# Meeting of the NGSP Clinical Advisory Committee Minutes

2024 ADA 83rd Scientific Sessions
Orlando, FL
Monday June 24, 2024 8:00 – 9:30 AM

| | |
|---|---|
| Brian Burke | VA |
| Chris Parkin | CGParkin Communications |
| Christopher Holliday | CDC, Division of Diabetes |
| Claire Meek | University of Cambridge |
| Curt Rohlfing | DDL, Univ of Missouri |
| David Leslie | St Bartholomews Hospital, UK |
| Davida Kruger | Henry Ford Health System |
| Elizabeth Selvin | Johns Hopkins |
| Irl Hirsch | Univ of Washington |
| Jared Watkin | Abbott |
| Jesica Baran | Univ of Washington |
| Jessica Castle | Dexcom |
| Jordan Perlman | Johns Hopkins |
| Julie Myers | Bio-Rad |
| Kevin Kaiserman | MannKind Corp |
| Kuanysh Kabytaev | DDL, Univ of Missouri |
| Linda Gaudiani | Marin Endo Care & Research |
| Marta Clendenin | Abbott |
| Ohad Cohen | Medtronic Diabetes |
| Paul Conlin | VA |
| Paul Hansen | |
| Richard Bergenstal | International Diabetes Center |
| Stewart Chalew | LSU |
| Tim Dunn | Abbott Diabetes Care |
| Viral Shah | Indiana University |
| William Herman | Univ of Michigan |
| Yongjin Xu | Abbott |
| Robert M Cohen | Univ of Cincinnati |
| Tracy J Sims | Eli Lilly and Co. |
| Carla Musso | Fundacion Favaloro, Univ of |
| Susan Garramone | Siemens Healthineers |
| Claire Tsai | Siemens Healthineers |
| Gary Keating | Trinity Biotech |
| John Gillard | Trinity Biotech |
| Guido Freckmann | Institute for Diabetes Tech/ULM |
| Heidi Diez | Univ of Michigan |
| Farah Daneshvar | Univ of Michigan |
| Ian de Boer | Univ of Washington |
| Rajiaxmi Bais | Univ of Washington |
| April Hopcroft | DiaTribe |

***Remote Via Zoom***

| | |
|---|---|
| Salvatore Secchi | NIDDK |
| Beena Akolkar | NIDDK |
| Ramiro Antuna | Clinica Diabetologica, Spain |
| Takuji Kohzuma | Asahi Kasei |
| Kate Redmond | |
| Allison Nathan | Close Concerns, Dartmouth |

**Welcome and introduction**: C. Holliday opened the meeting at 8:00 am and welcomed everyone. Participants introduced themselves. The 2023 NGSP Clinical Advisory Committee meeting minutes were approved.

**NGSP/CAP Update:** R. Little

- Structure of the NGSP
    1. The NGSP network consists of an administrative core, the Central Primary Reference Laboratory (CPRL), a backup PRL and 10 Secondary Reference Laboratories (SRLs).
    2. The NGSP network labs are located in the U.S., the Netherlands, Japan and China.
    3. NGSP network labs are monitored monthly via 10 fresh-frozen samples.
    4. The NGSP network is linked to the IFCC HbA1c network via an established master equation; twice-yearly sample exchanges between the networks ensure the stability of the relationship.

