Study Protocol

Title:	**Inequity in access to continuous glucose monitoring and health outcomes in paediatric diabetes, a case for national continuous glucose monitoring funding: A cross-sectional population study of children with type 1 diabetes in New Zealand.**
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1.0	New Document	*Martin de Bock, FRACP PhD*

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ABBREVIATIONS AND DEFINITIONS OF TERMS

AID	Automated Insulin Delivery
CGM	Continuous Glucose Monitoring
CSII	Continuous Subcutaneous Insulin Infusion
DPMS	Diabetes Patient Management System
DHB	District Health Board
HbA1c	Glycated Haemoglobin
isCGM	Intermittently Scanned Continuous Glucose Monitoring
MDI	Multiple Daily Injections
rtCGM	Real-Time Continuous Glucose Monitoring
SMBG	Self-Monitoring of Blood Glucose
T1D	Type 1 Diabetes

1 BACKGROUND INFORMATION AND RATIONALE

Less than one third of people with Type 1 Diabetes (T1D) achieve glycaemic control targets known to reduce the risk of long-term complications (1). Accordingly, rates of acute and chronic complications among people with T1D remain unacceptable.

Real-time Continuous Glucose Monitoring (rtCGM) and intermittently scanned CGM (iCGM) are valuable tools for personalized diabetes management, and the evidence that CGM improves glycaemic control and quality of life for adults and children with T1D is irrefutable (2-4). rtCGM tracks interstitial glucose concentrations, reflecting near real-time glucose data, and in a similar manner isCGM shows continuous glucose measurements retrospectively at the point of checking. rtCGM has the added benefit of being able to forewarn its users about impending hypoglycaemia or hyperglycaemia so the user can respond accordingly to avert the event.

Outside of the United States many people using CGM, are self-funding it. As the evidence base for CGM clinical value grows, rates of reimbursement grow also. In the United Kingdom, funded CGM has been available to a subset of people with diabetes who satisfy the National Institute for Health and Care Excellence clinical guidelines since 2015 (5), and access to fully subsidized CGM in Australia is becoming more pervasive (6). However, unlike many similar high-income countries, CGM is not currently funded in New Zealand, and the cost of self-funding it is often prohibitive.

Unfortunately, inequitable access to diabetes technology and inequitable glycaemic outcomes are commonplace within the diabetes expanse. Prior research has exposed sociodemographic disparities in the use of publicly funded insulin pump therapy in New Zealand, with differences existing between District Health Boards (DHBs), age, gender, ethnicity and socioeconomic position (7), and so vaster disparities are anticipated with CGM since there is no universal funding. Hence, the lack of funded CGM in New Zealand is likely to further fuel inequity, however no studies have assessed the sociodemographic and glycaemic characteristics of the limited cohort accessing CGM in New Zealand currently.

2 STUDY OBJECTIVES AND HYPOTHESES

The purpose of this study is to provide a snapshot of the frequency and characteristics of users of CGM in children and adolescents with T1D in New Zealand, to prove or refute that disparities with access to CGM exist. It is hypothesized that disparities in this context are real and palpable.

Furthermore, the study aims to assess the relationship between CGM use and HbA1c, to illuminate if inequitable access translates to inequitable glycaemic outcomes. This information could be used to inform the New Zealand Pharmaceutical Management agency (PHARMAC) of a digital diabetes divide, and contribute to the argument for CGM to become publicly funded in New Zealand.

3 METHODOLOGY

3.1 Study Synopsis

This cross-sectional study will involve collecting relevant diabetes data (patient demographics, diabetes treatment, HbA1c and CGM use) from all available children and adolescents <15 years with T1D managed by a secondary care diabetes center as of the 01 October 2021. The centers will be instructed and supported to complete an Excel spreadsheet supplied by the researchers. Data will be extracted from existing local databases, or established through electronic chart review in centres who do not collect data. Data returned to the researchers for analysis will be without identifiable information.

3.2 Research Site

This research will be based in the Paediatric Department, University of Otago, Christchurch in collaboration with DHBs across New Zealand.

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Date Range of Study

Data collection will be as of the 01 October 2021.

3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

All 20 District Health Board (DHB) secondary care sites in New Zealand managing children and adolescents with diabetes will be invited to provide relevant data for the study.

3.4 Study Population

The study will include all children and adolescents < 15 years with T1D in New Zealand under a secondary care paediatric diabetes service as of the 01 October 2021. No specific exclusionary criteria will be applied.

3.4.1 Inclusion Criteria

1. T1D diagnosed as per the American Diabetes Association classification as of the 01 October 2021
2. Under a secondary care paediatric diabetes service in New Zealand as of the 01 July 2021

4 STUDY PROCEDURES

4.1 Data Sources

Data for this study will be obtained primarily from the Diabetes Patient Management System (DPMS), which collects data such as patient demographics, diabetes treatments and glycaemic outcomes. DPMS is currently used by all five DHBs in the South Island. These five DHBs will be supplied a script which will facilitate the extraction of required data from DPMS. Dr Martin de Bock, the Principal Investigator for the current study, has been integral to the development and deployment of DPMS in New Zealand, and has authority to access patient data from DPMS.

DHBs who are yet to adopt DPMS will be able to draw the relevant diabetes data from local diabetes records/databases.

The individual centers will be asked to 'clean' their data to ensure that the information they provide about patients' ethnicity and device use etc. is accurate and up to date.

