

An Economic Evaluation of Continuous Glucose Monitoring for People with Type 1 Diabetes and Impaired Awareness of Hypoglycaemia within North West London Clinical Commissioning Groups in England

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Objective: To assess the economic impact of providing real time continuous glucose monitoring (CGM) for people with type 1 diabetes (T1D) and impaired awareness of hypoglycaemia (IAH) within North West (NW) London clinical commissioning groups (CCGs). **Methods:** The eligible population for CGM and inputs for the economic budget impact model developed were derived from published data. The model includes cost of CGM; cost savings associated with lower hypoglycaemia related hospital admissions, accidents and emergency visits; self-monitoring of blood glucose (SMBG) strip usage; and glycated haemoglobin (HbA1c) reduction-related avoided complications and insulin pump use. **Results:** The cost of CGM for T1D-IAH (n=3,036) in the first year is £10,770,671 and in the fourth year is £11,329,095. The combined cost off-sets related to reduced hypoglycaemia admissions, SMBG strip usage and complications are £8,116,912 and £8,741,026 in years one and four, respectively. The net budget impact within the NW London CCGs is £2,653,760; £2,588,068 in years one and four respectively. **Conclusions:** Introduction of CGM for T1D-IAH patients will have a minimal budget impact on NW London CCGs, driven by cost of CGM and offsets from lower hypoglycaemia-related costs, reduced SMBG strip usage, avoided HbA1c-related complications and lower insulin pump use.

Keywords

Continuous glucose monitoring, economics, type 1 diabetes, clinical commissioning group

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About 10% of adults with diabetes in the United Kingdom (UK) have type 1 diabetes (T1D) and are treated by daily insulin doses – taken either by injections or via an insulin pump.¹ Diabetes is a leading cause of morbidity and mortality and is associated with substantial healthcare and societal costs. The cost of diabetes to the National Health Service (NHS) is over £1.5m an hour or 10% of the total NHS budget for England and Wales. This equates to over £25,000 being spent on diabetes every minute.² Intensive therapy that lowers average glucose levels has been shown to reduce the risk of the long-term complications of diabetes but it also increases the risk of hypoglycaemia,^{3–5} which results in significant morbidity and mortality and may cause fear of hypoglycaemia which is a major barrier to optimising glucose control.²

Real-time continuous glucose monitoring (CGM) is the most advanced glucose monitoring technology that continuously measures interstitial glucose levels, displays the current glucose level and direction and rate of change, and uses alarms and alerts to inform patients and caregivers when glucose levels are exceeding or falling below specified thresholds.^{6,7} This complete picture of glycaemic activity helps guide diabetes management decisions (e.g., insulin dosage adjustments, changes in diet) to avoid glycaemic excursions.^{6,7} In the recently conducted DIAMOND randomised controlled trial (RCT) in T1D participants on multiple daily injections (MDI) with a mean baseline glycated haemoglobin (HbA1c) of 70 mmol/mol (8.6%), there was a 10.9 mmol/mol (1%) demonstrated reduction in HbA1c for the CGM group compared with 4.4 mmol/mol (0.4%) reduction in the self-monitoring of blood glucose (SMBG) group at 24 weeks from baseline. Participants in the CGM group also spent significantly less time (p=0.002) in hypoglycaemia (duration of hypoglycaemia) at <2.8 mmol/L, <3.3 mmol/L and <3.9 mmol/L; had a significant reduction in diabetes distress (p<0.001); less fear of hypoglycaemia (p=0.02); and an increase in hypoglycaemia confidence (p<0.001) and well-being (p=0.01), compared with conventionally monitored patients using SMBG alone.^{8,9} Similarly, in the GOLD RCT, T1D participants on MDI and HbA1c above target, a significant reduction in HbA1c was seen using CGM compared with SMBG alone.¹⁰

Recurrent hypoglycaemia induces a maladaptive response that impairs the ability of patients to detect the early warning signs of hypoglycaemia, a condition known as impaired awareness of hypoglycaemia (IAH). IAH significantly increases the risk of severe hypoglycaemia, which requires assistance from a third party to treat¹¹ and often requires costly emergency medical care.¹² Tools are needed that can help people with insulin-treated diabetes to lower their blood glucose levels

Table 1: Target population

Parameter	Age <16 years	Age ≥16 years	Reference
NW London CCGs Population	390,037	1,737,909	16
Persons with diabetes*		145,564	17
Prevalence of T1D	0.19%	10%	18, 1
Prevalence of IAH in T1D	29%	20%	19, 20

