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REVIEW ARTICLE

Innovative solution or cause for concern? The use of continuous glucose monitors in people not living with diabetes: A narrative review

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Abstract

Aims: Continuous glucose monitors (CGMs) have expanded their scope beyond indicated uses for diabetes management and are gaining traction among people not living with diabetes (PNLD). CGMs track in time glucose levels and are proposed as tools for the early detection of abnormal glucose and a potential solution for its normalisation through behavioural change, particularly, diet personalisation and motivation of physical activity. This becomes relevance given the growing incidence of metabolic conditions, such as type 2 diabetes mellitus (T2DM). Clinical guidelines, however, do not recommend CGMs in contexts outside type 1 diabetes (T1DM) or insulin-treated T2DM. Therefore, there is a visible disconnect between the indicated and real-world usage of these medical devices. While the commercial market for CGMs in PNLD is expanding rapidly, a comprehensive and evidence-based evaluation of the devices' utility in this population has not been done. Therefore, this review aims to formulate a working model for CGM utility in PNLD as proposed by the 'health and wellness' market that advertises and distributes it to these individuals.

Methods: We aim to critically analyse the available research addressing components of the working model, that is (1) detection of abnormal glucose; (2) behavioural change, and (3) metabolic health improvement.

Results: We find a lack of consistent and high-quality evidence to support the utility of CGMs for these purposes. We identify significantly under-reserved areas including clinical benchmarks and scoring procedures for CGM measures, device acceptability, and potential adverse effects of CGMs on eating habits in PNLD. We also raise concerns about the robustness of available CGM research.

Conclusion: In the face of these research gaps, we urge for the commercial claims suggesting the utility of the device in PNLD to be labelled as misleading. We argue that there is a regulatory inadequacy that fuels 'off-label' CGM distribution and calls for the strengthening of post-market clinical follow-up oversight

for CGMs. We hope this will help to avert the continued misinformation risk to PNLD and 'off-label' exacerbation of health disparities.

KEYWORDS

CGM regulations, continuous glucose monitor, medical devices, people not living with diabetes, wearable technology

1 | INTRODUCTION

Diabetes mellitus (DM) remains a predominant metabolic condition, with figures indicating over 415 million individuals worldwide living with it. Type 2 diabetes mellitus (T2DM) accounts for over 90% of all cases.[1] The condition is characterised by persistent hyperglycaemia combined with elevated glucose fluctuations.[1] The imperative of timely detection of these glucose fluctuations is underscored by its capacity to preserve pancreatic beta-cell (β-cell) function thus potentially preventing or delaying T2DM onset.[1] The importance of disease prevention is being increasingly recognised by the general population. In this way, the 'health and wellness' market has expanded with products for health monitoring and lifestyle optimisation being of particular interest to the consumer as ways to reduce their risk.[2] Continuous glucose monitors (CGMs) specifically have evolved beyond the certified indications for diabetes management and are now being increasingly adopted by people not living with diabetes (PNLD).[3] Minimally invasive, CGMs track glucose levels in the interstitial fluid (ISF) via a subdermal sensor electrode allowing a comprehensive insight into glucose dynamics.[4] Present CGM models enable measurement for up to 14 days, documenting durations and frequencies of both hypo- (low blood glucose < 3.9 mmol/L) and hyperglycaemic (high blood glucose > 10.0 mmol/L) episodes, in addition to postprandial (after meal) glucose spikes.[4,5] Therefore, in PNLD, CGMs are gaining traction as potential tools for detection of abnormal glucose spikes and a solution for glucose normalisation.[3] This becomes of relevance given the rapidly increasing incidence of T2DM and other non-communicable diseases linked to diet.

Glycated haemoglobin (HbA1c) and fasting plasma glucose (FPG) are the key glucose metrics used in T2DM screening and risk prediction.[5,6] Yet, their ability to spot those at risk has been questioned.[6] In turn, CGMs may allow for a more refined risk categorisation through glycaemic variability (GV).[7,8] GV represents the measurement of glucose oscillations over a period of time (within a day, between days or long-term)[7] and is the focal point used by commercial companies distributing CGMs.[9] The metric is suggested to anticipate both micro- and macrovascular complications, aligning with elevated HbA1c, FPG, postprandial glycaemia, and insulin resistance.[9,10] From this, the key objective communicated to PNLD is minimising GV to prevent these potential negative impacts on metabolic health outcomes.[3,9]

By continuously measuring and visualising daily GV, CGMs could detect the early onset of glucose dysregulation[8] and promote improvement by allowing the user to associate these fluctuations with their diet and lifestyle habits.[11] With the inter-individual differences in glucose responses to the same foods,[12,13] CGMs may provide effective personalised nutritional advice by addressing these variations. For instance, foods resulting in lower postprandial glucose responses (PPGRs) could be prioritised, and those causing higher PPGRs excluded or minimised.[3] Easy access and continuity of immediate feedback of glucose

What's new

- With the growing interest in wearable health technologies, continuous glucose monitoring systems (CGMs) have expanded their scope, transitioning from exclusive use in diabetes management to lifestyle enhancement for people not living with diabetes.
- This narrative review summarises current knowledge on the utility of CGMs for people not living with diabetes, as presented in the 'health and wellness' sector, and critically assessed its components, namely, detection of glucose abnormalities, behavioural change and metabolic health improvement.
- We identify significant gaps between the indicated, marketed, and real-world use of CGMs showing there is a lack of compelling evidence for the utility of CGM in this group. Furthermore, we emphasise the importance of refining CGM regulation in the UK, particularly when considering its 'off-label' use.

data suggest further functionality of CGMs to potentially motivating and fine-tuning physical activity for optimised metabolic health.[14] Leveraging these potential functions of the device, the 'health and wellness' market proposes CGM as a tool and an innovative solution for optimising metabolic health.[3] Commercial companies freely advertise and distribute the device throughout the EU and the UK, particularly to the health-conscious consumer and importantly, those that can afford them.[3] However, whether the CGM can actually produce the anticipated health improvements in PNLD remains uncertain. In fact, current clinical guidelines do not recommend CGMs outside of people living with type 1 diabetes (T1DM) or insulin-treated T2DM.[15] This disconnect between the indicated and real-world applications of CGMs, recognised by the Medicines and Healthcare products Regulatory Agency (MHRA) as a medical device,[16] is concerning and requires addressing.

Given the expanding market and evolving relevance of CGMs in PNLD, this narrative review aims to synthesise and critically analyse recent research on CGM application within this population. We anticipate the widespread adoption of this device by PNLD to be justified by a sufficient body of high-quality evidence, otherwise, concerns may arise regarding the efficacy and most importantly safety of CGM use in PNLD. We formulate a potential working model for CGM utility as a device for metabolic health improvement and T2DM prevention, and critically address its integral components: detection of abnormal glucose, behavioural change, and improvement of metabolic health (Figure 1). In untangling speculation from reality, we hope to bring clarity

