

Emerging Technologies

Bolus Calculators, Pumps And CGMs



Children With Diabetes
Orlando, FL
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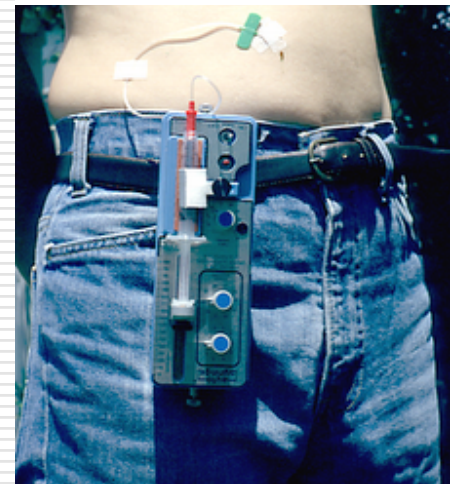
View slides at www.diabetesnet.com/presentations/

Disclosure

- Book sales – all pump companies
 - Advisory Boards – Tandem Diabetes, Unomedical, Spring, Halozyme
 - Consultant – Bayer, Roche, BD, Abbott, Tandem Diabetes, Medingo, Spring
 - Speakers Bureau – Tandem Diabetes
 - Sub-Investigator – Glaxo Smith Kline, Animus, Sanofi-Aventis, Bayer, Bidel, Dexcom, Novo Nordisk
 - Pump Trainer – Accu-Chek, Animas, Medtronic, Omnipod
 - Web Advertising – Sanofi-Aventis, Sooil, Medtronic, Animas, Accu-Chek, Abbott, etc.
-

What We'll Cover

- Bolus Calculators
- New Pumps
- CGMs
- Pump/CGM Combos
- Closed Loop
- Future Pump Features



Terms

- **TDD** – total daily dose (all basals and boluses) of insulin
 - **Basal** –background insulin released slowly through the day
 - **Bolus** – a quick release of insulin
 - Carb bolus – covers carbs
 - Correction bolus – lowers high readings that arise from deficits in basal rates or carb boluses
 - **Bolus Calculator (BC)** – calculates bolus recommendations
 - **Bolus On Board (BOB)** – bolus insulin still active from recent boluses, active insulin, insulin on board
 - **Duration of Insulin Action (DIA)** – how long a bolus will lower the BG – used to measure BOB
-

Bolus Calculator (BC)

Part of pump that gives bolus recommendation

Provides the “smarts” in smart pumps

First appeared in 2003 in Cosmo pump

Now appearing in meters, iPhones, apps, ???

Bolus Calculators

- Software recommends carb and correction boluses
- Settings: CarbF, CorrF, Corr target, DIA
- Tracking of BOB helps prevent insulin stacking
- Current BG is needed to measure BOB
- Accurate carb counts and BG values are needed
- Tracks and stores history

Unfortunately, no two BCs work the same way

Meter With Bolus Calculator – Abbott Freestyle InsuLinx



- Stores readings, bolus rec., meal markers, and carbs
- Touch screen
- Tracks BOB
 - Boluses can be entered retroactively
- Only 1 unit increments (injections)
- USB download, Windows or Mac
- FreeStyle Auto-Assist software

CE approved in Europe

BC Or Meter Via Phone



- In future, meter or pump controller may communicate with smart phone
 - No bolus calculator or pump control on phone itself
 - Wireless Bluetooth or cable interface
 - Not currently possible to use phone as medical device
-

BC or Meter in iPhone – Agamatrix



- Small meter attaches to iPhone
- Track blood glucose, carb intake and insulin dose
- Share BG data immediately with direct phone or internet access
- Agamatrix, Sanofi-Aventis, Apple
- Also: Wavesense Bolus Calc.

Submitted for CE approval

New Insulin Pumps

Remote Controls



- Meter sends BG to pump
- Bolusing from meter/PDA lets pump stay hidden
- Carb bolus, correction bolus, basal remotely controlled by meter/PDA
- Accurate, complete history
- Omnipod control must be present to bolus



Bolus and basal adjustments in Accu-Chek Combo (CE approved)

New Line Pumps



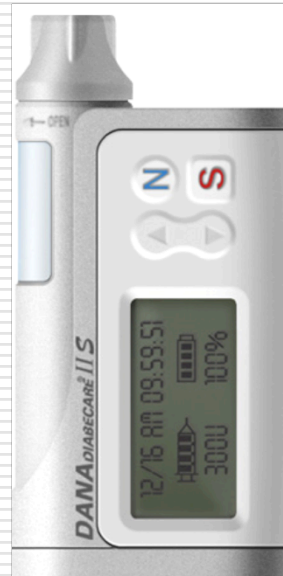
Tandem t:slim



CellNOVO



Asante Pearl



Dana Diabecare II-SG



D-Medical Spring

Pumps – Asante Pearl

- Uses prefilled pen cartridges
- Modular design
- 3.88" x 1.72" x 0.75"
- Pay as you go pricing
- Uses luer lock infusion sets
- Alarms gradually get louder
- Built-in flashlight



FDA and CE approved

Pumps – Sooil Dana Diabecare IISG



- Small, light 300 u pump
- Color screen controller communicates via phone
- Meter/controller communicate with pump
- Reverse luer lock sets available only from Dana
- Accurate bolus recommendations

CE approved in Europe

Wax Motor Pump – CellNovo

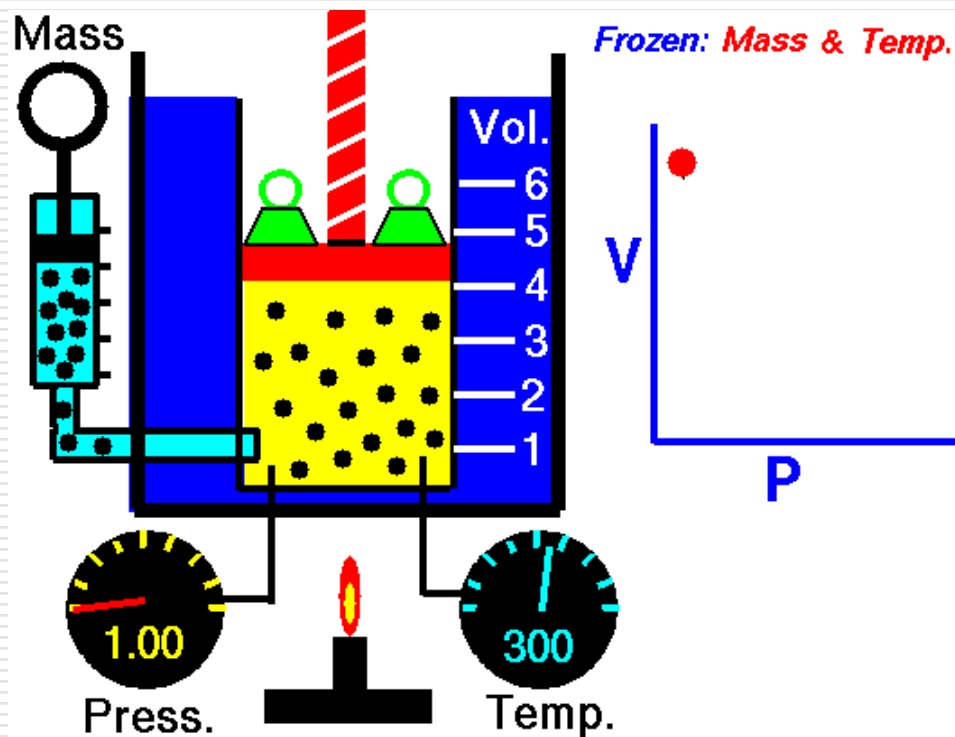


- Small wax cube is heated to pump 0.05 u volumes of insulin
- ? Slow boluses
- Controller sends data via phone lines to internet site/cell phone
- Connects to short infusion set
- 2 rechargeable pumps
- Unclear operation in heat/cold



CE approved in Europe

New Pressure Pumps



- Precise delivery – 1000ths of a unit
- No motor or gears
- Less weight
- No reservoir
- Some can detect leak or displacement of infusion set

Boyle's Law: $pV = k$ or $\Delta V = k / \Delta p$

Pressure Pump – Tandem T-Slim



- Pressure generated small solenoid pump
- Lightweight, I-Phone style
- Hi-res color touch screen
- Informative and VERY easy to use
- Standard luer lock sets

Submitted for FDA and CE approval

Pressure Pump – Spring



- Components:
 - Hardware & screen – permanent
 - Reservoir and spring that creates pressure – one time use
- Spring is only “moving” part
- Pressure generated by spring in reservoir
- Simple, small, light, low cost
- 300 u reservoir

Submitted for FDA and CE approval

Early Closed Loop – Animas Vibe



- Insulin pump with high contrast color screen
- 1 week Dexcom G4 sensor with smallest needle
- Internet access via Diasend software

CE approved in Europe

Early Closed Loop – Medtronic Veo



- Low Glucose Suspend (LGS)
- Uses CGM to suspend basal for up to 2 hrs when low
- User can reactivate basal
- Reduce prolonged nighttime lows
- Ability to detect low BGs remains an issue

CE approved in 2009

Patch Pumps

Patch applied directly to body, separate external controller

Patch Pumps Vs Line Pumps

Patch Pump

- Worn on body
- No external tubing in some
- Some require controller be present to bolus
- Can loosen, leak, be knocked off

Line Pump

- More body site options
 - Variety of needle and tubing lengths
 - Easy pump removal for showering, sports
 - Can loosen, leak, be knocked off
-

New Patch Pumps



Valeritas V-Go



Omnipod



Calibra



Roche/Medingo Solo



Debiotech Jewel

Also: Medtronic (2013), Medsolve, Altea

Pump – Roche Medingo Solo



- Precise dispensing screw
- Auto-inserter
- 200 units
- Weighs 1 oz
- Bolus button also on pump
- Controller has color screen, 5 ft range
- Accurate bolus calculations



Submitted for CE approval

Valeritas V-Go



- Simple design for Type 2 diabetes
- No controller
- Preselected basal rates
- Bolus button on pump
- No bolus calculator, BOB tracking, etc.