- NGSP Process
    1. Calibration: Informal process by which the NGSP works with manufacturers/laboratories to assist them in checking their calibration.
    2. Certification: Formal process by which manufacturers/labs perform a 40-sample comparison against a SRL using fresh or fresh-frozen whole blood; they must pass specific criteria to obtain certification.
    3. Proficiency Testing: Key to monitoring the progress and success of the NGSP in harmonizing HbA1c results. The CAP GH5 survey uses fresh whole blood with values assigned by the NGSP network.
- NGSP Certification: Year 1 to 27
    1. The NGSP certifies both methods and laboratories.
    2. There are two types of laboratory certification: Level 1 and Level 2. L1 labs generally perform clinical trials.
    3. Most certified labs are Level 1 and most are outside of the U.S.
    4. Level 1 criteria are a bit more stringent than for manufacturer or L2 certification, and they are monitored against the NGSP network quarterly.
    5. The number of certified methods continues to increase (currently there are ~330), the number of certified labs has leveled off due to consolidation of large lab groups.
    6. Certified laboratories are distributed throughout the world.
- Current Limits for NGSP and CAP criteria
    1. Manufacturer and Level 2 Lab Certification Criteria: 36/40 results must be within ±5%
    2. Level 1 certification: 37/40 results must be within ±5% (also quarterly monitoring)
    3. The CAP Survey Grading for HbA1c is still ±6%
    4. Certification must be renewed annually.
- 2024 CAP GH5A survey data (5 samples)
    1. There has been considerable improvement in the comparability of results since 1993 when the DCCT ended.
    2. CAP and NGSP criteria have been tightened over the years.
    3. The NGSP network assigns the values for the accuracy-based CAP GH-5 survey.
    4. Overall pass rates were 96.9% to 98.0% for the 5 2024 survey samples. Individual method pass rates were 86.2% - 100%.
    5. All-method CVs on the survey have decreased between 2000 and 2024. Our goal for all-method CVs is ≤3.0%. CVs for the current survey were 2.6% - 3.0%.
    6. Method-specific, between-laboratory CVs ranged from 0.6% to 4.3%.
    7. Overall, only 80% of laboratories are using methods with CVs < 3% at all five HbA1c levels.
    8. Most methods performed well on the most recent survey and showed small between-lab variability, but there are still several that demonstrate more pronounced variability.
- Updated PT Regulations for 2025
    1. CMS has decided to make HbA1c a CLIA-regulated analyte.
    2. Although the CAP survey criterion has been ±6% for some time, CLIA will adopt a criterion of ±8% effective in 2025.
    3. PT providers, including CAP, are not allowed to fail labs that participate in their surveys if they pass the CLIA criterion.
    4. Updated CAP PT Limits for 2025

- CAP-accredited laboratories that use accuracy-based proficiency testing for HbA1c (e.g. GH5) will be required to evaluate results based on acceptable performance criteria of ±6% in 2025.
- The CAP will provide two evaluations for the GH5-A 2025 mailing
  - To meet CLIA regulations (±8%)
  - To meet CAP checklist (±6%) requirements for CAP accredited laboratories.

**Discussion:**

*At one point there was discussion of CAP moving to ±5%, is this now off the table?*

R. Little said yes, because the new CMS guideline CAP is staying with 6%, although it is now part of the inspection checklist rather than the criterion for passing the CAP GH-5 survey.

There was a comment about the CAP survey criteria (6%) being different from the criteria for NGSP certification (5%). R. Little said that they are different. When the current NGSP criteria were being developed, the statistician on the Steering Committee at the time (C. Parvin) did some analyses to compare the NGSP criteria to the CAP survey. Based on these analyses it was determined that 36/40 samples within ±5% was the most comparable to the CAP 6% criterion.

*Two different criteria were mentioned, 8% for CLIA and 6% for CAP, will these apply to different surveys and what will be required from the labs?*

R. Little noted that CMS/CLIA does not actually supply surveys, they just set the acceptable limits for passing. The majority of labs in the U.S. subscribe to the CAP HbA1c survey, although there are a few others but they are not accuracy based. There are some other countries that have their own accuracy based surveys. Although labs will be able to pass CLIA if they are within 8%, CAP-accredited labs will effectively have to pass 6%, as they will have to show compliance with this when they are inspected.

**GMI-Pro: Using GMI Can Improve Diabetes Management:** I. Hirsch

- Disclosure: I am not an epidemiologist. I'm a clinician and clinical researcher who takes care of individual patients, not populations. I've been observing and studying HbA1c (and discordance with glucose) for over 40 years.
- In other words, I take care of individual patients, not populations
- One Concerning Example (not uncommon in my practice)
  1. 37 y/o male with ESRD receiving epoetin alpfa, dapsone and Bactrim
  2. HbA1c 5.9%; GMI 9.2%
  3. Important: I will treat the GMI, mean glucose, and TIR/TBR. I will also ignore the HbA1c (if I have a choice)
- What CGM Taught Us in 2008: Average Glucose Versus A1C (Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ. Diabetes Care. 2008;31:1473-1478) (ADAG Study)

| A1C (%) | AG (mg/dL [95% CI]) |
|---|---|
| 5 | 97 (76-120) |
| 6 | 126 (100-152) |
| 7 | 154 (123-185) |
| 8 | 183 (147-217) |
| 9 | 212 (170-249) |
| 10 | 249 (192-282) |
| 11 | 269 (217-314) |
| 12 | 298 (240-347) |

1. One can't compare the A1C levels between 2 people
2. Each A1C comprises a wide mean glucose range
3. This does not take away from A1C use in a clinical trial
4. No one seemed to talk about the wide CI's in 2008 (and some in 2024)!