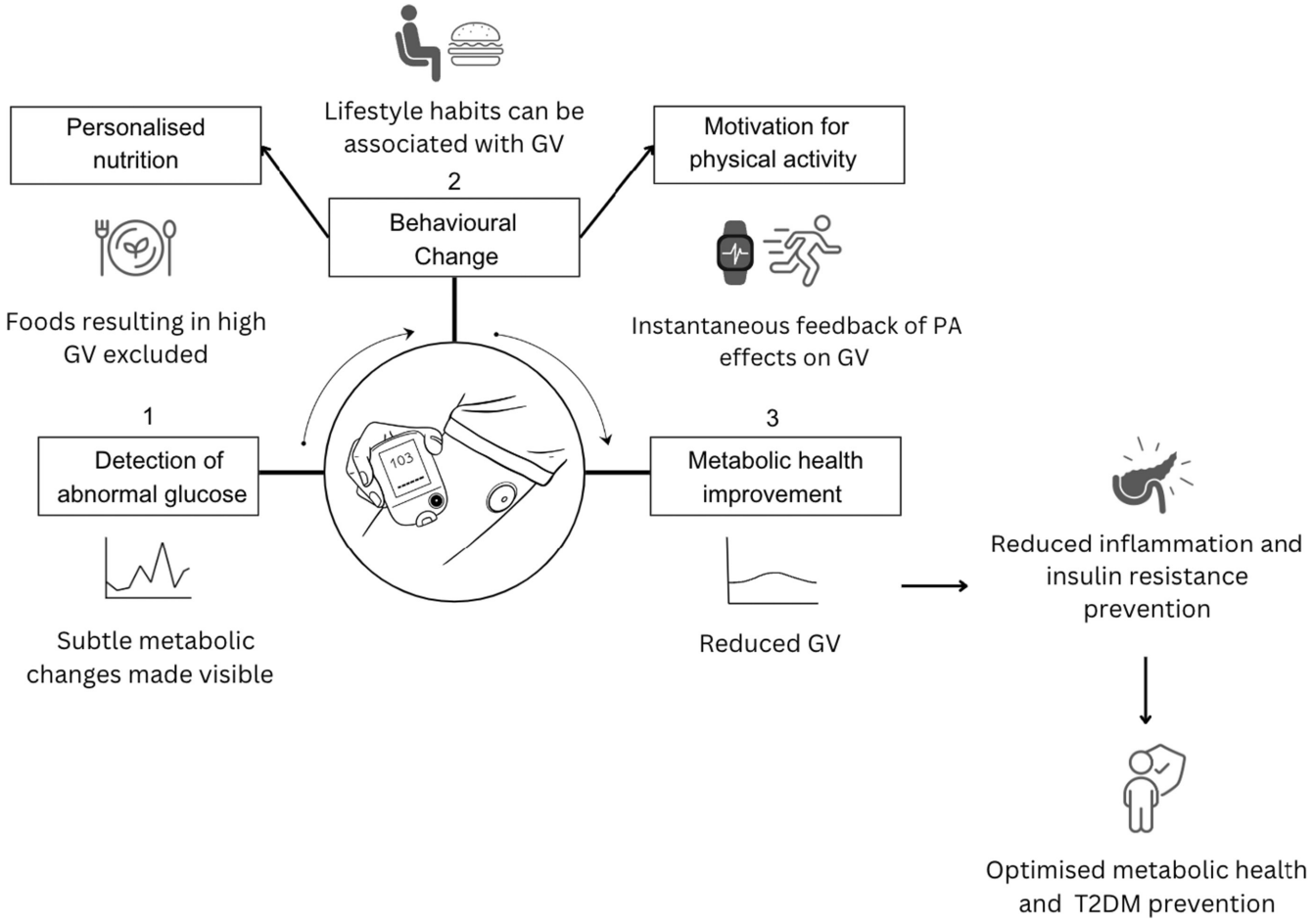

FIGURE 1 A visual representation of the mechanistic pathways as proposed in 'health and wellness' for improvement of metabolic health and T2DM prevention using a CGM: (1) Detection of abnormal blood glucose is enabled by CGM making subtle metabolic changes visible; (2) Lifestyle habits such as diet and physical activity can be associated with CGM data to induce behavioural change. Diet may be personalised based on CGM data with foods resulting in high PPGR avoided. Immediate glucose data feedback of the beneficial effects of physical activity on glucose regulation may motivate greater engagement and accountability; (3) Behavioural change results in reduced GV, inflammation, and insulin resistance improving metabolic health and potentially preventing T2DM. GV, glycaemic variability; PA, physical activity; PPGR, postprandial glucose responses; T2DM, type 2 diabetes.

to PNLD wishing to use CGMs, as well as to the regulatory bodies overseeing the distribution of these devices in the UK.

2 | METHODS

Electronic searches of the online databases PubMed (MEDLINE), EMBASE and Cochrane Library between January 1980 to May 2024 were conducted for studies examining aspects of CGM utility and performance in PNLD. Search terms used included 'Continuous glucose monitoring' AND 'healthy' OR 'without diabetes', (see Supplementary material for full terms). The references of the included articles were also screened manually to access relevant articles that were not identified during the database search. The PICO framework[17] was used to determine the selection criteria. Therefore, studies were included if they were studies of PNLD using CGMs in adults; and assessed either (1) CGM accuracy; or (2) CGM measures and clinical benchmarks; or (3) CGM-powered behavioural interventions including those in personalised nutrition and exercise; and (4) were peer-reviewed and available in English. Studies were excluded if they were: (1) in paediatric populations; (2) were studies on CGM accuracy or clinical benchmarks and were published earlier than 2018, given device accuracy has significantly improved since then. Other studies were not excluded based on location or date of publication. Overall, 27 eligible studies were identified (Supplementary Tables S1–S4).

2.1 | CGM for early detection of abnormal glucose

The main functionality of CGMs in PNLD is the real-time visualisation of glucose fluctuation in glucose response to foods and drinks which is reflected in greater glucose variability (GV).[7] With continuous glucose data easily accessible, early identification of short-term GV may be more easily detected allowing for a timely lifestyle intervention and potentially reduced risk of disease progression or development.[7,8] For this to be possible, CGMs have to provide a clear assessment of glucose metrics (Table S2 in Supplementary materials), set definitive clinical benchmarks for PNLD (Table S3 in Supplementary materials), and maintain a high degree of accuracy (Table S1 in Supplementary materials).[5] Absence of these features may at best compromise the tangible benefits, and worst lead to adverse health outcomes. Therefore, the following sections will evaluate the available evidence for these aspects of CGMs to confirm whether it can and should be used for early detection of abnormal glucose in PNLD.

2.2 | Glucose assessment metrics and clinical benchmarks for CGM data interpretation

In PNLD, assessment of glucose control and subsequent lifestyle change can be guided by CGM-derived composite metrics (CMs).[18] These capture multiple glucose variability (GV) indices, each recording different aspects of glucose fluctuations, including amplitude, frequency, duration, or pattern[19] (Table 1).[20,21] CMs are proposed to be indicative of an individual 'glucotype', reflecting their state of glucose control and metabolic health.[18] Computational approaches are used to produce CMs[18] with the end-result being visually accessible data using CGM-compatible software[22] That way, for PLWD Abbott's Freestyle Libre 2 and 3 sensors are certified together with a compatible Freestyle LibreLink App.[23]

Studies emphasise the importance of choosing the relevant components for CM calculation according to the clinical metrics of interest and the characteristics specific to the user.[21] For instance, 'CGMap' characterised CGM-derived measures in PNLD and revealed markers for early detection of diabetic retinopathy such as fractal dimension displaying significant associations with eA1C and J_index.[21] These may present potential digital biomarkers for early impaired glucose tolerance (IGT),[21] however, the limitations of this cross-sectional dataset need to be appreciated including relatively small sample size and self-reported dietary intake.

