

Effectiveness of telemedicine technologies for improving glucose control in patients with type 2 diabetes mellitus: A critical review

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Abstract

Uncontrolled diabetes mellitus is the seventh leading cause of mortality and the leading cause of blindness, kidney failure, and non-traumatic amputations in the United States. A high prevalence of type 2 diabetes mellitus (T2D) has placed a strain on health care systems due to costs associated with anti-diabetic medications as well as diabetes-associated morbidities and disabilities. Traditionally, medical care providers have prescribed lifestyle and medication changes during clinical face-to-face visits, however these visits are costly and are often not effective for producing desired changes in self-management techniques. Evidence shows that the current standard of care often fails to deliver on achieving evidence-based recommendations for glycemic control for patients with diabetes. Recent advancements in telemedicine technologies have emerged as promising platforms which can deliver diabetes management services while reducing unnecessary use of health care resources. Different technological approaches may vary with regard to patient glycemic control outcomes, and cost differences should be taken into consideration when selecting the technology that may provide the greatest overall benefit for the patient. Many newer glucometers have transmission capabilities, allowing these meters to link to smartphone Apps or websites. Patients can measure their glucose levels, share results with their healthcare team in real time, and talk over the phone or through video visits for medication or lifestyle interventions, all in a more expedient manner compared to traditional face-to-face visits. Remote monitoring of blood glucose levels by clinicians has been shown to be feasible and acceptable for patients with both type 1 diabetes mellitus (T1D) and T2D. With this background in mind, the aim of the current review was to evaluate the effectiveness of remote blood glucose monitoring compared to continuous glucose monitoring (CGM) for lowering HbA1c in adult patients with T2D. PubMed was searched for randomized controlled trials, clinical trials, and

systematic reviews that included either remote blood glucose monitoring, CGM, or both, and individual interventions had to be longer than six weeks in duration. Studies also had to include adult patients with T2D and had to examine the outcome of change in HbA1c as the primary or secondary outcome of interest. Inclusion and exclusion criteria were determined a priori, and searches included a variety of search terms yielding 92 records, of which 27 articles met the inclusion criteria. Study findings suggested that both remote blood glucose monitoring and CGM are effective for reducing HbA1c in patients with T2D compared to controls. Both the absolute treatment means, and the average treatment mean differences suggest larger reductions in HbA1c in the remote blood glucose monitoring interventions as compared to the CGM interventions. In agreement with previous research, side by side comparisons of the included studies revealed a trend toward greater absolute reductions in HbA1c among all studies where patients had higher baseline HbA1c levels, frequent engagement with the clinical team for more timely and responsive management, as well as algorithm-based treatment plans. Future studies should include a comparison of feasibility, cost of care to implement the interventions, and cost savings to inform clinical decision making, thereby identifying the technology with the greatest overall benefit for patients with diabetes.

Table of Contents

List of Figures	vi
List of Tables	vii
Acknowledgements.....	viii
Chapter 1 - Introduction.....	1
Chapter 2 - Methods.....	6
Statistical Analysis.....	7
Chapter 3 - Results.....	8
Chapter 4 - Discussion.....	15
Comparison to Systematic Review	16
Remote Blood Glucose Monitoring	17
Continuous Glucose Monitoring.....	19
Side by Side Comparison.....	21
Gaps in Current Knowledge.....	22
Conclusion	23
References.....	24

List of Figures

Figure 3.1. PRISMA Flow Diagram.....	10
Figure 3.2. Clinician Breakout Box	11

|

List of Tables

Table 3.1. Remote Blood Glucose Monitoring Study Results.....	12
Table 3.2. CGM Study Results	13
Table 3.3.Types of Devices	14

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Chapter 1 - Introduction

In the United States, uncontrolled diabetes mellitus is the seventh leading cause of mortality and the leading cause of blindness, kidney failure, and non-traumatic amputations.¹ In 2017, the Centers for Disease Control and Prevention reported that approximately 30.3 million adults in the United States were affected by diabetes mellitus, which is about one in every ten adults, 95% of whom are diagnosed with type 2 diabetes mellitus (T2D).² The American Diabetes Association's standard glycemic control target of Hemoglobin A1c (HbA1c) level is less than 7%.³ Research shows that fewer than 65% of patients who have T2D achieve the optimal HbA1c target, and many patients have suboptimal glucose control despite clear evidence that good glycemic control can prevent diabetic complications.^{1, 3, 4, 5}

A high prevalence of T2D has placed a strain on health care systems due to costs associated with anti-diabetic medications as well as diabetes-associated morbidities and disabilities.⁴ Long-term macrovascular and microvascular complications such as myocardial infarction and kidney failure are responsible for most morbidities and mortality in patients with diabetes.^{7, 8} The International Diabetes Federation estimates that health care costs for patients with T2D are two to three times higher than patients of similar age and sex without diabetes.⁸ Large-scale randomized trials have shown that microvascular complications can be reduced with optimal glycemic control, and by reducing the incidence of chronic complications, costs can also be substantially reduced.⁷

