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Resistance to data loss from the Freestyle Libre: Impact on glucose variability indices and recommendations for data analysis

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Abbreviations: (APE) absolute percent error, (CV) coefficient of variation, (CONGA) continuous overall net glycaemic action, (ICC) intraclass correlation coefficients, (MAGE) mean amplitude of glycaemic excursions, (MAPE) mean absolute percent error, (MAR) missing at random, (MCAR) missing completely at random, (MNAR) missing not at random,
(NHS) National Health Service, (SIGNAL) Sensing Interstitial Glucose to Nudge Active Lifestyles

Abstract

Like many wearables, flash glucose monitoring relies on user compliance and is subject to missing data. As recent research is beginning to utilise glucose technologies as behaviour change tools, it is important to understand whether missing data is tolerable. Complete Freestyle Libre data files were amputed to remove 1-6 hours of data both at random and over mealtimes (breakfast, lunch and dinner). Absolute percent errors (MAPE) and intraclass correlation coefficients (ICC) were calculated to evaluate agreement and reliability. Thirty-two (91%) participants provided at least one complete day (24-hours) of data (age: 44.8±8.6 years, female: 18 (56%); mean fasting glucose: 5.0±0.6 mmol/L). Mean and CONGA (60 minutes) were robust to data loss (MAPE ≤3%). Larger errors were calculated for standard deviation, coefficient of variation (CV) and MAGE at increasing missingness (MAPE 2-10%, 2-9% and 4-18%, respectively). ICC decreased as missing data increased, with most indicating excellent reliability (>0.9) apart from certain MAGE ICC, which indicated good reliability (0.84-0.9). Researchers and clinicians should be aware of the potential for larger errors when reporting standard deviation, CV and MAGE at higher rates of data loss in nondiabetic populations. But where mean and CONGA are of interest, data loss is less of a concern.

Abstract wordcount: 200 words

Keywords: data loss, flash glucose monitoring, glycaemic variability, mHealth, self-monitoring, Freestyle Libre

Novelty:

- As research now utilises flash glucose monitoring as behavioural change tools in nondiabetic populations, it is important to consider the influence of missing data.
- Glycaemic variability indices of mean and CONGA are robust to data loss, but MAGE and standard deviation are influenced at higher rates of missingness.

Introduction

Glucose monitoring is an essential component in the self-management of diabetes (Chico et al. 2020), with a wide range of devices available that provide real-time information on glucose concentrations and rates of change (Rodbard 2016). Most glucose monitoring devices are minimally-invasive and utilise a subcutaneous sensor to measure interstitial fluid (Vashist 2013), and transmit data to a reader or receiver device. As glucose sensing technologies have evolved, flash glucose monitoring has recently become available (Heinemann and Freckmann 2015). In contrast to continuous monitors, flash glucose devices require the user to retrieve data by hovering a reader device (smartphone or handheld reader) over the sensor at regular intervals (Rodbard 2017). Despite this subtle difference, the process of data transmission and retrieval is active (rather than automatic); demanding regular user interaction to avoid data loss, creating challenges that were previously non-existent.

The Freestyle Libre (Abbott, Illinois, USA) is a flash glucose device which provides advantages over previous continuous models by being able to sample glucose concentrations for up to 14 days without the need for calibrations. The device is widely discussed in the literature (n=161 studies from 2015-2020, PubMed) and is now being funded via National Health Service (NHS) England for individuals with Type 1 diabetes (NHS England 2019). The use of these technologies has been associated with improved glycaemic outcomes in people living with diabetes, due to ability to scan the devices frequently (Rodbard 2017; Dunn et al. 2018; Jangam et al. 2019). There is also growing literature on glucose monitoring technologies as a physical activity behaviour change tool in individuals without a current diagnosis of diabetes (Bailey et al. 2016; Ehrhardt and Al Zaghal 2019; Whelan et al. 2019). As use is expanding from medical care to prevention, users are not always reliant on these devices for their health and may feel less inclined to sustain strict scanning regimes. With ever-increasing sensor lifespans, it is possible to observe reductions in user engagement with the sensors (Whelan et al. 2019). The device requires users to interact with the sensor every eight hours to prevent data loss. Therefore, it is increasingly important for researchers and practitioners to ascertain how much error missing data introduces and whether this error is tolerable. This is especially important in individuals not currently diagnosed with diabetes, as the population is not commonly associated with glucose technologies but are beginning to be exposed to them as behaviour change tools.

