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Assessment of the effect of the COVID-19 lockdown on glycaemic control in people with type 1 diabetes using flash glucose monitoring

A. R. Dover[1] | S. A. Ritchie[2] | J. A. McKnight[2] | M. W. J. Strachan[2] | N. N. Zammitt[1] | D.J. Wake[2,3] | S. Forbes[1,4] | R. H. Stimson[1,4] | F. W. Gibb[1,4]

[1]Edinburgh Centre for Endocrinology and Diabetes, Royal Infirmary of Edinburgh, Edinburgh, UK

[2]Edinburgh Centre for Endocrinology and Diabetes, Western General Hospital, Edinburgh, UK

[3]Usher Institute, University of Edinburgh, Edinburgh, UK

[4]University/BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK

Correspondence
Fraser W. Gibb, Edinburgh Centre for Endocrinology and Diabetes, Royal Infirmary of Edinburgh, University/BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK.
Email: Fraser.gibb@ed.ac.uk

Abstract

Aim: To describe the effect of the stringent lockdown measures, introduced in the UK on 23 March 2020 to curtail the transmission of COVID-19, on glycaemic control in people with type 1 diabetes using flash glucose monitoring.

Methods: We undertook an observational study of 572 individuals with type 1 diabetes for whom paired flash glucose monitoring data were available between early March and May 2020. The primary outcome was change in flash glucose monitoring variables. We also assessed clinical variables associated with change in glycaemic control.

Results: Percentage of time in range increased between March and May 2020 [median (interquartile range) 53 (41–64)% vs 56 (45–68)%; $P < 0.001$], with associated improvements in standard deviation of glucose ($P < 0.001$) and estimated HbA_{1c} ($P < 0.001$). There was a small reduction in the number of individuals meeting the hypoglycaemia target of <5% per day (64% vs 58%; $P = 0.004$). Comparing changes in flash glucose monitoring data from March to May in 2019 with the same period in 2020 confirmed that these differences were confined to 2020. Socio-economic deprivation was an independent predictor of a ≥5% reduction in time in range during lockdown (odds ratio 0.45 for people in the two most affluent Scottish Index of Multiple Deprivation quintiles; $P < 0.001$).

Conclusions: Lockdown was not associated with a significant deterioration in glycaemic control in people with type 1 diabetes using flash glucose monitoring. However, socio-economic deprivation appeared to increase the risk of decline in glycaemic control, which has implications for how support is focused in challenging times.

1 | INTRODUCTION

A novel coronavirus strain (COVID-19) was identified as the cause of a severe acute respiratory distress syndrome (SARS-CoV-2), which emerged in Wuhan, China in December 2019.[1] In the following months, the virus rapidly spread across the world, with a marked increase in cases occurring in the UK from March 2020. In response to this, the UK government enacted a lockdown which included the closure of schools and all non-essential business, effective from 23 March 2020 (when just over 6000 cases were confirmed).[2] The lockdown also included a directive to the population to 'stay at home'

with the exception of essential work, food/medicine shopping and a single episode of daily exercise. Across the UK, diabetes services have generally cancelled all routine 'face-to-face' outpatient activity during the COVID-19 crisis and, where possible, have delivered consultations 'remotely' by telephone and/or video calls.[3] It is conceivable that the major upheaval in diet, physical activity, daily routine and stress associated with COVID-19, in addition to interruption in diabetes services, may have had a negative impact on glycaemic control in people with type 1 diabetes. To assess this, we interrogated our centre's database to compare glycaemic variables in those with type 1 diabetes using flash glucose monitoring, both before and approximately 7 weeks after lockdown (whilst lockdown was still in place). In addition, we explored the clinical and demographic factors associated with decline in glycaemic control across this period.

What's new?

- The COVID-19 pandemic is an unprecedented public health crisis and very little is known with respect to the effects of lockdown measures on glycaemic control.
- Interruption to standard diabetes services, stress and major upheaval to lifestyle and daily routines could all conceivably impact on glucose control in type 1 diabetes.
- We found no evidence of any clinically significant deterioration across a broad range of glycaemic variables in people with type 1 diabetes following the COVID-19 lockdown.
- If anything, some minor improvement was observed in percentage time in target glucose range (3.9–10 mmol/l) between March 2020 (pre-lockdown) and May 2020 (7 weeks into lockdown).
- Deterioration in time in range and estimated HbA_{1c} during lockdown was more likely in people with higher levels of socio-economic deprivation.
- Even greater focus on support for people with type 1 diabetes and socio-economic deprivation is important during the COVID-19 pandemic.

