Έξυπνες πένες ινσουλίνης (smart insulin pens)
Smart watches
Apps

Κωνσταντίνος Μαρκάκης, MD, PhD
Παθολόγος με εξειδίκευση στο σακχαρώδη διαβήτη
Επιμελητής Α', Β' Προπαιδευτική Παθολογική Κλινική,
Μονάδα Έρευνας και Διαβητολογικό Κέντρο,
Πανεπιστημιακό Γενικό Νοσοκομείο "ΑΤΤΙΚΟΝ"

Δήλωση σύγκρουσης συμφερόντων

Η ομιλία εκφράζει τις απόψεις του ομιλητή

Ο ομιλητής έχει λάβει τιμητική αμοιβή για ομιλίες από τις εταιρείες Abbott, Menarini, ΦΑΡΜΑΣΕΡΒ-ΛΙΛΛΥ ΑΕΒΕ και HEMOGLOBE HELLAS

Εκπαίδευση

- Διαβήτης – Επιπλοκές

- Διατροφή

- Μέτρηση υδατανθράκων

- Δυναμική προσαρμογή δόσης ταχείας ινσουλίνης (γεύμα – διόρθωση – στόχοι)

- Εκτίμηση βασικής και γευματικής ινσουλίνης

Εκπαίδευση

- Διαβήτης – Επιπλοκές
- Διατροφή

- Μέτρηση υδατανθράκων
- Δυναμική προσαρμογή δόσης ταχείας ινσουλίνης (γεύμα – διόρθωση – στόχοι)
- Εκτίμηση βασικής και γευματικής ινσουλίνης

- Αναλογία ινσουλίνης/ γρ. υδατανθράκων ή ισοδύναμο (Insulin to Carbohydrate Ratio, ICR) - Τεστ ICR
- Παράγοντας ευαισθησίας ινσουλίνης (Insulin Sensitivity Factor, ISF)
- Στόχοι Σχ (BG targets)

- Τήρηση ημερολογίου μετρήσεων
- Ερμηνεία μετρήσεων – λήψη θεραπευτικών αποφάσεων
- Τεστ βασικής ινσουλίνης και γευματικής ινσουλίνης

Σχήμα πολλαπλών ενέσεων (Basal Bolus)

- Αντιμετώπιση υπογλυκαιμίας

- Προσαρμογή σε αυξημένη φυσική δραστηριότητα – άσκηση (είδη άσκησης)

- Προσαρμογή θεραπείας σε ασθένεια

- Προσαρμογή σε ταξίδια - διακοπές

- Αναγνώριση υπογλυκαιμίας
- Αντιμετώπιση υπογλυκαιμίας
- Πρόληψη
- Επίγνωση υπογλυκαιμίας

- Αυξημένες ανάγκες σε ινσουλίνη
- Αποφυγή κετοξέωσης

- Μεταβολή σε διατροφικές συνήθειες – φυσική δραστηριότητα
- Συντήρηση – μεταφορά ινσουλίνης, αναλωσίμων
- Ζώνες ώρας

Σχήμα πο

- Αντιμετώπιση υπογλυκαιμ

  - Είδη άσκησης (αερόβια – αναερόβια)
  - Διάρκεια άσκησης
  - Αμεση επίδραση
    Επίδραση αργότερα- κίνδυνος νυκτερινής υπογλυκαιμίας
  - Στρατηγικές αποφυγής της επαγόμενης από την άσκηση υπογλυκαιμίας

- Προσαρμογή σε αυξημένη

- Προσαρμογή θεραπείας σε ασθένεια

  - Αυξημένες ανάγκες σε ινσουλίνη
  - Αποφυγή κετοξέωσης

- Προσαρμογή σε ταξίδια - διακοπές

  - Μεταβολή σε διατροφικές συνήθειες – φυσική δραστηριότητα
  - Συντήρηση – μεταφορά ινσουλίνης, αναλωσίμων
  - Ζώνες ώρας

Μέτρηση υδατανθράκων

Carbs&Cals

Calorie Counter & Carb Manager - Freshbit

Choose from 300,000+ Foods

← Greek Salad

281 calories   15 minutes

Greek Salad   + Log

Greek   Vegetarian

Published by: Delicious Salads Recipes

NUTRITION   INGREDIENTS   INSTRUCTIONS

Calorie Breakdown

← Γεμιστά (ντομάτες, πιπεριές, κολοκυ...

‹ 380 g › ≈   ‹ 1 μερίδα (... ›

Θερμίδες   **501.6**/2000kcal (25%)
Πρωτεΐνες   **5.7**/50
Συνολικά Λίπη   **34.6**/ε
Υδατάνθρακες   **44.8**/3
Σάκχαρα, συνολι... **14.4**/ε
Νάτριο   **30.4**/2

ⓘ σύρατε προς τα αριστερά περισσότερες πληροφορίες

‹ Σήμερα 23 Αυγ

Πρωί Μεσημέρι Βράδυ Ε

⊕ Καταγραφή

← Γεμιστά (ντομάτες, πιπεριές, κολοκυ...

‹ 380 g › ≈   ‹ 1 μερίδα (... ›

Υδατάνθρακες
35%

ⓘ πατήστε στα χρωματιστά τμήματα για ποσοστά επί συνόλου θερμίδων

‹ Σήμερα 23 Αυγ ↺ ›

Πρωί Μεσημέρι Βράδυ Ενδιάμεσο

⊕ Καταγραφή

titroo

Γευματικό – διορθωτικό bolus

Ρυθμίσεις → **Bolus** ← **Βοήθεια στη μέτρηση υδατανθράκων**

Δυνατότητα διαφορετικών ρυθμίσεων (αναλογία ινσουλίνης προς υδατάνθρακες, συντελεστής ευαισθησίας διόρθωση) για διαφορετικά διαστήματα της ημέρας

CONFIGURATION WIZARD

12:00 AM → 2.84;

+ Carbohydrates ratio (hourly)

12:00 AM → 14;

< BACK   NEXT >

Diabetes:M

Total bolus: 7.65 U = 6.02 + 1.63 → 3h

Active Insulin: **0 U**
Bolus type: Multiwave
Total bolus: 7.65 U
Standard: 6.02 U (79%)
Extended: 1.63 U (21%) over 3h
!!Glucose is above target level. If possible delay eating by
10 - 20 min after applying the bolus.
Press for details

Cal: 350; Fat: 15; Carbs: 50; Prot: 7.1;
Press to view the selected food

⬡ Glucose	137	mg/dL
⬡ Carbs	50	grams
✓ Extended Bolus		
Proteins	7.1	grams
Fats	15	grams
Calories	350	kcal

Food List

Search food ✕ 🎤 🌐

ⓘ Long press on items to add/edit food.