- Etiologies of HbA1c Discordance From Blood Glucose (DT&T, Published Online:13 Feb 2024 https://doi.org/10.1089/dia.2024.0028)

| | Falsely Decreased HbA1c | Falsely Elevated HbA1c |
|---|---|---|
| Hematologic conditions[26] | Hemolytic anemia:[27,28] sickle cell disease, thalassemia, glucose 6-phosphate deficiency, hemoglobin (Hb) Leiden,[29] sickle cell trait,[30] mechanical heart valves.[31] | Iron deficiency with and without anemia[55,56,57]; vitamin B12 & folate deficiency,[26,57] and megaloblastic anemia[26,57]. |
| | Reticulocytosis,[32] hereditary spherocytosis.[33] | Asplenia,[33] elevated red cell distribution width,[58] polycythemia[59], hemoglobin Wayne.[60] |
| Chronic disease | Chronic kidney disease,[34,35] hemodialysis.[35,36] | |
| | Chronic liver disease,[37] cystic fibrosis,[38,39] hypothyroidism.[40] | |

| | Falsely Decreased HbA1c | Falsely elevated HbA1c |
|---|---|---|
| Medication or toxicity related | Due to hemolysis:[41] antiretrovirals for HIV treatment,[42,43]dapsone,[44] ribavirin,[45,46] sulfasalazine,[44] trimethoprim sulfamethoxazole.[47] | Chronic alcohol use,[61] lead poisoning.[62] |
| | Effect of therapy: erythropoetin therapy,[32,48] iron supplementation,[32,49] exogenous testosterone.[50] | |
| Physiology | Pregnancy 1st and 3rd trimesters.[51,52] | Age[63,64], iron deficiency in late pregnancy[65] |
| Assay interference including altered Hb | Hydroxyurea,[41] aspirin.[28,53,A] | Aspirin,[26,50] uremia,[34,66,B] hypertriglyceridemia,[28,67] hyperbilirubinemia.[28] |

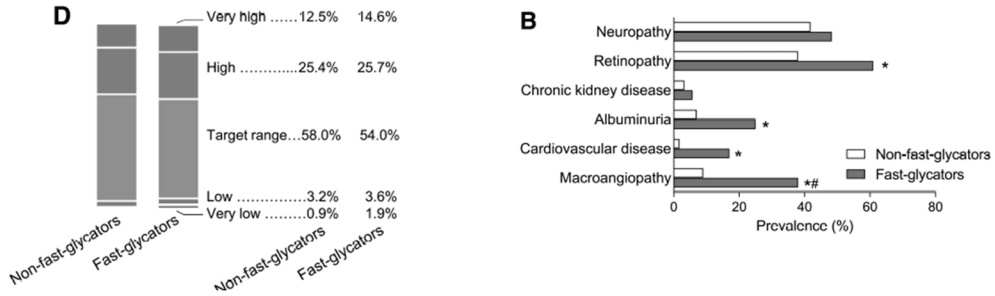
| | Falsely decreased HbA1c | Falsely elevated HbA1c |
|---|---|---|
| Altered glycation | Vitamin C, [28,53,A] Vitamin E.[28,53,A] | |
| Miscellaneous | Acute blood loss, blood donation, chronic opiate use.[54] | Smoking[68] |
| Variable Effect on A1c: Ethnicity and genetics,[69,70,71] hemoglobinopathy,[28,66,72] blood transfusion. | | |

A. Variable results have been seen for aspirin and vitamin c. Interference is assay-dependent & less common with modern assays.[28]
B. Assay interference from uremia is now uncommon. Details of modern assays available on NGSP site.[66]

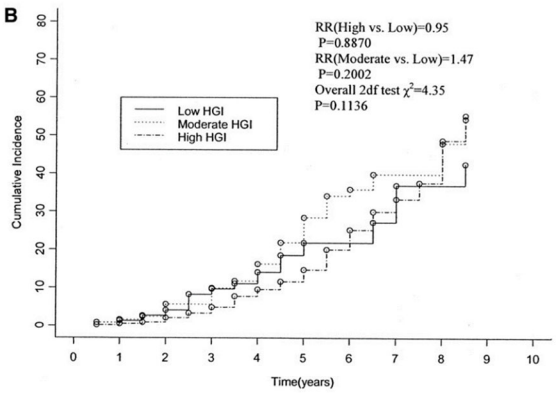
- To get into the ADAG study, one could not have:
    1. Anemia and or high reticulocyte count
    2. CKD
    3. Chronic liver disease
    4. High-dose vitamin C