When comparing time in range (TIR), GV and average glucose levels in people at-risk for T2DM, prediabetes, and T2DM[11] (Table 2), higher GV was identified during the day compared with night time for all groups.[8] Similar results were observed in PNLD in a study by Sofizadeh et al. (2020), with the differences attributed to glucose fluctuations linked to meals during the day, for this group, TIR (3.9–10.0 mmol/L) stood at 97.0%, with an SD of 1.0 mmol/L and a CoV of 20.0%.[24] In another study, prediabetes group had a significantly higher TIR (7.8–10.0 mmol/L) compared with those at risk of T2DM (5.4% [2.0; 9.7] and 1.1% [0.4; 3.7] respectively, $p < 0.01$), though overnight TIR (7.8–10.0 mmol/L) did not differ significantly between these groups.[8] In T2DM, however, TIR (7.8–10.0 mmol/L) was higher both overnight (15.2% [6.8, 35.6] vs. 0.4% [0, 1.5] for the prediabetes and 0% [0, 0.7] for the at-risk for T2DM group, $p < 0.0001$) and during the day.[8] These differences in night time TIR may provide a measure indicative of the early onset of impaired fasting glucose and potentially capture the progression from PNLD to prediabetes.[8] On the other hand, in another study, TIR showed weak correlations to clinical parameters in PNLD compared with other common metrics such as MODD and MAGE.[21]

TABLE 1 Continuous glucose monitoring metrics.

Metric	Description
MAGE	Measure of magnitude of glycaemic excursions that exceed 1 SD from the mean
SD	Measure of variation of all glucose measurements
CoV	Magnitude of variability relative to mean blood glucose $CoV = (SD)/(\text{mean glucose}) \times 100$
TIR, TBR, TAR	Proportion of time spent within, below or above blood glucose levels within the target range
CONGA	Combined measurement of timing and magnitude of blood glucose level fluctuations at specific time periods
GMI	Estimate of HbA1c, based on average glucose
eA1C	A linear transformation a of the mean glucose value, meant to estimate the HbA1c blood test. Calculated: $(46.7 + \text{mean(Glucose)})/28.7$
J_index	Index designed to stress the importance of the mean level and the variability of glycaemia. Calculated: $0.001 \times [\text{mean(Glucose)} + \text{SD(Glucose)}]^2$

Abbreviations: CONGA, continuous overall net glycemic action; CoV, coefficient of variation for glucose; eA1C, estimated A1c glycated haemoglobin; GMI, glucose management indicator; HbA1c, glycated haemoglobin; J_index, Youden's index; MAGE, mean amplitude of glycemic excursions; SD, Standard deviation of blood glucose levels; TAR, time above range; TBR, time below range; TIR, time in range.

TABLE 2 CGM measures for people not living with diabetes (PNLD), at risk for type II diabetes, with prediabetes and with type II diabetes.

	User cohort				ATTD target values
CGM measure	PNLD	At risk for T2DM	Prediabetes	T2DM	T1/2DM (%)
TIR (3.9–10.0 mmol/L)	97.3 [95.4, 98.7]	98.0** [95.6, 99.4]	97.8** [95.8, 98.7]	85.6** [67.7, 91.6]	>70
TBR (<3.9 mmol/L)	1.6 [0.6, 3.2]	2.0* [0.3, 4.4]	1.6* [0.5, 4.0]	0.2* [0, 1.1]	<4
TAR (>10.0 mmol/L)	0.25 [0, 1.29]	0** [0, 0]	0.2** [0, 0.6]	11.4** [4.6, 28.6]	<25
GV (%CoV)	20	16.0** [13.1, 18.4]	17.7** [15.6, 20.3]	23.2** [20.2, 27.9]	≤36

Note: Data are % medians [IQR]. Prediabetes defined by FPG (5.6–6.9 mmol/L) and/or HbA1c (5.7%–6.4% (39–46 mmol/mol)). At risk for T2DM is self-reported as at risk for developing T2D using the American Diabetes Association diabetes risk assessment tool. *p* values represent comparisons across prediabetes, T2DM and at-risk groups (Barua et al.[8]) using a Kruskal–Wallis test. CGM values for PNLD are findings of a comparable study by Sofizadeh et al.[24]

Abbreviations: ATTD, Advanced Technologies and Treatments for Diabetes; CGM, continuous glucose monitoring; FPG, fasting plasma glucose; GV, glycaemic variability; HbA1c, glycated haemoglobin; PNLD, people not living with diabetes; T2DM, type 2 diabetes mellitus; TAR, time above range; TBR, time below range; TIR, time in range.

**$p < 0.001$; *$p < 0.05$.

Despite there being statistically significant differences in GV values between PNLD, those at high risk, prediabetes and T2DM[8] (Table 2) all groups fell below the recommended threshold for T1 and T2DM of 36% (Cov).[5] This possibly indicates that on average, all have relatively stable glucose levels, at least as far as GV is concerned. However, whether this threshold is appropriate to be considered in PNLD is worth exploring in adequately powered longitudinal research. While GV is indeed higher in people with IGT compared with without, this is unsurprising given it is driven by PPGRs that are higher in the former group.[25] However, this does not suggest GV be a driver of disease progression, whereby its minimisation would be protective. GV does not appear to have clear associations with important diabetes related metrics such as insulin sensitivity, blood liver profile, or oxidative stress.[25] Its effects on micro- and macrovascular complications are also uncertain, with current evidence suggesting the strongest correlation with cardiovascular events only in people with coronary artery disease.[25] Notably, the magnitude as well as the directionality of these associations is unclear given the limitations of cross-sectional design in CGM studies. Further, the accuracy of CGM measurements and thus their associations with clinical outcomes may depend on the type of device used,[26] user body composition particularly fat mass,[27,28] or be affected by interferences from certain medications

including lisinopril and albuterol[29] (see Section 2.3). Therefore, current research is too limited to confirm the relationship between CGM-derived measures for appropriate scoring of CMs. Whether GV brings additional benefit in terms of diagnostic ability beyond current glucose measures in clinical practice remains equally uncertain. In this context, interpreting glucose data becomes challenging as it is both unclear what constitutes CGM-defined abnormal values and what is their clinical meaning in PNLD.

Current cut-offs for defining pathologic glucose levels in PNLD may not provide a valid evaluation if considered against CGM data. Notably, clinical values for IGT (75-g OGTT, 7.8–11.0 mmol/L) are established using large datasets of oral glucose tolerance tests (OGTTs) usually conducted after 10–16 h fast.[30] CGM-derived 2-h post-meal PPGRs will significantly differ from values seen following standardised OGTT as these can be affected by factors such as lack of sleep or previous meals prior to the OGTT.[30] Hence, judgement of CGM-captured PPGR using non-CGM specified benchmarking would be considered inappropriate and therefore cannot be used definitively for the assessment of metabolic health in PNLD. Long-term prospective studies are required to develop benchmarks constituting healthy GV that are relevant to clinical outcomes in PNLD. Therefore, commercial companies that advocate for GV minimisation to improve metabolic health and prevent disease progression appear to be doing so based on speculations only, as current data are overly fragmented to suggest the predictive power of GV in terms of heightened T2DM risks and reduction in disease development in PNLD.[25]

2.3 | CGM accuracy

The accuracy of CGMs has significantly progressed over recent years, with the mean absolute relative difference (MARD) reducing from 25% to a respectable 10%, especially in the context of T1DM.[4] Accuracy metrics for CGMs encompass point, trend, and threshold alarm accuracies[31] with MARD values reported to depend on glucose ranges (in people with vs without diabetes),[32,33] as well as on the model type of the CGM sensor.[4] For PNLD, given the relatively benign glucose fluctuations compared with T1DM and T2DM, point accuracy becomes the main criterion.[31] This metric reflects the alignment between an isolated glucose reading and an established reference benchmark.[31] However, relying on comprehensive metrics like MARD may be overshadowed by inaccuracies, specifically with hypoglycaemic episodes, potentially inducing unreasonable anxiety in PNLD.[34] where no concern is warranted.

