

Peer Review File

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Reviewer A

Comment 1: Overall, you present a very good history review of diabetes technology. Your article will be a good review for the general practitioner who cares for pediatric diabetes patients. I appreciate your efforts to trace the history for each testing device through its evolution. This illustrates our progress and encourages continued innovation. I appreciate your discussion of each device, offering the reader both strengths and weaknesses.

I am not clear if your manuscript had a chart or graph. I think that adding a chart with current technology devices citing the function of each, minimal age requirement, and strengths and weakness to each in comparison to other devices could be a useful quick reference.

Reply 1: Suitable graphs are limited by copyright.

Comment 2: For consistency and to prevent bias, would suggest using generic terms to describe CGM and insulin pumps or brand/manufacture specific names, but be consistent. If you use CGM, then use tubeless or tubed insulin pump, earlier generations vs newer generations.

Reply 2: Brand specificity has made it difficult to generalize above categories.

Comment 3: Line 107, remove “use”.

Reply 3: We have modified our text as advised. Line number is now 95.

Changes in text: Sentence now reads: The same concept was applied to test strips ... instead of “to use” test strips.

Comment 4: Line 113, remove “the”.

Reply 4: We have modified our text as advised. Line number is now 101.

Changes in text: Sentence now reads “...from office testing to home testing when portable glucometers ... “the” removed before “portable glucometers”.

Comment 5: Line 114-115, rewrite sentence to allow for better flow.

Reply 5: We have modified our text as advised. Lines now 100-102.

Changes in text: The text now reads: This concept has evolved dramatically over a few decades. It first revolutionized diabetes monitoring when portable glucometers made it possible to extend glucose testing from medical offices to the patients’ homes.

Comment 6: Line 116, add “over the past few decades...”.

Reply 6: We have modified our text as advised, it is now line 103.

Comment 7: Line 116, remove “the”.

Reply 7: We have modified our text as advised.

Changes in text: Sentence now reads: “Over the past few decades, glucometers became simpler, more accurate, more innovative, and less painful (physically and technologically) than any time before”

Comment 8: Line 126, change to “allows”.

Reply 8: Sentence was modified, it is now line 113.

Change in text: It now reads “Glucometers allow patients with diabetes to get more involved in their diabetes self- management and day to day decision...”

Comment 9: Line 129, rewrite sentence to allow for better flow.

Reply 9: Text has been modified. Lines 116-118

Changes in text: Sentence now reads: “However, the success of utilization of glucometer was always challenged by socio-economic determinants, literacy, and technology handiness (8).”

Comment 10: Line 132, include reasons why children may feel compelled to alter blood glucose log.

Reply 10: We have modified our text as advised. It is now Line 120

Changes in text: Added the following text: “Examples of compelling reasons for children doing this include: having to hide a dietary indiscretion or the result of a missed insulin dose that resulted from peer pressure situations. Secondary gain also plays a role. For example, an abnormal number in school, allows them to leave class”

Comment 11: Line 137, add urine ketone monitoring for at home monitoring.

Reply 11: We have modified our text. Now Line 127.

Changes in text: Sentences now read “An additional advance in home monitoring came with urine ketone strip monitoring and blood ketone meters. The latter allow monitoring of blood ketones detection for screening and monitoring of ketoacidosis in the setting of hyperglycemia and illness and allow more accuracy than urine ketones.”

Comment 12: Line 140, replace “my” with “may”.

Reply 12: We have modified our text as advised. Now line 130.

Comment 13: Line 147, replace “remained” with “remain challenging to patients...”.

Reply 13: we have modified our text as advised. Now line 136-137.

Comment 14: Line 162, edit sentence.

Reply 14: We have modified text. Resorted to broadening the statement to newer generations of CGM overall. Line 163.

Changes in text: It now reads: “The newer generations of CGM are now reliable enough that patients no longer need to confirm readings with glucometer for treatment decisions (16).”.

Comment 15: Line 175, please indicate time frame for improvement, including long term data (example: studies have demonstrated a 0.5% improvement in A1c over the first 6 months of utilization. Continued utilization of CGM therapy, patient demonstrate improved time in range or A1c at goal or better for # months)

Reply 15: text does already specify 6 months. Now line 167.

