

Evaluation of benefits on using diabetes technological devices in emerging adults with type 1 diabetes.

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Abbreviations: (ABC) Automated Bolus Calculator, (ADA) American Diabetes Association, (ASP) Augmented Sensor Pump, (CGM) Continuous Glucose Monitor (CSII) Continuous Subcutaneous Insulin Infusion, (DKA) Diabetes Ketoacidosis, (FGM) Flash Glucose Monitor, (FDA) Food and Drug Authority, (HbA1c) Glycated Hemoglobin, (HCL) Hybrid Closed Loop, (IDF) International Diabetes Federation, (MARD) Mean Absolute Relative Difference, (PICO) Population, Intervention, Comparator and Outcome, (PLGS) Predict Low Glucose Suspend, (PRISMA) Reporting Items for Systematic Reviews and Meta-analysis, (T1D) Type 1 diabetes.

Keywords: Benefits, Diabetes, Emerging Adults, Technological Devices.

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Abstract

Research title: Evaluation of benefits on using diabetes technological devices in emerging adults with type 1 diabetes.

Background: In the past few years advances in technology used in diabetes care has been observed. Achievement of glycemic control remains challenging in emerging adults with type 1 diabetes due to alternating adolescent behavior and despite of technological advancement until recently only minority of patients were using devices.

Objectives: This study aims to identify the clinical benefits of using diabetes technological devices in type 1 diabetes management in emerging adults. Illustrating clinical benefits in glycemic level control and prevention or reduction of diabetes complication like hypo- or hyperglycemia and diabetes distress.

Methods: Rapid review method of the scientific literature was conducted using PubMed and Cochrane database. Studies reported in English and published between 2010 and 2020 were included. PRISMA statement was employed in identification, screening and assessing eligibility criteria of studies in the review. From the 350 studies identified, 15 met inclusion criteria.

Results: Most of the reviewed studies showed clinical benefits of using insulin pumps and/or continuous glucose monitors related to glycemic control. Increase in the time spent within target glycemic range, reduction in glycated hemoglobin level (HbA1c), incidence of severe hypoglycemia or hyperglycemia and improvement in the quality of life.

Conclusion: This review study pointed out the clinical significance of using continuous glucose monitor and/or insulin pump with improvement glycemic control, reduce incidence of severe hypoglycemia and diabetes distress. As adolescents are increasingly accessing technologies. Further research is hence needed to assess accessibility of devices to emerging adults.

Background

Diabetes technology is the term used to describe the hardware, devices and software that people with diabetes use to help manage their condition, from lifestyle to blood glucose level. More recently, diabetes technology has expanded to include hybrid devices, that both monitor glucose and deliver insulin, some automatically, as well as software like online resources, mobile apps and telemedicine that serves as a medical device providing diabetes self-management support (Beck *et al.*, 2019) (Kubiack T *et al.*, 2020). Type 1 diabetes represents about 5% – 10% of diabetic cases world-wide, the incidence is increasing of which the burden is being eased by novel treatment modalities, particularly from the field of diabetic technologies (Tauschmann and Hovorka, 2018)(IDF, 2015). The use of technologies helps to reduce the risk of acute complications such as severe hypoglycemia and diabetic ketoacidosis as well as long-term macro- and microvascular complications (Prahalad *et al.*, 2018)(Zimmerman, Neill and Haller, 2019)(Costa *et al.*, 2009)(Ramchandani and Heptulla, 2012).

Diabetes technology is now becoming the delivering tool that have made their way into clinical care (Pettus and Herrath, 2018). In 2018 WHO Classification of digital health intervention with similar aims of providing government, technologists, clinicians, researchers and other communities in digital health a shared and standardized language for assessing digital health intervention (WHO, Digital health). Technological advances in type 1 diabetes care are rapidly moving us towards increasing automated devices which offer the promise of reduced disease burden (Zimmerman, Neill and Haller, 2019). By 2015 it is approximated that about 0.75 to 1.0 million diabetic patients are using continuous subcutaneous insulin infusion (Heinemann *et al.*, 2015). Adolescents is the challenging time for diabetes management and adherence, flash glucose monitoring may assist adolescents with self-monitoring glucose levels and inform treatment decisions that results in glycemic control (Boucher *et al.*, 2019). Diabetes technology

improvement has impacts on the diabetes distress in perspective of the effects of technology on the diabetes self-management care in the control of glycemic level and prevention of complication as shown by one of the study done in UK that the role of elevated diabetes distress in influencing HbA1c and self-management behaviors crucial for good diabetes health such as glucose monitoring and insulin administration or restriction (Sturt *et al.*, 2015). About 0.5 billion people (out of 2.7 billion using smartphones) in the world use mobile apps for diet, physical activities and chronic disease management particularly digital health apps for people with diabetes has developed a rapid pace and become an increasingly a common aspect of diabetes care and self-management in certain population (Heinemann *et al.*, 2015; Fleming *et al.*, 2020). One of the study done in Brazil and published on 2020 reported that it was the first study to be done among the developing countries that based on flash or scan glucose monitoring and the result have shown that increase in the use of scan technology was associated with improvement in the glycemic level (Calliari *et al.*, 2020). Intensive management of all aspect of diabetes, especially the glycemic control, is now the international gold-standard in children, adolescents and young adults (Dimeglio *et al.*, 2018). Study done in Colombia have shown about 58% of the enrolled patients have improved glycemic control by lowering in their HbA1c level after switching from MDI to sensor augmented pump therapy SAPT (Henaio *et al.*, 2019). The study done in Germany and published on 2019 showed that over the past decade, both the accuracy and usability of CGM devices have improved with considerably with expanded cost coverage of CGM by government statutory and private insurance (Miller *et al.*, 2019). The use of technology in the management of type 1 diabetes is beneficial medically, may in fact add to burden to disease management and reduce diabetes related distress including fear, feeling of guilt, anxiety, depression and being overwhelmed by diabetes (Barnard *et al.*, 2016). One of the randomized control trials done in Germany and published on 2017 had showed that use of technological

devices particularly real-time CGM have improved the glycemic level and lowered incidence of hypoglycemia by 72% of the enrolled study participants (Heinemann et al., n.d, 2018). The sample tables showing some of the selected both glucose monitoring and insulin delivery devices as shown in table 1 – 3.