2 | PARTICIPANTS AND METHODS

2.1 | Study design and participants

Approximately 3340 individuals with type 1 diabetes attend Royal Infirmary of Edinburgh and Western General Hospital (Edinburgh) diabetes clinics. A total of 1776 individuals

(i.e. approximately half of all people with type 1 diabetes attending our clinics) using flash glucose monitoring (FreeStyle Libre, Abbott, Witney, UK) have linked their glucose data to these clinics using the LibreView platform (libreview.com). Of 1776 LibreView users, we identified a cohort with glucose data uploaded within 7 days of 11 March 2020 (baseline) and again within 7 days of 14 May 2020 (follow-up 7 weeks into lockdown). Only individuals with ≥75% flash glucose monitoring data captured were included ($n = 572$). An additional analysis, comparing change in glycaemic variables between March to May 2019 and March to May 2020, was possible in 271/572 people (i.e. paired data available for both 2019 and 2020).

2.2 | Outcomes

The main study outcomes were assessment of flash glucose monitoring glycaemic variables between March 2020 and May 2020 (using 2-week data capture), including average glucose, standard deviation of glucose, interquartile range of glucose, coefficient of variation glucose, number of low glucose events per 2-week monitoring period, average low glucose event duration, percentage of time spent with glucose below 3.9 mmol/l, percentage of time spent with glucose in range of 3.9–10 mmol/l, percentage of time spent with glucose above 10 mmol/l, daily flash glucose monitoring scans, percentage of flash glucose monitoring data captured and estimated HbA_{1c}. The percentage of individuals meeting the international consensus targets for time in range and time below range were also recorded.[4] In addition to this, we compared change across a range of glycaemic variables between March and May 2019 (non-lockdown control period) and March and May 2020 (lockdown period). Clinical and demographic data including age, date of diabetes diagnosis, last clinic HbA_{1c} value, method of insulin therapy (continuous subcutaneous insulin infusion or multiple daily injections), obesity (BMI > 30 kg/m^2), smoking status and socio-economic deprivation [Scottish Index of Multiple Deprivation (SIMD); simd.scot] were collected from SCI-Diabetes. SIMD data were unavailable in 24 individuals. We also sought to identify independent predictors (clinical and demographic) of decline in glycaemic control following lockdown.

2.3 | Statistical analysis

Data were mostly non-normally distributed (as determined by Shapiro–Wilk test) and are presented as median and interquartile range (IQR). Paired data were analysed using the Wilcoxon signed-rank test and unpaired data using the Mann–Whitney *U*-test. Categorical data were analysed using the chi-squared or McNemar test, when comparing paired repeated measurements. Logistic regression [odds ratios (ORs) and 95% CIs] was performed to identify independent predictors of deterioration in

continuous glucose monitoring variables. No sample size calculation was performed. *P* values < 0.05 were taken to indicate statistical significance and no adjustment was made for multiplicity of statistical tests. All analyses were performed using RSTUDIO version 1.0.153 (https://www.rstudio.com).

2.4 | Ethics

The study was entirely observational (with no deviation from standard clinical care) and ethics approval was not required. Inclusion in our national clinic database system, SCI-Diabetes (https://www.sci-diabetes.scot.nhs.uk), includes permission to access data for audit purposes and individuals grant specific permission for clinic staff to access LibreView data when linking their devices to the clinic.

3 | RESULTS

3.1 | Participant characteristics

The median (IQR) age of the cohort was 39 (31–50) years, and the median (IQR) diabetes duration was 18 (9–27) years. Of 572 participants, 301 (53%) were men and 147 (26%) were continuous subcutaneous insulin infusion users. A total of 336 participants out of 548 (61%) belonged to the two least deprived quintiles of SIMD (4 and 5), 143/569 participants (25%) were obese and 41/569 (7.2%) were current smokers. The median (IQR) last clinic-recorded HbA_{1c} value was 60 (53–67) mmol/mol [7.6 (7.0–8.3)%].

3.2 | Flash glucose monitoring variables between March and May 2020

There were statistically significant changes in all reported flash glucose monitoring variables, with the exception of coefficient of variation glucose, low glucose event duration and number of daily flash glucose monitoring scans (Table 1). The direction of all change in glycaemic variables following lockdown was broadly consistent with improved glycaemic control (Table 1 and Figure 1), although a small but statistically significant increase in low glucose events and percentage of time with glucose below 3.9 mmol/l was noted. A greater proportion of individuals met the time in range target and a smaller proportion met the hypoglycaemia target between March and May 2020 (Table 1).

