

A SELECTION OF TEN READINGS ON TOPICS RELATED TO CONTINUOUS GLUCOSE MONITORING

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Selection of readings made by A/Prof Goh Lee Gan

READING 1 – CONTINUOUS GLUCOSE MONITORING FOR INPATIENT DIABETES MANAGEMENT

Zelada H,¹ Perez-Guzman MC,² Chernavvsky DR,³ Galindo RJ.⁴ Continuous glucose monitoring for inpatient diabetes management: an update on current evidence and practice. *Endocr Connect.* 2023 Sep 25;12(10):e230180. PMID: 37578799.

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ABSTRACT

Over the last few years, several exciting changes in continuous glucose monitoring (CGM) technology expanded its use and made CGM the standard of care for patients with type 1 and type 2 diabetes using insulin therapy. Consequently, hospitals started to notice increased use of these devices in their hospitalised patients. Furthermore, during the coronavirus disease 2019 (COVID) pandemic, there was a critical need for innovative approaches to glycaemic monitoring, and several hospitals started to implement CGM protocols in their daily practice.

Subsequently, a plethora of studies have demonstrated the efficacy and safety of CGM use in the hospital, leading to clinical practice guideline recommendations. Several studies have also suggested that CGM has the potential to become the standard of care for some hospitalised patients, overcoming the limitations of current capillary glucose testing. Albeit there is a need for more studies and particularly regulatory approval.

In this review, we provide a historical overview of the evolution of glycaemic monitoring in the hospital and review the current evidence, implementation protocols, and guidance for the use of CGM in hospitalised patients.

READING 2 – POST-PRANDIAL GLYCAEMIC RESPONSE IN HEALTHY INDIVIDUALS

Jarvis PRE,¹ Cardin JL,² Nisevich-Bede PM,³ McCarter JP.⁴ Continuous glucose monitoring in a healthy population: understanding the post-prandial glycaemic response in individuals without diabetes mellitus. *Metabolism.* 2023 Sep; 146:155640. PMID: 37356796

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ABSTRACT

Continuous glucose monitoring has become a common adjunct in the management of Diabetes Mellitus. However, there has been a recent trend among individuals without diabetes using these devices as a means of monitoring their health. ~~The increased visibility of glucose data has allowed users to study the effect lifestyle has upon post-prandial glucose levels.~~ Although post-prandial hyperglycaemia is well understood in the setting of diabetes, its impact in individuals without diabetes is less well defined.

This article reviews the factors that contribute to post-prandial hyperglycaemia in individuals without diabetes and how the data obtained from continuous glucose monitoring can be used to improve an individual's metabolic health.

READING 3 – DIABETES SPECIALISTS VALUE CONTINUOUS GLUCOSE MONITORING

Kompala T,¹ Neinstein A,^{1,3} Wong J.² Diabetes Specialists Value Continuous Glucose Monitoring Despite Challenges in Prescribing and Data Review Process. *J Diabetes Sci Technol.* 2023 Sep;17(5):1265-1273. PMID: 35403469.

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ABSTRACT

BACKGROUND: Diabetes clinicians are key facilitators of continuous glucose monitoring (CGM) provision, but data on provider behaviour related to CGM use and CGM generated data are limited.

METHODS: We conducted a national survey of providers caring for people with diabetes on CGM-related opinions, facilitators and barriers to prescription, and data review practices.

RESULTS: Of 182 survey respondents, 73.2% worked at academic centers, 70.6% were endocrinologists, and 70.7% practiced in urban settings. Nearly 70% of providers reported CGM use in the majority of their patients with type 1 diabetes. Half of the providers reported CGM use in 10% to 50% of their patients with type 2 diabetes. All respondents believed CGM improved quality of life and could optimise diabetes control. We found no differences in reported rates of CGM use based on providers' years of experience, patient volume, practice setting, or clinic type. Most providers reviewed CGM data each visit (97.7%) and actively involved patients in the data interpretation (98.8%). Only 14.1% of clinicians reported reviewing CGM data without any prompting from patients or their family members outside of visits. Most providers (80.7%) reported their CGM data review was valued by patients although only half reported having adequate time (45.1%) or an efficient process (56.1%) to do so.

CONCLUSIONS: Despite uniform support for CGM by providers, ongoing challenges related to cost, insurance coverage, and difficulties with prescription were major barriers to CGM use. Increased use of CGM in appropriate populations will necessitate improvements in data access and integration, clearly defined workflows, and decreased administrative burden in obtaining CGM.

READING 4 – CONTINUOUS GLUCOSE MONITORING IN ADULTS WITH TYPE 2 DIABETES

Jancev M,¹ Vissers TACM,¹ Visseren FLJ,¹ de Valk HW,¹ van Bon AC,² Serné EH,³ DeVries JH,³ van Sloten TT.⁴ Continuous glucose monitoring in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabetologia*. 2024 May;67(5):798-810. PMID:38363342.

