Champs Public Health Collaborative

Working together to improve health and wellbeing in Cheshire and Merseyside

Cheshire West and Chester

RAPID REVIEW:

Continuous glucose monitoring: Evidence update 2014-2017 and review of Cheshire and Merseyside policy

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CGM Policy

Adults with type 1 diabetes

CGM is not routinely commissioned.

CGM will only be considered for patients when the following criteria are met:

Currently using a continuous subcutaneous insulin pump of high specification in strict accordance with NICE appraisal TAG 151 and the local insulin pump policy.

AND

Managed by a recognised adult specialist centre of expertise. This will have a multidisciplinary team comprising a trained diabetes nurse specialist, physician and dietician with all patients trained to count carbohydrates.

AND

Willing to commit to using CGM at least 70% of the time and to calibrate it as needed.

PLUS

HbA1c ≥75 mmol/mol (9%) that persists despite blood glucose testing at least 10 times a day.

OR

Experiencing more than one severe hypoglycaemic episode a year with no obviously preventable precipitating cause. (Severe hypoglycaemia is generally recognised as hypoglycaemia involving convulsions/unconsciousness)

OR

Complete loss of awareness of hypoglycaemia

OR

Experiencing more than 2 episodes of hypoglycaemia per week that the patient has been unable to manage themselves and are causing problems with daily activities.

OR

Inability to recognise or communicate about symptoms of hypoglycaemia e.g. because of cognitive or neurological disabilities where other forms of glucose monitoring are not appropriate.

Pregnancy

CGM is not routinely commissioned in pregnancy unless all criteria for CGM in adults are met. Where CGM in pregnancy is used, funding is **only** for the duration of the pregnancy. Insulin doses are reduced to pre-pregnancy levels as soon as the baby is delivered and CGM should not be continued beyond this point.

FOR ALL PATIENTS

A CGM system with a low Mean Absolute Relative Difference (MARD) value should be chosen.
Where there is a CGM system with alarm function that will integrate and communicate directly with the patient's established insulin pump, then this CGM system must be used. However, an appropriate real-time Dexcom CGM system with alarm function may be considered for patients using other insulin pumps.

The device should be withdrawn from patients who fail to achieve a clinically significant response after 6 months.

There should also be an annual review to assure the clinically significant response is maintained and that CGM is still the most appropriate method of glucose monitoring for the patient.

Consideration should be given to switching to an integrated insulin pump/CGM system when seeking to replace the insulin pump at warranty expiry, if appropriate.

Children and young people with type 1 diabetes

CGM is not routinely commissioned.

CGM will only be considered for patients when the following criteria are met:

Currently using a continuous subcutaneous insulin pump of high specification, in strict accordance with NICE appraisal TAG 151 and the local insulin pump policy.

AND

When provided by a specialist centre with a multidisciplinary team including an active member who attends at least 67% (2/3) of the North West children and young people's diabetes network meetings. In addition, the specialist centre is achieving best practice tariff in paediatric diabetes and is also engaged with the national peer review programme in paediatric diabetes, to monitor the quality of its service.

AND

Willing to commit to using CGM at least 70% of the time and to calibrate it as needed.

PLUS

Experiencing more than 2 episodes per week of severe hypoglycaemia. This is defined as having low blood glucose levels that require assistance from another person to treat and that are happening often enough to have a **significant** impact on school work or quality of life.

OR

Inability to recognise or communicate about symptoms of hypoglycaemia e.g. because of cognitive or neurological disabilities.

OR

Impaired awareness of hypoglycaemia which is associated with significant adverse consequences e.g. seizures or severe anxiety.

Prior to transition to adult services, the child should be counselled on the transition process and advised that their CGM will be reviewed as part of the transition and their ongoing adult diabetes care. On transition to adult services there should be a review to assure there is still a clinically significant response and that CGM is still the most appropriate method of glucose monitoring for the patient.

INTRODUCTION

The paper "Continuous glucose meters and the management of diabetes" written in March 2014, raised questions about the accuracy, particularly around detection of hypoglycaemia, and also the effectiveness of continuous glucose monitoring. Reported reductions in HbA1c attributed to continuous glucose monitoring (CGM) were in the order of -0.5%. There were also issues about sensor comfort and data on pregnancy were conflicting.