Many patients with diabetes face barriers regarding adequate self-management and adherence to treatment plans, including lifestyle changes. Previous research suggests that one-on-one counseling focused on lifestyle interventions has a positive impact on diabetes outcomes, but high cost and time commitment are major challenges for successful intervention.⁵

Traditionally, medical care providers prescribe lifestyle and medication changes during clinical face-to-face visits three to six times per year, however these visits are costly and are often not effective for producing desired changes in self-management techniques.^{5, 6, 8, 9} Evidence shows that the current standard of care often fails to deliver on achieving evidence-based recommendations for glycemic control for patients with diabetes.^{5, 8}

With ongoing technological innovation, there is growing interest in leveraging new medical technologies to support diabetes management and to compliment traditional in-person care, especially in remote areas where access to care is limited.² Recent advancements in telemedicine technologies have emerged as promising platforms which can deliver diabetes management services while reducing unnecessary use of health care resources.^{5, 7} Telemedicine approaches vary, but many use telecommunication methods such as phone calls and video visits to deliver services.¹⁰ Telemedicine can provide remote consultations, personalized diet and lifestyle advice, and remove transportation barriers. These approaches are becoming more feasible since mobile phones are widely used across socioeconomic groups, making them promising tools for healthcare delivery.¹¹ Some studies with heterogeneous sample sizes and ethnicities have provided evidence that telemedicine may improve care for patients with diabetes, particularly with regard to remote monitoring and feedback related to glucose concentrations, lifestyle management programs, and video-based education programs.^{7, 12}

The American Diabetes Association recommends that people with diabetes mellitus perform self-monitoring of blood glucose (SMBG) four to eight times daily until normoglycemia is achieved.¹³ Traditionally, glucose assessment is performed by drawing a small amount of capillary blood from a fingertip, and using a portable glucometer to analyze the blood droplet for glucose content.¹³ Few patients adhere to the recommended measurement frequency due to pain,

hassle of testing, and limited utility of results.¹³ The cost of SMBG supplies might also be a barrier to adherence. Other limitations are that SMBG provides only a snapshot of current glucose levels, with many highs and lows going undetected and untreated.¹³ In standard practice, patients must remember to bring their SMBG log to their clinical face-to-face visit where provider-directed adjustments may take place, although considerable evidence shows that clinicians fail to follow clinical practice guidelines and recommendations.^{5, 6, 8, 9} Together, this evidence suggests that barriers to traditional SMBG limit successful management of T2D.

New payment models that reimburse providers based on outcomes rather than fees for services, are driving the exploration of new service delivery methods that result in improved patient outcomes.^{5, 9} Telemedicine is one method of particular interest, where clinicians utilize technology to deliver care from a distance.² There is heterogeneity in the tools and delivery methods used by clinicians, which can range widely from one practice to the next. Some clinicians use smartphone applications (Apps) or websites which may contain sophisticated learning modules, synchronous messaging, asynchronous messaging, video visit capabilities, or machine learning clinical algorithms to guide clinical decision making. Other clinicians use far less sophisticated tools and may only use telephone calls with either structured or unstructured patient interactions.

Many newer glucometers have transmission capabilities, allowing these meters to link to smartphone Apps or websites for remote monitoring by clinicians. There is heterogeneity in the tools and delivery methods, but typically patients can measure their glucose levels, share results with their healthcare team in real time, and talk via the phone or through video visits for medication or lifestyle interventions, all in a more expedient manner compared to traditional face-to-face visits. Remote monitoring of blood glucose levels by clinicians is one aspect of

telemedicine, and has been shown to be feasible and acceptable for patients with both type 1 diabetes mellitus (T1D) and T2D.¹³ The use of these services has been shown to be beneficial for weight loss, reducing HbA1c levels, supporting behavior change, increasing patient self-efficacy, and improving ability for patient self-management of their disease.² For the purpose of the current review, we will use the term remote blood glucose monitoring to encompass studies that include SMBG and transmission of glucose data to a clinician, combined with at least one telemedicine delivery method.

A newer technology for testing blood glucose is the use of a Continuous Glucose Monitoring System (CGM) which measures interstitial fluid glucose levels from a thin needle attached to a small sensor, which is typically worn on the back upper arm or abdomen for up to two weeks at a time.¹³ CGM provides real-time data, updating every five to 15 minutes, allowing for the determination of velocity and direction of glucose changes.¹³ CGM does not require finger pricks and can detect fluctuations in blood glucose that are often missed with traditional SMBG, such as overnight lows and postprandial highs. By viewing daily CGM trends, clinicians can improve medication titration, and reduce the occurrence of severe hypoglycemic and hyperglycemic events compared with SMBG.¹³

Since 2008, The American Diabetes Association “Standards of Medical Care in Diabetes” recommendations has included CGM as an adjunct tool to SMBG for certain individuals, such as patients with T1D and those with hypoglycemia unawareness.¹² Most CGM research has examined the effectiveness of CGM for reducing HbA1c in patients with T1D, however, benefits for patients with T2D have also been of interest.^{4, 12} Research is ongoing to investigate the use of CGM for T2D outcomes.^{4, 12} With technological advancements, expanding insurance coverage, and increasing prevalence of T2D in the United States, clinicians may

benefit from greater elucidation of the effectiveness of CGM for achieving HbA1c targets in addition to reducing T2D complications.

