State of the Art
Glucose Monitoring Technology

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Minneapolis, MN
Disclosure Statement
Richard M. Bergenstal, MD

RMB has participated in *clinical research, a scientific advisory board or served as a consultant* for:

- Eli Lilly
- Novo Nordisk
- Sanofi
- Hygieia
- T1D Exchange (Helmsley Charitable Trust)
- Roche Diabetes Care
- J&J
- Abbott Diabetes Care
- Bayer Diabetes
- Medtronic Diabetes Care
- DexCom
- Astra Zeneca
- Merck
- ResMed
- Takeda

RMB inherited Merck stock and is a member of AACE, ADA, Endocrine Society & JDRF

RMB’s employer, non-profit Park Nicollet Institute, contracts for his services and he receives no personal income from these contracts.
Glucose Monitoring
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

Optimal Glycemic Control
Diabetes Management

Glucose Monitoring ➡ Therapeutic Action (adjustment)

Urine Glucose ➡ Insulin

Orals (SU)

Animal - short, intermediate, long
Premixed
Recombinant – Human Analogs
  - Basal
  - Bolus
Inhaled

Optimal Glycemic Control
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

Urine Glucose ← ? → Insulin  

Orals (SU)

SMBG

Optimal Glycemic Control
SMBG Meters
SMBG Meters
SMBG Wireless Download / Data Management

Accu-Chek Connect Online
Full integration of Diabetes Management

207
TAKE ACTION !!!

OneTouch Verio Sync

Test N’GO™

All rights reserved
Glucose Meters

Evolution toward
- Smaller
- Faster
- **More Accurate**
- More Memory
- Downloadable
- Event markers
- Reminders
- Wireless – smart phone, Cloud

Accuracy
- How many “standards” do we need?
  - ISO
  - CLSI hospital standards
  - FDA
- Consistency from lot to lot is critical and should be evaluated

Reimbursement
- Pay for strips --- if **documentation** of use to help manage diabetes
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

Urine Glucose  ?  Insulin

SMBG  Orals (SU)

MDI (IIT)

Optimal Glycemic Control
Ideal Basal/Bolus Insulin Absorption Pattern

Plasma Insulin

Time

4:00  8:00  12:00  16:00  20:00  24:00  4:00  8:00

Breakfast  Lunch  Dinner
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

+ DATA

Urine Glucose → ? → Insulin

SMBG → Pattern Control → MDI (IIT)

Optimal Glycemic Control
Evidence of a Strong Association Between Frequency of Self-Monitoring of Blood Glucose and Hemoglobin A1C Levels in T1D Exchange Clinic Registry Participants

Miller K. et al for T1D Ex Diabetes Care online Feb 2013
Glucose monitoring

- Patients on multiple-dose insulin (MDI) or insulin pump therapy should do self-monitoring of blood glucose (SMBG) at least prior to meals and snacks, occasionally postprandially, at bedtime, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. (B)
Glucose monitoring

- When prescribing SMBG, ensure that patients receive ongoing instruction and regular evaluation of SMBG technique and SMBG results, as well as their ability to use SMBG data to adjust therapy. (E)
Step 4: Look for Glucose Patterns
Where are your glucoses above or below your targets?
Target Range:
- High: 160
- Low: 80

Date: Weekdays and Weekends
- From: 10/13/2008
- To: 11/11/2008
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Average: 147, 153, 120, 93, 107, 151, 120
In Target: 3%, 45%, 0%, 100%, 60%, 43%, 100%
# Results: 30, 22, 7, 8, 10, 23, 9
Universal Diabetes Data Uploading / Aggregating

Continue the Open Source Dialogue

- We need access to the DATA
- It must be STANDARIZED
  (data in & data out)
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment) +

DATA

Urine Glucose  ?  Insulin

SMBG  \textit{Pattern Control}  MDI (IIT)

CSII (± tubing)

Orals (SU)

Lifestyle  GLP 1 RA Orals (non-SU)

Optimal Glycemic Control
Insulin Pumps
Diabetes Management

Glucose Monitoring $\rightarrow$ Therapeutic Action (adjustment)

+ DATA

Urine Glucose $\rightarrow$ ? $\rightarrow$ Insulin

SMBG $\leftarrow$ Pattern Control $\rightarrow$ MDI (IIT)

CGM
- Retrospective
- Real-time

CSII (+ tubing)

Orals (SU)

Lifestyle

GLP 1 R A Orals (non-SU)

Optimal Glycemic Control
CGM Goals / Progress

- **Sensors**
  - Improved Accuracy / redundancy / calibration free
  - Smaller / more comfortable / more transmission distance
    --- straight to smart phone / Cloud

- **Algorithms**
  - Refine algorithms
  - Enhance Trend analysis – arrows/rate of change to refine manual or automated insulin dosing

- **Pumps**
  - Improved functions and surveillance/feedback

- **Glucose data analysis, display, action**
  - Standardize
    - Definitions, display, clinical decision support/guidance

- **Faster mealtime Insulin**

- **Studies with MDI, T2D assessment/treatment, AP at home**
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

