Continuous Glucose Monitoring: The Future of Diabetes Care

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Diabetes TeleHealth Series

Objectives

- Understand the principles of continuous glucose monitoring including indications, benefits and limitations thereof.
- Recognize the differences between currently available CGM systems.
- Review key uses of CGM data including real-time trending, retrospective trending, high and low alerts.
- Briefly discuss the future of continuous glucose monitoring.

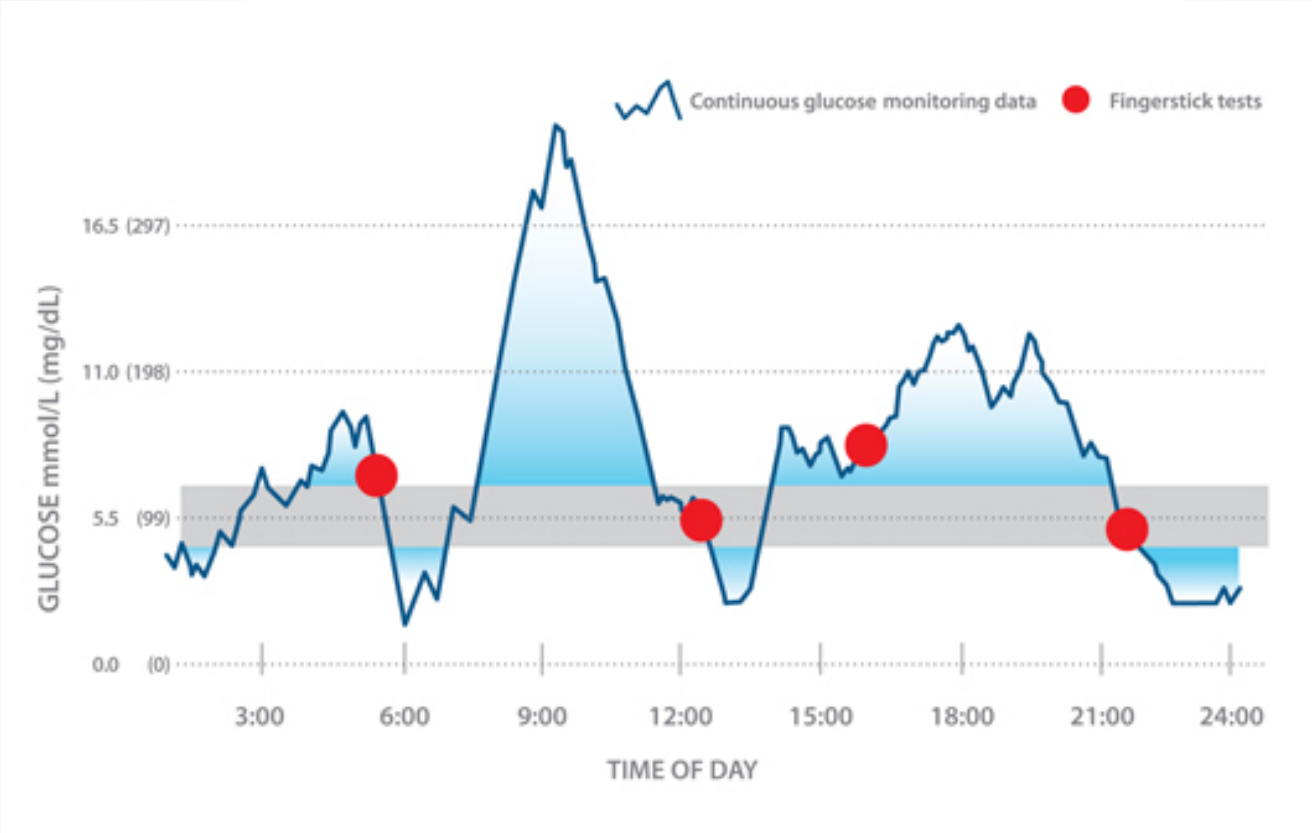
Introduction

- Diabetes mellitus is associated with long-term complications.
- Most glycemic control in patients with type 1 diabetes is suboptimal.
- Glycemic control is limited by poor adherence to prescribed regimens.
- Adherence is limited, in part, by fear of hypoglycemia.
- Recent evidence links severe hypoglycemia to morbidity and mortality.

Current Metrics for Diabetes Control

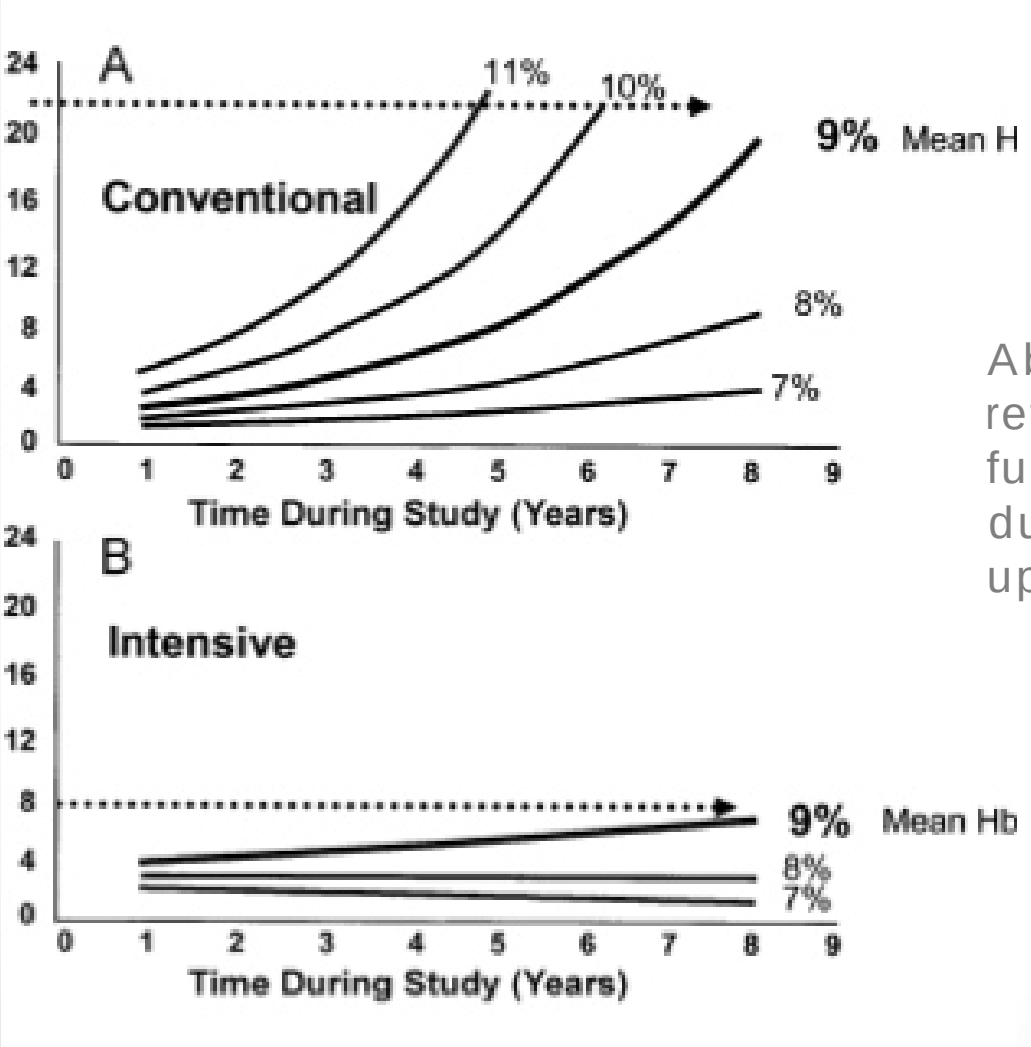
- DCCT established HbA1c as gold standard evaluating for glycemic control.
- Self monitored blood glucose (SMBG) protocols vary.
- Blood glucose measured during in-house study-day typically involves 10-24 measurements.
- Frequency of hypoglycemic events is analyzed using study criteria with pre-defined thresholds and patient reports.

Limitations of Current Metrics



- HbA1c reflects mean blood glucose for preceding 120 days.
- SMBG often misses peak post-prandial glucose.
- Self-report and SMBG data unreliable for hypoglycemia.

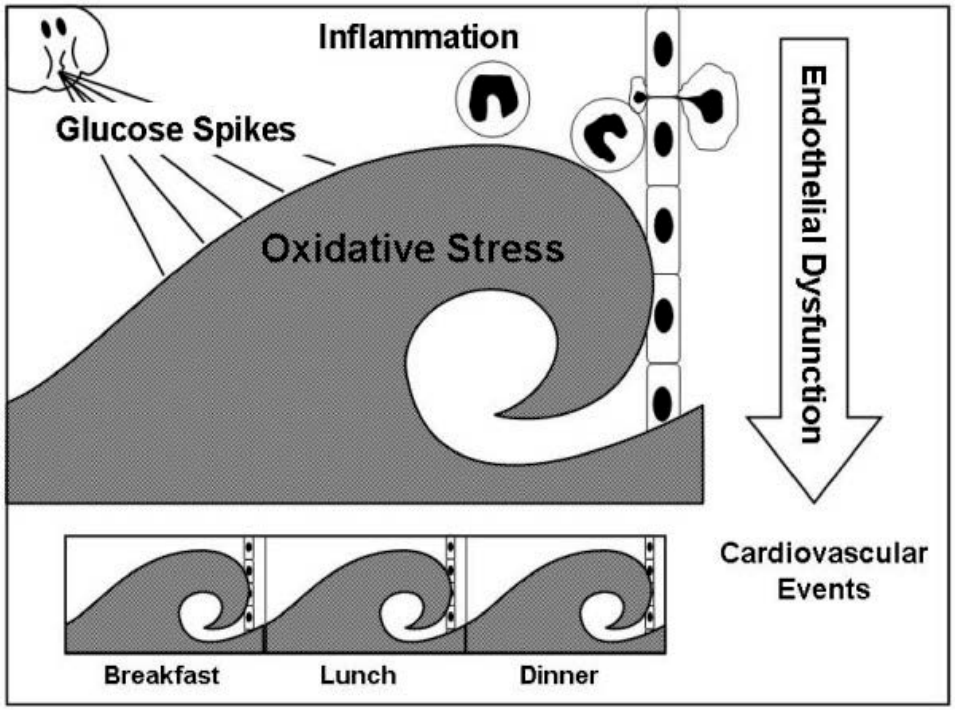
DCCT Observation



Absolute risk of sustained retinopathy progression as function of updated mean A1c during DCCT and time of follow-up during study years.

