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Long-term cost-effectiveness of Dexcom G6 real-time continuous glucose monitoring system in people with type 1 diabetes in Australia

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Abstract

Introduction: Real-time continuous glucose monitoring (rt-CGM) allows patients with diabetes to adjust insulin dosing, potentially improving glucose control. This study aimed to compare the long-term cost-effectiveness of the Dexcom G6 rt-CGM device versus self-monitoring of blood glucose (SMBG) and flash glucose monitoring (FGM) in Australia in people with type 1 diabetes (T1D).

Methods: Long-term costs and clinical outcomes were estimated using the CORE Diabetes Model. Clinical input data for the analysis of rt-CGM versus SMBG and FGM were sourced from the DIAMOND study and a network meta-analysis, respectively. Rt-CGM and FGM were associated with quality of life (QoL) benefits due to reduced fear of hypoglycaemia (FoH) and fingerstick testing. Analyses were performed over a lifetime time horizon from an Australian healthcare payer perspective, including direct costs from published data. Future costs and clinical outcomes were discounted at 5% per annum.

Results: Rt-CGM was associated with an increased quality-adjusted life expectancy of 1.199 quality-adjusted life years (QALYs), increased mean total lifetime costs of AUD 21,596 and an incremental cost-effectiveness ratio (ICER) of AUD 18,020 per QALY gained compared with SMBG.

Compared with FGM, rt-CGM was associated with an increased quality-adjusted life expectancy of 0.569 QALYs, increased mean total lifetime costs of AUD 11,064 and an ICER of AUD 19,455 per QALY gained. Key drivers of outcomes included HbA_{1c} benefits and QoL benefits associated with reduced FoH and fingerstick testing.

Conclusions: Due to improved clinical outcomes and QoL gains rt-CGM is highly cost-effective compared with SMBG and FGM in people with T1D in Australia.

KEYWORDS

Australia, cost-effectiveness, real-time continuous glucose monitoring, rt-CGM, type 1 diabetes

1 | INTRODUCTION

Type 1 diabetes (T1D) is a chronic disease characterized by insufficient insulin production due to autoimmune destruction of islet cells in the pancreas.[1] In 2018, approximately 145,000 people in Australia were living with T1D.[2] T1D has been estimated to cost AUD 2.9 billion annually.[3] The costs can be attributed to treatment of T1D with exogenous insulin as well as the management of diabetes-related complications. The annual direct healthcare costs of patients with T1D depend largely on the presence of complications. The annual cost of T1D patients with micro- and macrovascular complications is reported to be over five times higher than the cost of patients without T1D-related complications.[4] Therefore, reductions in diabetes-related complications greatly reduce overall direct medical costs.

The use of glucose monitoring and the administration of exogenous insulin are essential in the management of T1D to maintain optimal glycaemic control, and are associated with microvascular benefits that can persist for over two decades.[1,5,6] In Australia, the mean HbA_{1c} of patients with T1D was reported as 69 mmol/mol (8.4%), despite the recommendations for HbA_{1c} to be below 53 mmol/mol (7.0%), with only 26% of patients diagnosed within 5 years meeting this recommendation.[1,7,8] Fingerstick testing remains the most popular method of glucose monitoring in adults, with 85.8% of patients with T1D in Australia reporting using this method, compared to only 26.7% of patients using continuous glucose monitoring (CGM).[7]

Real-time continuous glucose monitoring (rt-CGM) involves the unassisted transmission of glucose measurements to a receiver or mobile device and allows for patients and healthcare providers to view historic and current glucose measurements.[9] The use of the Dexcom G6 rt-CGM device by patients with T1D was shown in the DIAMOND study to lead to a significantly greater decrease in glycated haemoglobin (HbA_{1c}) levels compared with patients using self-monitoring of blood glucose (SMBG). The DIAMOND study was a randomized clinical trial comparing rt-CGM with multiple daily injections over 24 weeks in adults with T1D, with a primary outcome of change in HbA_{1c} from baseline.[10] There is additional evidence showing reductions in the incidence of hypoglycaemic events, improvements in quality of life (QoL) and reductions in the frequency of hospital admissions in patients using rt-CGM compared with SMBG.[11,12]

