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Early Glycemic Control Assessment Based on Consensus CGM Metrics*

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Abstract— **Continuous glucose monitoring (CGM) has revolutionized the world of diabetes and transformed the approach to diabetes care. In this context, an expert panel has reached consensus on clinical targets for CGM data interpretation based on eight CGM metrics. At least 70% of 14 consecutive CGM days (referred to as a period) are recommended to assess glycemic control based on the metrics. In clinical practice less CGM data may be available. Therefore, the primary aim of this study is to explore the ability to recover the consensus metrics utilizing less than 14 days of CGM data (intra-period). As a secondary aim, we investigate the recovery considering two consecutive periods (inter-period). The analyses are based on real-world CGM data from 484 diabetes users (4726 periods) acquired from the Cornerstones4Care® Powered by Glooko app. Using up to 14 accumulated days, the consensus metrics are calculated for each user and period, and compared to the fully 14 accumulated intra- and inter-period days. Relatively low deviations were observed for time in range (TIR) and average based metrics when using less than 14 days, however, we observed large deviations in metrics characterizing infrequent events such as time below range (TBR). Furthermore, the consensus metrics obtained in two consecutive 14 day periods have clear discrepancies (inter-period). Recovering consensus metrics using less than 14 days might still be valuable in terms of interpreting CGM data in certain clinical contexts. However, caution should be taken if treatment decisions would be made with less than 14 days of data on critical metrics such as TBR, since the metrics characterizing infrequent events deviate substantially when less data are available. Substantial deviation is also seen when comparing across two consecutive periods, which means that care should be taken not to over-generalize consensus metric based glycemic control conclusions from one period to subsequent periods.**

I. Introduction

Over recent decades, diabetes prevalence has risen globally across all age groups. Currently, an estimate of 436 million people in the world have diabetes, and numbers are expected to increase further [1]. The major categories are type 1 (T1D), and the more prevalent type 2 diabetes (T2D) which accounts for approximately 90% of all cases.

Diabetes is a chronic disease characterised by abnormal levels of glucose in the blood due to either inadequate production of insulin or insufficient sensitivity of cells to use it effectively. An increased risk of developing life-threatening health complications is caused by prolonged elevated glucose levels. These consequences can be avoided or delayed if people with diabetes are treated adequately. Hence, diabetes management requires substantial effort from the person with diabetes in terms of independent self-care and adherence to treatment. A crucial factor is the regular assessment of glycemic control [2]. The traditional way of assessing glycemic control is to measure glycated haemoglobin, HbA1c, reflecting the last two-three months average glucose levels. Although it plays a major role and is a well-established tool for assessing the risk of diabetes complications, it has several limitations [3]. It is insensitive to rapid intra- and inter-day variation and cannot capture acute excursions. Similarly, Self-Monitoring Blood Glucose (SMBG) provide a limited number of glucose level measurements within a day and does not reflect the immediate glucose level trend [3].

Continuous glucose monitoring (CGM) technology addresses many of the limitations of HbA1c and SMBG, and is anticipated to replace them over time [3], [4]. CGM devices are worn up to two weeks and measure glucose values in 5 to 15 minute intervals. The dynamic information and trends enable visualization of immediate variability in glucose levels, including its two extremes, hypo- and hyperglycemia [5]. As a result, a CGM device can be a powerful tool to support immediate treatment decisions, e.g., prompt adjustment of insulin dosing and adherence detection [3], [6]–[8].

Even though benefits of the CGM technology are recognised and the technology has improved considerably in terms of increased robustness and accuracy, the successful utilization of CGM in clinical practice stays relatively low [3]. One reason has been the lack of a standardized approach to generate relevant insights from the CGM data and transfer these to the patient and the healthcare professionals (HCPs). Although recommendations have been put forward in separate peer-reviewed articles, formal adaption and application remained low [3], [9]–[11]. To address this, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress convened an international expert panel which established a standardized approach to evaluate CGM data for T1D and T2D patients [3]. A total of eight CGM metrics were established to guide glycemic control assessment [3]. It was further recommended that the minimum percentage of CGM readings should be 70% during 14 consecutive days of CGM data in order to perform a reliable assessment of the glycemic control [3]. This is supported by a prior study presented by

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Xing et al. [12] and a more recent study by Riddleworth et al. [13] showing that 14 days of CGM data are needed to reliably reflect a patient's glucose levels. Thus, there is consensus that for clinical use 14 days of CGM data suffices to reflect a patients glycemic control. However, in clinical reality less than 14 days of CGM data may be available, for instance due to gaps in CGM data which can occur for a variety of reasons based on human and/or sensor error or sensor compression [14].