Deserts (**59**)

Fats: 13, Carbs: 37, Prot. 2.4, Cal. 265

Apple Pie - piece (⅛ of ~9",23cm)
Fats: 19; Carbs: 58; Prot. 3.7; Cal: 411

Apple Strudel - 100g
Fats: 11; Carbs: 41; Prot. 3.3; Cal: 274

Apple Strudel - piece (~2"/2" 5cm/5cm)

➢ Υπολογισμός ενεργού ινσουλίνης (insulin on board)

Smart watches

Smart watch - CGM

Dexcom CGM

Dexcom mobile app is compatible with both Apple and Android watches.

Apple or Android watch syncs with the current CGM data from the app running on your iPhone or Android phone.

It displays your current glucose number and arrow trend, as well as graphs for 1-, 3-, 6-, and 24-hour periods.
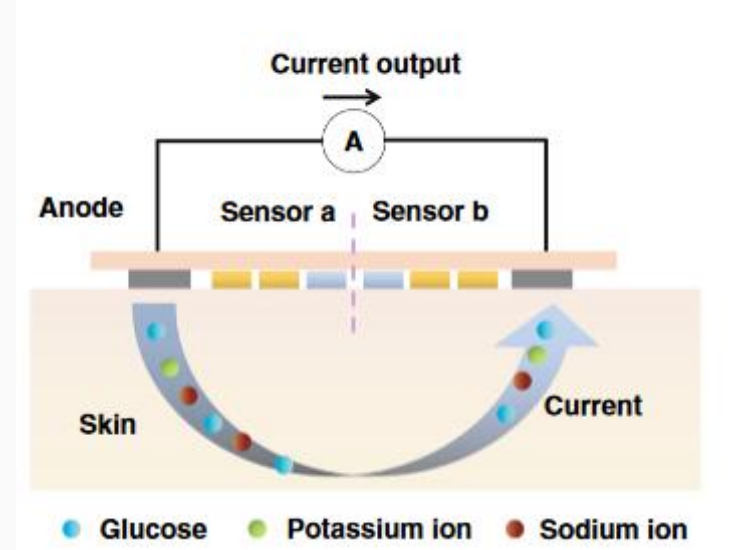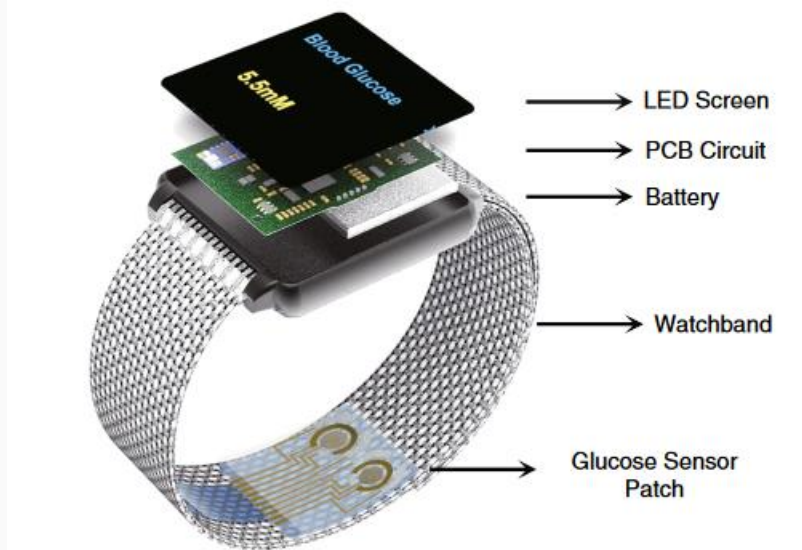
High or Low glucose Alerts

Dexcom CGM

Garmin watches and diabetes data

Real-time glucose levels as well as a trend arrow and a 3-hour history CGM line.

Alerts

K'Watch Glucose

84.34% clinical accuracy in the Clarke error grid analysis (zones A + B)

Chang et al. Microsystems & Nanoengineering (2022)8:25

Smart insulin pens /
Smart caps for insulin pens

JDRF

What makes an insulin pen 'smart'?

- It keeps a record of the time and dose of each injection.
- It can connect to a compatible smartphone app, so you can keep track of your data easily and can choose to share it with your clinic.
- It can enable more accurate dosage calculations through a bolus calculator and so ease the mental burden.
- It can help you avoid missed doses.

Novopen 5

Novopen Echo

Smart Insulin Pens
NovoPen

Novopen 6 / Novopen Echo Plus

NovoPen® 6))

NovoPen Echo® Plus))

Novopen 5

Novopen Echo

Dose memory

— Number of units last injected

— Time passed since last injection (hours: minutes: seconds)
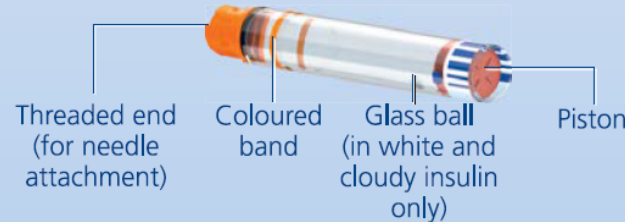
Novopen 6 / Novopen Echo Plus

Smart Insulin Pens NovoPen

NovoPen 6
NovoPen Echo Plus

Pen cap

Insulin window

Insulin scale

Cartridge holder

Piston rod head

Piston rod

Dose pointer

Dose counter

LOT number (on reverse side)

Pen ID

Dose button

Dose memory

Single-use needle (example)

Outer needle cap

Inner needle cap

Needle

Paper tab

Insulin cartridge (Penfill® cartridge 3 ml)

Threaded end (for needle attachment)

Coloured band

Glass ball (in white and cloudy insulin only)

Piston

NovoPen® 6:
60-unit maximum dose
1-unit dose increments

NovoPen Echo® Plus:
30-unit maximum dose
0.5-unit dose increments.