The Diabetes Control and Complications Trial (DCCT) Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. *Diabetes*, 1995; 44: 968-983[1].

Glycemic Variability

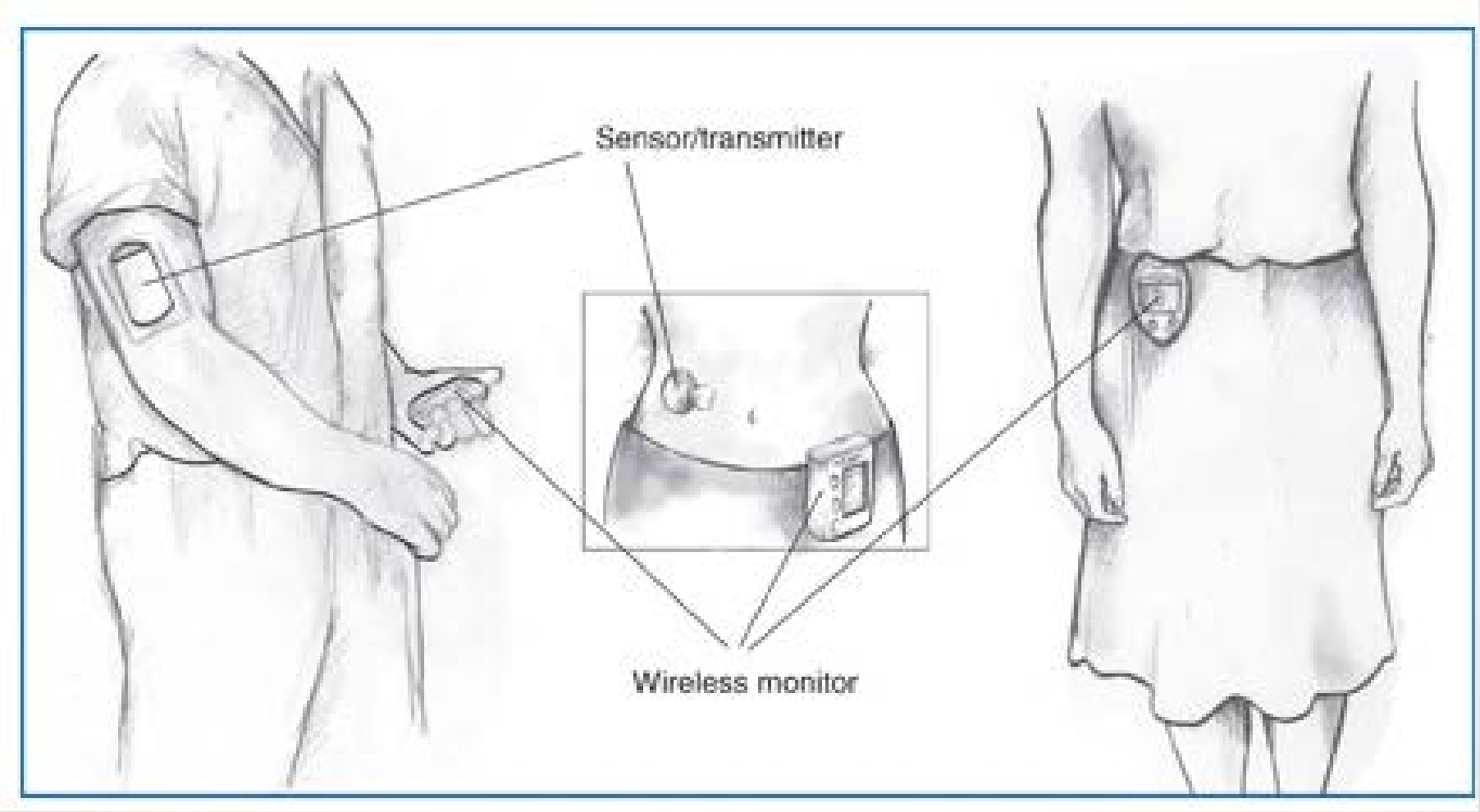


- DCCT illustrated importance of relative glycemic control to prevent microvascular complications
- Some data at that time suggested deleterious effects of glycemic variability
- Pathophysiologic data indicates increased oxidative stress with fluctuating glucose levels
- Epidemiologic studies suggest correlation between elevated PPG and micro/macrovascular outcomes
- Clinical trial data is limited

OVERVIEW: CGM

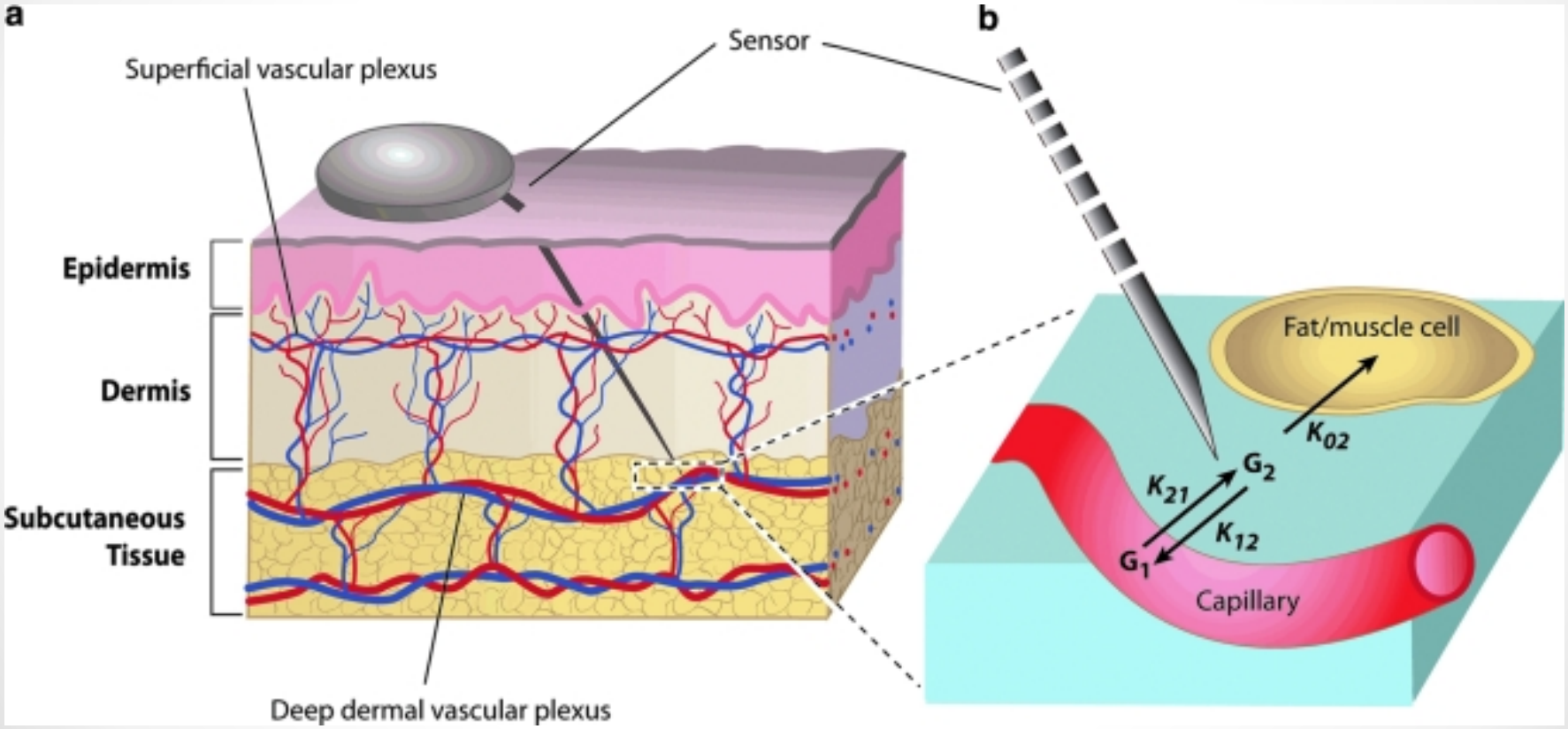
- Continuous Glucose Monitor = device that provides “real-time” glucose readings & data about trends in glucose levels
- Measures interstitial glucose every 5 minutes
- Alerts user to high and low glucose values
  - Also predicted “highs” and “lows”
  - Rate changes
- 4th era in diabetes management