Therefore, the primary aim of this study is to examine how the consensus metrics are impacted by the use of less than 14 days of data. This is examined in terms of the extent in which each consensus metric can be recovered using data from fewer days than the fully accumulated 14 days of CGM data. Unless treatment interventions or lifestyle changes are instituted, glycemic control changes gradually. Thus, consensus metric based glycemic control conclusions based on two consecutive 14 day periods should be reasonably consistent. The consistency of the metrics between consecutive periods is of interest in situations where CGM data are used for decision support algorithms which go beyond real-time or near real-time decision support. A secondary aim of this study is therefore to examine the extent to which each consensus metric can be recovered when compared to the consecutive 14 days of CGM data.

To the best of our knowledge, we are the first study to investigate the recovery of consensus metrics both within and between two consecutive 14 day periods based on a large self-reported *real-world* data across a diverse population. This is different from the mentioned studies based on *clinical* data by Xing et al. [12] and Riddlesworth et al. [13] including a recent study by Herrero et al. [15] proposing a new approach to define the minimum duration of CGM data based on T1D patient data.

II. Materials and Methods

A. Established consensus CGM metrics

This study is based on the recommendations of the expert panel as presented in Table 1. In order to facilitate more practical and easier data interpretation, the panel identified time in ranges as a combined, more intuitive metric of glycemic control [3], [16]. It includes a subset of the consensus metrics as depicted in Figure 1: time in range (TIR, metric six), time above range (TAR, metrics four and five) and time below range (TBR, metrics seven and eight), expressed either as time per day or as percentage of readings as illustrated in Figure 1. Acceptable glycemic control is achieved if all of the presented conditions are met. However, individual assessment is encouraged in each case [3], and different thresholds apply for specific patient groups (e.g. older/high risk patients and during pregnancy).

B. CGM data and inclusion criteria

Our analysis is conducted based on real-world CGM data acquired from the Cornerstones4Care® Powered by Glooko platform, which is a diabetes management application. The data are used for research purposes with consent from the users [17]. The data set covers the period from 2016 to 2019, and includes data from T1D and T2D patients, albeit a considerable proportion has not reported their diabetes type in the app. Therefore, the CGM data are pooled by considering the same consensus guidelines presented for T1D and T2D patients (apart from older/high risk patients and during pregnancy) and the uncertainties associated with self-reported data. For each user, we identified all available periods of 14 consecutive days of CGM data in the mentioned period. Only data from users with at least two consecutive periods of data, i.e., 28 consecutive days were included, and where CGM data were available for $> 70\%$ of each day. For each included period, the days were divided into 14 accumulated time spans from 1 to 14 days, thus gradually adding more CGM data. For each period, the established consensus CGM metrics were calculated for the accumulated days [18] using the same approach regardless of which CGM device the data originated from. Many users had more than two consecutive periods available (repeated measures), i.e., more than two consecutive periods at a time (e.g. four consecutive periods in a row) and/or two or several consecutive periods with breaks in between, over the observed time period.

C. Intra- and inter-period analyses

Two analyses are made, namely intra-period (within 14 days period) and inter-period (across two consecutive periods). The intra-period analysis quantifies the extent to which an assessment based on less CGM data can recover the assessment had the data from the full 14 days been available, the primary study aim. The inter-period analysis quantifies the extent an assessment based on CGM data from a full 14 days period can recover the assessment had it been based on the 14 days CGM data of the consecutive period, the secondary study aim.

In order to introduce consistency and a comparable setup between the two analyses, the last available period for each user was excluded for the intra-period analysis. This exclusion approach is performed in order to assure equal number of data samples between the two analyses, thus the possibility of direct comparison.

D. Statistical measures

As statistical measure, Relative Absolute Difference (RAD) is applied. In this context, results are provided as the estimated population mean with 95% confidence interval (CI). Since we consider repeated measures when estimating the population mean, RAD is modelled using a random effects model to incorporate both within and between user variation [19] as implemented using the 'lme4' package (version 1.1.21) in R (version 3.6).

The RAD captures how much the value of each accumulated day of CGM data differs from the value based on the corresponding fully accumulated 14 day period and is defined as:

$$RAD_m(p,s,d) = \left| \frac{x^{(m)}_{p,s,d} - x^{(m)}_{p',s,d=14}}{x^{(m)}_{p',s,d=14}} \right| \cdot 100\%, \qquad (1)$$

TABLE I

ESTABLISHED CONSENSUS CGM METRICS FOR CLINICAL CARE (2019) [3].