Furthermore, metrics without agreement values for PNLD could distort the proportion of clinically relevant readings, thus potentially endorsing CGMs with respectable averages yet erratic excursions.[35] Currently, the standards ratified by the United States Food and Drug Administration (FDA) for CGMs are the only published regulatory benchmarks that set out minimal accuracy requirements, using specified target ranges associated with agreement values.[36] Within these benchmarks, the point accuracy criteria explain the least proportion of readings required to align with the Advanced Technologies & Treatments for Diabetes (ATTD) consensus guidelines.[36] Presently, compliant devices include the Freestyle Libre 2, Freestyle Libre 3, Freestyle Libre 2 Plus, Free Style Libre 3 Plus Dexcom ONE, Dexcom G6, and Dexcom G7.[16] However, for PNLD, the precise values for gaining CGM benefits might deviate from these stringent CGM criteria. Thus, the lack of data makes diabetic target benchmarks potentially unsuitable for PNLD.

The available studies on CGM accuracy in PNLD exhibit overarching limitations, including small and unrepresentative sample sizes,[27–29,32,33,37] use of outdated device models[29,38] and low generalisability. Analysis is rarely supported with confidence intervals, thereby effect size, precision, and reliability of the findings are uncertain.[27–29,32,33,37] Furthermore, highly variable accuracy measured with MARD across contexts highlights the need for a nuanced understanding of device performance in the target population (Table S1 in Supplementary materials), which for PNLD is not available.

CGM precision can also vary depending on user characteristics, predominantly body composition.[27,28] Anthropometrics like overall body fat, body fat percentage, and body mass index (BMI) are inversely associated with CGM precision.[27,28] Factors stemming from shifts in subcutaneous fat and capillary networks, characteristic of obesity, potentially affect the diffusion impediment and subsequently CGM precision across different BMI categories.[27,28] Thus, considering body composition when interpreting CGM data, particularly for people living with obesity, is crucial. Given obesity is one of the leading drivers of T2DM,[1] people living with obesity may present the key subgroup that would be willing to uptake CGMs for metabolic health improvement and prevention of T2DM. The outlined accuracy limitations in this population require device optimisation for safe use by people living with obesity. Currently, the relationship between body composition and CGM accuracy should be considered when interpreting the results.

Another salient factor is the discrepancy between glucose concentrations in the ISF and blood glucose.[39] This is particularly problematic with rapid glucose fluctuations such as during high-intensity exercise or following the consumption of highly glycaemic foods such as refined carbohydrate.[32,37] Data shows that CGM overestimation

of ISF glucose after glucose loading has been previously highlighted.[32] During activity, studies in both PLWD and PNLD show higher CGM bias, with apparent blind spots in the early detection of hypoglycaemic episode.[37] Therefore, device reliability may be restricted to sedentary periods.[37] Mechanisms for this reduced accuracy may also include microcirculation perturbations caused by localised movement, increased body temperature, and rapid glucose shifts, termed 'sensor drift'.[37] Thus, PNLD partaking in physical activity may receive skewed data, potentially resulting in undue concerns or misinformed lifestyle adjustments based on glucose levels. In fact, Wong and colleagues (2020) report the overall lower accuracy of the Freestyle Libre sensor in PNLD comparing with previous studies in people with T1DM or T2DM.[33] This may be because people living with diabetes have compromised tissue glucose uptake, which is associated with higher ISF, making it more sensitive to changes in blood glucose levels.[33] Therefore, the difference between ISF and blood glucose might be smaller in PNLD, both in fasting and postprandial states. This speculation, however, is yet to be tested in human trials.[33]

To address these issues, several CGMs utilise algorithms to adjust for these physiological variances between the two compartments, aiming to approximate glucose levels. Such computational models insinuate that displayed readings might not genuinely correspond to either ISF or capillary glucose values.[39] CGM measurements also suffer from lower inter-day reproducibility in PNLD, especially among younger individuals as established using functional data analysis.[38] This emphasises the need for rigorous calibration processes and precise reference standards to compile best practice guidelines ensuring the reliability of CGM outputs. For PNLD, this aspect is visibly missing.

Furthermore, certain concurrent medications can adversely influence CGM precision. Notably, devices like Medtronic Guardian Sensors and Dexcom G4 Platinum have recorded accuracy reductions due to electrochemical interferences from specific agents like lisinopril and albuterol.[29,34] It is possible for these interferences to have a bigger role in accounting for the implausible CGM data than users and even clinicians assume.[34] Despite this, there is scarcity of publications addressing this limitation, with the majority testing outdated CGM systems.[34] While regulatory requirements mandate manufacturers to conduct interference studies for each new CGM model and generation, a considerable proportion of the data generated from these studies remains unpublished making it difficult to understand the true impact on CGM precision.[34]

Finally, ensuring accuracy limitations are effectively communicated to the end-user remains the responsibility of the manufacturer[40] and not those commercial companies utilising their products. CGM user manuals align with the intended purpose of the device and thus are generally diabetes-focused. PLWD can also seek professional advice from their clinician for any device-related concerns, this however, is not the case for PNLD. Therefore, if CGMs are to be used by PNLD, research addressing device accuracy in this context is required. Studies should focus on confirming the clinical significance of potential inaccuracies attributed to drug interferences, physical activity, or body composition of the user to develop guidelines and support systems tailored to PNLD. At present, the judgement of nocturnal hypoglycaemia and postprandial hyperglycaemia, as determined by CGM, in PNLD is inappropriate. Use of more reliable devices such as self-monitoring of blood glucose and subsequent CGM calibration is recommended.[32]

2.4 | Practical applications of CGMs for behavioural change aimed at metabolic health improvement

Effective blood glucose control is linked to lifestyle habits.[1] CGMs could reveal these interactions by graphically associating and visualising lifestyle factors with corresponding high or low glucose results, thus potentially fostering healthier lifestyle practices, as observed in people living with prediabetes, T1DM, and T2DM.[41] Similarly, CGMs may foster beneficial behavioural changes in PNLD by increasing accountability thereby improving glucose control and reducing T2DM risk. Particularly, increasing levels of physical activity and maintaining a healthy diet are fundamental in preventing T2DM.[42] Therefore, this section evaluates the utility of CGMs in supporting these behavioural changes in PNLD and assesses the resulting metabolic health outcomes (Table S4 in supplementary materials).