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ABSTRACT

AIMS/HYPOTHESIS: Continuous glucose monitoring (CGM) is increasingly used in the treatment of type 2 diabetes, but the effects on glycaemic control are unclear. The aim of this systematic review and meta-analysis is to provide a comprehensive overview of the effect of CGM on glycaemic control in adults with type 2 diabetes.

METHODS: We performed a systematic review using Embase, MEDLINE, Web of Science, Scopus, and ClinicalTrials.gov from inception until 2 May 2023. We included RCTs investigating real-time CGM (rtCGM) or intermittently scanned CGM (isCGM) compared with self-monitoring of blood glucose (SMBG) in adults with type 2 diabetes. Studies with an intervention duration <6 weeks or investigating professional CGM, a combination of CGM and additional glucose-lowering treatment strategies, or GlucoWatch were not eligible. Change in HbA1c and the CGM metrics time in range (TIR), time below range (TBR), time above range (TAR), and glycaemic variability were extracted. We evaluated the risk of bias using the Cochrane risk-of-bias tool version 2. Data were synthesised by performing a meta-analysis. We also explored the effects of CGM on severe hypoglycaemia and micro- and macrovascular complications.

RESULTS: We found 12 RCTs comprising 1,248 participants, with eight investigating rtCGM and four isCGM. Compared with SMBG, CGM use (rtCGM or isCGM) led to a mean difference (MD) in HbA1c of -3.43 mmol/mol (-0.31%; 95% CI -4.75, -2.11, $p < 0.00001$, $I^2 = 15%$; moderate certainty). This effect was comparable in studies that included individuals using insulin with or without oral agents (MD -3.27 mmol/mol [-0.30%]; 95% CI -6.22, -0.31, $p = 0.03$, $I^2 = 55%$), and individuals using oral agents only (MD -3.22 mmol/mol [-0.29%]; 95% CI -5.39, -1.05, $p = 0.004$, $I^2 = 0%$). Use of rtCGM showed a trend towards a larger effect (MD -3.95 mmol/mol [-0.36%]; 95% CI -5.46 to -2.44, $p < 0.00001$, $I^2 = 0%$) than use of isCGM (MD -1.79 mmol/mol [-0.16%]; 95% CI -5.28, 1.69, $p = 0.31$, $I^2 = 64%$). CGM was also associated with an increase in TIR (+6.36%; 95% CI +2.48, +10.24, $p = 0.001$, $I^2 = 9%$) and a decrease in TBR (-0.66%; 95% CI -1.21, -0.12, $p = 0.02$, $I^2 = 45%$), TAR (-5.86%; 95% CI -10.88, -0.84, $p = 0.02$, $I^2 = 37%$), and glycaemic variability (-1.47%; 95% CI -2.94, -0.01, $p = 0.05$, $I^2 = 0%$). Three studies reported one or more events of severe hypoglycaemia and macrovascular complications. In comparison with SMBG, CGM use led to a non-statistically significant difference in the incidence of severe hypoglycaemia (RR 0.66, 95% CI 0.15, 3.00, $p = 0.57$, $I^2 = 0%$) and macrovascular complications (RR 1.54, 95% CI 0.42, 5.72, $p = 0.52$, $I^2 = 29%$). No trials reported data on microvascular complications.

CONCLUSIONS/INTERPRETATION: CGM use compared with SMBG is associated with improvements in glycaemic control in adults with type 2 diabetes. However, all studies were open label. In addition, outcome data on incident severe hypoglycaemia and incident microvascular and macrovascular complications were scarce.

READING 5 – CONTINUOUS GLUCOSE MONITORING IN HIGH-RISK PREGNANT WOMEN

Barr E,¹ McLean A,^{1,2} Maple-Brown L,^{1,4} Tabuai G,² Murphy HR.³ Continuous Glucose Monitoring Metrics in High-Risk Pregnant Women with Type 2 Diabetes. *Diabetes Technol Ther.* 2023 Dec;25(12):836-844. PMID: 37902969.

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ABSTRACT

OBJECTIVE: To describe glucose metrics in a high-risk population of women with type 2 diabetes (T2DM) in pregnancy and to explore the associations with neonatal outcomes.

RESEARCH DESIGN AND METHODS: Prospective observational study of 57 women. Continuous glucose monitoring (CGM) trajectories were determined from metrics collected in early and late gestation using the first and last two (mean 16 and 35) weeks of Freestyle Libre data. Logistic regression was used to examine associations of CGM metrics with neonatal hypoglycaemia (glucose <2.6 mmol/L requiring intravenous dextrose) and large for gestational age (LGA) (>90th percentile for gestational age and sex). Pregnancy-specific target glucose range was 3.5-7.8 mmol/L (63-140 mg/dL).