Established consensus CGM metrics	
1. Mean glucose (MG)	
2. Glucose management indicator (GMI)	
3. Glycemic variability (%CV)	
4. Time above range (TAR)	% of readings and time >250 mg/dL (>13.9 mmol/L) [Level 2]
5. Time above range (TAR)	% of readings and time 181-250 mg/dL (10.1-13.9 mmol/L) [Level 1]
6. Time in range (TIR)	% of readings and time 70-180 mg/dL (3.9-10.0 mmol/L)
7. Time below range (TBR)	% of readings and time 54-69 mg/dL (3.0-3.8 mmol/L) [Level 1]
8. Time below range (TBR)	% of readings and time <54 mg/dL (<3.0 mmol/L) [Level 2]

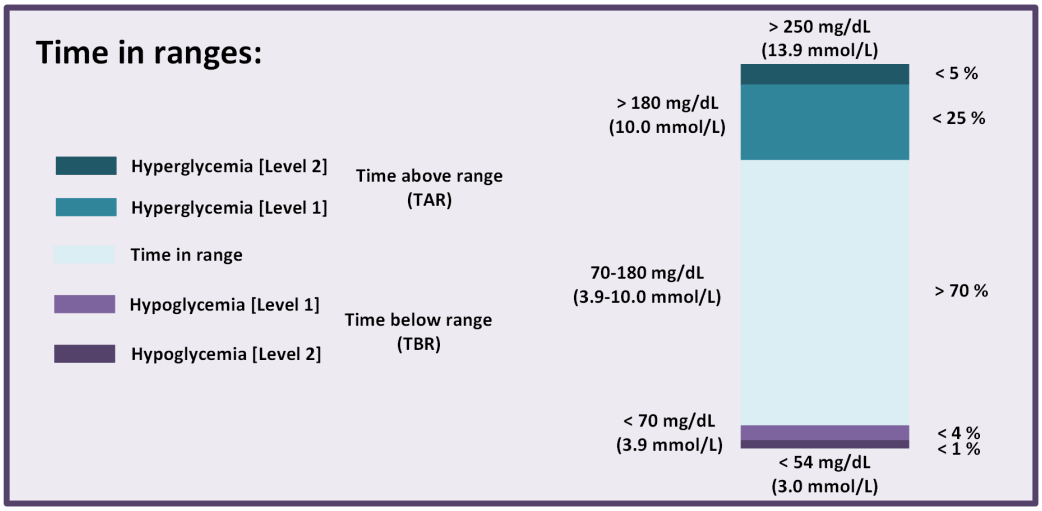

Fig. 1. Time in ranges (conditions) for glycemic control assessment represented by stacked bar (inspired from the international consensus on TIR [3]).

where $x^{(m)}_{p',s,d=14}$ represents the value of consensus metric m for period p of subject s accumulating d days of CGM data. For the intra-period analysis $p' = p$ (current period) and for inter-period analysis $p' = p+1$ (consecutive period).

Although the RAD measure is well-established and has previously been used in similar contexts comparing relative differences between CGM metrics when less data than the proposed duration are used [12], it is subject to an inherent limitation. RAD is impacted by the magnitude of each metric's full 14 days value, which must be taken into account when comparing and interpreting metrics with different magnitudes.

To clarify this, consider GMI, which is a scaled linear combination of MG [20]. Even though GMI and MG are based on the same value, the RAD will be different. Let d represent the considered day, x depict MG and y be GMI related to MG as $y = a \cdot x + b$ where $a = 0.02392$ and $b = 3.31$ for MG in [mg/dL] presented by Bergenstal et al. [20]. The following reduction is then applied:

$$\begin{aligned} RAD(x) &= \left| \frac{x_d - x_{d=14}}{x_{d=14}} \right| \\ RAD(y) &= \left| \frac{y_d - y_{d=14}}{y_{d=14}} \right| = \left| \frac{(a \cdot x_d + b) - (a \cdot x_{d=14} + b)}{(a \cdot x_{d=14} + b)} \right| \\ &= \left| \frac{x_d - x_{d=14}}{x_{d=14} + \frac{b}{a}} \right| = RAD(x) \cdot \frac{x_{d=14}}{x_{d=14} + \frac{b}{a}}, \end{aligned} \quad (2)$$

where we have used that $x_{d=14}$, a, and b all are positive. Hence, $RAD(y)$ will be reduced relative to $RAD(x)$ by the factor $\frac{x_{d=14}}{x_{d=14}+138.4}$, resulting in different RAD values even though they are based on the same value.

For the inter-period analysis, we further estimate the extent in which two consecutive CGM periods are correlated using repeated measures correlation [21] (accounting for the intra-user variability) as implemented using 'rmcorr' package (version 0.4.1) in R (version 3.6).

The random effects model approach for RAD and the repeated measures correlation are applied as these desirably exploit all available CGM data. These are preferred over either an averaging approach or manually selecting the periods/patients.

III. RESULTS

A. Available CGM data

The data set includes 50% T1D and 15% T2D users. 35% have not registered their diabetes type in the app (unknown). 29% of the users reported to be male, 24% female and 47% have not given information about their gender. The average age in 2019 was 42 years for T1D, 56 years for T2D and 44 years for unknown. A total of 4726 14 day periods of CGM data, representing 484 users were included into the study, distributed as shown in Figure 2. The average time with available CGM data for the included periods was 88.4%.

