Latest Developments in Diabetes Technology

Presented by
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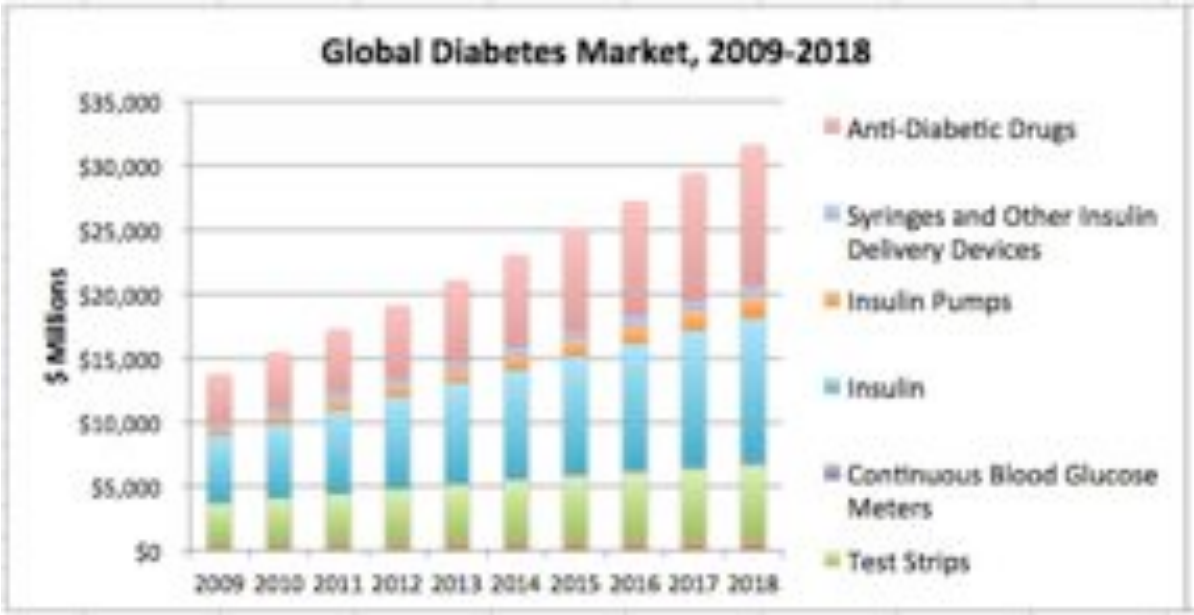
Speaker Disclosures

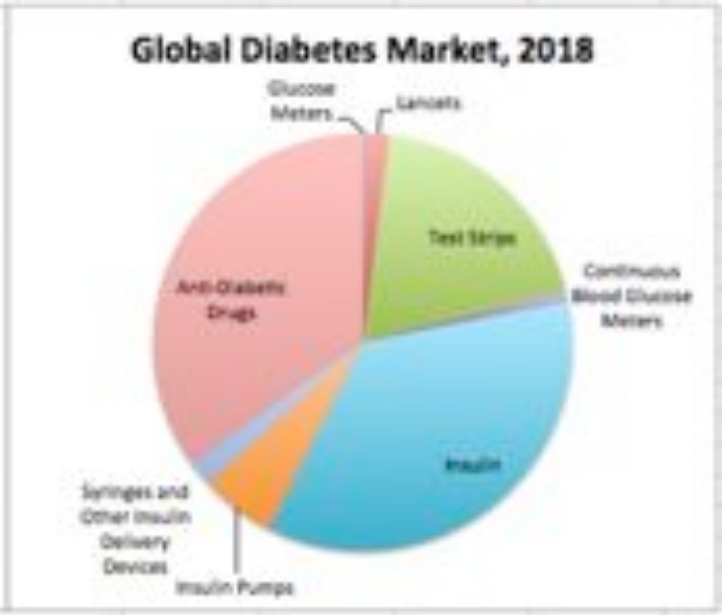
- Advisory Board for Becton Dickinson & Voluntis
- Speaker's Bureau for Program Management Services, Inc.

Objectives

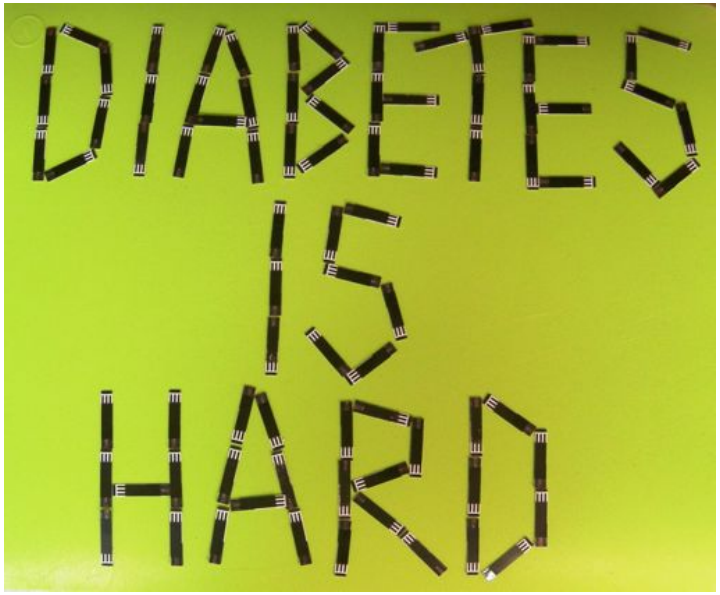
- Identify current technologies for treating diabetes including glucose meters, continuous glucose monitoring, insulin pumps, and mobile applications
- Discuss patient selection and engagement for using current diabetes technologies

Economic Perspective



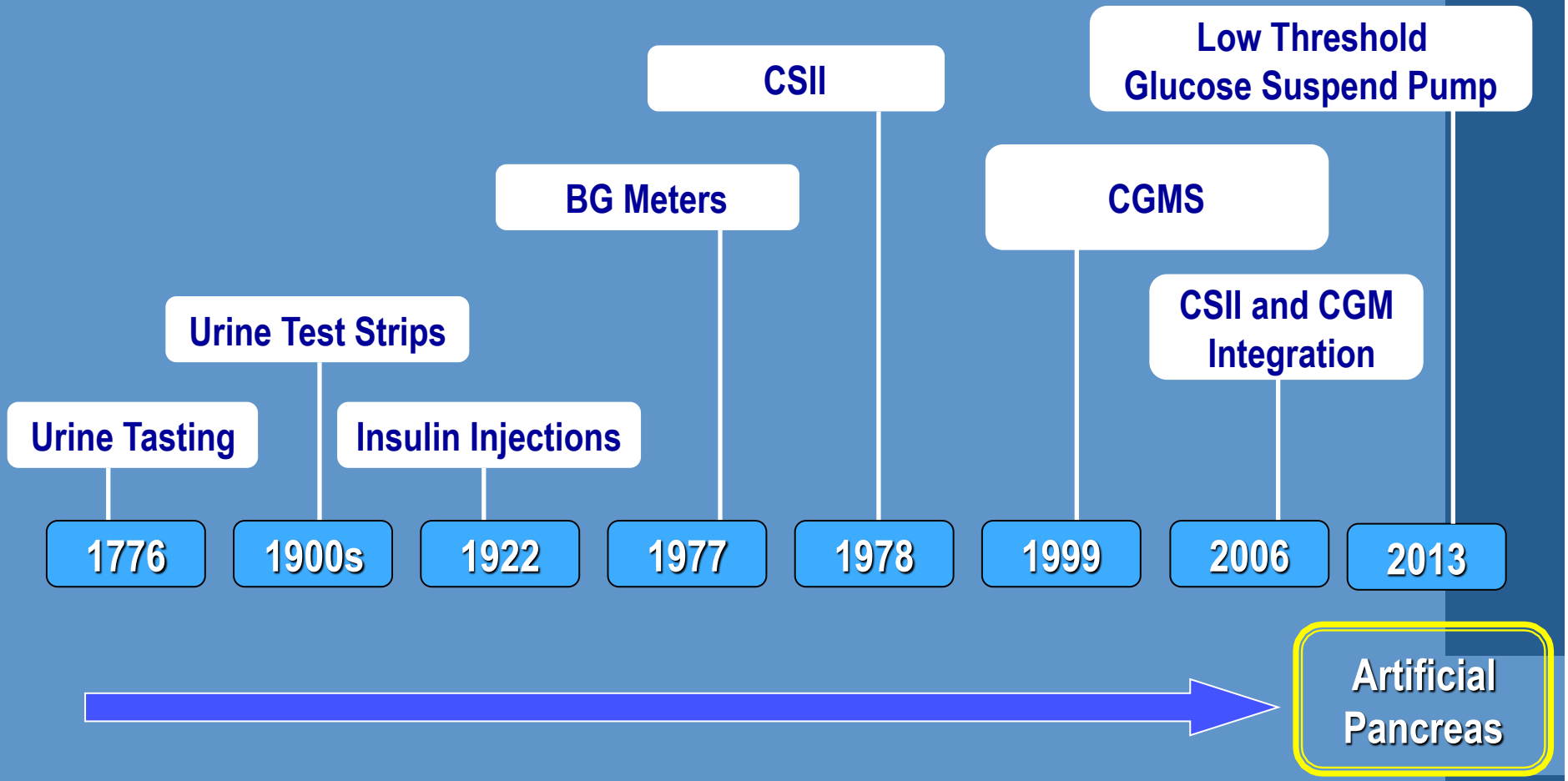


Source: MedMarket Diligence, LLC; Report #D510, "Diabetes Management: Products, Technologies, Markets and Opportunities Worldwide 2009-2018."