CGM Components

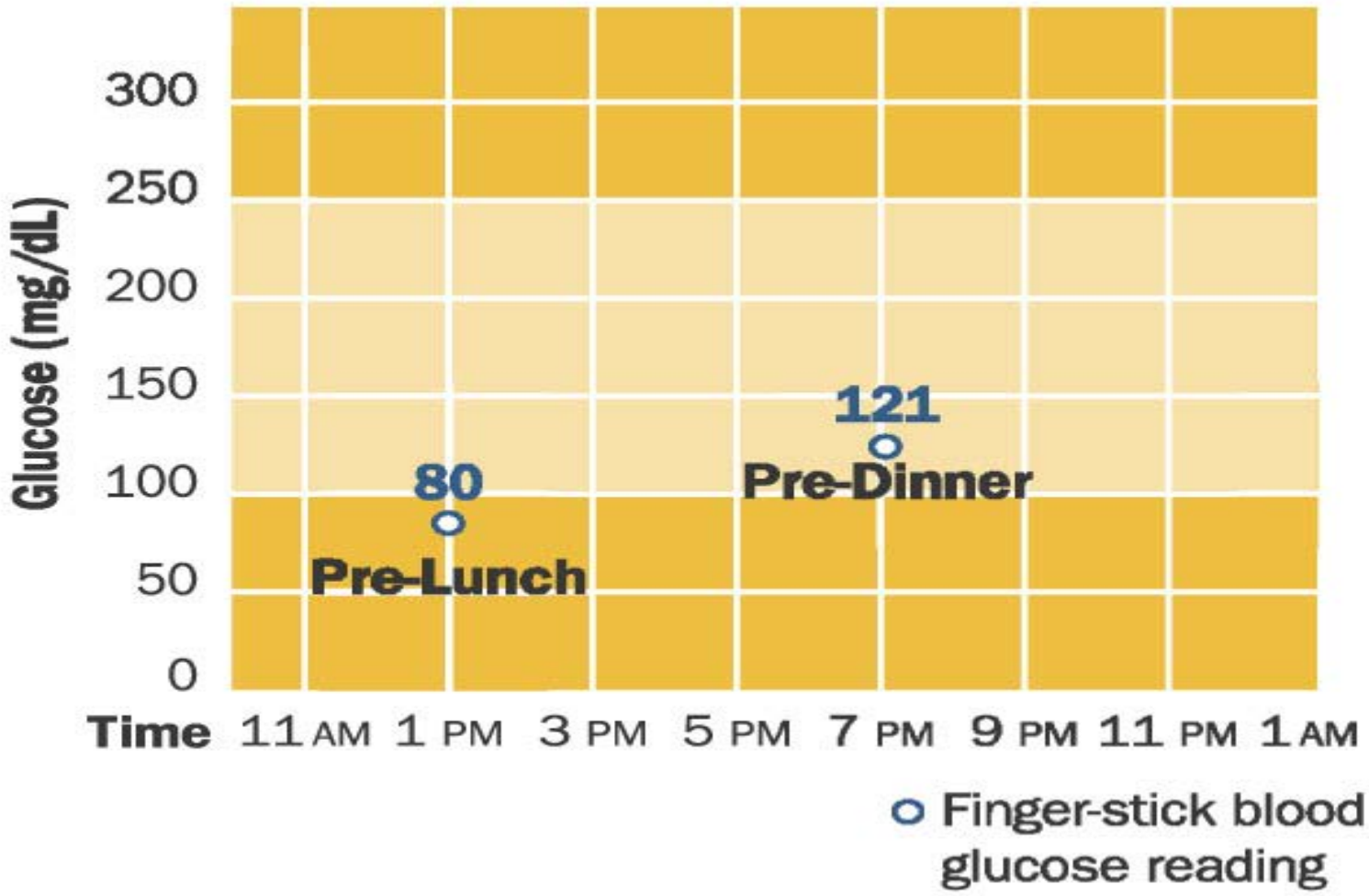


- http://diabetes.niddk.nih.gov/dm/pubs/glucosemonitor/

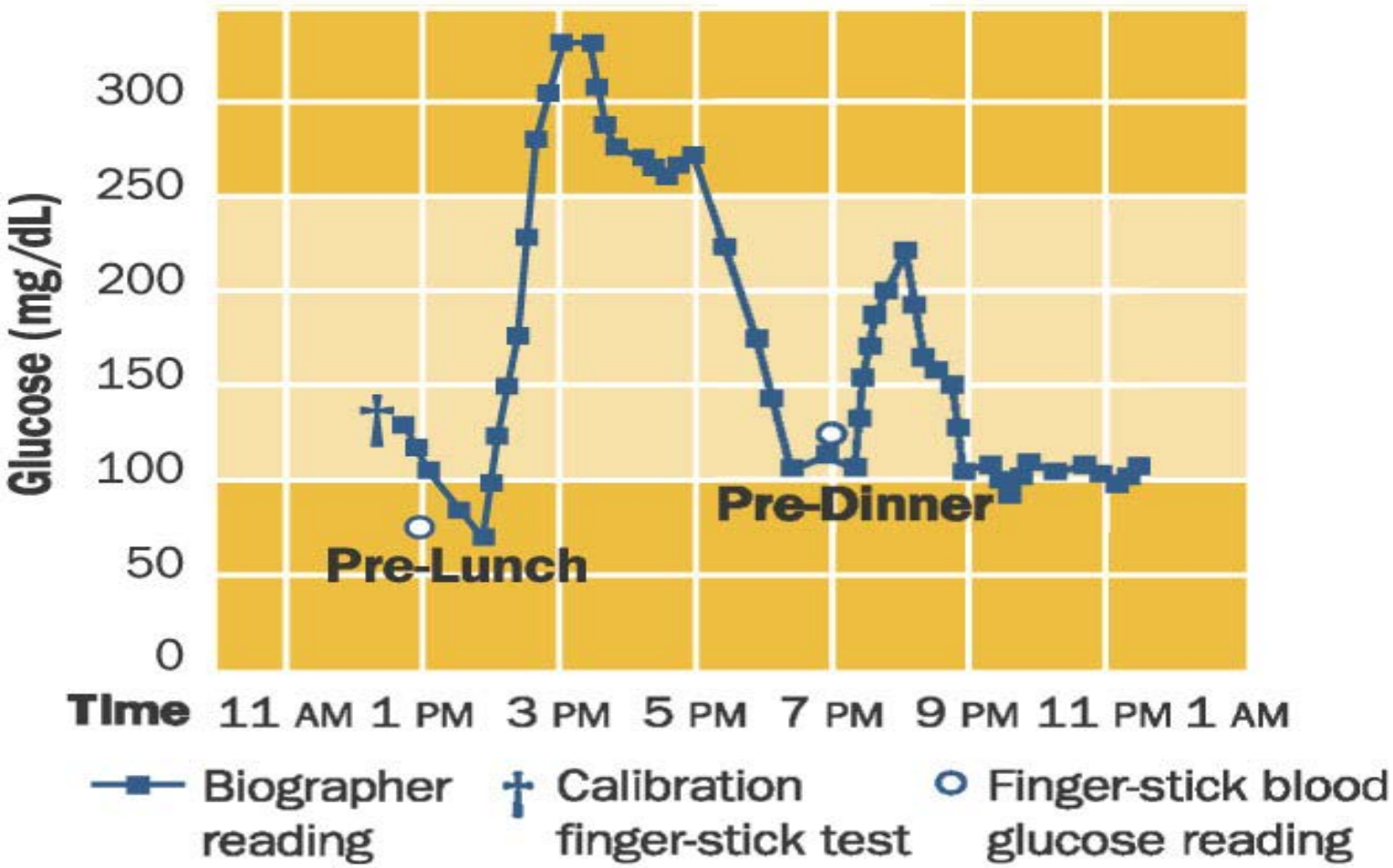
CGM: Subcutaneous Sensor



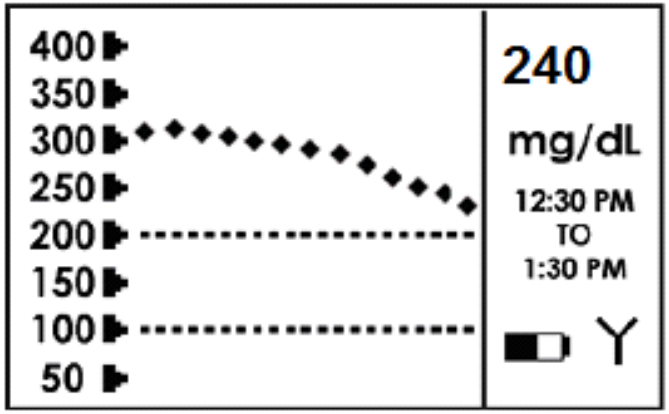
Fingerstick "Snapshot" of BG

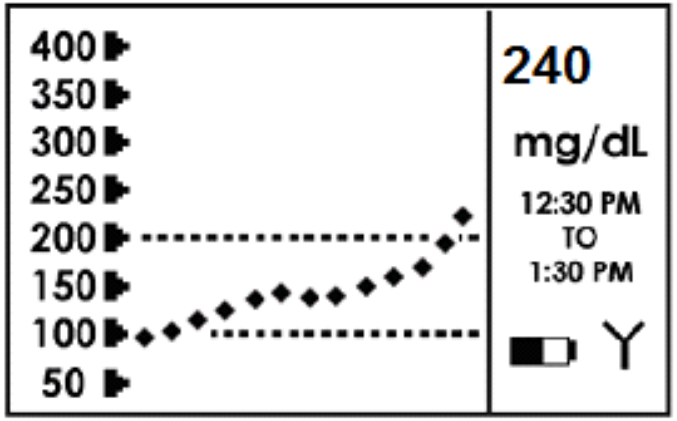


CGM "Full Disclosure" of BG Trends



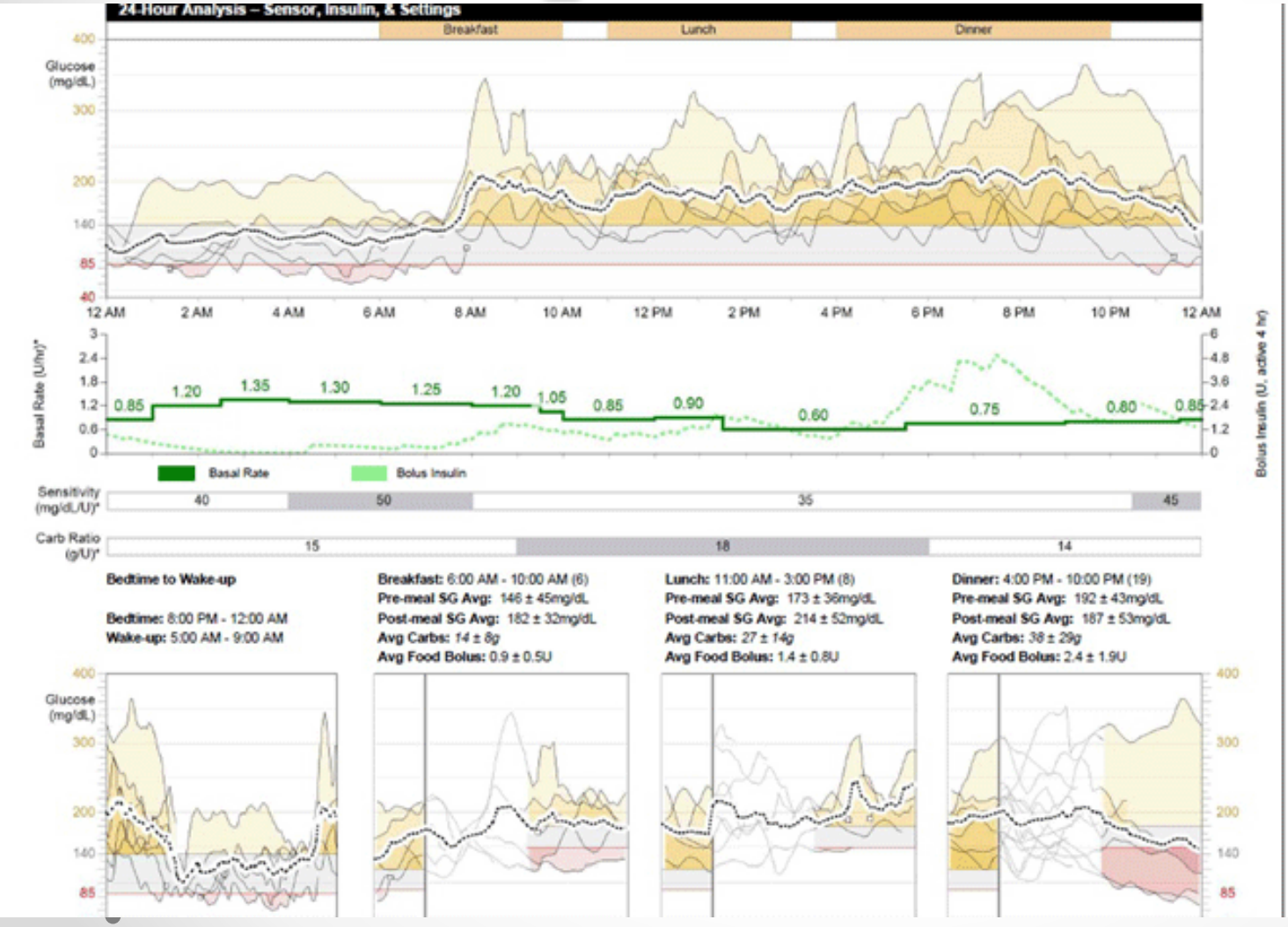
Types of Data: Real Time Trending





*(Understanding Pumps and CGMs, p.103)