*The estimate of prevalence of T1D in children in England is 187.7 per 100,000. Number of T1D patients was directly estimated from the population aged <16 years in NW London CCGs. This is because the diabetes prevalence model estimates for local authorities by Public Health England gave the prevalence estimates for population ≥16 years only so the prevalence estimates for population <16 years had to be derived separately. CCGs = clinical commissioning groups; IAH = impaired awareness of hypoglycaemia; T1D = type 1 diabetes.

without increasing their risk of hypoglycaemia, which can potentially reduce the incidence of severe hypoglycaemia in people at risk for this costly and potentially fatal adverse event. For people with IAH, the alarm function of CGM devices may be their only warning of emerging hypoglycaemia. In contrast, traditional fingerstick SMBG, which provides intermittent and limited information about blood glucose concentrations at single point in time,^{6,13} may fail to detect any potentially dangerous glycaemic excursions even when diligently performed.^{6,7}

The National Institute for Health and Care Excellence (NICE) recommends the use of CGM in their NG17 guidelines for adults with T1D who have any of the following despite optimised use of insulin therapy and conventional SMBG: 1. more than one episode a year of severe hypoglycaemia with no obviously preventable precipitating cause; 2. complete loss of awareness of hypoglycaemia; 3. frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities; 4. extreme fear of hypoglycaemia and 5. hyperglycaemia (HbA1c level of 75 mmol/mol [9%] or higher) that persists despite SMBG testing at least 10 times a day.¹⁴

In 2016, the North West London clinical commissioning groups (NW London CCGs) board approved a proposal to commission CGM for a defined cohort of T1D patients, in line with NICE NG17.¹⁵

With access to CGM secured in NW London CCGs, this study specifically estimates the budget impact of providing CGM for the highest-risk subgroup of T1D patients with IAH.

Methods

Model structure

This analysis evaluates the budgetary impact of providing CGM devices with alarms for people with T1D and IAH within NW London CCGs in England over a 4-year period. The starting cohort for the model was the entire population of NW London CCGs of Brent, Hillingdon, Harrow, Hounslow, Ealing, West London, Central London, Hammersmith and Fulham. The model was developed using Microsoft Excel (version 2016).

Using the data on age-distribution and diabetes prevalence within these CCGs, a cohort of people with T1D was created from the starting population. Finally, using the prevalence of IAH, the model arrived at the target population of people with both T1D and IAH. Age-specific and T1D-specific severe hypoglycaemia event rates were applied to the model cohort (references listed in *Table 1*). The model included only direct costs due to severe hypoglycaemia related health services utilisation such as ambulance call-outs, emergency attendance and hospital admissions. Costs related to SMBG as well as direct costs related to progression

Table 2: Clinical/outcomes inputs

	Value	Source
Average number of severe hypoglycaemic events per year in T1D children	0.32	20–23
Average number of severe hypoglycaemic events per year in T1D adults	1	24–31
Increased risk for severe hypoglycaemia among patients with hypoglycaemia unawareness	6-fold	19, 32
Severe hypoglycaemic events requiring ambulance	86%	48
Severe hypoglycaemic events requiring accident and emergency	59%	48
Severe hypoglycaemic events requiring hospital admissions	20%	48
Reduction in severe hypoglycaemic events conferred by CGM	59%	33
Reduction in HbA1c conferred by CGM versus SMBG	0.6%	8
SMBG group: Frequency of fingersticks use	*8	49
CGM intervention group: Frequency of fingersticks use	2.8	38
Avoided pump usage every year	30%	36, 8

*NICE guideline NG18 recommends self-monitoring ≥5 times per day in children, and one study in the report had a 90th percentile frequency of SMBG of 37/week. The target population will have diabetes that is more difficult to manage than average, and many will wish to test more often because of a fear of hypoglycaemia. On this basis, the model assumes a testing frequency of eight per day. CGM = continuous glucose monitoring; HbA1c = glycated haemoglobin; SMBG = self-monitoring of blood glucose; T1D = type 1 diabetes.

to complications and insulin pump usage in the short-term were also included in the model.

The number of severe hypoglycaemic (SH) events, the number of finger sticks used for SMBG by persons with diabetes (PwD)-IAH, and associated costs, were evaluated for both the non-intervention (SMBG only) and CGM intervention scenarios. For the CGM intervention scenario, reductions in rates of SH events were applied to the base case event rates. This rate of reduction was based on published clinical trials (references listed in *Table 2*). Sensitivity analyses were conducted by varying key model inputs and assumptions in order to assess the robustness of the model results.