4.2 Data Collected

The Excel spreadsheet/ DPMS script will facilitate the documentation of the variables outlined below, as of the 01 October 2021:

Patient demographic characteristics
Age in years. Gender. Ethnicity - prioritized, self-identified ethnicity. Meshblock to determine New Zealand Index of Deprivation 2018 Score as a validated measure of socioeconomic position.
General diabetes information:
Date of T1D diagnosis will be used to calculate the individual's age at diagnosis. DHB. HbA1c as a measure of glycaemic outcome - last recorded HbA1c in the six months between the 01 April 2021 - 01 October 2021. Insulin therapy - Multiple Daily Injections (MDI), Continuous Subcutaneous Insulin Infusion (CSII), or Automated Insulin Delivery (AID).
CGM information:
CGM use (yes/no) Type of CGM (if applicable) - Libre, Libre/MiaoMiao, Dexcom G5, Dexcom G6, Guardian 3. How CGM is funded (if applicable) - Self, Work and Income New Zealand, DHB, research, other.

5 STATISTICAL CONSIDERATIONS

The characteristics of the study sample (age, gender, DHB, ethnicity, NZ Deprivation score, …) will be summarized using standard descriptive measures (for example means and standard deviations for continuous variables such as age, and percentages for categorical variables such as gender). Differences in demographic variables (age, gender, DHB, ethnicity, NZ Deprivation score) between subjects using CGM versus subjects Self-Monitoring of Blood Glucose (SMBG) will be presented and assessed using Chi-square or Fisher exact tests. The relative importance of each demographic variable will be tested in a multivariable generalised linear regression model.

Inequities in outcomes will be assessed by investigating associations between children's glycaemic control, as measured by HbA1c, and demographic variables using ANOVA or unpaired t-tests. The importance of CGM use in influencing inequities will be explored by using linear regression analysis to estimate differences with 95% CI in HbA1c across variable categories before and after adjustment for CGM use. A multivariable linear regression model will be used to estimate fully adjusted differences in HbA1c.

The sample size will be one of convenience, that is all of the available cases. It is estimated that >99% of children with T1D are managed in secondary care in New Zealand (8).

6 STUDY ADMINISTRATION

6.1 Data Collection and Management

The individual centers will be responsible for data cleaning and collection. They will be responsible for ensuring their data is up to date, and that the final data set does not contain any identifiable information before it is returned to the researchers.

6.2 Regulatory and Ethical Considerations

6.2.1 Risk Assessment

There are no anticipated risks from the study other than the small risk of breach of confidentiality of data.

6.2.2 Potential Benefits of Study Participation

Possible indirect benefits that accrue to the individual and society in the future include CGM becoming publicly funded in New Zealand and diabetes inequity being better addressed.

6.2.3 Ethical Approval

The audit activity of this study was covered by "Clinical benchmarking utilising data from New Zealand Diabetes Centre Patient Management Systems/Databases and contributing to the Australasian Diabetes Database Network/ SWEET international diabetes database", Ethics Committee reference number HD18/098.

7 REFERENCES

1. Miller KM, Foster NC, Beck RW, Bergenstal RM, DuBose SN, DiMeglio LA, et al. Current state of type 1 diabetes treatment in the U.S.: updated data from the T1D exchange clinic registry.(Report). 2015;38(6):971.

2. New JP, Ajjan R, Pfeiffer AFH, Freckmann G. Continuous glucose monitoring in people with diabetes: the randomized controlled Glucose Level Awareness in Diabetes Study (GLADIS. Diabetic Medicine. 2015;32(5):609-17.

3. Wong JC, Foster NC, Maahs DM, Raghinaru D, Bergenstal RM, Ahmann AJ, et al. Real-time continuous glucose monitoring among participants in the t1d exchange clinic registry.(Report). Diabetes Care. 2014;37(10):2702.

4. Rachmiel M, Landau Z, Boaz M, Mazor Aronovitch K, Loewenthal N, Ben-Ami M, et al. The use of continuous glucose monitoring systems in a pediatric population with type 1 diabetes mellitus in real-life settings: the AWeSoMe Study Group experience. Acta Diabetologica. 2015;52(2):323-9.

5. Graham C. Continuous Glucose Monitoring and Global Reimbursement: An Update. Diabetes technology & therapeutics. 2017;19(S3):S-6-S-66.

6. [Available from: https://www.ndss.com.au/living-with-diabetes/managing-diabetes/continuous-glucose-monitoring/.

7. Wheeler BJ, Braund R, Galland B, Mikuscheva A, Wiltshire E, Jefferies C, et al. District health board of residence, ethnicity and socioeconomic status all impact publicly funded insulin pump uptake in New Zealand patients with type 1 diabetes. The New Zealand medical journal. 2019;132(1491):78-89.

8. de Bock M, Jones TW, Fairchild J, Mouat F, Jefferies C. Children and adolescents with type 1 diabetes in Australasia: An online survey of model of care, workforce and outcomes. J Paediatr Child Health. 2019;55(1):82-6.

8 APPENDIX

8.1 Excel Spreadsheet

Fig 1: Excel spreadsheet distributed to DHBs showing patient data collected

General									General Diabetes Information				CGM Information			
Unique Idenifier	Patient Age	Gender	Ethnicity (enter up to 6)						Meshblock	Date T1DM diagnosed	DHB	HbA1c (mmol/mol), last recorded between 01 Apr - 01 Oct 2021	Treatment Modality	Was the patient using CGM on 01 Oct 2021	Type of CGM	How CGM funded	If funded by 'other' please specify
			1	2	3	4	5	6									