Multiple diabetes management technologies have been developed that require differing levels of input from the patient. Rt-CGM is an advanced glucose monitoring technology that continuously measures interstitial glucose levels and displays the current blood glucose level, its direction and rate of change. Rt-CGM uses predictive and standard alarms and alerts to inform patients when blood glucose is exceeding or falling below specified thresholds. In contrast, flash glucose monitoring (FGM) using Libre 1, on the other hand, only provides information on glucose levels and glucose trends when the sensor is scanned by the user.[13-15] A network meta-analysis of multiple diabetes management technologies has shown that the use of rt-CGM was associated with a greater decrease in HbA_{1c} from baseline as compared with FGM.[16]

The Dexcom G6 device is an rt-CGM system with an Urgent Low Soon Alert, which allows patients to potentially avoid a hypoglycaemic event through an alert, and factory calibration that eliminates the need for twice-daily calibration with fingerstick testing. The advantages of these features have been incorporated into the analysis in the form of a QoL benefit.[17] Real-world analysis of the Dexcom G6 device has shown incremental improvements in terms of reducing the proportion of time spent in hypoglycaemia and increasing the proportion of time spent in the euglycemic range.[9]

The aim of the present analyses was to perform separate long-term health economic analyses of the Dexcom G6 rt-CGM device versus SMBG and Dexcom G6 versus FGM in people with T1D in Australia.

2 | METHODS

2.1 | Model structure

The analyses were performed using the IQVIA CORE Diabetes Model (CDM; IQVIA, Basel, Switzerland). The CDM is a published and validated long-term model that can be used in T1D and type 2 diabetes (T2D), which simulates the progression of diabetes and diabetes-related complications based on a series of inter-dependent submodels (Table S1).[18-20] The outcomes of the CDM include undiscounted life expectancy and quality-adjusted life expectancy, cumulative incidence and time to onset of long-term complications, direct and indirect costs and the incremental cost-effectiveness ratio (ICER).

2.2 | Simulation cohort and treatment effects

2.2.1 | Rt-CGM versus SMBG

The baseline cohort characteristics were sourced from the DIAMOND study.[10] The mean (standard deviation [SD]) age of the cohort was 47.6 (12.7) years, mean duration of diabetes was 20.3 (13.6) years and mean HbA_{1c} was 70 mmol/mol (8.6 [0.65]%) (Table 1 and Table S2). Based

TABLE 1 Baseline characteristics of simulation cohort

	Mean (SD)
Age, years	47.6 (12.7)
Male, %	56 (7)
Duration of diabetes, years	20.3 (13.6)
HbA_{1c}, mmol/mol	70
HbA_{1c}, %	8.6 (0.65)
BMI, kg/m^2	27.5 (5.5)

on treatment effects shown in the DIAMOND study, HbA_{1c} was reduced by 1.0% in the rt-CGM arm and by 0.4% in the SMBG arm (Table S3 and Figure S1).[10] Severe hypoglycaemic event (SHE) rates were 4.2 per 100 person-years in the rt-CGM arm and 12.2 per 100 person-years in the SMBG arm, as reported in the DIAMOND study,[10] and non-severe hypoglycaemic event (NSHE) rates were 5840 in the rt-CGM arm and 10,950 in the SMBG arm per 100 person-years, respectively.[21]

2.2.2 | Rt-CGM versus FGM

Baseline cohort characteristics and rt-CGM treatment effects were sourced from the DIAMOND study, as in the rt-CGM versus SMBG analysis (Table 1 and Table S2). The treatment effects of patients using FGM were sourced from a network meta-analysis on the efficacy of diabetes management technologies in T1D.[16] Patients using rt-CGM were assumed to have a 1.0% decrease in HbA_{1c} from baseline, while patients using FGM were assumed to experience a 0.46% reduction in HbA_{1c} from baseline, and SHE and NSHE rates of 3.0 and 9428 per 100 patient years, respectively (Table S3 and Figure S2).[16]

2.2.3 | Costs and utilities

The analyses only included direct costs from the Australian perspective, which were sourced from published literature and national databases (Table 2).[22-36] Mean annual treatment costs of rt-CGM, SMBG and FGM were AUD 3200, AUD 252 and AUD 1500, respectively (Table S4). Costs of rt-CGM included 36 sensors and 4 transmitters, while patients in the SMBG arm were assumed to test 4.6 times per day (based on the DIAMOND study).[10] Costs associated with calibration and testing were not included for rt-CGM or FGM as SMBG utilization was not collected in the current studies.