Telemedicine has been shown to improve adherence to treatment plans, quality of services, allocation and use of healthcare resources, and delivery of more timely and appropriate diabetes care regardless of the patient's location.¹⁴ Further, with remote monitoring, therapy effectiveness can be checked and adjusted in a timely and responsive manner.¹⁴ Two different telemedicine technologies, remote blood glucose monitoring and CGM, may differ with regard to effectiveness for patients with diabetes. Therefore, the purpose of this critical review was to compare the effectiveness of remote blood glucose monitoring to CGM for lowering HbA1c in adult patients with T2D. Our hypothesis was that in patients with T2D, CGM would be more effective for improving HbA1c as compared with remote blood glucose monitoring. We believed this newer technology, with a continuous view of glucose values may result in better awareness of glucose trends, and more timely interventions including lifestyle change, resulting in greater reductions in HbA1c. This critical review will provide important information for clinicians and patients regarding the strengths and limitations of each treatment technology in order to assist with clinical decision making, thereby providing the most clinical benefit for the patient, with consideration of costs and other potential barriers or limitations.

Chapter 2 - Methods

In order to achieve the study purpose, we performed a search for relevant studies in the published literature indexed in PubMed. Inclusion and exclusion criteria were determined a priori. We included randomized controlled trials, clinical trials, and systematic reviews. These studies included either remote blood glucose monitoring, CGM, or both, and had to be longer than six weeks in duration. Studies also had to include adult patients with T2D and had to examine the outcome of change in HbA1c as the primary or secondary outcome of interest. Studies were excluded when only T1D patients were included or when T1D and T2D results were not able to be differentiated. Studies that were focused on insulin management or medication titration were also excluded, as were studies that included only pediatric populations.

Relevant studies for inclusion were obtained through searching PubMed using a variety of search terms. Five records were identified using the search terms “telemedicine” [MeSH] AND “blood glucose self-monitoring/instrumentation” [MeSH] NOT “insulin infusion systems” [MeSH] NOT “diabetes mellitus, type 1” [MeSH] NOT “child” [MeSH]. Thirty-one records were identified using the search terms “diabetes mellitus, type 2” [MeSH] AND “blood glucose self-monitoring/instrumentation” [MeSH] NOT “insulin infusion systems” [MeSH] NOT “diabetes mellitus, type 1” NOT “child” [MeSH]. Twenty-one records were identified using the search terms “telemedicine/methods” [MeSH] AND “blood glucose self-monitoring/methods” [MeSH] NOT “insulin infusion systems” [MeSH] NOT “diabetes mellitus, type 1” [MeSH] NOT “child” [MeSH]. Thirty-five records were identified using search terms “diabetes mellitus, type 2” [MeSH] AND “blood glucose self-monitoring” [MeSH] AND “glycated hemoglobin a/analysis” [MeSH]. Filters were applied to limit searches to the highest quality studies and included

“humans”, “clinical trial”, “randomized controlled trial”, and “systematic review”. Following removal of duplicates, 82 records remained.

Manual screening of abstracts resulted in removal of 57 records, and a full text article review resulted in removal of 6 records due to a priori exclusion criteria. Reasons for exclusion were varied and can be seen in detail in Figure 1. Eighteen experimental studies and one systematic review matched our eligibility criteria. The systematic review was hand searched for individual studies that also fit the eligibility criteria, resulting in nine additional studies. A total of 27 experimental studies were included in our final descriptive critical analysis.

Statistical Analysis

While our intention was not to perform a meta-analysis given the lack of studies that directly compared remote blood glucose monitoring and CGM, we determined the change in HbA1c for the control and experimental groups in order to quantitatively determine any potential advantages for one technology, indirectly compared with the other, for patients with T2D. We utilized Google Sheets to perform our statistical analysis. The mean change in HbA1c, as reported using the Diabetes Control and Complications Trial (DCCT) percentage units, was compared between the control and the experimental groups for each study.³² In addition, we calculated the mean difference in change in HbA1c between the control and experimental groups, the standard deviation, the interquartile range, the median effects as the central tendency for the change in HbA1c, and the range of the overall effects. For our primary results, we compared the average effects for remote blood glucose monitoring to the average effects for CGM to get a sense of whether there are clinically meaningful differences in effectiveness regarding HbA1c outcomes when using these two different monitoring technologies.

