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Has subsidised continuous glucose monitoring improved outcomes in paediatric diabetes?

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Running head: Subsidised CGM and outcomes

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Metabolic outcomes in type 1 diabetes (T1D) in childhood and adolescence have improved little over the last 1-2 decades in Australia. In the 1990's and early 2000's, statewide mean/median HbA1Clevels in Western Australia, New South Wales and Queensland were reported to be 8.1%, 8.2% and 8.6% respectively (1-3). In 2017, data from the Australasian Diabetes Database Network (4) from paediatric tertiary centres showed a mean HbA1C level of 8.3% (5). Contemporaneous statewide data from Queensland in 2018 has shown that the mean HbA1C has in fact deteriorated to 9.1% (6). Similarly, static or deteriorating HbA1C outcomes have been reported in other paediatric registries (7). This lack of improvement in outcomes has not been due totherapeutic inertia. Over the last two decades insulin regimens have changed dramatically. Whilst twice daily injections were the norm in the mid to late 1990's (1, 3), nowover 80% of Australian children and adolescents with T1D use either multiple daily injections or insulin pump therapy (5). Such dramatic therapeutic change and effort begs the question- why haven't outcomes improved accordingly?Severe hypoglycaemia (SH) is arguably the most feared acute complication of T1D by patients and care-givers,and its perceived risk is one of the most significant obstacles to tighter metabolic control (8). However, the previous association of lower HbA1C and SH (1)is no longer inevitable (9). Despite this and the relatively low absolute incidence of SH (10), the perception of risk by patients and their care-givers continues (8).

Frequent measurement of blood glucose levels has been known to be associated with improved metabolic outcomes and reduced risk for SH for some time. Devices that could markedly increase the frequency of glycaemic data then could potentially lead to marked benefits in HbA1C levels whilst simultaneously further reducing the risk of SH. Continuous glucose monitoring (CGM) is

astrategy that is being increasingly used in type 1 diabetes (T1D), particularly in paediatric populations(11, 12). The first generation of devices only allowed retrospective data analysis, however iterative technologies have since allowed presentation of tissue glucose levels in real time and with frequent use being reported to be associated with lower HbA1Clevels (13).

In 2017 the Federal Australian Government fully subsidised CGM devices for patients under 21 years of age with T1D, with the aim of reducing rates of severe hypoglycaemia and improving metabolic control (14). The 54 million dollar investment over 4 years was one of the largest clinical initiatives in diabetes management in several decades, and as such there is an imperative for clinical outcome reports. The purpose of this study is to report outcomes associated with the subsidised CGM program at a large tertiary paediatric diabetes centre 24 months after its commencement.

Methods

Institutional research ethics approval was obtained (RCH HREC number QA/47340/RCHM-2018-154334). The study design was observational with both prospective (standardised intervention, pre-defined data fields from a defined subpopulation within our diabetes clinic) and retrospective (data retrieved and analysed post hoc) elements. Data was obtained on patients who commenced CGM between May 2017 andJuly 2019 at our institution. Data collection ceased December 2019 (ie all patients had at least 4 months of CGM use). Comparative data from the RCH Diabetes Clinic was accessed from the Australian Diabetes Database Network (ADDN) website (https://www.addn.org.au/- March 2018) for patient demographic, insulin regimen and HbA1C data.

Data pertaining to episodes of severe hypoglycaemia was obtained by manual chart review over the same time period. This time was chosen because it was the ADDN data load closest to the mid-way point of the CGM commencement period.

Study population

Patients self-referred for CGM use via our hospital website (https://www.rch.org.au/diabetes/). Patients and families had to be eligible for the Federal CGM subsidy (T1D and < 21 years of age) and part of our clinic, otherwise there were no exclusion criteria. Patients were seen in order of their applications.

CGM Education

Relevant webinar materials were produced as a resource for families to use prior to self-referral (https://www.rch.org.au/diabetes/learning-materials/webinars/). After self-referral and once the CGM device had been received, patients and their families attended a 2hour educational session with 1-2 families and adiabetes educator per session. The education included both use of the hardware and CGM data interpretation to achieve optimal glycaemic control. Education was tailored toboth the device chosen and insulin regimens. On-line assessment modules were completed by families prior to an additional follow up appointment, one month after CGM commencement.

Data obtained

Patient and clinical data were extracted from the electronic medical record (EMR) by one researcher (ES) and entered into a Excel database Clinical data were obtained at 4 monthly intervals (aligning with clinic visits) for 12months prior to and up to 24 months after commencing CGM. This data included age, gender, duration of diabetes, insulin regimen, HbA1C, episodes of severe

hypoglycaemia, number of daily finger-prick blood glucose measurements and reported percent time of CGM use (fields of "ceased CGM" or percentage time of use quartiles, eg 0-24%, 25-49% of the time etc estimated from CGM download).

Statistics

Mean HbA1c levels before and after commencing CGM were derived from one to three values up to 12 month period pre- and up to 24 month period post commencement according to available data from the Royal Children's Hospital Epic EMR. Pre- and post CGM patient HbA1C values were investigated by calculating a mean pre- and post-HbA1C value for each patient and then compared using paired samples t-tests. Further, independent samples t-tests were completed to compare HbA1c levels of patients using CGM more than 75% of the time to those using CGM less than 75% of the times at 4, 8, 12, 16, 20 and 24 months after commencing CGM. All statistical analyses were completed using Stata 14.

Results

Patient characteristics are shown in Table 1. Three hundred and forty one patients commenced CGM over the defined study period. This represents approximately 30% of the RCH diabetes clinic population. The mean age was 12.9 years and mean duration of diabetes 6.3 years. The mean baseline HbA_{1C} of the group was 7.8% which was close to the overall clinic mean HbA1C of 8.0%. Two CGM systems were utilised- the Medtronic Guardian Connect/Guardian 2 and the Dexcom G5 devices. The various patient numbers at each follow up time interval are shown in Figure 1.

Cessation and usage rates

Mean active CGM usage rates (any documented use) ranged between 54.4% and 68.4% of the total cohort at the follow up intervals of 4-24 months (Table 2). One in seven youth discontinued use of CGM within 4 months of its initiation; rates of ceasing CGM altogether increased to and remained stable between 27.9% and 32.8% of patients 12-24 months after CGM commencement. In51/74patients,a reason for cessation was recorded. The main reasons cited for cessation were a dislike of wearing the device, followed by technical/alarm issues and site issues (Table 3). The proportion of people who reported they were using their CGM > 75% of the time during the various follow up intervals ranged between 67.3% and 77.3% of CGM users (Table 4).

