

World Journal of *Clinical Cases*

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ABOUT COVER

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Clinical Trials Study

Performance of Dexcom G5 and FreeStyle Libre sensors tested simultaneously in people with type 1 or 2 diabetes and advanced chronic kidney disease

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Abstract

BACKGROUND

Advanced chronic kidney disease (CKD) is a common complication for people with type 1 and 2 diabetes and can often lead to glucose instability. Continuous glucose monitoring (CGM) helps users monitor and stabilize their glucose levels. To date, CGM and intermittent scanning CGM are only approved for people with diabetes but not for those with advanced CKD.

AIM

To compare the performance of Dexcom G5 and FreeStyle Libre sensors in adults with type 1 or 2 diabetes and advanced CKD.

METHODS

This was a non-randomized clinical trial that took place in two outpatient clinics in western Sweden. All patients with type 1 or 2 diabetes and an estimated glomerular filtration rate (eGFR) of < 30 mL/min per 1.73 m² were invited to participate. Forty patients (full analysis set = 33) carried the Dexcom G5 sensor for 7 d and FreeStyle Libre sensor for 14 d simultaneously. For referencing capillary

blood glucose (SMBG) was measured with a high accuracy glucose meter (HemoCue®) during the study period. At the end of the study, all patients were asked to answer a questionnaire on their experience using the sensors.

RESULTS

The mean age was 64.1 (range 41-77) years, hemoglobin A1c was 7.0% [standard deviation (SD) 3.2], and diabetes duration was 28.5 (SD 14.7) years. A total of 27.5% of the study population was on hemodialysis and 22.5% on peritoneal dialysis. The mean absolute relative difference for Dexcom G5 *vs* SMBG was significantly lower than that for FreeStyle Libre *vs* SMBG [15.2% (SD 12.2) *vs* 20.9% (SD 8.6)], with a mean difference of 5.72 [95% confidence interval (CI): 2.11-9.32; $P = 0.0036$]. The mean absolute difference was also significantly lower for Dexcom G5 than for FreeStyle Libre, 1.21 mmol/L (SD 0.78) and 1.76 mmol/L (SD 0.78), with a mean difference of 0.55 (95%CI: 0.27-0.83; $P = 0.0004$). The mean difference (MD) was -0.107 mmol/L and -1.10 mmol/L ($P = 0.0002$), respectively. In all, 66% of FreeStyle Libre values were in the no risk zone on the surveillance error grid compared to 82% of Dexcom G5 values.

CONCLUSION

Dexcom G5 produces more accurate sensor values than FreeStyle Libre in people with diabetes and advanced CKD and is likely safe to be used by those with advanced CKD.

Key Words: Type 1 diabetes; Type 2 diabetes; Chronic kidney disease; Continuous glucose monitoring; Accuracy; Mean absolute relative difference

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Core Tip: This study bridges a needed gap within the diabetes device area for people with diabetes and advanced chronic kidney disease and was done in a home setting for analyses as close to real life as possible. The study found that Dexcom G5 showed greater accuracy both in relation to the mean absolute relative difference and on a surveillance error grid, but participants rated their user experience for FreeStyle Libre higher but rated no difference in feeling safe.

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INTRODUCTION

For people with diabetes, good glycemic control is essential to avoid problems due to diabetes complications[1]. To reach recommended glucose levels, it is important to monitor glucose levels and for several years, self-measurement of blood glucose (SMBG) with capillary measurements has been the best way to do this[1,2]. Over the last decades, continuous glucose monitoring (CGM) and intermittent glucose monitoring (isCGM) has become more common within diabetes management and for many, has replaced the multiple capillary tests. Both systems are made up of a small sensor that is inserted under the skin where it measures glucose levels in the interstitial fluid. CGM measures glucose levels continuously and every 5 min sends a glucose value to a handheld receiver or mobile telephone. It sends alarms for high and low glucose levels. The isCGM collects data, and when the user scans the sensor with a handheld receiver or a mobile phone, it sends the glucose levels to the receiver[3,4].

Within the diabetes field, there are many discussions regarding who should be given CGM and isCGM. To date, CGM and isCGM are only approved for people with diabetes but not with chronic kidney disease (CKD)[3,4] and mainly recommended for those with type 1 diabetes and who have problems with recurrent hypoglycemia[1].

Advanced CKD is a common complication in people with type 1 and 2 diabetes. It is estimated that 20%-40% of people with diabetes will develop diabetic kidney disease, and it is the leading cause of end-stage renal failure[5,6]. A recent study showed that up to 5.1% of people with type 1 diabetes in Germany and Austria had an estimated glomerular filtration rate (eGFR) below 30 mL/min, and for Sweden and United States, the corresponding figures were 1.5% and 2.1%[7]. Advanced CKD increases the risk of hypoglycemia and great glycemic variation, and therefore it can be helpful to monitor blood

glucose with a CGM or isCGM[8,9]. There are very few studies available on the accuracy of CGMs or isCGMs for people with advanced CKD[10]. Two of the most common systems are Dexcom and FreeStyle Libre. Neither of these systems are approved for people in dialysis[3,4].

The aim of this study was to compare the performance of Dexcom G5 and FreeStyle Libre in adults with type 1 or 2 diabetes with CKD and an eGFR < 30 mL/min/1.73 m², including patients on maintenance dialysis.

MATERIALS AND METHODS

This study took place at NU Hospital Group and Sahlgrenska University Hospital, Sweden. It was a non-randomized, non-blinded clinical study over a 14 d period to compare the performance of FreeStyle Libre 1 and Dexcom G5 for people with diabetes and advanced CKD in an at-home situation. The protocol was approved by the regional ethics review board of Gothenburg, Sweden.