5. Recent blood loss and or transfusion

- Those 507 subjects participating in the most important study assessing the relationship between mean glucose and HbA1c had perfect hemoglobin levels without known interferences (not our clinic populations)!
- Therefore, It Is Clear: There is more than the known physiology of hemoglobin and other co-morbidities impacting HbA1c
- What Else Impacts HbA1c?
    1. RBC Survival Time (Cohen RM, Franco RS, Khera PK: Blood 2008;112:4284-4291)
    2. What about protein glycation rates?
- Are Glycation Rates The Same Between Individuals? Maran A, et al: Diabetes Care 2022;45:2439–2444
    1. Estimation of skin advanced glycation end products (AGEs) using skin autofluorescence (SAF)
    2. N = 135 with T1D
    3. Fast glycators defined as GMI/HbA1c < 0.9
    4. A Controversy That Won't Go Away: Fast vs. Non-Fast Glycation

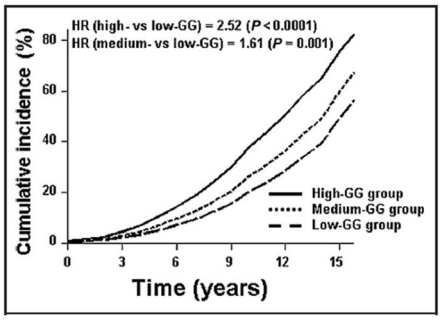



- "Fast Glycators" are not a New Hypothesis
    1. HGI: formula modeled in 2004 (Diabetes Care 2004;27:1259-1264)
    2. Mean Blood Glucose (MBG) from glucose levels of all DCCT subjects throughout the study (7-point profiles)
    3. A model was used to predict HbA1c from the MBG profiles from all encounters in DCCT
    4. HGI= observed HbA1c - predicted HbA1c, where observed HbA1c is the measured HbA1c for the quarterly clinic visit and predicted HbA1c is the value mathematically derived by inserting the profile set MBG for the same quarterly visit into the population regression equation.
- Did Fast Glycators Have More DR Progression in the DCCT (adjusted for baseline HbA1c)? No! Diabetes 56:1913–1921, 2007




- But Not All Agreed: Progression of DKD Clinical Chemistry 57:2264–271 (2011)

1. Hb A1c was regressed on fructosamine by using a repeated-measures longitudinal regression model and data for all visits of all patients
2. The raw glycation gap gg was calculated at each visit, as measured by HbA1c minus the value predicted by the regression

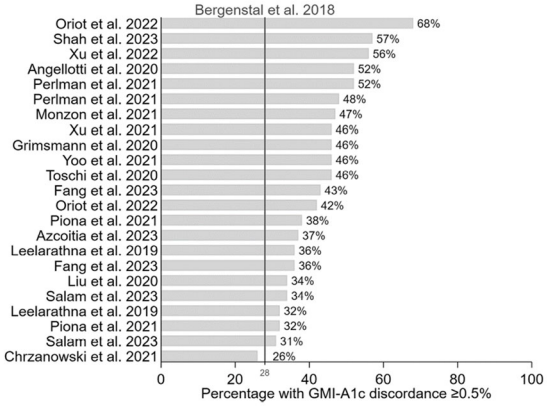



3. Is use of the GMI as the comparator instead of fructosamine or SMBG a better way to assess this glycation gap?

- Does It Make More Sense to Use GMI As A Strategy to Assess High Glycators? ADA Sci Session OR-107, 2023
    1. N = 661, 64% with > 20 years duration, 90% with T1D
    2. Fast glycator again defined as GR = GMI/HbA1c < 0.9

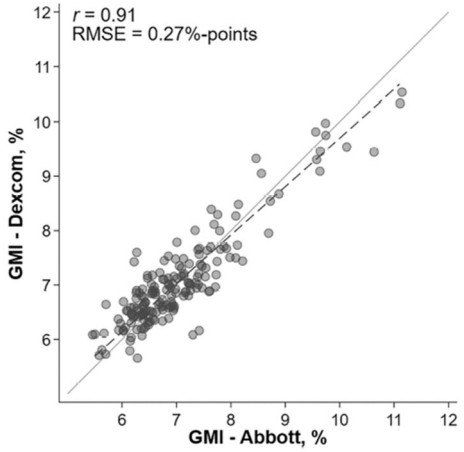
| Glycation Ratio (GMI/A1c) and Prevalence of Retinopathy and Nephropathy | | | | |
|---|---|---|---|---|
| | GR<0.9 | GR>0.9 | OR | p-value |
| Retinopathy | 41.12% | 25.45% | 2.05 (1.33-3.14) | 0.001 |
| Nephropathy | 24.30% | 10.18% | 2.83 (1.68-4.77) | 0.0001 |