HbA1c

In the overall cohort HbA1c did not change before or after baseline in patients who continued to use CGM (Figure 2). In this group mean HbA1C values were 7.7%, 7.7%. 7.7%, 7.6%. 7.5% and 7.6% at the follow up intervals of 4, 8, 12, 16, 20 and 24 months respectively (Table 2). Paired samples t-test of the mean HbA1c of individual patients prior to and after commencing CGM showed a p value of 0.9. At baseline 89/341 patients had a mean HbA1C level at target (< 7.0%). The corresponding number of CGM using patients with HbA1C < 7.0% were 64/236 (27.1%), 56/206 (27.2%), 37/165 (22.4%), 27/128 (21.1%), 28/104 (26.9%) and 16/68 (23.5%) at 4, 8, 12, 16, 20 and 24 months respectively.Overall, independent samples t-tests showed CGM use > 75% of the time compared to CGM use <75% of the time, was associated with a significantly lower HbA1C at 4, 16 and 24 months, with p values of 0.01, 0.06, 0.09, 0.02, 0.2, 0.01 at 4, 8, 12, 16, 20 and 24 months respectively (Figure 3). The mean differences in mean HbA1C were 0.4, 0.2, 0.2, 0.3, 0.2 and 0.5 and 95% confidence intervals were 0.1 to 0.70, -0.006 to 0.50, -0.03 to 0.52, 0.04 to 0.57, -0.11 to 0.51 and 0.15 to 0.89 at 4, 8, 12, 16, 20 and 24 months respectively (Figure 3). Mean HbA1C values after CGM start were not

impacted whether patients were younger or older than the group mean age at CGM onset of 12.9 years (Table 5).

Severe hypoglycaemia

In the 12 months prior to starting CGM 17 out of 341 patients had experienced 21 episodes of severe hypoglycaemia (5.0 episodes per 100 patient years) (Table 1). This was not significantly different (p=0.47) from the contemporaneous 'all of clinic' rate of severe hypoglycaemia at RCH of4.1 per 100 patient years (Table 1). In the 24 months after starting CGM there were 20 episodes of severe hypoglycaemia in 19 patients in the overall CGM cohort. Six of these occurred in patients who had ceased CGM, ten episodes occurred in patients whilst using CGM (all in the older patient group, Table 5) and four episodes occurred in patients for which there is no CGM usage data (Table 2). In the 4 months after starting and continuing to use CGM there were 5 episodes of severe hypoglycaemia in 291 patients (5.2 episodes per 100 patient years). The corresponding rates of severe hypoglycaemia in those continuing to use CGM at 8, 12, 16, 20 and 24 months, were 5.1, 1.6, 6.1, 2.4 and 0 per 100 patient years respectively. Eight of the 10 patients who experienced severe hypoglycaemia whilst using CGM were using CGM > 75% of the time when the episodes occurred (Table 4).

Discussion

In this study of outcomes of a fully subsidised CGM initiative with self-referrals and a structured educational program, we have shown little overall impact of CGM on glycaemic control as well as significant rates of cessation and intermittent use over time. Approximately one quarter to one third of patients ceased using CGM after 12 months. In the remainder,more than two thirds used CGM more than 75% of the time at all time points. In the total group of initiators, CGM usage was not associated with any significant change in HbA1C levels at 4, 8, 12, 16, 20, or 24 months, assessed either as mean HbA1C or as percentage with HbA1C < 7.0%. .There may have been a reduction in rates of severe hypoglycaemia over the 24 months follow up period, however theabsolute numbers of events were so low as to preclude meaningful statistical analysis. Interestingly, neither HbA1C outcomes nor rates of severe hypoglycaemia appeared to be consistently influenced by frequent (>75% of the time) use of CGM.

Our results seemingly run counter to the prevailing narrative of clinical utilityof CGM in T1D (15, 16). Given this, both our results and that narrative should be scrutinised. The strengths of our study are its 'real world' context in a large tertiary paediatric diabetes clinic whose metabolic outcomes (RCH mean HbA1c = 8.0%) are reflective of many international centres (17). Data was collected systematically with pre-determined fields through an electronic health record system. Most reported improvement seen afterCGM interventions occur with 3-6 months (18, 19) so our 4-24 month follow up period should have been adequate to observe significant changes in clinical outcomes. Finally we have been using various CGM systems within our diabetes clinic for nearly two decades in clinical care and research, hence our team is experienced in CGM use in a variety of contexts. The limitations of this study relate mostly to operational constraints. The Australian Federal CGM initiative did not support education and diabetes nurse educator time. Additionally, there were no widely accepted,evidence-based education modules for CGM use in the paediatric population. Thus the CGM support given at our hospital may vary from other centres. While this may potentially limit the generalise-ability of our findings, we suspect that our levels of CGM support were not entirely dissimilar to those of other centres after anecdotal reports from colleagues. We note that another short-term audit of the Australian Federal CGM initiative of 55 children also

showed no significant change in either HbA1C or rates of severe hypoglycaemia (20).An additional limitation is that some data points were not recorded by clinicians and hence unable to be included in comparative analyses. These though, were limited to percent of time CGM was used and represented less than 16 percent of the potential data set.We were also unable to record how patients used their CGM devices and whether parents used features such as remote monitoring. Given that patients self-referred, there is also the potential of bias for patients to be unrepresentative of the clinic as a whole- being either highly motivated and technology adept and/ormore afraid of hypoglycaemia. This might be reflected in 32.3% of the CGM starters using CSII compared to 25% of the total clinic population. The incidence of severe hypoglycaemia at baseline in our patient group was 5.0 per 100 patient years compared to the overall clinic figure at the Royal Children's Hospital of4.1episodes per 100 patient years. Both figures are comparable to the cited range of 3-7 per 100 patient years seen in most paediatric T1D registries (8). We were unable to control for these potential factors in our analyses and acknowledge that bias may have been introduced. However, we note that the mean age, duration of diabetes and HbA1C of the CGM cohort at baseline reflect the mean age, duration of diabetes and HbA1C of our clinic as a whole (12.9 vs 13.0 years; 6.3 vs 5.8 years; 7.8% vs 8.0% respectively),so suspect that the impacts of any potential bias in this regard upon metabolic control would have been minimal.

What then of the narrative as to the published benefits of CGM in children and adolescents?One could argue that the foundations of this are less than solid. The 2017 International Consensus statement on CGM cited36 supporting references in favour of CGM,however 22 of these were rated as Level C quality or "Supportive evidence from poorly controlled or uncontrolled studies" (15).What is the highest level (Level A) of evidence in this regard? The earliest randomised controltrial (RCT) data of real-time CGM highlighted that increased use was associated with greater improvements in HbA1C (21). The landmark JDRF CGM RCTsubsequently showed little overall benefit of real time CGM in youth due to high rates of underuse (22). Sub-analyses of this group though showed that after 12 months,in the 17 out of 80 youth who used CGM more than 6 days per week there was a lowering of HbA1Cof 0.9% compared to those who used it less frequently (23). Thus, a threshold of CGM use at least 80-85% of the time to be effective was established. More recent RCT data in US children with slightly better baseline metabolic control (mean baseline HbA1C 7.9%), have shown no

impact of CGM on either HbA1C or rates of severe hypoglycaemia (24). Again, only a minority of patients used CGM at least 6 days per week,but in this study there was no relationship between sensor use and HbA1C level (24).A French RCT showed an improvement in HbA1C of only 0.1% after 3 months in a group of children who used CGM > 80% of the time (25). In this study an unusually high baseline rate of severe hypoglycaemia (29.1 episodes per 100 patient years) was reduced after CGM to a more conventional 3.3 episodes per 100 patient years. Locally, Australian RCT data in primary school-aged children with an apparently higher mean CGM use of 75% (5.25 days per week) again showed no benefit in HbA1C (26).Alternatively, a very recent RCT of CGM use in US adolescents and young adults did show a 0.37% reduction in mean HbA1C from a high baseline value of 8.9 to 8.5% in the intervention group and no change in the control group (27).