Whilst the most promising evidence supported the use in adults aged 25 years or older to reduce HbA1c, the underpinning evidence was questionable in terms of low patient numbers, the open nature of the trials, the short-term outcomes and heavy industry sponsorship.

The paper concluded there was no clear consensus as to where the role of continuous glucose monitors lies. High quality, long-term research was required. Recommendations for use was therefore restricted to type 1 diabetes using a sensor augmented pump with high baseline HbA1c or experiencing severe hypoglycaemic attacks (which required intervention by a carer). Only pumps with high accuracy and recommended by a recognised centre of excellence should be available. All other requests should not be funded.

The purpose of this report is to review the evidence published since 2014. It will also review current recommendations in light of the new evidence.

METHOD

A literature search of Medline and Embase was performed using keywords "continuous glucose monitoring" (or variants) restricted to articles published 2014–17. In addition, all NICE guidance published during this time was reviewed and also the Cochrane database.

Articles considered relevant dealt with concepts such as effectiveness, hypoglycaemia, accuracy, pregnancy or cost effectiveness.

FINDINGS

Around 2,000 titles were identified and scanned, and of these, 134 were selected for closer inspection. Only the references considered to be most relevant were used in the final review.

Effectiveness

In adults, the majority of studies were short-term (usually six months or less), small numbers (around 100 – 300 participants), and principally in type 1 diabetes. The impact on HbA1c was modest, with an average reduction of -0.5%. In more detail, the reductions in HbA1c were reported as -0.276% [1],
-0.43% [2], -0.5% [3], -0.6% [4] and -0.9% [5].

Two other small studies in adults reported other evidence of effectiveness outcomes instead of HbA1c. The first was in 52 adults over 32 weeks when the time in "normal" glycaemia was increased from 55% for those self-testing to 65% in those who were on CGM. [6] In the second, 160 patients over 100 days on CGM, spent an average of approximately 1 hour per day less outside the normal blood sugar range. [7]

A third study examined the records of 10,501 types 1 and 2 diabetics over 2 years stratified according to high or low use of CGM devices. [8] This showed that high frequency CGM users were more likely to be in the normal blood sugar range. However, "normal" blood sugar was defined using a somewhat unusual (perhaps) method which calculated the mean blood sugar.

In children, two very small studies with 21 and 83 participants observed reductions in HbA1c of -1.46% [9] and -0.27% [10] respectively.

In conclusion, because of the limited patient numbers and short duration, these low quality studies mostly conclude, as with previous data, that CGM is responsible for a modest reduction (in the order of -0.5%) of HbA1c. This adds little to the body of knowledge already accumulated.

Hypoglycaemia and general safety

One of the reported benefits of CGM is its alleged ability to detect and therefore reduce the incidence of hypoglycaemia. A handful of studies provide some data on this particular aspect.

A study in *Lancet Diabetes and Endocrinology* examined 52 high risk, type I adults with hypoglycaemia unawareness. [6] Patients were studied over two, 16 week periods receiving either CGM or standard monitoring and then crossing over to the alternative treatment after an intervening washout period. In the CGM group, 14 episodes of severe hypoglycaemia were counted with 34 episodes in the standard treatment mode. This proportion is statistically significant although when adjusted for treatment duration, the difference is no longer significant.

In another crossover study [2], 161 type I adults over 26 weeks experienced 1 and 5 cases of severe hypoglycaemia in the CGM and control groups respectively. No statistics were performed but there were 19 dropouts at the end of the trial. In a separate trial, over six months, 77 control participants experienced one case of severe hypoglycaemia whilst the 149 CGM patients experienced no hypoglycaemia. [11] In a very similar trial, of 105 CGM and 53 controls over 24 weeks, there was only one severe hypoglycaemia in each group. [4]

Finally, reports from the CareLink database (10,501 people) indicated there were 50% fewer hypoglycaemic episodes for participants who were high users of CGM. [8] Unfortunately, the abstract doesn't give sufficient detail to allow a critical appraisal of the underlying data.