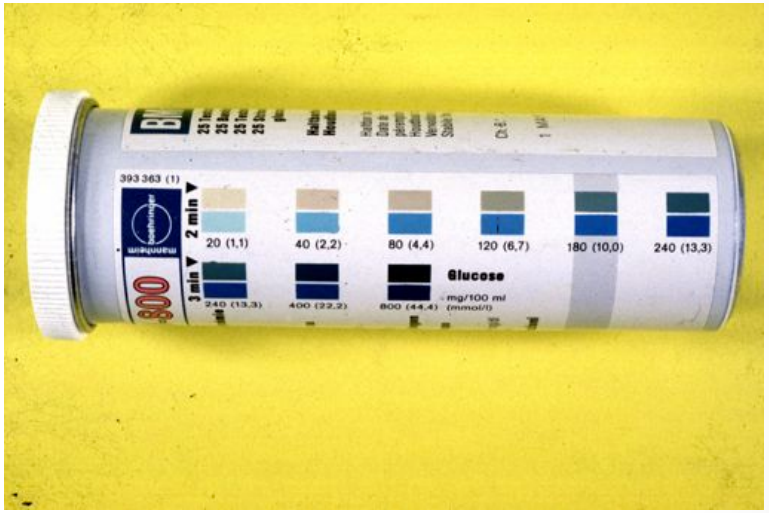


8 CBGs/day x 365 d/y x 40 yrs =116,800 tests in my lifetime so far…

Evolution of Diabetes Management Technologies



Glucose monitoring—Where we've been…

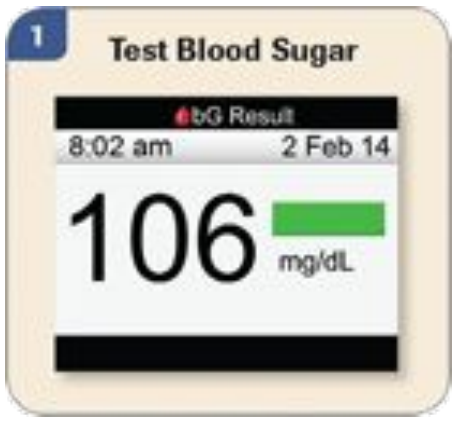


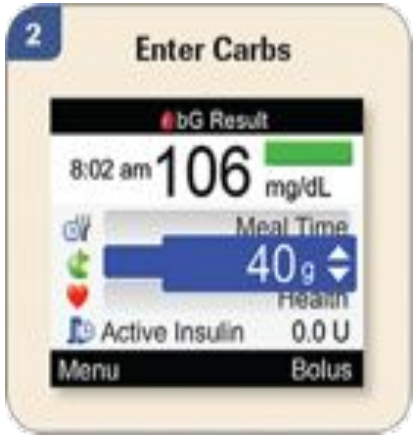
Glucose monitoring—Where we've been…

Glucose monitoring—where we are now…

Meters are connected to “your phone & computer”

Bolus Calculators – "Advisors"





- Calculates insulin dose based on blood glucose and expected carb amount
- Able to account for insulin on board
- Keeps history of patient's blood glucose, insulin and carb data (that was entered)
- Features hyper and hypo warning limits

What about Accuracy of SMBG?

Minimum Accuracy Criteria for BG Monitors From the 2013 ISO 15197 Standard

95% of glucose results must be:

For glucose ≤ 75 mg/dl – within 15 mg/dl of reference
For glucose ≥ 75 mg/dl – within 20% of reference

No clinical accuracy requirements

Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Minimum Accuracy Criteria for BG Monitors From the 2013 ISO 15197 Standard

95% of glucose results must be:

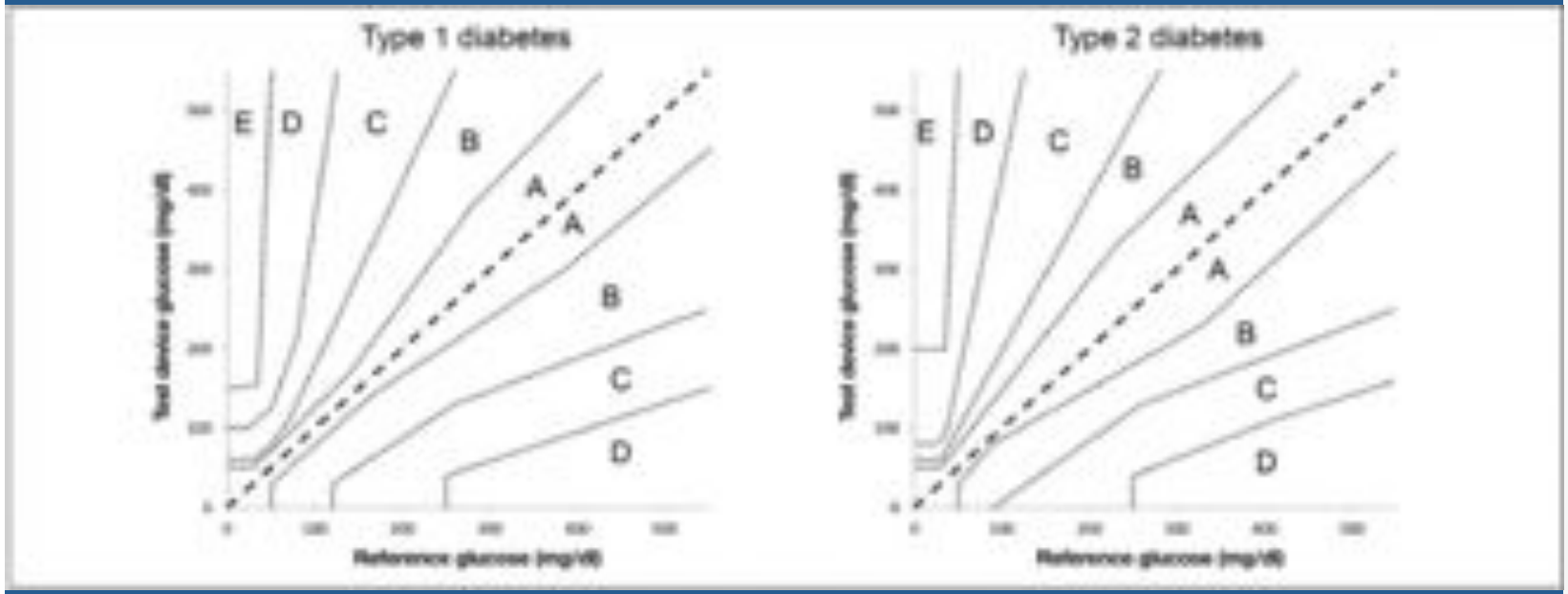
For glucose ≤ 100 mg/dl – within 15 mg/dl of reference
For glucose ≥ 100 mg/dl – within 15% of reference

99% of glucose results must be:

Within the Parkes (Consensus) Error Grid Zone A or B

Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

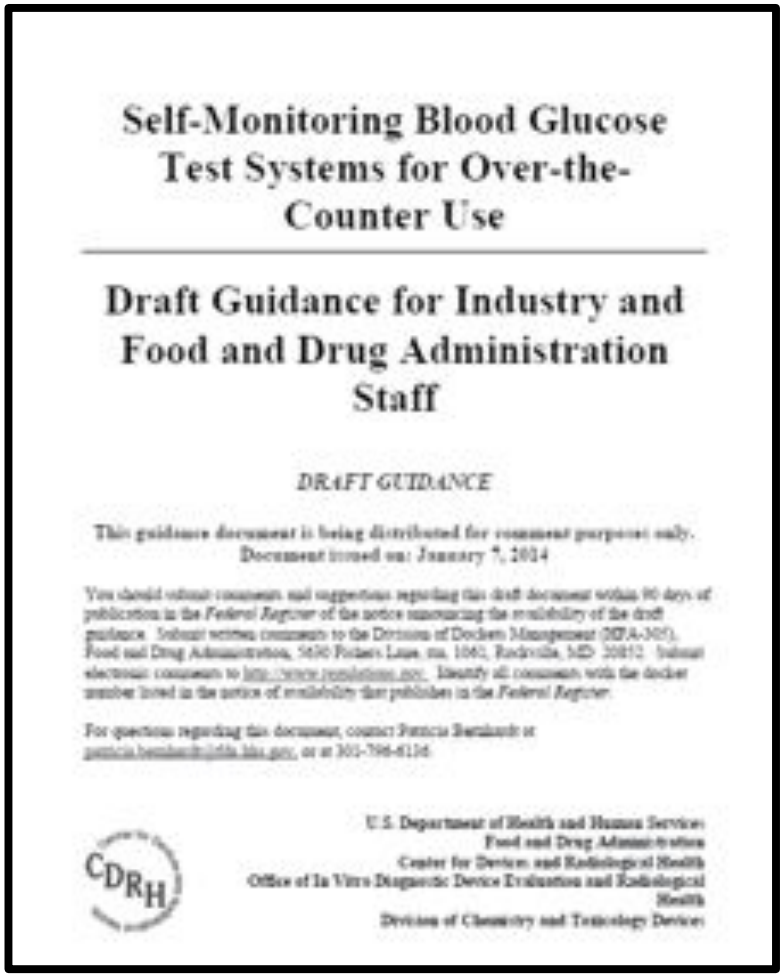
Parkes (Consensus) Error Grid Developed in 1994 for T1DM and T2DM



Parkes D Care 2000;23:1143

Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Proposed Standards…



Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

Draft Guidance for Industry and Food and Drug Administration Staff

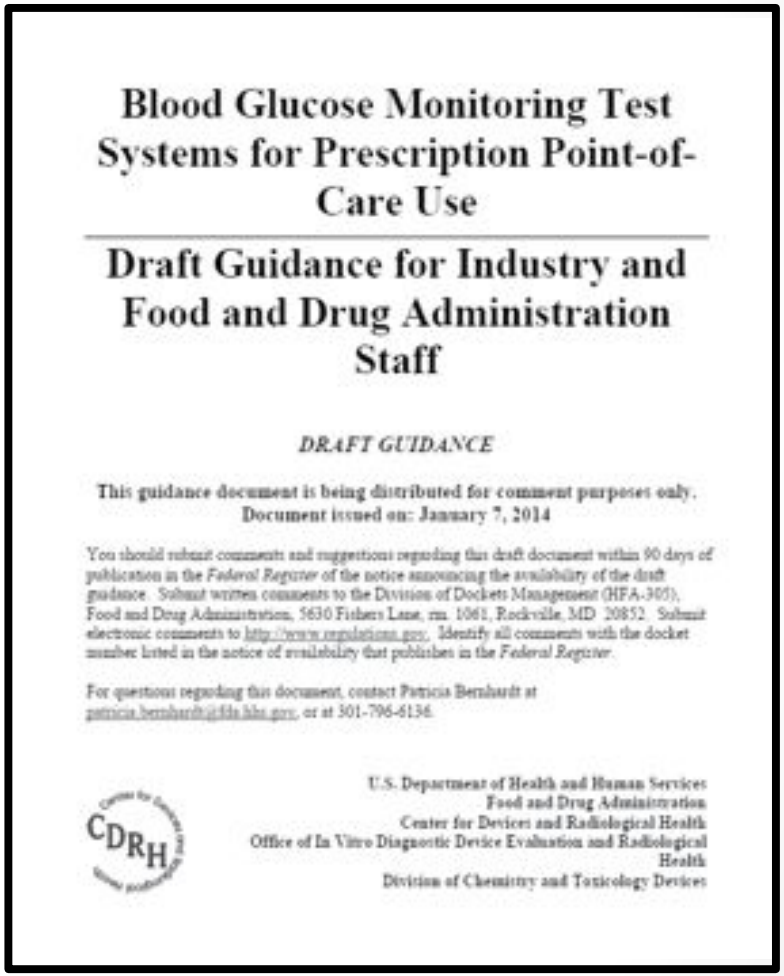
DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: January 7, 2014