Chapter 3 - Results

A total of 21 studies using remote blood glucose monitoring met the criteria for inclusion, all of which indicated reductions in HbA1c within their treatment groups. Of the studies that reported patient age, ages ranged from 40 to 86. The duration of the interventions ranged from three to 60 months. The mean change in HbA1c within the treatment groups was -1.01% with a median of -1.00%, standard deviation of 0.60, and interquartile range of 0.60. The mean change in HbA1c within the control groups was -0.34% with a median of -0.27%, standard deviation of 0.42, and interquartile range of 0.50. Two of the 21 studies did not include a control group. Of the 19 studies that included a control group, 16 showed a reduction in HbA1c, and three indicated an increase in HbA1c. The mean differences in changes in HbA1c between the treatment groups and control groups ranged from 0.01% to -1.10% with a standard deviation of 0.35 and interquartile range of 0.55. The average mean difference was -0.56%, favoring the remote blood glucose monitoring treatment group over the control condition with a median difference of -0.52%. (See Table 3.1)

A total of six studies using CGM met the criteria for inclusion, all of which indicated reductions in HbA1c within their treatment groups. Of the studies that reported patient age, ages ranged from 26 to 79. The duration of the interventions ranged from two to six months. The mean change in HbA1c within the treatment group was -0.92% with a median of -0.9%, standard deviation of 0.61, and interquartile range of 0.54. The mean change in HbA1c within the control groups was -0.56% with a median of -0.71%, standard deviation of 0.45, and interquartile range of 0.38. Two studies did not include a control group. Of the four studies that included a control group, one used the same participants to compare SMBG frequency with CGM. Three of the studies resulted in a statistically significant reduction in HbA1c, and one study showed an

increase in HbA1c. The mean differences in changes in HbA1c between the treatment groups and control groups ranged from 0.1% to -0.43% with a standard deviation of 0.27 and interquartile range of 0.32. The average mean difference was -0.26%, favoring the CGM treatment group over the control condition with a median difference of -0.31%. (See Table 3.2)

There was heterogeneity in the types of devices used for both remote blood glucose monitoring and CGM. For remote blood glucose monitoring there were six different modes by which data were delivered to clinicians. The most frequent type described were devices that uploaded data to clinicians, used in 43% of studies. For CGM there were four different modes by which data were delivered to clinicians. The most frequent type described were Dexcom and Medtronic devices used in 67% of the CGM studies. (See Table 3.3)

Figure 3.1.