Tresiba, Fiasp

NovoPen 6
NovoPen Echo Plus

Pen cap

Single-use needle (example)

Outer needle cap

Inner needle cap

Needle

Paper tab

rod d

Dose pointer

LOT number (on reverse side)

Dose button

ton od

Dose counter

Pen ID

Dose memory

2

10 units injected 35 minutes and 50 seconds ago

10
00:35:50

3

8.5 units injected, 36 hours, 45 minutes and 18 seconds ago

8.5
36:45:18

NovoPen® 6:
60-unit maximum dose
1-unit dose increments

NovoPen Echo® Plus:
30-unit maximum dose
0.5-unit dose increments.

Smart Insulin Pens
NovoPen
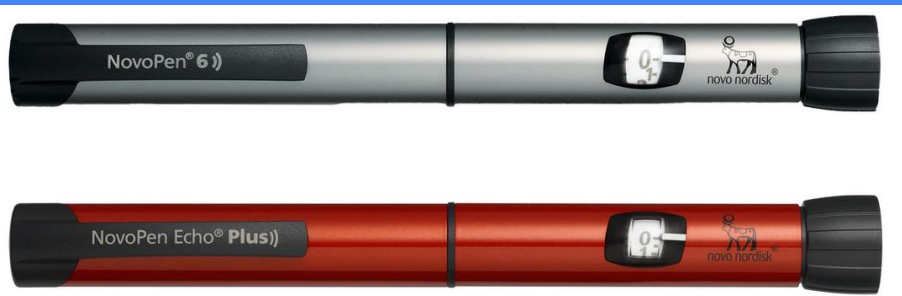
4 **Transfer your injection history to your device.**
- **Hold** the dose memory of the pen straight against the NFC spot on your device.
- **Wait** while the details of your latest injections are automatically transferred to your device.

Paired data

Bolus calculator

Smart Insulin Pens NovoPen

FreeStyle LibreLink

✔ Insulin doses recorded from the NovoPen® 6 or NovoPen Echo® Plus smart connected insulin pen can be easily transferred to the FreeStyle LibreLink app[2] with a scan.

✏ Helps patients see the effect of insulin doses with both glucose and insulin data on the same reports in LibreView[fh]

💬 Helps you to have more informed patient consultations

Smart Insulin Pens NovoPen

FreeStyle LibreLink

WHY FREESTYLE LIBRE SYSTEMS?	FREESTYLE PORTFOLIO	SCIENTIFIC RESOURCES & EDUCATION	FREESTYLE PORTAL	HELP & SUPPORT

Connect
Scan and add a compatible smart connected insulin pen[1] to automatically transfer insulin doses to the app[2,◊]

Review
Patients can easily track past insulin doses and their impact.
Seeing this information may help your patients avoid missing a dose or taking insulin doses too close together
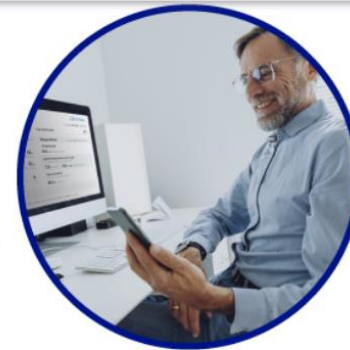
Share
Reports showing glucose and insulin data together for more informed patient consultations

Smart Insulin Pens
NovoPen

See insulin and glucose data together to support more efficient patient consultations
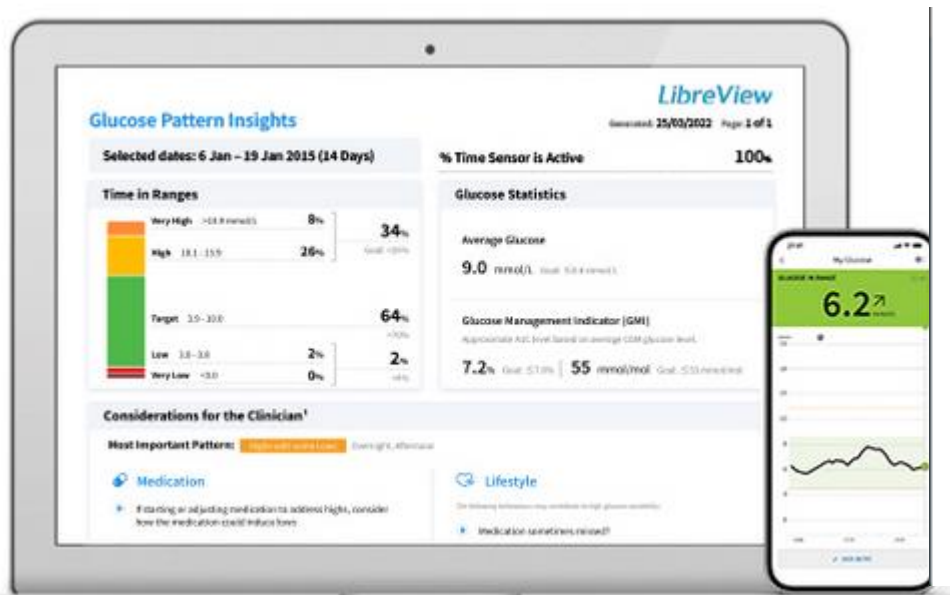
Smart Insulin Pens NovoPen