FDA approved

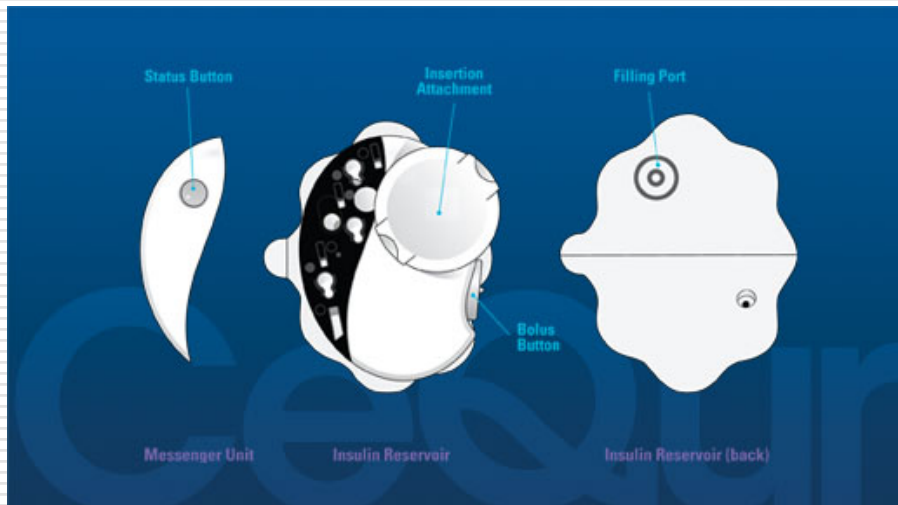
Patch Pump – Debiotech JewelPump



- Micro-Electro-Mechanical Systems tiny silicon motor
- Silicon wafer nanotechnology lets motor be mass produced
- Very light, 0.02 u delivery
- Separate infusion site
- Current 400 u insulin bladder makes it rather large
- ? Cost

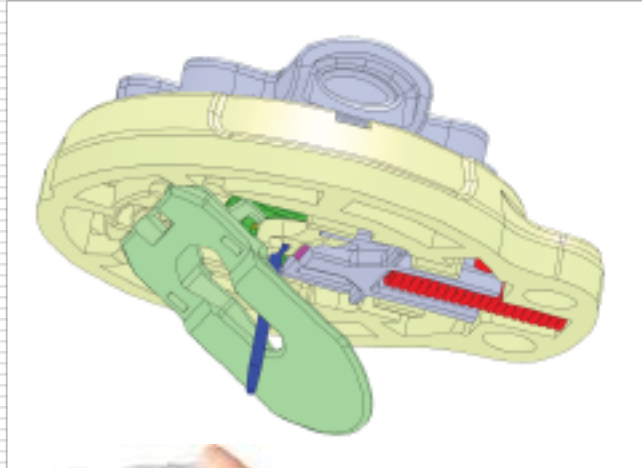
Submitted for CE approval

Patch Pump – CeQur



- Designed for Type 2
- Bolus button on pump
- No controller
- Montreux, Switzerland

Infusion Set With Detach Detector



- Nice spring auto-inserter
- Luer lock set for most pumps
- Current pumps don't alarm when infusion set detaches
- Set has another spring in base that occludes Teflon line if set detaches
- Faster detection of detached set when pump sounds occlusion alarm

Made by Spring/D-Medical – FDA & CE approved

Microneedles Speed Up Insulin



- Size of BD 1.5mm needle for injection

Compared to



- Current 0.5 to 3 mm microneedle rollers used to give facials

Color Screens

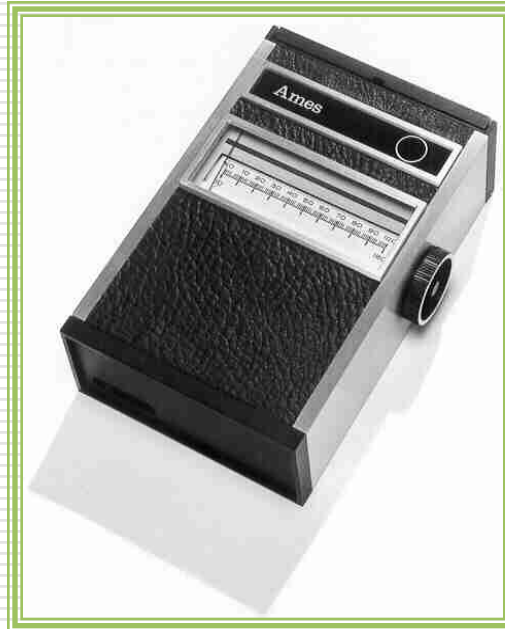


Progress In Monitoring

1300 BC



1971 AD



2011 AD



Continuous Glucose Monitors

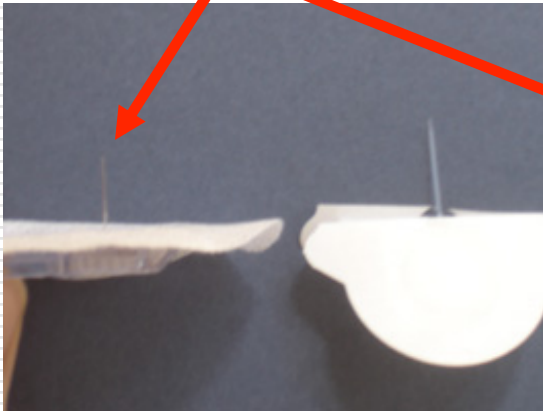
Real-Time Readings

plus

Retrospective Data

CGM Ingredients

Sensor



Dexcom sensor on left, Comfort infusion set on right
from insulinfactor.com

Receiver



Transmitter



CGM Benefits

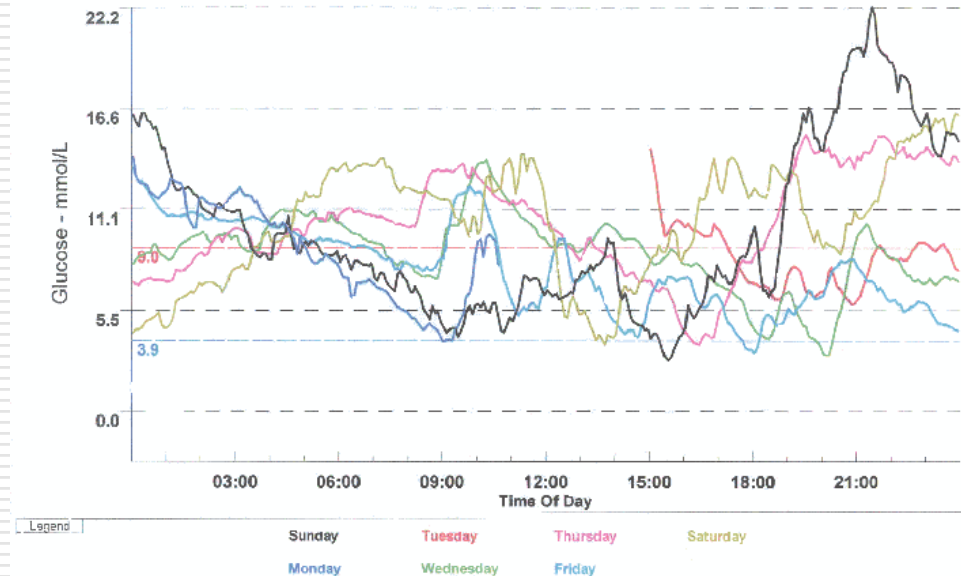
Real-Time

- The way most CGMs are used
 - Tracking and trending – fewer extremes
 - Avoid lows, especially night lows
 - Avoid foods that spike glucose
 - Immediate feedback – behavior mod made easy
 - Shows direction you're going
-

CGM Benefits

Retrospective View

- NOT used enough
- See patterns
- Test and tune basals, CarbF, CorrF
- Avoid night lows and hypo unawareness
- Peace of mind from fear of lows



Why Combine Pumps And CGMs?

Precise insulin delivery plus accurate glucose trends. Someone on a pump is more likely to handle 2nd device well.

CGM helps with:

dislodged infusion sets, missed meal boluses, detecting lows, lowering highs, basal and bolus testing, glucose stability, exercise, and stress, overriding bolus recommendations



Confidence For Performance



Clinical Indications For CGMs

- Frequent hypoglycemia (< 70 mg/dl, 2.9 mmol)
 - Hypoglycemia unawareness
 - Elevated A1c
 - Glycemic variability
 - Gastroparesis
 - Lives alone
 - Presence of complications
 - Small children not yet able to recognize and vocalize they are low
-

Drawbacks To CGM

- Cost, availability of reimbursement
 - False positive and false negative alarms
 - Inaccurate readings, not totally reliable – focus on trends
 - Calibration
 - Sensor failure
 - Need to do fingerstick to confirm CGM reading before treating
-

JDRF Study 2008:

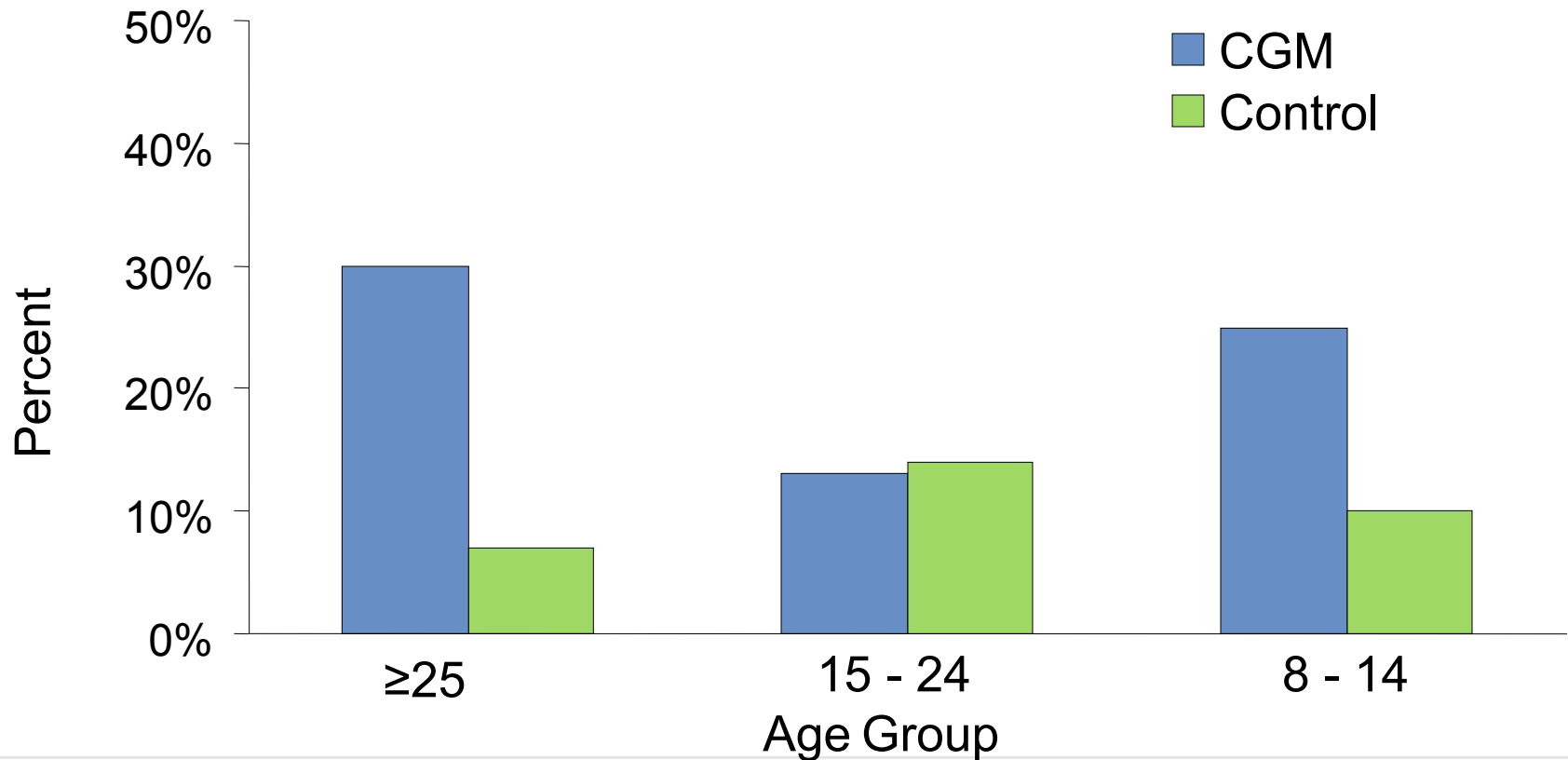
CGM substantially improves glycemic control in adults with T1DM, *without* increasing hypoglycemia.

JDRF CGM Trial

322 people, 8 to 72 years of age at 10 diabetes centers over 26 weeks			
Age	6 days use per week	A1c	Hypoglycemia
8 - 14 yo	50%	No change	No change
15 - 24 yo	30%	No change	No change
25 - 72 yo	83%	- 0.53%	No change

A significant reduction in A1c was seen in those who used CGMS frequently in those over 25 and in those 8-14. More CGM users achieved A1c below 7% and lowered A1c by 0.5% or more.

Patients With A1c <7.0 With GCM



CGM Systems

DexCom™
SEVEN® PLUS



Medtronic MiniMed
Revel® REAL-Time*



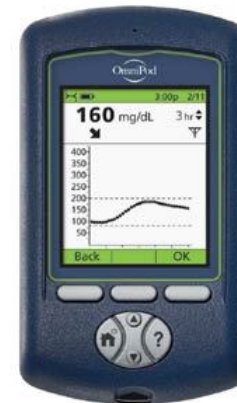
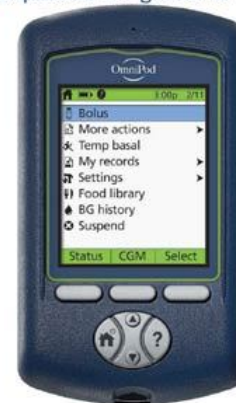
CGM Displays



Combines The OmniPod System with Dexcom continuous glucose monitoring system
Your one PDM now is your pump controller, CGM device and BGM device – eliminate the need for carrying 3 different meters / pumps

Upgrade path will be made available once product is approved

Expected filing date in Q1



CGM And Pump Choices

CGM:

Dexcom 7+

Pump:

Animas

Insulet

Tandem

Medtronic

Combo*

Available

2012?

2011?

2012?

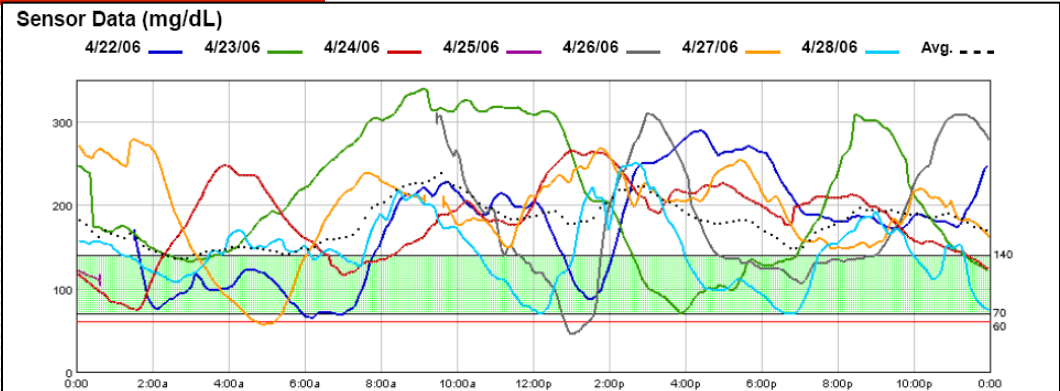
now

2013?

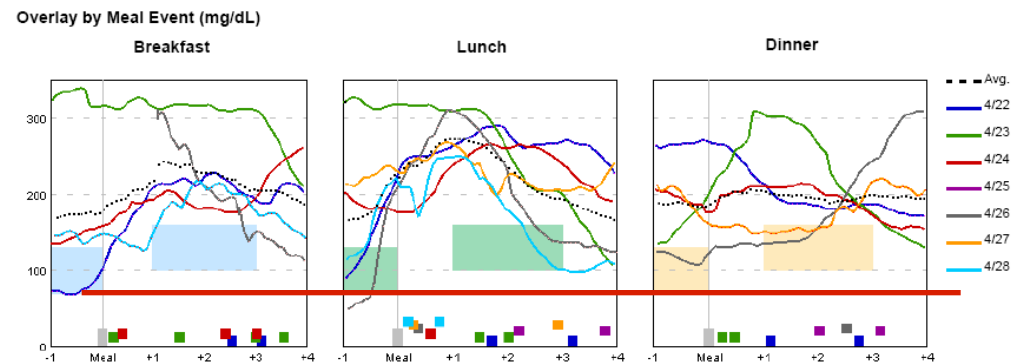


CareLink Online Reports

Sensor daily
overlay



Sensor results
by meal



	Sleeping 3:00 AM - 6:00 AM	Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Dinner	After Dinner	Evening 11:00 PM - 3:00 AM	All Time Periods
Range	100 - 150	70 - 130	100 - 160	70 - 130	100 - 160	70 - 130	100 - 160	100 - 150	
Average SG	146	173	227	190	234	186	195	162	185
High SG	248	340	318	326	312	270	302	308	340
Low SG	56	68	138	48	100	106	134	72	48
Standard Dev.	50	95	51	76	50	51	42	59	65
# of Readings	180	48	119	72	144	60	120	252	995