In the past decade have witnessed rapid advances in technology used to treat patient with type 1 diabetes while the disease burden is still high but this advance have contributed to improvements in both glycemic control and quality of life for many of those affected (Zimmerman, Neill and Haller, 2019)(Costa *et al.*, 2009). One of the comparison study have shown that despite of the diabetes technological advancement like use of CGM to improve glucose control in patient with type 1 diabetes but until recently only a minority of the patients are using devices as shown by USA, German and Australian type 1 diabetes registry (Miller *et al.*, 2019). We are in the middle of revolution of technological advancements in diabetic care. This technology boom and associated variety of diabetic management tools enable clinicians to develop new and innovative means of treating their patients, additionally this advancement have the potential to decrease burden of disease management on the patients themselves, improving patient care and its delivery (Ramchandani and Heptulla, 2012). Data from 54000 children and adolescents with type 1 diabetes from three large transatlantic registries showed that the use of insulin pump therapy was lowest in England and Wales 14% by 41% in German and Australia while USA has 47% (Beck *et al.*, 2019). Another study has found while adolescents are increasingly accessing technologies to support the self-management of type 1 diabetes the impacts of these tools on clinical outcome is not clear (Goyal *et al.*, 2017). Tight blood glucose control which is achieved by these technological advancements in type 1 diabetes delays onset of macro- and microvascular complications with monitor of glucose level to prevent hypoglycemia (Bolinder *et al.*, 2016). One of study published on August 2016 showed that data from randomized control

trials are limited on the use of medical devices, but existing studies support the use of diabetes technology for wide variety of indications (Peters *et al.*, 2016). One of the literature review has found that diabetes distress has shown to be 20 – 30% of the study participants that necessitate the benefits of technology utilization in the management of diabetes as it has also shown that glycemic level control and diabetes complications impacts diabetes distress (Sturt *et al.*, 2015). So, this study aims to identify the benefits of diabetic technological devices for the past ten years to enhance the use these devices in the management of type 1 diabetes as have been shown by different studies that they have improvement in the outcome.

Study to address the benefits of the use of diabetic technological devices in the management of diabetes particularly type 1 is of perhaps important so community may be aware to why they must initiate and keep using these technological devices (Heinemann *et al.*, 2015). Technological intervention in management of type 1 diabetes was shown to be accepted by children and young people as shown by the study done Knox *et al* (Knox *et al.*, 2019). One of the study done in New Zealand and published on 2019 have reported if improvements are found this will further encourage steps towards integrating FGM into regular diabetes care for youth with unhealthy glycemic control, with the expectation it will reduce daily diabetes burden and improve short and long term health outcomes in this high risk group (Boucher *et al.*, 2019). Study aims to bring awareness on the benefits of using technological devices in the management of type 1 diabetes among youth. According to WHO data from 24 countries in 2020 report from 2016 to 2019 human insulin was available only 61% of all health facilities and analogue insulin were only available in 13%, so this necessitate the need and use of technological advancement in diabetes management ([WHO2020](#)).

Table 1. *Characteristic of selected Continuous glucose monitoring devices (CGM) and Insulin delivery pumps (Ramchandani & Heptulla,*

| Device name | Accuracy Overall (%MARD) | Approval availability | Sensor lifetime | Calibration | Smart device compatibility | Remote monitoring |
|--|--|--|--------------------|--|--|---------------------------|
| Medtronic Paradigm Minimed Veo 530G | Enlite-sensor Adults 13.6% MARD | FDA in USA CE mark in Europe | Enlite 6 days | 2 per day | Minimed connect | Minimed connect |
| Dexcom G4 Platinum CGM 2012 | Adults above 18 years – 13%MARD Pediatric 2 – 17 years – 15% MARD | Approved by FDA CE mark: available in USA, EU, Middle East, South America, Australia, New Zealand | 7 days | 2 per day | No | Share |
| (Abbott) FreeStyle Libre Flash Glucose Monitoring system | 11.4% MARD 10.1% MARD | CE mark: for ages above 18 years in UK, France, German, Spain, Italy, Sweden | 14 days | Not required by end user | Librelink (Approved software for androids) | Summary report via E-mail |
| Insulin delivery devices | | | | | | |
| System | Basal | Bolus | Age | Meter/CGM Integration | Additional feature | |
| Insulet corporation OmniPod system | 0.05 – 30 units/hr in 0.05 units increment | 0.05 – 30 units in increment of 0.05 units whole insulin-to-carb ratio | All ages | PDM with built in glucose meter | Tubeless PDM with database of 1000 common food with nutrition information | |
| Medtronic MiniMed 670G | 0.025 – 35 units/hr in 0.025 units increment | 0.025 – 25 units in increment of 0.025 units insulin-to-carb ratios with fraction of grams | 14 years and older | Contour next 2.4 meter Medtronic Guardian 3 CGM | Hybrid closed-loop pump with SmartGuard technology Auto mode adjust basal insulin based on CGM readings and recent insulin requirements | |

| | | | | | |
|--------------------------------------|---|---|-------------------------|------------------|--|
| | | | | | Users input boluses Manual mode with PLGS feature |
| Tandem Diabetes care t:slim X2 | 0.1 – 15 units/hr in 0.01 units increment | 0.05 – 25 units in 0.01 units increment Insulin-to-carb ratio with fraction of grams | 6 years and older | Dexcom G6 CGM | Tandem device updater remotely updates software without purchasing a new device Basal-IQ technology with PLGS feature |

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Technological advancement has now been arising and widely spreading throughout the world necessitating use of technology in the management of chronic diseases like diabetes particularly type 1 diabetes (Beck *et al.*, 2019). There is various study which have shown emerging new technologies with the use of modern devices in the management. The use of technology has led to improved glycemic outcomes and quality of life of people with diabetes (Thabit and Hovorka, 2017). Advances in glucose monitoring and insulin delivery system has improved clinical outcomes and quality of life for people with type 1 diabetes in the study done at United Kingdom (Beck *et al.*, 2019). This study based on the review of the diabetic technological devices particularly those used in insulin delivery and glucose monitoring for the past ten years to date and their benefits to the diabetic care among youth aged 13 to 24 years. The use of technology in the management of type 1 diabetes is beneficial medically, may in fact add to burden to disease management and reduce diabetes related distress including fear, feeling of guilt, anxiety, depression and being overwhelmed by diabetes (Barnard *et al.*, 2016). Study done by McCarthy and Grey published on 2018 revealed that merging adults were less likely to use insulin pump (56%) or continuous glucose monitors (7%), but were more likely to miss at least one insulin dose per day (3%) and to have at least one episode of Diabetes ketoacidosis in the past year (7%) (McCarthy, 2018). This case necessitates the outline and highlight of study on the benefits of using technology in the management of type 1 diabetes particularly among young adults.