FreeStyle LibreLink

See insulin and glucose data together to support more efficient patient consultations
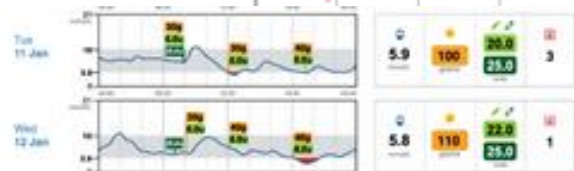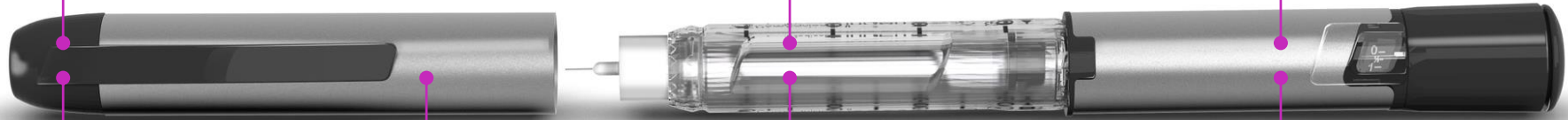
Smart Insulin Pens- InPen Medronic

InPen™ smart pen

Available in two colours

Blue: compatible with Novo Nordisk **NovoRapid**®, Novo Nordisk **Fiasp**® and Novo Nordisk Insulin Aspart Injection, 3 ml cartridges (300 units)

Grey: compatible with Lilly **Humalog**® and Lilly **Lyumjev**® cartridges

Delivers half unit doses (up to 30 units)

Share data from multiple InPen™ smart pens to the same app

Connects to the app via Bluetooth®

Monitors insulin temperature

Battery lasts a full year with no need to charge

Humalog® and Lyumjev® are registered trademarks of Eli Lilly and Company. Fiasp®, Novorapid® and Novo Nordisk Insulin Aspart are registered trademarks of Novo Nordisk A/S.

Smart MDI systemSmart MDI system with Simplera™ & InPen™ 2.0

InPen™ hardware

InPen™ app

Simplera™ sensor

Simplera™ app

Care partner app

Smart watch support

28

Simplera™ CGM

Key features

24hr — Real-time CGM tracing
Records glucose levels every 5 minutes, 24/7 with no fingersticks*

Predictive glucose alerts
Alerts of lows and highs up to 60 minutes ahead of time

Discreet design
Simple insertion & wear experience

NEW feature

NEW feature

App connectivity to Android and Apple phones, Apple watch & Care Partners app
* If CGM readings do not match symptoms or expectations, use a blood glucose meter to make diabetes treatment decisions. Refer to System User Guide

Introducing the Smart MDI system

InPen™ smart insulin pen

Tracks dosing data

Active insulin tracking, automatic dose logging and reminders to dose or change cartridges

Provides real-time dosing guidance

Bolus calculator and Missed dose detection technology recommends a corrective action when a mealtime bolus is missed or not enough to stay in range

Easy access to reports & insights

Your patients on MDI therapy's glucose and insulin data is available in a single CareLink™ system report

CGM & insulin dosing in one system

Glucose levels, active insulin, and dose calculations combined to recommend the right mealtime dose*

Insulin dosing

InPen™ smart insulin pen tracks dosing data and helps calculate dose

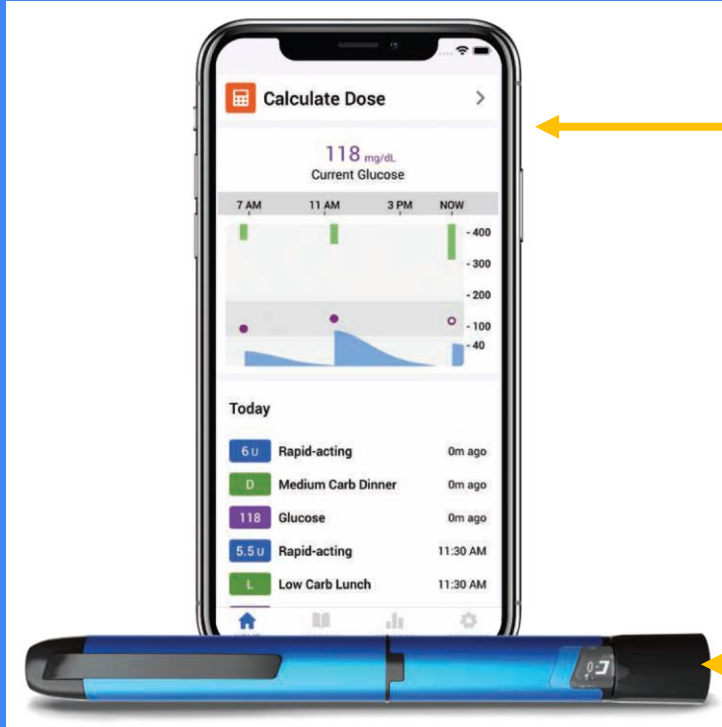### CGM

Records real-time glucose trends

Smart MDI system

Provides real-time dosing guidance for your patients

Medtronic

Smart Insulin Pens
InPen Medronic

CR, ISF, BG target
Active insulin time/
Insulin on board

up to 4
time intervals

Bolus calculator
Reminders
Logbook

InPen App

BG meter
CGM (Guardian)