Types of Data: Retrospective Trending



Statistics	
Avg BG	169 ± 68mg/dL
Estimated A1C	7.5%
BG Readings	13.3 per day
Carbs Entered	156± 51g per day

Hypoglycemic Patterns (3)	
	3:33 AM-7:49 AM (3)
Time Period	1:04 AM-2:19 AM (1)
	10:34 PM-11:44 PM (1)

Hyperglycemic Patterns (1)	
	7:40 AM-11:50 PM
Time Period	

Pump Use	Per Day
Insulin TDD	37.9 ± 4.4U
Basal/Bolus Ratio	55 / 45
Manual Boluses	0.3U (0.7 boluses)
Bolus Wizard	16.6U (10.2 boluses)
Food	9.5U (5.7 boluses)
Correction	14.5U (5.8 boluses)
Override (+)	0.3U (0.7 boluses)
Override (-)	-1.4U (0.7 boluses)
Suspend Duration	22m per day
Res./Site Change	Every 2.0 / 2.0 days

Sensor Use	
Avg SG	168 ± 58 mg/dL
Wear Duration	6d 15h per week
Low SG Alarms	5.8 per day

CGM: Short-Term Benefits

- Minimize extreme BG
- Immediate feedback impact of food/exercise/stress on BG
- Know direction BG is trending (whether pt needs more or less insulin)
- Adds meaning to fingersticks

Blinded vs Nonblinded CGM Tracings

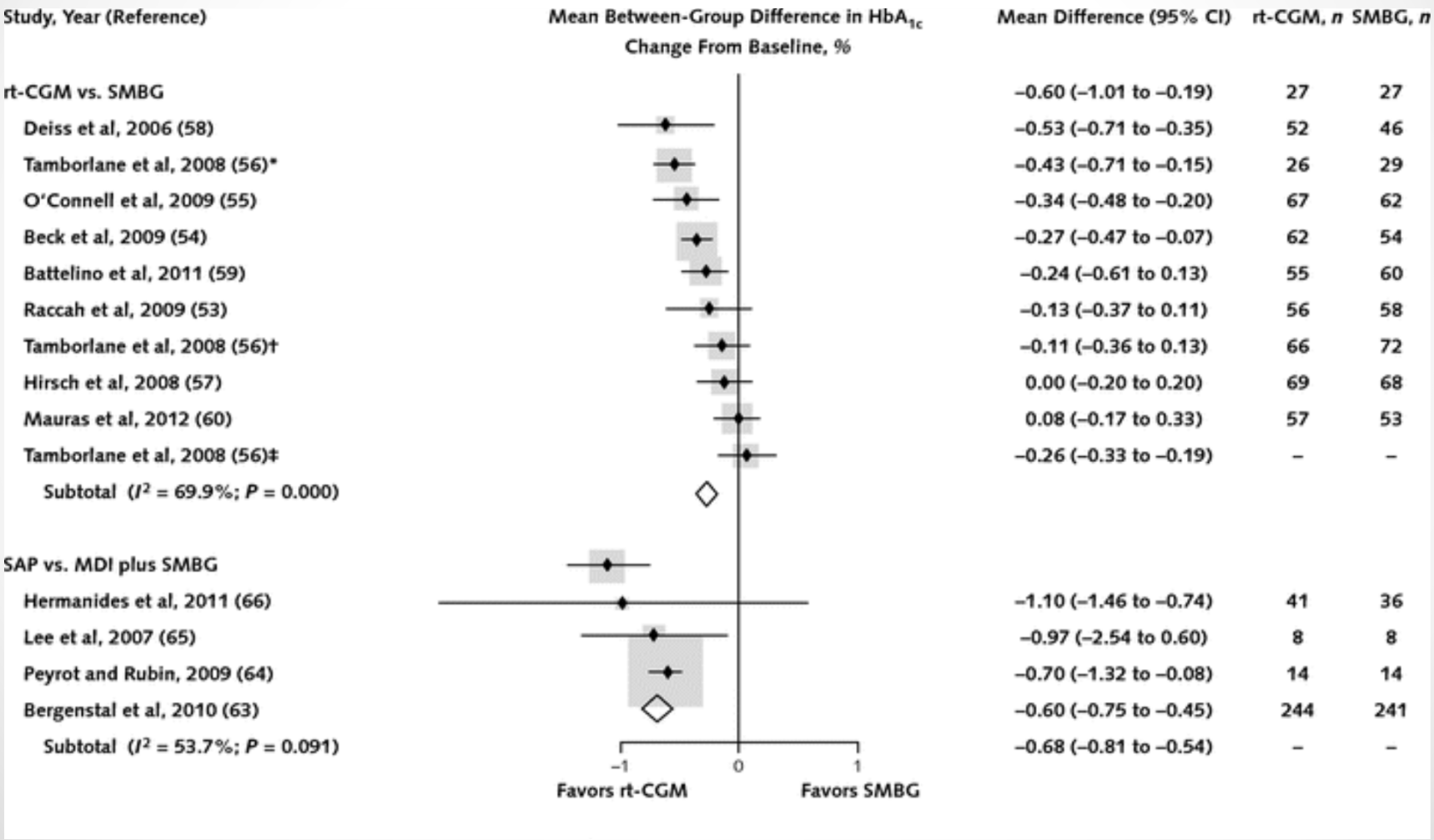
	p-value
• 21% less time <55 mg/dl	<0.001
• 23% less time >240 mg/dl	<0.001
• 26% more time in target	<0.001
• (81 – 140 mg/dl)	

•(Garg et al, Diabetes Care 27:1922,2004)

CGM: Long-Term Benefits

- Reduce HbA1c
- Identify patterns
- Test and fine-tune basal, ISF, and I:C
- Improve hypoglycemia unawareness

HbA1c: Comparing CGM with SMBG and SAP



Ann Intern Med. 2012;157(5):336-347. doi:10.7326/0003-4819-157-5-201209040-00508

From: Comparative Effectiveness and Safety of Methods of Insulin Delivery and Glucose Monitoring for Diabetes Mellitus: A Systematic Review and Meta-analysis

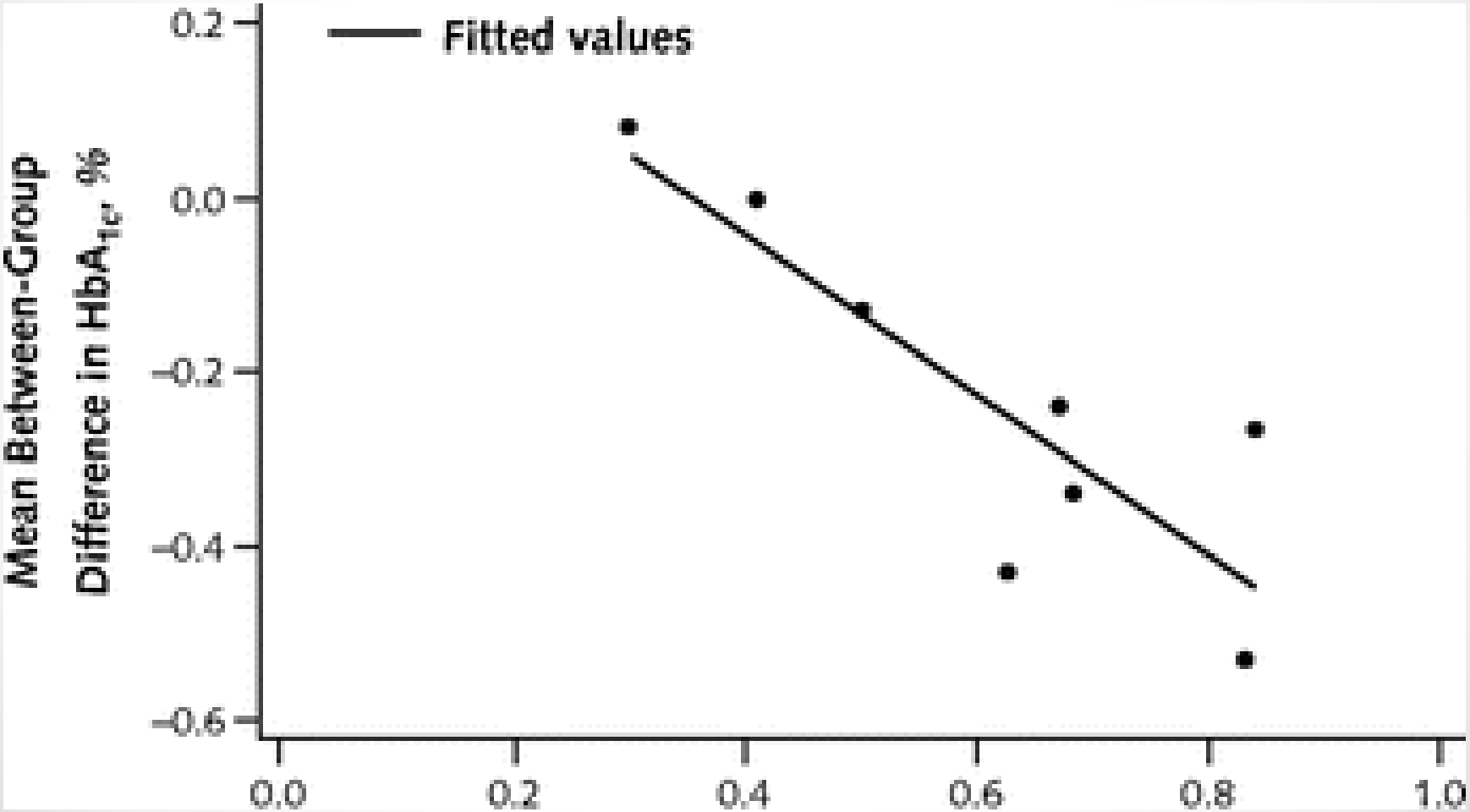
Table 2. **Summary of the Subgroup Analyses in the Between-Group Change From Baseline HbA_{1c} Among Patients With T1DM Comparing rt-CGM with SMBG**