Model inputs and parameter assumptions

The population of NW London CCGs was derived from the general practitioner (GP) registrations used by NHS England to build the financial allocation model for 2016–2017 budgets. The registrations represent all age-groups so that the population registered are adjusted to equal the NHS England estimate of actual population.¹⁶

The prevalence of diabetes in persons over 16 years of age was estimated from the diabetes prevalence model estimates for local authorities by Public Health England.¹⁷ Of these, 10% of the diabetes patients were estimated to have T1D.¹ The prevalence of T1D in children was estimated to be 187.7 per 100,000 people based on National Paediatric Diabetes Audit report.¹⁸ For persons with T1D, it was estimated that 20% of the persons over or equal to 16 years of age and 29% of the persons under 16 years of age have IAH based on published literature (*Table 1*).^{19,20}

Thus, the target population for this budget impact analysis was PwD-IAH. The incidence of SH events for T1D was derived from published literature. Five studies of children and adolescents with T1D have reported rates of severe hypoglycaemia ranging from 0.16–0.38 episodes per patient-year.^{20–23} The median incidence rate from these studies was 0.32 per patient-year after pooling the patients together. This is very close to the incidence rate for severe hypoglycaemia seen in the Katz et al. study that included children up to 15 years of age (0.38 per patient-

year).²³ Incidence rates for severe hypoglycaemia in adults with T1D range from 0.7–3.2 events per patient-year, with most studies reporting an incidence of ~1 episode per patient-year.^{24–31} Based on the review of the evidence published in literature, we assumed the annual rate of severe hypoglycaemia in the general adult T1DM population to be ~1 episode per patient-year, which we believe is a conservative estimate. It was assumed that on average children with T1D experience 0.32 SH events and adults experience one SH episode per year. Importantly, for this model, people that have IAH will have a six-fold increase in risk for hypoglycaemia.^{19,32}

The percentage of SH events resulting in hospitalisations, accident and emergency (A&E) visits and ambulance call-outs were derived from a UK study and are shown in *Table 2*. The IN-CONTROL trial, a randomised, open-label crossover study, found that CGM reduced the incidence of SH events by 59% in PwD-IAH,³³ which is what was used in the analyses. All other key inputs can be seen in *Table 2*. In the recently conducted DIAMOND RCT in people with T1D on MDI, patients who received CGM had a 6.6 mmol/mol (0.6%) greater reduction in HbA1c compared to those who used SMBG.⁹ Long-term (~11 years) follow-up data from studies such as the Diabetes Control and Complications Trial (DCCT) demonstrate that compared with patients who received conventional diabetes management, patients who were intensively treated during the DCCT experienced a significant (42%) reduction in cardiovascular (CV) events as well as a significant (57%) decrease in non-fatal myocardial infarctions, strokes, and CV deaths.³⁴ Analyses performed 20 years after the DCCT showed that a mean of 6.5 years of intensive therapy aimed at achieving near-normal glucose levels reduced the risk of development and progression of retinopathy by as much as 76% compared with conventional therapy.³⁵

The NICE guidance recommends insulin pump for T1D adults and children 12 years and older provided that: 1. attempts to achieve target HbA1c levels with MDI result in the person experiencing disabling hypoglycaemia, or 2. HbA1c levels have remained high (that is, at 8.5% [69 mmol/mol] or above) on MDI therapy (including, if appropriate, the use of long-acting insulin analogues) despite a high level of care.³⁶ In the DIAMOND RCT, 52% of the MDI patients with HbA1c \geq 8.5% at the baseline achieved target blood glucose control at the end of 24 weeks of the trial.⁹ However, clinical trials are conducted in a well-controlled environment, so in this analysis, it is conservatively assumed that in the real world, as a result of using CGM with MDI, glycaemic targets will be attained (based on DIAMOND RCT) and 30% of the T1D-IAH population will not progress to insulin pump. In our model, we estimated the number of T1D patients ages <16 years and \geq 16 years requiring insulin pump every year within NW London CCGs based on new pump prevalence from the insulin pump audit report for all of England.³⁷

The Dexcom G5[®] Mobile CGM System (San Diego, CA, US) is the only FDA-approved CGM device for the replacement of confirmatory self-monitoring blood glucose measurements when making therapeutic decisions. Evidence from REPLACE-BG, a multicentre, randomised, noninferiority clinical trial demonstrates that the use of CGM without confirmatory SMBG is as safe and effective as using CGM adjunctive to SMBG in adults with T1D and an HbA1c close to target.³⁸ Based on the trial results, the analyses assumes 2.8 fingersticks (2 fingersticks are required for CGM calibration) per day for people on CGM.