RESULTS: Forty-one women used CGM for 15 weeks (mean age 33 years, 73% Aboriginal or Torres Strait Islander, 32% living remotely). There was limited change in average metrics from early to late pregnancy. For the subgroup with sensor use >50% (n=29), mean time in range (TIR) increased by 9%, time above range reduced by 12%, average glucose reduced by 1 mmol/L, and time below range increased by 3%. Neonatal hypoglycaemia was associated with most CGM metrics, HbA1c, and CGM targets, particularly those from late pregnancy. LGA was associated with hyperglycaemic metrics from early pregnancy. Each 1% increase TIR was associated with a 4%-5% reduction in risk of neonatal complications.

CONCLUSION: In this high-risk group of women with T2DM, CGM metrics only improved during pregnancy in those with greater sensor use and were associated with LGA in early pregnancy and neonatal hypoglycaemia throughout. Culturally appropriate healthcare strategies are critical for successful use of CGM technology.

READING 6 – CGM IN PATIENTS WITH DIABETES IN PREGNANCY

Song Y,¹ Zhai X,¹ Bai Y,¹ Liu C,¹ Zhang L.¹ Progress and indication for use of continuous glucose monitoring in patients with diabetes in pregnancy: a review. *Front Endocrinol (Lausanne).* 2023 Aug 23;14:1218602. PMID: 37680884.

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ABSTRACT

Gestational diabetes mellitus is one of the most common endocrine diseases that occur during pregnancy. Disorders of blood glucose metabolism during pregnancy can increase the risk of adverse pregnancy outcomes, such as pregnancy-related hypertension, preeclampsia, eclampsia, miscarriage, macrosomia, and neonatal hypoglycaemia. Continuous glucose monitoring (CGM) can safely and effectively monitor blood glucose changes in patients with gestational hyperglycaemia, thereby reducing adverse pregnancy outcomes.

Hence, this article aims to provide a comprehensive review of the progress and indications for using CGM in pregnant patients with diabetes. CGM can reduce blood glucose fluctuations and the occurrence of serious hypoglycaemia and hyperglycaemia events and can provide time in range (TIR), which is an important indicator of blood glucose level. Patients with a higher TIR during pregnancy have better gestational outcomes.

READING 7 – ASIA-PACIFIC CONSENSUS RECOMMENDATIONS FOR CGM

Kong APS,¹ Lim S,² Yoo SH,³ Ji L,⁴ Chen L,⁵ Bao Y,⁶ Yeoh E,⁷ Chan SP,⁸ Wang CY,⁹ Mohan V,¹⁰ Cohen N,¹¹ McGill MJ,¹² Twigg SM.¹³ Asia-Pacific consensus recommendations for application of continuous glucose monitoring in diabetes management. *Diabetes Res Clin Pract.* 2023 Jul;201:110718. PMID: 37196707.

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ABSTRACT

Glucose monitoring has evolved from self-monitoring of blood glucose to glycated haemoglobin, and the latest continuous glucose monitoring (CGM). A key challenge to adoption of CGM for management of diabetes in Asia is the lack of regional CGM recommendations. Hence, 13 diabetes-specialists from eight Asia-Pacific (APAC) countries/regions convened to formulate evidence-based, APAC-specific CGM recommendations for individuals with diabetes. We defined CGM metrics/targets and developed 13 guiding-statements on use of CGM in: (1) people with diabetes on intensive insulin therapy, and (2) people with type 2 diabetes on basal insulin with/without glucose lowering drugs. Continual use of CGM is recommended in individuals with diabetes on intensive insulin therapy and suboptimal glycaemic control, or at high risk of problematic hypoglycaemia. Continual/intermittent CGM may also be considered in individuals with type 2 diabetes on basal insulin regimen and with suboptimal glycaemic control.

In this paper, we provided guidance for optimising CGM in special populations/situations, including elderly, pregnancy, Ramadan-fasting, newly diagnosed type 1 diabetes, and comorbid renal disease. Statements on remote CGM and stepwise interpretation of CGM data were also developed. Two Delphi surveys were conducted to rate the agreement on statements. The current APAC-specific CGM recommendations provide useful guidance for optimising use of CGM in the region.

READING 8 – BENEFITS OF CGM IN PRIMARY CARE

King J,¹ Govender RD,¹ Kieu A,^{1,2} Östlundh L.³ **The Benefits of Utilizing Continuous Glucose Monitoring of Diabetes Mellitus in Primary Care: A Systematic Review.** *J Diabetes Sci Technol.* 2023 May;17(3):762-774. PMID: 35100891.