In PNLD, greater postprandial glycaemia (PPGR) is associated with reduced insulin sensitivity and impaired β-cell function.[43] Importantly, visible inter-individual differences in PPGRs to the same foods have been observed, which are not explicitly considered by traditional carbohydrate or calorie-centric dietetic care approaches.[12,13] Instead, CGMs offer PNLD a chance to visualise and associate their PPGRs with the foods they consume, excluding items resulting in high PPGR.[12] Such personalisation is proposed to allow for improved insulin sensitivity and β-cell protection and reducing of disease development.[12,13]

Personalised nutrition (PN) is a dietary protocol tailored to an individual's genetic, microbiotic, metabolic, alimentary, and other key factors.[44] Scant research, to our knowledge, has delved into the clinical benefits of using CGMs for PN within the PNLD (Table S4 in Supplementary

materials). From the available published data, only six studies were found.[11–13,45–47]

Zeevi et al. (2015) assessed individual PPGRs, characterised the individual variabilities, and identified associated factors.[12] For uniform food items such as bread, significant inter-personal PPGR variations were noted as serving basis for the development of a predictive machine learning (ML) model.[12] Incorporating data gathered from participants' blood tests, microbiome evaluations, dietary diaries, and anthropometrics, the ML model's ability to predict individual PPGR was comparable to dietary guidance based on expert analysis of CGM data only.[12] Results were echoed in a subsequent study[45] to suggest potential application of the algorithm in PNLD. The authors reported a continuous relationship between PPGRs and risk factors for T2DM, such as BMI, HbA1c, and wakeup (fasting) glucose, and proposed its potential clinical utility.[12] However, without reported confidence intervals, the precision and reliability of these short-term associations are difficult to ascertain raising concerns about the external validity and generalisability of the findings. The predictions made require validation in appropriately powered longitudinal studies. Further, the use of self-report tools for gathering diet, sleep, and activity data can be prone to reporter bias or underreporting, and thus attenuating the potential diet–disease relationships identified in PN studies using CGMs.[48] Ultimately, a large proportion of the predictive features in these studies are related to the faecal microbiome with the underlying mechanisms currently being elusive.[12] Further research is essential to decipher the connections between the gut microbiome and glycaemic outcomes, guiding the formulation of appropriate and evidence-based PN interventions.

High inter-personal variability in PPGRs has also been supported by the findings from The Personalised Responses to Dietary Composition Trial-1 (PREDICT-1) trial, with further validation from an independent US cohort of PNLD.[13] This study identified higher variability in postprandial triglyceride and glucose rather than fasting values, suggesting the post-prandial response to be a better indicator of metabolic health.[13] However, PPGRs were less informative than FPG as a biomarker predicting IGT and atherosclerotic cardiovascular disease (ASCVD) 10-year risk score.[13] Therefore, the clinical decisions based solely on fasting glucose may already capture a reasonable proportion of the relevant information as indicated by only a minor improvement in ASCVD risk prediction being reported when PPGR was added (ROC AUC = 0.69 vs. 0.72, respectively).[13] The study emphasised the larger role of individual glucose over the macronutrient composition of meals in impacting the incremental area under the curve (iAUC) (18.74% vs. 16.73%).[13] Yet, contrastingly to its name, PREDICT 1 study did not establish long-term predictive values of these differences and currently does not show its relevance in better discrimination of metabolic tolerance. PREDICT 2 and 3 are set out to reaffirm the findings of PREDICT 1 in more expansive cohorts.[49] Unless PPGR predictions are translated into clinical outcomes, it is unclear as to how these studies will significantly update the working model meaningfully enough to increase the confidence in the value of PN using CGMs in PNLD.

More recently, a PN trial aimed at assessing the efficacy of short-term personalised dietary advice, using a personal dietary programme, compared with generic US dietary advice[50] on cardiometabolic health.[46] Here it was shown, in a relatively healthy US population living with obesity, that a PN intervention resulted in greater reductions in triglycerides, weight, waist circumference, HbA1c, but not low-density lipoprotein cholesterol.[46] In addition, there were improvements in diet quality and microbiome composition.[46] Despite these differences being statistically significant, it could be questioned whether they represent clinically relevant improvements[S1,S2] and how beneficial they were at risk reduction. Though it should be appreciated that the study population was healthy, and as such greater health improvements might be seen in those who are metabolically unhealthy or at greater risk of T2DM. Finally, the direct role and magnitude of the effect of using a CGM within the PN intervention were difficult to ascertain due to the complex nature of the study PN algorithm,[46] and so whether this is evidence for the beneficial use of CGMs in PNLD remains unclear.

The key assumption of PN studies is that an individual's unique response to the same meal is reproducible[12,13] has also been challenged.[S3] With recent data showing poor reliability of PPGR to multiple duplicate meals, with intra-individual GV similar to that seen across different meals.[S3] Even under controlled experimental conditions, obtaining two measurements was insufficient to accurately estimate PPGR; however, determining the number of CGM readings needed for accurate estimates remains ambiguous.[S3] Furthermore, the efficacy of CGM-driven meal assessments within PN may be dependent on the CGM device used, given observed variances in inter-personal PPGR with different devices,[26] prompting reflections on genuine personalisation and use in T2DM prevention and disease prevention. The discrepancy could, however, have arisen due to potential methodological challenges. Ad libitum feeding could have compromised sensor accuracy, especially during glycaemic extremes, with ambiguously composed meals distorting meal classification.[S4] Supportively, reduced variability indices were documented for carbohydrate-rich meals (>25 g),[S4] though results were not replicated in an independent data set.

Given these inconsistent findings, the transition of CGMs from a medical device measuring glucose dynamics in diabetes management to a comprehensive tool for PN possibly seems premature. Merely demonstrating inter-individual variations in PPGRs[12,49] appears insufficient to demonstrate using CGMs to optimise metabolic health in PNLD. Interestingly, research contrasting PN interventions with generic dietary advice revealed little effect on key indices such as HbA1c or GV in prediabetes.[S5,S6,S8,S9] Therefore, questioning whether the real-world metabolic improvements using CGM-informed nutritional interventions are truly 'personalised' remains questionable.

The 'Sugar Challenge' study assessed glucose patterns in 665 participants.[11] Using CGMs alongside a smartphone application, participants' glucose dynamics were measured relative to factors like dietary composition and physical activity.[11] Among PNLD with poor baseline TIR (time spent in range 3.3–7.8 mmol/L less than 83%), 91.7% displayed TIR improvement by an average 23.2%.[11] The authors suggested this effect was primarily attributed to avoidance of foods with high glycaemic index.[11] While the ATTD consensus for TIR is 3.9–10 mmol/L for T1DM,[5] the study defined TIR for PNLD as glucose levels 3.0–7.8 mmol/L, as PNLD can have non-pathologic Level 1 (below 3.8 mmol/L) hypoglycaemia.[11 S10] Given discrepancies in TIR definitions, the addition of percentages of TIR including normoglycaemia, hypoglycaemia and hyperglycaemia together with GV metrics would have been beneficial for greater clarity on clinical benefit.