Finally, two reviews give conflicting views on the impact of CGM on hypoglycaemia. The first (published in 2017) suggested there is evidence that sensor pumps reduce episodes of moderate and severe hypoglycaemia compared to multiple daily injections. [12] The second (published in 2016) concluded that current evidence doesn't demonstrate an effect on mild or severe hypoglycaemia. [13] However, the authors also suggested that the new machines, perhaps the ones with "insulin suspend" might be more effective.

Another review suggested that the limitations of CGM include the level of numeracy and literacy of the user, alarm fatigue and interfering substances which might lead to erroneous readings and high rates of discontinuation. [14] A systematic review which examined interventions to restore awareness of hypoglycaemia concluded that a stepped care approach is effective. This starts with structured diabetes education, flexible insulin therapy which may incorporate psychotherapeutic and behavioural therapies and then progress to the technology for those patients with persistent need. [15]

In conclusion, because of the small number of studies, few participants and short durations, the evidence to support the use of CGM to prevent significant hypoglycaemia isn't strong. Further work is still required.

Accuracy

An accuracy check of 2 sensors demonstrated an overall Mean Absolute Relative Difference (MARD) of 12.1% in the euglycaemic range. [16] The accuracy was much lower in the hypoglycaemic range (19.4%) but higher in the hyperglycaemic range (9.3%). In an experiment to compare sugar levels measured by CGM to those in arterial blood in 22 cardiac surgery patients, the accuracy varied between 88.7% – 72.9% depending on the setting and siting of the sensors. [17]

The value of the MARD is dependent on a number of factors. It can be affected by the way the CGM device is calibrated (using capillary or venous blood) [18], and also the number of paired data collection points. The greater the number of data points collected then the greater the accuracy. [19, 20]

It has previously been observed that there is a delay or timeshift of interstitial glucose behind that of the venous or capillary blood. However, this seems to be more complex than just a simple shift in time. [21, 22] One practical solution is to adjust the CGM's computer algorithm [23] and in one small study this reduced the time delay of 9.5 minutes by 4 minutes. [24] However, there is an argument that a CGM measured interstitial sugar is better than blood, particularly in a dynamic situation e.g. during a meal or exercise, because the general trend of changing glucose levels gives a better indication than a single point determination of a finger prick. [25]

In a review of the challenges related to development of an artificial pancreas i.e. where CGM is used as part of a system to detect and respond to sugar levels, the main drawback was thought to be the latency (5 – 10 minutes) of the CGM. [26]

Finally, one review concluded that on current evidence, it is risky to assume that CGMs are consistently accurate enough to be used non-adjunctively for the precise dosing of insulin. [27] To confirm this, perhaps, Shapiro performed a text analysis of error reports of CGM in the FDA's database since 2015. [28] Over 25,000 complaints about CGM sensors and accuracy were reported with instances directly leading to serious outcomes.

In conclusion, the most recent studies confirm problems in delayed glucose measurements and also inaccuracies which change over a range of sugar levels, being worse at the hypoglycaemic end. The problems are compounded by differences between different CGM devices and computer algorithms. More research is required.

Cost effectiveness

A small number of cost-effective studies have been performed. The first was a USA model in type II diabetes with 2 weeks on CGM and 1 week off. This returned incremental cost effectiveness ratios (ICERs) of between
$9,319–$13,030. [29] Although this is within the range of ICERs which is considered to be cost-effective by NICE*, data on clinical effectiveness for type II diabetes are not as strong as that for type I diabetes.

The second study examined the cost effectiveness of sensor augmented pumps in type 1 diabetes in Sweden. [30] The calculated ICER was 367,571 Swedish krona (which is equivalent to £34,235). Whilst this is not cost-effective according to NICE, the authors suggested the contrary view.

In a UK study of sensor augmented pumps with an insulin suspend feature, the economic model predicted an ICER of £12,233 for type 1 diabetes. [31] This is clearly cost-effective by NICE standards, but the main assumption was a reduction in HbA1c of 1.49% which is about three times the generally accepted reduction (i.e. -0.5%). Such a high reduction in HbA1c would result in a much more favourable ICER.