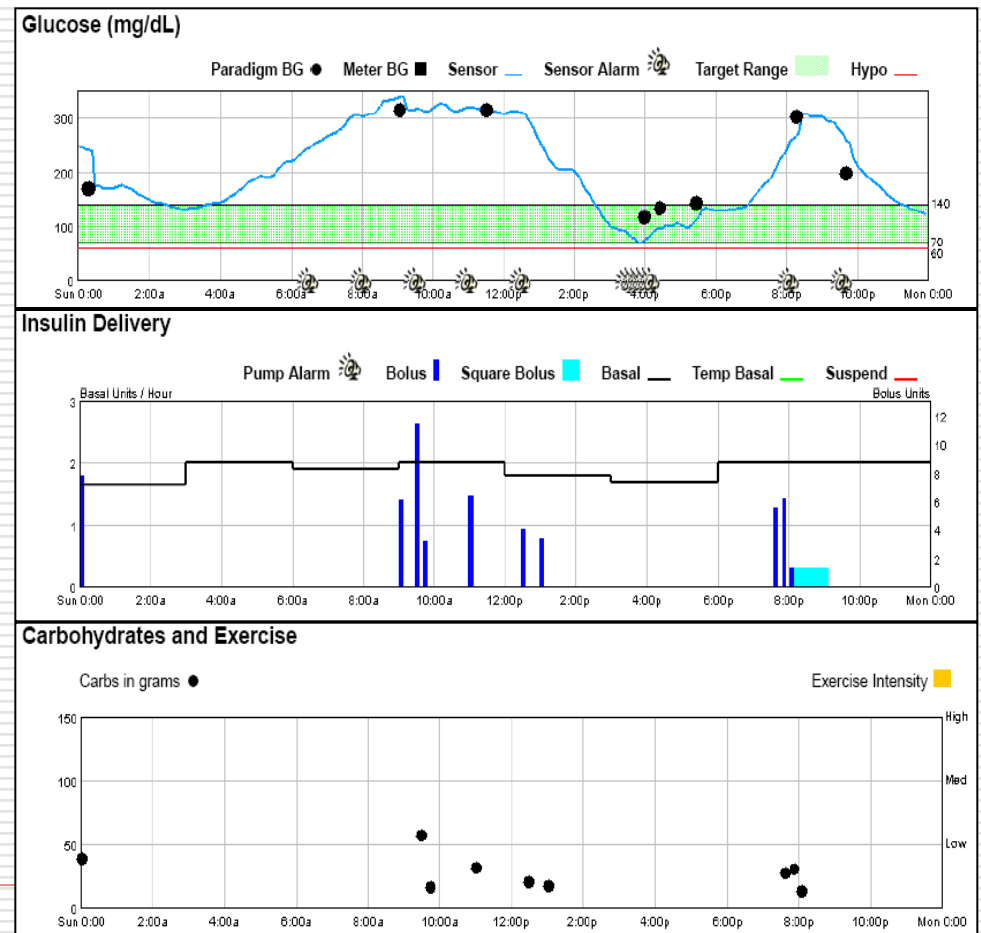
CareLink Online Reports

Daily summaries &
layered reports

Sensor tracing

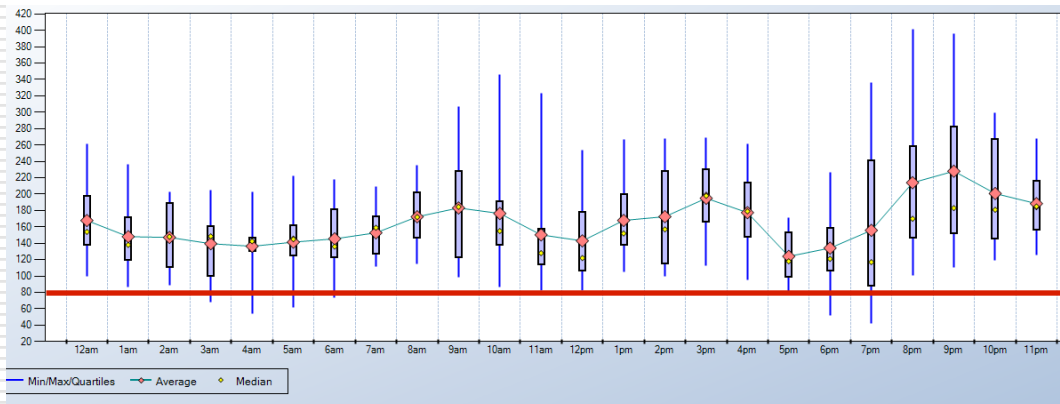
Basals & boluses

Carbs, exercise, etc

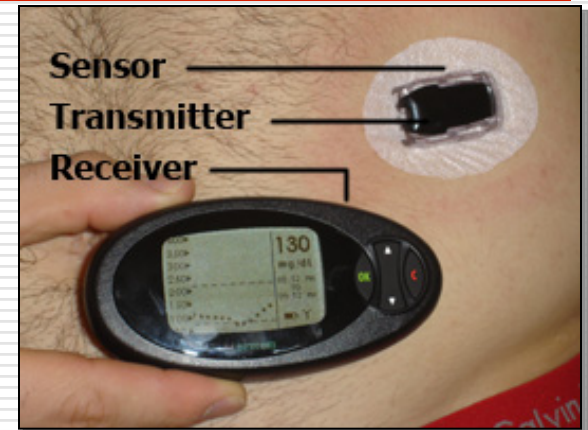


DexComTM 7 STS[®]

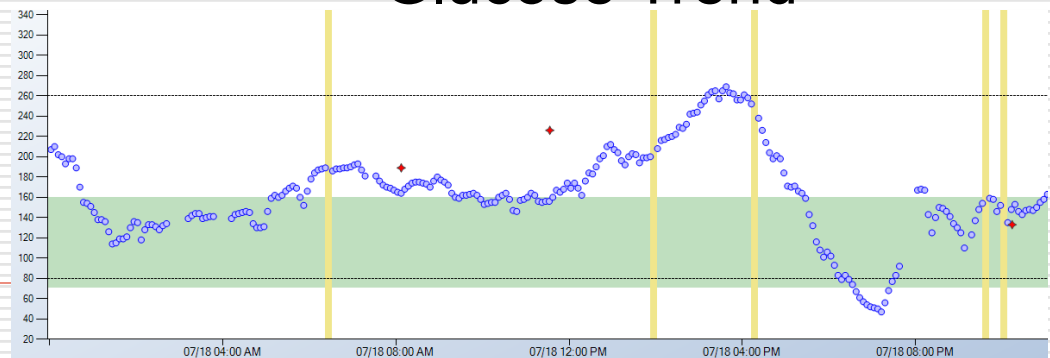
Dexcom DM2 Download Reports



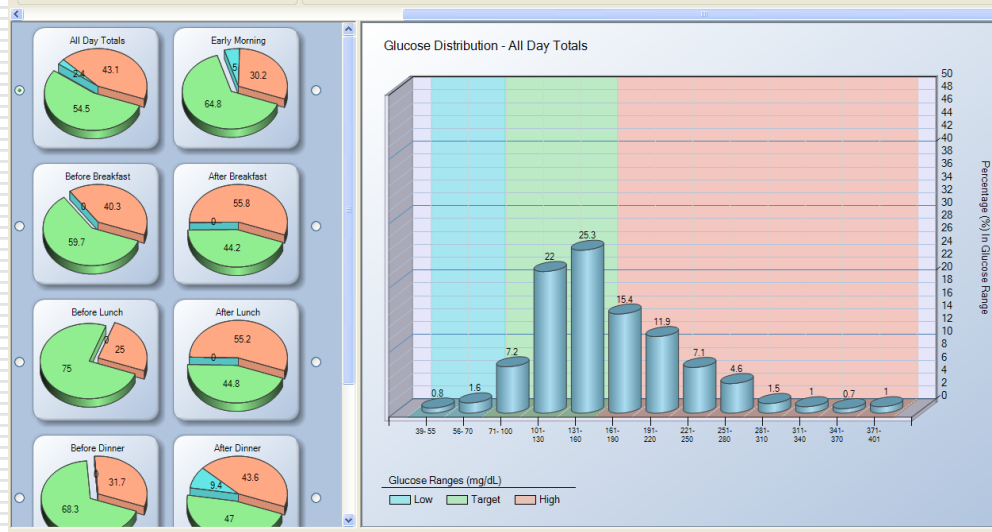
Hourly Stats



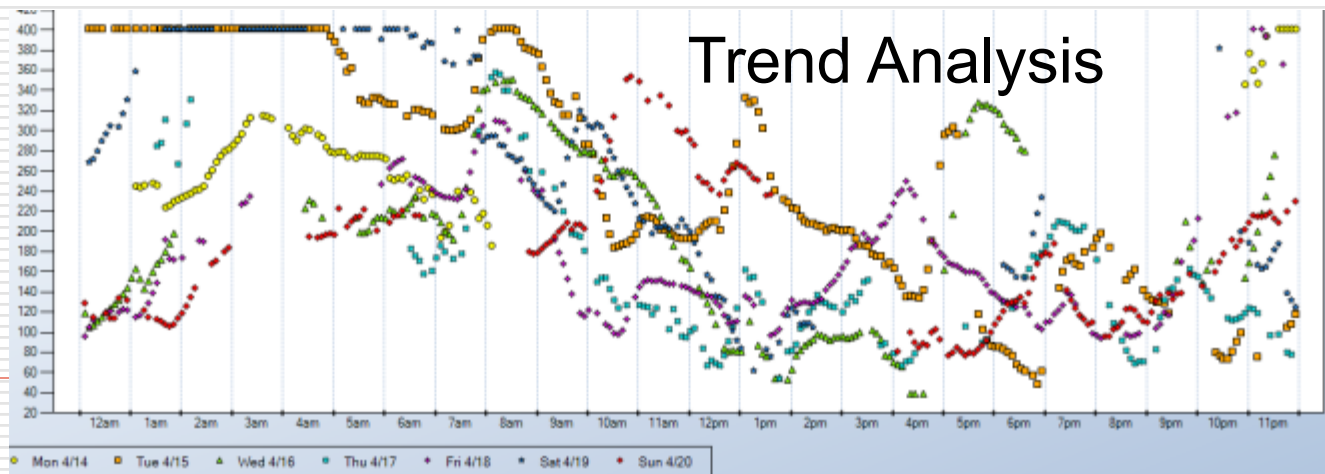
Glucose Trend



DexCom™ 7 STS®



BG Distribution





**Glucose Trends
Get Rid Of
Excursions**

Trends Show More Than Points

Insight



No clue
what to
do

Consistent Trend Data



Two Dexcom sensors worn by the same person

Trend line with ± 30 mg/dl accuracy is OK for dosing!