3.3 | Comparison of 2019 and 2020

When comparing changes in flash glucose monitoring variables in the period March to May 2019 with the same period in 2020,

TABLE 1 Flash glucose monitoring data for the whole cohort in March and May 2020 ($N = 572$)

	March 2020	May 2020	Median difference	*P* comparing March 2020 and May 2020
Average glucose, mmol/l	9.6 (8.5 to 10.9)	9.3 (8.1 to 10.4)	–0.4 (–1.1 to 0.3)	<0.001
SD glucose, mmol/l	3.6 (3.0 to 4.3)	3.5 (2.8 to 4.0)	–0.2 (–0.5 to 0.2)	<0.001
IQR glucose, mmol/l	5.0 (4.1 to 6.0)	4.8 (3.9 to 5.8)	–0.2 (–0.8 to 0.4)	<0.001
Coefficient of variation glucose, %	37 (33 to 42)	37 (33 to 42)	–0.1 (–3.2 to 2.9)	0.420
Low glucose events, number/14 days	7 (3 to 12)	7 (3 to 14)	1 (–2 to 3)	0.003
Low glucose event duration, min	90 (60 to 120)	92 (65 to 127)	3 (–26 to 34)	0.061
% time below target range: <3.9 mmol/l	3 (1 to 6)	3 (1 to 7)	0 (–1 to 2)	0.005
% time in range: 3.9–10.0 mmol/l	53 (41 to 64)	56 (45 to 68)	3 (–4 to 10)	<0.001
% time above range: >10.mmol/l	42 (29 to 56)	39 (25 to 51)	–3 (–11 to 3)	<0.001
Number of daily scans	10 (7 to 15)	10 (7 to 15)	0 (–2 to 1)	0.074
% flash glucose monitoring data captured	94 (90 to 97)	93 (88 to 96)	–1 (–4 to 1)	<0.001
Estimated HbA_{1c}				<0.001
mmol/mol	61 (53 to 69)	58 (50 to 66)	–2 (–7 to 2)	
%	7.7 (7.0 to 8.5)	7.5 (6.7 to 8.2)	–0.2 (–0.6 to 0.2)	
Time in range target met (>70%), *n*/*N* (%)	93/572 (16)	122/572 (21)	NA	0.001
Hypoglycaemia target met (<5%), *n*/*N* (%)	365/572 (64)	332/572 (58)	NA	0.004
Time in range and hypoglycaemia targets met, *n*/*N* (%)	55/572 (9.6)	65/572 (11)	NA	0.261

Note Data are median (IQR), unless otherwise indicated.

Abbreviation: IQR, interquartile range.