Previous research investigating up to 80% of missing glucose data in a sample of adults living with type 1 diabetes reported glucose measurements to be robust to data loss, with calculated mean absolute percentages errors (MAPE) remaining below 5% (Kucharski et al. 2018). This analysis was conducted on data collected using the Medtronic Enlite Sensor which passively transmits data automatically. However, quantifying the effect that missing data have on common glycaemic indices has not been conducted for flash glucose monitoring, which may have larger amount of missing data due to the active requirement for data acquisition. Therefore, the aim of this study was to investigate the influence of missing data on common glucose variability indices (mean, standard deviation, coefficient of variation (CV), continuous overall net glycaemic action (CONGA) and mean amplitude of glycaemic excursions (MAGE)) from data collected via flash glucose monitoring.

Materials and methods

Data source

Data were collected as part of the Sensing Interstitial Glucose to Nudge Active Lifestyles (SIGNAL) programme of research in 2016 that aimed to investigate the association between physical activity behaviours and glycaemic variability. This project involved 35 participants, who all provided written informed consent, and the study was approved by the Loughborough University Human Participants Ethical Sub-Committee (R15-P142).

The Freestyle Libre is a minimally-invasive sensor that was inserted into the interstitial fluid of the upper arm and a handheld reader was provided to collect the data. Due to a data storage restriction, participants were asked to scan once every 8 hours otherwise earlier data points would be overwritten sequentially. For example, if the wearer last scanned at 9am and did not scan again until 6pm, data between 9am-10am would be lost.

Height and weight were measured once using a stadiometer (SECA 213, SECA, Germany) and an electronic scale (Tanita MC780MA, Tanita, The Netherlands). Additionally, a fasting capillary blood test (> 8 hours) was undertaken to determine diabetes status via a point-of-care capillary blood device (Lipid Profile•Glucose Cartridge, Cholestech LDX® Analyzer, Alere, Massachusetts, USA). Individuals were deemed at high risk of diabetes if their fasting plasma glucose level was between 5.5 and 6.9 mmol/L (NICE 2017).

Data processing decisions

Files were downloaded into a .txt file format, screened and evaluated to determine the number of valid data points within a file. The theoretical maximum number of datapoints was 96 per day (four per hour per 24 hours). Due to temporal drift within the data, where data were collected at roughly 13 to 17 (rather than 15) minute intervals, this daily total number of datapoints could instead be 95 or 97. To model missing data, complete datasets, defined as ≥95 datapoints, were identified. Other days containing 93 or 94 data points, which were defined as near complete, underwent linear interpolation before being pooled. These days formed the reference dataset to which all subsequent analyses were compared against. Any days which did not meet these criteria were removed from the analyses.

Missing data are usually described as being either: (i) missing completely at random (MCAR) when the missingness is not related to the data being observed i.e. errors are unrelated to other variables and is completely random, (ii) missing at random (MAR) when there is some relationship between the missingness and the data being observed i.e. missingness depends on the variables collected, or (iii) missing not at random (MNAR) when errors depend on variables with missing data or variables that have not been collected (Rubin 1976; Goretzko et al. 2019). Data were modelled as MCAR to account for the variety of possible explanations. Missing data could have been due to the user forgetting to scan, misplacing the reader, being too busy to scan at the expected frequency or by sleeping >8 hours. As a result of how the Freestyle Libre stores and overwrites data, missing data occurs in blocks of consecutive values with the duration of missingness directly related to the delay in scanning after the eight-hour threshold. The missing data was amputed (removed) within the datafile in blocks of time to reflect real life Freestyle Libre data loss. Ninety-eight percent of available days were classed as having no more than six hours of missing data, indicating that participants were relatively compliant with scanning the sensor. To contextualise this number, to gain up to 6 hours of missing data, the wearer would not have scanned for 14 consecutive hours. Therefore, it was decided that this study would model up to 6 hours of missing data in 1-hour blocks of time.