Analysis	Studies Included (Participants Included), *n (n)*	Mean Difference in HbA_{1c} (95% CI), %	I^2, %
All studies*	8 (1066)†	−0.26 (−0.33 to −0.19)	66.6
Adults ≥18 y‡	3 (312)§	−0.38 (−0.53 to −0.23)	77.3
Children <18 y‖	5 (434)¶	−0.13 (−0.27 to 0.01)	46.0
Adherence >60%	7 (705)**	−0.36 (−0.44 to −0.27)	40.8

HbA_{1c} = hemoglobin A_{1c}; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose; T1DM = type 1 diabetes mellitus.
* Three studies (53–55) reported results combining all age groups.
† References 53 to 60.
‡ Only patients aged >25 y in reference 56 were included in this subgroup analysis.
§ References 56, 57, and 59.
‖ Only patients aged <15 y in reference 56 were included in this subgroup analysis.
¶ References 56 to 60.
** References 53 to 59.

Ann Intern Med. 2012;157(5):336-347. doi:10.7326/0003-4819-157-5-201209040-00508

Sensor Adherence and Difference in HbA1c Between rt-CGM and SMBG



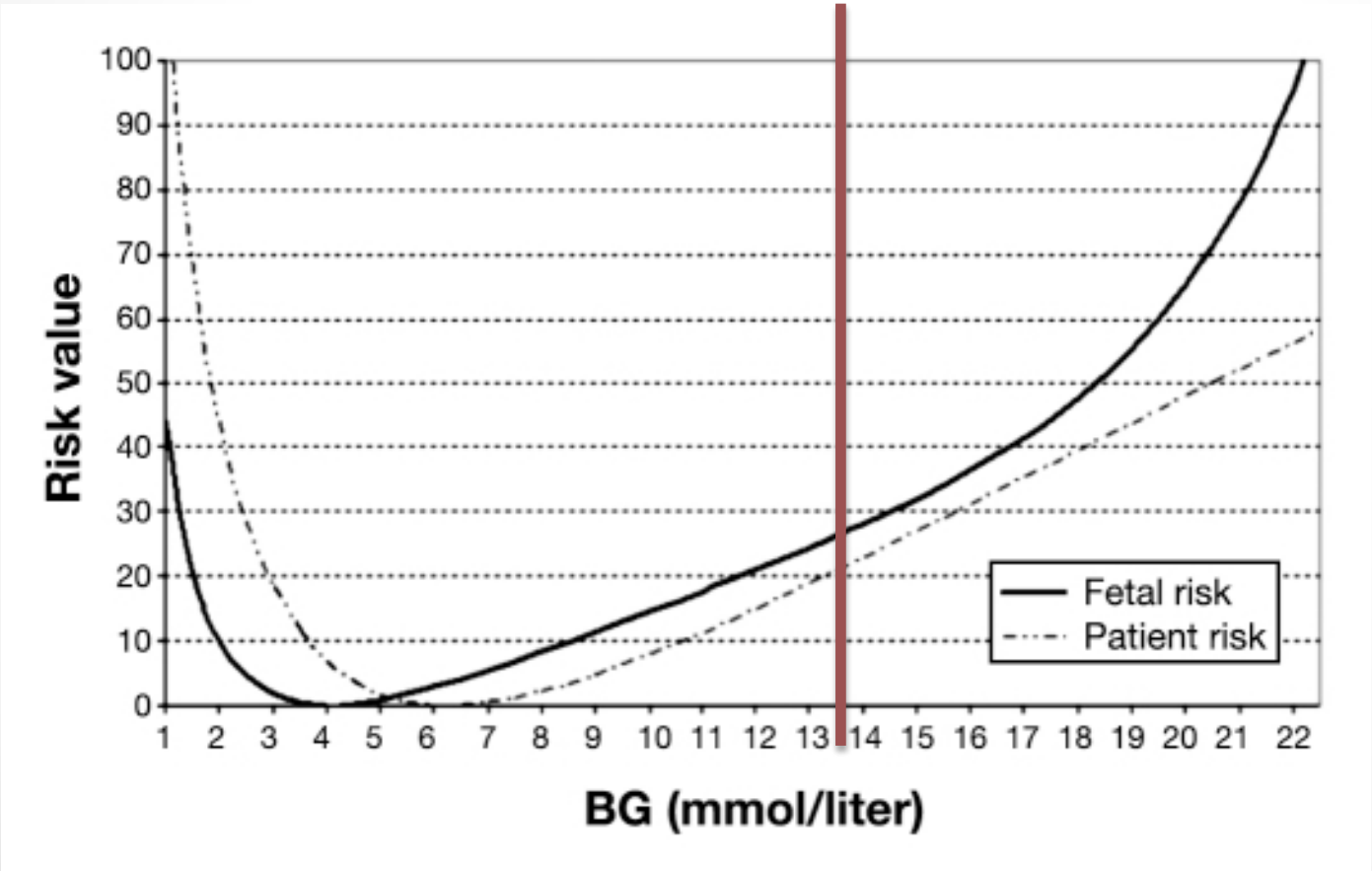
Ann Intern Med. 2012;157(5):336-347. doi:10.7326/0003-4819-157-5-201209040-00508

CGM in Pediatrics: Consensus Statement

- RT-CGM: effective for lowering HbA1c, reaching target HbA1c and reducing MAGE without increased frequency of severe hypoglycemia
- RT-CGM: Effective for reducing severe hypoglycemia & reducing time spent in hypoglycemic range.
- Effectiveness of RT-CGM in pediatric population with T1D significantly related to amount of sensor use.
- SAP effective means to treat youth of all ages at onset of disease
- SAP effective in lowering HbA1c among those with elevated HbA1c on MDI with SMBG
- Intermittent, retrospective or real-time CGM can be used to detect dawn phenomenon, post-prandial hyperglycemia, asymptomatic & nocturnal hypoglycemia & evaluating effects of changes in treatment.

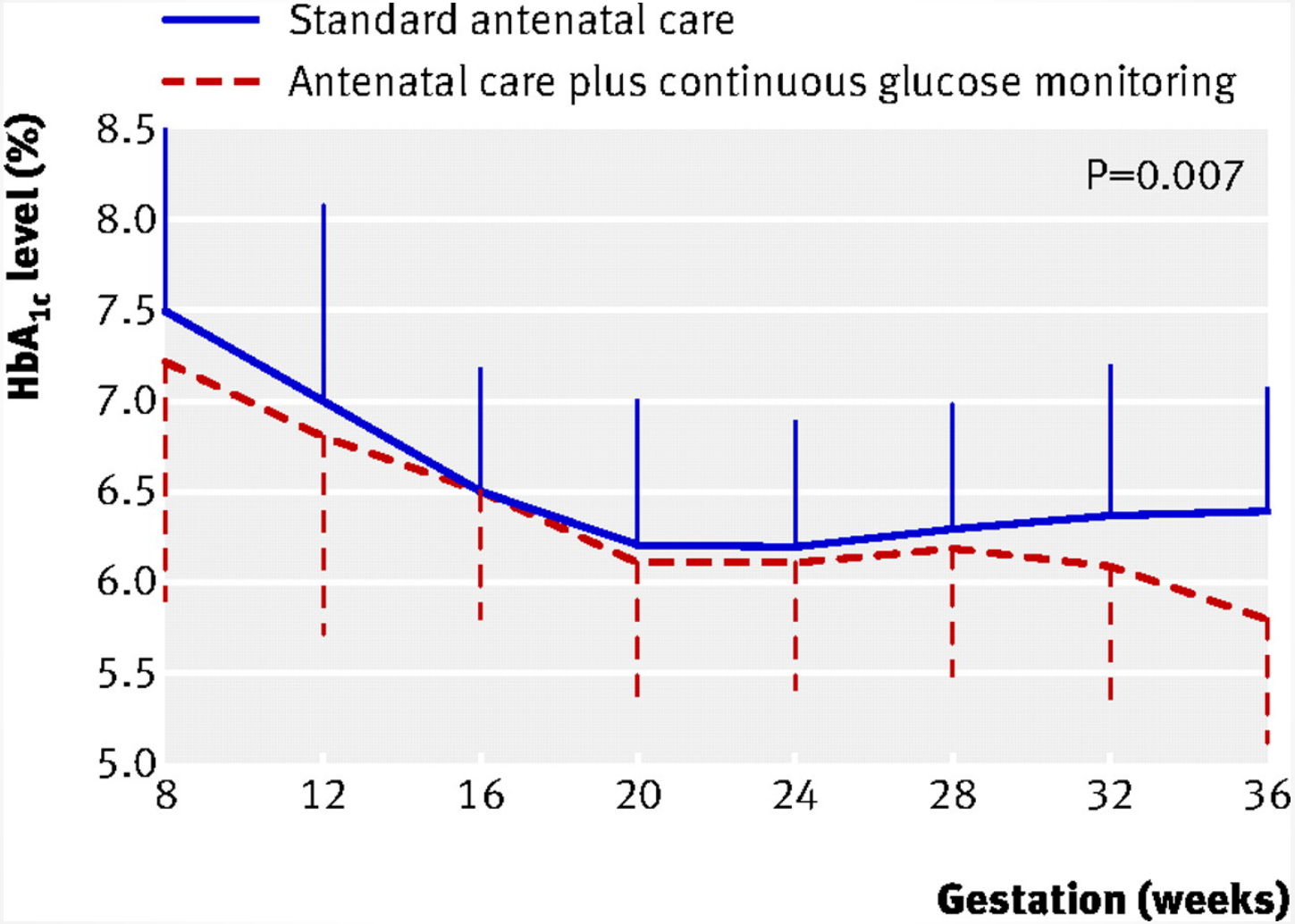
CGM in Pregnancy

Comparison of risk transform functions



- J Diabetes Sci Technol. 2010 November; 4(6): 1368–1373. Published online 2010 November 1.