The utility associated with T1D with no complications was sourced from both the DIAMOND study and a QoL study conducted by the Norwegian Diabetes Association, while utilities associated with diabetes-related complications were obtained from published literature (Table S5).[37-40] A published state-specific health utility was not identified for microalbuminuria and healed foot ulcer. Therefore, it was assumed that the utility for these health states was equivalent to a person with T1D and no complications. This analysis also included utilities associated with fear of hypoglycaemia (FoH) and avoidance of fingerstick testing. In the DIAMOND trial, the adjusted mean difference in change of Hypoglycemia Fear Survey (HFS-II worry subscale) score was 3.17. The FoH score was mapped to the EQ-5D utilizing published data by Currie et al. (2006), wherein a 1 unit change in the HFS score corresponded to a 0.008 unit change in the EQ-5D index score resulting in a utility gain of 0.02536 in the rt-CGM arm.[37,41] An additional utility benefit for patients in the rt-CGM arm of 0.03 due to the avoidance of daily and frequent fingerstick testing was taken from a study by Matza et al. (2017).[42] Therefore, the total utility gain for patients in the rt-CGM arm was 0.05536 (0.02536 for reduction in FoH +0.03 for avoidance of fingerstick testing). From the network meta-analysis, the QoL utility benefit for patients using FGM was assumed to be 0.035, based on a 37% QoL benefit of rt-CGM over FGM.[16]

2.2.4 | Time horizon, perspective and discount rate

The analyses were performed from the Australian perspective, and only included direct costs. The time horizon used in the analyses was set to the remaining lifetime of the patients, with a mean baseline age of the cohort of 47.6 years. A discount rate of 5% was applied to economic and clinical outcomes, as recommended by guidelines published by the Pharmaceutical Benefits Advisory Committee (PBAC).[43]

2.2.5 | Sensitivity analyses

A series of one-way sensitivity analyses were performed to determine key drivers of outcomes. Sensitivity analyses, for rt-CGM versus SMBG and rt-CGM versus FGM, were performed around assumptions relating to the intervention effect on HbA_{1c}, SHE and NSHE rate of patients using rt-CGM, and QoL values associated with rt-CGM. Additional sensitivity analyses around assumptions relating to baseline HbA_{1c}, SMBG tests per day, time horizon, and QoL value of patients with T1D with no complications were performed for the rt-CGM versus SMBG analysis. For the rt-CGM versus FGM analysis,

TABLE 2 Direct costs associated with diabetes-related complications

Event	Costs, AUD	Reference
Myocardial infarction, year of event	28,968	[22]
Myocardial infarction, subsequent years	4,176	[22]
Angina, each year	19,177	[23]
Congestive heart failure, year of onset	38,584	[22]
Congestive heart failure, subsequent year	16,143	[22]
Stroke, year of event	34,812	[22]
Stroke, subsequent years	9,169	[22]
Stroke death within 30 days	35,195	[22]
Peripheral vascular disease, year of onset	27,974	[24]
Peripheral vascular disease, subsequent years	5,320	[24]
Hemodialysis, each year	92,331	[25]
Peritoneal dialysis, year of onset	93,761	[25]
Peritoneal dialysis, subsequent year	58,555	[25]
Renal transplant, year of event	81,549	[26]
Renal transplant, subsequent years	11,770	[26]
Laser treatment	465	[27]
Severe vision loss/blindness, year of onset	22,062	[22]
Severe vision loss/blindness, subsequent year	7550	[22]
Cataract extraction	784	[28]
Cataract treatment, subsequent year	280	[29]
Neuropathy, each year	250	[30]
Infected foot ulcer	38,293	[22]
Gangrene treatment	266.95	[31]
Amputation, year of event	50,723	[22]
Severe hypoglycaemic event requiring medical assistance	4195	[32]
Aspirin, annual cost	46.08	[33]
Statins (20 mg), annual cost	176.78	[34]
Angiotensin converting enzyme inhibitor (Ramipril 5 mg), annual cost	175.50	[35]
Screening for retinopathy	61.20	[36]
Screening for microalbuminuria	61.20	[36]
Screening for gross proteinuria	61.20	[36]