Insulin supply

Diabetes technology on the insulin supply was of great advancement as the impacts of technology as evidenced by the following studies. First insulin pump was invented in 1974, but it was only used during DKA and hospitalization, technologies still advances as time goes leading to the transformation of devices to an extent that in June 2018 the FDA approved Insulin

Management system which includes a Bluetooth enabled pod and updated touch screen PDM, currently there is hybrid closed loop system and the smart devices will be used to monitor blood glucose level, insulin delivery and automatically administer prandial insulin boluses (Zimmerman, Neill and Haller, 2019)(Pettus and Herrath, 2018)(American Association of Diabetes Educators, 2018). Insulin pump therapy also known as CSII is an important and evolving form of insulin delivery, which is mainly used for patient with type diabetes (Heinemann *et al.*, 2015). Closed loop control is more effective as shown by the study done which revealed T1D improved glycemic control and reduced exposure to hypoglycemia even during intense winter sport activities (Forlenza, Deboer, *et al.*, 2017). According to WHO data from 24 countries in 2020 report from 2016 to 2019 human insulin was available only 61% of all health facilities and analogue insulin were only available in 13%. Due technological advancement like apps and technological diabetic devices inflation in 2017 National practice survey found that 88% of diabetes educators indicated that they have influence on insulin initiation and use of technology (American Association of Diabetes Educators, 2018). Studies shows that automated insulin delivery studies remain low in number and sample size (Priesterroth, 2020). Another study done in Barcelona, Spain have shown that the use of automated bolus calculator (ABCs) coupled with advanced carbohydrate counting have shown glycemic level improvements, increase in treatment satisfaction and reduction in both episodes and fear of hypoglycemia (Alcántara-aragón, 2019). People with type 1 diabetes need insulin for their very survival and to maintain their blood glucose levels to reduce the risk of common complications ([WHO2020](#)).

Glucose monitor

Moreover, technology have improved the glucose monitoring strategies in terms of time, accuracy and regulation. Home blood glucose monitors came into clinical use in the late 1980s and replaced urine testing, as technology advances to 1990s we got Continuous glucose monitor which has improved accurate and provide patient continual, real time information about their blood glucose level (Pettus and Herrath, 2018). The study done in Germany and published on 2019 showed that over the past decade, both the accuracy and usability of CGM devices have improved with considerably with expanded cost coverage of CGM by government statutory and private insurance (Miller *et al.*, 2019). The use of this devices has shown to improve diabetes self-treatment when used consistently (Uirassu Borges and Kubiak, 2016).

An individualized approach to the patient is emphasized and a decrease in target HbA1c to < 7% is recommended for those using the new technologies constituent with the goal for children, adolescents and young adults with type 1 diabetes (Dimeglio *et al.*, 2018). Use of CGM is generally associated with an improvement in the HbA1c level and reduction in the risk of hypoglycemia (Rodbard, 2016). An observational data on T1D Exchange shows that only a small percentage of patients with T1D are using CGM on the ongoing basis, surprisingly on beneficial effects observed in clinical trials and survey users (American Association of Diabetes Educators, 2018)(Rodbard, 2016). CGM provides information unattainable by intermittent capillary blood glucose, including instantaneous real-time display of glucose level and rate of exchange of glucose, alert and alarm for actual or impending hypo- or hyperglycemia and ability to characterize glycemic variability (Rodbard, 2016). There is a study done USA which showed, patient with type 1 diabetes who use real time continuous glucose monitoring about 60-70% of time have significant improvements in glycemic control (Ramchandani and Heptulla, 2012). One of the randomized control trials done in Germany and published on 2017 had showed that use of technological devices particularly rt-CGM have improved the glycemic level and lowered

incidence of hypoglycemia by 72% of the enrolled study participants (Heinemann et al., n.d, 2018)(Alcántara-aragón, 2019). A systematic review study done by Sturt et al showed that the evidence suggests that 20 – 30% of people with type 1 diabetes will experience elevated diabetes distress that will be affecting their self-management behavior and their glycemic control (Sturt *et al.*, 2015).

METHODOLOGY

Study design

In this study a Rapid effectiveness review was used. This is within the family of systematic reviews, but it specifically reviews whether the health system intervention works including its intended and unintended effects (WHO, 2017)(Ask Us, 2018). Of which this study reviewed on the benefits of using technological devices in the management of type 1 diabetes for the published studies for past ten years to date, it also responsive, timely can be within days to week, accurate and reproducible (WHO, 2017). Rapid effective review is composed of six phases (Ask Us, 2018). Preparing the guiding questions, literature search, data collection, critical analysis of the studies included, discussion of the results and presentation of the rapid effective review (Messina *et al.*, 2018).

Review steps

In this rapid review each step was as analyzed below

Search strategy and screening

A systematic search was conducted using PubMed and Cochrane electronic databases combining the responsible keywords of the studies published from January 2010 to January 2020.

Keywords was; type 1 diabetes, T1D, T1DM + youth(s), adolescents, young adults, emerging adults + technological device(s), diabetes technology, technology utilization, CSII, CGM, FGM, SAP, SAPT, hybrid closed loop + benefits, significances, improvements + glycemic control, diabetes complication, episodes of, incidence of hypoglycemia, hyperglycemia, DKA, diabetes distress, emotional wellbeing.

Inclusion/Exclusion criteria

The following inclusion criteria was used in the selection of the study to be used in this study: (a) any study design reporting data from/on young or emerging adults from 13 to 25 years of age (b) published from January 2010 to January 2020 as it is the period when the technology had widely spread on the management of T1D, as reported by different studies (Zimmerman, Neill and Haller, 2019)(Miller *et al.*, 2019) (c) exclusively with type 1 diabetes (d) using diabetes technological devices in insulin delivery and glucose monitoring (e) with outcome of interest (i) improved glycemic control (lowering HbA1c) (ii) decrease in the episodes or incidence of hypoglycemia, DKA, hyperglycemia (iii) improve from diabetes distress like emotional stability and wellbeing (Miller *et al.*, 2019). Exclusion criteria that will be applied are (i) type 1 diabetes in adults not including young adults or adolescents (ii) papers reporting on mixed samples where type 1 diabetes were not presented separately from other conditions (iii) papers where there are use of diabetes technology but no specific use of either insulin delivery devices or glucose monitoring devices (Miller *et al.*, 2019)(Messina *et al.*, 2018).