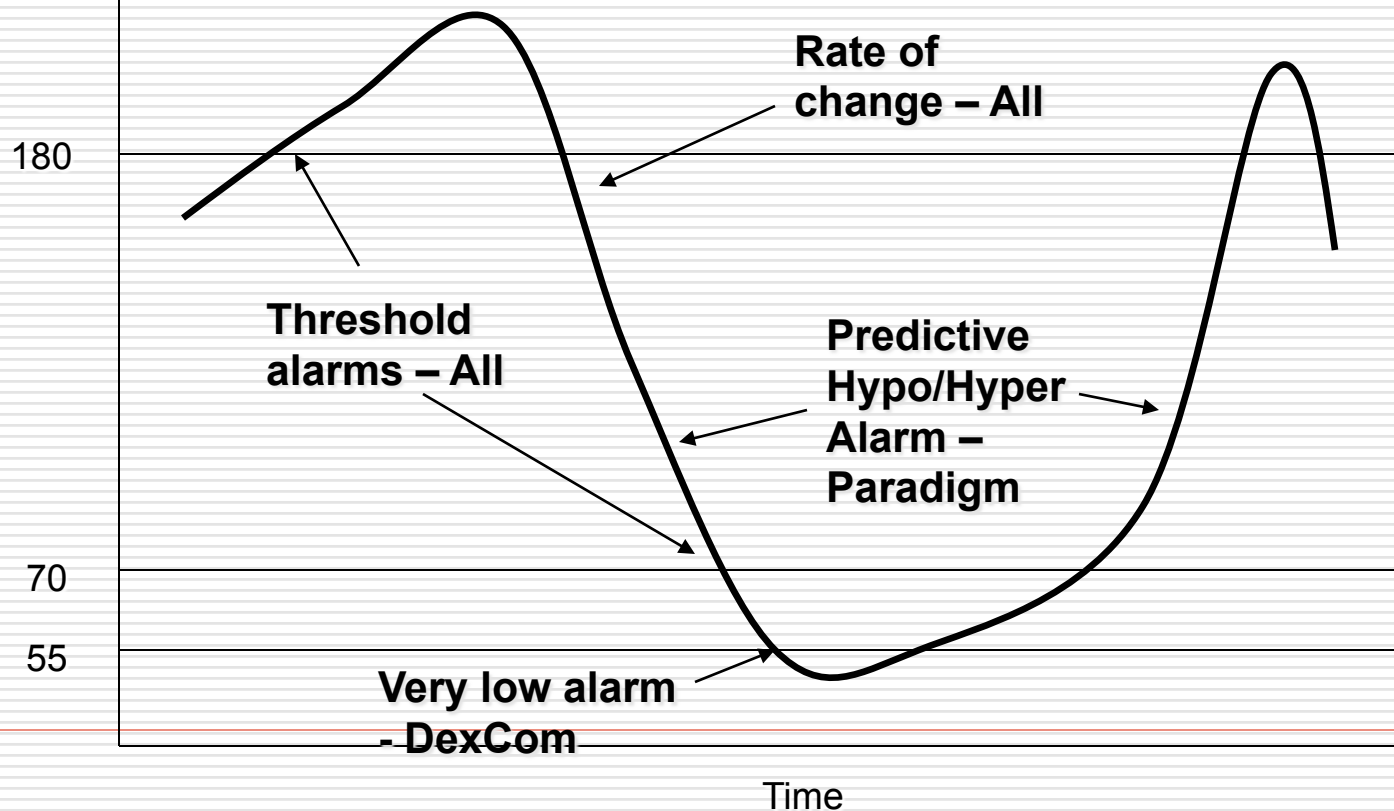
Real Time Data – Off The Screen

- Glucose read every 5 min – 288 readings/day
 - Trends
 - Rate of change arrows
 - Alarms – highs, lows, rate of change, predicted high or low
-

Types Of Alarms

BG – mg/dL

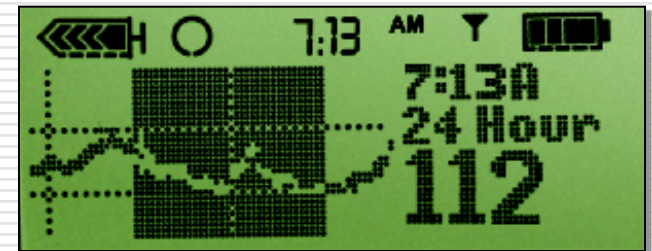
High and low alarms are set by user – features such as predictive alarms and alarm vol./type vary by manufacturer



Paradigm/Guardian[®] CGM Screens

On-Screen Reports

- 3 / 6 / 12 / 24-hr graphs
- Can scroll back for specific data points
- ↑↓ “direction” indicators
- Updates every 5 minutes
- Hi/Low Alerts
- Predictive Alerts (Guardian)



DexCom™ Seven Plus®

On-Screen Reports



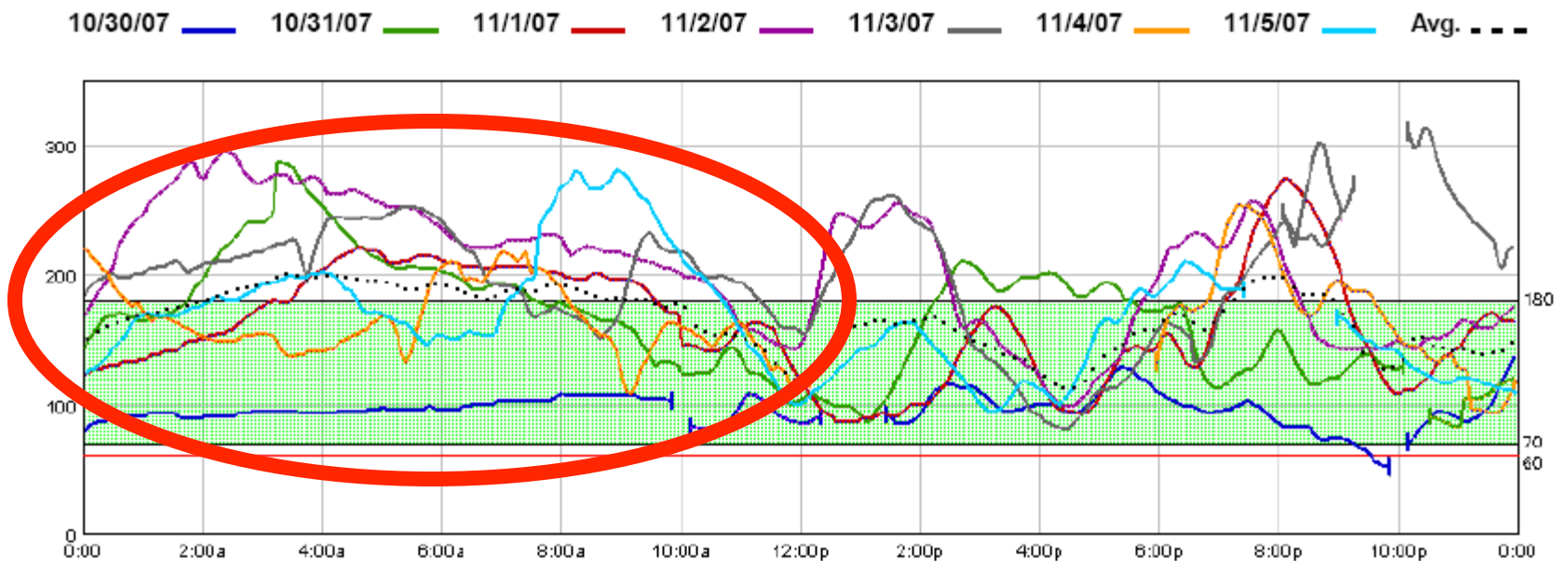
- 1, 3, 6, 12, 24-hr graphs
 - Updates every 5 minutes
 - Hi/Low alerts
 - Rate of Change alerts
 - Immediate feedback from screen
-

Retrospective Data – From Download

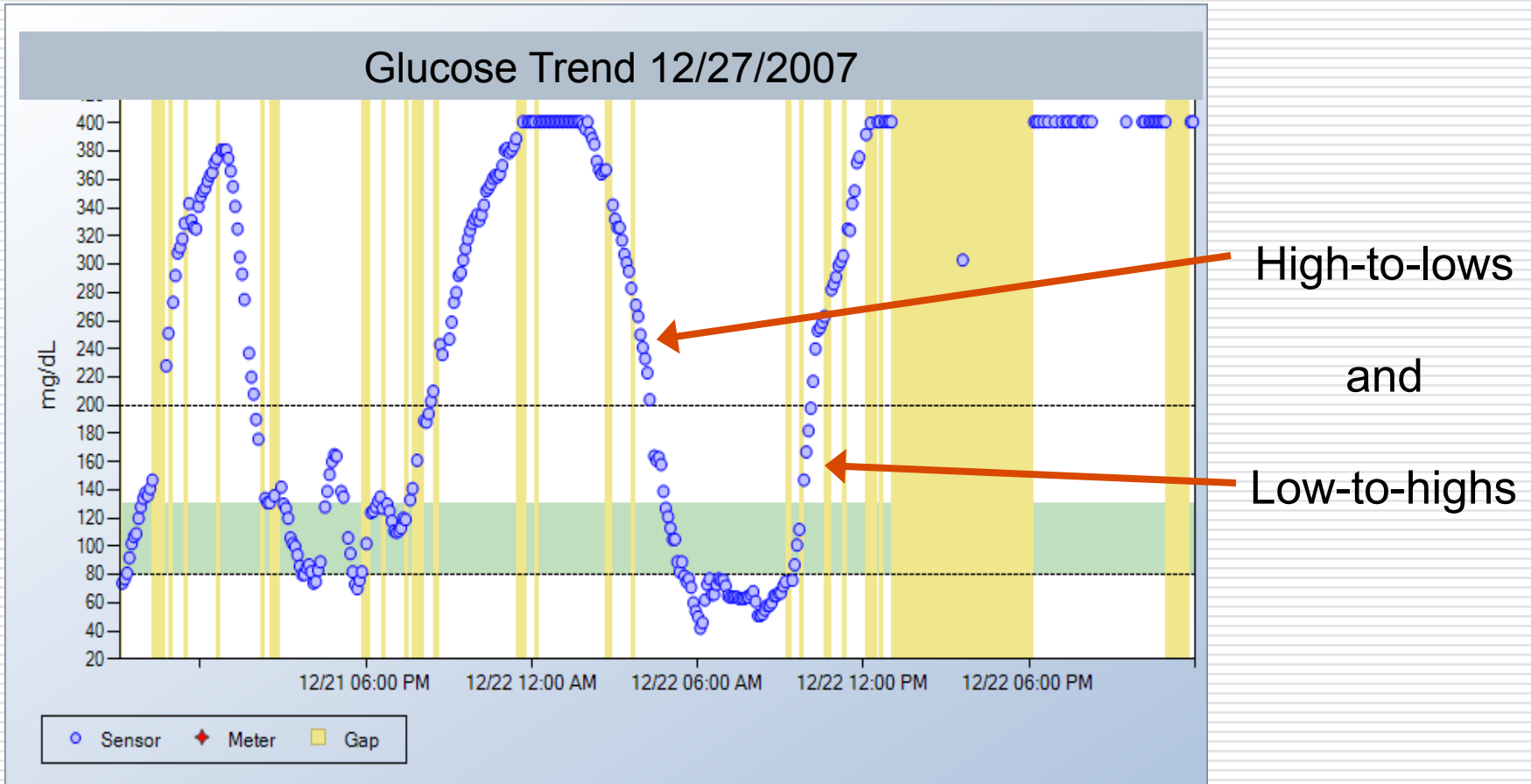
- Data downloaded to computer or internet
 - Trend graphs, tables, pie charts, modal day, % in and out of glucose goal range, averages, variability
 - Feedback available only after data is downloaded
-