Study procedures

All participants provided written informed consent before the study began. The inclusion criteria were: type 1 or type 2 diabetes, between 18-years-old and 80-years-old, and eGFR < 30 mL/min per 1.73 m² for people undergoing or not undergoing dialysis. The exclusion criteria were pregnancy, patients with severe cognitive dysfunction or other diseases that makes glucose monitoring difficult, continuous use of paracetamol, history of allergic reaction to chlorhexidine or alcohol antiseptic solution, abnormal skin at the anticipated glucose sensor attachment sites, and eGFR ≥ 30 mL/min per 1.73 m².

After obtaining written and informed consent, a diabetes nurse inserted two different sensors in accordance with instructions from the manufacturer. Dexcom G5 was inserted in the abdomen and FreeStyle Libre on the upper arm. Participants were instructed on how they should use each monitor and instructed how to calibrate the Dexcom G5. Calibrations were done using the HemoCue® DM RD 201 (Ängelholm, Sweden). All HemoCue meters were calibrated before being assigned to participants using the absolute isotope dilution gas chromatography/mass spectrometry measurement system[11]. The total measurement error/reproducibility imprecision of HemoCue is less than 6.5%[12]. Earlier studies using HemoCue showed a strong correlation between capillary and venous HemoCue concentrations, and capillary concentrations were considered to be a suitable reference[13]. All participants were instructed by a diabetes nurse on how to use the HemoCue meter. Participants were instructed to simultaneously document their blood glucose measured by HemoCue and the value of the FreeStyle Libre and Dexcom G5 in a diary a minimum of three times per day. Participants were instructed to calibrate their Dexcom G5 twice daily in accordance with the manufacturer's instructions and to do so after recording its value in the diary. Participants on maintenance dialysis (peritoneal dialysis or hemodialysis) were also asked to register the start and finish of each session in their diary. After 7 d, Dexcom G5 was removed by the participants but they continued to record results from the FreeStyle Libre and HemoCue. After the 14 d period, participants returned the meters to the site. The study personnel downloaded data from the meters using the Glooko-Diasend system. HemoCue measurements were manually validated by personnel going through each value and comparing to the diary. When each sensor was finished, participants rated their experience on a 10-item visual analogue scale. Similar questionnaires have been used in earlier studies[14,15].

Predefined endpoints

All endpoints were predefined and registered on ClinicalTrials.gov. The primary endpoint was the difference of mean absolute relative difference (MARD) between Dexcom G5 and FreeStyle Libre using HemoCue (capillary glucose meter) as a reference. Secondary endpoints were the difference in mean absolute difference (MAD) between the Dexcom G5 and FreeStyle Libre sensors, the difference in mean difference (MD) between the Dexcom G5 and FreeStyle Libre sensors, and the correlation between the different systems. Predefined subgroup analyses for glucose ranges below 3.9 mmol/L, between 3.9 and 10 mmol/L, and above 10 mmol/L as well as for those without dialysis and undergoing dialysis.

Independence of the study

The manufacturers of FreeStyle Libre and Dexcom G5 were not involved in the design, performance, data analysis, or publication of the article. No support was received from the manufacturers.

Statistical analysis

After sample size analysis, 40 patients were included in the study (see supplement). All main analyses between Dexcom G5 and FreeStyle Libre were performed with paired analyses. All statistical analyses were predefined in the statistical analysis plan before database lock. All participants having at least 10 matched time points, with evaluable blood glucose values from both sensors and HemoCue (reference capillary value) during the whole study period, were included in the Full Analysis Set (FAS). All matching time points were used. For paired analysis regarding continuous variables, Fisher's non-parametric permutation test for paired observations was used and for dichotomous and ordered

categorical variables sign test was used. For comparison between dialysis subjects and subjects not in dialysis, Fisher's non-parametric permutation test was used for continuous variables.

The primary variable was MARD, which is the mean absolute relative difference between the estimated sensor glucose value of FreeStyle Libre or Dexcom G5 and blood glucose measured with HemoCue. For each individual mean of following differences from each time point was evaluated for both sensors: $|(sensor_i - HemoCue_i)| / HemoCue_i$. The secondary variables were MAD and MD.

MAD is the mean absolute difference between estimated sensor glucose value of FreeStyle Libre or Dexcom G5 and blood glucose measured with HemoCue. For each individual mean of following differences from each time point was evaluated for both sensors: $|sensor_i - HemoCue_i|$. MD is the mean difference between estimated sensor glucose value of FreeStyle Libre or Dexcom G5 and blood glucose measured with HemoCue. For each individual mean of following differences from each time point was evaluated: $(sensor_i - HemoCue_i)$, where i = time-point during the analyzed days in the study.

The MD between Dexcom G5 and FreeStyle Libre with 95% confidence intervals (CIs) was calculated based on Fisher's non-parametric permutation test for paired observations for continuous variables. All analyses for different glucose ranges were based on HemoCue values within respective range.

To study the covariation between Dexcom G5/FreeStyle Libre and HemoCue Pearson correlation coefficient between each of the devices and HemoCue was calculated for each subject. These correlations were also analyzed both for Dexcom G5 and FreeStyle Libre with Fisher's non-parametric permutation test one sample test.

Agreement between each of the devices and HemoCue were analyzed with Bland-Altman' methods. The main result was the limit of agreement. If one got a value measured with one of the sensors, you can calculate an interval where 95% of the HemoCue values would have been. The distributions of the difference between each of the sensor and HemoCue was also given together with Intraclass correlation coefficient (ICC), Bland-Altman plots, and scatterplots.

All significance tests were two-sided and conducted at the 5% significance level. All statistical analyses were performed with SAS System Version 9.4 (Cary, NC, United States).