Food consumption is complex and multifaceted, moulded by a combination of physiological, social and psychological facets.[47] For instance, emotional eating can predispose individuals to weight gain and T2DM.[47] One investigation on 'hunger training' assessed the alignment between perceived hunger and glucose data. Two groups used CGMs and SMBG to measure pre-meal glucose. Both saw noteworthy weight loss, regardless of the glucose assessment technique used,[47] though no significant differences in acceptability, adherence or behaviour change were noted between the two methods. Qualitative data, however, suggested at a more positive experience and a greater inclination to explore a variety of foods in the CGM group.[S7] Conversely, the discomfort inherent in finger pricking may have motivated greater mindfulness of eating behaviours.[S7]

Physical activity, paramount for controlling post-meal glucose fluctuations and T2DM risk, may be enhanced by CGMs.[S8] Witnessing the immediate glycaemic benefits of exercise may help to stimulate activity adherence.[S8,S9] An 8-week investigation contrasting traditional exercise with a CGM-enhanced routine revealed superior fitness outcomes and attendance in the CGM group.[S13] Paired with fitness trackers, CGMs prompt improved motivation for weight loss in people living with overweight.[S8] Though the sustainability of these behavioural improvements are currently uncertain given the short-term nature of the studies available.[S8,S9] Further randomised controlled trials exploring the prolonged effect of physical activity on CGM-based measures are warranted.[S9]

While CGMs' benefits seem evident in PLWD, their adoption by PNLD demands further scrutiny.[14] One study indicated that 90% of users found the CGM easy to use and enlightening, but only 40% foresaw its health utility.[14] This diminished adoption could stem from gaps in people understanding the meaning of the CGM data thus deterring full engagement. Crucially, this research did not probe the CGM's potential behavioural influence or conduct qualitative assessments to enhance comprehension in PNLD.[14] Future behavioural studies using CGMs in PNLD should consider provision of concise information sessions on how dietary choices and physical activity impact glycaemia and how it reflects in CGM data, appreciating inter-individual variability. This could help motivate users by bridging gaps in understanding and fostering greater engagement. Ultimately, practical relevance of CGM-enhanced interventions will depend on the specific needs of the target user. It is therefore crucial to carry out qualitative assessments of PNLD experiences of using CGM to better understand the unique demands and objectives of this user group.

3 | DISCUSSION

This current review underscores a lack of compelling evidence for the utility of CGM in PNLD. Despite their popularity CGMs currently appear not to be suitable for repurposing from a device for diabetes management to a comprehensive tool for metabolic health improvement and disease prevention at present.

The most substantial potential barrier to CGMs utility in PNLD is the visible lack of prospective longitudinal research to allow consensus on the thresholds for CGM measures.[S10] Current absence of accepted standards for CGM glucose assessment metrics specific to PNLD complicates both research, clinical implementations, and their commercial viability.[S11] Until these data become available, CGMs should not be used as tools for screening and T2DM risk stratification in PNLD. Similarly, very little data exist on how to select the optimal CGM components for CMs, as well as how to best score and correlate them with clinical outcomes.[S11] Given the outlined gaps, it is unclear as to what guides the development of commercial procedures for CM scoring used by PNLD for metabolic health assessment. Highly variable and minimally transparent, these

approaches require robust scrutiny in terms of reliability and clinical efficacy before wider scale use.

At the same time, studies advocating for the beneficial effects of CGMs in behavioural change lack real-world validity and fail to prove clinical significance and long-term effects of CGM-powered interventions. The magnitude, as well as directionality, of the associations found in these studies are unclear and arguably inadequate to support viability of using CGMs for population-wide interventions which are currently being advocated. As it stands, notions suggesting minimising GV can be protective of T2DM or other non-communicable diseases feed off anecdotal evidence. This way, PN approaches proposed to PNLD targeting GV may potentially overlook the actual underlying pathophysiology of T2DM and contrastingly, result in poorer health outcomes.[3] For instance, GV-focused PN could potentially lead PNLD to replace carbohydrates with foods higher in animal proteins or fat.[3] This may not only, not reduce T2DM risks but potentially have adverse impact on β-cell function and insulin resistance and increase cardiovascular risk.[3]

Notably, a proportion of studies reporting positive results of these interventions compared with classical dietary advice, are sponsored or directly affiliated with companies functioning in the PN space.[13,46 S4] In fact, more than 50% of total research on blood glucose measurement is industry sponsored.[S12] Such prevalence underscores the pervasive influence of corporate interests in shaping research output in the field. This highlights the need for independent studies to establish a more comprehensive understanding of CGM's role in health improvement and disease prevention for PNLD. Addressing the robustness of CGM studies becomes imperative given how quickly the commercial market is expanding. In 2023, the global CGM market was valued at $9277.16 million, and is forecasted to grow at a compound annual growth rate (CAGR) of 21.8% between 2024 to 2032.[S13] Given CGMs have witnessed extensive application in the broader commercial setting, despite the absence of according guidelines, concerns arise regarding the regulatory strictures overseeing their usage in PNLD.

As medical devices, CGMs gain market entry in Europe post-acquisition of the Conformité Européenne (CE) marking, among other global validations.[16] However, questions surround the robustness of CGM precision evaluations via the CE marking, with criticisms highlighting an absence of unified study methodologies and established performance criteria.[16] For instance, variances have been detected in the MARD values of a CGM between company-sponsored studies and independent research.[S8,S9]

Post the EU Medical Devices Regulation (MDR) 2017/745, CGMs must now have a CE marking for UK marketability.[40] Yet, post-Brexit regulations indicate that CE-labelled medical tools will only have access to the UK market until 31 December 2024.[16] Subsequent to this, compliance with the UK Medical Devices Regulation 2002 (UK MDR 2002) and the acquisition of the UK Conformity Assessed (UKCA) marking becomes imperative.[16] Therefore, manufacturers are responsible for presenting and substantiating clinical evidence in line with overarching safety and efficacy parameters.[40] These directives are primarily diabetes-centric, often sidelining considerations for PNLD.

Exceptions do exist, such as the Abbott Libre Sense Glucose Sport Biosensor (Supersapiens) which obtained a CE marking solely for athletic applications.[S14] The manufacturer outlines that this device is not made for diagnosis, treatment, or any medical purpose.[S14] The designated utility and categorisation determine the evidence threshold for CE marking attainment.[40] Nonetheless, CGMs, originally designated for PLWD, are gaining traction among PNLD, surpassing their CE certificatory bounds. A case in point is the Freestyle Libre 2 Flash which is CE-certified for ISF glucose measurement in PLWD, yet being sold by med-tech companies for providing dietary guidance in PNLD.[9,49 S15]

This presents a regulatory puzzle, amplifying concerns over CGM distribution controls and the latent risks for PNLD utilising devices outside of intended purposes. While the EU MDR 2017/745 outlines the regulations for distributors and post-market observation, it remains silent on the consequences of unsanctioned medical device distribution.[40] This creates uncertainty over matters of accountability, liability, and patient safety. Importantly, the term 'off-label use' remains vague within EU MDR 2017/745, given its limited emphasis on manufacturers identifying, but not clearly defining such use.[S16] In fact, the ramifications of this regulatory insufficiency have already adversely impacted the diabetes care market. Following a surge in off-label prescribing of glucagon-like peptide-1 receptor agonists (GLP-1RAs), a National Patient Safety Alert has been declared by the Department of Health and Social Care (DHSC) and the NHS.[S17] The current severe shortages of GLP-1RAs are illustrative of the inherent flaws in the regulation, underscoring the pressing need for forward-thinking measures to prevent such crises. Given CGMs are certified for T1DM and insulin-dependent T2DM contexts only, while med-tech companies have retailed CGMs for 'off-label use' since 2017, reveals a clear regulatory oversight and is a cause for concern.

The Medicines and Healthcare products Regulatory Agency (MHRA) undertook a public consultation in 2022 to rearticulate the 'intended purpose' for medical devices, CGMs included.[S18] Considering the escalating adoption of CGMs outside their prescribed use, an urgent requirement has arisen to unambiguously term 'off-label' and provide exhaustive guidelines on its implications. Such mandates

should help encapsulate precision benchmarks, manufacturer duties vis-à-vis device constraints, and responsibility for untoward events stemming from 'off-label use'. Echoing this sentiment, the International Federation of Clinical Chemistry and Laboratory Medicine has advocated for stringent study protocols and performance criteria, as evidenced in a detailed scoping review.[S18]

Despite CGMs not being officially endorsed for abnormal glucose detection or shaping behavioural changes in PNLD, marketing narratives suggesting the opposite abound increasing off-label demand for these devices.[9] [S15] Such claims risk being labelled 'misleading' in the face of significant evidential gaps as outlined in this review. Addressing regulatory and research gaps remains imperative to prevent the continued misinformation risk to PNLD.