Cost inputs

The cost of ambulance call-outs, hospital admissions and A&E visits were derived from a database developed by New Economy and

Table 3: Cost inputs

Parameter	Costs (2016)	Reference
Cost per ambulance callout	£240	39
Tariff per accident and emergency attendance	£126	39
Tariff for hypoglycaemia admission	£1,834	39
Average cost of insulin pump per year	£2,284	45
Savings due to avoided complications per year	£63*	40
Cost per 50 blood glucose monitoring fingerstick tests	£6.78†	14
Cost per 100 lancets	£4.28	41
G5 Mobile CGM costs for year one with receiver	£3,740	42
G5 Mobile CGM costs for year one with no receiver	£3,465	42

*Baxter et al. 2016 demonstrated cost reductions between £66 and £184 over 5 years from avoided complications if HbA1c was reduced by 0.4% from baseline. Based on this, we assume a median cost-reduction of £125 over 5 years that translates into cost-reduction of £25 per year due to avoided complications. If HbA1c reduction were equal to 1% from baseline (as seen in DIAMOND RCT for CGM), this equates to £63 in cost-reductions every year due to avoided complications. †Back calculated - Costing statement: type 1 diabetes in adults. CGM = continuous glucose monitoring; HbA1c = glycated haemoglobin; RCT = randomised controlled trial.

Her Majesty's Government.³⁹ The average cost savings per year due to avoided complications as a result of %HbA1c reduction for patients using CGM was derived from published literature (*Table 3*).⁴⁰ The cost per fingerstick was derived from published literature¹⁴ and the cost of lancets was derived from drug tariff published by NHS.⁴¹ The cost of Dexcom G5 Mobile CGM was provided by the manufacturer.⁴² The G5 Mobile CGM system consists of an interstitial sensor, a transmitter and a dedicated receiver. A smart phone (or mobile device) can be used in lieu of the dedicated receiver. The labelled sensor usage is 7 days. The Dexcom G5 Mobile device has CE mark approval for use without the need for a receiver, and patients will use their existing smart phone to function as the CGM receiver. In this analysis, it was assumed (based on user experience) that 30% of the patients will use the G5 Mobile system receiver with the remainder of the patients using their mobile phone as the receiver. The model assumes 2.5% increase in prices every year in the analyses. All other cost inputs can be seen in *Table 3*.

Sensitivity analysis

Sensitivity analysis was performed on the following parameters:

- Sensor and receiver usage**
Sensitivity analysis was conducted on Dexcom G5 sensor usage. More specifically, it was assumed that sensors are replaced every 10 days instead of 7 days in the base case. It was also assumed in this sensitivity scenario that patients do not use the receiver.
- Fingerstick usage in SMBG group**
Sensitivity analysis was performed assuming SMBG group using a maximum of 10 fingersticks per day and a minimum of four fingersticks per day.
- Reduction in SH events conferred by CGM**
Sensitivity analysis was performed assuming a minimum of 46% mean reduction in the incidence of SH based on the Juvenile Diabetes Research Foundation (JDRF) RCT.⁴³ Because the JDRF study excluded people with a history of SH and those with IAH, and was not powered to determine the impact of CGM on SH, the study may underestimate the potential efficacy of CGM for reducing SH in a high-risk population, and is therefore a conservative estimate. Sensitivity analysis was also performed using a maximum of 93% reduction in the incidence of SH events based on a retrospective audit of 35 patients with T1D and IAH.⁴⁴

Table 4: Total impact on the budget of North West London clinical commissioning groups (£)

	Year 1	Year 2	Year 3	Year 4
SMBG strip and lancet savings	10,66,314	1,092,972	1,120,296	1,148,304
Savings due to reduced severe hypoglycaemia	6,620,735	6,786,253	6,955,910	7,129,807
Savings from avoided pump usage*	238,586	244,551	250,665	256,931
Savings from avoided or postponed HbA1c related complications†	191,276	196,058	200,960	205,984
Total savings	8,116,912	8,319,835	8,527,830	8,741,026
Net budget impact on NW London CCGs	2,653,760	2,463,361	3,402,143	2,588,068

*Savings from avoided pump usage = % reduction in pump usage every year multiplied by the total cost to NHS every year for new pump starts; †Savings from avoided or postponed HbA1c related complications = Savings from avoided or postponed HbA1c related complications per person (£63) multiplied by the number of T1D-IAH patients (target population). CCGs = clinical commissioning groups; HbA1c = glycated haemoglobin; NHS = National Health Service; NW = North West; SMBG = self-monitoring of blood glucose; T1D-IAH = type 1 diabetes with impaired awareness of hypoglycaemia.