Post-hoc analyses

The surveillance error grid graph for Dexcom G5/FreeStyle Libre *vs* HemoCue was calculated by using <https://www.diabetestechology.org/seg/>. The proportion of sensor values within 15%, 20%, and 30% of reference values HemoCue for blood glucose > 100 mg/dL (5.6 mmol/L) or within 15, 20, and 30 mg/dL (0.8, 1.1, 1.7 mmol/L) of reference values for blood glucose ≤ 100 mg/dL (5.6 mmol/L), respectively, was calculated (%15/15, %20/20, %30/30). MARD FreeStyle Libre *vs* HemoCue the first week was compared with the second week with the same requirements as main study with Fisher's nonparametric permutation test for paired observations.

RESULTS

The study included 40 participants with type 1 and 2 diabetes and advanced CKD; 33 (FAS) met the criteria for data analysis and at least 10 time points with evaluable values from both systems and the HemoCue within 5 min during the whole study period (June 2016-March 2019). Of the 7 patients who were not included in FAS, 2 chose not to participate after starting the study and 5 did not meet the criteria for data analysis described above; that is, they did not have 10 matched time points for both sensors. Mean hemoglobin A1c (HbA1c) was 7.0%, 25.6% were women, mean age was 64.1 (range 41-77), and 50% were on dialysis. Additional baseline characteristics are shown in [Table 1](#).

Accuracy evaluations

The MARD analyzed for all participants for Dexcom G5 was significantly lower than that for FreeStyle Libre *vs* SMBG (15.2% [SD 12.2] *vs* 20.9% [SD 8.6]), respectively, with mean difference of 5.72 (95%CI: 2.11-9.32; $P = 0.0036$). The MAD was also significantly lower for Dexcom G5 than for FreeStyle Libre, 1.21 mmol/L (SD 0.78) and 1.76 mmol/L (SD 0.78), with a mean difference of 0.55 (95%CI: 0.27-0.83; $P = 0.0004$). There was also a significant difference between the MD of the systems. There was a systematic MD between FreeStyle Libre and HemoCue of -1.10 mmol/L (95%CI: -1.55 to -0.66 mmol/L; $P < 0.0001$) but no systematic MD between Dexcom G5 and HemoCue -0.107 (95%CI: -0.439 to 0.225; $P = 0.052$) ([Table 2](#)).

We found that for glucose values that were in range (3.9-10.0 mmol/L) and above range (> 10 mmol/L), there was a significantly lower MARD, MAD, and MD for Dexcom G5 than for FreeStyle Libre ([Table 2](#)). For glucose values in range, the MARD was 14.8% (SD 10.6) for Dexcom G5 and 22.6% (SD 8.9) for the FreeStyle Libre, with a mean difference of 7.83 (95%CI: 4.32-11.33; $P < 0.0001$). The MARD for hyperglycemic values were 12.3% (SD 11.6) and 16.6% (SD 11.1), respectively, with a mean difference of 4.22 (95%CI: 1.06-7.39; $P = 0.010$). There were few values below range (< 3.9 mmol/L), 14 values from 9 individuals ([Table 2](#)).

Table 1 Baseline characteristics

Variable	All, <i>n</i> = 40	FAS population, <i>n</i> = 33
Age in yr	64.1 (9.2)	63.2 (9.2)
	66 (41; 77)	65.5 (41; 77)
	<i>n</i> = 39	<i>n</i> = 32
HbA1c in mmol/mol	53.1 (11.0)	53.9 (11.5)
	53 (31; 75)	54 (31; 75)
	<i>n</i> = 40	<i>n</i> = 33
HbA1c %	7 (3.2)	7.1 (3.2)
	53 (5; 9)	7.1 (5; 9)
	<i>n</i> = 40	<i>n</i> = 33
Dialysis		
Not in dialysis	20 (50.0%)	17 (51.5%)
Hemodialysis	11 (27.5%)	7 (21.2%)
Peritoneal dialysis	9 (22.5%)	9 (27.3%)
Diabetes duration	28.5 (14.7)	29.2 (15.4)
	27.5 (5.3; 64.5)	28.5 (5.3; 64.5)
	<i>n</i> = 32	<i>n</i> = 26
Sex		
Man	29 (74.4%)	22 (68.8%)
Woman	10 (25.6%)	10 (31.3%)
Smoking		
No	25 (71.4%)	19 (67.9%)
Yes	3 (8.6%)	3 (10.7%)
Do not know	7 (20.0%)	6 (21.4%)
Systolic blood pressure in mmHg	145.6 (24.2)	146.5 (24.7)
	145 (95; 213)	142.5 (95; 213)
	<i>n</i> = 37	<i>n</i> = 30
Diastolic blood pressure in mmHg	77.4 (13.7)	78.6 (13.8)
	80 (52; 103)	80 (52; 103)
	<i>n</i> = 37	<i>n</i> = 30
Insulin delivery		
Basal insulin only	12 (32.4%)	10 (33.3%)
Mix insulin	2 (5.4%)	2 (6.7%)
MDI	24 (64.9%)	20 (66.7%)
Other glucose lowering treatment	5 (13.5%)	3 (10.0%)
Total insulin dose per day	73.0 (60.3)	65.7 (63.8)
	45 (8; 277)	41 (8; 277)
	<i>n</i> = 25	<i>n</i> = 20
Type of diabetes		
Type 1	11 (30.6%)	10 (33.3%)
Type 2	25 (69.4%)	20 (66.7%)

For categorical variables n (%) is presented. For continuous variables mean (SD)/median (min; max)/ n is presented. FAS: Full analysis set; MDI: Multiple daily injection.