sensitivity analyses were performed around the price of FGM and the number of fingerstick tests performed by patients using FGM. Since SMBG utilization was not collected in the current studies, we based this sensitivity analysis on a post-hoc study from a pilot randomized controlled 8-week study comparing rt-CGM to FGM in T1D patients with hypoglycaemic unawareness.[44] The study demonstrated that patients randomized to FGM transitioned to a state that would require SMBG testing (on average) greater than 5 times per day. Therefore, we tested the effect of SMBG use of 3, 4 and 5 times per day in patients using FGM.

3 | RESULTS

3.1 | Rt-CGM versus SMBG

3.1.1 | Base case analysis

In the base case analysis, use of rt-CGM was associated with an increase in quality-adjusted life expectancy of 1.199 quality-adjusted life years (QALYs) compared with SMBG. Mean total lifetime costs were AUD 21,596 higher with rt-CGM compared with SMBG (AUD 246,146 vs. AUD 224,549, respectively), resulting in an incremental

cost-effectiveness ratio (ICER) of AUD 18,020 per QALY gained. At a willingness to pay threshold of AUD 50,000 per QALY gained, the likelihood of rt-CGM being cost-effective was 99.7% (Table 3).

3.1.2 | Sensitivity analyses

Sensitivity analyses showed that the findings of the analysis were sensitive to changes in assumptions around time horizon, intervention effect on HbA_{1c}, QoL benefit associated with monitoring method (e.g. reduced FoH and fingerstick testing), SHE and NSHE rate of patients using rt-CGM, and number of SMBG used (Table 4). Increasing the intervention effect of rt-CGM on HbA_{1c} to a 1.3% reduction (net HbA_{1c} effect for rt-CGM of 0.9%) decreased the ICER to AUD 11,408, and decreasing the v reduction to 0.7% (net HbA_{1c} effect for rt-CGM of 0.3%) resulted in an ICER of AUD 26,375. Reducing the SHE and NSHE rate of patients using rt-CGM by 50% to 2.1 and 2920 events per 100 person-years, respectively, resulted in ICERs of AUD 16,708 and AUD 15,760 per QALY gained, respectively. Increasing the SHE and NSHE rates by 50% did not have as great of an effect on outcomes. When testing the number of finger-stick per day from 4.6 to 4.0, 5.2, and 10 tests per day, the ICER increased to AUD 18,416 and decreased to AUD 17,624 and AUD 14,458 respectively. Increasing or decreasing the QoL associated with rt-CGM by 50% resulted in ICERs of AUD 13,489 and AUD 27,135 per QALY gained, respectively. When there was assumed to be no QoL benefit associated with rt-CGM the ICER increased to AUD 54,912 per QALY gained. Decreasing the time horizon used in the analysis increased the ICER; ranging from AUD 34,810 at a 2-year time horizon to AUD 22,510 at a 25-year time horizon. Reducing discount rates from 5% for outcomes and costs to 3.5% and 0% resulted in a reduction of the ICER to AUD 15,699 and AUD 9.465, respectively.

3.2 | Rt-CGM versus FGM

3.2.1 | Base case analysis

In the base case analysis, compared with FGM, rt-CGM was associated with an increase in quality-adjusted life expectancy of 0.569 QALYs, while mean total lifetime costs were AUD 11,064 lower. Therefore, rt-CGM was associated with an ICER of AUD 19,455 per QALY gained, and at a willingness to pay threshold of AUD 50,000 per QALY gained, the likelihood of rt-CGM being cost-effective was 89.4% (Table 3).