A more pragmatic trial (as described in a conference abstract) performed an economic evaluation of CGM in type 1 diabetes with impaired awareness in a group of North West London CCGs (total population just over 2 million). [32] Over one year, the total outlay for 3,036 participants was £9,671,972. Savings associated with reductions in hypoglycaemia -related

* NICE consider an intervention to be cost-effective if the ICER is less than £20 – £30,000.

admissions, blood testing strip usage and HbA1c reduction-related complications were thought to amount to £4,050,257. This leaves an annual outlay of £5,621,714 which is just over £1800 per annum per person. The abstract doesn't state the assumed reduction in HbA1c; neither has the study been properly peer-reviewed.

In summary, the data on cost effectiveness are low quality and do not provide convincing evidence that CGM is a cost-effective intervention.

Pregnancy

A Cochrane review (published in 2017) compared the impact of self-monitoring, CGM or clinic monitoring during pregnancy for women with pre-existing diabetes. [33] The review found no evidence that one technique was superior to another in women with either types 1 or 2. The authors concluded that the evidence is weak and larger, well-designed RCTs are required.

Reviews

An early review (2014) suggested that CGM is justified in selected patients in those who have shown substantial improvement in HbA1c and also in those with unawareness who have encountered severe hypoglycaemia in the past. [34] The authors concluded that more data are required.

There seems to be some enthusiasm for widespread use of CGM in the USA. [35] A consensus conference of the American Association of clinical endocrinologists advocated expansion of the use of CGM. The conference stated that the meters have the *potential* to reduce the risk of acute and chronic complications. [36]

Further, the American "Endocrine Society" recommended real-time CGM in patients with above target HbA1c and who are willing to use devices on a nearly daily basis. [37] However, a BMJ commentary on this article noted the recommendation for use in type 2 diabetes despite the limited evidence and also the authors' declaration of multiple, potential competing interests. [38] Another BMJ commentary concluded that additional clinical trials are needed to determine the long-term effect [39]

Other reviews have been less sympathetic in their assessment. One in particular noted that "not all that is new is necessarily better". [40] Current evidence does not demonstrate convincing arguments for generalised application.

Perhaps a more balanced assessment in a review of CGM suggested that CGM is medically indicated for patients with frequent, severe or nocturnal hypoglycaemia especially in the presence of unawareness. It noted limited uptake and also barriers such as cost, need for recalibration, replacement of sensors, inexperience and lack of training of physicians and lack of standardised software. [41] Use of a pump with automated suspension of insulin might increase the uptake.

More practical advice for users has included wearing the CGM as much as possible, frequent monitoring of the readout, realising that CGM isn't perfect and the importance of calibration and also recognising that finger prick readings are sometimes needed. Users should also have a plan (without overreacting) for responding to low glucose. [42]

Conclusions

In summary, the new tranche of articles adds little to the current body of knowledge. Some of the apparent enthusiasm has to be tempered by the fact that this is based on consensus and opinion and low quality data rather than hard facts.

NICE GUIDANCE

This has been published for type 1 diabetes in adults (NG17 – 2015), types 1 and 2 in children (NG18 – 2015) and in pregnancy (NG3 – 2015). All 3 guidelines make reference to CGM. The recommendations on CGM are listed in table 1. For ease of comparison, the various indications are listed in table 2 to allow a comparison to be made between the different guidelines. For adults and in pregnancy, NICE state that CGM should not be routinely used.

For children and young people, CGM should be "offered" for frequent severe hypoglycaemia or impaired awareness of hypoglycaemia which is associated with adverse effects or the inability to recognise or communicate symptoms of hypoglycaemia because of cognitive impairment. It is important to emphasise the definition of "offer" which in this context means that NICE are confident that for the vast majority of patients, an intervention will do more good than harm and be cost-effective.

In contrast, NICE state that CGM should be considered in children according to strict criteria for a variety of other indications. "Consider" means the intervention may do more good than harm for most patients and be cost-effective but there are other options which are similarly cost-effective. One interpretation is that "offer" is a "must do" whereas "consider" means there are other options available and the recommendation is by no means compulsory.

In this way, NICE recommend CGM in children and young people for severe hypoglycaemia (although "severe" is not defined) and also for complete loss of awareness of hypoglycaemia when associated with adverse effects such as seizures or anxiety. It is surprising to see the long list of other indications to be considered and the relatively low quality of evidence which NICE used to justify their recommendations. It is interesting to note that one of NICE's research recommendations is the need to determine the clinical and cost effectiveness of CGM compared to frequent finger prick tests in children aged 5 years or younger using insulin pump therapy.