PRISMA Flow Diagram

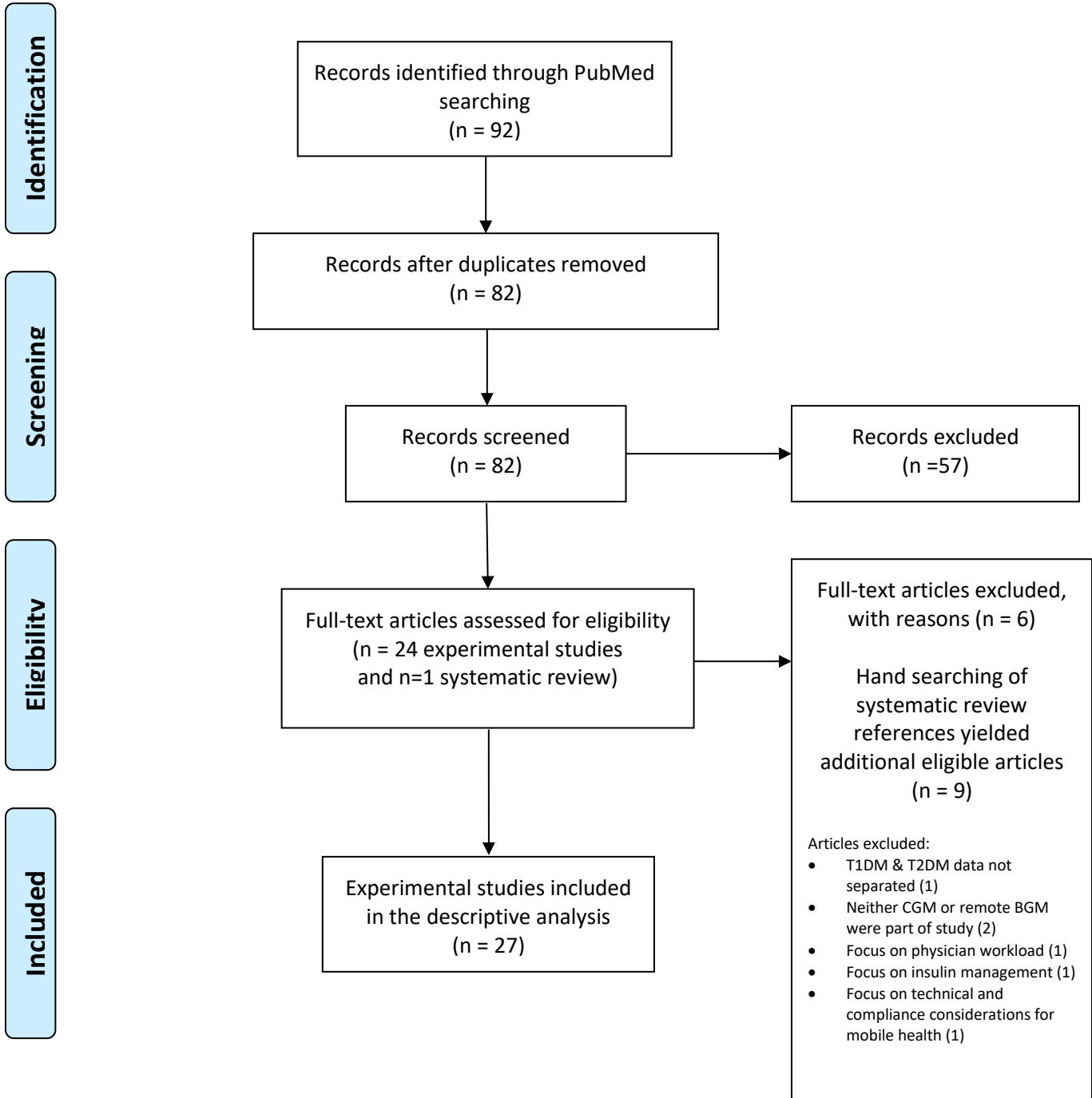


Figure 3.2.

Clinician Breakout Box

Highlights

- While evidence clearly shows that improved glycemic control can prevent diabetic complications, the current standard of care is failing to meet optimal HbA1c targets for T2D patients.^{1, 3, 4}
- The current critical review suggested that both remote blood glucose monitoring and CGM are effective for reducing HbA1c in T2D patients compared to controls.
- Contrary to our hypothesis, both the absolute treatment means, and the average treatment mean differences suggested a larger reduction in HbA1c in the remote blood glucose monitoring interventions as compared to the CGM interventions.
- Side by side comparisons of the included studies revealed a trend toward a greater absolute reduction in HbA1c in studies, in agreement with previous research, where patients had higher starting HbA1c levels, frequent engagement with the clinical team for more timely and responsive management, as well as algorithm-based treatment plans.
- Insurance coverage and cost differences between the two technologies should be taken into consideration when selecting the technology with the greatest overall benefit for the patient.

Table 3.1.*Remote Blood Glucose Monitoring Study Results*

Study	Participants	Duration in Months	Mean Baseline HbA1c (%) ± SD	Absolute Change in HbA1c Control Group (%)	Absolute Change in HbA1c Treatment Group (%)	Mean Difference ± SE (%)	p-value
Greenwood et al, ¹ 2015	90	6	8.3 ± 1.1	-0.70	-1.11	-0.41 ± 0.08	0.009
Storch et al, ⁵ 2019	115	3	6.9 ± 1.01	0.05	-0.47	-0.52 ± 0.17	0.038
Jeong et al, ⁷ 2018	338	6	8.3 ± 1.14	-0.66	-0.81	-0.15	0.162
Wild et al, ⁸ 2016	321	9	8.9 ± 1.3	-0.40	-1.00	-0.60	0.007
Watson et al, ⁶ 2009	7	3	6.8	X	-1.00	X	NR
Sun et al, ¹⁰ 2019	91	6	7.9	-0.38	-1.00	-0.62	0.020
Dario et al, ¹⁴ 2017	299	12	7.9	-0.27	-0.26	0.01	0.760
Lee et al, ²⁰ 2017	85	3	8.7 ± 1.1	-0.24	-1.07	-0.83	<0.01
B-Fedak et al, ²¹ 2011	100	6	7.6	-0.01	-0.29	-0.28	0.720
Tildesley et al, ²² 2011	50	12	8.6	-0.10	-1.20	-1.10	0.350
Cho et al, ²³ 2006	80	30	7.6	-0.10	-1.00	-0.90	0.022
Kwon et al, ²⁴ 2004	110	3	7.4	0.33	-0.54	-0.87 ± 0.13	<0.001
Ralston et al, ²⁵ 2009	83	12	8.1	0.20	-0.90	-1.10	<0.01
Shea et al, ²⁶ 2009	1665	60	7.4	-0.06	-0.31	-0.25 ± 0.06	0.001
Biermann et al, ²⁷ 2002	43	8	8.2	-1.20	-1.20	0	NR
Stone et al, ²⁸ 2010	150	6	9.5	-0.80	-1.70	-0.90	<0.001
Bind et al, ²⁹ 2007	62	6	7.1	-0.10	-0.60	-0.50	<0.01
McMahon et al, ³⁰ 2005	104	12	10.0 ± 0.8	-1.20	-1.60	-0.40	<0.05
Magee et al, ³¹ 2016	89	3	11.3	X	-3.00	X	NR
Parsons et al, ⁹ 2019	446	12	8.6 ± 1.15	-0.30	-1.20	-0.90	<0.0001
Nagrebetsky et al, ¹¹ 2013	14	12	8.1 ± 1.1	-0.50	-0.90	-0.40	0.35

Note X indicates no control group was part of the study; NR indicates data was not reported; Absolute Change in HbA1c Treatment Group (%) - Absolute Change in HbA1c Control Group (%) = Mean Difference (%)