Eligibility criteria

Studies was eligible when has showed the benefits of using diabetes technological devices including either insulin delivery or glucose monitoring devices in the improvement of glycemic

level (lowering in HbA1c), decrease in diabetes complication like episodes of hypo/hyperglycemia, DKA and also in diabetes distress.

Study selection and Data extraction

Studies was reviewed to check for eligibility (title and abstract, and if necessary full text article) and extracts appropriate information in full text articles using either qualitative or quantitative tool. There was double extraction to validate the eligibility of the extracted data even of at least 50% of the studies selected for extraction (WHO, 2017). Data to be extracted from article includes the year of publication, country, study design, period of data collection, baseline characteristics of participants, intervention and comparators, and outcomes.

Intended outcomes was on the improvement of glycemic level particularly using HbA1c level, episodes of hypo/hyperglycemia, diabetes distress (Jeronimo *et al.*, 2019)(WHO, 2017) as shown in the Table.

Statistical analysis

The main characteristics of the study was summarized including the study's objectives and design, characteristics of study participants, intervention and comparators. Effects across the studies was summarized with (a) improvement of glycemic level (b) episodes of hypoglycemia, hyperglycemia or DKA (c) emotional instability due to diabetes distress.

Study limitations

One of the obvious limitations in this review was lack of studies with clinical benefits as the primary endpoint.

A potential bias when comparing these studies was difference in the use of reference range of glycemic level and severity of hypoglycemia. Lower level of glycemic ranging from 50mg/dl to 70mg/dl while higher ranges from 180mg/dl, 200mg/dl, 250mg/dl and above.

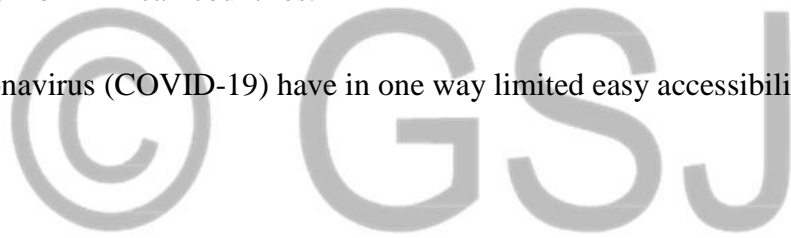
Limited number of studies that have collectively work on emerging adult with type 1 diabetes and use of diabetes technological devices.

Different inclusion criteria were used in some studies reviewed. Because some studies have included different age group in the same studies but have specified their results to target age group.

Difference in study design, participants age, study location/setting

No reported study from African countries.

Outbreak of Coronavirus (COVID-19) have in one way limited easy accessibility of resources.



RESULTS

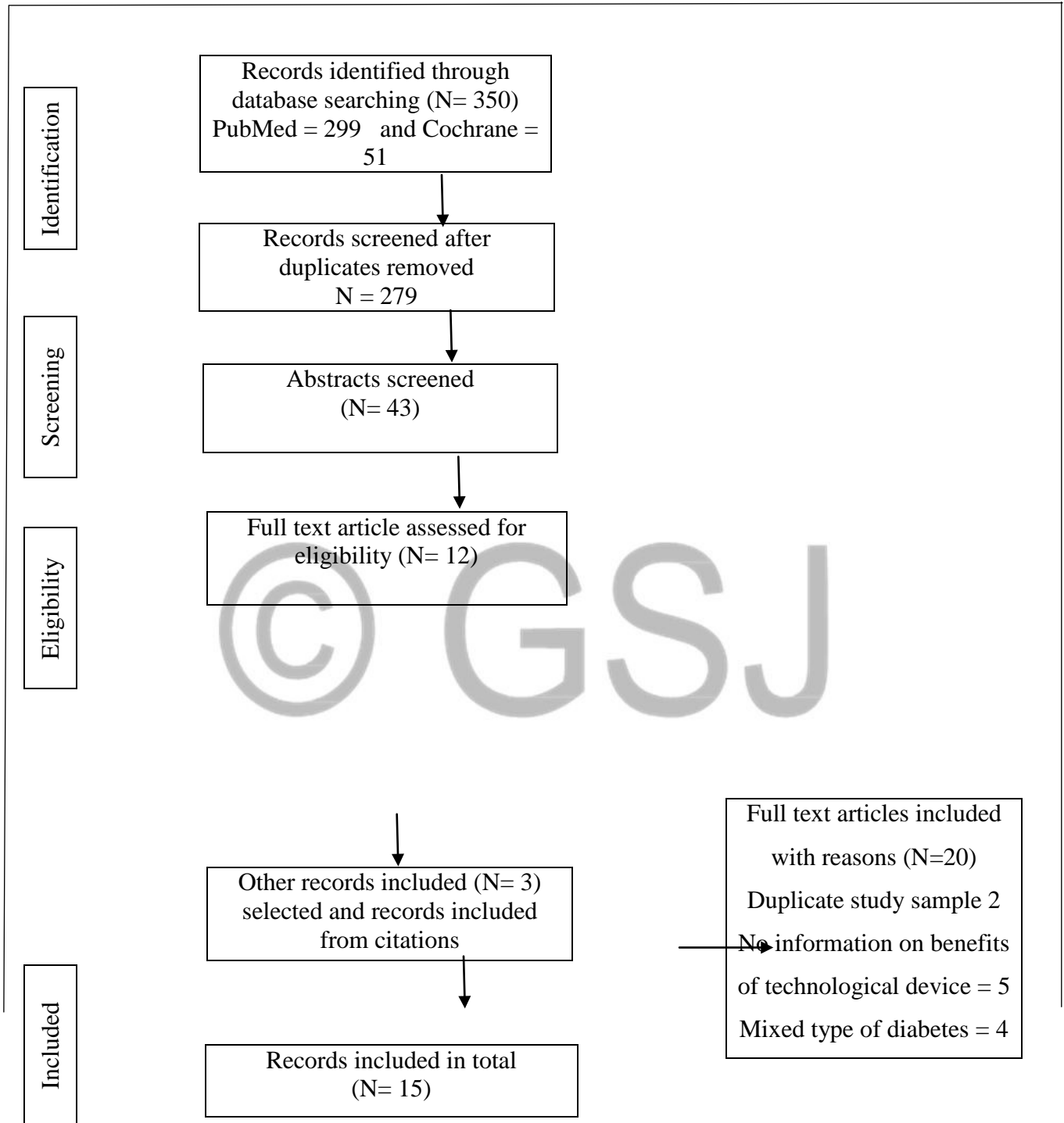


Figure 2. PRISMA 2009 Flow diagram. Source (Moher *et al.*, 2009).