Systematic reviews of the benefits of CGM in children and adolescents with T1D by independent health care authorities have beensimilarly underwhelming. The UK National Institutes for Health Care Research review of RCT data compared integrated CGM/CSII to either CGM/MDI or SMBG/CSII combinations. In the case of the CGM/CSII compared to SMBG/MDIthe review concluded that that the integrated CGM/CSII combination resulted in a statistically lower HbA1C (0.5%) with no change in severe hypoglycaemia or quality of life compared to SMBG/MDI. However, when integrated CGM/CSII was compared to SMBG/CSII there was no statistically significant effect upon HbA1C (28).The inference being that when insulin delivery modalities were matched the impact of CGM upon HbA1C was negligible. AWashington State Health Care Authority review of RCT data found that in children, CGM use compared to SMBG was not associated with lower mean HbA1C and it did not increase the number of patients achieving a target HbA1C of < 7.0%. Additionally, CGM use did not ameliorate either overall or severe hypoglycaemic events, DKA or impaired QOL (29).

Anecdotal reports and uncontrolled observations from registries and uncontrolled studies suggest that significant clinical benefits of CGM do appear to be possible in motivated and adherent individuals (13, 16). Some would argue these testimonial reports have been given more weight by

regulatory authorities than would normally occur (30). In reality though, repeated reports of non-acceptability and under-use remain common in children and adolescents (31-35). Our experience of 23% of patients ceasing CGM was less than reportedin the US Type 1 Diabetes Exchange (T1DE),with a 12 month cessation rateof 41% (33), but are nonetheless still very high. The reasons for paediatric and adolescent patients finding CGM unacceptable have been well documented and relate both to operator characteristics, accuracy issuesand lack of perceived benefit (32, 33). An additional factor associated with poor CGM adherence and discontinuation may be lower executive function skills and hence ability to optimally utilise CGM data (35, 36). Of those who remain CGM-users, there appears to be an increasing total reliance on the technology with more than half patients decreasing the frequency of traditional finger-prick testing and only 8-12% of patients reviewing their CGM data weekly (33). Thus outcomes from uncontrolled case series and registry data appear to be highly nuanced according to acceptability and unforeseen changes in patient behaviour. Baseline patient characteristics also appear to be determinative. In 2014 in the 45-55% of T1DE paediatric patients who used CGM > 6 days per week, there was a reported 0.3% reduction in mean HbA1C in young children with no difference seen in adolescents. There were no differences seen in either group for rates of severe hypoglycaemia or DKA (33). More recent data from German/Austrian Diabetes-Patienten-Verlaufsdokumentation (DPV) and T1DE registries between 2011 and 2016 again showed variable outcomes. At all-of-registry levels, despite a 5-7 fold increase in the use of CGM over the follow-up period there was a 0.1% decrease and 0.3% increase in mean HbA1C levels in the DPV and T1DE registries respectively (11).Amongst paediatric patients in the DPV registry (mean baseline HbA1C 7.9%) CGM use was associated with a 0.3% reduction in mean HbA1C, whereas in the T1DE group (mean baseline HbA1C 8.5%) the reductions in were 0.5-0.9%, depending on treatment group (11). The 2019 outcome data from the T1DE are even more impressive, with CGM use associated with mean HbA1C levels that are 0.8-1.0% lower compared to intermittent glucose testing (mean HbA1C of the paediatric patients 8.2-9.2%) (7). Thus in these studies, the greatest benefits are found in the T1DE which has mean HbA1C levels that higher than most national and international comparators (36). At an individual or therapy group level, higher pre-CGM HbA1C has also been associated with a greater HbA1C benefit (7, 11). These disparate improvements in HbA1C between registries and individuals appear to speak to a ‘floor effect’ whereby benefits in HbA1C with CGM diminish in those whose baseline control is better. In cohorts such as that reported in this study,

where baseline mean HbA1C is lower, the HbA1C benefits do not appear to be apparent.Additionally, a limitation of “real-world” observational studies such as ours is the lack of a contemporaneous control group. Given the well-known phenomenon of deteriorating metabolic control through adolescence seen in various registries (37),it is conceivable that CGM usein theolder adolescent half of our cohort may have mitigated against this.

Much is made of the potential of CGM to improve non-glycaemic outcomes such as quality of life, hypoglycaemia awareness and fear of hypoglycaemia (38). Most studies have shown no impact of CGM upon generic or diabetes-specific quality of life scores (39). Similarly several studies have shown little impact of CGM upon specific parental issues such as parental quality of life, fear of hypoglycaemia or diabetes-related distress (38). On the other hand, two recent Australian studies showed that CGM use impacted upon parental QOL with reduced parental fear of hypoglycaemia, parental stress and improved parental sleep quality (20, 26). Although we did not measure quality of life in this study, since many of our patients either ceased CGM use or under-used it, it seems reasonable to assume that quality of life experiences were variable and not universally shared.

Despite international guidelines recommending that CGM be used in all T1D patients not achieving target HbA1C (15), our experience is that CGM has thus far not proved itself to be a therapeutic panacea. Given the high expense of CGM systems, the consistently reported suboptimal rates of effective usage and high rates of cessation, it is logical to consider patient selection in CGM use. It is possible to predict CGM adherence with a high degree of accuracy using demographic and individual factors (40) but in practice this appears to be rarely considered. In out-of-trial contexts, high usage of CGM in of itself does not appear to be a guarantee of improved metabolic or quality of life outcomes. This is perhaps related to issues of over-reliance and non-reflective interpretation of CGM data by some patients who are otherwise avid wearers of the device. This may change in the future with improved education, more discriminating patient selection and potentially improved CGM-dependent hybrid closed loop CSII systems. Although in this instance we have not shown an improvement in HbA1C, other outcomes such as glucose variability or total daily insulin dose, which

were not captured, may be relevant in long term diabetes-related outcomes and would be worth monitoring in future trials.

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Table 1: Baseline patient characteristics at time of commencement of CGM

	RCH Diabetes Clinic	**RCH CGM Cohort**
Number	1123	341
Females (%)	547 (49)	180 (52.8)
Mean age (yrs) [SD]	12.3 [4.0]	12.9 [4.2]
Mean duration of diabetes (yrs) [SD]	5.0 [3.8]	6.3 [3.6]
Mean HbA1C over last 12 months (%) [SD]	8.0 [1.2]	7.8 [1.0]
Using CSII (%)	265 (24%)	110 (32.3)
Total number of SH events	23*	21
Number of patients having at least one SH event	23*	17

*RCH Diabetes Clinic data obtained from the Australasian Diabetes Database Network March 2018 dataset. * All of clinic severe hypoglycaemia data obtained by manual chart review of 1146 patient files from December 2017 to June 2018.*

Figure 1: Number of patients using and not using CGM at 4 month intervals for 24 months. Inclusive of patients for which there is no CGM usage data. *Terminology- "Not using CGM" means that patients had ceased using the CGM completely. "No % usage data" means that patients were recorded as actively using CGM but the amount of time they were wearing the device was not recorded. "Using CGM" means that patients were actively using the device with the percentage of time (1-100%) of use recorded in the EMR.*