Subgroup analysis: People needing and not needing dialysis

Subgroup analyses for MARD, MAD, and MD were done for people requiring and not requiring dialysis. The MARD for FreeStyle Libre for people in dialysis was 19.3% (SD 7.4) compared to 22.5% (SD 9.5) for those not in dialysis ($P = 0.29$). The corresponding values for Dexcom G5 were 15.5% (SD 14.8) and 15.0% (SD 9.6), respectively ($P = 0.91$). For people not in dialysis, there was a significant difference between the sensors MARD and MAD ($P = 0.0033$ and $P = 0.0057$, respectively). For people in dialysis, there was a significant difference between the systems MAD ($P = 0.035$), whereas a numerical difference was found between the sensors MARD, although not statistically significant (Table 2). Further subgroup analysis with people on peritoneal dialyses showed numerically lower MARD and MAD for Dexcom G5 compared to FreeStyle Libre as in the total population, and there was a significant systematic difference between FreeStyle Libre and HemoCue -1.58 ($P = 0.01$). There were 7 people on hemodialysis and Dexcom G5 showed a numerically lower MARD and MAD compared to FreeStyle Libre in this subgroup, but the differences were less (Table 2).

Correlation between the systems

Analyses were done to see how well the systems correlated with the capillary reference system. Values obtained by Dexcom G5 and FreeStyle Libre significantly correlated with those obtained by the HemoCue capillary reference system [$r = 0.784$, (SD 0.29) $P < 0.0001$, and 0.777 , (SD 0.34) $P < 0.0001$, respectively]. Interclass correlation coefficient (ICC) was 0.68 for FreeStyle Libre and 0.88 for Dexcom G5 and limits of agreement (-3.54- 1.34) for FreeStyle Libre and (-1.94- 1.73) for Dexcom G5 (Supplementary Table 1). This could clearly be seen on the Bland-Altman plot in Figure 1 and Supplementary Figures 1 and 2.

Patient experience

After using the systems, participants evaluated their experience (Table 3). Participants were significantly more positive towards FreeStyle Libre than Dexcom G5 in all factors except feeling safe, for which there was no significance between the two systems. FreeStyle Libre scored 7.94 of 10 and Dexcom G5 scored 7.19 of 10 ($P = 0.32$; Table 3).

Post hoc analysis

For Dexcom G5, %20/20 = 79.6, which indicates that 79.6% of the values above 5.6 mmol/L were within 20% of the reference instrument and within 1.11 mmol/L (20 mg/dL) for values below 5.6 mmol/L. The corresponding figure for FreeStyle Libre was 61.3%. For %15/15 the values were 70.3% for Dexcom G5 and 43.9% for FreeStyle Libre. For %30/30 the corresponding figures were 89.1% and 84.6% respectively. The surveillance error grid (Figure 2) showed that 82% of the values for Dexcom G5 were within the no risk zone (green color) compared to 66.3% of the values for FreeStyle Libre. Data from the second week of Libre showed that there was a greater MARD during this week, 24.8% (95%CI: 20.4-29.2 mmol/L) compared to the first week when it was 19.4%, $P = 0.0042$. MARD for participants with type 1 diabetes was 11.8 % (SD 10.0) for Dexcom G5 and 17.4% (SD 5.7) for FreeStyle Libre with a mean difference of 5.6 (95%CI: (-0.4-11.8, $P = 0.068$). Corresponding results for participants with type 2 diabetes were 16.2 % (SD 12.7) for Dexcom G5 and 21.6% (SD 8.6) for FreeStyle Libre with a mean difference of 5.4 (95%CI: (0.25-10.49, $P = 0.042$).

DISCUSSION

Dexcom G5 showed greater overall accuracy than FreeStyle Libre. Dexcom G5 also showed greater accuracy for glucose values within range (3.9-10 mmol/L) and above range (> 10 mmol/L). Furthermore, in a subgroup analysis, Dexcom G5 showed greater accuracy for people not in dialysis. However, for people in dialysis, Dexcom G5 had a numerically lower MARD and a significantly lower MAD compared with FreeStyle Libre. On the surveillance error grid, Dexcom G5 had 82% of values within the no risk zone compared to 66% for FreeStyle Libre. Glucose values from both sensors correlated well with the reference instrument, HemoCue. FreeStyle Libre showed a greater systematic deviation than Dexcom G5. Participants rated their user experience of FreeStyle Libre higher after a 2 wk period than Dexcom G5 but did not experience a difference in safety.

Earlier studies with similar methodology and the same reference instrument showed that the FreeStyle Libre had a MARD of 13.2% and an earlier Dexcom sensor (Dexcom 4G) had a MARD of 13.8% when tested in people with type 1 diabetes [14,15]. A recent study analyzed how well FreeStyle Libre correlates with capillary measurements (Medisafe® Fit) during hemodialysis in people with type 2

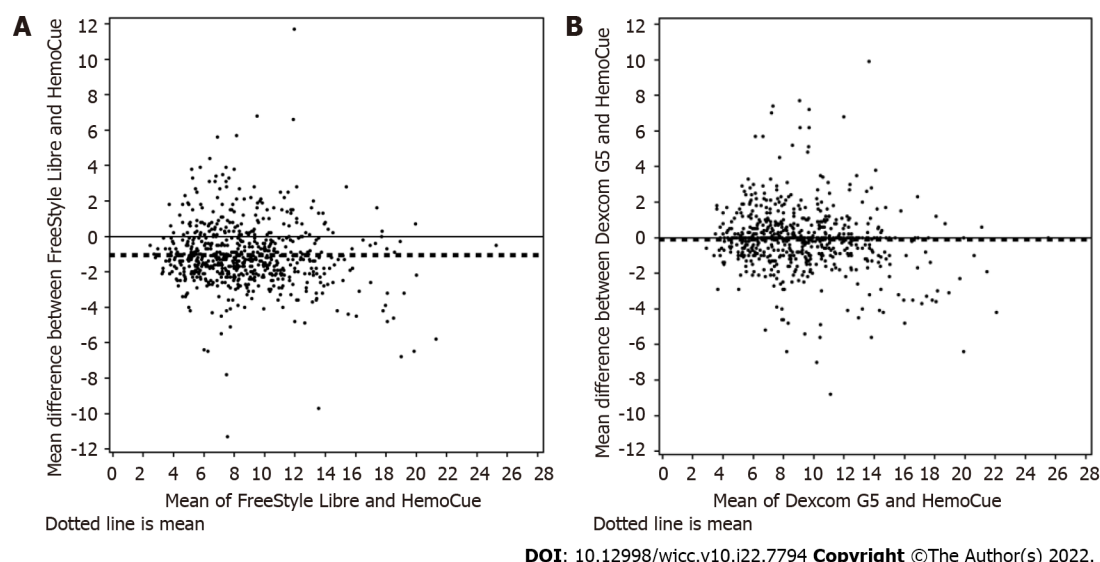
Table 2 Mean absolute relative difference, mean absolute difference and mean difference for Dexcom G5 and FreeStyle Libre