InPen

30-unit maximum dose
0.5-unit dose increments

Cartridges:
Novorapid, Fiasp
Humalog, Lyumjev

Smart Insulin Pens
InPen Medronic

BMG/CGM

Calculator/Recommendation Bar

Current Glucose measurement

Trend Graph

Real-time* with Guardian™ Connect CGM

Daily timeline

Time and size of last entry
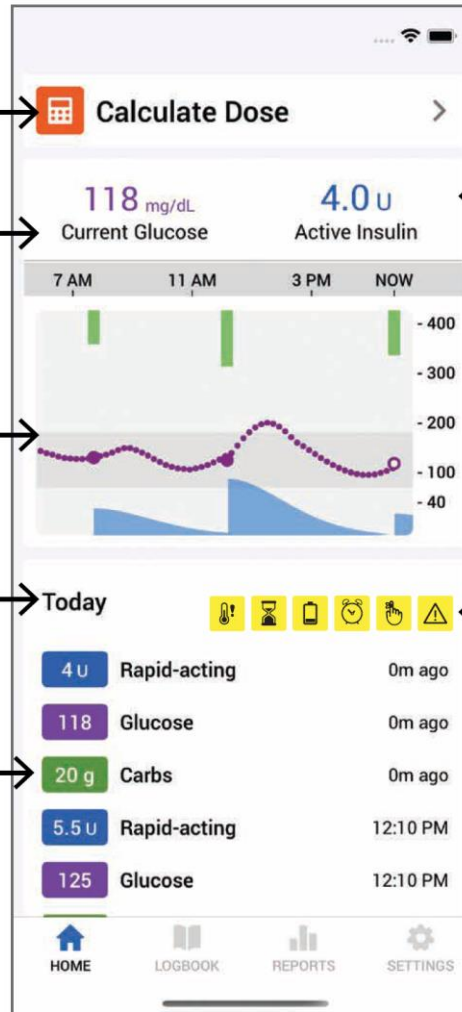
Current Active Insulin

(if enabled)

Notification icons:

Calculate Dose

118 mg/dL
Current Glucose

4.0 U
Active Insulin

7 AM   11 AM   3 PM   NOW

- 400
- 300
- 200
- 100
- 40

Today

4 U   Rapid-acting   0m ago
118   Glucose   0m ago
20 g   Carbs   0m ago
5.5 U Rapid-acting   12:10 PM
125   Glucose   12:10 PM

HOME   LOGBOOK   REPORTS   SETTINGS

Smart Insulin Pens- InPen Medronic

Comprehensive reports

Of a patients' glucose, insulin dosing, and meal data

Providing healthcare teams

Data and information to facilitate informed discussions with patients

All in one report

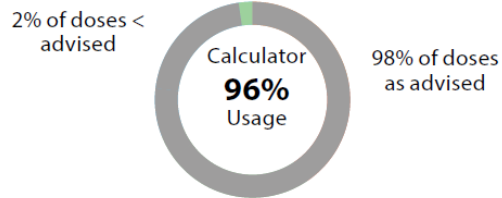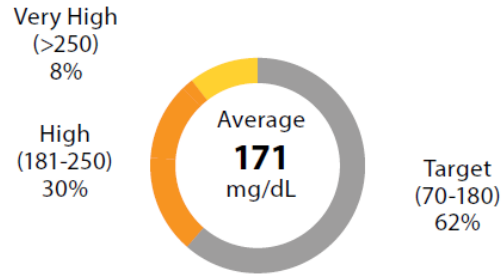Insights reports integrate insulin, BG, CGM, insulin dose and dose calculator information in an all-in-one report format

Fine-tuning based on data

Fine-tune insulin regimen and care plan based on data

Access to your patients' glucose and insulin data in a single CareLink™ report.

Medtronic

Smart Insulin Pens
InPen Medronic
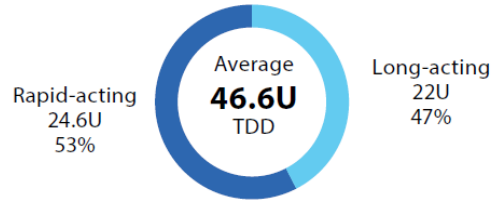
Missed doses:
Rapid-acting doses not logged within the time range configured in meal dose reminders are considered missed doses, unless you indicated that you did not eat that meal in the 24 missed dose reminder response.

Long-acting doses not logged within three hours before or after the long acting reminder time are considered missed doses.

Smart Insulin Pens - Roadmap

Kerr D, Warshaw H, Choi NY. Smart Insulin Pens Will Address Unmet Needs for People With Diabetes Using Insulin. Endocrine Today, 2019;17(5):20-21.