In pregnancy, although NICE say that CGM should not be offered routinely, it may be considered for problematic severe hypoglycaemia or unstable blood glucose or to gain information about blood glucose. These recommendations were published 2 years before the most recent (2017 Cochrane systematic review described above [33] which found no difference between CGM and self-monitoring.

In adults, although not to be routinely commissioned, the list of possible "considerations" includes severe hypoglycaemia, complete loss of awareness of hypoglycaemia, frequent episodes of hypoglycaemia causing difficulties with daily activities, extreme fear of hypoglycaemia and hyperglycaemia that persists despite testing at least 10 times per day.

Table 1: *NICE guidance on Continuous Glucose Monitors (CGM)***:** *Summary*

Guidance/ Population	**Adults**	**Children and YP**	**Pregnancy**
NG3 (2015) Diabetes in pregnancy			• **Do not offer** CGM routinely. • **<u>Consider</u>** in:- Problematic severe hypoglycaemia† (+/- impaired awareness). OR unstable blood glucose OR to gain info about blood glucose. • Support must be available from team with expertise.
NG17 (2015) Type 1 diabetes in adults	• **Do not offer** rT CGM routinely. • **<u>Consider</u>** rT CGM in adults willing to commit to >=70% wearing & attempts at optimisation, despite optimised insulin use AND any of the following :- >1 episode p.a. of severe hypoglycaemia† OR Complete loss of awareness of hypoglycaemia OR >2 episodes per week of asymptomatic hypoglycaemia causing difficulties with daily activities OR Extreme fear of hypoglycaemia OR Hyperglycaemia‡ that persists despite testing at least x10 per day. Continue with CGM only if HbA1c is reduced to 7% or less or a fall of 2.5%. • CGM provided by centre with expertise and in combination with either multiple daily insulin or continuous infusion. **<u>Research required</u>** • CGM not considered cost effective even with impaired awareness. • May still be of value in CGM in high HbA1c – need to know if newer technologies may be more cost effective.		
NG18 (2015) Diabetes		• **<u>Offer</u>** real time CGM with alarms in type 1 for:-	

† "Severe hypoglycaemia" not defined in NG17, NG3 or NG18.

‡ "hyperglycaemia" defined as HbA1c 9% (75 mmol/mmol) or greater

(types 1 and 2) in children and YP.		Frequent severe hypoglycaemia†. OR impaired awareness of hypoglycaemia associated with adverse effects (eg seizures or anxiety). OR inability to recognise/communicate about symptoms because of cognitive impairment. • **Consider** rT CGM for:- Neonates, infants and pre-school children. Children and young people who undertake high levels of physical exercise (eg sport at a regional level). Children and YP with comorbidities eg anorexia or drugs which affect blood sugar. • **Consider** *intermittent* CGM (rT or retrospective) to improve blood sugar in C & YP with *hyperglycaemia* despite insulin adjustment and support.	
QS125 (2016) Diabetes in children and young people.		Statement 4 • **Offer** real time CGM with alarms in type 1 for:- Frequent severe hypoglycaemia† (This is consistent with NG18 above.)	
DG21 (2016) Integrated sensor-augmented pump therapy systems for managing blood glucose in type 1 diabetes.§	• MPV recommended as an option in type 1 DM if:- Disabling hypoglycaemia** despite optimal management with insulin infusions (company must collect and publish usage data). Supervised by an experienced MDT and only if person agrees to use >=70% of the time along with support programme. Must demonstrate a decrease in hypoglycaemic episodes. • VGP is not recommended.		

rT= Real time

§ MiniMed Paradigm Veo (MPV) and the Vibe & G4 PLATINUM (VGP). MPV is able to suspend insulin delivery if there's no response to low glucose warning.

** Hypoglycaemic episodes occurring frequently or without warning causing constant anxiety and impact on quality of life.