Variable	FreeStyle Libre (isCGM)	Dexcom G5 CGM	Difference (isCGM-CGM)	P value [†]
Mean MARD	20.9 (8.6)	15.2 (12.2)	5.72 (10.17)	0.0036
	19.8 (8.5; 43.1)	11.9 (2.2; 60.5)	6.5 (-26.75; 24.68)	
	<i>n</i> = 33	<i>n</i> = 33	(2.11; 9.32)	
			<i>n</i> = 33	
Mean MAD	1.76 (0.78)	1.21 (0.78)	0.548 (0.795)	0.0004
	1.65 (0.48; 4.48)	0.95 (0.23; 3.12)	0.679 (-1.662; 2.11)	
	<i>n</i> = 33	<i>n</i> = 33	(0.267; 0.830)	
			<i>n</i> = 33	
Mean MD	-1.10 (1.24)	-0.107 (0.937)	-0.998 (1.278)	0.0002
	-1.46 (-4.48; 1.63)	-0.229 (-2.47; 3.007)	-1.1 (-3.586; 2.431)	
	<i>n</i> = 33	<i>n</i> = 33	(-1.451; -0.545)	
			<i>n</i> = 33	
Persons in dialysis				
Mean MARD	19.3 (7.4)	15.5 (14.8)	3.80 (11.09)	0.19
	17.7 (8.5; 33.7)	8.6 (4.1; 60.5)	6.51 (-26.75; 15.75)	
	<i>n</i> = 16	<i>n</i> = 16	(-2.11; 9.71)	
			<i>n</i> = 16	
Mean MAD	1.74 (0.91)	1.26 (0.85)	0.489 (0.828)	0.035
	1.65 (0.77; 4.48)	0.99 (0.43; 3.12)	0.611 (-1.236; 1.65)	
	<i>n</i> = 16	<i>n</i> = 16	(0.048; 0.931)	
			<i>n</i> = 16	
Mean MD	-1.29 (1.29)	0.056 (1.232)	-1.34 (1.30)	0.0019
	-1.32 (-4.48; 0.96)	-0.252 (-2.47; 3.007)	-1.46 (-3.59; 1.07)	
	<i>n</i> = 16	<i>n</i> = 16	(-2.03; -0.65)	
			<i>n</i> = 16	
People not in dialysis				
Mean MARD	22.5 (9.5)	15.0 (9.6)	7.53 (9.19)	0.0033
	19.8 (8.8; 43.1)	12.5 (2.2; 38.5)	6 (-15.59; 24.68)	
	<i>n</i> = 17	<i>n</i> = 17	(2.80; 12.25)	
			<i>n</i> = 17	
Mean MAD	1.77 (0.65)	1.16 (0.72)	0.604 (0.784)	0.0057
	1.67 (0.48; 3.22)	0.95 (0.23; 2.77)	0.679 (-1.662; 2.11)	
	<i>n</i> = 17	<i>n</i> = 17	(0.201; 1.007)	
			<i>n</i> = 17	
Mean MD	-0.934 (1.211)	-0.260 (0.529)	-0.673 (1.209)	0.037
	-1.482 (-2.586; 1.632)	-0.223 (-1.323; 0.932)	-0.855 (-2.348; 2.431)	
	<i>n</i> = 17	<i>n</i> = 17	(-1.295; -0.052)	
			<i>n</i> = 17	
Glucose values < 3.9 mmol/L				
Mean MARD	53.0 (37.1)	89.8 (66.8)	-36.9 (42.0)	0.027
	35.3 (12.8; 115.2)	66.7 (7.7; 197.4)	-44.7 (-127.2; 7.1)	