InPen integrated data report
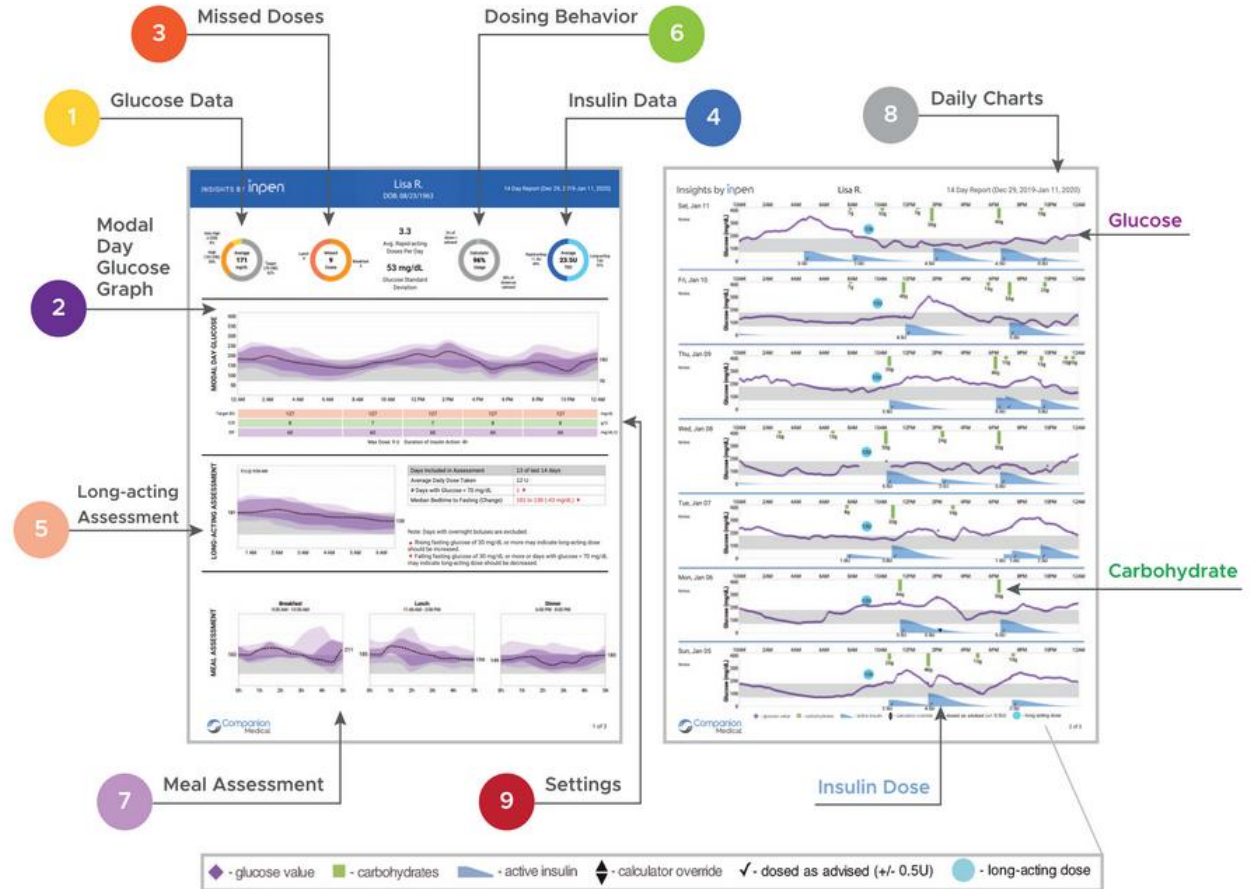
Warshaw H, Isaacs D, MacLeod J. The Reference Guide to Integrate Smart Insulin Pens Into Data-Driven Diabetes Care and Education Services. The Diabetes Educator. 2020;46(4_suppl):3S-20S.

Smart cap for insulin pens

Bigfoot Unity™
Diabetes Management System
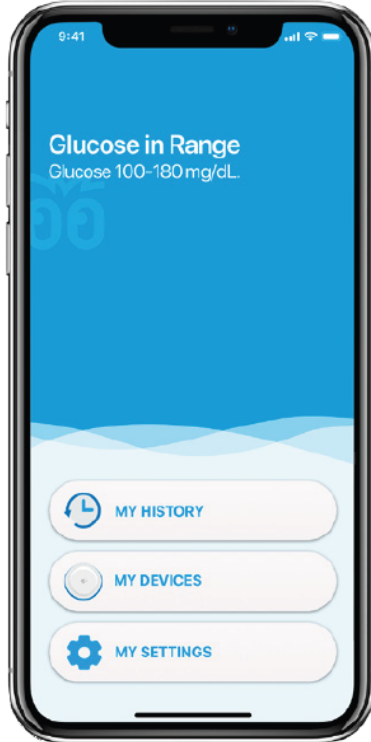
9:41

Glucose in Range
Glucose 100-180 mg/dL.

MY HISTORY

MY DEVICES

MY SETTINGS

3hr 10 min
since last dose

Lantus SoloStar®
insulin glargine injection
For Single Patient Use Only
100 units/mL (U-100)
3 mL Prefilled Pen

Black Cap for Long-Acting Insulin

disposable pens

320 mg/dL → | Correction
3u

Humalog
KwikPen®
insulin lispro injection, USP
(rDNA origin)

White Cap for Rapid-Acting Insulin

102 mg/dL

Bigfoot Unity App

Abbott FreeStyle
Libre 2 Sensor

Bigfoot Blood
Glucose Meter

Smart cap for insulin pens

Bigfoot Unity™ Diabetes Management System

Cap is off Pen
For Lantus

For Lantus

...ulin

disposable pens

Cap is off Pen
For Humalog

...g Insulin

For Humalog

320 Correction

2 mg/dL

Bigfoot Unity App

Abbott FreeStyle Libre 2 Sensor

Bigfoot Blood Glucose Meter

Bigfoot Unity™
Diabetes Management System

Black Cap for Long-Acting Insulin

χρόνος από την τελευταία ένεση

➢ Δυνατότητα λήψης alert στο κινητό τηλέφωνο ότι ίσως έχει χαθεί δόση

Smart cap for insulin pens

Bigfoot Unity™
Diabetes Management System

The White Cap for Rapid-Acting Insulin

Τιμή Σχ
Σύνδεση με BGM ή Freestyle Libre 2

βέλος τάσης

Δόση τελευταίας ένεσης
Γεύμα/διόρθωση

➢ White Cap → προσλαμβάνει και στέλνει στο App
τα δεδομένα των τελευταίων 8 ωρών από το Freestyle Libre2

Smart cap for insulin pens

Bigfoot Unity™ Diabetes Management System

Meal

Smart cap for insulin pens

Bigfoot Unity™ Diabetes Management System

Correction

Notes

Screen 1 (Correction):

9:41

‹Back   Insulin Settings   Edit

Correction Insulin

Enter the units of <Insulin>
for each range below.

GLUCOSE RANGE (mg/dL)	<INSULIN> (units)
150 - 200	1
201 - 250	2
251 - 300	3
301 - 350	4
351 - 400	5
Over 400	6

Need help?

Next

Screen 2:

9:41

‹Back   Insulin Settings

I take <Insulin> to lower glucose to a target of 120 mg/dL .