- We Can All Agree
    1. HbA1c is a not-perfect biomarker for an individual due to both hematologic and other biologic processes that make it imperfect for everyone
    2. GMI is also flawed for a variety of reasons
- How Common Do We See A1C/GMI Discordance > 0.5% Selvin E: Diabetes Care. 2024 Jun 1;47(6):906-914




1. Problems with GMI
    - Lack of accuracy with CGM (day of wear, “compression lows”, lag time, etc.)
    - HbA1c = glycation of RBCs; GMI = mean of ISF glucose
    - GMI based on adults using Dexcom G4 in mostly T1D subjects, therefore equation may be flawed.
    - Is it fair to compare GMI using Dexcom G4 to today’s sensors using Dexcom G6/7, Abbott Libre 2/3, Sensionics, and Medtronic? (is our equation for GMI incorrect?)

2. What About GMI Discordance?




- My Thoughts
    1. HbA1c has many limitations-it is often dangerous to use for clinical management
    2. GMI is far from perfect. The hope is as CGM improves, the GMI will improve with it.
    3. At the end of the day, as clinicians (in addition to patients and family members) we need to treat the glucose, not its biomarkers.
    4. GMI and HbA1c may be most useful when used together to assess those individuals who are high glycators.
- More Thoughts
    1. For patient care, we had no issues using GMI during the pandemic when we did not have access to HbA1c
    2. For those without CGM, use of HbA1c by itself can be inappropriate
        - Starting insulin in a patient with T2D when not needed
        - Telling a women it is safe to get pregnant when it is not
        - Payors grading us as clinicians!
        - But it actually gets worse than this
- Reuters series: Out of Control Part Two (How drugmakers pushed diabetes patients into a danger zone (reuters.com) November 2021)-- Overly aggressive HbA1c treatment goals can be dangerous to patients.
- We All Realize the Emotional Trauma to Patients and Families From the HbA1c Result: The "failure" one feels when HbA1c is discordant high. Do most clinicians understand the nuances of HbA1c discordance to explain to the patient they are not "failures" despite their efforts?
- My Belief:
    1. We need to use GMI from CGM to assess discordance from HbA1c in everyone, even though both tests have limitations. For the typical type 2 patient, it needs to be done once to assess for discordance
    2. GMI will continue to improve as CGM improves
    3. GMI may be the best tool to assess the controversy of high glycators
    4. The bottom line: in 2024 we need both biomarkers
- Finally, most of us in the room today treat patients with diabetes, not Excel spreadsheets.

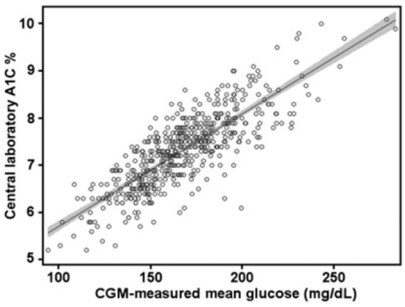
**Con: Time to rethink the use of GMI in diabetes management:** E. Selvin

- Hemoglobin A1c (HbA1c): Strengths and Limitations
    1. Hemoglobin A1c (HbA1c) – Fundamental to Diabetes Care
        - Standard measure used to monitor glycemic control in persons with diabetes-- Used to monitor and guide treatment

- Screening and diagnostic test for prediabetes and diabetes
- Surrogate endpoint for clinical trials of glucose-lowering therapies in type 1 and type 2 diabetes (US FDA criteria)

2. Advantages of HbA1c for Diagnosis and Monitoring of Diabetes
   - Much less biologic variability (vs fasting or 2-hr glucose)
   - Better index of overall glycemic exposure
   - Strict standardization
   - No need for fasting or timed samples
   - Relatively unaffected by acute factors
   - Standard measure used to guide and adjust treatment
   - Robust associations with long-term macro- and micro-vascular outcomes
3. Limitations of fasting glucose (Glucose: A Simple Molecule That Is Not Simple to Quantify, Gambino Clin Chem 2007)
   - Diurnal variation
   - Pre-analytical issues
   - Laboratory calibration
   - Patient preparation (i.e., fasting)
   - High within-person variability, esp. compared to HbA1c
   - Captures a single moment in time (not an integrated measure)
4. Limitations of HbA1c?
   - Assay interferences: Some Hb traits interfere with interpretation of HbA1c assays, although not for the majority of Hb variants: www.ngsp.org
   - Some conditions interfere with HbA1c test results--Altered red cell turnover, e.g. hemolytic anemia, transfusions, pregnancy, major blood loss