To model MCAR data points, complete data files were assigned a number using a random number function within Excel i.e. one number per row (Microsoft, Redmond, USA). The random number with the highest value for each hour condition of missing data acted as the starting point for the missing data removal and assessment. We calculated the estimates by removing (deleting) between 1 and 6 hours of missing data. This involved removing 4 data points for each hour of missing data, until 24 data points for 6 hours of missing data. To model postprandial missing data or MNAR, mealtime periods were defined as 06:00-10:00 for breakfast, 12:00-15:00 for lunch and 18:00-21:00 for dinner (Leech et al. 2015). To determine the mealtime peak between those times, the highest average glucose value was determined and then 60 minutes was subtracted to identify the time of consumption (ADA 2001). Missing data points for these mealtime periods were initiated from 07:15 (datapoint 30) for breakfast, 13:15 (datapoint 58) for lunch and 18:15 (datapoint 74) for dinner, across all files. Blocks of missing data lasting between one and six hours were amputed starting from the second datapoint of the hour. Missing data points were represented as blank cells.

Glucose variability measures

The following indices were chosen for this study to reflect the most easily understood and commonly used to represent glycaemic variability. Mean daily glucose as a measure of glucose exposure was calculated as the average of all datapoints for a given data file, which has been reported as a metric which both patients and clinicians can understand (Bergenstal et al. 2013), and characterises daily variations in glucose concentrations. Standard deviation of daily glucose is the variation of glucose datapoints from the average daily glucose (Hill et al. 2011), and CV is the standard deviation adjusted on the 24 hour mean glucose and is calculated by (SD / mean) x 100 (Monnier et al. 2018a, 2018b). Both standard deviation and CV are considered one of the most popular and appropriate assessment metrics for within day glucose variability (Monnier et al. 2018a; Rodbard 2018). Additionally, CONGA is the standard deviation of differences between observations separated by a period of 1-4 hours (Rodbard 2009). For this analysis, the difference in time was set at 60 minutes and a higher CONGA value signals a greater glycaemic variability (McDonnell et al. 2005). Finally, MAGE is the mean amplitude of glucose excursions that occur above one standard deviation, which reflects postprandial excursions (Service et al. 1970). MAGE was calculated on the continuous data using a fuzzy logic algorithm available within the processing software (Hill 2010).

Data analyses

Data were downloaded using Freestyle Libre software (Abbott, Illinois, USA) and then cleaned and structured in Excel (Microsoft, Washington, USA). Following re-structuring, data were then processed using the EasyGV software (V9.0, University of Oxford, Oxford, UK; Hill 2010). Mean absolute percent errors (APE: Absolute(((Missing Data Point – Complete Data Point) / Missing Data Point) × 100) were calculated using glucose variability estimates of (i) the complete datasets (Complete Data Point) and (ii) for each of the six missing data conditions (Missing Data Point). Intraclass correlation coefficients (ICC) were also calculated to determine the consistency between the complete and missing datasets using a Two-Way mixed model with absolute agreement. The following ICC thresholds were used: poor reliability (<0.5), moderate reliability (0.5-0.75), good reliability (0.75-0.9) and excellent reliability (>0.9) (Koo and Li 2016). Mean absolute percent errors and ICC analyses were calculated at the day level and then averaged across all available datapoints available. Statistical analyses were performed using SPSS v24 (IBM, New York, USA).

Results

Data processing

Thirty-two participants out of 35 (91%) provided at least one complete day of data (≥95 datapoints). Due to the timing of sensor deployment, the first day and last days were incomplete, resulting in a potential 416 recorded days (13 days x 32 participants). From these, 288 complete data files (69%) were available for amputation, with a further 88 files (21%) containing between 1-3 hours and 40 datafiles between 4-24 hours of missing data, respectively. Each participant provided on average 9 full days, with contributions ranging from 2-13 days. Datafiles could have been missing for several reasons including sensor malfunctions / errors (including premature removal due to adhesive issues; n=21, 16%) or non-compliance (e.g. failing to scan within the required 8 hour period; n=107, 84%). From the available dataset, one data file proved incompatible with EasyGV and was removed, leaving 287-day comparisons.

Of the 32 participants, 26 were not considered high risk of type-2 diabetes from their fasting capillary blood samples, and six were deemed at high risk (5.5-6.9 mmol/L (NICE 2017)). Participant characteristics are displayed within Table 1.