Retrospective

Sensor Data (mg/dL)

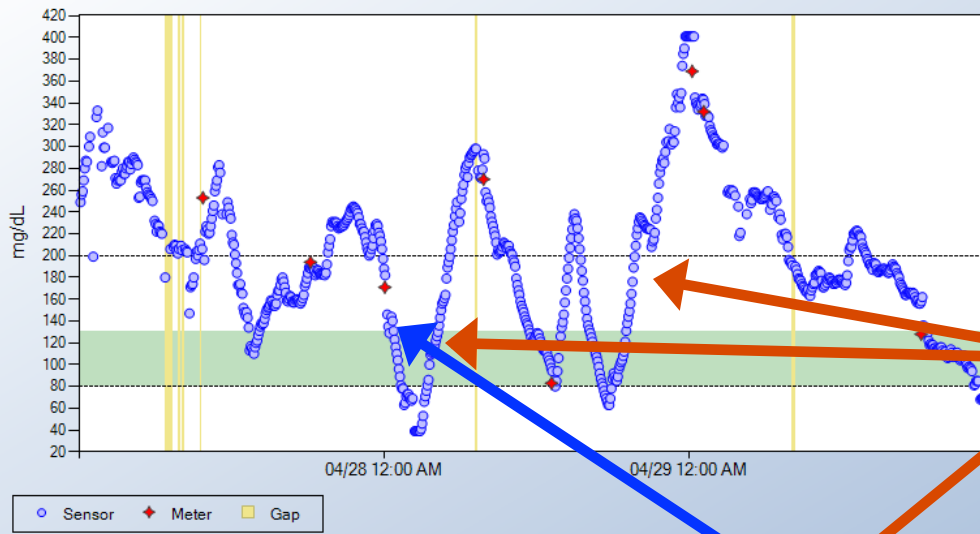


Some Glucose Trend Patterns



Glucose Trends

Glucose Trend : H, T [24312]

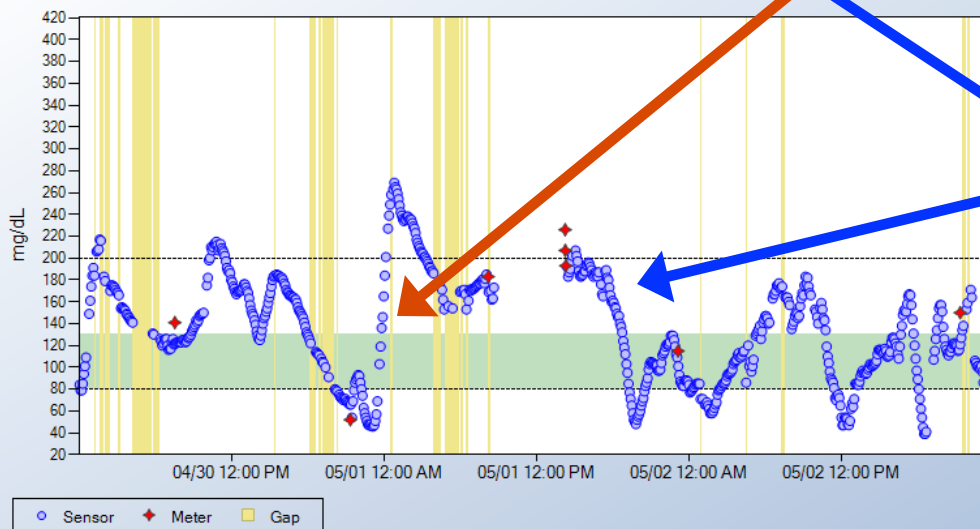


Excess low-to-highs

Control improves
by avoiding both

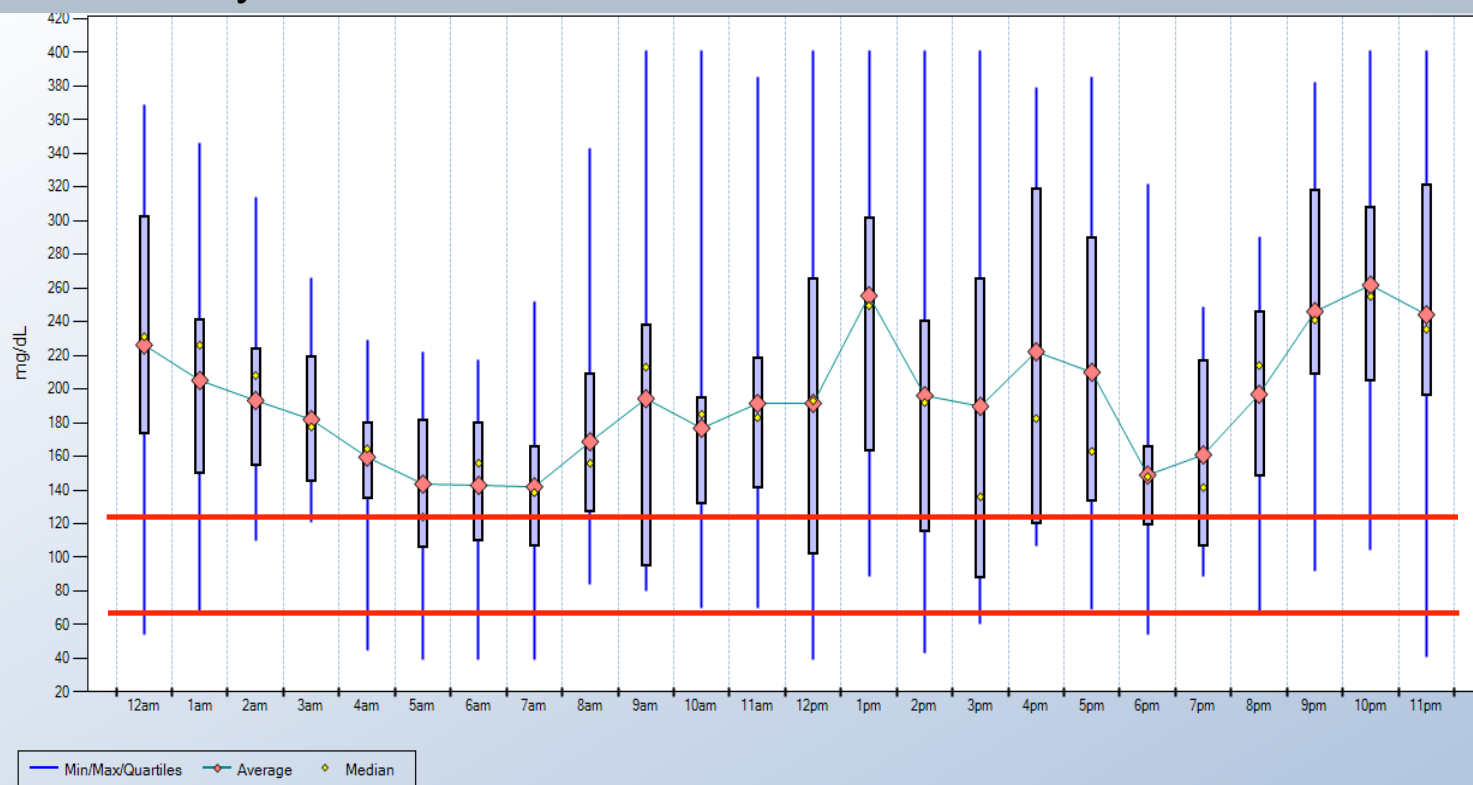
Excess high-to-lows

Glucose Trend : H, T [24312]