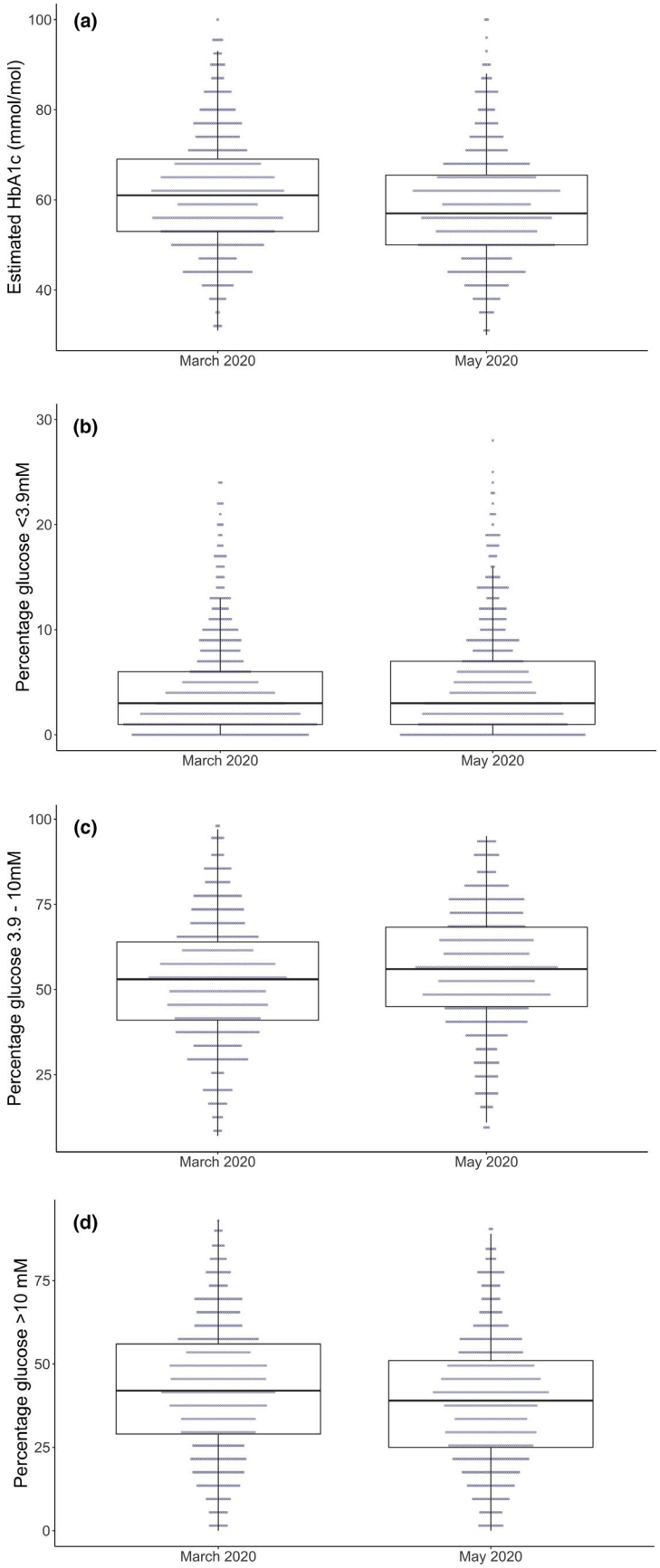

FIGURE 1 Change in (a) estimated HbA_{1c}, (b) percentage glucose below range, (c) percentage glucose in range and (d) percentage glucose above range between March 2020 and May 2020

TABLE 2 Comparing flash glucose monitoring variables in March and May 2019 with those in March and May 2020 (cohort with paired 2019 and 2020 data, $N = 271$)

	March 2019	May 2019	March 2020	May 2020	Median difference 2019	Median difference 2020	*P* comparing change between 2019 and 2020
Average glucose*, mmol/l	9.6 (8.6 to 11.0)	9.7 (8.4 to 11.1	9.5 (8.5 to 10.7)	9.2 (8.1 to 10.2)	0.1 (–0.6 to 0.7)	–0.4 (-1.0 to 0.2)	<0.001
SD glucose*, mmol/l	3.8 (3.2 to 4.5)	3.8 (3.2 to 4.5)	3.5 (3.0 to 4.1)	3.3 (2.8 to 3.9)	0.0 (–0.3 to 0.3)	–0.1 (-0.5 to 0.2)	<0.001
Coefficient of variation glucose* (%)	39 (34 to 43)	39 (34 to 44)	36 (32 to 41)	36 (32 to 41)	0.1 (–2.7 to 2.9)	–0.1 (–3.4 to 3.2)	0.382
Low glucose events*, number/14 days	8 (4 to 14)	7 (3 to 14)	6 (3 to 12)	7 (3 to 15)	0 (–4 to 2)	1 (–2 to 4)	<0.001
Low glucose event duration, min	93 (65 to 124)	86 (64 to 118)	89 (60 to 120)	86 (61 to 116)	0 (–27 to 23)	0 (–34 to 29)	0.482
% below range*	4 (2 to 7)	4 (2 to 7)	3 (1 to 6)	3 (1 to 7)	0 (–2 to 2)	0 (–1 to 2)	0.031
% in range*	52 (40 to 63)	51 (41 to 63)	54 (44 to 64)	58 (47 to 71)	0 (–5 to 5)	3 (–3 to 11)	<0.001
% above range	42 (30 to 57)	43 (30 to 56)	40 (30 to 53)	37 (24 to 49)	0 (–6 to 6)	–3 (–12 to 3)	<0.001
Number of daily scans	11 (8 to 15)	10 (7 to 15)	11 (7 to 16)	11 (7 to 16)	0 (–2 to 1)	0 (-2 to 1)	0.086
Estimated HbA_{1c}*						–2 (–7 to 1)	<0.001
mmol/mol	61 (53 to 69)	61 (52 to 70)	60 (53 to 68)	57 (50 to 64)	0 (–4 to 5)	–0.2 (0.6 to 0.1)	
%	7.7 (7.0 to 8.5)	7.7 (6.9 to 8.6)	7.6 (7.0 to 8.4)	7.4 (6.7 to 8.0)	0 (–0.4 to 0.5)		

Note: Data are median (interquartile range). *P* compares the median difference in 2019 (May to March 2019) and the median difference in 2020 (May to March 2020).