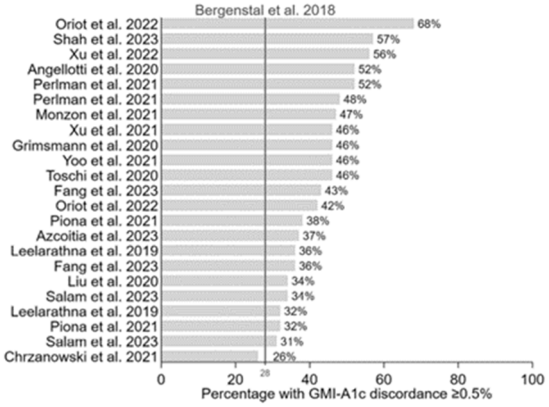
- What is GMI?
  1. GMI: An equation to estimate HbA1c from CGM mean glucose (Bergenstal et. al, Diabetes Care 2018;41(11):2275–2280)
     - In 2017, an equation was proposed for translating CGM mean glucose into an estimated HbA1c value, initially referred to as “eA1C”.



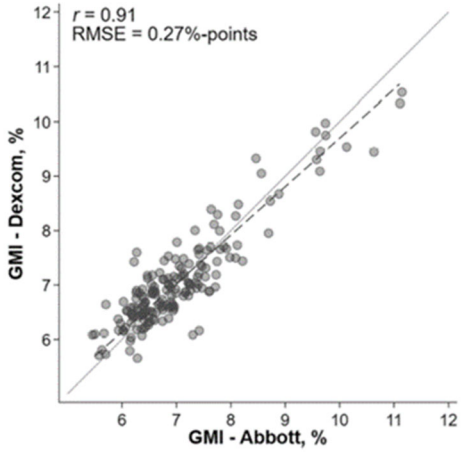

     - GMI (%) = 3.31+ 0.02392 x [CGM mean glucose in mg/dL]
     - GMI (mmol/L) = 12.71 + 4.70587 x [mean glucose in mmol/L]
     - In response to concerns raised by the US Food and Drug Administration (FDA) that people could confuse eA1C with laboratory HbA1c, it was later renamed the Glucose Management Indicator (GMI).
     - GMI is incorporated into CGM summary (AGP) reports, providing patients and providers a familiar “HbA1c-like” value.
     - GMI Basics
       - Study population, N=528 adults with type 1 or type 2 diabetes receiving insulin
       - 4 trials examining effectiveness of CGM (3 funded by Dexcom)

- Dexcom G4--Mean CGM glucose prior to A1C measurement (48 days, range 13-89)
- HbA1C (Tosoh G8)
- Ordinary least squares regression of CGM mean glucose on HbA1C
    A. GMI (%) = 3.31+ 0.02392 x [CGM mean glucose in mg/dL]
    B. GMI (mmol/L) = 12.71 + 4.70587 x [mean glucose in mmol/L]

- Questions re. GMI
    1. Unknown details regarding performance of GMI equation--SE, RMSE, measures of model fit
    2. Performance of GMI equation across population subgroups
        - Trial control vs intervention arms
        - Age
        - Sex
        - Anemia, kidney function, etc
        - Duration of CGM wear
    3. External generalizability?
        - Children and adolescents, pregnancy, persons not on insulin, persons without diabetes
        - Other CGM sensors
- Advantages of GMI
    1. Translates CGM mean glucose values into an estimated HbA1c which is familiar to patients and providers
        - Same units
        - HbA1c ranges and targets are well-established
    2. Provides an 'estimated HbA1c' if you don't have a laboratory HbA1c
- GMI's Persistent Discordance with Lab HbA1c
    1. Percentage of participants with clinically significant discordance (≥0.5%-points) between GMI and HbA1c

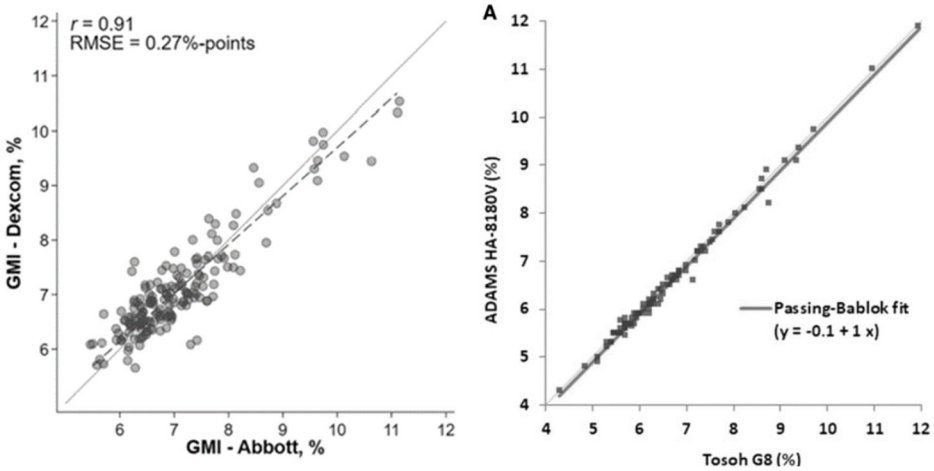



    2. Many studies have shown significant discordance between GMI and lab HbA1c
    3. GMI – Comparison of Two Different CGM Sensors (Sources: Selvin et al 2024 Diab Care)