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact Patricia Bernhardt at patricia.bernhardt@fda.hhs.gov, or at 301-796-6136.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of In Vitro Diagnostic Device Evaluation and Radiological Health
Division of Chemistry and Toxicology Devices



Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use

Draft Guidance for Industry and Food and Drug Administration Staff

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of In Vitro Diagnostic Device Evaluation and Radiological Health
Division of Chemistry and Toxicology Devices

Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Minimum Accuracy Criteria for OTC Blood Glucose Monitors from the 2014 Draft FDA Guidance

95% OF GLUCOSE RESULTS MUST BE WITHIN 15% OF REFERENCE

99% OF GLUCOSE RESULTS MUST BE WITHIN 20% OF REFERENCE

ACROSS THE RANGE

Within +/- 5 mg/dL	Within +/- 7 mg/dL	Within +/- 10 mg/dL	Within +/- 15 mg/dL
X/Y (%)	X/Y (%)	X/Y (%)	X/Y (%)

Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Minimum Accuracy Criteria for Point-of-Care Blood Glucose Monitors from the 2014 Draft FDA Guidance

99% of glucose results must be:

For glucose ≤ 70 mg/dl – within 7 mg/dl of reference
For glucose ≥ 70 mg/dl – within 10% of reference

And 100% of glucose results must be:

For glucose ≤ 75 mg/dl – within 15 mg/dl of reference
For glucose ≥ 75 mg/dl – within 20% of reference

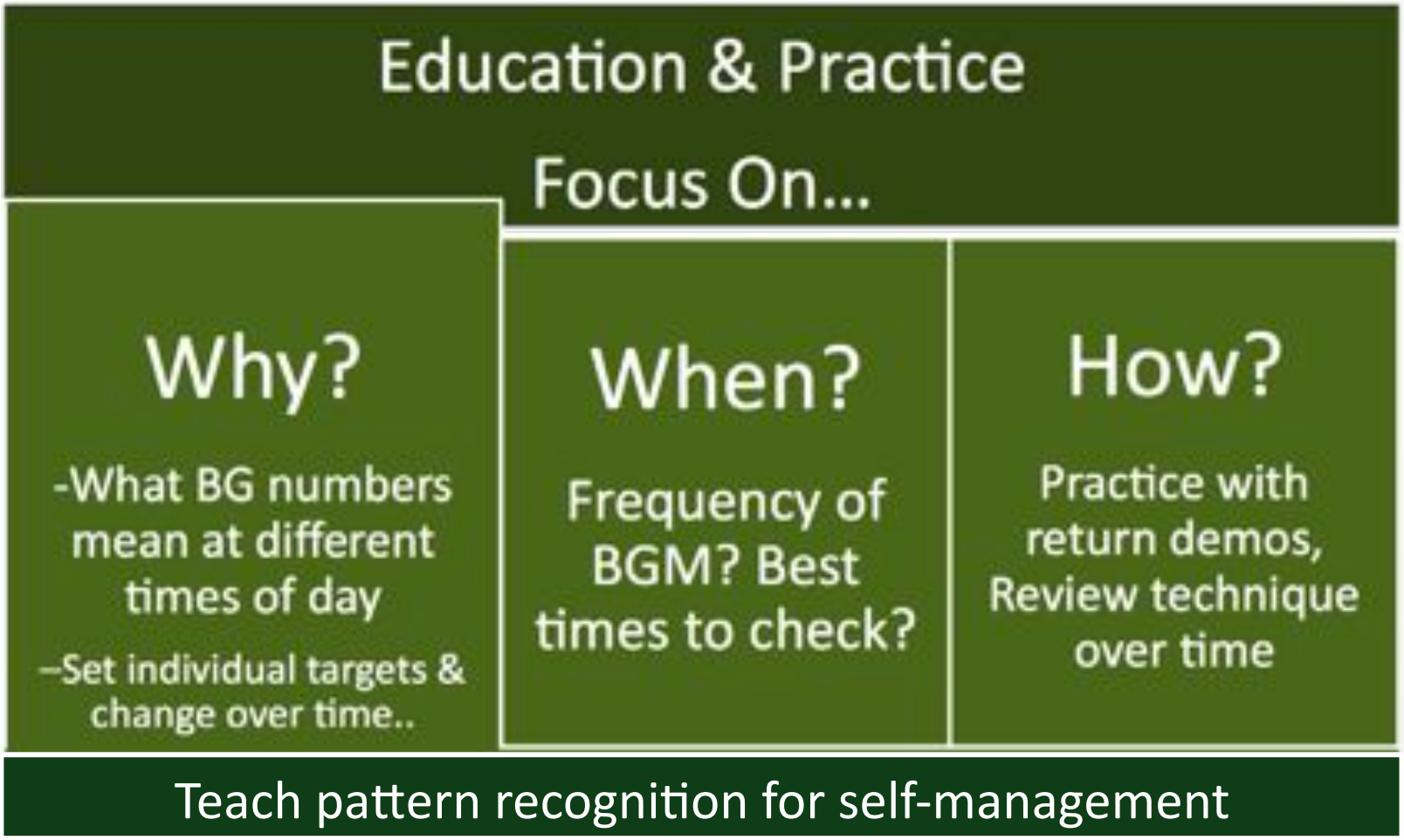
Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Who should monitor Capillary Blood Glucose (CBG)? (patient selection)

- All individuals using insulin[1-5]
- Woman with pregnant with Overt or GDM[2]
- Consider for persons using oral anti-hyperglycemic medications as optional component of self-management, in tandem with A1c [3]
- Individuals on sulfonylureas and glinides—check when sx [1,5]
- Individualize intensity and frequency [1-5]
- Generally agreed, not used as part of routine care when diabetes well controlled by by MNT or antihyperglycemic medications [3,5]
- SMBG is for any DM patient, including NIT T2DM patients on structured testing[6]

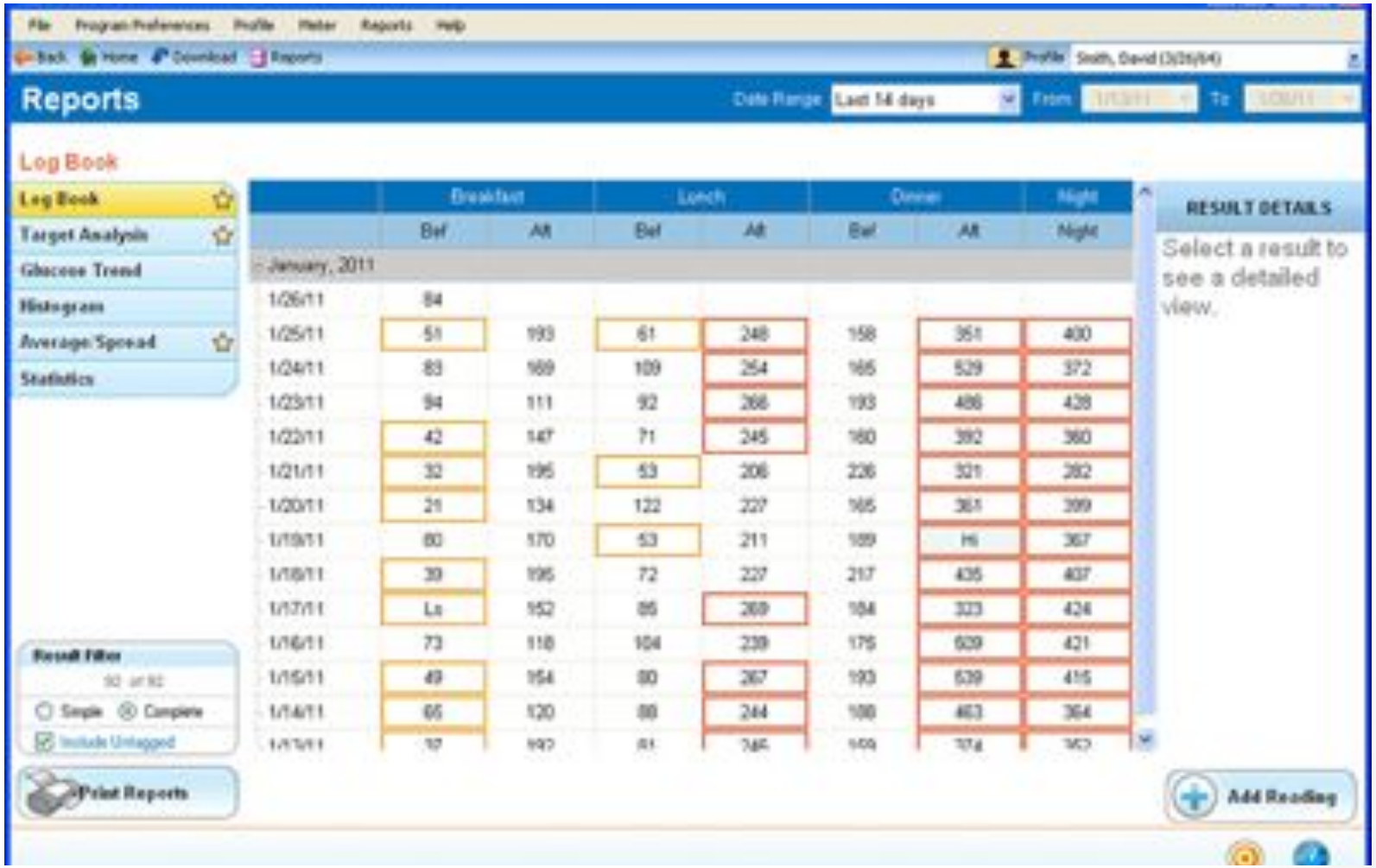
1. AACE/ACE 2015 Guidelines; 2. Endocrine Society Diabetes & Pregnancy Guidelines 2013; 3. IDF Clinical Guidelines Task Force Global guidelines for T2DM 2012; 4. ADA T1DM Position Statement 2014; 5. ADA 2015 Guidelines; 6. Cochrane Database Syst Rev 2012.

How to Engage Patients to Monitor?