In order to give an overview of the included CGM periods, Figure 3 provides the estimated population mean with 95% CI (based on random effects model) of the average time spent in the different ranges (TIR, TBR and TAR level 1 and 2) expressed as percentages [%], grouped by diabetes type. As expected, TBR is quite low for both level 1 and 2, followed by TAR level 1 and 2. In contrast, high values of TIR are present for all cases. The same plots are presented for the average based metrics, i.e., MG, GMI and CV.

B. Intra-period analysis results

Figure 4 shows the estimated population mean RAD [%] with 95% CI considering the eight consensus CGM metrics by accumulating days compared to the fully accumulated 14 days. The magnitude varies considerably amongst the different metrics. The RAD is recognizably highest for TBR level 1 and 2, and TAR level 2 over all accumulated days, exceeding $> 90\%$ at day one. In contrast, the RAD for TIR, MG, GMI and CV are relatively low even when assessing only one day of CGM data: 24% (TIR), 11% (MG), 6% (GMI) and 19% (CV). It is further reduced to 5% (TIR), 2% (MG), 1% (GMI) and 4% (CV) after 10 accumulated days. However, bearing in mind the limitations of RAD being impacted by the magnitude of each metric, this does not necessarily imply a better robustness of these metrics. Nevertheless, TIR and the average based metrics (MG, GMI and CV) still deviate least. In contrast, this is not the case for the critical consensus metrics represented by TBR level 1 and 2 as these are rare events which therefore deviate more with reducing amounts of CGM data. For all metrics, we observe a reduction in RAD as more days are included and there appears to be no clear point in which RAD no longer improves.

C. Inter-period analysis results

For the inter-period analysis (Figure 5, top panel), we observe that the RAD decreases for all the CGM metrics as more CGM data are included. However, the RADs are substantially higher than in the intra-period analysis. The observable difference is that the intra-period analysis converges towards zero as expected, while the inter-period assessment even after accumulated 14 days differs substantially. The lowest RADs are found when accumulating all 14 days as the following: 9% (CV), 4% (GMI), 7% (MG), 14% (TIR), 96% (TAR level 2), 43% (TAR level 1), 89% (TBR level 1), 81% (TBR level 2). In other words, even between two consecutive periods we observe clear discrepancies for the metrics and most noticeable for the critical metrics comprising TBR level 1 and 2.

For the estimated inter-period repeated measure correlation coefficient (Figure 5, bottom panel), we observe that the correlation gradually increases with increasing accumulating days and reaches a level of approximately 0.5 when the fully accumulated 14 days of the first period is compared to the fully accumulated 14 days of the second consecutive period. Compared to the other metrics, TBR level 2 and CV reach the lowest correlation coefficient of approximately 0.3.

IV. Discussion

A. Discussion of results pertaining to the primary study aim

The primary aim of this study was to examine how the consensus metrics are impacted by the use of less than 14 days of CGM data. In brief, as expected and illustrated by Figure 4, increasing amounts of data steadily improve the representation of the consensus metrics obtained when using 14 days of CGM data.

Although the RAD is relatively small for TIR and the average based metrics (MG, GMI and CV), this does not necessarily imply that less CGM data on these metrics can give adequate insight into glycemic control compared to the insights obtained by the recommended (70% of) 14 days of data. Instead, these results are biased by the high impact of the described full 14 days mean magnitude for each respective metric. For this reason, all the outcomes should be analysed carefully and always compared to the magnitude as presented in Figure 3.

TIR and the average based metrics obtained with less than 14 days of data can to a degree still reflect the same metrics obtained with the full 14 days of data. Thus, being aware of the clinical question to be addressed, TIR and the average based metrics may still provide valuable information on the average glycemic levels, even when based on fewer days of data.

In contrast, using less data significantly impacts the robustness of the information about the infrequent events, notably TBR level 1 and 2. In the clinical context these low glucose values are critical to avoid. Even though a strength of real-time CGM is to empower the patient to closely navigate their glucose levels and avoid hypoglycemia, our data illustrate a potential pitfall; If a patient's CGM data are pooled, but less than 14 days of data are available, the risk of missing critical low glucose information is increased. Combined, the limited impact on the average metrics and the significant impact on the metrics on infrequent events, calls for caution. For instance, an automated insulin titration algorithm should in a risk based way take this into account in the determination of minimum required data for dose recommendations.