	<i>n</i> = 9	<i>n</i> = 9	(-69.2; -4.5)	
			<i>n</i> = 9	
Mean MAD	1.81 (1.33)	3.10 (2.47)	-1.29 (1.52)	0.027
	1.2 (0.47; 3.9)	1.8 (0.27; 7.2)	-1.3 (-4.65; 0.2)	
	<i>n</i> = 9	<i>n</i> = 9	(-2.46; -0.12)	
			<i>n</i> = 9	
Mean MD	1.18 (1.96)	3.03 (2.54)	-1.85 (1.42)	0.0078
	1.2 (-1.2; 3.9)	1.8 (0.27; 7.2)	-1.8 (-4.65; 0.2)	
			(-2.94; -0.76)	
	<i>n</i> = 9	<i>n</i> = 9	<i>n</i> = 99	
Glucose values 3.9-10.0 mmol/L				
Mean MARD	22.6 (8.9)	14.8 (10.6)	7.83 (9.88)	< 0.0001
	21 (8.7; 44.1)	11.9 (1.5; 40.5)	8.05 (-13.18; 28.95)	
	<i>n</i> = 33	<i>n</i> = 33	(4.32; 11.33)	
			<i>n</i> = 33	
Mean MAD	1.60 (0.62)	1.03 (0.71)	0.568 (0.689)	< 0.0001
	1.45 (0.5; 2.98)	0.82 (0.13; 2.59)	0.633 (-0.918; 2.045)	
	<i>n</i> = 33	<i>n</i> = 33	(0.323; 0.812)	
			<i>n</i> = 33	
Mean MD	-0.868 (1.183)	0.136 (0.859)	-1.00 (1.19)	< 0.0001
	-1.067 (-2.9; 2.508)	-0.017 (-2.1; 2.445)	-1.07 (-3.57; 1.38)	
	<i>n</i> = 33	<i>n</i> = 33	(-1.43; -0.58)	
			<i>n</i> = 33	
Glucose values > 10.0 mmol/L				
Mean MARD	16.6 (11.1)	12.3 (11.6)	4.22 (8.63)	0.010
	15.3 (1.9; 59)	7.9 (1.9; 50.4)	4.69 (-25.08; 16.94)	
	<i>n</i> = 31	<i>n</i> = 31	(1.06; 7.39)	
			<i>n</i> = 31	
Mean MAD	2.06 (1.29)	1.54 (1.31)	0.520 (1.139)	0.016
	1.9 (0.2; 6.45)	1.04 (0.2; 5.5)	0.533 (-3.4; 2.18)	
	<i>n</i> = 31	<i>n</i> = 31	(0.102; 0.938)	
			<i>n</i> = 31	
Mean MD	-1.82 (1.56)	-0.944 (1.633)	-0.875 (1.777)	0.0087
	-1.89 (-6.45; 1.16)	-0.563 (-5.5; 2.7)	-0.95 (-4.1; 5.72)	
	<i>n</i> = 31	<i>n</i> = 31	(-1.527; -0.223)	
			<i>n</i> = 31	
Hemodialysis				
Mean MARD	21.4 (9.1)	20.3 (18.9)	1.13 (14.27)	0.86
	20.7 (8.5; 33.7)	17 (5.6; 60.5)	2.88 (-26.75; 15.75)	
	<i>n</i> = 7	<i>n</i> = 7	(-12.07; 14.33)	
			<i>n</i> = 7	
Mean MAD	1.79 (0.69)	1.44 (0.87)	0.354 (1.012)	0.38
	1.89 (0.77; 2.73)	1.28 (0.56; 3.12)	0.211 (-1.236; 1.614)	

	<i>n</i> = 7	<i>n</i> = 7	(-0.582; 1.290)	
Mean MD	-0.905 (1.451)	0.378 (1.185)	-1.28 (1.47)	0.063
	-1.606 (-2.733; 0.96)	0.056 (-0.433; 3.007)	-1.99 (-2.54; 1.07)	
	<i>n</i> = 7	<i>n</i> = 7	(-2.65; 0.08)	
			<i>n</i> = 7	
Peritoneal dialysis				
Mean MARD	17.6 (5.9)	11.7 (10.4)	5.88 (8.16)	0.078
	14.9 (12.1; 28.8)	6.9 (4.1; 36.7)	7.18 (-14.64; 13.35)	
	<i>n</i> = 9	<i>n</i> = 9	(-0.39; 12.15)	
			<i>n</i> = 9	
Mean MAD	1.71 (1.09)	1.11 (0.86)	0.595 (0.700)	0.043
	1.4 (0.96; 4.48)	0.77 (0.43; 2.83)	0.736 (-0.89; 1.65)	
	<i>n</i> = 9	<i>n</i> = 9	(0.057; 1.132)	
			<i>n</i> = 9	
Mean MD	-1.58 (1.15)	-0.193 (1.278)	-1.39 (1.23)	0.0039
	-1.25 (-4.48; -0.8)	-0.442 (-2.47; 2.195)	-1 (-3.59; -0.33)	
	<i>n</i> = 9	<i>n</i> = 9	(-2.34; -0.44)	
			<i>n</i> = 9	

¹For comparison between FreeStyle Libre and Dexcom G5 the Fisher's Non-Parametric Permutation test for matched pairs was used. For continuous variables, distribution of differences is given by mean (SD)/median (min; max)/(95% confidence interval for mean)/*n* = is presented and the distribution of values within the two sensors is given by mean (SD)/median (min; max)/*n* = is presented. CGM: Continuous glucose monitoring; MAD: Mean absolute difference; MARD: Mean absolute relative difference; MD: Mean difference; isCGM: Intermittent glucose monitoring.



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Figure 1 Bland-Altman plot, scatterplot. A: All individual measurements FreeStyle Libre vs HemoCue; B: All individual measurements Dexcom G5 vs HemoCue. Thick dotted line represents the mean difference.

diabetes, and showed that the FreeStyle Libre had a MARD between 13% and 22% depending on the glycemic range and that it showed a 18.4 mg/dL (1.0 mmol/L) lower value than the capillary reference instrument. The same study found that the Medtronic iPro Enlite sensor had a MARD between 5% and 30% depending on the glycemic value and showed a 4.7 mg/dL (0.3 mmol/L) lower value than the reference instrument[10]. It was previously shown that the FreeStyle Libre deviates systematically by -

Table 3 Patient experience of FreeStyle Libre and Dexcom G5 measured on a visual analogue scale

