Challenges of Statistical Inference Applied to Real World Data in Diabetes Care

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OBJECTIVE

Assessing diabetes therapy performance from Real World Data (RWD) is difficult as the data quantity of SMBG readings shows strong variability. Meeting the measurement regimens used in clinical setups is difficult for the majority of patients and potentially leads to a strong selection bias. Analyses for SMBG constraints applicable to RWD are missing but seem necessary, given the increasing interest in RWD studies and the lack of standardization.

METHOD

We found that previous studies using SMBG based metrics often lack predictive performance assessment (with respect to SMBG frequency.)* [1, 2, 3], with ADRR being an exception (3 SMBG / 14 days) 4. We see two potential risks when applying no or unvalidated constraints. Using loose inclusion criteria such as mean frequency, one might falsely include patients with skewed SMBGs. Second, hard constraints might favour highly motivated users. In order to leverage these biases, we formalized a flexible inclusion criteria.

RESULTS

$G^k_{n/N} \Leftrightarrow$ *n out of N days: |SMBG| ≥ k* formalizes data constraints as an observational period of N days in which a subset of n days are required to each contain ≥ k blood glucose readings. The formalism can easily be applied to published ADRR constraints (3 SMBG/day in 14 out of 30 days) as $G^3_{14/30}$. Our previous work modeled hypoglycemic excursion probabilities using kernel density functions and found $G^4_{14/30}$ using CGM based predictive performance assessment.[5]

We looked at a random selection of mySugr app registrations (n = 947) for a time period of 1 month and classified them into 4 groups based on SMBG logging habits. ***Figure 1*** shows the results of the classification.