1 unit of <Insulin> lowers my glucose by | mg/dL

Done

1	2 ABC	3 DEF
4 GHI	5 JKL	6 MNO
7 PQRS	8 TUV	9 WXYZ
	0	⌫

Screen 3 (Notes):

9:41

‹Back   Insulin Settings

Notes

Use this space to enter notes about
your diabetes care. Notes are
displayed only in the App and are not
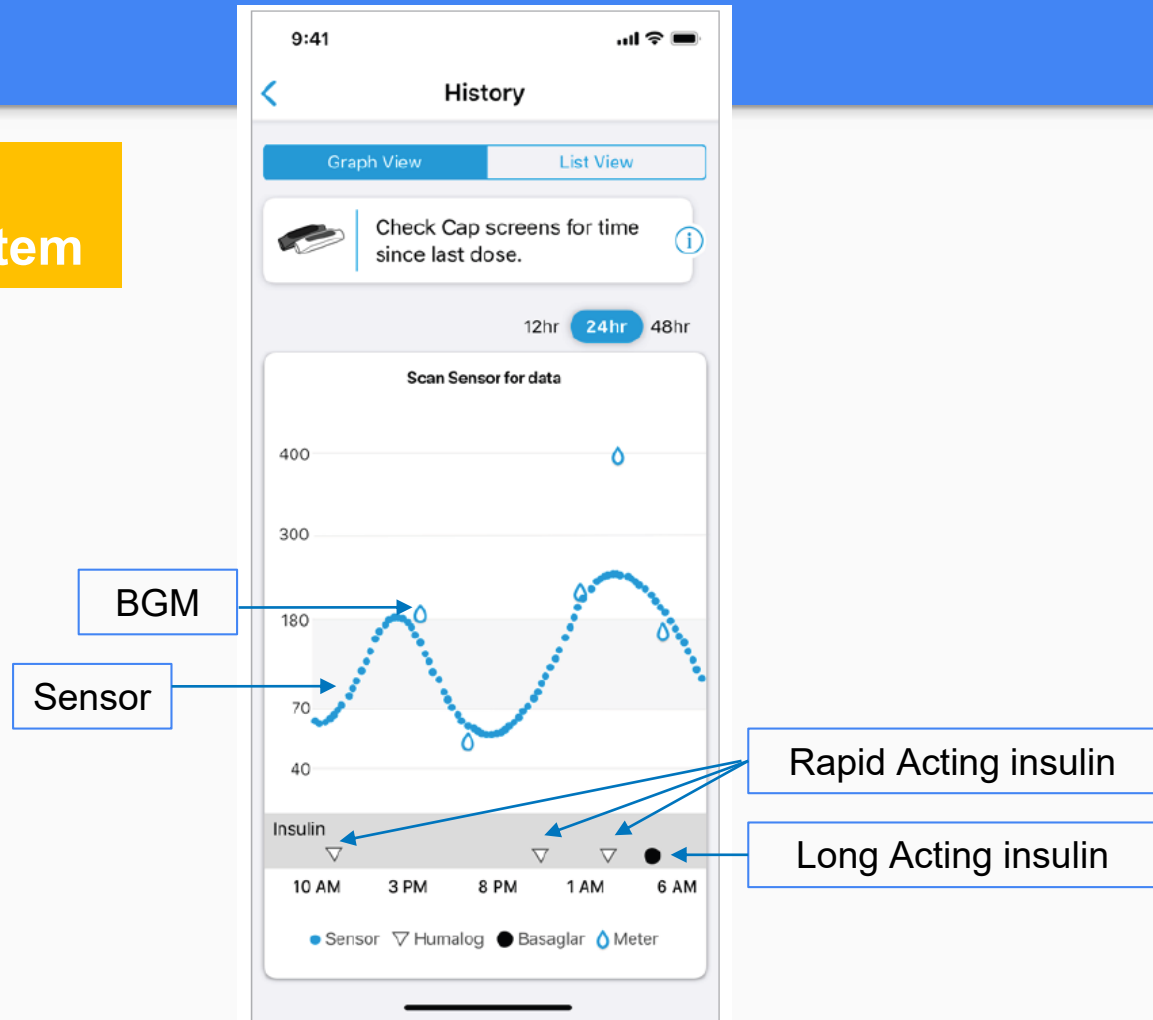used by Bigfoot Unity Caps.

Enter notes here (limit 1000
characters and 3 images)

Skip   Next

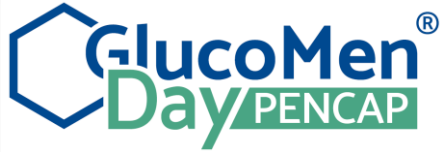# Smart cap for insulin pens

Bigfoot Unity™
Diabetes Management System

Smart cap for insulin pens

GlucoMen Day PENCAP®

Smart Insulin Pen Cap

02:10 07

disposable pens

Adherence Check

Check if insulin injections correctly occurred. Provides alarms in case a due injection is missed.

Record insulin data

Automatically record insulin dosing data and collect them with the other data from the GlucoMen Day line (CGM, SMBGs, Fitbit) in the same organized space (GlucoLog, Diasend (TBC)).

Check insuling storage

Monitor insulin storage temperature in real-time and provide alarms in case of improper conditions.

Build up a closed loop for MDI patients

The combination of the CGM, the bolus calculator and this cap could allow to build up a sort of closed loop system for MDI patients, where the user is assisted in dose calculation, and monitored for the correct insuling injection.

Compatible with insulin pens
Compatible with most common insulin pens

Injection Reminder
allow to remind insulin injection

Track Insulin Injection
track injection time

Data sharing via BT
Bluetooth sharing

Smart cap for insulin pens

Patient Diary App

GlucoLog Lite

GlucoLog RapidCalc
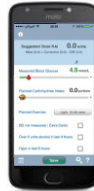
Insulin Bolus Calculator and Diary App

ICR, ISF,
BG target, active insulin time
Insulin on board

GlucoLog web

Data Management and Analysis Software

Συμμόρφωση στην ινσουλινοθεραπεία
Παράλειψη ενέσεων ινσουλίνης
(missed insulin injections)

Insulin adherence behaviours and barriers

Insulin adherence behaviours and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study

Peyrot et al. Diabet Med. 2012 May;29(5):682

Internet survey
China, France, Japan, Germany, Spain, Turkey, UK, USA
1530 insulin-treated patients (180 T1DM, 1350 T2DM)
1250 physicians

Patients:

33.2% reported insulin omission∕non-adherence at least 1 day in the last month, with an average of 3.3 days.