Variable	FreeStyle Libre isCGM, <i>n</i> = 31	Dexcom G5 CGM, <i>n</i> = 31	Change from FreeStyle Libre isCGM to Dexcom G5 CGM	
				<i>P</i> value
My experience of the system was very positive	8.35 (2.03)	6.84 (2.70)	-1.52 (3.41)	0.023
	9.00 (3.00; 10.00)	8.00 (2.00; 10.00)	-2.00 (-7.00; 7.00)	
	(7.61; 9.10)	(5.85; 7.83)	(-2.77; -0.26)	
	<i>n</i> = 31	<i>n</i> = 31	<i>n</i> = 31	
The insertion of the sensor was easy	9.03 (1.71)	8.27 (2.29)	-0.767 (1.455)	0.0084
	10.00 (2.00; 10.00)	9.00 (1.00; 10.00)	0.000 (-5.000; 2.000)	
	(8.39; 9.67)	(7.41; 9.12)	(-1.310; -0.223)	
	<i>n</i> = 30	<i>n</i> = 30	<i>n</i> = 30	
I felt safe during my time using the system	7.94 (2.67)	7.19 (2.46)	-0.742 (3.916)	0.32
	9.00 (0.00; 10.00)	8.00 (3.00; 10.00)	-1.000 (-7.000; 9.000)	
	(6.96; 8.91)	(6.29; 8.09)	(-2.178; 0.694)	
	<i>n</i> = 31	<i>n</i> = 31	<i>n</i> = 31	
It was easy to use the system	9.52 (0.96)	7.60 (2.62)	-1.93 (2.21)	< 0.0001
	10.00 (6.00; 10.00)	9.00 (2.00; 10.00)	-1.00 (-7.00; 0.00)	
	(9.16; 9.87)	(6.62; 8.58)	(-2.76; -1.11)	
	<i>n</i> = 31	<i>n</i> = 30	<i>n</i> = 30	
It was easy to interpret the information on the receiver screen	9.42 (0.99)	7.97 (2.46)	-1.45 (1.98)	< 0.0001
	10.00 (7.00; 10.00)	9.00 (1.00; 10.00)	-1.00 (-7.00; 1.00)	
	(9.06; 9.78)	(7.07; 8.87)	(-2.18; -0.73)	
	<i>n</i> = 31	<i>n</i> = 31	<i>n</i> = 31	
I was not in pain or had discomfort in connection to my use of the system	9.74 (0.73)	8.48 (2.78)	-1.26 (2.68)	0.0078
	10.00 (7.00; 10.00)	10.00 (0.00; 10.00)	0.00 (-10.00; 0.00)	
	(9.47; 10.01)	(7.46; 9.50)	(-2.24; -0.27)	
	<i>n</i> = 31	<i>n</i> = 31	<i>n</i> = 31	
I experienced no problem scanning/contact with the system	9.55 (0.93)	7.19 (3.29)	-2.35 (3.23)	< 0.0001
	10.00 (7.00; 10.00)	9.00 (0.00; 10.00)	-1.00 (-10.00; 2.00)	
	(9.21; 9.89)	(5.99; 8.40)	(-3.54; -1.17)	
	<i>n</i> = 31	<i>n</i> = 31	<i>n</i> = 31	
The sensor was comfortable to have on my body in my daily life	9.20 (1.40)	7.23 (2.69)	-1.90 (2.34)	< 0.0001
	10.00 (4.00; 10.00)	8.00 (1.00; 10.00)	-1.00 (-8.00; 1.00)	
	(8.68; 9.72)	(6.24; 8.21)	(-2.77; -1.03)	
	<i>n</i> = 30	<i>n</i> = 31	<i>n</i> = 30	
The system did not disturb my daily life	9.33 (1.09)	7.74 (2.62)	-1.50 (2.43)	0.0024
	10.00 (6.00; 10.00)	9.00 (3.00; 10.00)	0.00 (-7.00; 4.00)	
	(8.93; 9.74)	(6.78; 8.70)	(-2.41; -0.59)	
	<i>n</i> = 30	<i>n</i> = 31	<i>n</i> = 30	
I would like to use the system in my daily life	8.45 (2.86)	5.42 (3.49)	-2.66 (4.98)	0.0096
	10.00 (0.00; 10.00)	6.00 (0.00; 10.00)	-3.00 (-10.00; 9.00)	
	(7.36; 9.54)	(4.14; 6.70)	(-4.55; -0.76)	

	<i>n</i> = 29	<i>n</i> = 31	<i>n</i> = 29
It was easy to calibrate the Dexcom G5		8.40 (2.21)	
		10.00 (3.00; 10.00)	
		(7.58; 9.22)	
		<i>n</i> = 30	
The alarms did not disturb my daily life		7.97 (2.74)	
		9.00 (0.00; 10.00)	
		(6.95; 8.99)	
		<i>n</i> = 30	

For categorical variables *n* (%) is presented. For continuous variables mean (SD)/median (min; max)/(95% confidence interval for mean)/*n* is presented. For comparison over time, Fisher's non-parametric permutation test for paired observations was used for continuous variables. The evaluation of questions of the flash glucose monitoring/continuous glucose monitoring were expressed on a visual analogue scale with lowest value (0) meaning Not true at all and highest value (10) meaning completely true.