*Significantly different baseline (i.e. comparing March 2019 vs March 2020).

there were modest but significant improvements in percentage of time in range, estimated HbA_{1c} and standard deviation in 2020. There were statistically significant increases in low glucose events and percentage of time below range (Table 2).

3.4 | Predictors of change in glycaemic variables during lockdown

Of 572 participants, 125 (22%) experienced a decrease in percentage of time in range of ≥5% during lockdown. The only statistically significant baseline associations in univariate analysis were lower estimated HbA_{1c}, greater time in range and greater socio-economic deprivation (Table 3). 61/212 (28.8%) of those in the three most deprived quintiles (SIMD 1 - 3) experienced a decrease in percentage of time in range of ≥5%, compared to 60/336 (17.9%, P = 0.003) in the least deprived two quintiles (SIMD 4 & 5). Logistic regression analysis identified a lower risk in those belonging to the two SIMD quintiles with least deprivation [OR 0.45 (95% CI 0.29–0.70); $P < 0.001$] and a greater risk for those with higher percentage of time in range at baseline [OR 1.03 per % (95% CI 1.02–1.05); $P < 0.001$]. Socio-economic deprivation was the only independent predictor of a ≥5-mmol/mol (0.5%) increase in estimated HbA_{1c} [which occurred in 89/572 participants (16%)], with a lower risk observed in those belonging to the two quintiles with least deprivation [OR 0.41 (95% CI 0.25–0.67); $P < 0.001$ (Table 4)]. A ≥5% increase in percentage of time spent below 3.9 mmol/l was observed in 63/572 participants (11%) and the only independent predictor was greater time in range at baseline [OR 1.02 per % (95% CI 1.01–1.04); $P = 0.008$ Table 4)].

4 | DISCUSSION

COVID-19 has resulted in an unprecedented public health emergency and extreme disruption to the lives of people across the world. Whilst there are a number of reasons to suspect that lockdown conditions could have a deleterious effect on glycaemic control in people with type 1 diabetes, this was not observed in a large cohort of individuals using flash glucose monitoring. In fact, these data suggest that, overall, there has been a small but significant improvement in important metrics such as time in range and estimated HbA_{1c}. Although we have also shown statistically significant increases in low glucose metrics, these were negligible and unlikely to be clinically relevant. Two recently reported smaller series have shown similar results, with no evident deterioration in glycaemic control during lockdown

TABLE 3 Comparison of clinical characteristics and how these related to subsequent change in time in range between March and May 2020 ($n = 572$) in people in the Scottish Index of Multiple Deprivation quintiles 1 to 3 (most deprived) and those in quintiles 4 and 5 (least deprived)

	TIR fell by ≥5% between March and May 2020 ($n = 125$)	TIR did not fall by ≥5% between March and May 2020 ($n = 447$)	*P*
Age, years	38 (29–50)	39 (31–50)	0.735
Age at diagnosis, years	20 (13–31)	20 (11–29)	0.534
Diabetes duration, years	17 (9–25)	18 (10–28)	0.202
Men, *n* (%)	69 (55)	232 (52)	0.514
Women, *n* (%)	56 (45)	215 (48)	
Baseline estimated HbA_{1c}			<0.001
mmol/mol	57 (50–62)	62 (53–70)	
%	7.4 (6.7–7.8)	7.8 (7.0–8.6)	
Baseline %TIR	59 (51–71)	51 (39–62)	<0.001
Last clinic HbA_{1c} value			0.361
mmol/mol	59 (52–67)	60 (53–68)	
%	7.5 (6.9–8.3)	7.6 (7.0–8.4)	
Continuous subcutaneous insulin infusion, *n*/*N* (%)	29/125 (23)	118/447 (26)	0.469
SIMD quintile categories ($n = 548$), *n*/*N* (%)	1–3: 61/121 (50) 4 and 5: 60/121 (50)	1–3: 151/427 (35) 4 and 5: 276/427 (65)	0.003
Obese, *n*/*N* (%)	29/124 (23)	114/445 (26)	0.613
Current smoker, *n*/*N* (%)	9/123 (7.3)	32/446 (7.2)	0.956

Note: Data are median (interquartile range). *P* compares those in whom TIR fell by ≥5% between March and May 2020 and those in whom this did not occur.
Abbreviations: SIMD, Scottish Index of Multiple Deprivation; TIR, time in range.