Reviewed studies characteristics

The search revealed 350 abstracts and titles, after reviewing abstracts 43 studies were involved in the full text review. 15 studies met eligibility criteria for review of which 3 potential studies were identified from the reference lists. 8 out of the selected studies were randomized control trials, 6 were either systematic, meta-analysis or both review and 1 was cross-sectional study. Studies reported in English and published between 2010 and 2020 were included. Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement was employed in identification, screening and assessing eligibility criteria of studies in the review. Included studies used quantitative methods and come from USA (6), UK (3), Denmark (2), Netherlands (2), Australia (1) and Spain (1). Study characteristics are presented in Table 1. The sample size of the studies ranged from 14 to 2000 and included a total of about more than 26700 participants. Some studies have not reported or differentiated number of participants according to the gender. For studies which have reported on gender it was estimated to be about 60 by 50 percentage of female and male respectively. The lowest mean age of study participants was 16 years (Hillard *et al.*, 2014) and the highest was 23 years (Forlenza, Deboer, *et al.*, 2017)(Forlenza, Deshpande, *et al.*, 2017), some of the studies didn't report age. The oldest study being published 10 years ago (Davey, Jones and Fournier, 2010) while the latest study being just about 6 months ago (Rosner and Id, 2019). In the reviewed studies, important and different technological devices used for diabetes management among type 1 diabetes patients were identified for various significance pertaining to glycemic control, reduction or prevention of diabetes complications like severe hypoglycemia or hyperglycemia and diabetes related distress. Employed intervention were use of diabetes technological devices such as insulin delivery devices and glucose monitoring devices. Studies have shown that some use one of the device or others use both devices. Studies found to use both devices were named as closed loop system or artificial pancreas as an extended use of

insulin infusion set and continuous glucose monitors which are both designed to the common target of monitoring glucose and reduction or prevention of severe hypoglycemia as well as diabetes distress prevention or reduction.

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| Author, Year, Country | Study design/ Method | Devices used | Aim | Sample | Main results/themes |
|---|---|----------------------------|--|---|--|
| Forlenza G.P and Associates August 2017 America | Randomized Cross-over controlled home-use trial | Dexcom G4 Platinum and IIS | Artificial pancreas become standard of care, consideration of extended use of insulin infusion sets and continuous glucose monitor | Population = Young adults Sample size = 19 Gender (M/F) = 8/11 Age (mean) = 23years | Glycemic control has shown statistical significance with the use of insulin infusion set and continuous glucose monitor by 71.6% with $P = 0.008$ with glycemic range of 70-180mg/dl HbA1c target of 7% attained with 68% Reduction in the episodes of hypoglycemia both overall and overnight hypoglycemia with $P = 0.001$ |
| Cornelis A.J and J. Hans DeVries 2016 Netherlands | Literature review | | To assess impact of continuous glucose-monitor in hypoglycemia | Type 1 diabetes using CGM 18 studies used Age (N/A) | Use of CGM for purpose of preventing hypoglycemia was found to reduce episodes of hypoglycemia |
| Battelino T <i>et al</i> April 2011 Europe | Randomized controlled Multicenter study | FreeStyle glucose meter | To assess impact of continuous glucose-monitor in hypoglycemia | Population = Young adults with type 1 diabetes Sample size = 62 Gender (M/F) =30/26 Age (mean) = 23years | Time spent in hypoglycemia below 63, 55, 70mg/dl was significantly reduced in CGM with $P = 0.03$, $P = 0.05$ and $P = 0.01$ respectively. Glycemic control was significantly attained in the meantime of the study to those using CGM found to have HbA1c of 6.69% with $P = 0.008$. Most of the time they had normoglycemia in the range of 70 to 180mg/dl with $P = 0.009$ |

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| Bally L <i>et al</i> November 2017 UK and USA | Randomized multicenter clinical trials Medtronic MinMed 640G | | To assess the effectiveness of closed-loop control with pump and sensor- augmented pump in youth with type 1 diabetes | Population = youth with type 1 diabetes Sample size = 84 Age (mean) = 18years | Glycemic control attained and significantly improved in use of closed- loop control with target range of 70 to 180mg/dl $P < 0.0001$ Had HbA1c of 7.4% which was improved with $P < 0.0001$ Most of the time they we're in the normoglycemic level day and night compared to the control group $P =$ 0.0002 |
| Jennifer L. Sherr August 2018 USA | Randomized cross-over clinical trial | Medtronic MiniMed 670G | To assess the use of closed loop in managing youth with type 1 diabetes | Population = youth with type 1 diabetes Sample size = 30 Age (mean) = 17years | 8.5% increase in time of target range of glycemia of 70 to 180mg/dl and 0.6% reduction in HbA1c level with $P < 0.001$ Reduction in time spent as hyperglycemia above 180mg/dl 10-20% increase in time target range with a concomitant reduction of frequency of hypoglycemia. |
| Davey R J <i>et al</i> November 2010 CA, USA | Cross- sectional study | Medtronic, MiniMed Guardian | To assess the effect of real-time CGM in incidence and duration of hypoglycemia to type 1 diabetes | Population = youth with type 1 diabetes Sample size = 14 Gender (M/F) = 7/7 Age (mean) = 20years | The real-time CGM has significantly reduced the time spent below hypoglycemic thresholds defined operationally as CGMs readings <65mg/dl by 64% ($P < 0.05$) and decreased hypoglycemic incidence by 44% ($P < 0.05$) |
| Russell S J <i>et al</i> July 2014 | Random order crossover | Dexcom G4 | To evaluate glycemic control of adolescents | Population = youth with type 1 diabetes | Glycemic control: Percentage of time with glycemic level target at 70 to 180mg/dl was high above 80% |