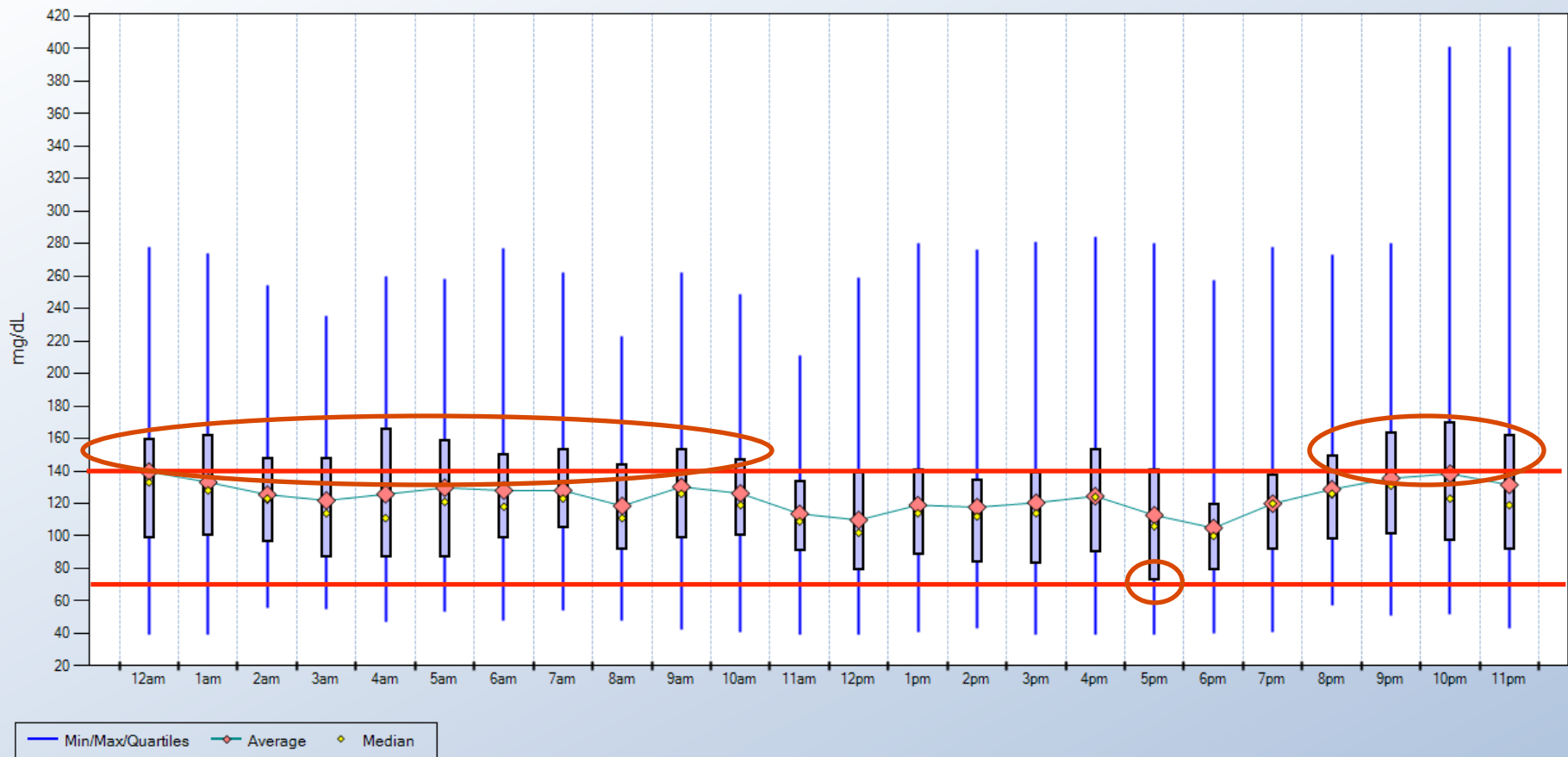
What Hourly Stats Tell Us

Hourly Statistics from 12/11/2007 12:00 AM to 12/19/2007



Hourly Stats For One Month

Hourly Statistics from 7/9/2008 12:00 AM to 8/8/2008 12:00 AM

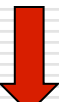




**Use CGM and
get off the
Rollercoaster!**

Decision Time – Look At BG, Trend, AND BOB!

CGM:

BG & Trend	110 	110 	110 
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Pump:

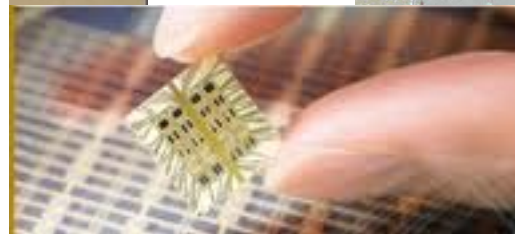
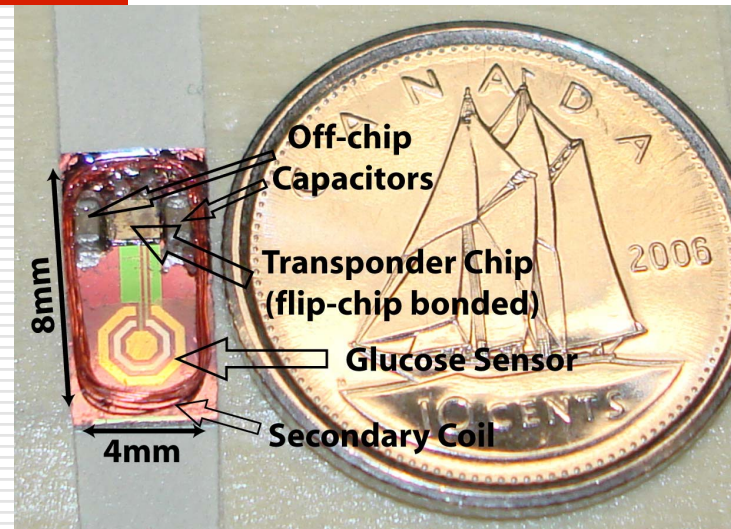
BOB	3 u	3 u	3 u
Time since bolus	2 hr	1/2 hr	2 hr

THEN decide on action to take.

Experimental CGMs

Invasive and Non-Invasive

Implanted CGM Systems

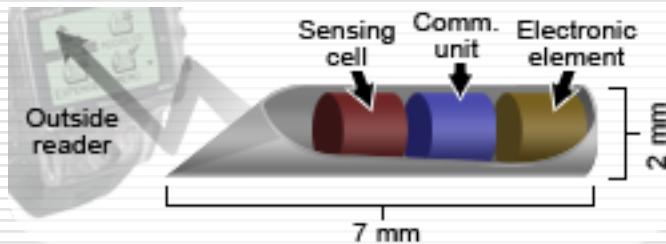


MicroCHIPS Illume



GlySens

CGM – Osmotic Pressure



- Future CGM implanted without surgery
- Measures osmotic pressure from glucose
- Currently testing immune system compatibility

LifeCare, Bergen, Norway

CGM – Implanted Fluorescent

Certain molecules fluoresce and change color as glucose rises and falls.

- Small size
 - Low power
 - Long life
 - Very good accuracy
-

CGM – Near Infrared



Near infrared light scattering measures glucose levels

- Bulky
 - Easy to use
 - Less accurate than current CGMs
 - Investigational
-

CGM – Eye Patch



Nanoparticles embedded in hydrogel lens

Lens color changes with glucose in tears

Device or glasses read glucose from color change

Greater lag time?

Accuracy?

Advances Underway

Advances In Pumps

- Smart phone communication
 - Smaller, flatter patch pumps with bolus buttons
 - Dual chamber pumps – glucagon, amylin, or GLP-1 agonists along with insulin
 - Basal shutoff for lows
 - More reliable infusion sets
 - CGM integration into closed loop
-

Future Pump Features

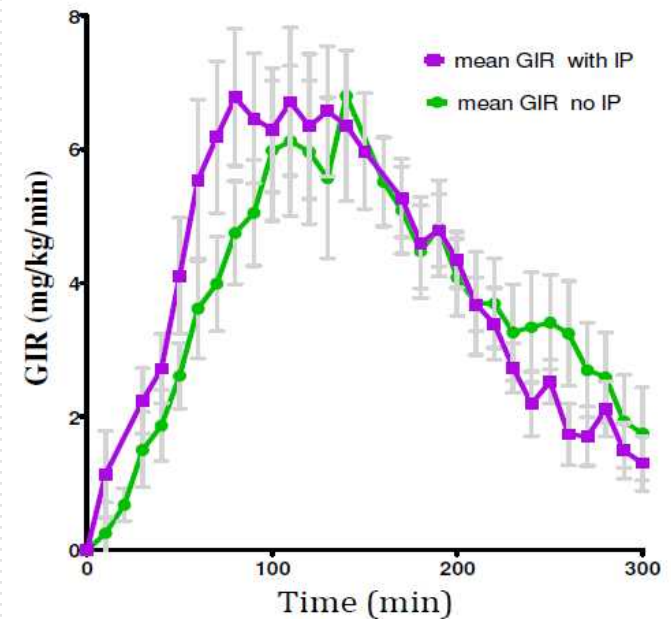
- Show How Setting Changes Impact TDD & BG
 - Temp Basal + Bolus Doses
 - Super Bolus
 - Meal Size Boluses
 - Excess BOB Alert
 - Exercise Compensator
 - Infusion Set Monitor
 - Automated Bolus and Basal Testing
-

Advances In Closed Loop

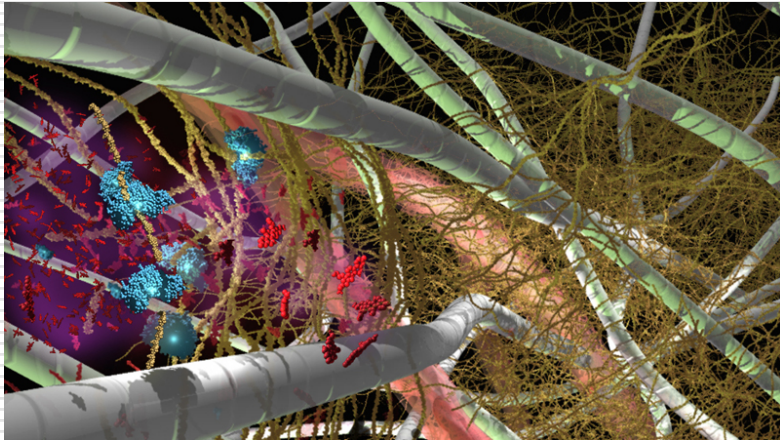
- Dual BG sensors reduces sensor error
 - Manual plus automatic control
 - Dual hormone delivery
 - insulin for highs
 - glucagon for lows
-

Faster Insulin Action

- Warm the infusion site
 - InsuPatch by InsuLine
- Faster insulins
 - Novo Nordisk
 - Bodel
- Speed up insulin absorption
 - Halozyme
- Intradermal 1.5 mm microneedles
 - BD



Halozyme Rapid Insulin



- Ultrafast, DIA ~ 3.75 to 4 hrs?
 - Combines recombinant human hyaluronidase with rapid insulins
 - Temporarily degrades local hyaluran, a structural protein in the interstitial space
 - Might lower peaks and cause fewer lows
 - In phase 2 clinical trials
-

Communication – Meter + Phone



- Several companies are developing meters for phones using Bluetooth
- Rapid alerts for care-givers of young, elderly, hypo-unaware
- Adds food databases, carb counters, apps, analysis
- Eventually management via cell phone