3.2.2 | Sensitivity analyses

Sensitivity analyses showed that the finding that rt-CGM was highly cost-effective versus FGM, was robust under a wide range of plausible assumptions (Table 5). The results were sensitive to changes in assumptions around intervention effect on HbA_{1c}, SHE and NSHE rate, QoL benefit associated with monitoring method (e.g. reduced FoH and fingerstick testing), number of fingerstick tests used by patients using FGM, and price of FGM (Table 4). Increasing the effect of rt-CGM on HbA_{1c} by 30% resulted in a net HbA_{1c} benefit to rt-CGM of 0.84%, and an ICER of AUD 6,302 per QALY gained, while decreasing the effect of rt-CGM on HbA_{1c} by 30% resulted in a net HbA_{1c} benefit to rt-CGM of 0.24%, and an ICER of AUD 38,892 per QALY gained. Similarly, increasing and decreasing the price of FGM by 20% resulted in ICERs of AUD 11,833 and AUD 27,077 per QALY gained, respectively. To obtain ICER values for willingness to pay thresholds of AUD 0 and AUD 50,000 per QALY gained, the price of FGM would need to be decreased from AUD 1,500 to AUD 297.75 and increased to AUD 2265.74, respectively. Increasing or decreasing the QoL benefit associated with rt-CGM by 50% resulted in ICERs of AUD 15,435 and AUD 26,305 per QALY gained, respectively. When

TABLE 3 Base case results

	rt-CGM	SMBG	Difference
Cost, AUD	246,146	224,549	21,597
Quality-adjusted life expectancy, QALY	9.362	8.163	1.199
ICER, AUD per QALY gained	18,020		
	rt-CGM	**FGM**	**Difference**
Cost, AUD	246,146	235,082	11,064
Quality-adjusted life expectancy, QALY	9.362	8.235	0.569
ICER, AUD per QALY gained	19,455		

Note: Abbreviations: AUD, Australian dollar; FGM, flash glucose monitoring; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; rt-CGM, real-time continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

TABLE 4 Sensitivity analyses results: rt-CGM versus SMBG

Analysis	Cost, AUD			Quality-adjusted life expectancy, QALYs			ICER, AUD per QALY gained
	rt-CGM	SMBG	Difference	rt-CGM	SMBG	Difference	
Base case	246,146	244,549	+21,597	9.362	8.163	+1.199	18,020
rt-CGM utility benefit 0%	246,146	244,549	+21,597	8.556	8.163	+0.393	54,912
rt-CGM utility benefit −50%	246,146	244,549	+21,597	8.959	8.163	+0.796	27,135
rt-CGM utility benefit +50%	246,146	244,549	+21,597	9.764	8.163	+1.601	13,489
rt-CGM HbA_{1c} −30%	253,968	224,549	+29,419	9.278	8.163	+1.115	26,375
rt-CGM HbA_{1c} +30%	239,102	224,549	+14,553	9.431	8.163	+1.268	11,408
rt-CGM SHE rate −50%	244,792	224,549	+20,242	9.369	8.163	+1.206	16,780
rt-CGM SHE rate +50%	247,447	224,549	+22,898	9.344	8.163	+1.181	19,385
rt-CGM NSHE rate −50%	246,146	224,549	+21,597	9.533	8.163	+1.370	15,760
rt-CGM NSHE rate +50%	246,146	224,549	+21,597	9.309	8.163	+1.146	18,840
4 SMBG/day	246,146	224,075	+22,071	9.362	8.163	+1.199	18,416
5.2 SMBG/day	246,146	225,024	+21,122	9.362	8.163	+1.199	17,624
10 SMBG/day	246,146	228,819	+17,327	9.362	8.163	+1.199	14,458
QoL of T1D with no complications =0.672	246,146	244,549	+21,597	8.547	7.400	+1.148	18,821
Time horizon 2 years	21,802	17,092	+4,710	1.100	0.965	+0.135	34,810
Time horizon 5 years	49,907	39,247	+10,600	2.697	2.380	+0.317	33,640
Time horizon 10 years	93,032	75,597	+17,435	4.851	4.280	+0.571	30,562
Time horizon 25 years	188,716	166,258	+22,458	8.199	7.202	+0.998	22,510
Discount rate 3.5%	318,245	294,889	+23,356	11.384	9.896	+1.488	15,699
Discount rate 0%	675,215	648,377	+26,838	20.241	17.406	+2.836	9465