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|---|--|--|--|---|---|
| USA | design | Insulin pump | using bionic pancreas (CGM and Insulin pump) | Sample size = 32 Gender (M/F) = 16/16 Age (mean) = 16years | compared to control group ($P < 0.001$) Hypoglycemia, was lower as only found by 4% as compared to more than 7% of control group with $P < 0.01$ |
| Pickup J C et al July 2011 UK | Meta-analysis of randomized controlled trial | | To evaluate glycemic control in real-time CGM | Population = youth with type 1 diabetes (6trials) Sample size = 449 Age (mean) = 20years | Glycemic control as patients using rtCGM experiences reduction in the HbA1c of about 0.9%. 23% reduction in exposure of hypoglycemia |
| Calhoun P M et al 2016 USA and Canada | Clinical trial | MiniMed Paradigm Enlite Medtronic With Pump | To examine for efficacy of PLGS in relation to hypoglycemia among youth with type 1 diabetes | Population = youth with type 1 diabetes Sample size = 41 Gender (M/F) = 20/21 Age (mean) = 16years | PLGS was shown to be ineffective in prevention of hypoglycemia as it has shown the episodes of hypoglycemia appeared by 8% with $P > 0.01$ |
| Bastian Rosner and Andres Roman-Urrestarazu August 2019 Netherlands | Systematic review and Meta-analysis | Insulin pump (CSII) | To evaluate quality of life in pediatric patients with type 1 diabetes using CSII | Population = youth with type 1 diabetes Sample size = 2000 Gender (M/F) = N/A | Glycemic control, estimate mean difference in HbA1c between study group was bigger at follow-up as CSII group reported lower HbA1c with significance difference $P = 0.005$ Three-folds decrease of the hypoglycemia incidence in CSII |

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| | | | | Age (mean) = 16years | subjects. Improvement in Quality of life of children and youth using CSII |
| Gimenez M et al February 2018 Spain | Randomized control trial | CGM and insulin pump (CSII) | To identifies an inverse relationship between HbA1c and severe hypoglycemia among type 1 DM | Population = youth with type 1 diabetes Sample size = 160 Gender (M/F) = 70/90 Age (mean) = 16years | Glycemic control was achieved in the group using CSII with improved HbA1c by lowering it by 10% with statistical significance $P = 0.05$ Reduced number of episodes of hypoglycemia significantly with $P < 0.0001$ |
| Steineck I et al 2017 Denmark | Narrative review summary | CSII (sensor-augmented pump) Medtronic 640 | To assess hypoglycemia prevention in type 1 diabetes patients using SAP | Population = youth with type 1 diabetes Sample size = 156 Gender (M/F) = 70/86 Age (mean) = 16years | From the three trials found solid evidence that SAP treatment reduces glycated hemoglobin without increasing incidence of hypoglycemia from 8.3% to 8.1% $P < 0.001$ as compared to other study group |
| Martin Tauschmann and Roman Hovorka 2014 UK | Systematic review | | To review the efficacy and effect of closed loop system in type 1 diabetes managements in adolescents | Population = youth with type 1 diabetes Sample size = Gender (M/F) = N/A Age (mean) = 16years | Use of SAP has significant reduction in the episodes of hypoglycemia it has found to reduce hypoglycemic episodes by more than 80% with nocturnal hypoglycemia reduction by more than 70%. It also reported to improve the quality of life that is reduction in diabetes stress by reducing hypoglycemic fear among |

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|--------------------------------|--|--------------------------|--|---|--|
| | | | | | patients and their parents. |
| Neylon OM et al 2014 Australia | Randomized crossover trial | Medtronic Animas Omnipod | To assess improvements of self-care behavior in youth with type 1 diabetes using Automated pump function | Population = youth with type 1 diabetes Sample size = 26 Gender (M/F) = 8/18 Age (mean) = 16years | Improvement in the glycemc control as HbA1c was reduced by about 0.9% with statistical significance $P = 0.003$ There was personal satisfaction on the use of automated pump with other group using their own devices with statistical significance. |
| Sherr JL et al 2016 USA | Comparison results (pediatric diabetes registry follow-up) | | To evaluate Impacts of insulin pump therapy on metabolic control in type 1 diabetes children and adolescents | Population = youth with type 1 diabetes Sample size = 54410 Gender (M/F) =N/A Age (mean) = 16years | Glycemic control of the reported registries on the group using insulin pump was found to be higher compared to the group which does not use the insulin pump in the management with statistical significance $P < 0.001$ Across all the registries use of pump was associated with lower HbA1c. |

Table 2. Reviewed study characteristics

Glycemic control

In the management of diabetes attaining of or even nearly norm glycemic level is an individual and everyone goals, attaining through different methods and devices to be employed is an underlying cofactor. Target normal glycemic range is 70 – 180mg/dl (3.5 – 11.1mmol/dl) (Forlenza, Deboer, *et al.*, 2017)(Forlenza, Deshpande, *et al.*, 2017). Glycemic control can also be monitored by using level of glycated hemoglobin (HbA1c) which is assumed to below 7.5% (Battelino, 2011).

In this review study there are different studies which have shown to attain glycemic control as a result of using diabetes technological devices. Study done by Bottellino T with his fellows involving the participants enrolled for using continuous glucose monitor and an insulin pump as an intervention group revealed to attain a good glycemic control as glycated hemoglobin (HbA1c) was reduced by 0.27% and 0.39% respectively (95% CI – 0.47 to 0.07, $P = 0.008$) (Battelino, 2011). Another study done have revealed the improvement in the glycemic level as a result of using closed loop system in the diabetes management it had revealed significant decrease in glycated hemoglobin by 8.3% during screening to 8.0% after an intervention compared to the control group which was found to reduce from 8.2% of screening to 7.8%, HbA1c were significantly lowering in the intervention group compared to control group, with mean difference between the group favoring the closed-loop group by 0.36% (95% CI – 2.2 to 5.8, $P < 0.0001$), it has also reported that the proportion of time when the glucose was within the target range was significantly increased in closed-loop compared to control group in both day and night ($P < 0.0001$) (Tauschmann *et al.*, 2018). Jennifer L. Sherr in her study named Closing the loop on managing Youth with type 1 diabetes has found 8.5% increase in time in target range which was 70 to 180mg/dl glycemic level after switching from Open to Hybrid closed-loop

(HCL) insulin delivery with 670G ($P < 0.001$) and also glycated hemoglobin was reduced by 0.6% in adolescents compared to the baseline values ($P < 0.001$) (Sherr, 2018). One of the study done by Russell SJ with his fellows on the use bionic pancreas in the management of type 1 diabetes revealed that the mean glucose level on continuous glucose monitoring was within the target range as was between 130mg/dl to 150mg/dl as compared to control group with glucose range between 130mg/dl to 185mg/dl and the percentage of glucose in the target range of 70 to 180mg/dl was higher than that of the control group (80% Vs 60%) with both having a statistical significance as $P = 0.004$ and $P < 0.001$ respectively (Hillard *et al.*, 2014). One of the meta-analysis done on the glycemic control using real time glucose monitoring in comparison with self-monitoring of blood glucose reported to confirm hypothesis that the improvement in glycemic control with continuous glucose monitoring was greatest in those with highest baseline glycated hemoglobin while using sensor very frequently, it has reported a reduction in glycated hemoglobin (HbA1c) by 0.9% with about 10% baseline HbA1c level compared to self-monitoring blood glucose with reduction of just 0.56% (Pickup and Freeman, 2011). A systematic and meta-analysis on health-related quality of life in pediatric patients with type 1 diabetes mellitus using insulin infusion have revealed significance improvement in the glycated hemoglobin with significant mean difference with lower HbA1c in both measurement between the study group favoring CSII group ($P = 0.019$) (Rosner and Id, 2019). Review study done on the sensor-augmented insulin pump in prevention of type 1 diabetes have revealed that 156 children had greater reduction in glycated hemoglobin to Sensor-augmented pump compared to multiple insulin injection group (8.3% to 7.5% Vs 8.3% to 8.1%, $P < 0.001$) (Steineck *et al.*, 2017). Another Randomized Control trial on the use of technology in improving self-care behavior in youth with type 1 diabetes has reported significant improvement in glycemic control