B. Discussion of results pertaining to the secondary study aim

The secondary aim of this study was to examine the extent to which each consensus metric can be recovered when compared to the consecutive 14 days of CGM data. Figure 5 (top panel) displays a similar trend as in Figure 4, i.e., improved performance with increasing number of accumulating days. However, two consecutive periods substantially differ as the RADs do not converge towards zero. This means that even when basing the consensus metrics on a full period with 14 days of data, these calculated metrics only correspond to metrics calculated from the consecutive 14 day period to a limited degree. For instance, the RADs after 14 days of accumulated data (Figure 5, top panel, 14 days data) only represent the consecutive 14 days period equivalent to what 1-2 days of accumulated data from the same consecutive

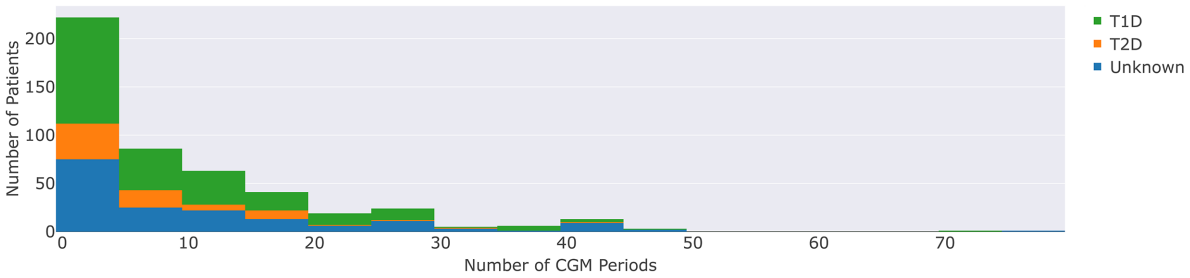

Fig. 2. Number of 14 day periods represented by stacked bar (grouped by diabetes type).

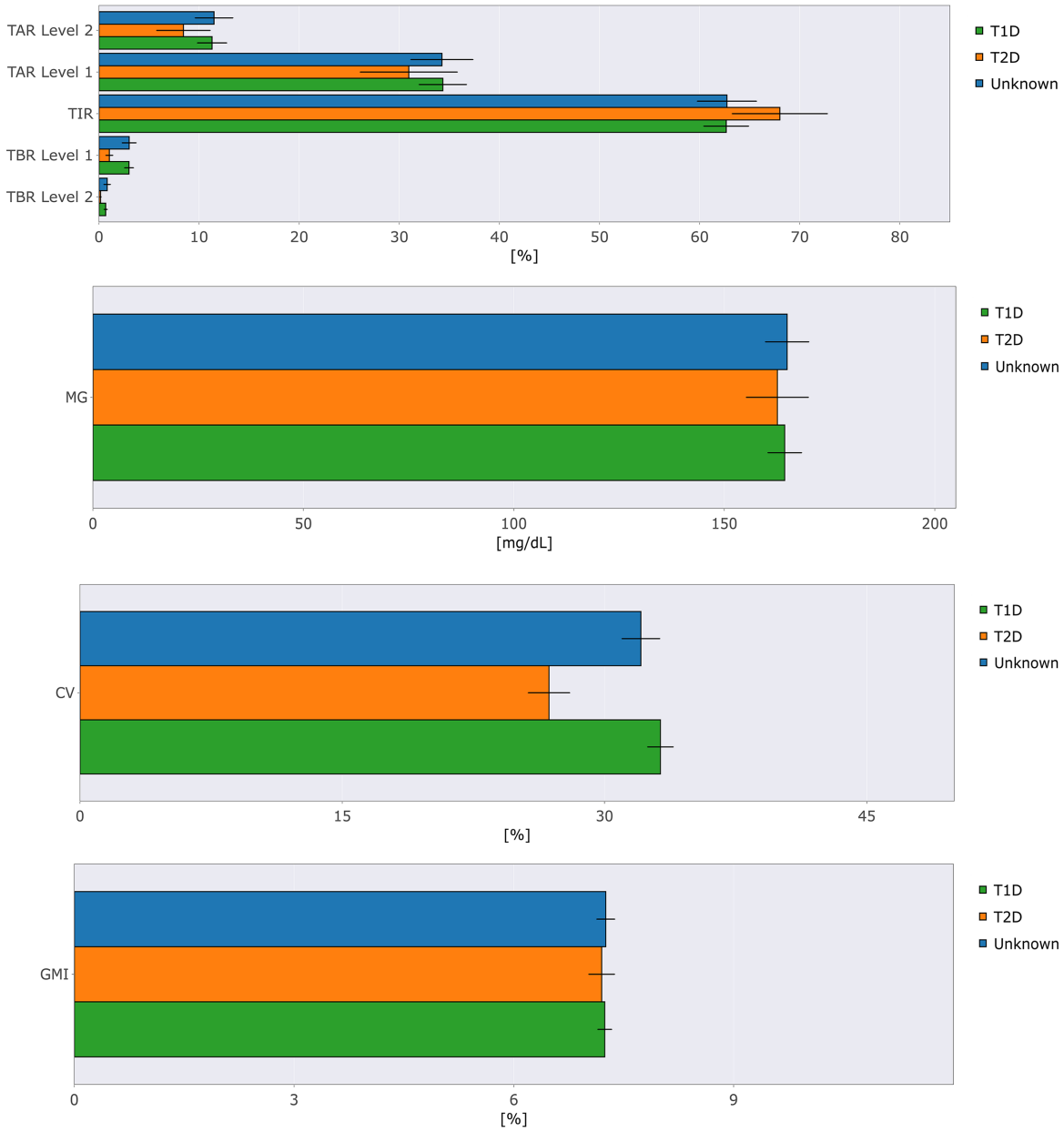

Fig. 3. Estimated population mean with 95% confidence interval considering the time spent in the different ranges (Time in range (TIR), Time below range (TBR) and Time above range (TAR) level 1 and 2) in terms of percentages [%], MG [mg/dL], CV [%] and GMI [%] for the included 14 day periods (grouped by diabetes type).