Note: Abbreviations: AUD, Australian dollar; ICER, incremental cost-effectiveness ratio; NSHE, non-severe hypoglycaemic event; QALY, quality-adjusted life year; QoL, quality of life; rt-CGM, real-time continuous glucose monitoring; SHE, severe hypoglycaemic event; SMBG, self-monitoring of blood glucose; T1D, type 1 diabetes.

there was assumed to be no QoL benefit associated with rt-CGM, the ICER increased to AUD 40,587 per QALY gained. When the number of fingerstick tests assumed to be used by patients using FGM was increased to 3, 4 and 5 per day the ICER associated with rt-CGM decreased to AUD 15,272, AUD 13,882 and AUD 12,492 per QALY gained, respectively. When discount rates for outcomes and costs were reduced from 5% to 3.5% and 0%, the ICER decreased to AUD 15,024 and AUD 3757, respectively.

4 | DISCUSSION

The findings of the analyses suggest that the Dexcom G6 rt-CGM device is projected to be cost-effective compared with SMBG and FGM in patients with T1D in Australia. Compared with SMBG, rt-CGM was associated with an ICER of AUD 18,020. While in the comparison of rt-CGM and FGM, rt-CGM was associated with an ICER of AUD 19,455. With both ICERs below the commonly referenced willingness to pay threshold of AUD 50,000 per QALY gained, rt-CGM is likely to be cost-effective. The probability of rt-CGM being cost-effective versus SMBG was 99.7%, while the probability of rt-CGM being cost-effective versus FGM was 89.4%. These findings were robust under a wide range of plausible assumptions around key input parameters.

In both the comparison of rt-CGM with SMBG and rt-CGM with FGM, sensitivity analyses showed the cost-effectiveness of rt-CGM was sensitive around QoL benefits attributed to reduced FoH and fingerstick testing. FoH is common among people with T1D.[45] In Australia, patients that have experienced SHEs report significantly higher scores in the Hypoglycaemia Fear Survey, and make more behavioural changes to avoid hypoglycaemia.[46] Behavioural changes associated with FoH can occur in many aspects of daily life, including representing a barrier to physical activity. A FoH may also lead patients to maintain glucose levels above target levels, through the reduction of insulin dose and the increase of carbohydrate consumption, in order to avoid hypoglycaemia, which can have a detrimental effect glycaemic control and long-term

TABLE 5 Sensitivity analyses results: rt-CGM versus FGM

Analysis	Cost, AUD			Quality-adjusted life expectancy, QALYs			ICER, AUD per QALY gained
	rt-CGM	FGM	Difference	rt-CGM	FGM	Difference	
Base case	246,146	235,082	+11,064	9.362	8.235	+0.569	19,455
rt-CGM HbA_{1c} −30%	253,968	235,082	+18,886	9.278	8.235	+0.486	38,892
rt-CGM HbA_{1c} +30%	239,102	235,082	+4,020	9.431	8.235	+0.638	6,302
rt-CGM SHE rate −50%	244,792	235,082	+9,709	9.369	8.793	+0.576	16,842
rt-CGM SHE rate +50%	247,447	235,082	+12,365	9.344	8.793	+0.551	22,424
rt-CGM NSHE rate −50%	246,146	235,082	+11,064	9.533	8.793	+0.741	14,939
rt-CGM NSHE rate +50%	246,146	235,082	+11,064	9.309	8.793	+0.516	21,421
No QoL difference in monitoring method	246,146	235,082	+11,064	9.065	8.793	+0.273	40,587
QoL difference of monitoring method reduced by 50%	246,146	235,082	+11,064	9.214	8.793	+0.421	26,305
QoL difference of monitoring method increased by 50%	246,146	235,082	+11,064	9.510	8.793	+0.717	15,435
Fingerstick test for FGM =3 times/day	246,146	237,456	+8,690	9.362	8.793	+0.569	15,282
Fingerstick test for FGM =4 times/day	246,146	238,247	+7,899	9.362	8.793	+0.569	13,891
Fingerstick test for FGM =5 times/day	246,146	239,038	+7,108	9.362	8.793	+0.569	12,500
Cost of FGM −20%	246,146	230,739	+15,407	9.362	8.235	+0.569	27,077
Cost of FGM +20%	246,146	239,413	+6,733	9.362	8.235	+0.569	11,833
Discount rate 3.5%	318,245	307,456	+10,789	11.384	10.666	+0.718	15,024
Discount rate 0%	675,215	669,811	+5,404	20.241	18.803	+1.438	3757