Adapted with permission J Seley, Blood Glucose Monitoring, DTS presentation, Orlando 2015

Meter Download of Electronic Log Book



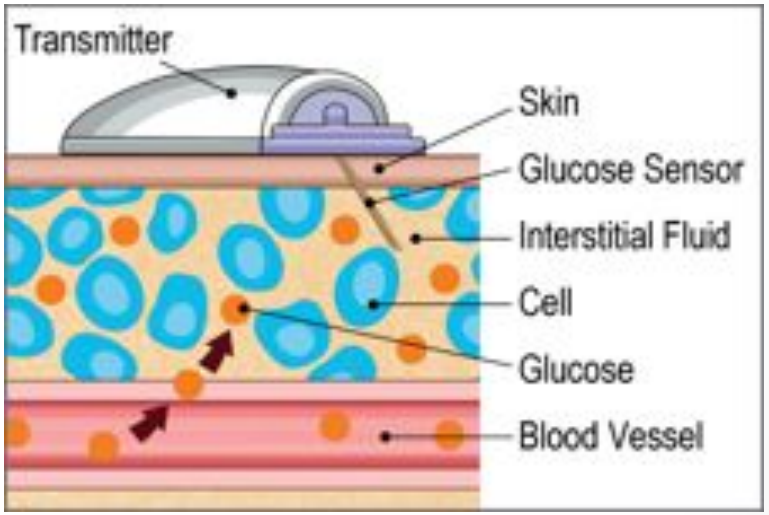
Adapted with permission by Jane Seley, DNP, CDE. CDTC course. Orlando, 2015

Continuous Glucose Monitoring (CGM)

Continuous Glucose Monitoring (CGM)

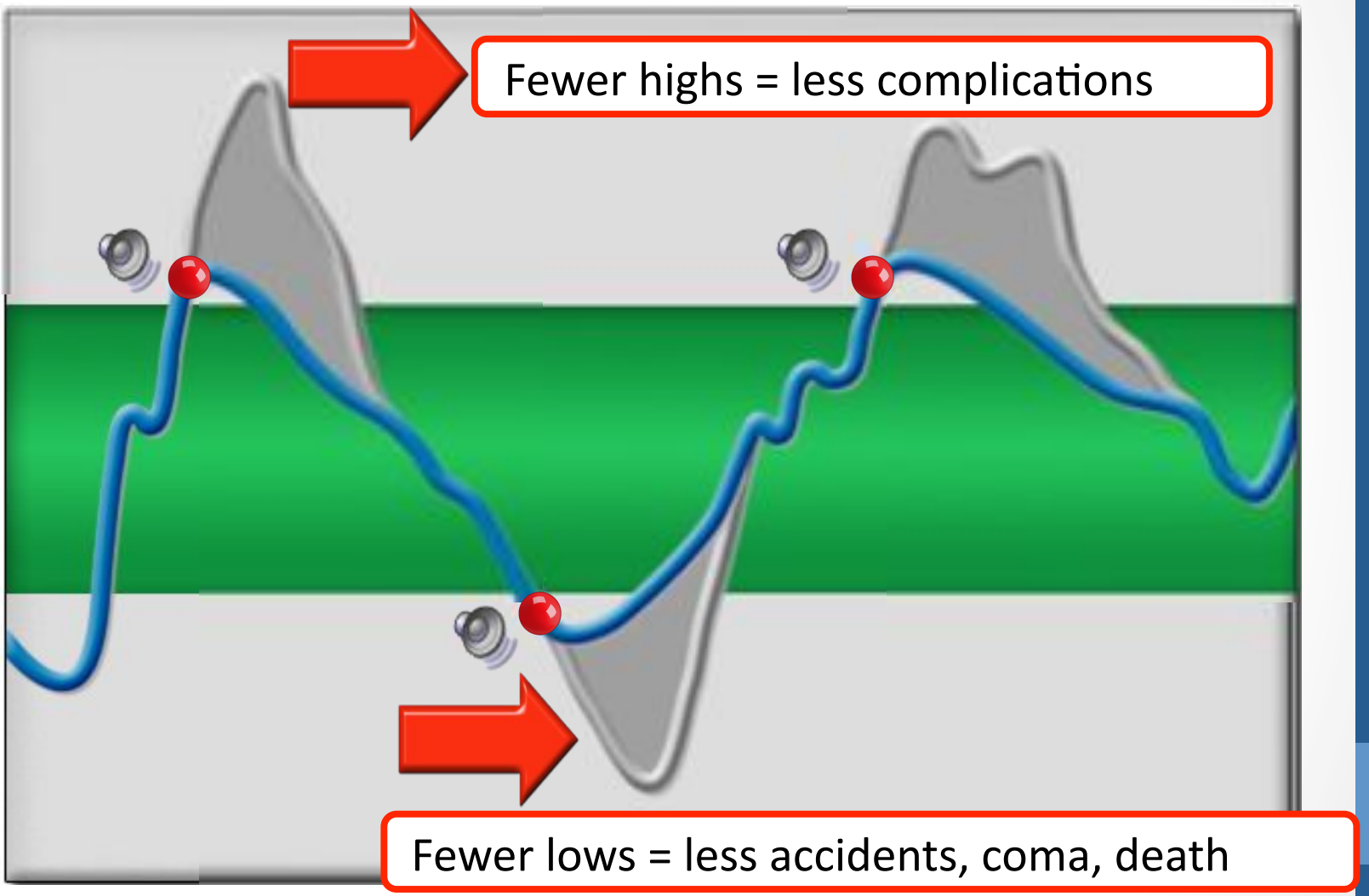
DEFINED TO HAVE 5 FEATURES…

- A wearable body sensor
- Always in contact with the body
- Measures glucose in a defined fluid, e.g., interstitial fluid (ISF) within the skin
- Provides values at least every 15 minutes
- Makes measurements automatically without patient effort



Adapted from D Klonoff, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

The Value of Continuous Glucose Monitoring…the future is all about glucose sensing