Table 5: Sensitivity analysis

Parameters	Base case (year 1: £2,653,760)
Sensor usage 10 days and no receiver	£815,094
SMBG usage: 10 fingersticks per day	£2,353,219
SMBG usage: 4 fingersticks per day	£3,254,840
Severe hypoglycaemia reduction on CGM – 93%	-£1,161,579
Severe hypoglycaemia reduction on CGM – 46%	£4,112,566

CGM = continuous glucose monitoring; SMBG = self-monitoring of blood glucose.

Results

For a population of 2,127,946 within NW London CCGs, it was estimated that there are 15,213 people with T1D, of whom 3,036 were estimated to have IAH.

The cost of CGM for PwD-IAH (n=3,036) is £10,770,671 in year one, £10,783,195 in year two, £11,317,177 in year three and £11,329,095 in year four. The combined cost offsets related to reduced hypoglycaemia admissions, SMBG strips usage and complications is £8,116,912; £8,319,835; £8,527,830 and £8,741,026 in years one through four, respectively. The net budget impact within the NW London CCGs is £2,653,760; £2,463,361; £3,402,143; £2,588,068 in years one through four respectively (Table 4).

Sensitivity analysis

In sensitivity analysis, the net budget impact of introducing CGM within NW London CCGs is £815,094 in year one when it is assumed that patients use a sensor for 10 days each. This also assumes no receiver usage. When the number of fingersticks used by patients in the SMBG group is increased from eight fingersticks to 10 per day in sensitivity analysis, the net budget impact on the NW CCGs decreases

to £2,353,219. When the number of fingersticks used by the patients in the SMBG group is decreased from eight fingersticks to four per day, the net budget impact increases to £3,254,840. When the reduction in the SH events is increased from 59% to 93% in the sensitivity analysis, the net budget impact in year one decreases to -£1,161,579 (cost-savings) and when the reduction in SH events is decreased from 59% to 46%, the net budget impact increases to £4,112,566 in year one (Table 5).

Discussion

The introduction of CGM for the high-risk sub-group of patients with IAH has a minimal budget impact (£2,653,760) in year one and remains stable for subsequent 3 years. Sensitivity analyses demonstrate the robustness of the model results and shows minimal budget impact due to CGM introduction in each of the scenarios assessed and cost-savings observed when the rate of severe hypoglycaemia reduction on CGM is increased to 93%. The results of this model are intended to provide a population-level estimate of the healthcare costs and savings associated with reduction in SH events, decreased complications in the short-term due to optimised HbA1c control and reduced insulin pump usage within NW London CCGs.

Several analyses have evaluated the cost-effectiveness of CGM in terms of incremental cost-effectiveness ratios and quality-adjusted life years.⁴⁵⁻⁴⁷ While these evaluations are important for determining the long-term societal impact of new medical interventions, they do not provide cost data in a context that is directly relevant to CCGs in England. This analysis adds to the literature by demonstrating the short-term budgetary impact of introducing real time CGM for T1D-IAH patients within NW London CCGs. However, this study is not without limitations, primarily because of the assumptions made in the model and data availability. Specifically, clinical trial data used to model the efficacy of the CGM intervention in terms of reduction in SH events for patients using CGM and the fingersticks usage by patients in the SMBG group may not be representative of the clinical benefits experienced in real-world practice. In order to address this limitation, one-way sensitivity analyses were conducted using a range of values around these inputs in the analyses. In addition, not all model inputs were available for T1D patients; therefore, certain data inputs were assumed. For instance, the percentage of patients delaying/avoiding going on insulin pumps due to better HbA1c control with CGM and MDI was derived from NICE guidance,³⁶ clinical judgement/expert opinion and results of the DIAMOND clinical trial.⁸

Finally, it is important to note that short-term budget impact analysis does not incorporate the long-term clinical and economic benefits related to reduction in HbA1c and thus better glucose control in terms of reduced microvascular and macrovascular complications.

Conclusions

Introduction of real time CGM for PwD-IAH will have a minimal budget impact on NW London CCGs, driven by cost of CGM and offsets from lower hypoglycaemia-related costs, reduced SMBG strip usage, avoided near term HbA1c-related complications and insulin pump usage. Given the established clinical benefits associated with CGM use compared with the potential budget impact, UK CCGs should consider providing real time CGM access to high-risk T1D patients. □

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