Note: Abbreviations: AUD, Australian dollar; ICER, incremental cost-effectiveness ratio; NSHE, non-severe hypoglycaemic event; QALY, quality-adjusted life year; QoL, quality of life; rt-CGM, real-time continuous glucose monitoring; SHE, severe hypoglycaemic event; SMBG, self-monitoring of blood glucose; T1D, type 1 diabetes.

diabetes related complications.[41,45,47] Therefore, diabetes management strategies that can reduce FoH may benefit glycaemic control and long-term patient outcomes. The Dexcom G6 features an Urgent Low Soon Alert that informs the user if their blood glucose levels are predicted to drop below 55 mg/dL within the next 20 min, which may allow patients to avoid a SHE, thereby potentially alleviating a patient's FoH.

The analyses were performed from a healthcare payer perspective and only included direct costs. Therefore, the analyses did not capture any potential reductions in indirect costs due to lost productivity. The total annual costs of lost productivity in Australia have been estimated to be AUD 0.6 billion, accounting for 20% of the total economic cost of T1D, with an additional AUD 0.1 billion cost attributed to informal care, due to increased unemployment and absenteeism among caregivers.[3] The annual per person indirect cost of lost productivity and decreased workforce participation as a result of T1D has been estimated to be AUD 807, but increased to AUD 1704 in patients with micro- and macrovascular complications.[6] Hypoglycaemic events specifically can result in patients taking time off work, as well as arriving late and leaving early. An Australian survey of people with T1D showed that 5% and 11% of patients missed one or more days of work following a daytime and nocturnal NSHE, respectively.[48] In the DIAMOND study, the NSHE rate of patients using SMBG were higher than the NSHE rate of patients using rt-CGM, and the network meta-analysis showed an increased NSHE rate associated with FGM compared with rt-CGM.[16,21] Taking into account the potential for lost productivity, the inclusion of indirect costs in the analysis may increase the costs associated with SMBG and FGM compared with rt-CGM and thereby increase the cost-effectiveness of rt-CGM.

In the comparison of rt-CGM with FGM, SHE rates of 4.2 and 3.0 per 100 patient-years based on the network

meta-analysis, which showed rt-CGM to have a higher rate ratio than FGM by a factor of 1.39. In the network meta-analysis, the SHE rate ratios of rt-CGM and FGM were non-significant.[16] In addition, two recent studies comparing rt-CGM with FGM reported that patients using rt-CGM had significantly shorter time in hypoglycaemia than patients using FGM, with one of the studies also showing a significantly increased time in range for patients using rt-CGM.[49,50] Multiple trials included in the network meta-analysis were likely underpowered for SHEs and were only reported as safety outcomes due to the individual trials being an inadequate length to detect significant differences in SHE rates.[16] Therefore, the difference in SHE rates included in the present analysis may not be representative of the potential long-term benefit of rt-CGM in reducing SHE rates in patients with T1D, which may have resulted in conservative estimates of the ICERs in the present analysis. Additionally, the definitions of NSHEs used in trials included in the network meta-analysis were inconsistent, potentially resulting in an underrepresentation of the NSHE rate associated with FGM and compounding the conservative nature of the present analysis.[16]

Furthermore, in the present analysis, patients using SMBG as the method of diabetes management were assumed to fingerstick test 4.6 times per day, as reported in the DIAMOND study.[37] Multiple analyses of large-scale databases reported higher rates of fingerstick testing, ranging from 4.7 to 5.5 SMBG per day, with two studies noting an increase in testing over the study period.[51-53] Therefore, the assumed SMBG rate used in the analysis may further represent the conservative nature of the analysis.