Table 2: *NICE guidance on Continuous Glucose Monitors (CGM)***:** *by indication*

Indication	**NG17 (adults)***	**NG18 (C&YP)**	**NG3 (pregnancy)**
Severe hypoglycaemia	Consider in >1 episode p.a	Offer for "frequent"	Consider in problematic
Complete loss of awareness of hypoglycaemia	Consider	Offer when associated with adverse effects††	Not covered
>2 episodes per week of asymptomatic hypoglycaemia causing difficulties with daily activities	Consider	Not covered	Not covered
Extreme fear of hypoglycaemia	Consider	Not covered	Not covered
Hyperglycaemia that persists despite testing at least x10 per day	Consider	Consider	Not covered
Neonates, infants and pre-school children.		Consider	
Children and young people who undertake high levels of physical exercise (eg sport at a regional level).		Consider	
Children and YP with comorbidities eg anorexia or drugs which affect blood sugar.		Consider	
Unstable blood glucose	Not covered	Not covered	Consider
To gain info about blood glucose	Not covered	Not covered	Consider

***** Adults willing to commit to >=70% wearing & attempts at optimisation, despite optimised insulin use

RECOMMMENDATIONS

Based on the above, the following recommendations are suggested:-

1. CGM in pregnancy is not routinely commissioned.
2. In children and young people, CGM is recommended as an option for severe hypoglycaemia or complete loss of awareness of hypoglycaemia associated with severe adverse effects such as seizures or anxiety (i.e. the indications which must be "offered" according to NG18).
3. The indications in the current Cheshire and Merseyside policy are modified slightly to take into account recommendations in NG17.
4. Overall, however, CGM continues not to be commissioned as a routine intervention.
5. The commissioning policy will state clearly that CGM is only commissioned by centres of expertise. These centres will be specified in the policy.

†† Eg Seizures or anxiety.

REFERENCES

1. Benkhadra K, Alahdab F, Tamhane S, Wang Z, Prokop LJ, Hirsch IB, et al. Real-time continuous glucose monitoring in type 1 diabetes: a systematic review and individual patient data meta-analysis. *Clinical endocrinology*. 2017;**86**(3):354-60.

2. Lind M, Polonsky W, Hirsch IB, Heise T, Bolinder J, Dahlqvist S, et al. Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections: The GOLD Randomized Clinical Trial. *JAMA*. 2017;**317**(4):379-87.

3. Kesavadev J, Vigersky R, Shin J, Pillai PBS, Shankar A, Sanal G, et al. Assessing the Therapeutic Utility of Professional Continuous Glucose Monitoring in Type 2 Diabetes Across Various Therapies: A Retrospective Evaluation. *Advances in therapy*. 2017.

4. Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, Haller S, et al. Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections: The DIAMOND Randomized Clinical Trial. *JAMA*. 2017;**317**(4):371-8.

5. Ruedy KJ, Parkin CG, Riddlesworth TD, Graham C, Group DS. Continuous Glucose Monitoring in Older Adults With Type 1 and Type 2 Diabetes Using Multiple Daily Injections of Insulin: Results From the DIAMOND Trial. *Journal of diabetes science and technology*. 2017:1932296817704445.

6. van Beers CAJ, DeVries JH, Kleijer SJ, Smits MM, Geelhoed-Duijvestijn PH, Kramer MHH, et al. Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): a randomised, open-label, crossover trial. *The lancet Diabetes & endocrinology*. 2016;**4**(11):893-902.

7. New JP, Ajjan R, Pfeiffer AFH, Freckmann G. Continuous glucose monitoring in people with diabetes: the randomized controlled Glucose Level Awareness in Diabetes Study (GLADIS). *Diabetic medicine : a journal of the British Diabetic Association*. 2015;**32**(5):609-17.

8. Battelino T, Liabat S, Veeze HJ, Castañeda J, Arrieta A, Cohen O. Routine use of continuous glucose monitoring in 10 501 people with diabetes mellitus. *Diabetic medicine : a journal of the British Diabetic Association*. 2015;**32**(12):1568-74.

9. Lewis KR, McCrone S, Deiriggi P, Bendre S. Effectiveness of continuous glucose monitoring in children, adolescents, and young adults with poorly controlled type 1 diabetes. *Journal for specialists in pediatric nursing : JSPN*. 2017;**22**(1).