Table 2: Interval outcomes at 4, 8, 12, 16, 20 and 24 months

	4 mths	8 mths	12 mths	16 mths	20 mths	24 mths
Total Patient Numbers	**341**	**301**	**261**	**216**	**172**	**125**
Number using CGM 1-100% of the time: (%)	**236 (65.4)**	**206 (68.4)**	**165 (63.2)**	**128 (59.3)**	**104 (60.5)**	**68 (54.4)**
Mean HbA1C [SD]	7.7 [1.0]	7.7 [0.9]	7.7 [1.0]	7.6 [0.8]	7.5 [0.9]	7.6 [0.8]
Number with HbA1C < 7.0% (%)	64 (27.1)	56 (27.2)	37 (22.4)	27 (21.1)	28 (26.9)	16 (23.5)
Number of SH events	2	4	1	3	0	0
Number of patients having at least one SH event	2	3	1	3	0	0
Number using CSII (%)	71 (30.0)	70 (34.0)	61 (37.0)	55 (43.0)	47 (45.2)	32 (47.1)
Number ceased CGM (%)	**50 (14.7)**	**65 (21.6)**	**73 (27.9)**	**68 (31.5)**	**49 (28.5)**	**41 (32.8)**
Mean HbA1C [SD]	8.0 [1.5]	8.2 [1.4]	7.9 [1.3]	7.8 [1.1]	7.9 [1.0]	8.1 [1.2]
Number with HbA1C < 7.0% (%)	13 (26.0)	11 (16.9)	17 (23.2)	17 (25.0)	10 (20.4)	6 (14.6)
Number of SH events	1	0	0	2	3	0
Number of patients having at least one SH event	1	0	0	2	3	0
Number using CSII (%)	15 (30.0)	17 (26.1)	33 (45.2)	32 (47.0)	21 (42.9)	19 (46.3)
Number using CGM but no data on amount of usage (%)	**55 (16.1)**	**30 (10.0)**	**23 (8.8)**	**20 (9.3)**	**19 (11.0)**	**16 (12.8)**
Mean HbA1C [SD]	7.8 [1.2]	7.9 [1.7]	7.4 [0.9]	7.4 (1.2)	7.4 (1.0)	7.1 (0.9)
Number with HbA1C < 7.0% (%)	13 (23.6)	7 (23.3)	8 (34.8)	7 (35.0)	7 (36.8)	8 (50.0)
Number of SH events	3	0	0	0	1	0
Number of patients	3	0	0	0	1	0

having at least one SH event						
Number using CSII (%)	14 (25.5)	7 (23.3)	2 (8.7)	3 (15.0)	6 (31.6)	11 (68.8)

Table 3: Reasons cited for stopping CGM

Main Reason for Stopping CGM	Number of Patients
Didn't like wearing device	21
Technical issues and alarms	11
Sensor site painful or annoying	9
Tape allergies or irritation	8
Insertion issues	2
Unknown/non-specific	23
Total	**74**

74 = the total number of patients who stopped using CGM by the time data collection stopped

Table 4: Percent usage CGM and outcomes at 4, 8, 12, 16, 20 and 24 months

	4 mths	**8 mths**	**12 mths**	**16 mths**	**20 mths**	**24 mths**
Total Patient Numbers	**236**	**206**	**165**	**128**	**104**	**68**
Using CGM 1-24% of the time (%)	**18 (7.6)**	**22 (10.7)**	**10 (6.1)**	**7 (7.8)**	**7 (6.7)**	**2 (2.9)**
Mean HbA1C [SD]	8.2 [0.8]	7.6 [0.9]	8.3 [1.0]	7.7 [0.8]	7.4 [0.8]	7.7 [0.2]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0
Using CGM 25-49% of the time (%)	**20 (8.5)**	**8 (3.9)**	**8 (4.8)**	**5 (3.9)**	**6 (5.8)**	**2 (2.9)**
Mean HbA1C [SD]	7.6 [1.2]	7.6 [0.8]	7.8 [0.4]	7.4 [0.3]	7.6 [0.6]	8.0 [0.1]
Number of SH events	0	2	0	0	0	0
Number of patients having at least one SH event	0	2	0	0	0	0
Using CGM 50-74% of the time (%)	**19 (8.1)**	**17 (8.3)**	**11 (6.7)**	**8 (6.3)**	**5 (4.8)**	**5 (7.4)**
Mean HbA1C [SD]	7.2 [0.7]	7.8 [1.0]	7.9 [0.8]	7.9 [0.8]	7.6 [0.4]	8.1 [0.5]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0
Using CGM 75-100% of the time (%)	**166 (70.3)**	**149 (72.3)**	**124 (75.1)**	**99 (77.3)**	**70 (67.3)**	**50 (73.5)**
Mean HbA1C [SD]	7.6 [0.9]	7.7 [0.9]	7.7 [1.0]	7.5 [0.8]	7.5 [0.9]	7.5 [0.8]
Number of SH events	2	2	1	3	0	0
Number of patients having at least one SH event	2	1	1	3	0	0
Using CGM – active but amount unspecified (%)	**13 (5.5)**	**10 (4.9)**	**12 (7.3)**	**9 (0.7)**	**16 (15.4)**	**9 (13.2)**
Mean HbA1C [SD]	7.8 [1.2]	7.4 [1.1]	7.4 [1.2]	8.1 [1.0]	7.4 [1.0]	7.6 [0.9]
Number of SH events	0	0	0	0	0	0
Number of patients	0	0	0	0	0	0

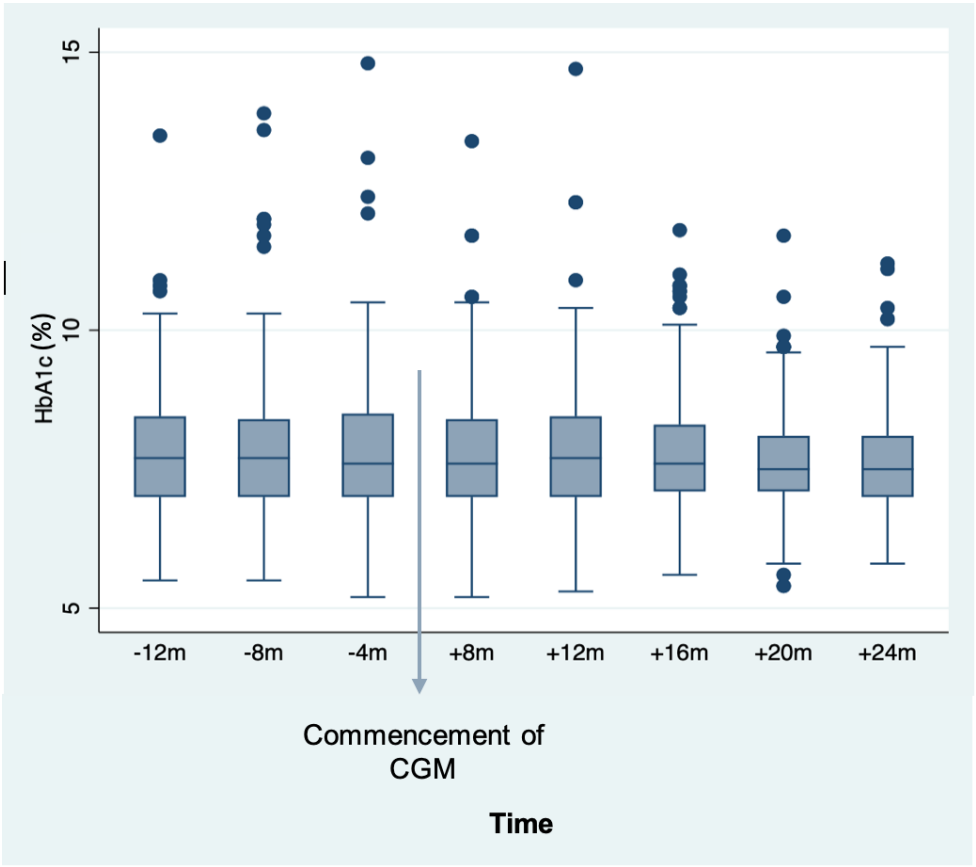
having at least one SH event						

Table 5: Clinical outcomes in CGM users above and below the mean age of 12.9 years at CGM start