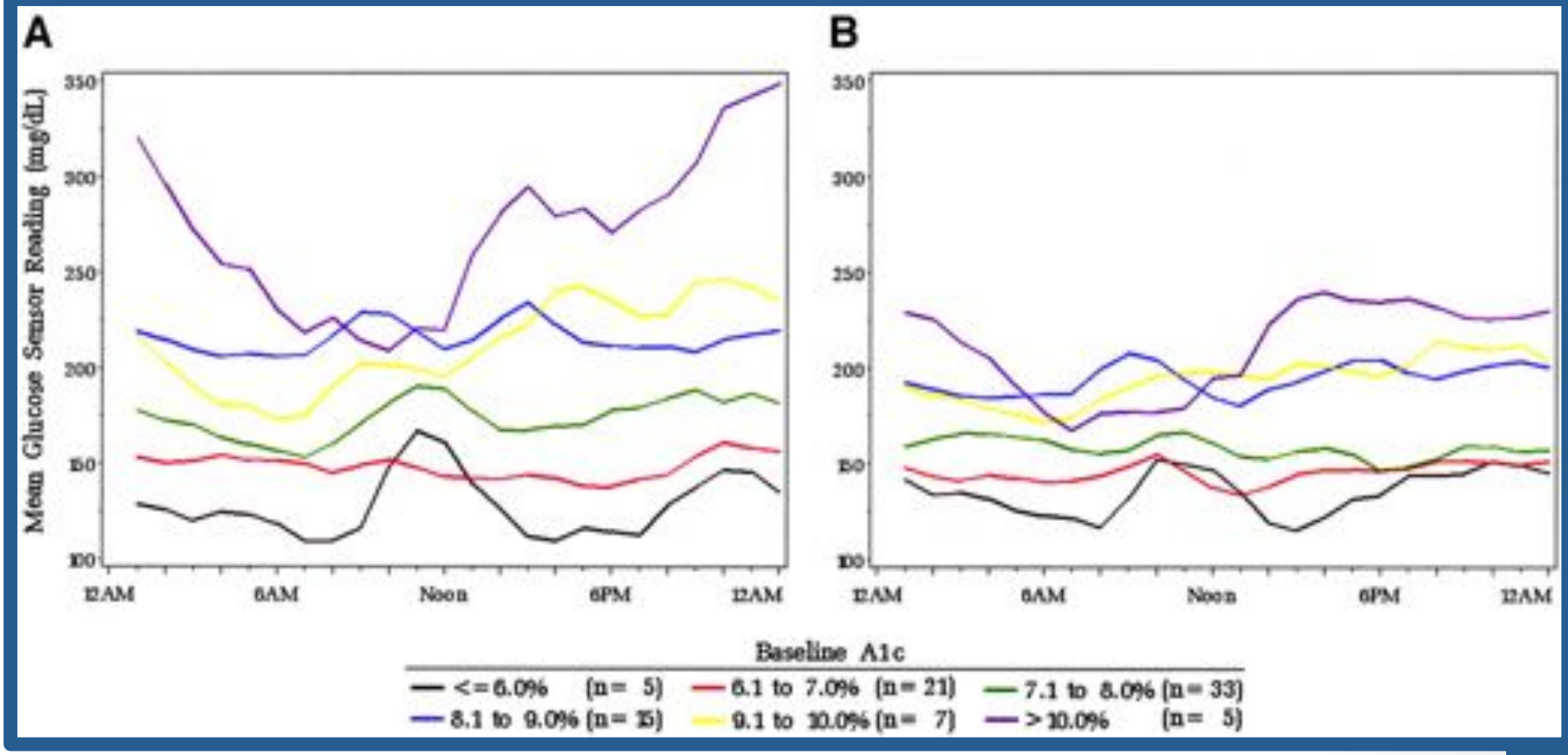


Beyond SBGM…Where we've been…

Modal Day by A1C

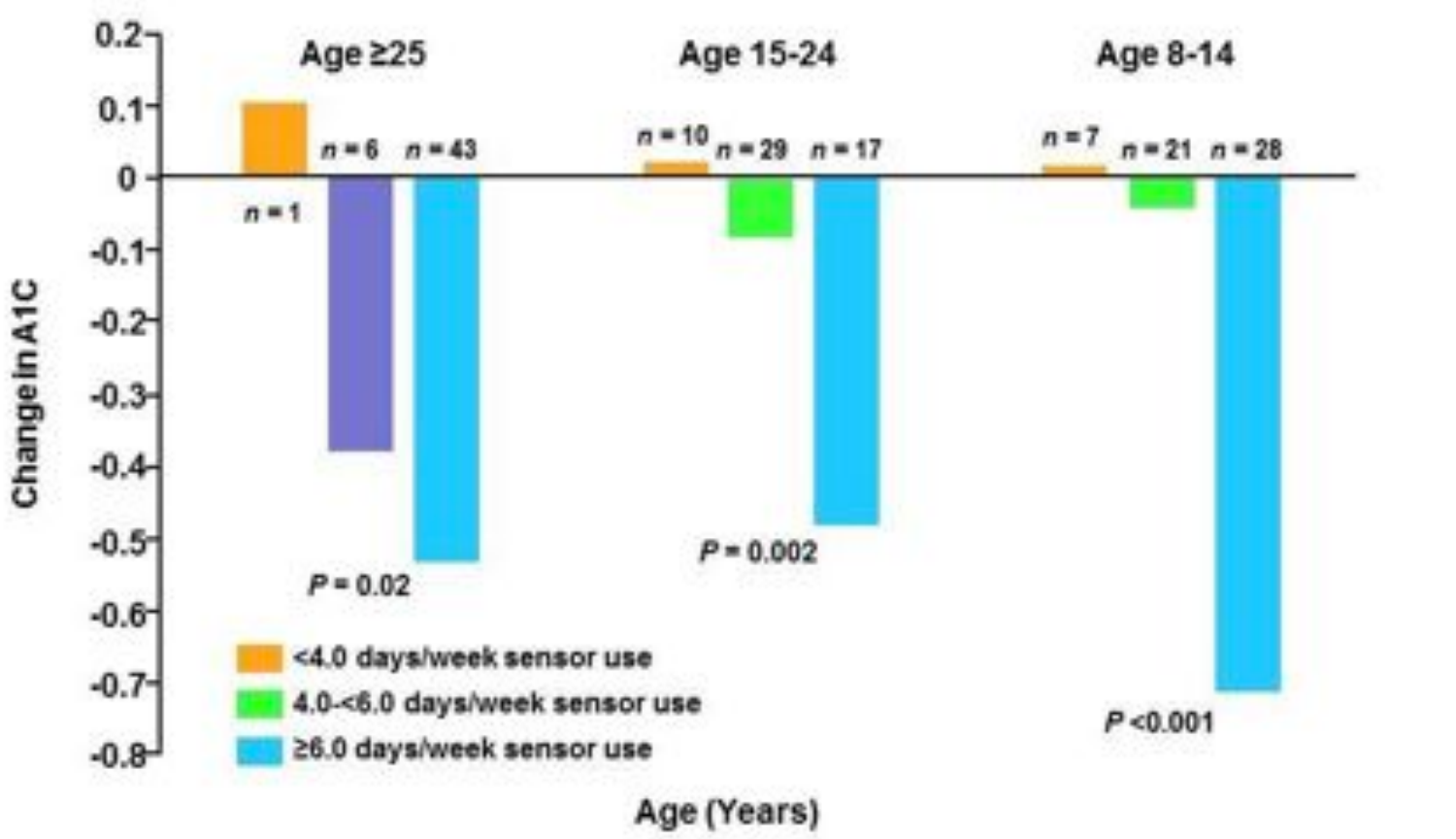
(Higher the A1c → Greater reduction in A1c)

Baseline Blinded Data **Access to Real-Time Data**



Garg & Jovanovic. Diabetes Care. 29:2544-2649

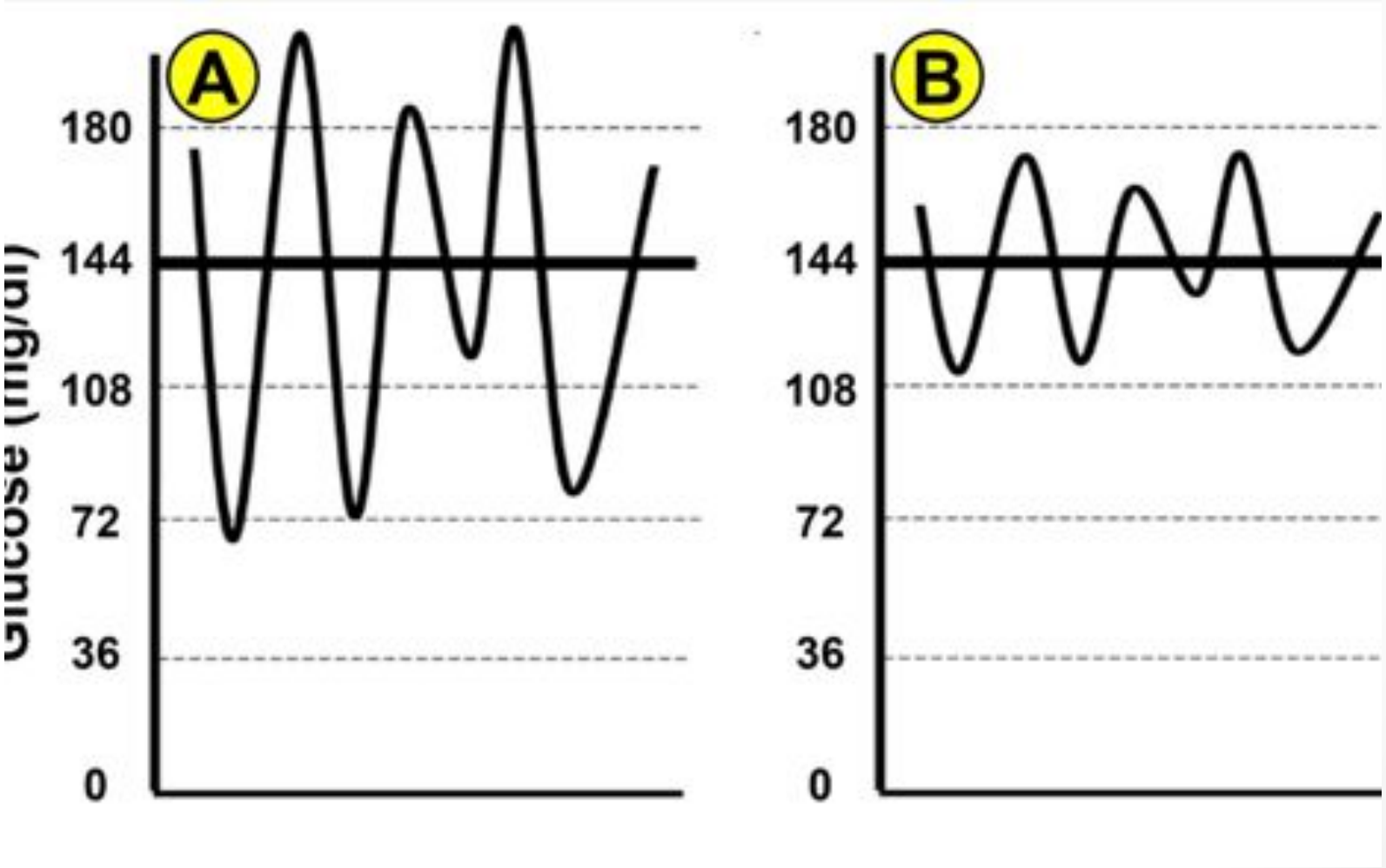
Change in A1C by Sensor Use



Diabetes Care. 2009;32:1947-5193.

LBL-012178 Rev 01

Glucose Variability –A1C 7%...



CGM…Where we're now…

FDA Approved CGM Devices

DEXCOM G4 SHARE

Sensor length: 13 mm

Sensor Life: 7 days

MEDTRONIC GUARDIAN

Sof-Sensor length: 14 mm

Sensor life: 3 days

CGM Shows If Trend Is Up or Down (Indicates Different Clinical Situations)

Based on simulated data.

LBL 010399 Rev 01

Comparative Features

Feature	Dexcom	Medtronic
Sensor Life	7 days	3 days Sof-sensor 6 days Enlite
Receiver Range	20 ft	8 ft
Pump Integration	Animas Vibe	All Revel / 530 models
Linked meter	No	Bayer Contour
Calibrations	2 x daily	2-3 x required daily 3-4 x daily optimal
Accuracy (MARD)	9-11%	13.6% (Enlite) 19.7% (Sof-sensor)

Who should use CGM? (patient selection)

- Consider GGM for patients with **TYPE 1 AND TYPE 2 ON BASAL-BOLUS THERAPY** –to improve A1C levels and reduce hypoglycemia. [1]
- Use in **PREGNANT WOMEN** with overt or GDM when SMBG levels insufficient to assess glycemic control (including hyper-and-hypoglycemia). [2]
- CGM is useful to **REDUCE A1C IN ADULTS** without increasing hypoglycemia; can reduce glycemic excursions in **CHILDREN** [3]
- **OTHER CLINICAL APPLICATIONS**—Pre-diabetes, Stress diabetes, Clinical trials of glucose lowering drugs, Hospitalized patients with know diabetes or with transient hyperglycemia, CABG surgical patients [4]

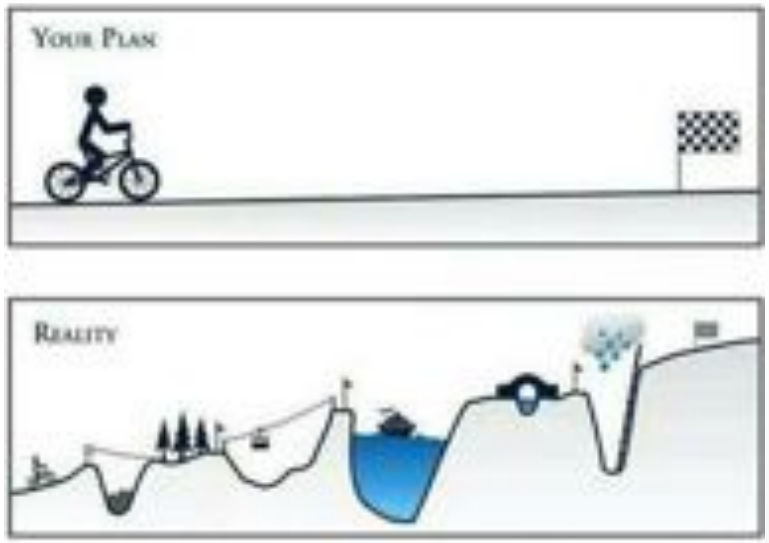
1. Handelsman Y, et al. AACE/ACE 2015 Guidelines. 2. Blumer I, et al. J Clin Endocrinol Metab. Endocrine Society Diabetes & Pregnancy Guidelines. 3. Chiang JL et al. ADA Type 1 Diabetes Position Statement 2014. 4. Klonoff D, "Clinical Need & Technology (SMBG). CDTC course Orlando, 2015