Particularly concerning is the lack of studies inquiring into the unanticipated psychological impact of commercial CGM use.[3] Excessive glucose monitoring has the risk of unintentionally creating maladaptive dietary changes in PNLD (e.g., exclusion of health food to avoid glucose excursion; whole grain bread), especially if inexperienced users struggle to understand what the glucose excursions actually mean. Similarly, calorie and fitness monitoring has been linked to the development of anxiety, compulsive behaviours, or disordered eating patterns,[S19] though the consequences of CGM data on exacerbating these issues has not been extensively explored. Studies measuring the effect of CGMs on the quality of life, disordered eating and other potential non-clinical factors such as would help to provide guidance for PNLD should they want to use these devices.

4 | CONCLUSION

CGMs, in their present form, appear not appropriate to optimise metabolic health or prevent metabolic conditions in PNLD. The available studies lack comprehensive assessments of long-term benefits and fail to prove the clinical significance of the interventions on health outcomes at present. Aspects including device accuracy, data analysis metrics, user acceptability, and potential adverse effects of CGMs in PNLD, remain under-researched. This review is one of the first to highlight the evidential gaps in CGM in PNLD for what appears to be a rapidly expanding off-label use of a medical device and is the first to our knowledge to suggest that the current regulatory frameworks are inadequate to protect wellbeing and safety of PNLD. There exists an urgent need for regulatory bodies to strengthen post-market clinical follow-up oversight for medical devices, including CGMs, to prevent off-label use further widening health inequalities. The ongoing evolution of UK regulatory frameworks presents a timely opportunity to address these gaps, and further investigation into CGMs' role in PNLD in the format of more robust approaches including meta-analyses is highly advised.

AUTHOR CONTRIBUTIONS

AB and ZO were responsible for the study conceptualisation. ZO was responsible for original draft. AB and ZO were responsible for the reviewing and editing. AB, ZO and JSP contributed to the final reviewing and editing. All authors agreed the final version.

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CONFLICT OF INTEREST STATEMENT

AB reports honoraria from Novo Nordisk, Office of Health Improvement and Disparity, Johnson and Johnson and Obesity UK outside the submitted work and is on the Medical Advisory Board and shareholder of Reset Health Clinics Ltd. JSP is on the Advisory Board for ROCHE Diabetes and has received speaker payments from Dexcom. ZO reports no conflicts of interest.

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REFERENCES

1. Galicia-Garcia U, Benito-Vicente A, Jebari S, et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci*. 2020;21(17):6275. doi:10.3390/ijms21176275
2. McKinsey and Company. Feeling good: the future of the $1.5 trillion wellness market. 2021. Accessed March 25, 2024. https://www.mckinsey.com/industries/consumer-packaged-goods/our-insights/feeling-good-the-future-of-the-1-5-trillion-wellness-market
3. Guess N. The growing use of continuous glucose monitors in people without diabetes: an evidence-free zone. *Pract Diab*. 2023;40(5):19. doi:10.1002/pdi.2475
4. Kumar Das S, Nayak KK, Krishnaswamy PR, Kumar V, Bhat N. Review- electrochemistry and other emerging Technologies for Continuous Glucose Monitoring Devices. *ECS Sens Plus*. 2022;1(3):031601. doi:10.1149/2754-2726/ac7abb
5. Battelino T, Danne T, Bergenstal M, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care*. 2019;42(8):1593-1603. doi:10.2337/dci19-0028
6. Penn L, Rodrigues A, Haste A, et al. NHS diabetes prevention Programme in England: formative evaluation of the programme