	4 mths	**8 mths**	**12 mths**	**16 mths**	**20 mths**	**24 mths**
Total Patient Numbers	**236**	**206**	**165**	**128**	**104**	**68**
Less than or equal to 12.9 years old, using CGM 1-100% of the time (%)	**122 (51.7)**	**100 (48.5)**	**83 (50.3)**	**63 (49.2)**	**55 (52.9)**	**39 (57.4)**
Mean HbA1C [SD]	7.7 [0.9]	7.7 [0.8]	7.7 [1.0]	7.6 [0.8]	7.3 [0.8]	7.5 [0.7]
Number of SH events	0	0	0	0	0	0

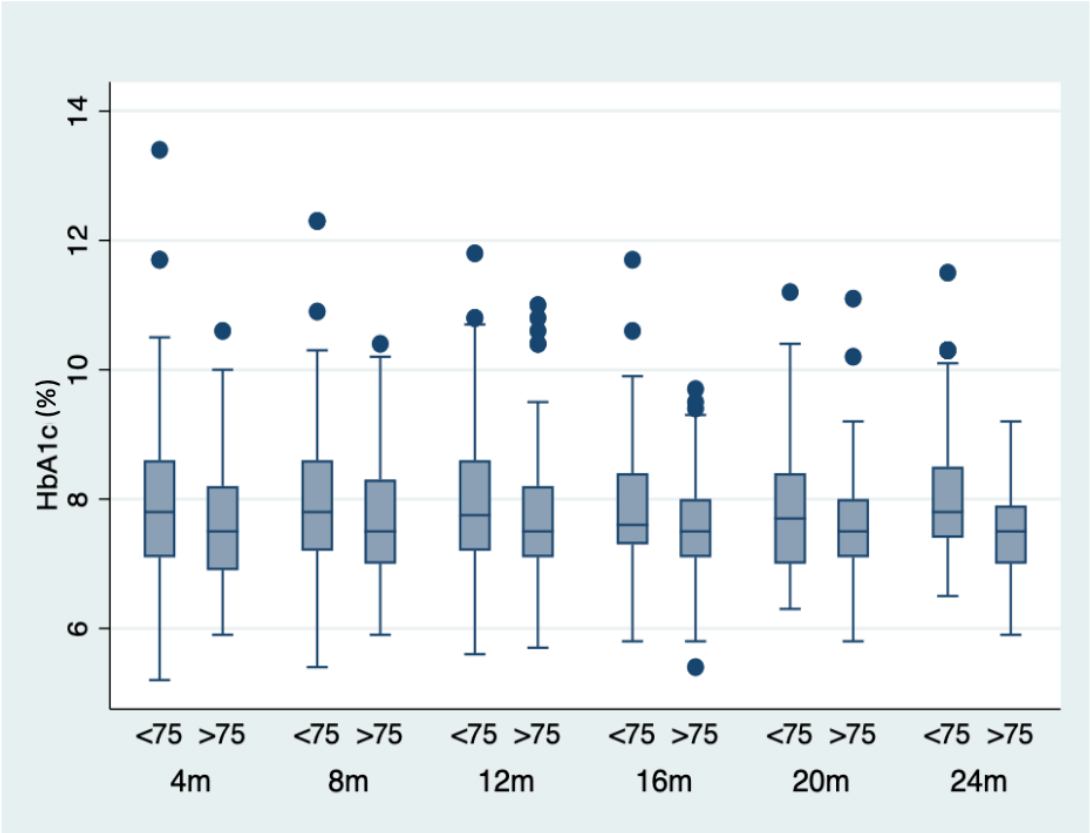
Number of patients having at least one SH event	0	0	0	0	0	0
Greater than 12.9 years old, using CGM 1-100% of the time (%)	**114 (48.3)**	**106 (51.5)**	**82 (49.7)**	**65 (50.8)**	**49 (47.1)**	**29 (42.6)**
Mean HbA1C [SD]	7.7 [0.9]	7.7 [1.0]	7.7 [1.0]	7.6 [0.8]	7.7 [1.0]	7.8 [0.8]
Number of SH events	2	4	1	3	0	0
Number of patients having at least one SH event	2	3	1	3	0	0

Figure 2: HbA1c of CGM users with 12 months of continuous usage, 12 months before and 24 months after commencement of CGM – inclusive of Patients Using CGM 1-100% of the time



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers.

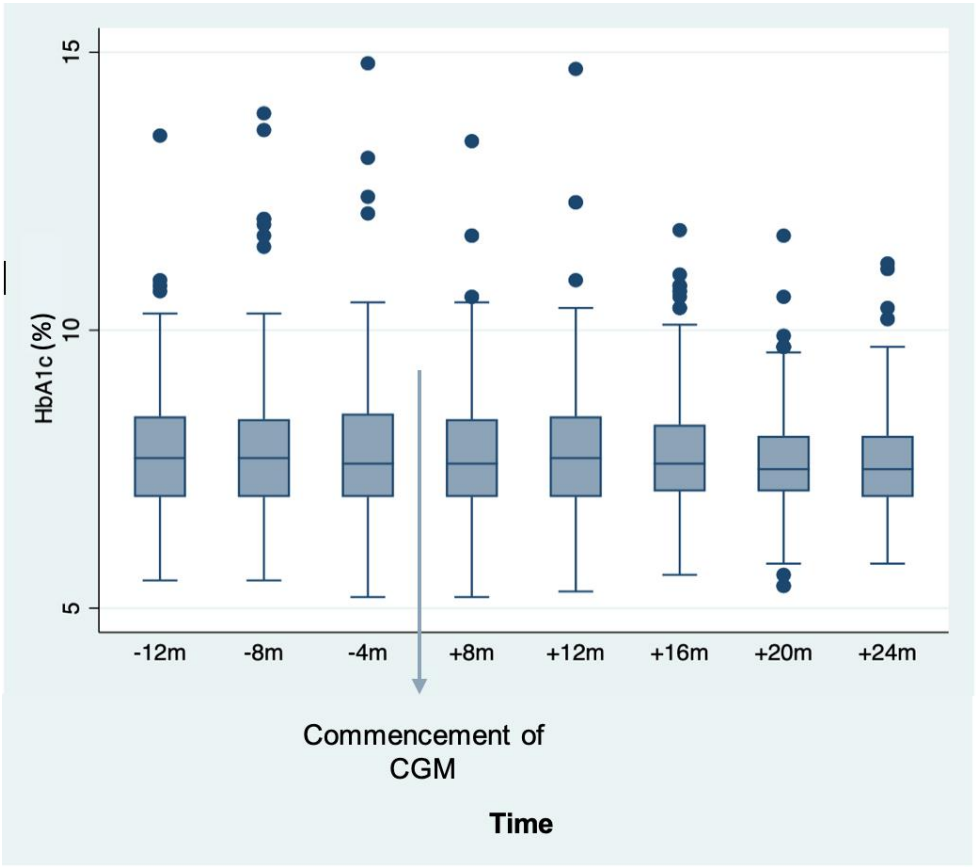
Figure 3: HbA1C of Patients Using CGM more or less than 75% of the time at 4 month intervals after CGM commencement



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers. P < 0.05 at 4, 16 and 24 months.