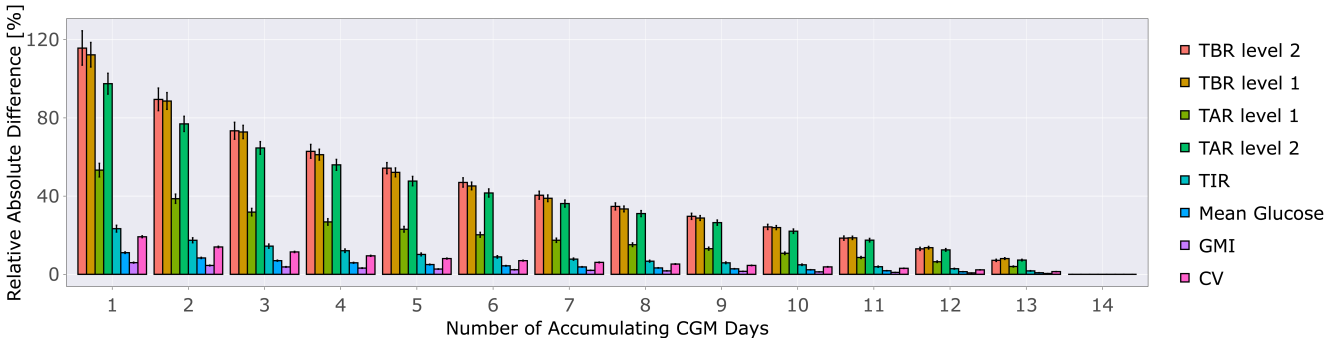

Fig. 4. Estimated population mean Relative Absolute Difference [%] with 95% confidence interval considering the eight consensus CGM metrics by accumulating days compared to the fully accumulated 14 days (intra-period analysis).

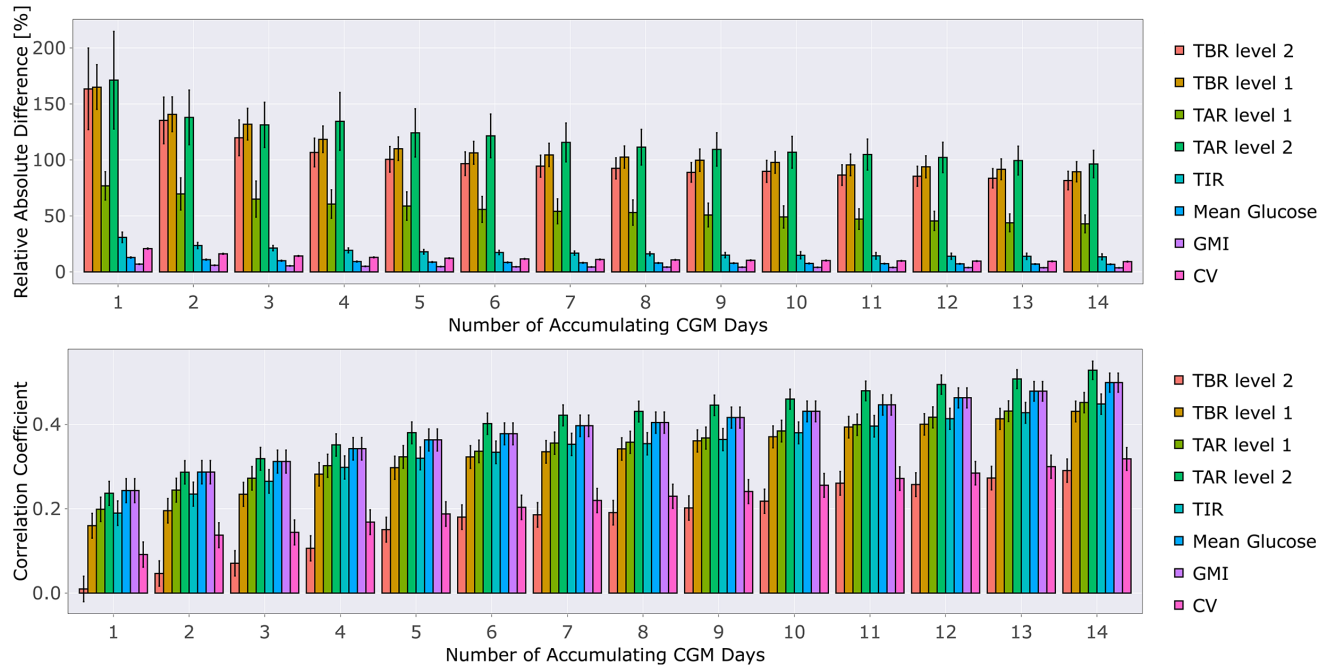

Fig. 5. Top panel: Estimated population mean Relative Absolute Difference [%] with 95% confidence interval considering the eight consensus CGM metrics by comparing accumulating days in the first period to the second fully accumulated 14 days period (inter-period analysis). Bottom panel: Same analysis but quantifying the estimated repeated measures correlation coefficient with 95% confidence interval.

period would have achieved (Figure 4, 1 and 2 days of CGM data).