Mean HbA1c levels every four weeks in women receiving standard antenatal care (n=33) or antenatal care plus continuous glucose monitoring (n=38).



Murphy H R et al. BMJ 2008;337:bmj.a1680

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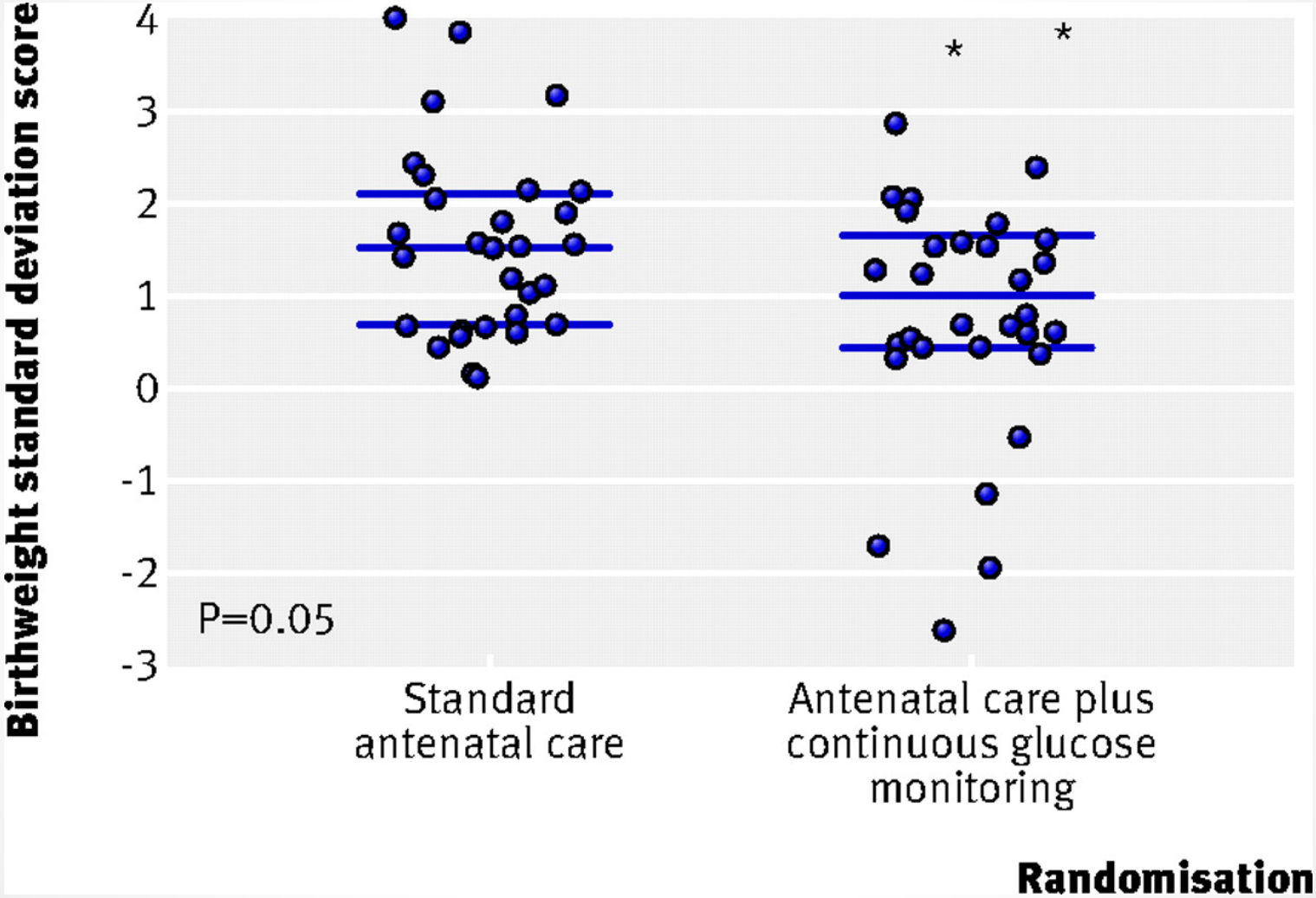
Distribution of birthweight standard deviation scores for 62 healthy living singletons of mothers in continuous glucose monitoring arm (n=32) or standard antenatal care arm (n=30). *Infants of mothers who withdrew from intervention arm (included in intention to treat analysis).



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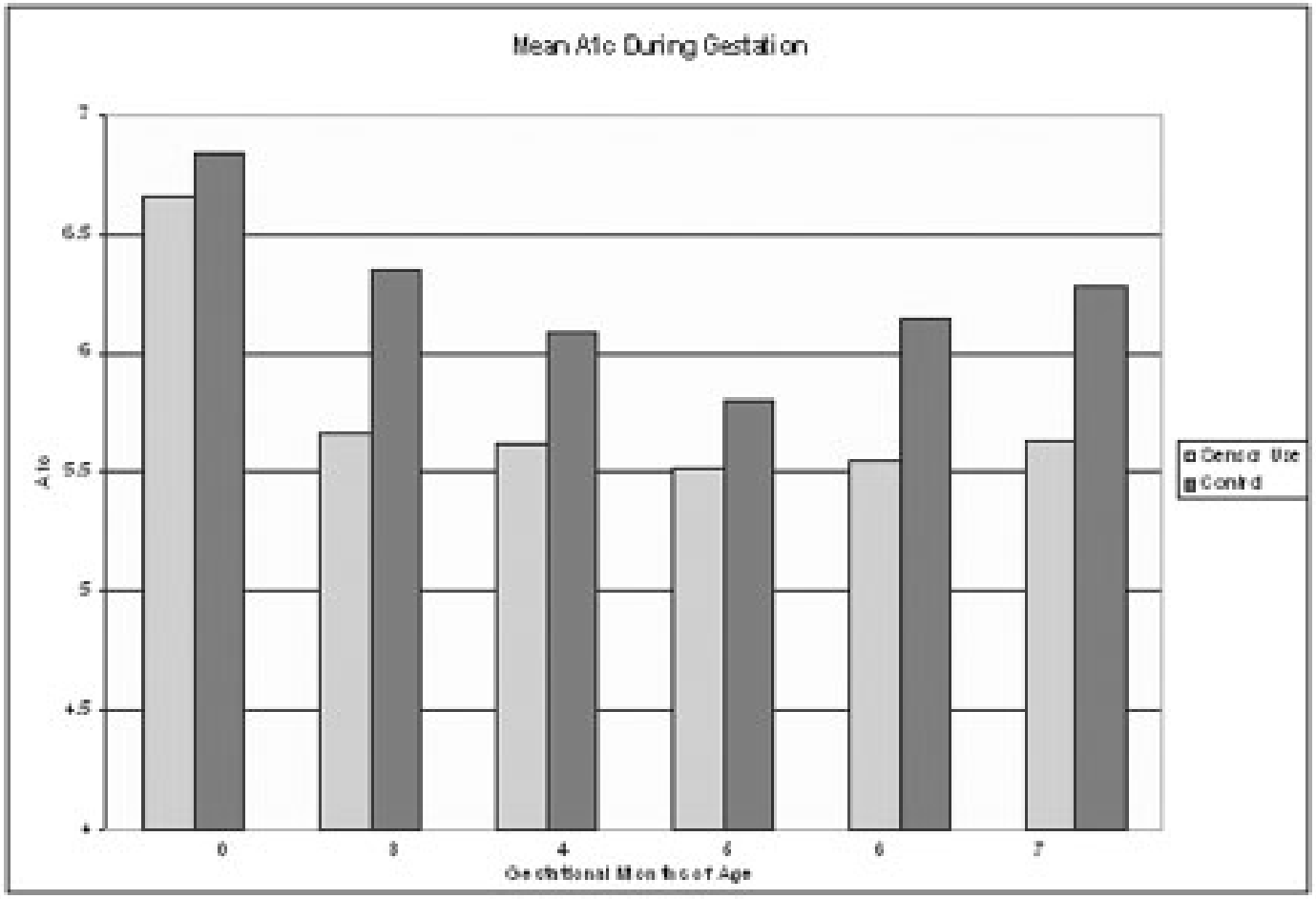
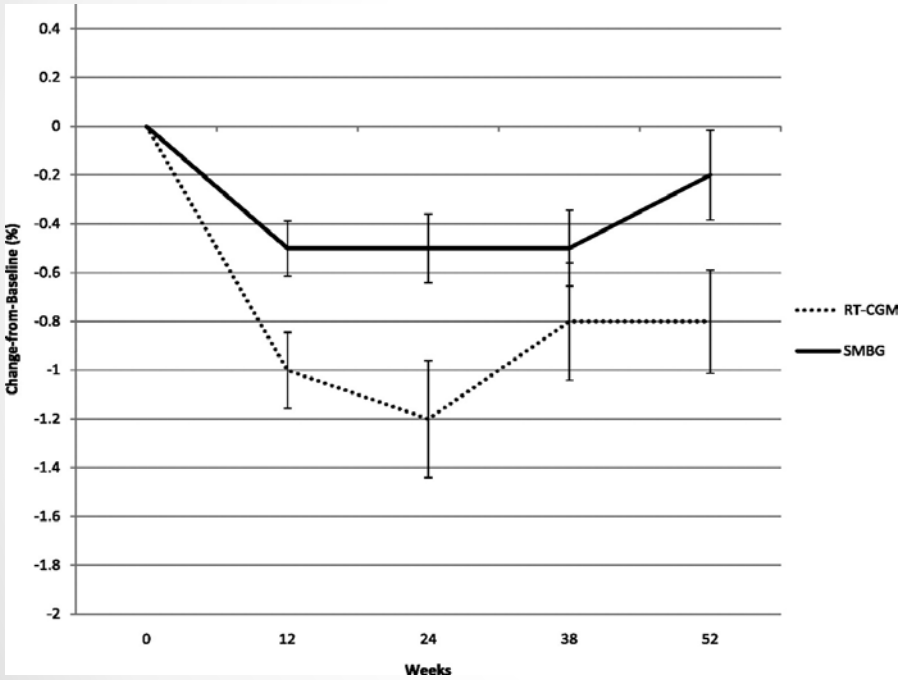
RT-CGM in Pregnancy



Copied from *Voelmle MA, Gottliebe P, Ellis S, Wallace A & Gerard L. 2007. DiabetesPro Abstract # 0440-P.*

CGM in Type 2 Diabetes

Change in HbA1c from Baseline



- Adults with type 2 diabetes NOT on prandial insulin had A1c decrease (mean – 1.16% over a year) with RT-CGM used intermittently for 12 weeks.
- CGM tracings can prompt changes in lifestyle or adherence to medications moreso than SMBG

Vigersky R A et al. Dia Care 2012;35:32-38

CGM: Indications

CGM: Indications

- Those with type 1 diabetes and …
  - Hypoglycemic unawareness/frequent hypoglycemia "judged to be excessive, potentially disabling or life-threatening"
  - Excess glycemic variability
  - Requiring HbA1c reduction without increased hypoglycemia
  - Preconception and pregnancy
- Children and adolescents with HbA1c <7% (highly motivated patient and family)
- Youth with HbA1c >7% who will use it on a near-daily basis

CGM: Indications (cont)

- Good candidates but trial for 2-4 weeks recommended
  - Youth with frequent SMBG
  - Committed families of young children (<8 years), especially if problems with hypoglycemia.