Potential Benefits of CGM Use… (patient en

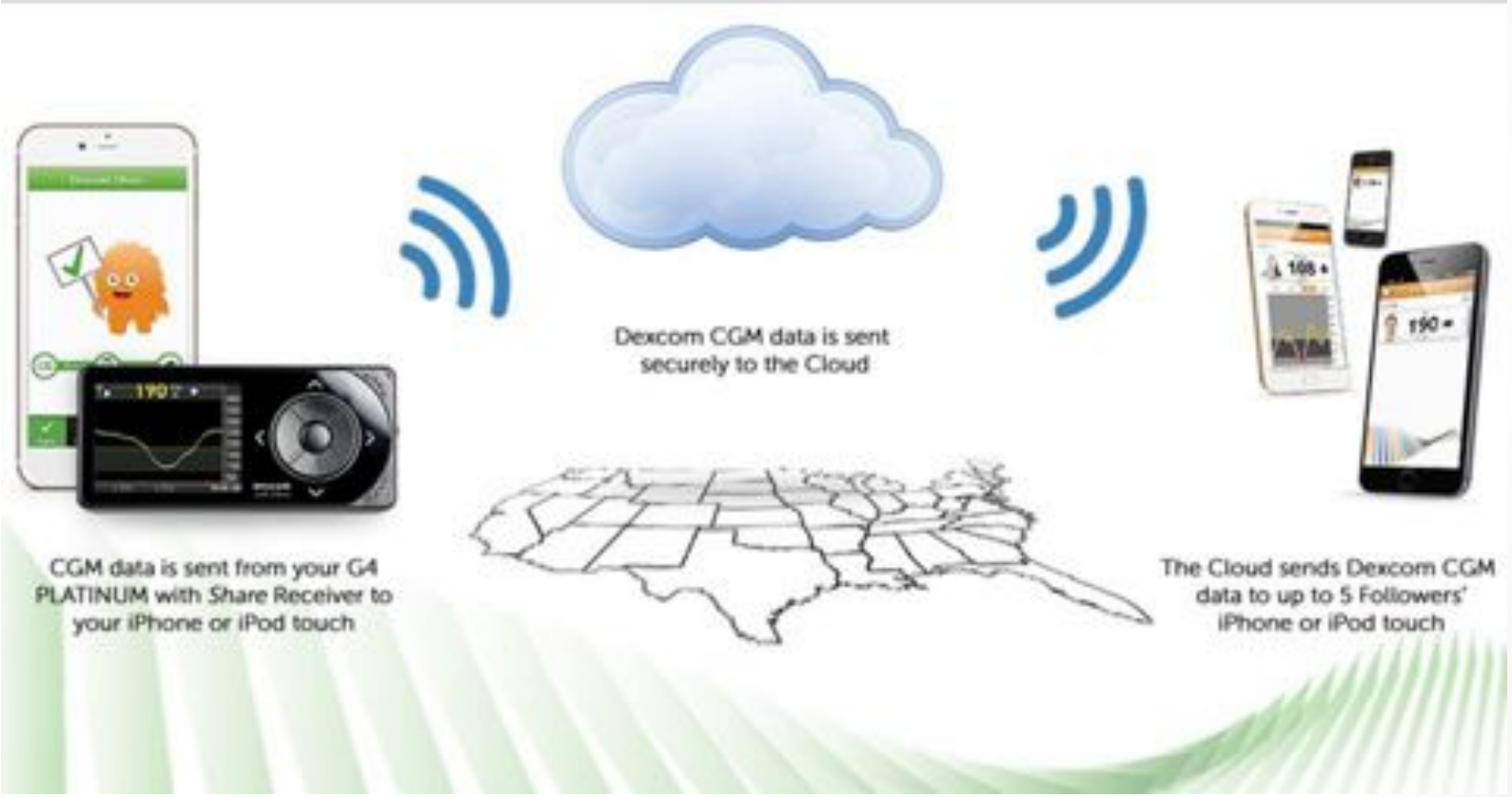
- **IDENTIFY**/confirm glycemic excursions
- **DETECT** dawn phenomenon, impact of hormones/stress
- **KNOWING** the direction of glucose levels
- **EARLY WARNING** of hypoglycemia
- **INSIGHTS** into effects of physical activity, food, stress, etc.
- **ALERTS** for highs and lows
- **ANTICIPATE** highs & lows to take action
- **VALIDATION** of therapeutic adjustments
- **EMPOWERMENT** to improve decision making regarding self-management

Potential Risks and Drawbacks

- Overly aggressive correction of elevated glucose levels
- For pump users, having a second "site" and/or device
- Alarm fatigue
- Skin irritation
- Accuracy issues
- Costs



Dexcom G4 Platinum with Share



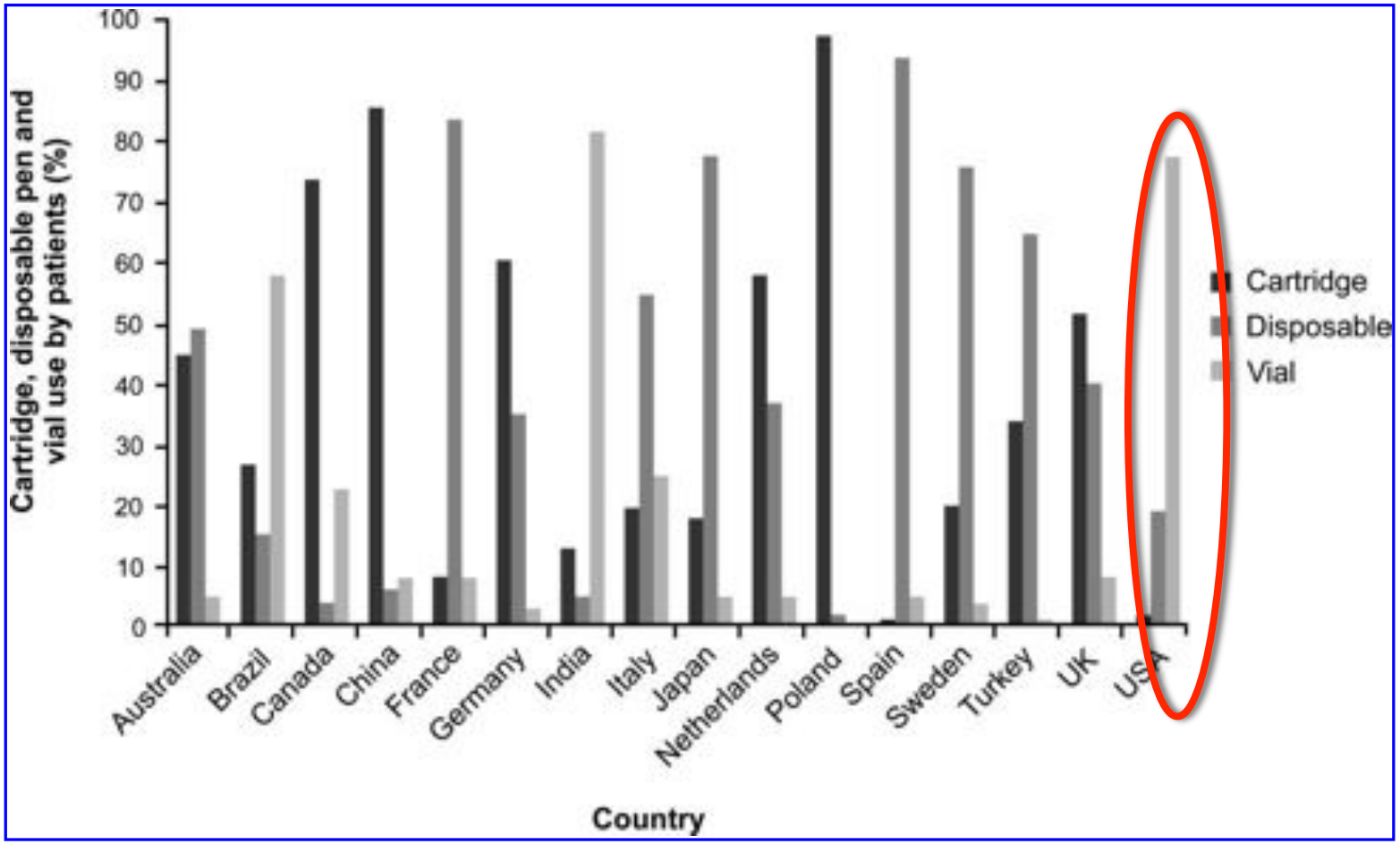
MiniMed Connect (pending)

Insulin Replacement Therapy

Insulin Syringes, Pens, Pumps and Beyond

Insulin Replacement Therapy…
Where we've been…

Worldwide Pen Use: 2009…Where we're now…



Diabetes Tech Therap 12 (Suppl 1)S79-S85, 2010

Pen Delivery of Injectables

Echo Pen (not just for kids…)

Shorter Pen Needles

Future technology….Timesulin (not available US)

- Shows how long since last insulin injection administered
- Replaces your plastic cap with battery activated timer
- Smart cap starts counting up to 99 hrs from time pen last capped
- Restarts counting if cap removed for > 8 sec

Where we might go….

“GoCap”

Where we've been with insulin pumps…

ADA Statement on CSII Therapy

Most people with type 1 diabetes should be treated with MDI injections (3 to 4 injections per day of basal and prandial insulin) or continuous subcutaneous insulin infusion (CSII).

Evidence category A

Standards of Medical Care-2014, Diabetes Care 37 (suppl 1), 2014

Where we're now… 2015

Medtronic

Tandem

OmniPod

Animas

Roche

V-Go

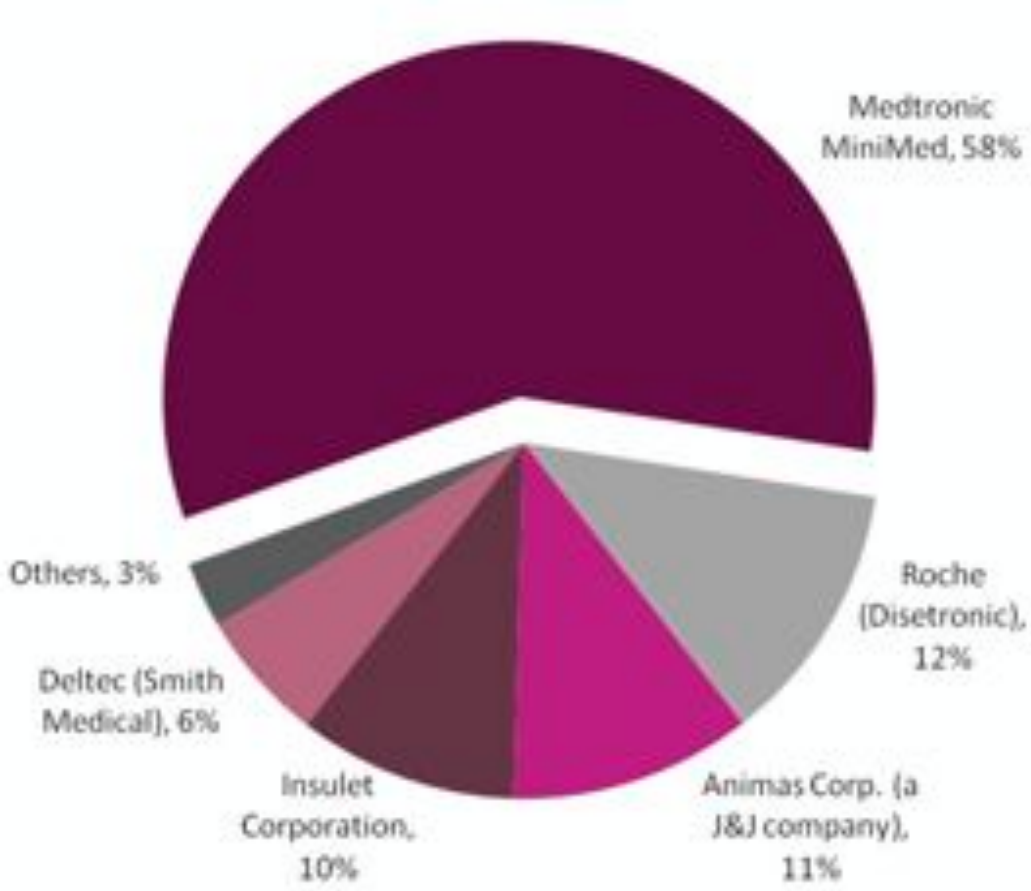
Consumer Guide 2015. Diabetes Forecast, Mar/Apr 2015

Insulin Pumps in the spotlight!