Table 3.2.*CGM Study Results*

Study	Participants	Duration in Months	Mean Baseline HbA1c (%) \pm SD	Absolute Change in HbA1c Control Group (%)	Absolute Change in HbA1c Treatment Group (%)	Mean Difference \pm SE (%)	p-value
Ajjan et al, ⁴ 2019	148	6	8.7 \pm 1.0	0.10	-0.40	-0.50 \pm 0.16	0.004
Puhr et al, ¹³ 2018	175	6	8.6	-0.90	-0.80	0.10	NR
Yeoh et al, ¹² 2018	30	3	9.9 \pm 1.2	-0.80	-1.00	-0.20	0.869
Thielen et al, ¹⁷ 2010	10	6	9.6	X	-2.05	X	NR
Billings et al, ¹⁸ 2018	316	6	8.5 \pm 0.6	-0.63	-1.05	-0.43	NR
Zick et al, ¹⁹ 2007	367	2	6.9 \pm 0.7	X	-0.23	X	NR

Note X indicates no control group was part of the study; NR indicates data was not reported; Absolute Change in HbA1c Treatment Group (%) - Absolute Change in HbA1c Control Group (%) = Mean Difference (%)

Table 3.3.*Types of Devices*

Described Device	Study
Libre	Ajjan et al, ⁴ 2019
Dexcom	Puhr et al, ¹³ 2018
	Billings et al, ¹⁸ 2018
Medtronix	Yeoh et al, ¹² 2018
	Zick et al, ¹⁹ 2007
CGM	Thielen et al, ¹⁷ 2010
USB Cables	Greenwood et al, ¹ 2015
Uploaded	Storch et al, ⁵ 2019
	Watson et al, ⁶ 2009
	Parsons et al, ⁹ 2019
	Tildesley et al, ²² 2011
	Cho et al, ²³ 2006
	Kwon et al, ²⁴ 2004
	Ralston et al, ²⁵ 2009
	Shea et al, ²⁶ 2009
	McMahon et al, ³⁰ 2005
Transmitted	Jeong et al, ⁷ 2018
	Dario et al, ¹⁴ 2017
	B-Fedak et al, ²¹ 2011
	Biermann et al, ²⁷ 2002
	Stone et al, ²⁸ 2010
Bluetooth	Wild et al, ⁸ 2016
	Sun et al, ¹⁰ 2019
	Nagrebetsky et al, ¹¹ 2013
	Lee et al, ²⁰ 2017
Entered Online	Bind et al, ²⁹ 2007
Cellular-enabled	Magee et al, ³¹ 2016

Chapter 4 - Discussion

The purpose of this critical review was to elucidate the effectiveness of remote blood glucose monitoring compared to CGM for lowering HbA1c in adult patients with T2D. Given the evidence suggesting that patients with T2D often do not meet glycemic control targets, and considering the new medical technologies to support diabetes management, we aimed to evaluate the available research in order to assist clinical decision making that results in the most benefit for the patient in terms of clinical outcomes.

Our hypothesis was that in patients with T2D, CGM would be more effective for improving HbA1c. However, the studies included in this review did not support our hypothesis. Both the absolute treatment means, and the average treatment mean differences suggested a larger reduction in HbA1c in the remote blood glucose monitoring interventions as compared to the CGM interventions, though no studies actually included direct comparisons of these two technologies. Overall, our findings suggested that both remote blood glucose monitoring and CGM are effective for reducing HbA1c in T2D, with the largest effects seen in the remote blood glucose monitoring interventions.

Side by side comparisons of included studies revealed a trend towards a greater absolute reduction in HbA1c in studies that had a higher starting HbA1c, frequent engagement with the clinical team, and algorithm-based treatment plans. While the CGM groups had access to real-time glucose levels around the clock, which we speculated would result in greater improvement in HbA1c, our hypothesis was not supported possibly due to more frequent engagement by clinical teams supporting a greater sense of self-care in the remote blood glucose monitoring groups.

Comparison to a previous Systematic Review

The results from our review aligned well with a previously published 2015 systematic review which focused on remote blood glucose monitoring in T1D and T2D.³ Authors of the systematic review hypothesized that patients in remote blood glucose monitoring groups would test their glucose more often than the control groups.³ The benefit of SMBG as an explanation for improvements in HbA1c was examined. Increased SMBG use was expected with remote blood glucose monitoring, however, several studies showed no correlation with frequency of SMBG and improvements in HbA1c.³ The systematic review concluded that SMBG may contribute to improved glycemic control, but does not fully explain the benefits of remote blood glucose monitoring.³ Patients using remote blood glucose monitoring reported increased self-motivation because they were being monitored more closely by their healthcare provider.³ A significant association between data upload frequency and improvement in HbA1c was observed, providing a quantitative measure of self-motivation, which correlated well with the effectiveness of remote blood glucose monitoring.³