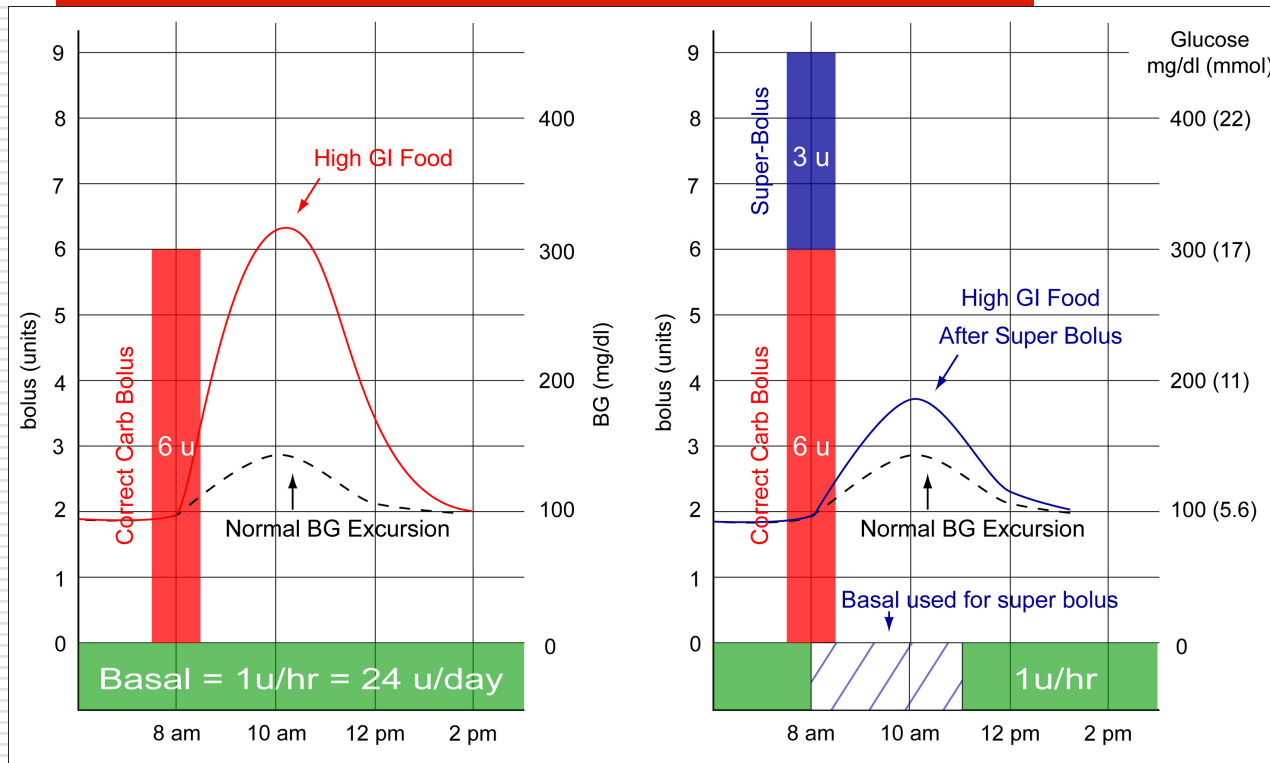
Diabetes Phone Apps



- Wavesense Diabetes Manager, Gluco Buddy, Diabetes Log, Bant, Glucose Mate, Diabetic Meal Planner Lite
- Many apps available for I–Phones, Pre, Blackberry
- Help for dosing, logging, carb counting, bolus calcs



Super Bolus – Shift Basal To Bolus



Helps when eating over 30 or 40 grams of carb

Max carbs/meal =

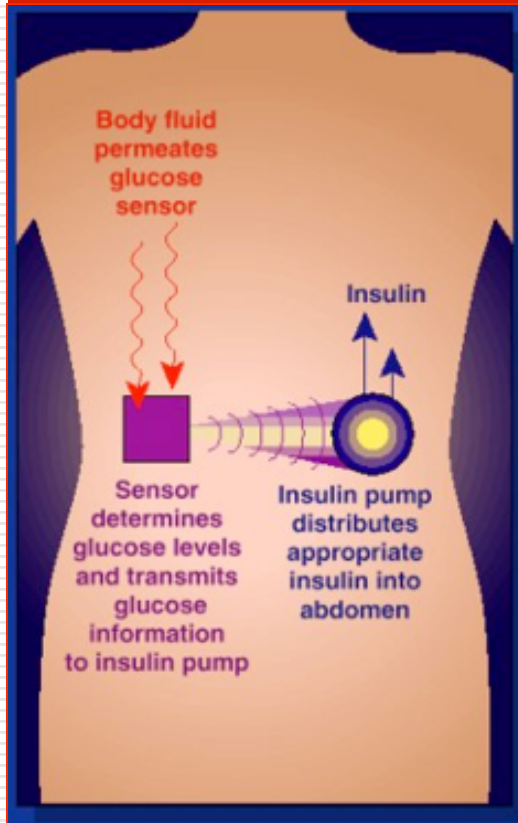
$$Wt(lb) \times 0.36$$
 to stay in control ²

Future: Super Bolus shifts part of the next 2 to 3.5 hrs of basal insulin into the bolus with less risk of a low later.^{1,2}

¹ J. Walsh: http://www.diabetesnet.com/diabetes_presentations/super-bolus.html September, 2004

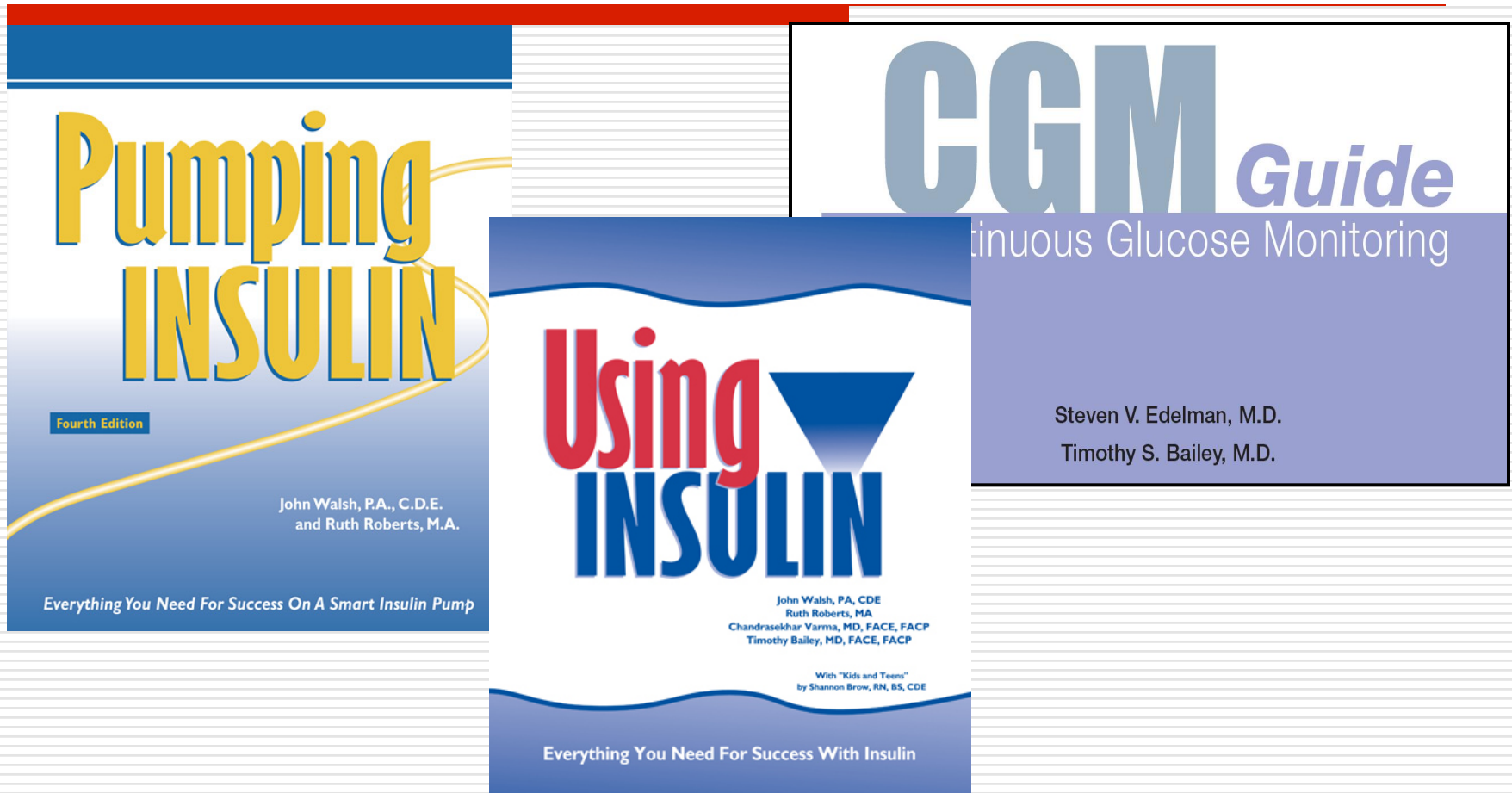
² J. Bondia, E. Dassau, H. Zisser, R. Calm, J. Vehí, L. Jovanovic, F.J. Doyle III, Coordinated basal-bolus for tighter postprandial glucose control in insulin pump therapy, Journal of Diabetes Science and Technology, 3(1), 89-97, 2008

How Long To A Closed Loop?



- ❑ Needed:
 - Faster insulin
 - Better CGM accuracy
 - Less sensor lag time
 - Better handle on life's variables
 - ❑ Dual pumps with glucagon
 - ❑ Glucose control algorithms and hardware that don't fail
-

Reading – Still The Best Way To Learn



Slides at www.diabetesnet.com/diabetes-resources/diabetes-presentations/
Books at www.diabetesnet.com/dmall/ or 800-988-4772