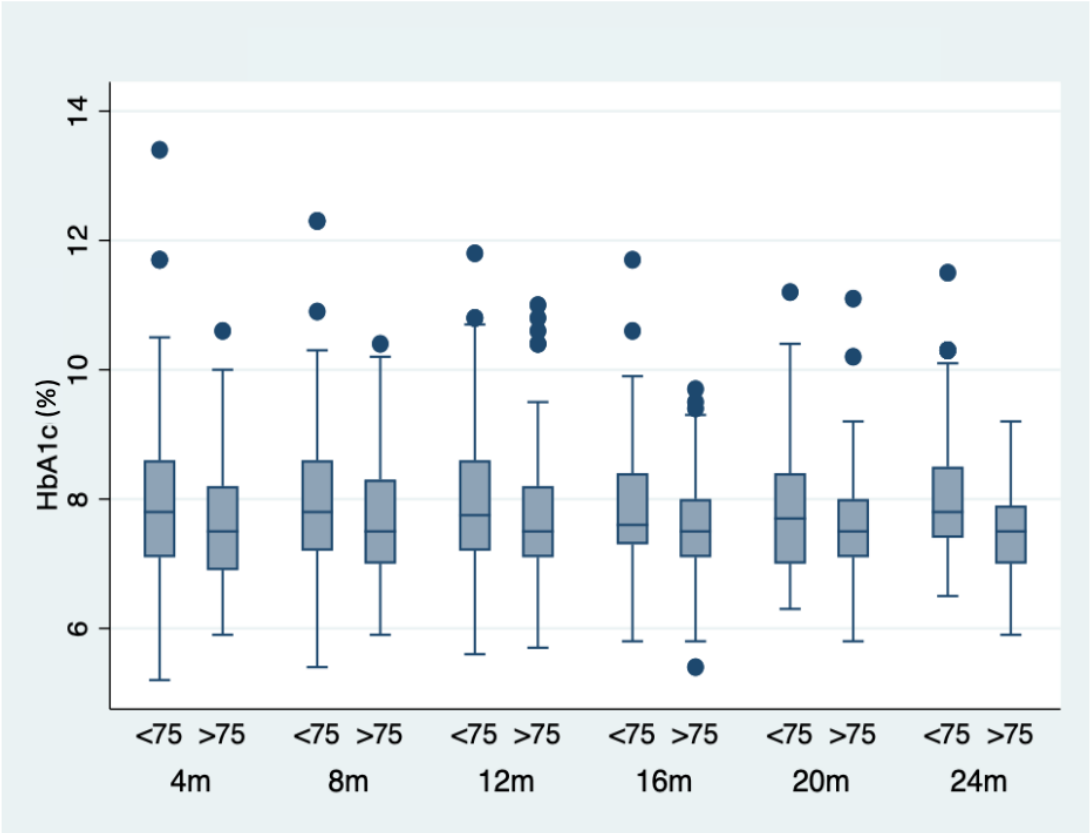
Figure 1: Number of patients using and not using CGM at 4 month intervals for 24 months. Inclusive of patients for which there is no CGM usage data. *Terminology- "Not using CGM" means that patients had ceased using the CGM completely. "No % usage data" means that patients were recorded as actively using CGM but the amount of time they were wearing the device was not recorded. "Using CGM" means that patients were actively using the device with the percentage of time (1-100%) of use recorded in the EMR.*

Figure 2: HbA1c of CGM users with 12 months of continuous usage, 12 months before and 24 months after commencement of CGM – inclusive of Patients Using CGM 1-100% of the time



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers.

Figure 3: HbA1C of Patients Using CGM more or less than 75% of the time at 4 month intervals after CGM commencement



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers. P < 0.05 at 4, 16 and 24 months.

Table 1: Baseline patient characteristics at time of commencement of CGM

	RCH Diabetes Clinic	**RCH CGM Cohort**
Number	1123	341
Females (%)	547 (49)	180 (52.8)
Mean age (yrs) [SD]	12.3 [4.0]	12.9 [4.2]
Mean duration of diabetes (yrs) [SD]	5.0 [3.8]	6.3 [3.6]
Mean HbA1C over last 12 months (%) [SD]	8.0 [1.2]	7.8 [1.0]
Using CSII (%)	265 (24%)	110 (32.3)
Total number of SH events	23*	21
Number of patients having at least one SH event	23*	17

*RCH Diabetes Clinic data obtained from the Australasian Diabetes Database Network March 2018 dataset. * All of clinic severe hypoglycaemia data obtained by manual chart review of 1146 patient files from December 2017 to June 2018.*

Figure 1: Number of patients using and not using CGM at 4 month intervals for 24 months. Inclusive of patients for which there is no CGM usage data. *Terminology- "Not using CGM" means that patients had ceased using the CGM completely. "No % usage data" means that patients were recorded as actively using CGM but the amount of time they were wearing the device was not recorded. "Using CGM" means that patients were actively using the device with the percentage of time (1-100%) of use recorded in the EMR.*