in early phase implementation. *BMJ Open*. 2018;8:e019467. doi:10.1136/bmjopen-2017-019467
7. Acciaroli G, Sparacino G, Hakaste L, et al. Diabetes and prediabetes classification using glycemic variability indices from continuous glucose monitoring data. *J Diabetes Sci Technol*. 2017;12(1):105-113. doi:10.1177/1932296817710478
8. Barua S, Sabharwal A, Glantz N, et al. Dysglycemia in adults at risk for or living with non-insulin treated type 2 diabetes: insights from continuous glucose monitoring. *ECLinicalMedicine*. 2021;35:100853. doi:10.1016/j.eclinm.2021.100853
9. The Levels Team. What is glycemic variability and why does it matter. 2024. Accessed March 25, 2024. https://www.levelshealth.com/blog/what-is-glycemic-variability-and-why-does-it-matter
10. Lind M, Tuomilehto J, Uusitupa M. The association between HbA1c, fasting glucose, 1-hour glucose and 2-hour glucose during an Oral glucose tolerance test and cardiovascular disease in individuals with elevated risk for diabetes. *PLoS One*. 2014;9(10):e109506. doi:10.1371/journal.pone.0109506
11. Dehghani Zahedani A, Shariat Torbaghan S, Rahili S, et al. Improvement in glucose regulation using a digital tracker and continuous glucose monitoring in healthy adults and those with type 2 diabetes. *Diabetes Ther*. 2021;12(7):1871-1886. doi:10.1007/s13300-021-01081-3
12. Zeevi D, Korem T, Zmora N, et al. Personalized nutrition by prediction of glycemic responses. *Cell*. 2015;163(5):1079-1094. doi:10.1016/j.cell.2015.11.001
13. Berry SE, Valdes AM, Drew DA, et al. Human postprandial responses to food and potential for precision nutrition. *Nat Med*. 2020;26(6):964-973. doi:10.1038/s41591-020-0934-0
14. Liao Y, Schembre S. Acceptability of continuous glucose monitoring in free-living healthy individuals: implications for the use of wearable biosensors in diet and physical activity research. *JMIR Mhealth Uhealth*. 2018;6(10):e11181. doi:10.2196/11181
15. NHS King's College Hospital, NHS Foundation Trust. Flash and real time continuous glucose monitoring: NICE diabetes guidance update. 2022. Accessed September 22, 2023. https://www.kch.nhs.uk/wp-content/uploads/2023/01/pl-1038.1-flash-and-real-time-continuous-glucose-monitoring-nice-diabetes-guidance-update.pdf
16. Pemberton JS, Wilmot EG, Barnard-Kelly K, et al. CGM accuracy: contrasting CE marking with the governmental controls of the USA (FDA) and Australia (TGA): a narrative review. *Diabetes Obes Metab*. 2023;25(4):916-939. doi:10.1111/dom.14962
17. Stern C, Jordan Z, Mcarthur A. Developing the review question and inclusion criteria. *AJN*. 2014;114(4):53-56. doi:10.1097/01.NAJ.0000445689.67800.86
18. Hall H, Perelman D, Breschi A. Glucotypes reveal new patterns of glucose dysregulation. *PLoS Biol*. 2018;16(7):e2005143. doi:10.1371/journal.pbio
19. Olawsky E, Zhang Y, Eberly LE, Helgeson ES, Chow LS. A new analysis tool for continuous glucose monitor data. *J Diabetes Sci Technol*. 2022;16(6):1496-1504. doi:10.1177/19322968211028909
20. Kovatchev BP. Metrics for glycaemic control — from HbA1c to continuous glucose monitoring. *Nat Rev Endocrinol*. 2017;13(7):425-436. doi:10.1038/nrendo.2017.3
21. Keshet A, Shilo S, Godneva A, et al. CGMap: characterizing continuous glucose monitor data in thousands of non-diabetic individuals. *Cell Metab*. 2023;35(5):758-769.e3. doi:10.1016/j.cmet.2023.04.002
22. Klonoff DC, Kerr D. Overcoming barriers to adoption of digital health tools for diabetes. *JDST*. 2017;12(1):3-6. doi:10.1177/1932296817732459
23. LibreLinkUp. Manage diabetes together with LibreLinkUp. Accessed March 25, 2024. https://www.librelinkup.com/
24. Sofizadeh S, Pehrsson A, Ólafsdóttir AF, Lind M. Evaluation of reference metrics for continuous glucose monitoring in persons without diabetes and prediabetes. *J Diabetes Sci Technol*. 2020;16(2):373-382. doi:10.1177/1932296820965599
25. Hjort A, Iggman D, Rosqvist F. Glycemic variability assessed using continuous glucose monitoring in individuals without diabetes and associations with cardiometabolic risk markers: a systematic review and meta-analysis. *Clin Nutr*. 2024;43(4):915-925. doi:10.1016/j.clnu.2024.02.014
26. Howard R, Gue J, Hall KD. Imprecision nutrition? Different simultaneous continuous glucose monitors provide discordant meal rankings for incremental postprandial glucose in subjects without diabetes. *Am J Clin Nutr*. 2023;112(4):1114-1119. doi:10.1093/ajcn/nqaa198
27. Röhling M, Martin T, Wonnemann M, et al. Determination of postprandial glycemic responses by continuous glucose monitoring in a real-world setting. *Nutrients*. 2019;11(10):2305. doi:10.3390/nu11102305
28. Zhang X, Sun F, Wongpipit W, Huang WYJ, Wong SHS. Accuracy of flash glucose monitoring during postprandial rest and different walking conditions in overweight or obese young adults. *Front Physiol*. 2021;12:732751. doi:10.3389/fphys.2021.732751
29. Basu A, Slama MQ, Nicholson WT, et al. Continuous glucose monitor interference with commonly prescribed medications: a pilot study. *J Diabetes Sci Technol*. 2017;11(5):936-941. doi:10.1177/1932296817697329
30. Phillips PJ. Oral glucose tolerance testing. *Aust Fam Physician*. 2012;41(6):391-393.
31. CLSI, ed. Performance metrics for continuous interstitial glucose monitoring. *CLSI guideline POCT05*. 2nd ed. Clinical and Laboratory Standards Institute; 2020. Accessed September 23, 2023. https://clsi.org/media/tqkj5mmn/poct05ed2_sample.pdf
32. Sekido K, Sekido T, Kaneko A, et al. Careful readings for a flash glucose monitoring system in nondiabetic Japanese subjects: individual differences and discrepancy in glucose concentration after glucose loading [rapid communication]. *Endocr J*. 2017;64(8):827-832. doi:10.1507/endocrj.ej17-0193
33. Wong THT, Wan JMF, Louie JCY. Flash glucose monitoring can accurately reflect postprandial glucose changes in healthy adults in nutrition studies. *Am J Clin Nutr*. 2020;40(1):1-7. doi:10.1080/07315724.2020.1734990
34. Heinemann L, Schoemaker M, Schmelzeisen-Redecker G, et al. Benefits and limitations of MARD as a performance parameter for continuous glucose monitoring in the interstitial space. *J Diabetes Sci Technol*. 2020;14(1):135-150. doi:10.1177/1932296819855670
35. Freckmann G, Pleus S, Grady M, Setford S, Levy B. Measures of accuracy for continuous glucose monitoring and blood glucose monitoring devices. *J Diabetes Sci Technol*. 2019;13(3):575-583. doi:10.1177/1932296818812062
36. Food and Drug Administration. CFR – Code of Federal Regulations Title 21. 2022. Accessed September 23, 2023.

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=862.1355
37. Clavel P, Tiollier E, Leduc C, Fabre M, Lacome M, Buchheit M. Concurrent validity of a continuous glucose-monitoring system at rest and during and following a high-intensity interval training session. *Int J Sports Physiol Perform*. 2022;17(4):627-633. doi:10.1123/ijspp.2021-0222
38. Matabuena M, Pazos-Couselo M, Alonso-Sampedro M, Fernández-Merino C, González-Quintela A, Gude F. Reproducibility of continuous glucose monitoring results under real-life conditions in an adult population: a functional data analysis. *Sci Rep*. 2023;13(1):13987. doi:10.1038/s41598-023-40949-1
39. Mian Z, Hermayer KL, Jenkins A. Continuous glucose monitoring: review of an innovation in diabetes management. *Am J Med Sci*. 2019;358(5):332-339. doi:10.1016/j.amjms.2019.07.003
40. Official Journal of the European Union. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC 2017. Accessed September 24, 2023. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32017R0745&from=EN
41. Ehrhardt N, Al ZE. Behavior modification in prediabetes and diabetes: potential use of real-time continuous glucose monitoring. *J Diabetes Sci Technol*. 2019;13(2):271-275. doi:10.1177/1932296818790994
42. de Hoogh IM, Pasman WJ, Boorsma A, van Ommen B, Wopereis S. Effects of a 13-week personalized lifestyle intervention based on the diabetes subtype for people with newly diagnosed type 2 diabetes. *Biomedicine*. 2022;10(3):643. doi:10.3390/biomedicines10030643
43. Blaak EE, Antoine JM, Benton D, et al. Impact of postprandial glycaemia on health and prevention of disease. *Obes Rev*. 2012;13(10):923-984. doi:10.1111/j.1467-789x.2012.01011.x
44. Berciano S, Figueiredo J, Brisbois TD, et al. Precision nutrition: maintaining scientific integrity while realizing market potential. *Front Nutr*. 2022;9:979665. doi:10.3389/fnut.2022.979665
45. Mendes-Soares H, Raveh-Sadka T, Azulay S, et al. Assessment of a personalized approach to predicting postprandial glycemic responses to food among individuals without diabetes. *JAMA Netw Open*. 2019;2(2):e188102. doi:10.1001/jamanetworkopen.2018.8102
46. Bermingham KM, Linenberg I, Polidori L, et al. Effects of a personalized nutrition program on cardiometabolic health: a randomized controlled trial. *Nat Med*. 2024. doi:10.1038/s41591-024-02951-6
47. Jospe MR, de Bruin WE, Haszard JJ, Mann JI, Brunton M, Taylor RW. Teaching people to eat according to appetite – does the method of glucose measurement matter? *Appetite*. 2020;151:104691. doi:10.1016/j.appet.2020.104691
48. Ravelli MN, Schoeller DA. Traditional self-reported dietary instruments are prone to inaccuracies and new approaches are needed. *Front Nutr*. 2020;7(90):1-6. doi:10.3389/fnut.2020.00090
49. Zoe Global Limited. Whitepaper: The PREDICT program 2023. Accessed September 24, 2023. https://zoe.com/whitepapers/the-predict-program
50. USDA. Dietary Guidelines for Americans 2020–2025. 2020. Accessed May 12, 2024. https://www.dietaryguidelines.gov/sites/default/files/2020-12/Dietary_Guidelines_for_Americans_2020-2025.pdf

SUPPORTING INFORMATION

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