after 6 months of automated pump use with reduction in glycated hemoglobin by 0.9% and had a statistical significance ($P = 0.003$) (Neylon *et al.*, 2014).

Diabetes complication

This rapid review study was looking on the significance of using diabetes technological devices to prevention or reduction of diabetes complication among youth with type 1 diabetes, of which it mainly or particularly based on the complication like hypoglycemia, hyperglycemia and diabetes distress as changes in the quality of living of a patient due to underlying diabetes condition. The reviewed studies were analyzed as to find out results about these complication as follows,

Hypoglycemia and Hyperglycemia

Blood glucose level which can either by using sensor or glucometers can be used to check for amount of glucose in the blood. Lowest normal blood glucose is 70mg/dl (3.9mmol/l) while the highest normal blood glucose is 180mg/dl (10mmo/l) (Forlenza, Deboer, *et al.*, 2017). One of the study randomized control trial on the extended use of infusion set and sensor as an artificial pancreas have shown an improvement in incidence of hypoglycemia as has showed successful decrease of both overall and overnight hypoglycemia percent time $<70\text{mg/dl}$ by about 2.7% in about 90% of study participants with statistical significance $P = 0.001$ (Forlenza, Deshpande, *et al.*, 2017). Another study done to find an impact of using continuous glucose monitor on hypoglycemia have found that nocturnal hypoglycemia which was defined $<55\text{mg/dl}$ was reduced in the display by 38% in the display group compared to control group $P < 0.00$, in the reduction of severe hypoglycemia study expected that CGM would reduce incidence of severe hypoglycemia but unfortunately, evidence supporting this belief is still lacking because the

overall severe hypoglycemia incidence rate ratio on SMBG compared to CGM was same (Beers *et al.*, 2015). Another study on the effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes have revealed time spent in hypoglycemia below 63mg/dl was reduced in the continuous glucose monitoring group by 48% in pediatric subjects of study group ($P = 0.03$), study also have reported that time spent per day in hyperglycemia was shorter in the continuous monitoring group compared to the control group although it was not statistically significant (Battelino, 2011). A multicenter randomized control trial on the use of closed-loop insulin delivery controlling type 1 diabetes has found time spent with glucose concentration below 3.9mmol/l was reduced by 0.83% (95%CI – 1.4 to 0.16, $P = 0.0013$) and that above 10mmol/l was reduced by about 10.3% (95%CI – 13.2 to 7.5, $P < 0.0001$) (Tauschmann *et al.*, 2018). Study on the use of hybrid closed-loop in managing youth with type 1 diabetes has shown during most of the free-living outpatient studies, there was about 10 – 20% increase in time in target range with concomitant reduction in frequency of hypoglycemia while it has also reported reduction in the time spent in glucose level above 180mg/dl (Sherr, 2018). Another study on the use of real-time continuous glucose monitor with low glucose alarm in incidence and duration of hypoglycemia has found CGM with alarm set at 80mg/dl significantly reduced the time spent below hypoglycemic threshold defined operationally as CGM reading <65mg/dl by about 64% ($P < 0.05$) and it also has decreased incidence of hypoglycemic episode by 44% ($P < 0.05$), it was also found to be better on the use of sensor as total time below alarm hypoglycemic threshold relative to the duration of sensor wear was reduced significantly by more than 52% in the alarm condition compared to control group (Davey, Jones and Fournier, 2010). A random-order crossover study on the glycemetic control with use of bionic pancreas among type 1 diabetes has reported significant decrease in the percentage of time with a glucose level below 70mg/dl by

3.2% ($P = 0.001$) while that below 60mg/dl by 2.2% ($P = 0.02$) compared to that of the control group (Hillard *et al.*, 2014). A meta-analysis of randomized control trial of glycemic control in type 1 diabetes during real-time glucose monitoring compared to self-monitoring of glucose has shown that there was significant reduction of median exposure to hypoglycemia by 23% of continuous glucose monitor compared to self-monitoring blood glucose (Pickup and Freeman, 2011). One of the study done on the efficacy of predictive low glucose suspend PLGS in relation to hypoglycemia risk factor in youth with type 1 diabetes have shown that PLGS system was effective in preventing hypoglycemia for each patient-level and night-level factor sub-group, though there was no strong evidence that PGLS system was more or less effective in preventing hypoglycemia than in other subgroups based on that factor (Calhoun *et al.*, 2016). Study done on the assessment of improvement in the quality of life (distress) to children and adults with type 1 diabetes using continuous glucose monitoring has found that there were slight improvement in the quality of life among individuals using continuous glucose monitoring compared to the control group ($P < 0.05$) (Laffel *et al.*, 2010). Another study done on revising the relationship between glycemic control and hypoglycemic incidence to patients using continuous glucose monitor have shown that the mean reduction in percentage time in hypoglycemia was 57.3%, with maximum reduction of 75% of time in hypoglycemia between 6.5% to 7.5% of HbA1c while the mean reduction in percentage in time in hypoglycemia is 46.3% across the HbA1c of 6 – 9.5% and maximum reduction of 43% achieved between HbA1c of 6 and 7.5% (Gimenez *et al.*, 2018). Study involving use of sensor augmented pump on prevention of hypoglycemia has found the reduction in the time spent on glucose level among 45 children and adolescents below 70mg/dl was reduced by about 50% (Steineck *et al.*, 2017).