TABLE 4 Logistic regression analysis of associations with reduction in time in range and increase in time below range between March and May 2020 ($N = 539$ included in models)

	TIR fell by ≥5% between March and May 2020			TBR increased by ≥5% between March and May 2020		
	OR	95% CI	*P*	OR	95% CI	*P*
% in range at baseline (per % change)	1.01	1.00–1.02	0.189	1.02	1.01–1.04	0.008
Multiple daily injections	0.87	0.50–1.56	0.640	1.82	0.93–3.80	0.092
Age (per year)	1.00	0.98–1.02	0.896	1.00	0.98–1.03	0.959
Diabetes duration (per year)	0.99	0.97–1.01	0.357	1.02	1.00–1.04	0.120
Male	1.02	0.62–1.69	0.927	0.98	0.56–1.73	0.946
SIMD quintile 4 or 5 (vs quintiles 1–3)	0.41	0.25–0.67	<0.001	1.20	0.68–2.18	0.530
Obese	0.88	0.49–1.54	0.670	0.94	0.47–1.75	0.844
Ever smoked	0.89	0.50–1.55	0.690	1.00	0.52–1.85	0.995

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; TBR, time below range; TIR, time in range.

in Italy and Spain.[5,6] In fact, the Italian study showed that individuals who were not working during lockdown experienced improvements in key glucose metrics, consistent with the present findings.[5] This suggests that standardization of daily routine may have mediated some of the benefits observed.

It is perhaps unsurprising that individuals with higher levels of time in range and lower estimated HbA_{1c} are at greater risk of subsequent deterioration, as this may simply reflect regression to the mean. Of potentially greater interest is the observation that higher levels of socio-economic deprivation were a strong, independent predictor of deteriorating glycaemic control during lockdown. The negative impact of socio-economic deprivation on glycaemic control is well recognized[7] and there are several plausible explanations as to why the COVID-19 crisis may have exacerbated this effect. For example, socio-economic deprivation may be disproportionately associated with poorer diet and reduced exercise during lockdown, as well as increased stress from childcare commitments and uncertainty around employment and income. Even greater challenges may exist for those not currently using modern glucose monitoring technologies and remote data-sharing. These individuals tend to have higher levels of socio-economic deprivation[8] and may be at greater risk of deteriorating glycaemic control in the midst of this crisis. Emerging evidence also suggests that socio-economic deprivation and elevated HbA_{1c} values are associated with adverse outcomes in individuals with COVID-19.[9]

A key strength of the present study is the cohort size, with the study representing the largest assessment of the effect of COVID-19 lockdown on glycaemic control in type 1 diabetes. An observational study is the only possible method of addressing this research question but raises the possibility that changes observed are not directly attributable to lockdown. We sought to address this potential confounder by comparing changes across the same months (March to May) in both 2019 and 2020, with the former acting as a control. In doing so, we showed that our results are unlikely simply to represent seasonal variation in glycaemic control[10] or incremental improvement in glycaemic control with longer duration of flash glucose monitoring. Another potential criticism of the study is that it is not generalizable to the wider type 1 diabetes population. Flash glucose monitoring, even in the era of National Health Service funding, is skewed towards younger and more affluent individuals[8] and continuous subcutaneous insulin infusion users were also over-represented in the present cohort. Our data were also limited to people with at least 75% data capture and therefore skewed towards more proactive flash glucose monitoring users. The reassuring findings from this study are likely to be generalizable to populations proactively using flash glucose monitoring, but not beyond this. This study was also limited to interstitial glucose monitoring metrics and we cannot comment on the psychological impact and other person-centred outcomes, which may be equally important to people with diabetes during this crisis. The large sample size identified statistically significant differences in several flash glucose monitoring variables, the magnitude of which would not be considered to be clinically meaningful.

In conclusion, these data provide reassurance that people with type 1 diabetes using flash glucose monitoring have not, in general, experienced significant deterioration in glycaemic control during the COVID-19 lockdown; however, the association between deteriorating control and socio-economic deprivation, even in those using flash glucose monitoring, is concerning. This has important implications for service

design to provide more effective support to those who require it most, particularly in challenging times.

COMPETING INTERESTS

F.W.G. and A.R.D. have received speaker fees from Abbott Diabetes Care.

ORCID

J. A. McKnight https://orcid.org/0000-0002-8214-7625
F. W. Gibb https://orcid.org/0000-0002-5576-6463

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