Most individual studies included in our review, as well as those included in the aforementioned systematic review, were short in duration. However, two studies from the systematic review demonstrated that remote blood glucose monitoring can help lower and maintain HbA1c levels over several years compared to control groups.³ While insulin dose changes have the potential to lower HbA1c, several studies from the systematic review demonstrated improvements in HbA1c that were independent of insulin dose adjustments, reinforcing the benefit of lifestyle interventions as important factors supporting remote blood glucose monitoring.³

The included systematic review identified several studies that included patients with over 8% HbA1c at baseline. They found greater improvements in HbA1c in the intervention groups, which was also observed in the current review.³ The systematic review also identified several studies that included patients with low HbA1c at baseline. Results still showed greater improvements in the intervention group with a significant decrease in mean HbA1c of 6.70% to 6.50% ($p=.045$), compared to no significant change in HbA1c in the control group.³ The systematic review concluded patients with a range of HbA1c could benefit from remote blood glucose monitoring and low HbA1c at baseline was not a limitation.³

Remote Blood Glucose Monitoring

Our review included a total of 21 studies that used remote blood glucose monitoring, all of which indicated reductions in HbA1c within the treatment groups. Absolute reductions in HbA1c ranged from a high of 3.00% to a low of .26%. The remote blood glucose monitoring study with the largest effect for HbA1c reduction of 3.00% used an intensive algorithm-based diabetes medication management program along with education and communication from the clinical care team which may explain why results were so high.³¹ The study did not have a control group and therefore mean difference was not calculated.³¹ There were similarities between this study and the CGM study with the largest effect on HbA1c reduction. In the CGM study, which took place in Belgium, an educational program combined with CGM was administered to a very small sample size of six participants who completed three months of the study, of which only four participants continued on to complete the entire six month duration of the study.¹⁷ The study did not include a control group, therefore a mean difference was not calculated.¹⁷ The intensive nature of both the remote blood glucose monitoring study and CGM

study interventions along with targeting a small sample, may have allowed for individualized attention and therefore may not be reflective of most interventions used in clinical practice.

One remote blood glucose monitoring study provided a two-hour education class and timely messaging or telephone follow-up with education or medication adjustments based on remotely transmitted glucose data over a six-month intervention period.²⁸ The intervention resulted in an average absolute reduction of 1.70% in HbA1c, which was among the largest reductions reported in our review. Another study, with results showing similar effectiveness, provided a half-day education class and used treatment algorithms combined with messaging or telephone follow-up based on remotely transmitted glucose data over a 12-month intervention duration.³⁰ In this study, the control group, who also participated in the half-day education class, also saw a substantial improvement with an average absolute reduction of 1.20% in HbA1c.³⁰

Six studies had similar average absolute reductions in HbA1c, ranging from 1.11% to 1.00%, and similar treatment methods.^{1, 6, 8, 10, 20, 23} One study provided monthly telephone calls to discuss remotely transmitted data and make treatment changes over six months.¹ One study took place over three months during Ramadan and provided telephone calls to discuss remotely transmitted data.²⁰ An alarm system was also used to notify the clinical team of three consecutive hypoglycemic readings.²⁰ One study provided clinician messaging and recommendations every two weeks based on remotely transmitted data over 30 months.²³ One study provided personal messaging with advice and reminders based on remotely transmitted data every two weeks over the course of six months.¹⁰ One study was based in the United Kingdom and provided treatment and lifestyle advice over the phone based on remotely transmitted data over the course of nine months.⁸ And one study was a pilot study with no control group and only included seven

participants, but provided personal messaging with feedback based on remotely transmitted data over three months.⁶

Several studies had similar treatment group methods, with clinicians sending individual feedback and making medication adjustments as needed over 12 months and six months respectively, based on remotely transmitted data.^{7, 25} It was concluded that telemedicine supported greater self-decision making among patients and was a driver in better self-care.⁷ Studies with the smallest average absolute reduction in HbA1c of 0.29% and 0.26% had similar treatment group methods, with clinicians providing individualized feedback when preset alarms sounded indicating glucose was outside of target range.^{14, 21} One study took place in Poland and was six months in duration, and one study took place in Italy and was 12 months in duration.^{14, 21} These studies were the least proactive regarding engagement with patients, which may explain why absolute reductions in HbA1c were among the lowest of the studies included in the current review.

Continuous Glucose Monitoring

A total of six studies were included that used CGM, all of which indicated reductions in HbA1c within the treatment groups. Average absolute reductions in HbA1c ranged from a high of 2.05% to a low of 0.23%. The study with the greatest reported average reduction took place in Belgium and showed an average reduction in HbA1c of 2.05%.¹⁷ The study did not include a control group, therefore a mean difference was not calculated.¹⁷ One reason that the reported effect may have been larger as compared with other studies is that a specific educational program combined with CGM was administered to a very small sample size of six participants who completed three months of the study, of which only four participants completed the entire six month duration of the study.¹⁷ Those who dropped out before six months did so because of

technical difficulties with use of the CGM device.¹⁷ The intensive nature of the intervention and the small sample may have allowed for individualized attention and therefore may not be reflective of most interventions used in clinical practice.