In addition to this, the estimated repeated measure correlation coefficient, Figure 5 (bottom panel), illustrates how much a consecutive period for an individual user correlates accounting for the intra-user variability. We observe substantial correlation indicating that even though two consecutive periods differ as described above, they are more similar in comparison to the more distant periods. This supports the clinically intuitive conclusion, that e.g. a predictive decision support algorithm will deteriorate with increasing timespan.

C. Considerations regarding CGM applications

CGM is becoming a well-established part of clinical care of people with diabetes. When used as part of clinical care, the physician assesses the person with diabetes holistically, and the person with diabetes uses the CGM as daily real-time support for decision making. In these situations, the CGM derived consensus metrics can be used to increase the understanding of the CGM data.

The consensus metrics can make it easier and more convenient to interpret periods of CGM data. In addition, some of the metrics may even be valuable when periods contain less than 14 days of CGM data in certain clinical contexts. However, our results call for caution if important treatment decisions are made based on the consensus metrics, in particular in situations where less than the recommended amount of data are available because infrequent events such as low glucose levels may be missed [15], [22].

D. Limitations and strengths of the study

This study uses real-world CGM data with limited and self-reported user information. In this data set, factors which are known to impact glucose level are largely unspecified,

e.g. diabetes type, demographics, lifestyle. Furthermore, treatment regimens, whether the users are optimally titrated and have achieved steady-state in their current treatment is also unknown. However, the real-world data are also the primary strength of the study as our analyses are based on large amounts of CGM data acquired in real-life situations across a diverse population. Hence, the data are not constrained by the limitations associated with the controlled setup of traditional clinical trials.

V. Conclusion

Using less than 14 days, increasing amounts of data steadily improve the representation of the consensus metrics obtained when using 14 days of CGM data. Some of the consensus metrics (TIR and average metrics) might still be valuable in terms of interpreting CGM data in certain clinical contexts. However, caution should be taken if treatment decisions would be made with less than 14 days of data on critical metrics such as TBR, since the metrics characterizing infrequent events deviate substantially when less data are available. Substantial deviation is also seen when comparing across two consecutive periods, which means that care should be taken not to over-generalize consensus metric based glycemic control conclusions from one period to subsequent periods.

References

[1] P. Saeedi, I. Petersohn, P. Salpea, B. Malanda, S. Karuranga, N. Unwin, S. Colagiuri, L. Guariguata, A. A. Motala, K. Ogurtsova, *et al.*, "Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition," *Diabetes Research and Clinical Practice*, vol. 157, p. 107843, 2019.

[2] American Diabetes Association, "Standards of Medical Care in Diabetes–2020," *Diabetes Care*, vol. 43 Suppl 1, 2020.

[3] T. Battelino, T. Danne, R. M. Bergenstal, S. A. Amiel, R. Beck, T. Biester, E. Bosi, B. A. Buckingham, W. T. Cefalu, K. L. Close, *et al.*, "Clinical targets for continuous glucose monitoring data interpretation: Recommendations from the international consensus on time in range," *Diabetes Care*, vol. 42, no. 8, pp. 1593–1603, 2019.

[4] C. Fabris, L. Heinemann, R. W. Beck, C. Cobelli, and B. Kovatchev, "Estimation of Hemoglobin A1c from Continuous Glucose Monitoring Data in Individuals with Type 1 Diabetes: Is Time in Range All We Need?," *Diabetes Technology & Therapeutics*, vol. 22, no. 7, 2020.

[5] S. V. Edelman, N. B. Argento, J. Pettus, and I. B. Hirsch, "Clinical implications of real-time and intermittently scanned continuous glucose monitoring," *Diabetes Care*, vol. 41, no. 11, pp. 2265–2274, 2018.

[6] D. N. Thyde, A. Mohebbi, H. Bengtsson, M. L. Jensen, and M. Mørup, "Machine Learning-Based Adherence Detection of Type 2 Diabetes Patients on Once-Daily Basal Insulin Injections," *Journal of Diabetes Science and Technology*, 2020.

[7] A. Mohebbi, A. R. Johansen, N. Hansen, P. E. Christensen, J. M. Tarp, M. L. Jensen, H. Bengtsson, and M. Morup, "Short Term Blood Glucose Prediction based on Continuous Glucose Monitoring Data," in *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, pp. 5140–5145, 2020.