Absolute percent errors

The absolute (mmol/L) difference and MAPE were calculated for both MCAR and MNAR data removal conditions for all glucose variability indices (Table 2). Lower errors were calculated for MCAR mean and CONGA calculations, and errors increased for all indices apart from MAGE as the degree of missing data also increased, albeit not entirely linearly.

A greater level of missing data increased mean and CONGA absolute values compared to the reference average values for the breakfast condition, whilst values decreased for both lunch and dinner with increasing missingness. Standard deviation, CV and MAGE values decreased for all mealtime conditions compared to their reference categories. Absolute magnitudes of change for standard deviation, CV and MAGE were lower across all conditions. MCAR absolute values were also varied, reflecting that missing data were randomly amputed (and were not anchored to specific mealtimes).

Figure 1 represents a visual representation of MAPE values (%) per glycaemic variability measures. The most stable glucose variability indices were CONGA and mean values with MAPE values consistently ≤3% for up to 6 hours of missing data. Missing data influenced standard deviation, CV and MAGE the greatest; however missing data introduced the largest errors for MAGE, as percentages reaching 12-18% error over the three mealtimes. However, MAGE MAPE values were slightly lower for increasing missingness for breakfast compared with lunch and dinner.

A sensitivity analysis was conducted to ascertain the difference in MAPE values after removing those participants who were deemed at higher risk of developing diabetes (n=6), leaving 228 days (79%) in the analyses. Mean and CONGA MAPE values were calculated at similar error magnitudes and whilst standard deviation, CV and MAGE absolute values decreased, MAPE values generally increased by ≤1%.

Intraclass correlations

Table 3 outlines the ICC that compared missing data values across all missing data conditions and glycaemic variables. ICC generally decreased over the duration of missing data, with most indicating excellent consistency (>0.9) apart from several MAGE ICC which indicated good consistency (0.75-0.9 (Koo and Li 2016)).

Discussion

Main findings

Findings from the present study offer unique insight into the impact of missing data on the representativeness of glucose indices provided by flash glucose monitoring. Our analysis shows that missing data has little impact on mean glucose and CONGA, but standard deviation, CV and MAGE can exhibit larger errors at increasing durations of missingness. The fact that degree of missingness does not influence average values for both MCAR and across mealtimes is an important finding for studies using the Freestyle Libre device within behavioural interventions, or those with average glucose as the primary outcome. End-users of the technology can therefore be somewhat confident that glycaemic variables are relatively stable at higher levels of missingness, and that enforcing participants to scan their sensors every 8 hours at the expense of participant burden is not necessary.

Our findings are comparable to another study that collected data using an Enlite Sensor (Medtronic, Dublin, USA) that found glucose variability measurements were robust to data loss in Type 1 diabetics (Kucharski et al. 2018). Absolute errors were similar, with MAPE values consistently below 5% and MAGE being the most “vulnerable to missing data” (Kucharski et al. 2018). Considering those devices had a greater data resolution of data transfer (5 minutes), it is encouraging to note that mean errors were comparable. Particularly given that flash glucose monitoring may obtain different estimates of important glycaemic variability compared to more traditional continuous monitoring devices (Michalak et al. 2019).

Comparison of missingness was derived to model the influence of MCAR and MNAR data whilst retaining contextual awareness of how the devices collected the data. The results of this study suggest that the MCAR analyses represent the interactions of the missing data across the defined mealtime periods. Reconfirming that mealtimes are an important source of error due to potentially large diet related deviations in glucose levels, it is again encouraging to note that mean and CONGA indices are relatively unaffected by data loss. Given the missing data structures of MCAR and MNAR, the results are generally consistent with other investigations regarding missing data mechanisms (Schouten and Vink 2018). Indeed, knowing the body’s ability to maintain homeostatic balance by returning postprandial glucose concentrations to normal within 2-3 hours (ADA 2001), it is logical to

conclude that for a large proportion of time, glucose levels are stable, and the mean will smooth over any short-term peaks in the data. Measures of deviations such as standard deviation, CV and MAGE will therefore be impacted, which has been demonstrated by higher MAPE values. Nevertheless, the lower magnitudes of values of both standard deviation and MAGE suggest that relatively small changes will exhibit larger MAPE values.