* DATA *

Urine Glucose → ? → Insulin

SMBG → Pattern Control → MDI (IIT)

CGM
- Retrospective
- Real-time
- Flash Glucose Monitoring

CSII (+ tubing)

Orals (SU)

Lifestyle

GLP 1 R A Orals (non-SU)

Optimal Glycemic Control
We need to keep moving toward:

- CGM replacement of SMBG
- Cost-effective
Diabetes Management

Glucose Monitoring \(\rightarrow\) Therapeutic Action \((\text{adjustment})\)

\[\text{+ \hspace{1cm} DATA}\]

Urine Glucose \(\leftarrow\) ? \(\rightarrow\) Insulin

SMBG \(\leftarrow\) Pattern Control \(\rightarrow\) MDI \((\text{IIT})\)

CGM \(\leftarrow\) Standardized Data \(\rightarrow\) Display – AGP \(\rightarrow\) CSII \((\pm \text{tubing})\)

Retrospective \hspace{1cm} Real-time

Flash Glucose Monitoring

Orals \((\text{SU})\)

Lifestyle

GLP 1 R A Orals \((\text{non-SU})\)

Optimal Glycemic Control
A common problem in practice
Different Devices - Different Outputs

Guardian RT

DexCom

Navigator
It is time for an EKG for Glucose Data

08-NOV-1970 (25 yr)
Male Caucasian
71 in 185 lb

11-MAR-1996 17:05
Recommendations for Standardizing Glucose Reporting and Analysis to Optimize Clinical Decision Making in Diabetes: The Ambulatory Glucose Profile (AGP)

Richard M. Bergenstal, MD, Andrew J. Ahmann, MD, Timothy Bailey, MD, Roy W. Beck, MD, PhD, Joan Bissen, Bruce Buckingham, MD, Larry Deeb, MD, Robert H. Dolin, MD, Satish K. Garg, MD, Robin Goland, MD, Irl B. Hirsch, MD, David C. Klonoff, MD, Davida F. Kruger, MSN, APN-BC, BC-ADM, Glenn Matfin, MB, ChB, MSc (Oxon), Roger S. Mazze, PhD, Beth A. Olson, BAN, RN, CDE, Christopher Parkin, MS, Anne Peters, MD, Margaret A. Powers, PhD, RD, CDE, Henry Rodriguez, MD, Phil Southerland, Ellie S. Strock, ANP-BC, CDE, William Tamborlane, MD, and David M. Wesley, BA

2012 Panel Supported by Helmsley Charitable Trust

March 2013 DTT and DTS Publication

**Statistical Summary**
- Glucose exposure (mean and eA1C)
- Variability (SD, IQR & CV)
- % in target, above and below

**Visual Display**
- Modal day (14 if possible)
- Smoothing algorithm - 5 glucose curves
- Median (orange line), 25th & 75th % (solid lines), 10th and 90th percentiles (dotted lines)

**Daily View**
- Thumbnail view - each day in the overall profile
- Calendar format
  - work vs. non-work, weekend vs. weekday
- Target range
Continuous Glucose Monitoring

These devices may offer the opportunity to reduce severe hypoglycemia for those with a history of nocturnal hypoglycemia. CGM forms the underpinning for the “artificial pancreas” or the closed-loop system. However, before CGM is widely adopted, data must be reported and analyzed using a standard universal template that is predictable and intuitive (75).

Identifying Glycemic Trouble Spots

Frequent Hyperglycemia

Frequent Hypoglycemia

High Variability

Ambulatory Glucose Profile (AGP)

Recommendations for Standardizing Glucose Reporting and Analysis to Optimize Clinical Decision Making in Diabetes: The Ambulatory Glucose Profile (AGP) March 1, 2013 online DTT and JDST Bergenstal et al.
Diabetes Management

Glucose Monitoring → Therapeutic Action (adjustment)

DATA

Urine Glucose → Insulin

SMBG → Pattern Control → MDI (IIT)

CGM → Standardized Data → CSII (± tubing)

Retrospective
Real-time

Flash Glucose Monitoring

SAP

Orals (SU)
Lifestyle
GLP 1 R A Orals (non-SU)

Optimal Glycemic Control
Sensor Augmented Pump (SAP)

Improved A1c in Adults and Children if the Sensor is Worn

Effectiveness of Sensor-Augmented Insulin-Pump Therapy in Type 1 Diabetes
Richard M. Bergenstal, M.D., William V. Tamborlane, M.D., Andrew Ahmann, M.D., John B. Buse, M.D., Ph.D., George Dailey, M.D., Stephen N. Davis, M.D., Carol Joyce, M.D., Tim Peoples, M.A., Bruce A. Perkins, M.D., M.P.H., John B. Welsh, M.D., Ph.D., Steven M. Willi, M.D., and Michael A. Wood, M.D., for the STAR 3 Study Group

Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes
The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group
Diabetes Management

Glucose Monitoring ➔ Therapeutic Action (adjustment)