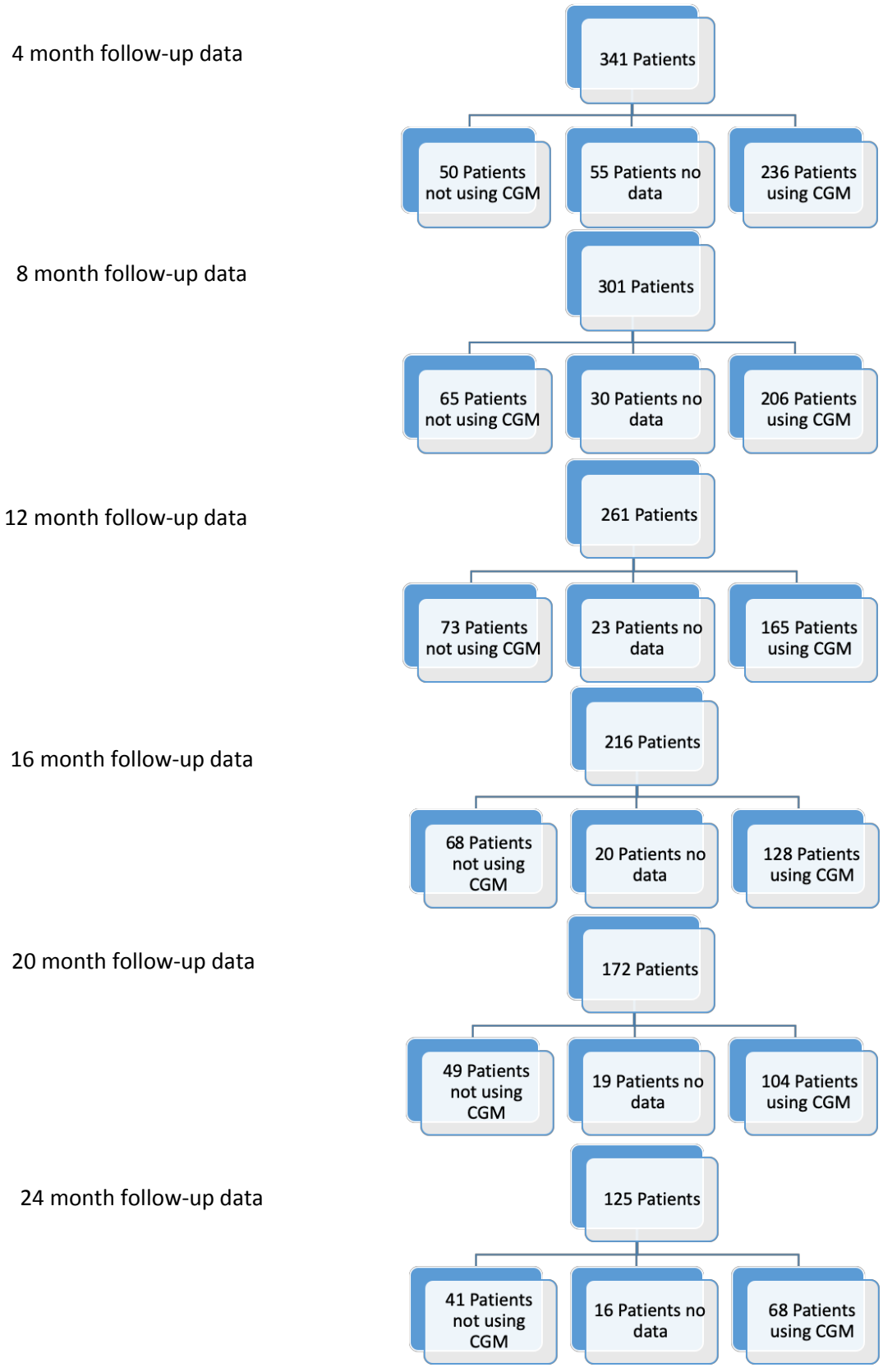


Table 2: Interval outcomes at 4, 8, 12, 16, 20 and 24 months

	4 mths	8 mths	12 mths	16 mths	20 mths	24 mths
Total Patient Numbers	**341**	**301**	**261**	**216**	**172**	**125**
Number using CGM 1-100% of the time: (%)	**236 (65.4)**	**206 (68.4)**	**165 (63.2)**	**128 (59.3)**	**104 (60.5)**	**68 (54.4)**
Mean HbA1C [SD]	7.7 [1.0]	7.7 [0.9]	7.7 [1.0]	7.6 [0.8]	7.5 [0.9]	7.6 [0.8]
Number with HbA1C < 7.0% (%)	64 (27.1)	56 (27.2)	37 (22.4)	27 (21.1)	28 (26.9)	16 (23.5)
Number of SH events	2	4	1	3	0	0
Number of patients having at least one SH event	2	3	1	3	0	0
Number using CSII (%)	71 (30.0)	70 (34.0)	61 (37.0)	55 (43.0)	47 (45.2)	32 (47.1)
Number ceased CGM (%)	**50 (14.7)**	**65 (21.6)**	**73 (27.9)**	**68 (31.5)**	**49 (28.5)**	**41 (32.8)**
Mean HbA1C [SD]	8.0 [1.5]	8.2 [1.4]	7.9 [1.3]	7.8 [1.1]	7.9 [1.0]	8.1 [1.2]
Number with HbA1C < 7.0% (%)	13 (26.0)	11 (16.9)	17 (23.2)	17 (25.0)	10 (20.4)	6 (14.6)
Number of SH events	1	0	0	2	3	0
Number of patients having at least one SH event	1	0	0	2	3	0
Number using CSII (%)	15 (30.0)	17 (26.1)	33 (45.2)	32 (47.0)	21 (42.9)	19 (46.3)
Number using CGM but no data on amount of usage (%)	**55 (16.1)**	**30 (10.0)**	**23 (8.8)**	**20 (9.3)**	**19 (11.0)**	**16 (12.8)**
Mean HbA1C [SD]	7.8 [1.2]	7.9 [1.7]	7.4 [0.9]	7.4 (1.2)	7.4 (1.0)	7.1 (0.9)
Number with HbA1C < 7.0% (%)	13 (23.6)	7 (23.3)	8 (34.8)	7 (35.0)	7 (36.8)	8 (50.0)
Number of SH events	3	0	0	0	1	0
Number of patients having at least one SH event	3	0	0	0	1	0
Number using CSII (%)	14 (25.5)	7 (23.3)	2 (8.7)	3 (15.0)	6 (31.6)	11 (68.8)

Table 3: Reasons cited for stopping CGM

Main Reason for Stopping CGM	Number of Patients
Didn't like wearing device	21
Technical issues and alarms	11
Sensor site painful or annoying	9
Tape allergies or irritation	8
Insertion issues	2
Unknown/non-specific	23
Total	**74**

74 = the total number of patients who stopped using CGM by the time data collection stopped

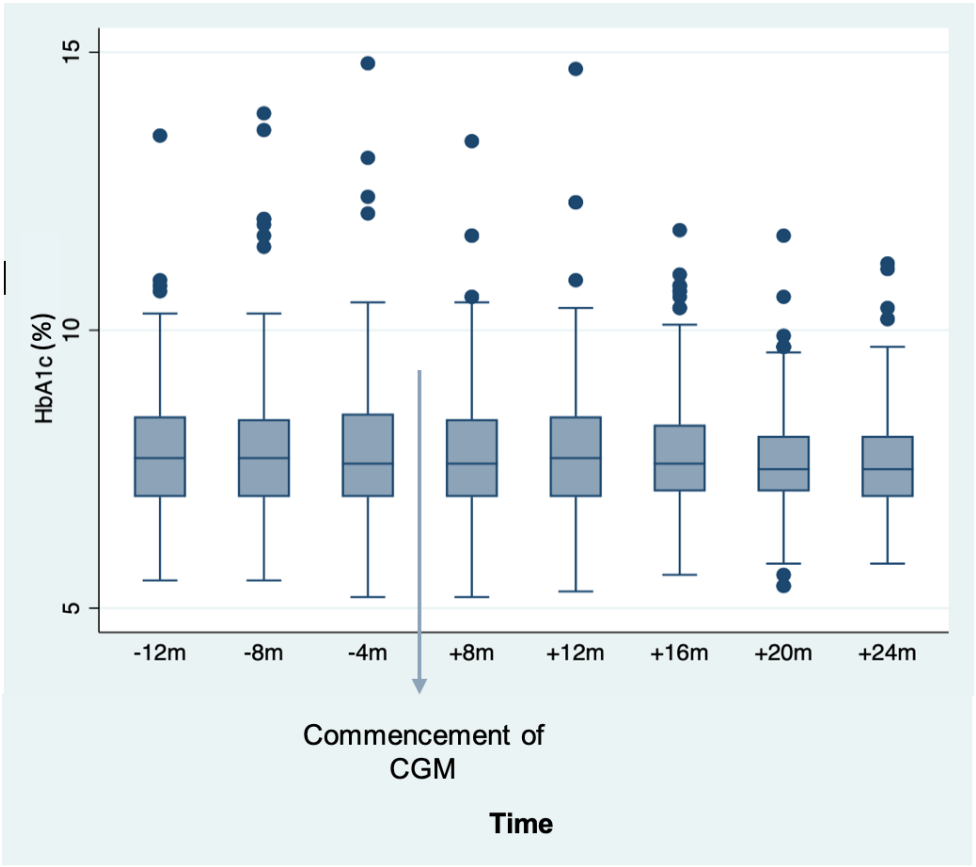
Table 4: Percent usage CGM and outcomes at 4, 8, 12, 16, 20 and 24 months