We have shown that whilst MAPE values remain below 3% for mean and CONGA indices, calculated errors for standard deviation, CV and MAGE range between 2-18% for up to 6 hours of data loss. There are a lack of clinically meaningful thresholds related to changes in short-term changes in glycaemic variability compared to more established chronic exposure metrics such as HbA1c (Wilmot et al. 2019), therefore making it difficult to define an acceptable level of introduced error. However, a minimum of 70% of data over 14 consecutive days has been proposed to optimise clinical decision making (Danne et al. 2017), equating to 7 hours of data loss per day. Whilst this criterion relates to an overview of glycaemic variability for the individual and not a valid day criterion, only 2% (8 days) of data within our sample were deemed to have >6 hours of missing data. Considering the low MAPE % and the excellent ICC values (Koo and Li 2016), for mean and CONGA across all missing data conditions indicates that up to 6 hours is tolerable. On comparison, the largest MAPE values for SD, CV, and MAGE range between 9-18% across all conditions. Yet bearing in mind the absolute differences of 0.029, 0.25% and 0.05 mmol/L for the largest errors, it could be considered that all glycaemic variability indices can be utilised with up to 6 hours of missing data. However, users should be aware of the potential larger errors above 2-3 hours of missing data for short-term glycaemic variability indices of SD, CV and MAGE.

Glycaemic variability can be considered the evaluation of the amplitude, frequency and duration of fluctuations in glucose data (Danne et al. 2017), that has been associated with a range of diabetes complications (Peyser et al. 2018). Deviating from equilibrium into both hypoglycaemic and hyperglycaemic ranges carry risks that increase with the amplitude of the change (Danne et al. 2017), but the detrimental effect of short-term fluctuations in glucose exposure have been less understood, compared with exposure of a chronic nature (Ceriello et al. 2019). Yet, the use of continuous monitoring devices is beginning to be extended beyond diabetes management to be used as a

preventative behavioural change tool (Whelan et al. 2019). The relatively low cost and lack of calibration of the devices has meant a wider possibility of the use of such devices in individuals with and without diabetes. As such, missing data may only be of concern for populations without diabetes as they may be less invested to interact with the devices (Whelan et al. 2019), and do not rely on them for clinical management. Yet, the growing literature on the associations between movement behaviours and short-term glycaemic variability indices (Kingsnorth et al. 2018), support the use of short-term, inter-day indices and the quantification of the influence of missing data.

The complete datasets within this present study were artificially amputed both randomly and over mealtimes by removing data between specific time points. Whilst it can be concluded that certain glycaemic variability measures will not be influenced by data structure and missing timestamps within analyses files, it is important to note that for measures such as CONGA, which does have a temporal component, and for MAGE which is determined by unique deviations, file structure should be prioritised. The Freestyle Libre data export does not impute data rows if data is missing and if files are not re-structured to represent complete data matrices, glucose variability metrics may not conform to the error rates reported within this study. Nevertheless, missing data are largely unique to flash glucose monitoring technologies and the intermittent nature of the device functionality.

Limitations

There are some limitations within the data and study design that need to be discussed. A large number of days were processed but the analyses did not constrain the contribution of certain participants in line of similar studies and certain influential cases (individuals) may influence the MAPE and ICC values calculated. The error and reliability estimates are also only applicable to the Freestyle Libre sensors as MAPE estimates could be altered using devices with a higher sampling frequency. The analyses do not also account for variations in eating behaviours (e.g. snacking) or physical activity that can cause short term changes in glucose concentrations. Finally, the blocks of time chosen to reflect mealtime periods may not reflect every possible meal schedule but captured the overall pattern of the participants within the present study. Additionally, the data were obtained from individuals without a diagnosis of diabetes and therefore the estimates may vary in populations with greater glucose excursions in their daily data, such as those with Type 2 Diabetes.