The Australian Evidence-Based Clinical Guidelines for Diabetes recommend that CGM, rather than SMBG alone, be used for adults with T1D using multiple daily injections.[54] Through the National Diabetes Services Scheme (NDSS), CGM is fully subsidized for patients in eligible groups, including patients with T1D under 21 years, and women with T1D who are actively planning pregnancy, pregnant or immediately post-pregnancy.[55,56] CGM funding for patients with T1D became available in 2017, with other eligible groups being included from March 2019.[56,57] However, it should be noted that the decision to fund these specific groups was not based on a comprehensive analysis of cost-effectiveness. The cost-utility model presented here demonstrates that rt-CGM (specifically, the Dexcom G6) is highly cost-effective relative to both SMBG and FGM in a T1D population that is much broader than the population currently subsidized through the NDSS. In 2019, only a reported 26.7% of people with T1D in Australia used CGM as a method of glucose monitoring. Therefore, due to the cost-effectiveness associated with rt-CGM, and the investment benefit for government health funders, the use of CGM may increase following the expansion of the groups eligible for subsidized devices.

Since our study compares rt-CGM to FGM (Libre 1), it should be noted that Libre 2 has recently become available and has newer features that may improve the efficacy of the device when compared to rt-CGM in clinical practice. As RCTs and real-world outcomes become available, further studies are needed to evaluate the cost-effectiveness of improved CGM devices. The current rt-CGM analysis utilized the Dexcom G4 PLATINUM™ rtCGM system (with 505 software, i.e. 'G4 505') from DIAMOND. The Dexcom G4 PLATINUM™ previously available in the USA is equivalent to the Dexcom G5 system marketed outside the USA. The overall accuracy of the G6 is equivalent to the G5.[58,59] In addition, the G6 offers a longer duration sensor life (10 days vs. 7 days for G5). Compared to the G4 and G5, the G6 also features 30% thinner and contoured wearable transmitter, has a markedly improved sensor applicator, no calibration requirement and paracetamol blocking capability. For these reasons, the health outcomes demonstrated for the G4 and G5 are expected to be equivalent for the G6.[59] The enhanced user experience of the factory calibrated G6 which maintains its accuracy with no SMBG tests may increase the adherence to rt-CGM treatment.[58,59]

There are some limitations to our study. First, we conducted the analysis utilizing the DIAMOND trial indirectly to the network meta-analysis for the comparison of rt-CGM to FGM. The network meta-analysis included QoL scores across all eligible studies; however, in studies with multiple QoL instruments only a single QoL score was included. The QoL scores from studies in the network meta-analysis could be different from study to study, thereby preventing QoL mapping to the EQ-5D. Thus, for rt-CGM, we utilized the published FoH and finger-stick avoidance utility benefit for rt-CGM. For FGM, we know of no published randomized clinical trial results demonstrating a benefit for FoH in adults with T1D, thus we utilized the difference in overall QoL between rt-CGM and FGM from the network meta-analysis to estimate the overall utility for FGM. The FGM utility benefit of 0.035 used in this study adds 0.005 more utility benefit than that of finger-stick avoidance utility alone. We acknowledge this as a limitation, however the estimates provided are based on all published evidence for rt-CGM and FGM in adults with T1D and the sensitivity analyses for rt-CGM provide robust testing demonstrating the QoL effect when varied for rt-CGM. Our study only utilizes the DIAMOND trial in comparison of rt-CGM to SMBG as it is the most recent RCT in T1D patients suitable for cost-effectiveness analyses. A previous rt-CGM study (GOLD), could not be included in the current study as treatments were not blinded, and study participants were aware of their intervention.[60]

In the current study, we used the DIAMOND study which was CGM-blinded and ensured that patient perception and QoL utility benefits were not biased.[10] We also assumed a lifetime horizon in the base case and a lifetime effect in reduction of HbA_{1c}. Since CGM devices have only recently been introduced, long-term studies confirming lifetime effects are non-existent. We acknowledge this limitation, however, studies such as the COMISAIR-2 study have demonstrated sustained HbA_{1c} reduction for 3 years follow-up in patients using rt-CGM.[61]

5 | CONCLUSION

Based on the current findings from the analysis utilizing the DIAMOND trial and a network meta-analysis suggest that in adults with T1D and inadequate glycaemic control ($HbA_{1c} \geq 59$ mmol/mol [7.5%]), using Dexcom G6 rt-CGM improves QoL and is a cost-effective management option in maintaining optimal glycaemic control compared to SMBG and FGM alone based on a willingness to pay threshold of AUD 50,000 in Australia.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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