risk-of-bias for each study, individually. (B) Risk-of-bias in the combined 35 studies.

conclusions regarding the cost-effectiveness of telemedicine in improving self-management outcomes for type 2 DM patients. For accurate, unbiased assessment of cost-effectiveness, additional studies of the financial burden associated with the various telemedicine approaches, compared to conventional medicine alone, will be required.

In addition to our inability to effectively determine the cost-effectiveness of telemedical approaches, important questions remain as to the impact that these treatment strategies

could have on outcomes over conventional, face-to-face approaches. Clearly, telemedicine offers a potential mechanism for reaching traditionally hard-to-treat populations, such as those living in geographically and/or socioeconomically isolated communities, far from medical facilities, or those with limited mobility. As recently reported in a report on telemedicine by the WHO, however, is the likely inability for telemedicine to address treatment barriers prevalent in the developing world, where a widespread lack of access to technology and

resources precludes applicability. Regardless, further investigations into the direct effect of telemedicine on closing treatment gaps and improving outcomes in populations with unmet needs will be required before any firm conclusions can be drawn regarding the potential efficacy of this technology.

Telemedicine, which is traditionally defined as healthcare provided at a distance, encompasses a wide variety of devices. This meta-analysis is a perfect illustration of the broad definition of “telemedicine,” with approaches spanning telephones, Bluetooth, modems, mobile phones, wireless devices, and websites. Given this diversity, it is no wonder that the costs and clinical efficacy associated with telemedicine appear to vary widely across studies, and could complicate the assessment of such approaches.

One limitation of this meta-analysis was that no included study successfully blinded its participants. As stated by Rodriguez-Idigoras (2009), given the nature of the intervention, it is almost impossible to blind the patients, as well as their healthcare providers.⁴⁰ Of all those involved in the studies, the outcome assessors demonstrated the greatest opportunity and frequency of blinding. The introduction of this potential bias might affect the quality of both the individual studies and the overall systematic review. For instance, some have suggested that the so-called Hawthorne effect, which says that the very awareness of monitoring will lead to inherent self-consciousness and behavioral adaptations in study participants, skewing the resultant data.⁶⁸ Since only one study included here investigated longitudinal effects, continuing for a duration of 60 months, the Hawthorne effect cannot be discounted.

As mentioned, the longest length of intervention among the included studies was 60 months, while the shortest was 3 months. This heterogeneity is not only a limitation of our systematic review, but also might affect our estimations. Further investigation is necessary to determine both the efficacy and durability of telemedicine intervention.

While patients receiving intervention failed to demonstrate marked improvement over that of the control group, their knowledge and attitudes might have been changed, inducing potential long-term effects. Indeed, Zurovac (2011) reported such an observation in a study examining the effect of text message reminders, sent to healthcare workers in Kenya, on adherence to outpatient malarial treatment guidelines.⁶⁹ While initial response to telemedicine in this study was nominal, improvements continued up to 6 months post-intervention. Indeed, some outcomes that showed no change from baseline immediately following intervention demonstrated significant improvement at the 6-month follow-up. Thus, the seemingly weak results presented here may not reflect the actual effectiveness of telemedicine in promoting glycemic control. More longitudinal studies of both the intervention and control group would better elucidate treatment efficacy.

Here, we found that the addition of telemedicine approaches into conventional, face-to-face disease management strategies elicited a slight decrease on HbA_{1c}, compared with those receiving the conventional therapy alone. Despite the failure of this review to illustrate a robust response to intervention by type 2 DM patients, we still believe that telemedicine holds promise in facilitating self-management of disease. Further, though no clear conclusions could be drawn regarding the cost-effectiveness of such approaches, this is only a small component of the metric that is needed to assess the true impact of telemedicine, especially in hard-to-treat populations, where treatment gaps arise from patient isolation, due to geographic, socioeconomic, or other constraints. Indeed, the rapidly

changing nature of telecommunications technologies, coupled with the potential ability of telemedicine to transform the way we manage chronic diseases like type 2 DM, suffice as reason enough to continue to explore this avenue of healthcare.

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