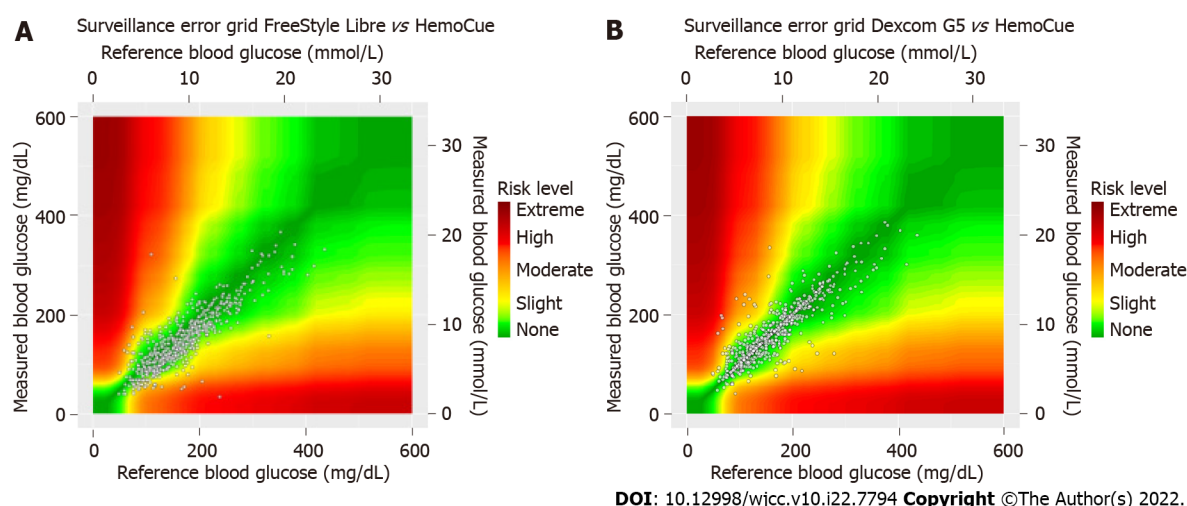


Figure 2 Surveillance error grid. A: FreeStyle Libre vs HemoCue -66.3% of values fall within the dark green area; B: Dexcom G5 vs HemoCue -82% of values fall within the dark green area.

0.5 mmol/L in people with type 1 diabetes using HemoCue capillary measurements as a reference[15]. The Dexcom G5 was found to have a MARD of 7.1%-15.7% when tested in people with type 1 diabetes and using a Yellow Spring Instrument as a reference[16].

People with advanced CKD more frequently experience glycemic excursions[15]. During hemodialysis, there is an increased risk for hypoglycemia, whereas patients with peritoneal dialysis have an increased hyperglycemia risk[17,18]. It is therefore important that this group of patients receives all possible help to monitor their glucose levels and to increase their possibility of better glycemic control. It is possible to speculate if these increased glucose excursions can possibly be the cause to the lower accuracy of these sensors for people with advanced CKD. This study found that the accuracy of FreeStyle Libre and Dexcom G5 while being used by people with advanced CKD is similar to the accuracy of earlier sensors which were used as glucose indicators and not for insulin dosing decisions [14,15]. An earlier study has found that when people on dialysis used CGM it led to more frequent treatment changes and better glycemic control[19].

This study showed that even people undergoing peritoneal dialysis, which can have high glucose fluctuations, had a MARD which is similar to previous systems. The peritoneal dialysis fluids did not seem to affect the MARD.

FreeStyle Libre had a higher MARD and MAD than Dexcom G5 and there was a greater percentage of values within the safe zone for Dexcom G5. This can partly be explained by the fact that the FreeStyle Libre showed a systematic deviation of -1.1 mmol/L. It is important that users of the system are aware of the systems tendency of reporting lower glucose values. This systematic deviation is not only evident when the sensor is used by people with advanced CKD although it seems to be greater for this patient group[15]. The surveillance error grid showed that only 66% of FreeStyle Libre values were in the no risk zone whilst 82% of Dexcom G5 values were within the no risk zone.

Participants rated the user experience of the FreeStyle Libre significantly higher than for the Dexcom G5. They found the system easier to use and easier to interpret the data on the receiver. The sensor was more comfortable, and it was less painful to insert. There was a greater interest to use the system in their daily life. This might be different with Dexcom's latest sensors which do not require calibration by the user. It is important to note that the users did not experience any difference of safety when using the system.

The strength of this study is that it was done independently from the manufacturers of this study. The study was done in a real-life environment as patients used the sensors in their daily life. All analyses were predefined. The limitations of this study were the short duration the participants used the sensors, and the evaluation of the user experience might change if the users become more comfortable and confident in the use of the sensors, and the questionnaire used is not validated. For certain subgroup analysis the number of participants or values obtained was low, therefore these analyses have to be interpreted with caution. It should be noted that Dexcom G5 was calibrated with the same capillary method as the reference system, and it cannot be excluded that more novel generations of Dexcom sensors which do not need calibrations may have a greater systematic deviation from HemoCue. Neither Dexcom G5 nor FreeStyle Libre are approved to be used by people with advanced chronic kidney disease. Another limitation is that the most novel sensors often used today were not evaluated. However, these data must be viewed in the light that CGM accuracy data are overall lacking in people with Diabetes and advanced CKD and data are therefore urgently needed.

CONCLUSION

In conclusion, this study supports that Dexcom G5 has a similar accuracy in people with diabetes and advanced CKD as in people with diabetes without advanced CKD. The FreeStyle Libre system showed similar correlations between sensor value and blood glucose values as Dexcom, but a lower number of values in the no risk zone indicating that greater caution should be taken to use it in the current population. The FreeStyle Libre showed a systematic deviation at least partly explaining the lower accuracy.

ARTICLE HIGHLIGHTS

Research background

People with diabetes and advanced chronic kidney disease (CKD) often have fluctuating blood glucose levels and today no blood glucose sensors are approved to be used in this patient group.

Research motivation

It is of great importance to give the best possible care to all people with diabetes. This is a patient group with difficult complications due to their diabetes and need all the help they can get.

Research objectives

The objective of this study was to see if the sensors FreeStyle Libre and Dexcom G5 were accurate when used by people with advanced CKD.

Research methods

This was a non-randomized clinical study. The results were evaluated by using mean absolute relative difference as a main analysis. Mean absolute difference and mean difference was also calculated. A surveillance error grid was even used for accuracy evaluations.

Research results

The main analysis found that the Dexcom G5 had a mean absolute relative difference of 15.2% while it was 20.9% for the FreeStyle Libre. There was no significant difference if the patients were on maintenance dialysis or not. There was no significant difference between those with type 1 or 2 diabetes. The surveillance error grid showed that Dexcom G5 had 82% of its values within the safe zone while FreeStyle Libre had 66% within the safe zone.

Research conclusions

The study concludes that the Dexcom G5 produces more accurate values than the FreeStyle Libre.

Research perspectives

This study is a great start for evaluating how we can use glucose sensors for this patient group, but further studies have to be done with more novel glucose sensors.

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FOOTNOTES

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