- GMI (CGM mean glucose) has within-person variability
- GMI varies significantly when comparing CGM sensors from two different manufacturers, worn at the same time on the same person
- 26% of participants had clinically significant discordance (≥0.5%-points) between GMI1 and GMI2

4. GMI – two different sensors; HbA1c – two different assays (Sources: Selvin et al 2024 Diab Care; Altawallbeh et al JALM 2020)




5. Why might HbA1C and CGM glucose (GMI) be discordant?
   - CGM measurements have error
     - Especially at the low range
     - Non-glycemic determinants (placement, lag time, pressure, inflammation, calibration, rapid changes in glucose, interferences, etc)
   - HbA1c measurements have error and have non-glycemic determinants
   - HbA1c and CGM glucose are distinct entities – would not expect them to align perfectly
   - Duration of CGM wear and timing of HbA1c measurement
   - GMI equation is imperfect--Not validated in external populations (different CGM sensors, pediatric populations, etc)

- Where do we go from here?
  1. Discordance between GMI and HbA1c causes confusion
  2. Instead of relying on GMI as a surrogate for HbA1c, emphasize mean CGM glucose alongside laboratory HbA1c testing
  3. HbA1c is a gold standard for diagnosis, strongly linked to outcomes and is one of the most important clinical biomarkers in the practice of medicine

4. Strengths of CGM systems
    - Detailed data on glucose patterns, trends
    - Real-time feedback
    - Reducing hypoglycemia
5. CGM mean glucose is one metric among many and is a helpful summary measure

- HbA1c and CGM: Better Together
    1. HbA1c is central to diabetes diagnosis and management
    2. Estimating HbA1c from CGM is problematic
        - CGM captures different aspects of glycemia
        - Different sources of error
        - CGM not linked to long-term outcomes
        - Understand strengths and limitations
    3. Embracing CGM mean glucose, time in range, and other CGM metrics while retaining regular laboratory HbA1c testing can optimize glucose control and prevent complications in patients with diabetes

**Discussion:**

*CGM and HbA1c*

W. Herman asked E. Selvin if all of the manufacturers use the same equation to calculate GMI. E. Selvin said yes, adding that although they could try to use different equations or optimize the equations incorporating other factors like hemoglobin, age, sex, etc., or utilize machine learning, you will never obtain a perfect estimate of laboratory HbA1c from CGM. Clinical equations are used in many aspects of medicine, although there is not a strong history of using them in Endocrinology/Diabetes. Given that HbA1c is easy to measure, there would not seem to be a need to utilize an equation to estimate it. V. Shah commented that defining fast and low glycators based on two imperfect measures, HbA1c and GMI, is very difficult. Their group looked at a group of subjects over 7 years and found that the discordance was in one direction in only 30% of them. The group also examined data from a large number of patients (n=2800) and tried to develop a new equation to define the relationship. The discordances between HbA1c and GMI did not go away no matter what kind of equation was used, linear, non-linear, etc. He also had concerns about the use of CGM metrics in patients without diabetes. It was noted that both speakers said many of the same things re. the limitations of the tests. For HbA1c we have defined clinical targets, if mean glucose should not be expressed as GMI, how do we frame mean glucose in terms of targets? E. Selvin responded that in the short term, the tables that currently show the relationship between mean glucose and HbA1c should be updated. There is an issue with variability, HbA1c methods are cleared on the basis of ±6%, the equivalent for CGM is 15-20% vs. venous glucose. So when we try to line up mean glucose with HbA1c there is a lot of "noise". We should be using regression models that better account for this rather than just linear regression. Then we should help people get familiar with the idea that at a given level of HbA1c your CGM glucose level is likely to be within a certain range. The idea that they are two different things is not too difficult for providers and patients to understand in her opinion. I. Hirsch said that HbA1c should not be used as the target in a clinical trial. That what was done in ACCORD, in a recent paper they showed that high glycators (based on fasting glucose as they did not have CGM) in the trial had higher mortality rates. It shows the potential of dangerous consequences. Also, for patients on dialysis HbA1c is almost worthless, yet for many in the U.S. and around the world it is the only measure of glucose control available for these patients and this will likely not change anytime soon. GMI has to change as the technology changes, it would be difficult but not impossible to step

