

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

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

3
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22 **Abbreviations:** (APE) absolute percent error, (CV) coefficient of variation, (CONGA) continuous
23 overall net glycaemic action, (ICC) intraclass correlation coefficients, (MAGE) mean amplitude of
24 glycaemic excursions, (MAPE) mean absolute percent error, (MAR) missing at random, (MCAR)
25 missing completely at random, (MNAR) missing not at random,
26 (NHS) National Health Service, (SIGNAL) Sensing Interstitial Glucose to Nudge Active Lifestyles

27 **Abstract**

28 Like many wearables, flash glucose monitoring relies on user compliance and is subject to missing
29 data. As recent research is beginning to utilise glucose technologies as behaviour change tools, it is
30 important to understand whether missing data is tolerable. Complete Freestyle Libre data files were
31 amputated to remove 1-6 hours of data both at random and over mealtimes (breakfast, lunch and
32 dinner). Absolute percent errors (MAPE) and intraclass correlation coefficients (ICC) were calculated
33 to evaluate agreement and reliability. Thirty-two (91%) participants provided at least one complete
34 day (24-hours) of data (age: 44.8±8.6 years, female: 18 (56%); mean fasting glucose: 5.0±0.6
35 mmol/L). Mean and CONGA (60 minutes) were robust to data loss (MAPE ≤3%). Larger errors were
36 calculated for standard deviation, coefficient of variation (CV) and MAGE at increasing missingness
37 (MAPE 2-10%, 2-9% and 4-18%, respectively). ICC decreased as missing data increased, with most
38 indicating excellent reliability (>0.9) apart from certain MAGE ICC, which indicated good reliability
39 (0.84-0.9). Researchers and clinicians should be aware of the potential for larger errors when
40 reporting standard deviation, CV and MAGE at higher rates of data loss in nondiabetic populations.
41 But where mean and CONGA are of interest, data loss is less of a concern.

42

43 **Abstract wordcount:** 200 words

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

46 **Novelty:**

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

51 **Introduction**

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

62

63 The Freestyle Libre (Abbott, Illinois, USA) is a flash glucose device which provides advantages over
64 previous continuous models by being able to sample glucose concentrations for up to 14 days without
65 the need for calibrations. The device is widely discussed in the literature (n=161 studies from 2015-
66 2020, PubMed) and is now being funded via National Health Service (NHS) England for individuals
67 with Type 1 diabetes (NHS England 2019). The use of these technologies has been associated with
68 improved glycaemic outcomes in people living with diabetes, due to ability to scan the devices
69 frequently (Rodbard 2017; Dunn et al. 2018; Jangam et al. 2019). There is also growing literature on
70 glucose monitoring technologies as a physical activity behaviour change tool in individuals without a
71 current diagnosis of diabetes (Bailey et al. 2016; Ehrhardt and Al Zaghaf 2019; Whelan et al. 2019).
72 As use is expanding from medical care to prevention, users are not always reliant on these devices
73 for their health and may feel less inclined to sustain strict scanning regimens. With ever-increasing
74 sensor lifespans, it is possible to observe reductions in user engagement with the sensors (Whelan et
75 al. 2019). The device requires users to interact with the sensor every eight hours to prevent data loss.
76 Therefore, it is increasingly important for researchers and practitioners to ascertain how much error
77 missing data introduces and whether this error is tolerable. This is especially important in individuals
78 not currently diagnosed with diabetes, as the population is not commonly associated with glucose
79 technologies but are beginning to be exposed to them as behaviour change tools.

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

90 **Materials and methods**

91 ***Data source***

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

97

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

103

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

110

111 ***Data processing decisions***

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

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

136

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

150 ***Glucose variability measures***

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

166

167 ***Data analyses***

168 Data were downloaded using Freestyle Libre software (Abbott, Illinois, USA) and then cleaned and
169 structured in Excel (Microsoft, Washington, USA). Following re-structuring, data were then processed
170 using the EasyGV software (V9.0, University of Oxford, Oxford, UK; Hill 2010). Mean absolute percent
171 errors (APE: $\text{Absolute}(\frac{\text{Missing Data Point} - \text{Complete Data Point}}{\text{Missing Data Point}}) \times 100$) were
172 calculated using glucose variability estimates of (i) the complete datasets (Complete Data Point) and
173 (ii) for each of the six missing data conditions (Missing Data Point). Intraclass correlation coefficients
174 (ICC) were also calculated to determine the consistency between the complete and missing datasets
175 using a Two-Way mixed model with absolute agreement. The following ICC thresholds were used:
176 poor reliability (<0.5), moderate reliability (0.5-0.75), good reliability (0.75-0.9) and excellent reliability
177 (>0.9) (Koo and Li 2016). Mean absolute percent errors and ICC analyses were calculated at the day
178 level and then averaged across all available datapoints available. Statistical analyses were performed
179 using SPSS v24 (IBM, New York, USA).