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ABSTRACT

BACKGROUND: Continuous glucose monitoring (CGM) and intermittently scanned CGM (is-CGM) have shown to effectively manage diabetes in the specialty setting, but their efficacy in the primary care setting remains unknown. Does CGM/is-CGM improve glycaemic control, decrease rates of hypoglycaemia, and improve staff/physician satisfaction in primary care? If so, what subgroups of patients with diabetes are most likely to benefit?

METHODS: A comprehensive search in seven databases was performed in June 2021 for primary studies examining any continuous glucose monitoring system in primary care. We excluded studies with fewer than 20 participants, specialty care only, or hospitalised participants. The National Heart, Lung, and Blood Institute and Grading of Recommendations Assessment, Development, and Evaluation were used for the quality assessment. The weighted mean difference (WMD) of HbA1c between CGM/is-CGM and usual care with 95% confidence interval was calculated. A narrative synthesis was conducted for change of time in, above, or below range (TIR, TAR, and TBR) hypoglycaemic events and staff/patient satisfaction.

RESULTS: From 10 studies and 4,006 participants reviewed, CGM was more effective at reducing HbA1c compared with usual care (WMD -0.43%). There is low certainty of evidence that CGM/is-CGM improves TIR, TAR, or TBR over usual care. The CGM can reduce hypoglycaemic events and staff/patient satisfaction is high. Patients with intensive insulin therapy may benefit more from CGM/is-CGM.

CONCLUSIONS: Compared with usual care, CGM/is-CGM can reduce HbA1c, but most studies had notable biases, were short duration, unmasked, and were sponsored by industry. Further research needs to confirm the long-term benefits of CGM/is-CGM in primary care.

READING 9 – CGM IN ADVANCED CKD DIABETIC PATIENTS

Galindo RJ,¹ de Boer IH,² Neumiller JJ,³ Tuttle KR.^{4,5} **Continuous Glucose Monitoring to Optimize Management of Diabetes in Patients with Advanced CKD.** *Clin J Am Soc Nephrol.* 2023 Jan 1;18(1):130-145. PMID: 36719162.

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ABSTRACT

Treatment of patients with diabetes and CKD includes optimising glycaemic control using lifestyle modifications and drugs that safely control glycaemia and improve clinical kidney and cardiovascular disease outcomes. However, patients with advanced CKD, defined as eGFR <30 ml/min per 1.73 m² or kidney disease treated with dialysis, have limitations with regards to the use of some preferred glucose-lowering medications, are often treated with insulin, and experience high rates of severe hypoglycaemia. Moreover, haemoglobin A1c accuracy decreases as GFR deteriorates. Hence, there is a need for better glycaemic monitoring tools. Continuous glucose monitoring allows for 24-hour glycaemic monitoring to understand patterns and the effects of lifestyle and medications. Real-time continuous glucose monitoring can be used to guide the administration of insulin and noninsulin therapies. Continuous glucose monitoring can overcome the limitations of self-monitored capillary glucose testing and haemoglobin A1c and has been shown to prevent hypoglycaemic excursions in some populations. More data are needed to understand whether similar benefits can be obtained for patients with diabetes and advanced CKD.

This review provides an updated approach to management of glycaemia in advanced CKD, focusing on the role of continuous glucose monitoring in this high-risk population.

READING 10 – SHOULD CGM BE USED TO MANAGE NEONATES AT RISK OF HYPOGLYCAEMIA?

Kalogeropoulou MS,¹ Beardsall K,^{1,3,4} Iglesias-Platas I.² Should continuous glucose monitoring be used to manage neonates at risk of hypoglycaemia? *Front Pediatr.* 2023 Mar 21;11:115228. PMID:37025284.

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The National Institute for Clinical Excellence (NICE) now recommends that continuous glucose monitoring (CGM) be offered to adults and children with diabetes who are at risk from hypoglycaemia.

Hypoglycaemia is common in the neonatal period, and is a preventable cause of poor neurodevelopmental outcome, but is CGM helpful in the management of neonates at risk of hypoglycaemia?

Neonatal studies have shown that CGM can detect clinically silent hypoglycaemia, which has been associated with reduced executive and visual function in early childhood. Intervention trials have further shown that CGM can support the targeting of glucose levels in high-risk extremely preterm neonates. In spite of significant advances in technology, including smaller sensors, better accuracy, and factory calibration, further progress and adoption into clinical practice has been limited as current devices are neither designed nor have regulatory approval for the specific needs of the newborn.

The use of CGM has the potential to support clinical management and prevention of hypoglycaemia but must be set within its current limitations. The data from CGM however also provides an important opportunity to improve our understanding of the potential risks of hypoglycaemia and the impact of clinical interventions to prevent it.