Comment 16: Line 186: define blood glucose ranges for time above range, time in range and time below range.

Reply 16: Text has been modified. Starting on line 180.

Change to our text: Added the following sentence: “For non-older and no high-risk Type 1 and Type 2 diabetes patients, “very high” is defined as over 250 mg/dL, “high” is over 180 mg/dl, “in range” is defined as 70-180 mg/dL, “low” as below 70 mg/dL and “very low” is defined as below 54 mg/dL. Goals for these populations are respectively, less than 5% of the time very high, less than 25% of the time “high, 70% of the time in range, less than 4% of the time “low”, and less than 1% of the time, “very low”.”

Comment 17: Line 187-188: sentence needs to be rewritten.

Reply 17: Text has been modified Line 179.

Changes to text: Clarified the sentence and it now reads “The report needs to include at least 2 weeks of data, having been used by the patient over 70% of the time in that time frame.”

Comment 18: Line 196-197, duplicate statement, “use of CGM over 6 months demonstrated greater reduction in A1c...”.

Reply 18: It specifies further the benefit for the groups of lower socioeconomic status. Line 196-197.

Comment 19: Line 206, you may want to mention that CGM sensors continually evolve providing the wearer smaller sensors and quicker warm up times reducing wait times (Dexcom G7).

Reply 19: Text has been modified to include G7. Of note, G7 had not been approved at the time of initial submission. Starts at line 198.

Changes to text: Now it reads: “There are currently four FDA approved, non-adjunctive, real-time continuous glucose monitors. The two models by Dexcom, G6 and G7, are approved for ages 2 years and above (23, 27), whereas the Abbott models, Freestyle Libre 2 and 3, are approved for ages 4 years and up (26). The Dexcom models, are designed for a 10-day duration. G6 is the only non-adjunctive sensor used in sensor augmented pumps for now. G7 has a shorter warm up period of 30 minutes than its predecessor that requires a two-hour period. The Freestyle Libre models are approved for a 14-day duration. Freestyle libre 2 requires scanning of the sensor to view actual glucose numbers. Freestyle Libre 3 does not require scanning anymore and the warmup period is 60 minutes. The latest models of each brand are about the size of a penny, have customizable alarms, and are also approved for gestational diabetes and pregnancy as well.”.

Comment 20: Line 207, include the recent change eliminating requirement of 4 blood sugar checks daily as requirement for CGM coverage (The Centers of Medicare and Medicaid) improving equity of care.

Reply 20: Text has been modified. Line 212.

Changes to text: Added this fact to the following paragraph and it now reads: “The Center for Medicare and Medicaid has eliminated the requirement of a minimum of four finger sticks in order to cover CGM’s. While this has improved equity of care, economic barriers for private payor patients and challenges of wearability logistics remain. Children are less tolerant to wearing devices. Real life implementation varies greatly as well as parental fund of knowledge interpreting numbers and taking correct actions.”.

Comment 21: Line 212, smart watches have recently been developed and marketed to measure BG via a smart watch like sensor.

Reply 21: Added as above. Please see line 219.

Comment 22: Line 222, define the types of insulin, including duration of action and advantage and limitations of each type of insulin.

Reply 22: Elaborated more on this. See line 231.

Changes to text: Added the following sentence: “The long acting or basal insulins such as detemir, glargine and degludec, are designed to mimic background insulin production. The fast and short acting, also called bolus insulins, aspart and lispro, mimic the immediate pancreatic acute insulin release that occurs with a meal.”.

Comment 23: Line 246, edit sentence to define more clearly how basal vs bolus dosing differs with CSII (example- In CSII, rapid or fast acting insulin is delivered continuously replacing the need for daily long-acting injections.).

Reply 23: We have modified text as advised. Now line 257.

Changes to text: Sentence now reads: “In CSII, insulin is delivered as basal and bolus dosing. The basal rate is continuous delivery of insulin throughout the day, thus eliminating the need for long-acting insulin injection. Basal rates can be customized for time of day, physical activity, illness, dawn phenomenon and allows greater flexibility than subcutaneous dosing of long-acting insulin injections.”