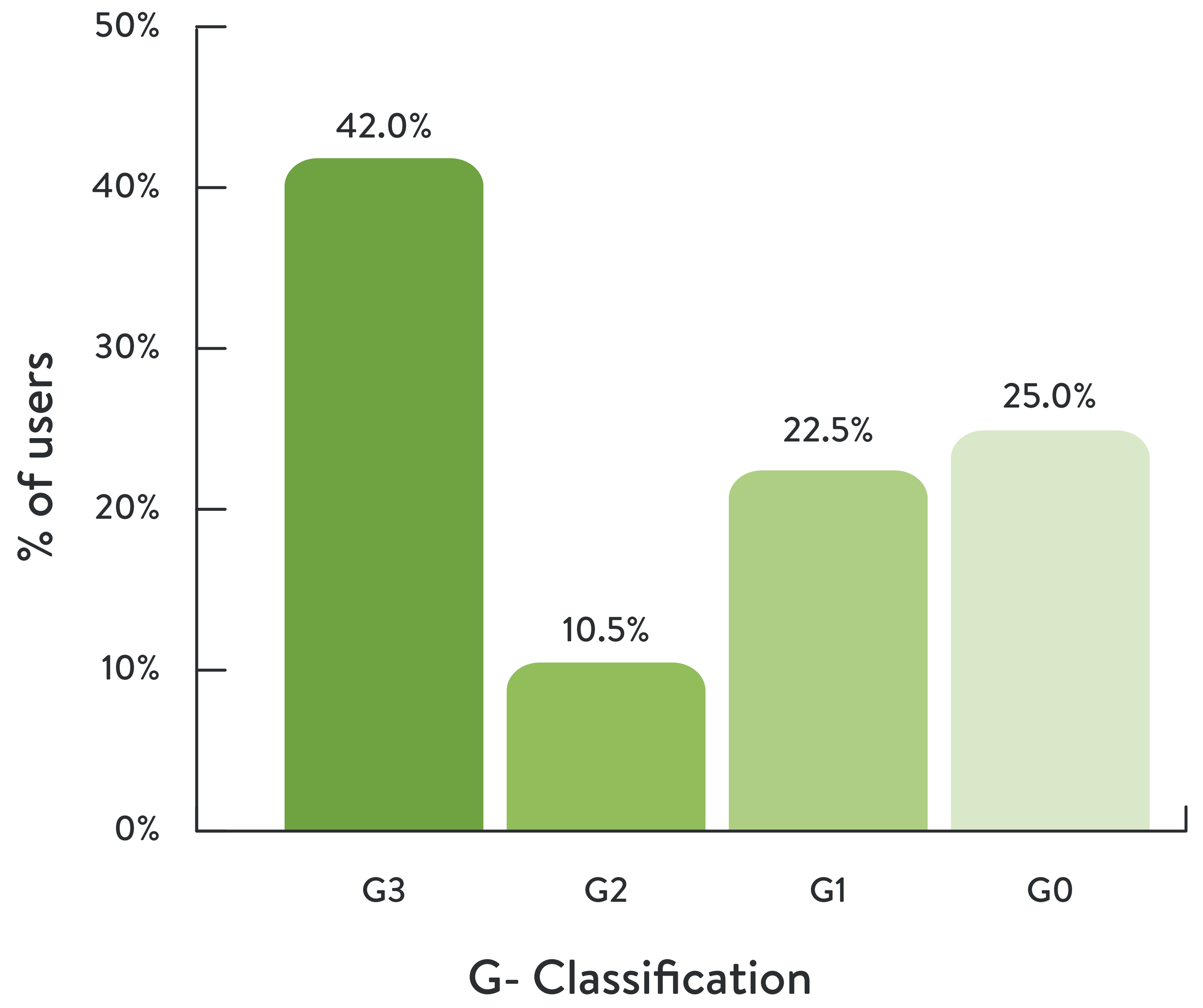

Figure 1: *The classifying logging habits (G-Classification) for 947 randomly selected users for a time period of 1 month.*

The classification allows us to easily understand our users' logging habits as well as provide them flexibility in logging. Each of the 4 groups from ***Figure 1*** are described below in detail:

- **G3 - Highly engaged users:** G3 represents k = 3 in the formalized equation for a minimum of 3 logs in 14 out of 30 days in the month. This logging rate allows us to feel confident in using industry standard metrics: estimated HbA1c, LBGI, HBGI, ADRR.
- **G2 - Engaged users:** logging habits are enough to draw some insights from the data: mean BG, Number of hypo- / hyperglycemic events. However, we would not calculate the industry standard metrics on this group.
- **G1 - Minimum engaged users:** These users' logging habits are not suitable for medically relevant insights and only minimal insight can be drawn from the readings.
- **G0 - No engagement:** This group shows users which have not used the mySugr app for SMBG logging.

The following 2 tables show the benefits of using our flexible metric. Even though User A in ***Table 1*** has an average of 2.0 readings per day, he/she will fall into the G1 classification. That is because the user only has 7 out of 30 days with more than 2 readings but 14 out of 30 days with >= 1 readings.

Table 1: *User A's daily SMBG readings for 1 month. User has an average readings per day of 2.0*

MON	TUE	WED	THU	FRI	SAT	SUN
10	10	10	5	5	0	10
3	0	0	0	0	0	1
1	0	0	1	0	0	0
1	0	0	0	1	1	0
1	0					

We include the user in ***Table 2*** to the G3 classification because while User B only has 1.7 readings per day on average, he/she has 17 distinct days with at least 3 readings.

Table 2: *User B´s daily SMBG readings for 1 month. User has an average readings per day of 1.7*

MON	TUE	WED	THU	FRI	SAT	SUN
3	0	3	0	3	0	3
3	0	3	0	3	0	3
3	0	3	0	3	0	3
3	0	3	0	3	0	3
3	0					

CONCLUSION

The proposed G-classification provides flexible criteria for RWD metric assessment while limiting inclusion biases. Applied to glucose control metrics, it can help to ensure data quality in RWD centric studies. We are currently conducting minimum data requirements for mean glucose, GMI, estimated HbA1c, CV and other metrics.

* *References 1,2,3 are looking at calculating estimated HbA1c. Other metrics were similar.*

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