Conclusions

Missing data may largely be attributed to the flash glucose monitoring technology itself; yet, as represented by low MAPE and high ICC values, mean and CONGA measures of glycaemic variability collected via flash glucose monitoring are resistant to 6 hours or less of missing data (MCAR) in individuals without a diagnoses of diabetes. In contrast, standard deviation, CV and MAGE display larger errors, which increases in proportion to the duration of missingness. Researchers and clinicians should therefore be aware of the potential for larger errors when reporting standard deviation, CV and MAGE at higher rates of data loss, but where mean and CONGA are indices of interest, data loss is less of a concern.

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Tables

Table 1 – Participant characteristics of the sample included within the missing data analyses

Characteristics	Mean	SD
Age (years)	44.8	(1.5)
Sex (n)		
Male	14	
Female	18	
Body mass index (kg/m^2)	24.9	(0.7)
Fasting glucose (mmol/L)	5.0	(0.1)

Abbreviations: SD (standard deviation).

454 Table 2 – Mean absolute percent errors for all glycaemic variables for data missing at random and missing over key mealtimes.

	Mean		SD		CV		CONGA		MAGE		
	mmol/L	MAPE %	mmol/L	MAPE %	%	MAPE %	mmol/L	MAPE %	mmol/L	MAPE %	n
Complete data	5.06	-	0.873	-	17.20	-	4.47	-	2.40	-	287
MCAR											
1 hour	5.04	0.52	0.870	2.50	17.18	2.34	4.46	0.68	2.38	4.15	287
2 hours	5.05	0.80	0.876	3.31	17.29	3.08	4.47	0.95	2.37	9.35	287
3 hours	5.03	1.19	0.862	5.38	17.06	4.79	4.47	1.31	2.35	11.55	284
4 hours	5.16	2.15	0.877	4.51	16.89	5.12	4.52	1.59	2.41	7.68	287
5 hours	5.21	3.01	0.876	5.71	16.68	6.80	4.52	1.86	2.42	7.04	286
6 hours	4.97	2.31	0.844	10.30	16.92	9.02	4.43	1.86	2.33	18.20	275
MNAR - Breakfast											
1 hour	5.06	0.49	0.873	2.01	17.19	1.86	4.47	0.59	2.38	4.74	287
2 hours	5.06	0.82	0.871	3.31	17.16	3.07	4.47	0.79	2.37	7.08	286
3 hours	5.07	1.12	0.869	4.44	17.10	4.20	4.48	1.05	2.37	10.02	285
4 hours	5.08	1.44	0.868	5.65	17.03	5.30	4.49	1.33	2.36	11.41	285
5 hours	5.10	1.70	0.866	7.17	16.92	6.78	4.50	1.57	2.37	14.08	284
6 hours	5.12	1.96	0.868	8.10	16.90	7.74	4.51	1.80	2.36	15.13	283
MNAR - Lunch											
1 hour	5.04	0.63	0.861	2.74	17.03	2.45	4.47	0.64	2.32	8.90	286
2 hours	5.02	1.04	0.854	4.76	16.95	4.19	4.46	0.95	2.32	12.55	286
3 hours	5.01	1.33	0.851	6.07	16.93	5.40	4.45	1.15	2.32	14.30	285
4 hours	4.99	1.63	0.847	7.65	16.90	6.70	4.44	1.39	2.31	16.33	281
5 hours	4.98	1.95	0.846	9.02	16.92	7.84	4.44	1.63	2.35	16.27	279
6 hours	4.97	2.25	0.846	10.15	16.95	8.83	4.43	1.90	2.35	18.38	278
MNAR - Dinner											
1 hour	5.05	0.48	0.872	2.06	17.19	1.95	4.48	0.68	2.36	7.11	285
2 hours	5.04	0.87	0.866	3.92	17.11	3.57	4.48	0.98	2.36	9.13	284
3 hours	5.03	1.19	0.862	5.38	17.06	4.79	4.47	1.31	2.35	11.55	284
4 hours	5.02	1.49	0.858	6.48	17.02	5.75	4.47	1.53	2.34	13.69	283
5 hours	5.01	1.83	0.852	8.20	16.96	7.27	4.46	1.75	2.33	15.33	278
6 hours	4.99	2.19	0.848	9.48	16.95	8.39	4.45	2.10	2.29	17.48	279

Notes: n = number of MAGE comparisons as some did not compute during analyses. Abbreviations: SD (standard deviation); CV (coefficient of variation); CONGA (continuous onset of net glycaemic action); MAGE (mean amplitude of glycaemic excursions); MAPE (mean absolute percentage errors); MCAR (missing cases at random); MCNAR (missing cases not at random); SD is presented to 3 decimal places to account for smaller variations.