CGM: Available Options

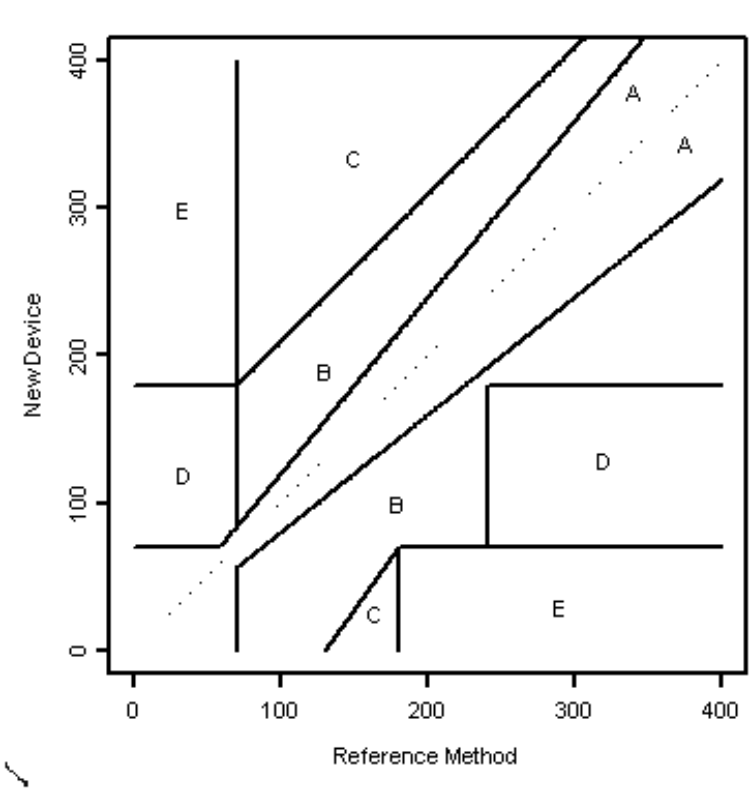
Medtronic Guardian® Real-time

- Integrated with MiniMed Paradigm® Revel insulin pump
- Predictive alerts
- FDA approved for children
- FDA approved for 3 day use
- Data downloadable to online program with detailed analysis & excellent graphics
- Accuracy: MARD = 20%
- Introducer needle: 22 gauge
- Lag time 10-20 minutes
- Data withheld if miss calibration
- Must calibrate when blood glucose is stable

Dexcom G4™Platinum

- Can be worn with any therapy
- Can input insulin, activity, illness
- Customizable alerts (including high-volume)
- FDA approved for 7 days
- Data downloadable to software with detailed analysis and graphic
- Accuracy: MARD = 13%
- Introducer needle 26 gauge
- Lag time 5-10 minutes
- Can calibrate regardless of rate o change
- Acetaminophen falsely elevates readings
- Plans for integration with: Animas (Vibe), Tandem etc.

Differences Between Systems



	MARD	% in Clark A
SMBG	10-15%	
Dexcom Seven Plus™	15.9%	69%
Dexcom G4™	14%	78%
Medtronic Paradigm®	19.7%	61.7%

Using CGM Data in Patient Care

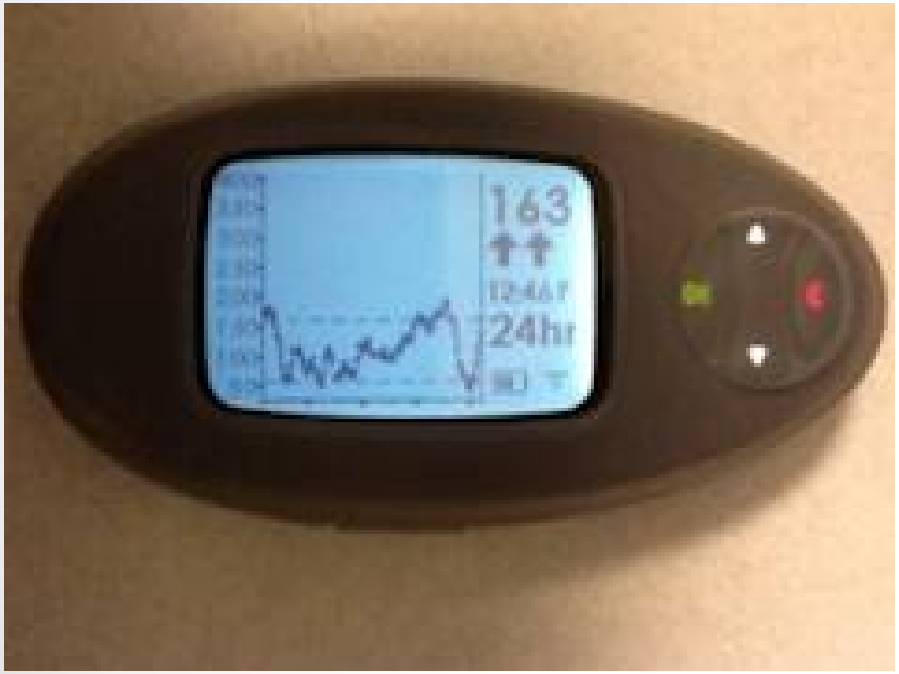
Using CGM Info

- Download review:
  - Basal check
  - Insulin:carb check
  - Correction factor check
  - Trending
- Real-time data:
  - Adjust correction factor and I:C for hyper- and hypoglycemia
  - Glucose if dropping
  - “Stay between the lines”

Downtrending Blood Glucose

- Predictive hypo or 1 arrow down and stabilizing:
  - Less treatment
    - Less than usual carbs for correction
    - Medium GI food
    - Decrease bolus 10%
- Hypo alert or rapid drop (2 arrows down):
  - Aggressive treatment:
    - High GI food
    - Full or increased carbs
    - Decrease bolus 20%

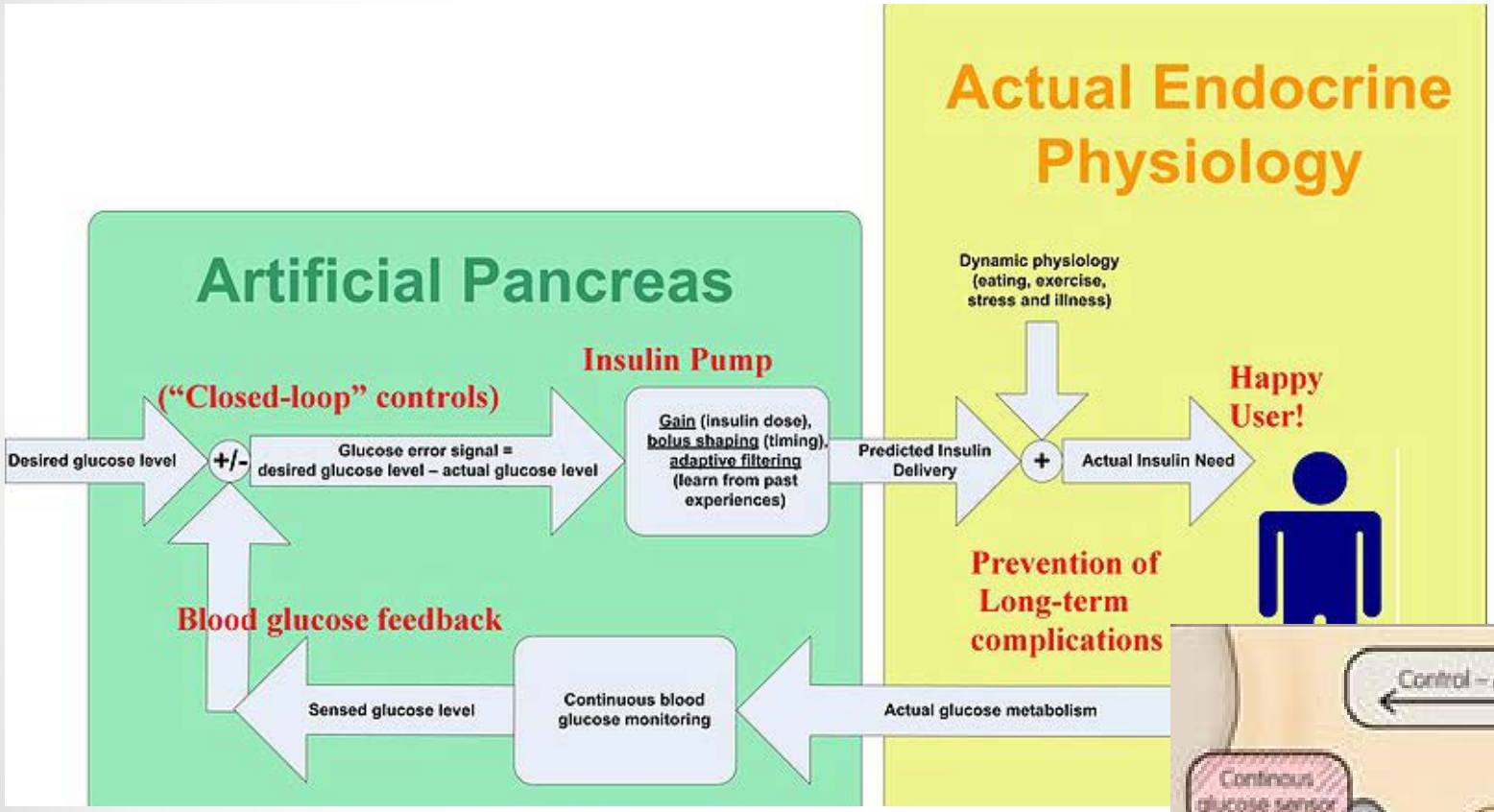
Uptrending Blood Glucose

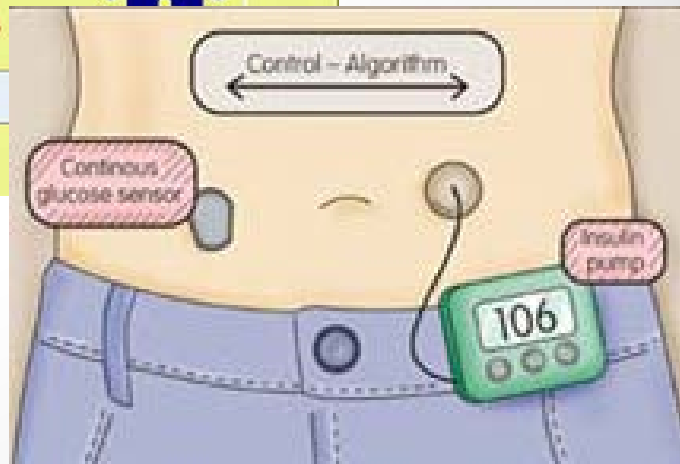


- BG stable – flat
  - Usual I:C + ISF
- BG rising gradually (1 arrow up)
  - Increase bolus 10%
- BG rising sharply (2 arrows up)
  - Increase bolus 20%