Urine Glucose ➔ ? ➔ Insulin

Lifestyle
Orals (SU)
GLP 1 R A
Orals (non-SU)

SMBG ➔ Pattern Control ➔ MDI (IIT)

CGM ➔ Standardized Data Display – AGP ➔ CSII (± tubing)

Retrospective
Real-time
Flash Glucose Monitoring

Optimal Glycemic Control

SA-MDI

Sensor Augmented MDI
Eagerly await DATA

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AP Strategy – Iterative Increases in Automation

1. Very Low Glucose
   Insulin Off Pump
   
   Pump shuts off when user not responding to low-glucose alarm

2. Hypoglycemia
   Minimizer
   
   Predictive hypoglycemia causes alarms followed by reduction or cessation of insulin delivery below low threshold

3. Hypoglycemia/
   Hyperglycemia
   Minimizer
   
   Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dl)

4. Automated
   Basal / Hybrid
   Closed Loop
   
   Closed loop at all times with meal-time manual assist bolusing

5. Fully Automated
   Insulin Closed Loop
   
   Manual meal-time bolus eliminated

6. Fully Automated
   Multi-Hormone
   Closed Loop

A. Kowalski  JDRF
Primary efficacy outcome: Nocturnal hypoglycemia (↓ 38%)
Primary safety outcome: Change in HbA1c (no change)

Diabetes Management

Glucose Monitoring ➔ Therapeutic Action (adjustment)

+ DATA

Urine Glucose ➔ Insulin

SMBG ➔ Pattern Control ➔ MDI (IIT)

CGM ➔ Standardized Data Display – AGP

Retrospective ➔ Real-time

Flash Glucose Monitoring

Optimal Glycemic Control

Hybrid CL or Bihormonal CL

Sensor Augmented MDI

SA-MDI

SA-MDI

Hybrid CL or Bihormonal CL

GLP 1 RA

Orals (non-SU)

Lifestyle

Orals (SU)

Optimal Glycemic Control

International Diabetes Center

Park Nicollet

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AP Strategy – Iterative Increases in Automation

1. Very Low Glucose
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4. Automated
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   Closed Loop

   Closed loop at all times with meal-time manual assist bolusing

5. Fully Automated
   Insulin Closed Loop

   Manual meal-time bolus eliminated

6. Fully Automated Multi-Hormone
   Closed Loop

   JDRF IMPROVING LIVES: CUREING TYPE I DIABETES.
Hybrid Closed Loop in an Adolescent (24 hrs) (Manual meal boluses)


Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes


A Mean Glucose Levels in Adults

This article was published on June 15, 2014, at NEJM.org.
Diabetes Management

Glucose Monitoring $\rightarrow$ Therapeutic Action (adjustment)

- **DATA**
  - Orals (SU)
  - GLP 1 R A
  - Lifestyle
- Orals (non-SU)

Urine Glucose $\leftrightarrow$ Insulin

SMBG $\leftrightarrow$ Pattern Control $\rightarrow$ MDI (IIT)

- CGM
  - Retrogressive
  - Real-time
  - Flash Glucose Monitoring
  - Standardized Data Display – AGP
- AGP
- MDI (IIT)
  - CSII ($\pm$ tubing)
- SA-MDI
  - Surveillance
  - Cost-effectiveness
  - Sensor Augmented MDI

**Optimal Glycemic Control**

Beyond A1c

A1c +

CGM based: Time in Range (TIR) with minimal Hypoglycemia ($\pm$ glucose variability)

**Triple Aim**

- ↑ Quality
- ↑ Pt Experience
- Reasonable Cost
1. All people with diabetes benefit from some glucose monitoring – if they use the data.

- Need agreement on how to document acceptable use of data
- T1D (pump & MDI) and T2D (MDI): unlimited SMBG
- For T1D pts. who are indicated for CGM use - the CGM must be covered by Medicare
- MDI pts.: likely will benefit from CGM (need data).
- T2D non-MDI: benefit from some SMBG as a guide to understanding their diabetes and making timely lifestyle or medication changes/advances
2. **Remote** glucose pattern control analysis (SMBG, CGM) and med adjustment should be reimbursed.

3. **CGM as a replacement for SMBG** deserves study:
   - Promising for MDI, CSII, SAP and AP patients.

4. **Standardization of glucose data** is essential:
   - **Collection** (universal aggregation, open source over time)
   - **Analysis** – agree on definitions of TIR and buckets of hypo & hyperglycemia and GV.
   - **Display** – shared decision making critical and rapid action based on the visualized data.
   - **Clinical decision making** aids and guides need development.
4. Outpatient Artificial Pancreas work is a priority
   • Hybrid Closed Loop – ready for larger testing program to determine real world benefit and refinement
   • Bihormonal Closed Loop - ready for select testing and refinement

5. **Post marketing surveillance** for all diabetes devices and system components (e.g. infusion sets) must be enhanced and standardized

6. **Optimal yet Individualized Glycemic Control needs redefinition**
   • A1c + TIR with minimal hypoglycemia (specific targets need to be defined)
Thank You

Questions?