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Table 3 – Intraclass correlation coefficients for all glycaemic variables over 24 hours for data missing at random and missing over key mealtimes.

	Mean	SD	CV	CONGA	MAGE
MCAR					
1 hour	0.998	0.993	0.993	0.997	0.982
2 hours	0.996	0.991	0.989	0.994	0.943
3 hours	0.992	0.971	0.970	0.990	0.918
4 hours	0.978	0.984	0.974	0.986	0.955
5 hours	0.957	0.975	0.941	0.979	0.967
6 hours	0.975	0.922	0.919	0.981	0.844
MNAR - Breakfast					
1 hour	0.998	0.995	0.995	0.998	0.971
2 hours	0.995	0.985	0.987	0.996	0.951
3 hours	0.992	0.976	0.978	0.993	0.919
4 hours	0.987	0.965	0.965	0.989	0.899
5 hours	0.982	0.952	0.946	0.985	0.872
6 hours	0.977	0.943	0.934	0.980	0.858
MNAR - Lunch					
1 hour	0.997	0.989	0.989	0.997	0.923
2 hours	0.994	0.976	0.975	0.994	0.901
3 hours	0.991	0.964	0.961	0.992	0.881
4 hours	0.986	0.950	0.946	0.989	0.864
5 hours	0.981	0.936	0.933	0.985	0.868
6 hours	0.975	0.923	0.920	0.981	0.842
MNAR - Dinner					
1 hour	0.998	0.994	0.993	0.997	0.958
2 hours	0.995	0.981	0.980	0.995	0.937
3 hours	0.992	0.971	0.970	0.990	0.918
4 hours	0.988	0.960	0.960	0.987	0.901
5 hours	0.983	0.945	0.944	0.984	0.883
6 hours	0.977	0.931	0.930	0.978	0.866

Abbreviations: SD (standard deviation); CONGA (continuous onset of net glycaemic action); MAGE (mean amplitude of glycaemic excursions); CV (coefficient of variation); MCAR (missing cases at random); MCNAR (missing cases not at random).

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Figure captions

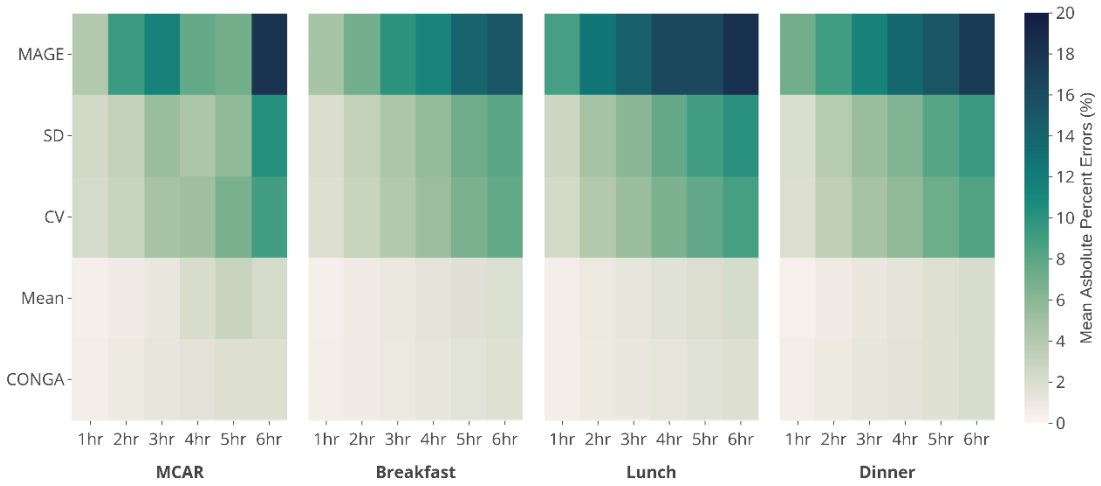

Figure 1 – Mean absolute percent errors (MAPEs) across all data removal conditions (missing at random and across breakfast, lunch and dinner meal conditions) and glycaemic variability measures (continuous overall net glycaemic action (CONGA), mean glucose, coefficient of variation (CV), standard deviation (SD) and mean amplitude of glycaemic excursions (MAGE). The grey colour represents lower MAPE, whilst green and blue indicates higher MAPE values. The glycaemic variability measures have been ordered according to MAPE values.