10. Rachmiel M, Landau Z, Boaz M, Mazor Aronovitch K, Loewenthal N, Ben-Ami M, et al. The use of continuous glucose monitoring systems in a pediatric population with type 1 diabetes mellitus in real-life settings: the AWeSoMe Study Group experience. *Acta diabetologica*. 2015;**52**(2):323-9.

11. Aleppo G, Ruedy KJ, Riddlesworth TD, Kruger DF, Peters AL, Hirsch I, et al. REPLACE-BG: A Randomized Trial Comparing Continuous Glucose Monitoring With and Without Routine Blood Glucose Monitoring in Adults With Well-Controlled Type 1 Diabetes. *Diabetes care*. 2017;**40**(4):538-45.

12. Steineck I, Ranjan A, Nørgaard K, Schmidt S. Sensor-Augmented Insulin Pumps and Hypoglycemia Prevention in Type 1 Diabetes. *Journal of diabetes science and technology*. 2017;**11**(1):50-8.

13. van Beers CAJ, DeVries JH. Continuous Glucose Monitoring: Impact on Hypoglycemia. *Journal of diabetes science and technology*. 2016;**10**(6):1251-8.

14. Anhalt H. Limitations of Continuous Glucose Monitor Usage. *Diabetes technology & therapeutics*. 2016;**18**(3):115-7.

15. Yeoh E, Choudhary P, Nwokolo M, Ayis S, Amiel SA. Interventions That Restore Awareness of Hypoglycemia in Adults With Type 1 Diabetes: A Systematic Review and Meta-analysis. *Diabetes care*. 2015;**38**(8):1592-609.

16. Biagi L, Hirata Bertachi A, Conget I, Quirós C, Giménez M, Ampudia-Blasco FJ, et al. Extensive Assessment of Blood Glucose Monitoring During Postprandial Period and Its Impact on Closed-Loop Performance. *Journal of diabetes science and technology*. 2017:1932296817714272.

17. Song I-K, Lee J-H, Kang J-E, Park Y-H, Kim H-S, Kim J-T. Continuous glucose monitoring system in the operating room and intensive care unit: any difference according to measurement sites? *Journal of clinical monitoring and computing*. 2017;**31**(1):187-94.

18. Andelin M, Kropff J, Matuleviciene V, Joseph JI, Attvall S, Theodorsson E, et al. Assessing the Accuracy of Continuous Glucose Monitoring (CGM) Calibrated With Capillary Values Using Capillary or Venous Glucose Levels as a Reference. *Journal of diabetes science and technology*. 2016;**10**(4):876-84.

19. Reiterer F, Polterauer P, Schoemaker M, Schmelzeisen-Redecker G, Freckmann G, Heinemann L, et al. Significance and Reliability of MARD for the Accuracy of CGM Systems. *Journal of diabetes science and technology*. 2017;**11**(1):59-67.

20. Kirchsteiger H, Heinemann L, Freckmann G, Lodwig V, Schmelzeisen-Redeker G, Schoemaker M, et al. Performance Comparison of CGM Systems: MARD Values Are Not Always a Reliable Indicator of CGM System Accuracy. *Journal of diabetes science and technology*. 2015;**9**(5):1030-40.

21. Cobelli C, Schiavon M, Dalla Man C, Basu A, Basu R. Interstitial Fluid Glucose Is Not Just a Shifted-in-Time but a Distorted Mirror of Blood Glucose: Insight from an In Silico Study. *Diabetes technology & therapeutics*. 2016;**18**(8):505-11.

22. Sinha M, McKeon KM, Parker S, Goergen LG, Zheng H, El-Khatib FH, et al. A Comparison of Time Delay in Three Continuous Glucose Monitors for Adolescents and Adults. *Journal of diabetes science and technology*. 2017:1932296817704443.

23. Facchinetti A. Continuous Glucose Monitoring Sensors: Past, Present and Future Algorithmic Challenges. *Sensors (Basel, Switzerland)*. 2016;**16**(12).

24. Schmelzeisen-Redeker G, Schoemaker M, Kirchsteiger H, Freckmann G, Heinemann L, Del Re L. Time Delay of CGM Sensors: Relevance, Causes, and Countermeasures. *Journal of diabetes science and technology*. 2015;**9**(5):1006-15.