Nicole Johnson – Miss America
1999

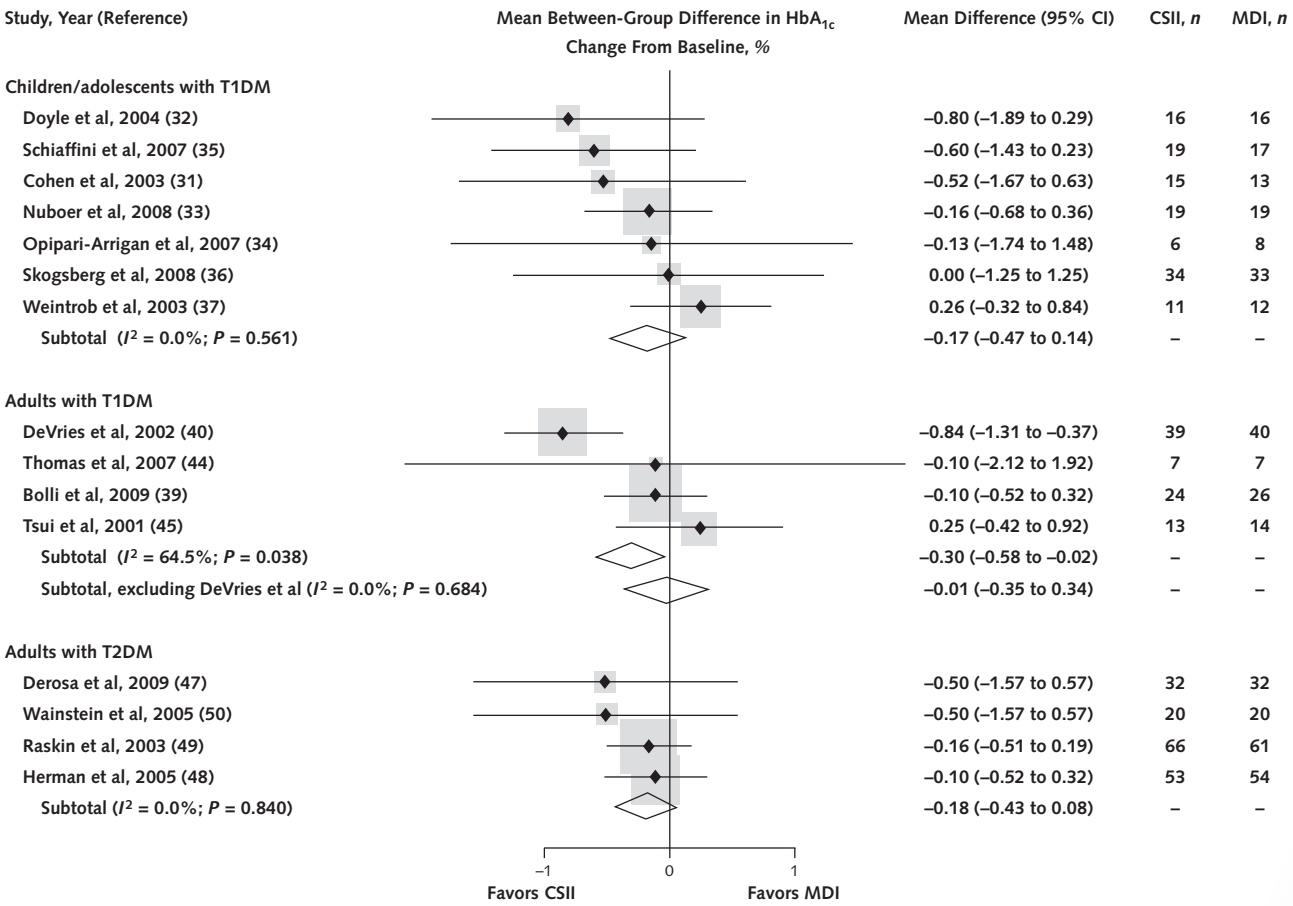
Sierra Sandison –Miss Idaho
2014

Global Share Of Insulin Pump Market
(Based On Revenue)



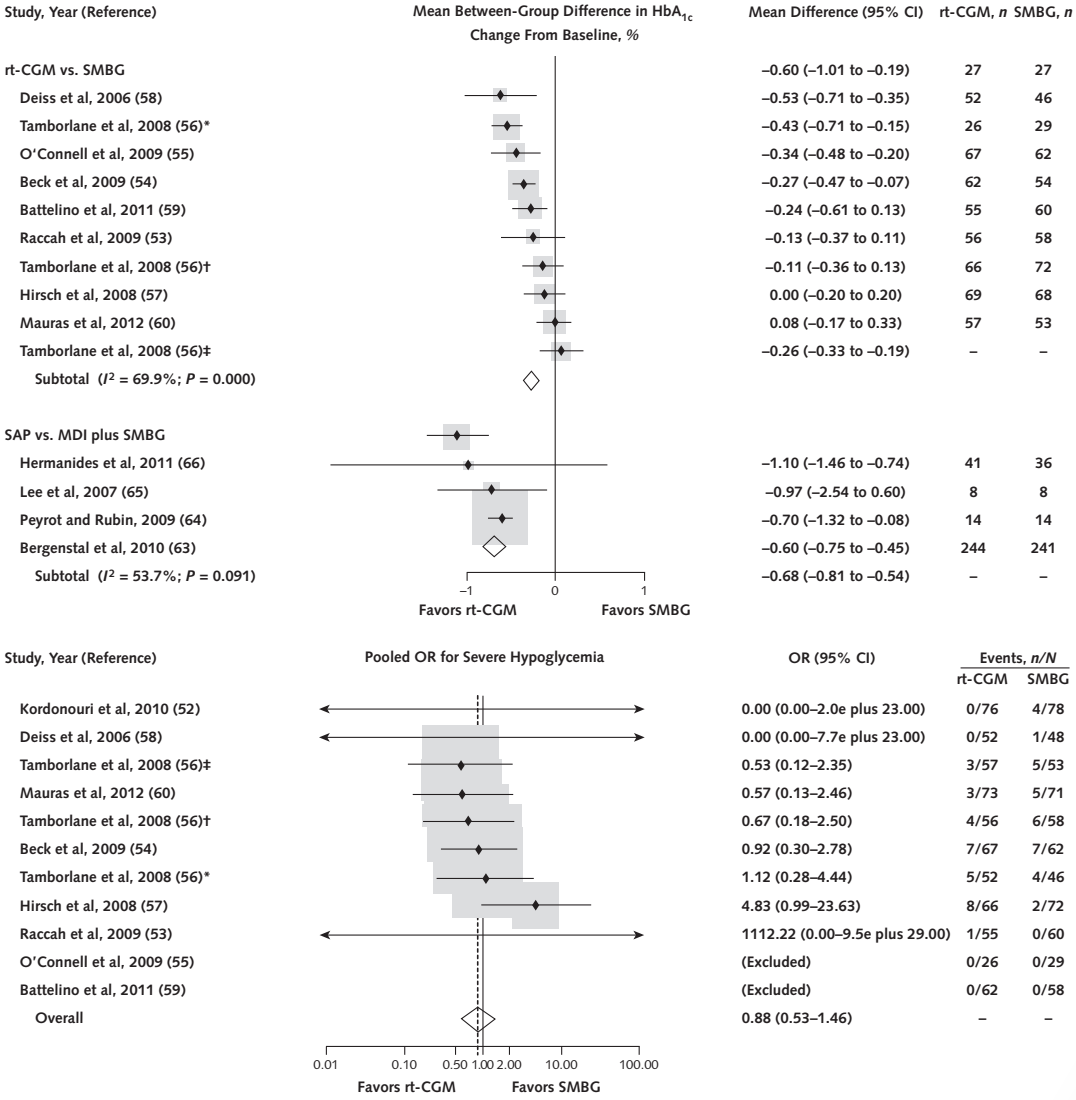
Source: D. Medical Industries LTD. - 2012 SEC Form 6-K
http://www.sec.gov/Archives/edgar/data/1487525/000117891312003364/zk1212349.htm

AHRQ Review Insulin Pumps - Mean Between-group Difference in the Change from Baseline HbA1c: CSII vs MDI



Ann Int Med 157:336-347, 2012

AHRQ Review Insulin Pumps—Sensor Augmented Pump (SAP) vs MDI + SMBG



Who would benefit?

- Suboptimal glycemic control despite optimized multiple daily injection therapy
- Wide glycemic excursions
- Dawn phenomenon with elevated fasting blood glucose levels
- Frequent severe hypoglycemia and/or hypoglycemic unawareness
- Pregnant or planning conception
- Inconsistent daily schedule not well managed with injections
- Insulin sensitivity and requirement of low doses of insulin
- Gastroparesis
- Early neuropathy or nephropathy
- Renal transplantation

Keeping Patients Engaged in Healthy Self-Care…

- Regular appointments with review of A1C, download of insulin pump settings and glucose or CGM monitoring
- Screen for “Diabetes” Burnout as needed based on biochemical indicators
- Provide ongoing Diabetes Self-Management Education and Support (DSMES) as needed
- Provide ongoing support for life changes and events
- Provide expert measuring, monitoring, and management with focus on safe and effective pump therapy
- Offer new and improved technology when available and appropriate

Where we've been… Artificial Pancreas!!