Comment 24: Line 256, delete “continuous subcutaneous insulin infusion” and insulin pump therapy. These terms are the same. CSII is fine to use since you defined the abbreviation earlier in the article.

Reply 24: We have modified text as advised. Now line 267.

Changes in text: It now reads, “CSII has been shown to improve glucose control and to reduce hypoglycemic episodes (34).”.

Comment 25: Line 263, include data to support this statement.

Reply 25: Text was modified to better explain that pumps allow for the option of changing basal rates to mimic what happens with circadian rhythms. Now line 271.

Changes in text: It now reads “Insulin pump therapy offers a close resemblance to normal physiological insulin delivery due to the feasibility to change the basal insulin rate within circadian rhythms (36)”.

Comment 26: Line 270, include why education is important to reduce unintended hypoglycemia.

Reply 26: See reply below.

Comment 27: Line 272-273, how does this allow better flexibility? (Allows the user to use/program multiple time intervals setting defined basal rates, carb ratios, correction factors).

Reply 27: See reply below.

Comment 28: Line 287-300, important to highlight the importance of diabetes education before insulin pump initiation and each follow up, particularly steps to take in case of pump failure. Also, important to mention importance of careful evaluation and assessment in patient's knowledge in pump failure and sick day management to ameliorate risk you have mentioned in this section.

Reply 28: All above was addressed. Text was rearranged and modified. Please see lines now numbered 266 to 315.

Comment 29: Line 327, the future and promise for an artificial pancreas or dual hormone (DH) closed loop systems is more promising with the release of liquid stable glucagon. There have been several studies published comparing insulin only closed loop systems with DH closed loop systems with promising results to prevent hypoglycemia.

Reply 29: Please see lines 368-371.

Comment 30: Line 348, please spell out what HCL means.

Reply 30: It means Hybrid closed loop. This was defined in a prior sentence. Please refer to sentence in line 344 that reads "Advances from SAP to automated insulin delivery (AID), also referred to as hybrid closed loop (HCL) allows adjustment of insulin delivery based on CGM Data by a software algorithm."

Comment 31: Line 357-358, this statement feels derogatory. And does not appear to have any context utility. While I don't think you meant anything negative, I would suggest removing it or rephrasing your statement.

Reply 31: We have modified text as advised.

Reviewer B

Comment 1: The manuscript is well written. However, it is not clear to me what is new in terms of content. There are many reviews on the subject that have already been published.

Reply 1: This article focuses in pediatrics. Not all devices are approved or are suitable for pediatrics.

Reviewer C

Comment 1: I read with great interest the paper. The authors presented an overview focused on the role of technology in the management of diabetes highlighting the recent advances which have led to a huge variety of benefits for people with diabetes.

Although the objective of the study is a real current hot topic, the paper requires several revisions.

One of the main limitations is related to the methodology. The search strategy is not declared and also the table included in the main text makes me doubtful. It is not clear the reasons why the authors decided to consider also RCTs, reviews, and some recommendation guidelines for this type of review, excluding other types of papers from their literature search.

Furthermore, I'm not quite sure that all the cited references belong to those categories. I strongly suggest re-evaluating this search strategy. I'm afraid that the review covers a too huge variety of aspects and I think that some of these were not addressed. It is quite ambitious to reduce the evolution of CSII therapy to a few pages and some data are missing. Currently, other AID systems have been approved and routinely used in addition to those cited by the authors. No mentions of the algorithms which allow the automatic delivery of insulin are present. Some figures and tables could help the authors to summarize some relevant aspects of this review.

I appreciated that the authors also remark on the barriers to the universal use of technology for diabetes management and the key role of patients and their caregivers' education in the use of these devices but some references are missing. I suggest considering the following papers: doi: 10.23736/S2724-5276.21.06531-9; doi: 10.2147/MDER.S312858; doi: 10.1089/dia.2023.2511.

Finally, I feel that the abstract is too long in the current version, especially in the background section and should be carefully revised in order to guide quite rapidly the reader on the core of the manuscript.

Reply 1: The extent of the literature search was nonsystematic as customary for narrative review. But it is important to highlight how the current technology changes outcomes, hence, the citation of RCT's as the best evidence. We were unable to access, and review referenced article above despite attempting to reach authors. Abstract was shortened.