	4 mths	**8 mths**	**12 mths**	**16 mths**	**20 mths**	**24 mths**
Total Patient Numbers	**236**	**206**	**165**	**128**	**104**	**68**
Using CGM 1-24% of the time (%)	**18 (7.6)**	**22 (10.7)**	**10 (6.1)**	**7 (7.8)**	**7 (6.7)**	**2 (2.9)**
Mean HbA1C [SD]	8.2 [0.8]	7.6 [0.9]	8.3 [1.0]	7.7 [0.8]	7.4 [0.8]	7.7 [0.2]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0
Using CGM 25-49% of the time (%)	**20 (8.5)**	**8 (3.9)**	**8 (4.8)**	**5 (3.9)**	**6 (5.8)**	**2 (2.9)**
Mean HbA1C [SD]	7.6 [1.2]	7.6 [0.8]	7.8 [0.4]	7.4 [0.3]	7.6 [0.6]	8.0 [0.1]
Number of SH events	0	2	0	0	0	0
Number of patients having at least one SH event	0	2	0	0	0	0
Using CGM 50-74% of the time (%)	**19 (8.1)**	**17 (8.3)**	**11 (6.7)**	**8 (6.3)**	**5 (4.8)**	**5 (7.4)**
Mean HbA1C [SD]	7.2 [0.7]	7.8 [1.0]	7.9 [0.8]	7.9 [0.8]	7.6 [0.4]	8.1 [0.5]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0
Using CGM 75-100% of the time (%)	**166 (70.3)**	**149 (72.3)**	**124 (75.1)**	**99 (77.3)**	**70 (67.3)**	**50 (73.5)**
Mean HbA1C [SD]	7.6 [0.9]	7.7 [0.9]	7.7 [1.0]	7.5 [0.8]	7.5 [0.9]	7.5 [0.8]
Number of SH events	2	2	1	3	0	0
Number of patients having at least one SH event	2	1	1	3	0	0
Using CGM – active but amount unspecified (%)	**13 (5.5)**	**10 (4.9)**	**12 (7.3)**	**9 (0.7)**	**16 (15.4)**	**9 (13.2)**
Mean HbA1C [SD]	7.8 [1.2]	7.4 [1.1]	7.4 [1.2]	8.1 [1.0]	7.4 [1.0]	7.6 [0.9]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0

Table 5: Clinical outcomes in CGM users above and below the mean age of 12.9 years at CGM start

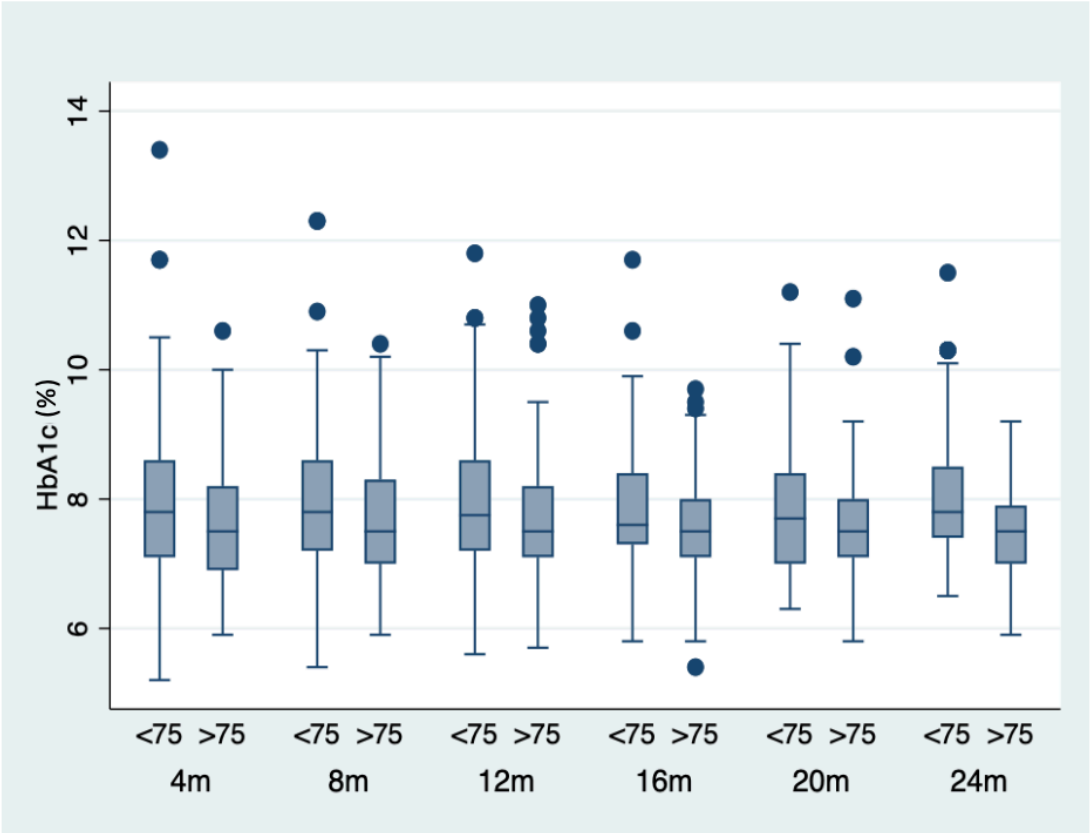
	4 mths	**8 mths**	**12 mths**	**16 mths**	**20 mths**	**24 mths**
Total Patient Numbers	**236**	**206**	**165**	**128**	**104**	**68**
Less than or equal to 12.9 years old, using CGM 1-100% of the time (%)	**122 (51.7)**	**100 (48.5)**	**83 (50.3)**	**63 (49.2)**	**55 (52.9)**	**39 (57.4)**
Mean HbA1C [SD]	7.7 [0.9]	7.7 [0.8]	7.7 [1.0]	7.6 [0.8]	7.3 [0.8]	7.5 [0.7]
Number of SH events	0	0	0	0	0	0
Number of patients having at least one SH event	0	0	0	0	0	0
Greater than 12.9 years old, using CGM 1-100% of the time (%)	**114 (48.3)**	**106 (51.5)**	**82 (49.7)**	**65 (50.8)**	**49 (47.1)**	**29 (42.6)**
Mean HbA1C [SD]	7.7 [0.9]	7.7 [1.0]	7.7 [1.0]	7.6 [0.8]	7.7 [1.0]	7.8 [0.8]
Number of SH events	2	4	1	3	0	0
Number of patients having at least one SH event	2	3	1	3	0	0

Figure 2: HbA1c of CGM users with 12 months of continuous usage, 12 months before and 24 months after commencement of CGM – inclusive of Patients Using CGM 1-100% of the time



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers.

Figure 3: HbA1C of Patients Using CGM more or less than 75% of the time at 4 month intervals after CGM commencement



Standard box plot legend- whiskers show maximum and minimum values with boxes showing first to third quartiles and median results. Solid dots represent outliers. P < 0.05 at 4, 16 and 24 months.