EVOLUTION OF AP SYSTEMS

VERY LOW GLUCOSE→ Insulin Off Pump

HYPOGLYCEMIA MINIMIZER →Predictive hypoglycemia Causes Alarms →Followed by reduction in – or – Cessation of Insulin Delivery below LOW THRESHOLD

HYPOGLYCEMIA – AND – HYPERGLYCEMIA MINIMIZER --Same as (2), but Added feature allowing insulin dosing above HIGH THRESHOLD

AUTOMATED BASAL / HYBRID –CLOSED LOOP
Closed loop at all times – With – Meal-time manual assist Bolusing

Fully Automated INSULIN CLOSED LOOP

Fully Automated INSULIN + AUTOMATED MULTI-HORMONE CLOSED LOOP

Adapted from A Kowalski, "From Research to Clinical Practice: Upcoming Advances in Diabetes Care", AADE 2015, New Orleans

AP Systems are Coming…

- MDT: Hybrid Closed Loop: April 2017
- Animas Hypo-Hyperglycemia minimizer
- Bigfoot Biomedical: Hybrid Closed Loop
- Type Zero: Hybrid Closed Loop
- Boston University: Dual-hormone
- Inreda: Dual-hormone
- Tandem
- Insulet
- Roche
- Medtronic

Adapted from A Kowalski, JDRF "From Research to Clinical Practice: Upcoming Advances in Diabetes Care", AADE 2015, New Orleans

Telehealth Technology

Smartphones apps, Social Media, Telemedicine

Telehealth Terminology

- Telehealth
- Connected Health
- E-health
- E-community
- Telematics
- M-Health
- Telemedicine

Telehealth Defined

- "Telehealth encompasses a broad variety of technologies and tactics to deliver virtual medical, health, and education services. Telehealth is not a specific service, but a collection of means to enhance care and education delivery." [1]
- State and federal agencies often differ on how they define telehealth.
  - The federal HRSA defines *"The use of electronic information and telecommunications technologies to support long-distance clinical health care, patient and professional health-related education, public health and health administration."*[1]

1. Center for Connected Health Policy. The National Telehealth Resource Center. http://cchpca.org/what-is-telehealth

Where we're now…Telemedicine

- New Mexico enacted legislation for telemedicine:

- "The law mandates coverage under private health insurance plans, and defines telemedicine as the use of real-time interactive audio, video, or other telecommunications technology, including store-and-forward-technology, by a health care provider to deliver health care services at a site other than the site where the patient is located."

Telehealth Modalities

- **LIVE VIDEO** (synchronous): Live, two-way interaction between a person (patient, caregiver, or provider) and a provider using audiovisual telecommunications technology. This type of service is also referred to as "real-time" and may serve as a substitute for an in-person encounter when it is not available.

Telehealth Modalities

- **STORE-AND-FORWARD (asynchronous):** Transmission of recorded health history (for example, pre-recorded videos and digital images such as x-rays and photos) through a ecure electronic communications system to a practitioner, usually a specialist, who uses the information to evaluate the case or render a service outside of a real-time or live interaction.

As compared to a real-time visit, this service provides access to data after it has been collected, and involve communication tools such as secure email.

Telehealth Modalities

REMOTE PATIENT MONITORING (RPM): Personal health and medical data collection from an individual in one location via electronic communication technologies, which is transmitted to a provider (sometimes via a data processing service) in a different location for use in care and related support.

This type of service allows a provider to continue to track healthcare data for a patient once released to home or a care facility, reducing readmission rates.

Telehealth Modalities

- **MOBILE HEALTH (MHEALTH)**: Health care and public health practice and education supported by mobile communication devices such as cell phones, tablet computers, and PDAs.
- Applications can range from targeted text messages that promote healthy behavior to wide-scale alerts about disease outbreaks, to name a few examples.

Mobile Phone Use in USA

SMARTPHONE USE HAS INCREASED

- 2011—35% American adults owned a smartphone
- 2014—64% American adults owned a smartphone
- Some smartphone owners (particularly younger adults, minorities and lower-income Americans) depend on their smartphone for internet access

SMARTPHONE USES

- Texting
- Talking
- Emailing
- Internet
- Social Networking
- Photos or Videos
- Reading news

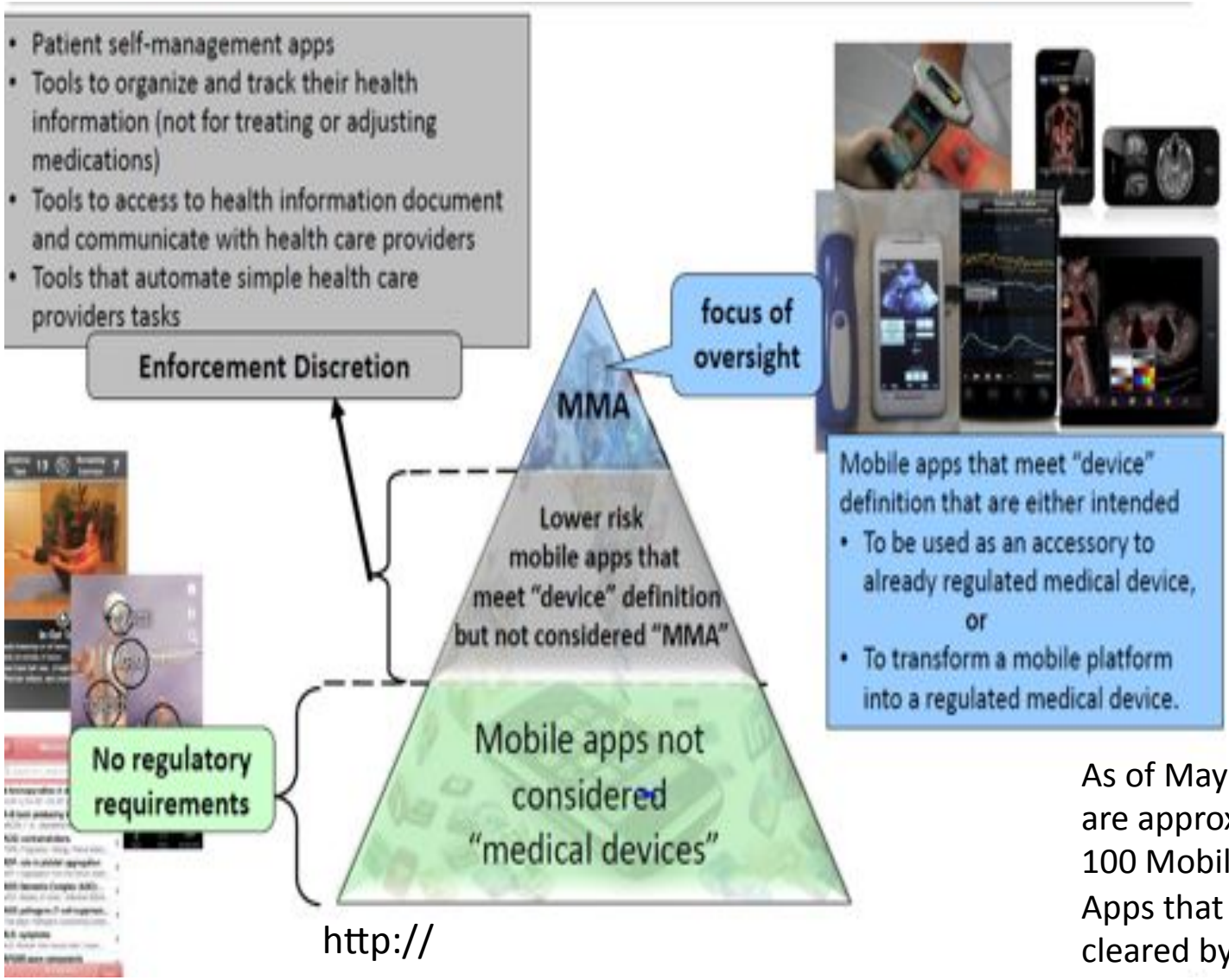
Mobile Health (mHealth) Apps

- **500 million** Smartphone users globally are using health apps [1]
- By 2018—**>50% of the more than 3.4 billion** smartphone and tablet users will have downloaded **mHealth applications** [2]
- **Apple App Store** – 43,000 apps (health related categories)
  - 23,728-(Healthcare & Fitness) + 19,484 (Medical)3
- "The **Healthcare Apps Market is dominated by <u>exercise apps</u>**

  Sleep and meditation, and weight loss apps are expected to grow at the highest rate during the forecast period." [4]
- Breakdown of available health-related apps [5]
  - **96 % consumer focused** -- Calorie counting, Cardiovascular fitness, Strength training, Sleep improvement → **remaining 4 %** -- more specialized apps, for e.g. remote patient monitoring."

1. Sasan A,ed (2/19/15). Mobile Health: A Technology Road Map. Springer. ISBN 978-3-319-12817-7; 2.Research to Guidance, 2010; 3. http://148apps.biz/ as reported on 9/9/13; 4. September 2013 Research and market report -- http://www.researchandmarkets.com/research/6hlqd6/mhealth_apps; 5. *M. Shaw., Health digest news*

Mobile Medical Apps→FDA Regulation



http://

http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf

As of May 2015, there are approximately 100 Mobile Medical Apps that have been cleared by the FDA.

Mobile Technology & Health

- Few apps with evidence-based studies to demonstrate
  - Effectiveness and outcomes
  - Safety
  - Application of clinical, behavioral, and user interface expertise
  - Workflow and practice integration into the current health care delivery system
- Patients are challenged to find and use technology resources for diabetes self-management

Nilsen, et al. News from NIH. TBM

What's your Favorite Health & Fitness App?

What About Social Media & Diabetes?

Consumers Have Many Choices

Diabetes Online Community Fact Sheet

https://www.diabeteseducator.org/patient-resources/tip-sheets-and-handouts

“Deepening dependency on technology raises risk of breakdowns”

- “Technology has become so indispensable that when it breaks down, people’s lives go haywire, too.”
- Technology already controls critical systems, e.g., airline route, electricity grids, financial markets, military weapons, commuter trains, street traffic lights and our lines of communications

By MICHAEL LIEDTKE and BARBARA ORTUTAY Associated Press/fi:/csp/mediapool/sites/Shared/assets/csp/helper/getByline.csp, e:.001028 Thursday, July 9, 2015

In Summary…

- Technology is gaining strides in diabetes care and education
- Technology choices makes life “fun and challenging”
- Cost of health care keep rising with hopes that technology will offer new ways to deliver cost effective care
- Technology is our bridge to a cure for diabetes

Thank you …