Diabetes distress

Modern diabetes technology and use of devices has great potential to ease burdens and associated psychosocial distress, it also places additional demands including training, competency and problem solving. Review study on use of closed loop in youth with type 1 diabetes have shown that closed loop has prevented hypoglycemia by about 84% of the cases while it has also prevented nocturnal hypoglycemia by about 50%, the study has also reduces significantly the fear of hypoglycemia and diabetes distress thus has improved quality of life to group of individual using such system (Tauschmann and Hovorka, 2014). Systematic and meta-analysis review have on the health-related quality of life in pediatric patients with type 1 diabetes using insulin infusion system based on Diabetes Quality of Life for Youth Questionnaire (DQOL-Y) have shown that at the follow-up the pooled estimates suggest significantly better quality of life in the insulin infusion set group compare to the control group $P = 0.002$ (Rosner and Id, 2019). Result from this study are more consistent with one of the study on psychosocial aspect of diabetes technology reported that there is reduction in the diabetes distress due to anxiety, insecurity and fear as a result of using insulin pump and CGM (Priesterroth, 2020).

DISCUSSION

Findings from this rapid review study suggested that the use of technological diabetes devices like insulin delivery and glucose monitoring devices have both clinical benefits particularly in glycemic level control, prevention or reduction of diabetes complication like severe hypo- or hyperglycemia and reduction in the diabetes distress.

This is evidenced by the fact that most of the reviewed studies showed statistical significance on benefits of using technological diabetes devices among youths or adolescents with type 1

diabetes. On the glycemic control the use of technological devices have resulted in the improved norm glycemic level in most of the reviewed studies, the target normal glycemic level was assessed using either blood glucose ranging from 70 to 180mg/dl (3.5 to 10mmol/l) or glycated hemoglobin (HbA1c) level which was below 7%. Some of studies used percentage of time spent in the norm glycemic target range and the finding was that the use of diabetes technological devices has increased the percentage time spent in the norm glycemic range. Like one of the reviewed studies showed percentage of glucose in the target range of 70 to 180mg/dl was higher than that of the control group (80% Vs 60%) (Hillard *et al.*, 2014; Sherr, 2018). Other reviewed studies showed improvement in the glycemic level by increase in the percentage of reduction of glycated hemoglobin level, two of the studies have showed reduction of the glycated hemoglobin by 0.9% from their baseline values (Pickup and Freeman, 2011; Neylon *et al.*, 2014). This study have shown higher reduction of HbA1c to one of the review reported by American Diabetes Association under Diabetes Care 2020 that use of CGM have reduced glycated hemoglobin by 0.6% and 0.43% in two different studies from their baseline value (American Diabetes Association, 2020).

In the prevention or reduction of diabetes complication mostly hypo- or hyperglycemia have shown to be improved in most of the reviewed studies of which severe hypoglycemia was counted as glycemic level below 70mg/dl (3.5mmol/l) while severe hyperglycemia as glycemic level above 250mg/dl. It was reported in percentage of time spent below or above normal ranges, as this study found that most of the reviewed studies have reduced percentage time in below glycemic level and that of above glycemic level. Reduction in the percentage time spent below target glycemic value was ranging from about 10% to 48% reduction (Pickup and Freeman, 2011; Hillard *et al.*, 2014; Beers and Devries, 2016; Steineck *et al.*, 2017; Gimenez *et al.*, 2018;

Tauschmann *et al.*, 2018). Using insulin infusion system based on Diabetes Quality of Life for Youth Questionnaire (DQOL-Y) have shown that at the follow-up the pooled estimates suggest significantly better quality of life in the insulin infusion set group compare to the control group $P = 0.002$ (Rosner and Id, 2019). This study is consistent with one of the review study that have revealed that, continuous glucose monitor and sensor-augmented pump therapy in control of blood glucose reduces diabetes distress as compared to control group using multiple daily injection (Sturt *et al.*, 2015).

The review study have found improvement in the quality of life on using diabetes technological devices like diabetes distress which was found to be associated with fear of hypoglycemia and psychological distress (Laffel *et al.*, 2010; Tauschmann and Hovorka, 2018; Rosner and Id, 2019). Three randomized control trial reported under American Diabetes Association have reported that use of CGM have reduced both hypoglycemia and hyperglycemia children, adolescents and young adults (Beck *et al.*, 2019).

Somewhat surprisingly, one of the study in this review was found there was no evidence of statistical significant on benefits of using diabetes technological devices in the management of youth as it reported there was no significant difference with self-monitoring blood glucose in the improving glycemic level or prevention or reduction of hypoglycemic incidence (Calhoun *et al.*, 2016).

This review study finding is consistent to one of the study on the advances in type 1 diabetes technology which reported that the use of diabetes device have shown to improve regulation of blood glucose to closely normal range and reducing the frequency of hypoglycemia, a combination that allows for a potential reduction of both short term and long-term diabetes complications as a results improve quality of life (Pettus and Herrath, 2018; Zimmerman, Neill

and Haller, 2019). Other finding which was found to be similar with this review study have reported the improvement in the glycemic level by reduction in the level of glycosylated hemoglobin and reduction in frequency of hypoglycemia (Rodbard, 2016; Dimeglio *et al.*, 2018). The use of closed loop system has been shown to reduce severe hypoglycemia by study done by Breton MD with his fellows (Breton *et al.*, 2018).

From this finding we found that use of diabetes technological devices in the management of youths or adolescents with type 1 diabetes to be effective and it was shown to have statistical significance as these devices can provide adequate information of the glycemic level trends and even sometimes there are devices which can sense lowering or raising in the glycemic level then give an alarm or to shoot required amount of insulin if using closed loop system. By this mechanism there is high pace of regulating glycemic level which led to prevention or reduction of hypoglycemic incidence as a result improve an individual quality of life with no stress, distress or fear of hypoglycemia.

CONCLUSION

Generally, this review study points out the clinical significance of using continuous glucose monitor and/or insulin pump that it improves glycemic control, reduce incidence of severe hypoglycemia and diabetes distress. Reduction of glycosylated hemoglobin by about 0.9% of its baseline value, about 8% increase in time spent in nearly norm glycemic range, reduction of incidence of hypoglycemia by about 10 to 48%. As adolescents are increasingly accessing technologies it is paramount important to address benefits of using diabetes technological devices further research is hence needed to assess accessibility of devices to emerging adults.

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Authors' Contributions

MSG conceptualized the project, undertook the systematic review and drafted the manuscript. RM contributed to the supervision of the junior researchers and manuscript review. AK contributed to the conceptualization of the project, planning methodology, supervision of the junior researchers and manuscript review.

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Declaration

Ethical approval and consent to participants

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All authors agree to have this paper published

Competing interest

The authors declare that they have no conflicts of interests



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