back from GMI and start a new education platform based on mean interstitial glucose. However, we have spent decades teaching primary providers about HbA1c, now we would need to spend years trying to get them to understand the limitations and back off of it. Nonetheless he thought it would be possible. P. Conlin said that HEDIS now accepts both HbA1c and GMI as quality measures with the same metric applied. This means that a patient could have GMI results throughout the duration of their diabetes without ever having HbA1c measured and still be in compliance with HEDIS, is this appropriate? E. Selvin thought it is a problem, as GMI is not a good measure of laboratory HbA1c. I. Hirsch said we do not have a DCCT-like study involving GMI. However, a practical reality is that with the explosion of telemedicine and the fact that we can look at GMIs from the cloud, we can use these tools with rural elderly patients where it is very difficult to get them into a clinic. Right now GMI is not approved for Medicare, but this will hopefully change. Right now elderly rural patients have to have their HbA1cs done every 3-4 months no matter what. For taking care of the patient he doesn't need the HbA1c, I would much rather have the GMI. More important than the GMI is the TBR and TIR. R. Bergenstal was not sure that going to mean glucose is the best approach. He envisioned the GMI as a bridge to eventual precision management using CGM using metrics like TBR and TIR to better manage patients more safely. He sees HbA1c as a measurement tool and CGM as a management tool. C. Meek said that equation, if used in pregnancy, would have to be adjusted in a trimester specific way. Meanwhile we know that HbA1c in pregnancy, despite its limitations, is still a strong predictor of outcomes in these patients. She did not think that GMI in pregnancy would be feasible, at least with the current systems we have. It was noted that data from closed-loop systems has shown that the GMI/HbA1c discordances increase with increasing HbA1c and are highest at very high HbA1c levels. R. Little noted that HbA1c is not a mean glucose but is a weighted average where the most recent glucose levels contribute much more than the levels from several months earlier. T. Dunn asked about the next steps as far as updating the HbA1c/MBG relationship using newer data. E. Selvin said she wants to do this, but would not want to update it before obtaining more data in different populations looking at different CGM sensors, etc. She is wanting to reach out to manufacturers who have performed trials to see if they would share data. She drew an analogy to the use of serum creatinine and cystatin-C in nephrology, where both are utilized and they can be discordant. We understand their strengths and limitations and still utilize both tests. She sees an irony in that the strengths of CGM are the nuanced pattern data and real-time feedback, but then these data are being reduced to a single number. J. Castle said that as a trained Endocrinologist she saw the main value of CGM in terms of TBR and TIR, but most patients see primary care providers and for them there is value in summary statistics. From her perspective we need to look at how to improve CGM and make it more applicable across different populations and A1c ranges, pediatric populations, etc. There was a comment that we should not place so much reliance on a single measurement as is currently done with the use of HbA1c as a quality measure. C. Parkin said from his perspective, it seems that GMI provides the "gateway drug" into CGM, in that the physician sees a number they are familiar with. The value of HEDIS adopting GMI is recognizing the value of CGM data, not GMI as such but TIR and TBR. Whether we improve GMI or not may not be that critical if we can get the providers to pay more attention to the detailed information CGM provides. L. Gaudiani suggested that since most patients with diabetes see primary care physicians, pediatricians and internists, it would be useful to publish a paper in a journal that is read by them that discusses the differences between GMI and HbA1c to lessen the distress of providers and their patients. W. Herman asked how people feel about HEDIS quality management guidelines emphasizing GMI, HbA1c or both. E. Selvin said focusing on any one measure is an exercise in frustration. Quality measures like HEDIS can drive everyone crazy because it is taking information that is nuanced and bringing it down to one metric. However, she does not think relying on GMI as an estimate of HbA1c is a good idea. We have spent decades standardizing and gaining a better understanding of HbA1c, if we want to look at HbA1c we should just measure it directly. I. Hirsch said

his only issue with that is that in his practice he sees a lot of patients with comorbidities where HbA1c simply does not work. Another issue is the OTC CGMs that are about to hit the market. Physicians will likely get more and more phone calls and e-mails asking about why the GMI and HbA1c do not match up. As L. Gaudiani suggested, more education, especially of primary providers, is needed.

*C. Holliday thanked everyone for their attendance and the discussions, and noted that the CAC will meet again next year in Chicago. The meeting was adjourned at 9:45 AM.*

*Minutes prepared by Curt Rohlfing 7/17/2024.*