[8] D. Rodbard, "Continuous glucose monitoring: A review of recent studies demonstrating improved glycemic outcomes," *Diabetes Technology and Therapeutics*, vol. 19, pp. S25–S37, 6 2017.

[9] G. Agiostratidou, H. Anhalt, D. Ball, L. Blonde, E. Gourgari, K. N. Harriman, A. J. Kowalski, P. Madden, A. H. McAuliffe-Fogarty, M. McElwee-Malloy, *et al.*, "Standardizing clinically meaningful outcome measures beyond HbA1c for type 1 diabetes: A consensus report of the American Association of Clinical Endocrinologists, the American Association of Diabetes Educators, the American Diabetes Association, the Endo," *Diabetes Care*, vol. 40, no. 12, pp. 1622–1630, 2017.

[10] T. Danne, R. Nimri, T. Battelino, R. M. Bergenstal, K. L. Close, J. H. DeVries, S. Garg, L. Heinemann, I. Hirsch, S. A. Amiel, *et al.*, "International consensus on use of continuous glucose monitoring," *Diabetes Care*, vol. 40, no. 12, pp. 1631–1640, 2017.

[11] J. R. Petrie, A. L. Peters, R. M. Bergenstal, R. W. Holl, G. A. Fleming, and L. Heinemann, "Improving the clinical value and utility of CGM systems: issues and recommendations: A joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group," *Diabetologia*, vol. 60, no. 12, pp. 2319–2328, 2017.

[12] D. Xing, C. Kollman, R. W. Beck, W. V. Tamborlane, L. Laffel, B. A. Buckingham, D. M. Wilson, S. Weinzimer, R. Fiallo-Scharer, and K. J. Ruedy, "Optimal sampling intervals to assess long-term glycemic control using continuous glucose monitoring," *Diabetes Technology and Therapeutics*, vol. 13, no. 3, pp. 351–358, 2011.

[13] T. D. Riddlesworth, R. W. Beck, R. L. Gal, C. G. Connor, R. M. Bergenstal, S. Lee, and S. M. Willi, "Optimal Sampling Duration for Continuous Glucose Monitoring to Determine Long-Term Glycemic Control," *Diabetes Technology and Therapeutics*, vol. 20, no. 4, pp. 314–316, 2018.

[14] S. J. Fonda, D. G. Lewis, and R. A. Vigersky, "Minding the gaps in continuous glucose monitoring: A method to repair gaps to achieve more accurate glucometrics," *Journal of Diabetes Science and Technology*, vol. 7, no. 1, pp. 88–92, 2013.

[15] P. Herrero, A. Alalitei, M. Reddy, P. Georgiou, and N. Oliver, "Robust determination of the optimal continuous glucose monitoring length of intervention to evaluate long-term glycaemic control," *Diabetes Technology & Therapeutics*, vol. 44, no. February, pp. 19–22, 2020.

[16] D. Rodbard, "Glucose Time In Range, Time Above Range, and Time Below Range Depend on Mean or Median Glucose or HbA1c, Glucose Coefficient of Variation, and Shape of the Glucose Distribution," *Diabetes Technology & Therapeutics*, vol. 22, no. 7, pp. 492–500, 2020.

[17] A. K. Böhm, M. L. Jensen, M. R. Sørensen, and T. Stargardt, "Real-World Evidence of User Engagement With Mobile Health for Diabetes Management: Longitudinal Observational Study," *JMIR mHealth and uHealth*, vol. 8, p. e22212, 11 2020.

[18] A. Mohebbi, J. M. Tarp, M. L. Jensen, S. Puthusserypady, E. Hachmann-Nielsen, H. Bengtsson, and M. Morup, "Fast Assessment of Glycemic Control based on Continuous Glucose Monitoring Data," in *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, pp. 7185–7188, 2019.

[19] M. Borenstein, L. V. Hedges, J. P. T. Higgins, and H. R. Rothstein, "A basic introduction to fixed-effect and random-effects models for meta-analysis," *Research Synthesis Methods*, pp. 97–111, 2010.

[20] R. M. Bergenstal, R. W. Beck, K. L. Close, G. Grunberger, D. B. Sacks, A. Kowalski, A. S. Brown, L. Heinemann, G. Aleppo, D. B. Ryan, *et al.*, "Glucose management indicator (GMI): A new term for estimating A1C from continuous glucose monitoring," *Diabetes Care*, vol. 41, pp. 2275–2280, 11 2018.

[21] J. Z. Bakdash and L. R. Marusich, "Repeated Measures Correlation," *Frontiers in Psychology*, vol. 8, p. 456, 4 2017.

[22] A. Advani, "Positioning time in range in diabetes management," *Diabetologia*, vol. 63, no. 2, pp. 242–252, 2020.