One of the CGM studies used data from the DIAMOND study and had a primary aim of identifying whether baseline HbA1c could predict the magnitude of glycemic improvement.¹⁸ The intervention resulted in an average absolute reduction of 1.05% in HbA1c which was among the largest reductions reported in our review. A significant number of participants had a high baseline HbA1c >9%.¹⁸ Results of the study showed a positive relationship between high baseline HbA1c and improvements in glycemic status in both the treatment group and the SMBG control group.¹⁸

Two studies that indicated similar effectiveness for CGM had different intervention methods. One used data from the DIAMOND study and had a primary aim of measuring the effect of reduced SMBG testing after adopting CGM.¹³ All participants were provided with guidelines for supplemental treatment decisions based on their CGM data.¹³ The other study focused on a T2D patient population in Singapore with stage three or higher diabetic kidney disease not on dialysis.¹² Since all participants had diabetic kidney disease, the relatively large effect size may have been influenced by improved patient adherence to positive lifestyle choices due to greater health risk consequences.¹²

Of the CGM studies, one was unique in that the primary aim was to evaluate differences in detection of hypoglycemia using conventional methods versus CGM. In this study, the reductions in HbA1c were the smallest of the six CGM studies, likely because the participants baseline HbA1c levels were lower compared with other studies, and there was not a focus on an overall lifestyle intervention based on blood glucose readings.¹⁹

Side by Side Comparison

There are cost differences between the two technologies that should also be taken into consideration when selecting the technology that may provide the greatest overall benefit for the patient. Private insurance, Medicaid, and Medicare coverage vary greatly between plans and from state to state³⁴. Traditional glucose monitoring devices and test strips are most often covered, and may or may not contain remote monitoring capabilities. CGM has had limited insurance coverage, often requiring that the patient needs multiple daily insulin injections to qualify for the option to use this technology. Out of pocket costs can be quite expensive without insurance coverage. One recently published study in T1D patients compared the cost of SMBG to CGM over a six-month trial.³³ Results showed that the average cost for the use of SMBG was \$7,236 compared to \$11,032 for CGM.³³ The main difference in these costs was the upfront price of the CGM device; overall, the average cost was reduced with longer-term use.³³

The current critical review did not reveal any studies that directly compared remote blood glucose monitoring and CGM technologies. Because of this lack of direct comparison, the current results should be interpreted with caution. While not an a priori focus of the current review, we noticed that there was heterogeneity in the methods and devices used in the remote blood glucose monitoring and CGM interventions. Some research reveals differences in accuracy, reliability, and precision among devices.¹⁶ Differences in technical skills required of users to operate the devices should also be taken into consideration when evaluating results of our comparisons, as technical difficulties were reported as the cause of participants withdrawing from several studies.^{16, 17} (See Table 3.3)

While new technology has the potential to support better metabolic improvements in diabetes care through more timely and responsive management, it appears that frequent follow-

up for the remote blood glucose monitoring groups may have resulted in greater reductions in HbA1c compared to the CGM group. Algorithm-based treatment plans might also support greater reductions in HbA1c by providing more timely lifestyle and medication interventions as compared with clinical expertise alone, to ensure a better outcome for patients.

Gaps in Current Knowledge

As indicated previously, the current critical review did not reveal any studies that directly compared remote blood glucose monitoring and CGM technologies. Directly comparing both methods with the same controls would best answer our study question. Additionally, there was heterogeneity in the methods, devices, and controls used in the remote blood glucose monitoring and CGM interventions. Future studies should address these limitations by conducting rigorously designed randomized controlled trials to directly test the effectiveness of remote blood glucose monitoring compared with CGM.

While evidence clearly shows that improved glycemic control can prevent and mitigate diabetic complications, the current standard of care is failing to meet optimal HbA1c targets for T2D patients.^{1,3,4} The current critical review suggests that both remote blood glucose monitoring and CGM can play an important role for achieving positive clinical outcomes for patients, however technical skills by participants might be a limitation. Several studies, particularly with use of CGM, reported participants dropping out due to technical difficulties. While the current critical review did not compare feasibility or cost of these two different monitoring technologies, there are gaps in current knowledge which may be barriers for widespread patient adoption of either technology. Future studies should include a comparison of feasibility, cost of care to implement the interventions, and cost savings to inform clinical decision making, thereby identifying the technology with the greatest overall benefit for the patient.

Conclusion

The current critical review suggested that both remote blood glucose monitoring and CGM are effective for reducing HbA1c in T2D patients when compared to controls. Overall, larger effects were seen in the studies that included remote blood glucose monitoring interventions as compared with the studies that included CGM. Side by side comparisons of the included studies agreed with previous research and indicated a tendency for greater absolute reductions in HbA1c where patients had higher starting HbA1c levels, frequent engagement with the clinical team for more timely and responsive management, as well as algorithm-based treatment plans.

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