25. Siegmund T, Heinemann L, Kolassa R, Thomas A. Discrepancies Between Blood Glucose and Interstitial Glucose-Technological Artifacts or Physiology. *Journal of diabetes science and technology*. 2017:1932296817699637.

26. Christiansen SC, Fougner AL, Stavdahl Ø, Kölle K, Ellingsen R, Carlsen SM. A Review of the Current Challenges Associated with the Development of an Artificial Pancreas by a Double Subcutaneous Approach. *Diabetes therapy : research, treatment and education of diabetes and related disorders*. 2017;**8**(3):489-506.

27. Shapiro AR. The Safety of Nonadjunctive Use of Continuous Glucose Monitors for Insulin Dosing: Still Not Resolved. *Journal of diabetes science and technology*. 2017:1932296817704446.

28. Shapiro AR. Nonadjunctive Use of Continuous Glucose Monitors for Insulin Dosing. *Journal of diabetes science and technology*. 2017:1932296816688303.

29. Fonda SJ, Graham C, Munakata J, Powers JM, Price D, Vigersky RA. The Cost-Effectiveness of Real-Time Continuous Glucose Monitoring (RT-CGM) in Type 2 Diabetes. *Journal of diabetes science and technology*. 2016;**10**(4):898-904.

30. Roze S, Saunders R, Brandt AS, de Portu S, Papo NL, Jendle J. Health-economic analysis of real-time continuous glucose monitoring in people with Type 1 diabetes. *Diabetic medicine : a journal of the British Diabetic Association*. 2015;**32**(5):618-26.

31. Roze S, Smith-Palmer J, Valentine WJ, Cook M, Jethwa M, de Portu S, et al. Long-term health economic benefits of sensor-augmented pump therapy vs continuous subcutaneous insulin infusion alone in type 1 diabetes: a U.K. perspective. *Journal of medical economics*. 2016;**19**(3):236-42.

32. Chaugule S, Oliver N, Klinkenbijl B, Graham C. An economic evaluation of the introduction of continuous glucose monitoring (CGM) devices for people with Type 1 diabetes and impaired awareness of hypoglycaemia within North West London clinical commissioning groups in England. *Diabetic Medicine*. 2017;**34**:187.

33. Moy FM, Ray A, Buckley BS, West HM. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. *The Cochrane database of systematic reviews*. 2017;**6**:CD009613.

34. Heinemann L, Devries JH. Evidence for continuous glucose monitoring: Sufficient for reimbursement? *Diabetic Medicine*. 2014;**31**(2):122-5.

35. Castle JR, Jacobs PG. Nonadjunctive Use of Continuous Glucose Monitoring for Diabetes Treatment Decisions. *Journal of diabetes science and technology*. 2016;**10**(5):1169-73.

36. Toschi E, Wolpert H. Utility of Continuous Glucose Monitoring in Type 1 and Type 2 Diabetes. *Endocrinology and metabolism clinics of North America*. 2016;**45**(4):895-904.

37. Peters AL, Ahmann AJ, Battelino T, Evert A, Hirsch IB, Murad MH, et al. Diabetes technology-continuous subcutaneous insulin infusion therapy and continuous glucose monitoring in adults: An endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism*. 2016;**101**(11):3922-37.

38. McCarthy M. US doctors recommend continuous glucose monitoring for patients with type 1 diabetes. *BMJ (Clinical research ed)*. 2016;**354**:i5247.

39. Wise J. Continuous glucose monitoring can benefit patients with type 1 diabetes. *BMJ (Clinical research ed)*. 2017;**356**:j364.

40. Acerini C. The rise of technology in diabetes care. Not all that is new is necessarily better. *Pediatric diabetes*. 2016;**17**(3):168-73.

41. Rodbard D. Continuous Glucose Monitoring: A Review of Successes, Challenges, and Opportunities. *Diabetes technology & therapeutics*. 2016;**18**.

42. Pettus J, Edelman SV. Recommendations for Using Real-Time Continuous Glucose Monitoring (rtCGM) Data for Insulin Adjustments in Type 1 Diabetes. *Journal of diabetes science and technology*. 2017;**11**(1):138-47.