Supplementary material

Table S1 - sensitivity analyses for glycaemic variability indices without individuals categorised as 'high risk'.

	Mean		SD		CV		CONGA		MAGE		
	mmol/L	MAPE %	mmol/L	MAPE %	%	MAPE %	mmol/L	MAPE %	mmol/L	MAPE %	n
Complete data	4.86	-	0.819	-	16.85	-	4.30	-	2.23	-	228
MCAR											
1 hour	4.84	0.47	0.817	2.441	16.85	2.32	4.30	0.64	2.21	4.47	228
2 hours	4.85	0.74	0.825	3.295	16.97	3.02	4.31	0.92	2.20	9.06	228
3 hours	4.83	1.19	0.807	5.475	16.70	4.88	4.31	1.29	2.16	12.10	226
4 hours	4.96	2.19	0.820	4.471	16.49	5.25	4.37	1.64	2.26	7.73	228
5 hours	5.01	3.07	0.817	5.627	16.27	6.93	4.37	1.92	2.26	6.73	227
6 hours	4.76	2.37	0.786	11.074	16.49	9.56	4.26	1.84	2.16	18.86	216
MNAR - Breakfast											
1 hour	4.86	0.47	0.820	1.884	16.84	1.78	4.31	0.58	2.23	4.68	228
2 hours	4.87	0.76	0.820	3.052	16.83	2.88	4.32	0.76	2.23	6.94	227
3 hours	4.88	1.03	0.819	4.159	16.78	4.04	4.32	1.02	2.21	10.51	226
4 hours	4.89	1.33	0.819	5.314	16.73	5.10	4.33	1.27	2.21	11.90	226
5 hours	4.91	1.60	0.818	6.927	16.64	6.69	4.35	1.51	2.24	14.47	226
6 hours	4.93	1.89	0.821	7.889	16.61	7.66	4.36	1.74	2.24	15.59	225
MNAR - Lunch											
1 hour	4.84	0.62	0.807	2.899	16.67	2.58	4.31	0.61	2.16	9.15	227
2 hours	4.82	1.04	0.799	5.064	16.56	4.42	4.30	0.92	2.16	13.23	227
3 hours	4.80	1.36	0.794	6.614	16.52	5.83	4.29	1.13	2.16	15.22	226
4 hours	4.79	1.69	0.788	8.413	16.45	7.28	4.27	1.35	2.14	17.40	222
5 hours	4.77	2.02	0.787	9.769	16.48	8.43	4.26	1.59	2.17	17.33	220
6 hours	4.76	2.32	0.788	10.950	16.51	9.42	4.26	1.84	2.16	18.95	219
MNAR - Dinner											
1 hour	4.85	0.46	0.818	2.190	16.84	2.04	4.31	0.67	2.19	7.31	226
2 hours	4.84	0.86	0.812	4.065	16.76	3.66	4.31	0.97	2.18	9.41	226
3 hours	4.83	1.19	0.807	5.475	16.70	4.88	4.31	1.29	2.16	12.10	226
4 hours	4.81	1.51	0.801	6.683	16.64	5.93	4.30	1.51	2.15	14.37	226
5 hours	4.79	1.89	0.795	8.517	16.57	7.58	4.28	1.74	2.15	16.29	222
6 hours	4.77	2.29	0.791	9.895	16.57	8.73	4.27	2.07	2.12	18.42	221

Notes: 6 individuals were categorised as ‘high risk’ and were removed; 228 days (79%) remained within the above analysis); n = number of MAGE comparisons as some did not compute during analyses. Abbreviations: SD (standard deviation); CV (coefficient of variation); CONGA (continuous onset of net glycaemic action); MAGE (mean amplitude of glycaemic excursions); MAPE (mean absolute percentage errors); MCAR (missing cases at random); MCNAR (missing cases not at random); SD is presented to 3 decimal places to account for smaller variations.