Future of CGM

Combined Technologies → Artificial Pancreas

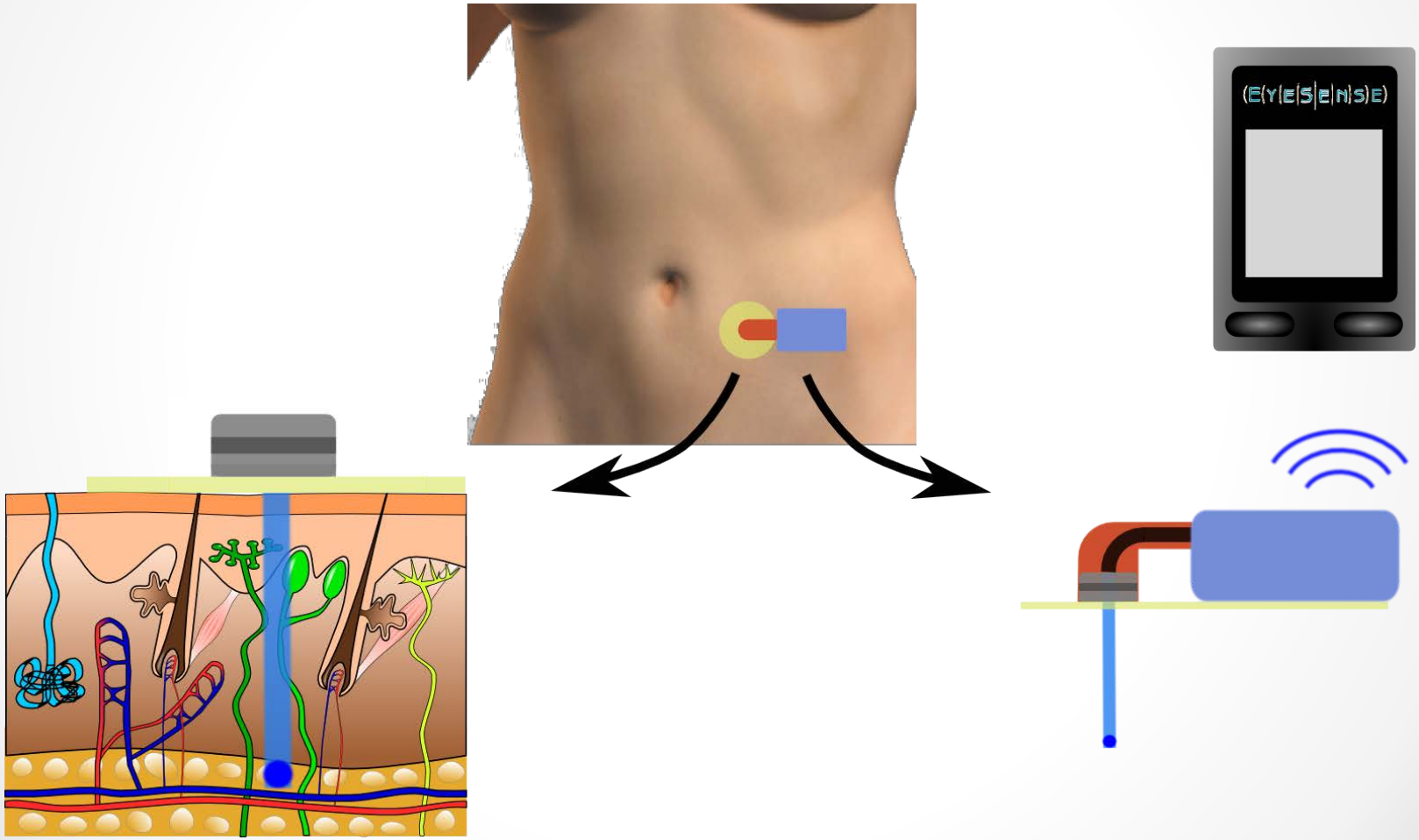




Multiple Studies

- Multiple Groups
  - JDRF
  - Helmsley Trust
  - Government funding bodies
  - Medical device companies
  - Independent research groups
- Variations: CGM +
  - Insulin + glucagon
  - Insulin + pramlintide
  - Insulin + Heat patch

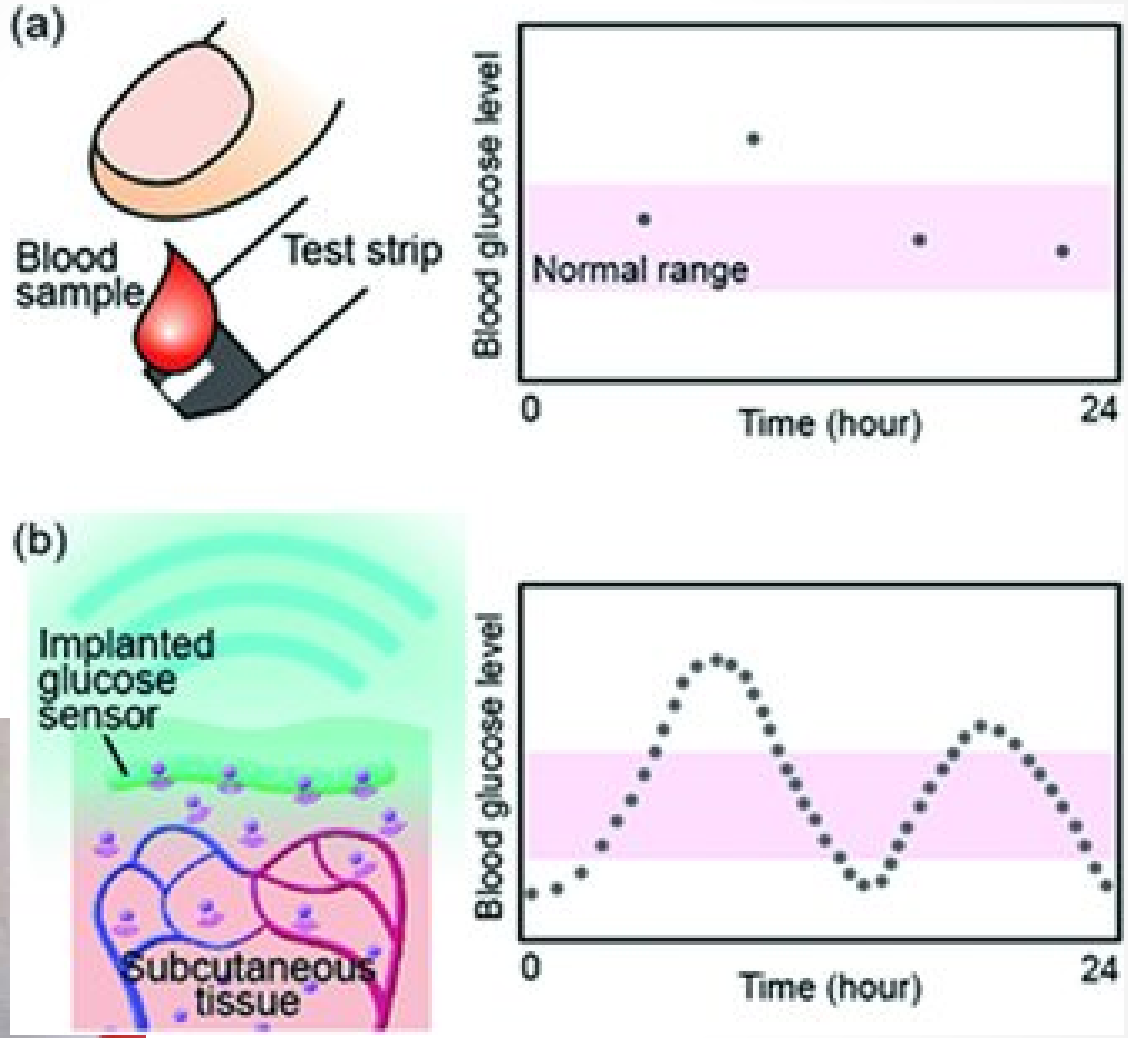
Fiber-Optic Sensors



http://www.eyesense.com/en/konzept_fiber.htm

"Smart" Tattoos

From: http://www.diabetesmine.com/2011/08/the-tiny-tattoo-that-could-monitor-blood-sugar-in-florescent-light.html



From Techdigitt Technology News. Michaelraj AM. Jan 30, 2013

Advanced Healthcare Materials
Volume 2, Issue 1, pages 43-56, 26 NOV 2012 DOI: 10.1002/adhm.201200167

Eye Sensor

http://www.eyesense.com/en/results_eye.htm

Functional Contact Lens

http://www.research.microsof.com/en-us/collaboration/stories/functionalcontactlens.aspx

Conclusions

- Diabetes is associated with long-term complications caused by "dysglycemia."
- Adequately controlling blood glucose values without increasing the risk of hypoglycemia is difficult.
- Continuous glucose monitoring can help patients and their health care providers to optimize their diabetes regimen while limiting hypoglycemia.
- Current CGM systems use subcutaneous sensors that measure interstitial glucose electrochemically.
- Alternative approaches to continuous glucose monitoring are in development.
- Prediction: continuous glucose monitoring will be the standard of care.

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Questions?