180 **Results**

181 ***Data processing***

182 Thirty-two participants out of 35 (91%) provided at least one complete day of data (≥ 95 datapoints).
183 Due to the timing of sensor deployment, the first day and last days were incomplete, resulting in a
184 potential 416 recorded days (13 days x 32 participants). From these, 288 complete data files (69%)
185 were available for amputation, with a further 88 files (21%) containing between 1-3 hours and 40
186 datafiles between 4-24 hours of missing data, respectively. Each participant provided on average 9
187 full days, with contributions ranging from 2-13 days. Datafiles could have been missing for several
188 reasons including sensor malfunctions / errors (including premature removal due to adhesive issues;
189 $n=21$, 16%) or non-compliance (e.g. failing to scan within the required 8 hour period; $n=107$, 84%).
190 From the available dataset, one data file proved incompatible with EasyGV and was removed, leaving
191 287-day comparisons.

192

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

196

197 ***Absolute percent errors***

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

202

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

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

216

217 A sensitivity analysis was conducted to ascertain the difference in MAPE values after removing those
218 participants who were deemed at higher risk of developing diabetes (n=6), leaving 228 days (79%) in
219 the analyses. Mean and CONGA MAPE values were calculated at similar error magnitudes and whilst
220 standard deviation, CV and MAGE absolute values decreased, MAPE values generally increased by
221 $\leq 1\%$.

222

223 ***Intraclass correlations***

224 Table 3 outlines the ICC that compared missing data values across all missing data conditions and
225 glycaemic variables. ICC generally decreased over the duration of missing data, with most indicating
226 excellent consistency (>0.9) apart from several MAGE ICC which indicated good consistency (0.75-
227 0.9 (Koo and Li 2016)).

228 **Discussion**

229 ***Main findings***

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

239

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

248

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

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

263

264 We have shown that whilst MAPE values remain below 3% for mean and CONGA indices, calculated
265 errors for standard deviation, CV and MAGE range between 2-18% for up to 6 hours of data loss.

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

280

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

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

295

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

305

306 ***Limitations***

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

318

319 **Conclusions**

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

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330

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450

451 **Tables**

452

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).

453

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		n
	mmol/L	MAPE %	mmol/L	MAPE %	%	MAPE %	mmol/L	MAPE %	mmol/L	MAPE %	
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

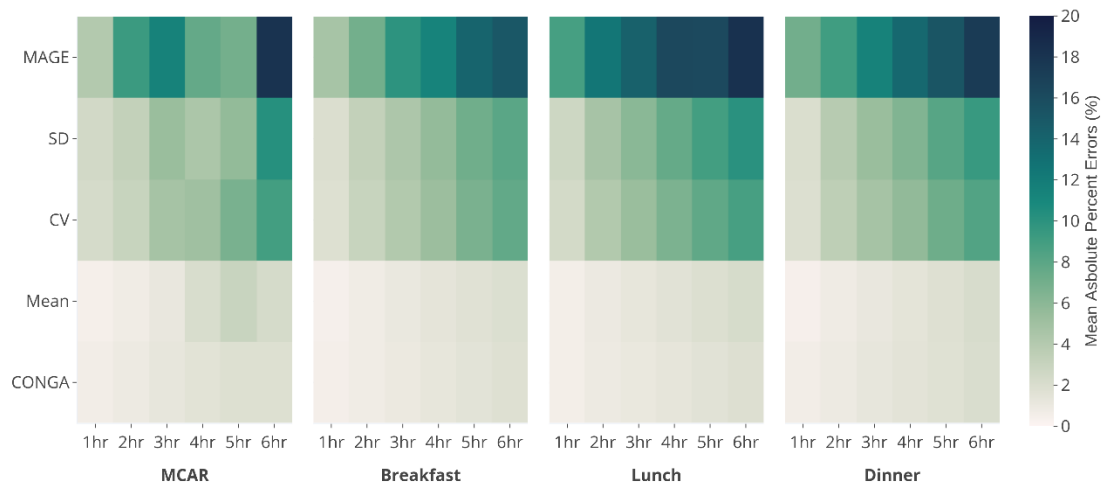
Notes: n = number of MAGE comparisons as some did not compute during analyses. Abbreviations: SD (standard deviation); CV (coefficient of variation); CONGA (continuous onset of net glycaemic action); MAGE (mean amplitude of glycaemic excursions); MAPE (mean absolute percentage errors); MCAR (missing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

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).

457 **Figure captions**



458

459 Figure 1 – Mean absolute percent errors (MAPEs) across all data removal conditions (missing at
460 random and across breakfast, lunch and dinner meal conditions) and glycaemic variability measures
461 (continuous overall net glycaemic action (CONGA), mean glucose, coefficient of variation (CV),
462 standard deviation (SD) and mean amplitude of glycaemic excursions (MAGE). The grey colour
463 represents lower MAPE, whilst green and blue indicates higher MAPE values. The glycaemic
464 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		n
	mmol/L	MAPE %	mmol/L	MAPE %	%	MAPE %	mmol/L	MAPE %	mmol/L	MAPE %	
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.