Physicians:

72.5% report that their typical patient does not take their insulin as prescribed, with a mean of 4.3 days per month of basal insulin omission∕non-adherence and 5.7 days per month of prandial insulin omission∕non-adherence

Insulin adherence behaviours and barriers

Reason	Patients % and rank	Physicians % and rank
Too busy	18.9% 1	41.9% 3
Travelling	16.2% 2	43.6% 2
Skipped meal	15.0% 3	44.8% 1
Stress or emotional problems	11.7% 4	32.2% 5
Embarrassing to inject in public	9.7% 5	36.8% 4
Challenging to take it at the same time everyday	9.4% 6	29.1% 6
Forgot	7.4% 7	2.0% 11
Too many injections	6.0% 8	26.4% 7
Avoid weight gain	4.0% 9	13.4% 9
Regimen is too complicated	3.8% 10	16.8% 8
Injections are painful	2.6% 11	7.8% 10

Παράλειψη γευματικής ινσουλίνης

Παράλειψη bolus

BG profile with insulin (blue), without (red)
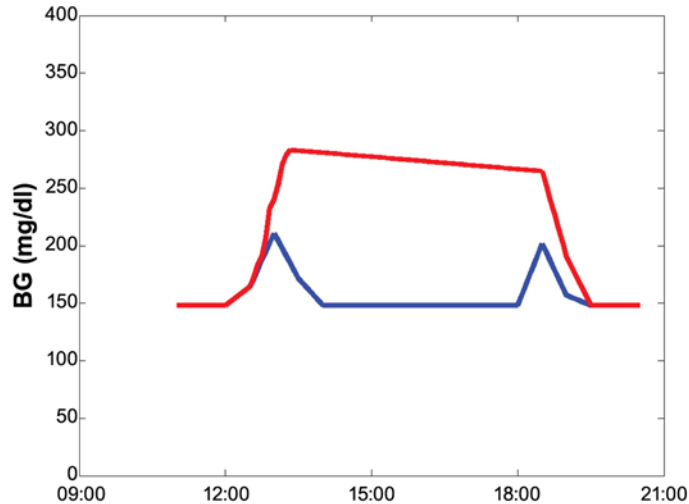
Figure 4. Omitting a meal bolus. The red curve is based on data from the DirecNet study.[8]

Παράλειψη ινσουλίνης βραδείας δράσης
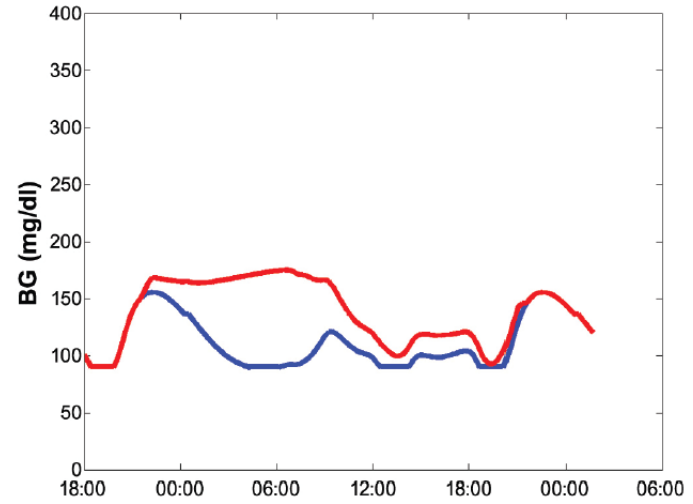

BG profile with insulin (blue), without (red)

Figure 6. Forgetting bedtime long-acting insulin. Simulated profiles from AIDA.

Jette Randløv et al., Journal of Diabetes Science and Technology Volume 2, Issue 2, March 2008

Παράλειψη γευματικής ινσουλίνης

Increased average glycaemia

Increased HbA1c

2.1 omissions per week

2.1 omissions per week

Case—bolus	ΔHbA1c using Rohlfing's relation	ΔHbA1c using Kilpatrick's relation
Forgetting breakfast bolus (**Figure 1**)	0.383 (±0.014)	0.617 (±0.022)
Omitting a meal bolus (**Figure 4**)	0.265 (±0.009)	0.426 (±0.015)
Forgetting lunch insulin. AIDA simulation (**Figure 5**)	0.278 (±0.010)	0.448 (±0.016)

Case—basal	ΔHbA1c using Rohlfing's relation	ΔHbA1c using Kilpatrick's relation
Forgetting long-acting insulin in the early afternoon (**Figure 2**)	0.171 (±0.006)	0.276 (±0.010)
Forgetting bedtime long-acting insulin. AIDA simulation (**Figure 6**)	0.333 (±0.012)	0.536 (±0.019)

Παράλειψη γευματικής ινσουλίνης

Injection remember rate	Injection forget rate	HbA1c deviation from optimum
100%	0%	Optimum treatment
90%	10%	0.3 to 0.4% points
80%	20%	0.6 to 0.8% points
70%	30%	0.9 to 1.2% points
61.5%	38.5%	1.8% points

Average Insulin remember rate (missing about 1 injection every 3!)

A Novo Nordisk study (2014) reported 59%

Randlov & Poulson 2015, Cramer 2004

Nonadherence to Insulin Therapy Detected by Bluetooth-Enabled Pen Cap Is Associated With Poor Glycemic Control

Munshi et al. Diabetes Care 2019;42:1129

USA
n=75
Young adults T1DM
older adults T1DM or T2DM on two or more insulin injections/day

Gocap Bluetooth-enabled pen for basal and bolus

Glycemic Control by Tertile of Adherence

■ A1c (%)

7,7%

8,6%

P=0.03

10

9

8

7

6

5

Most adherent tertile

Least adherent tertile
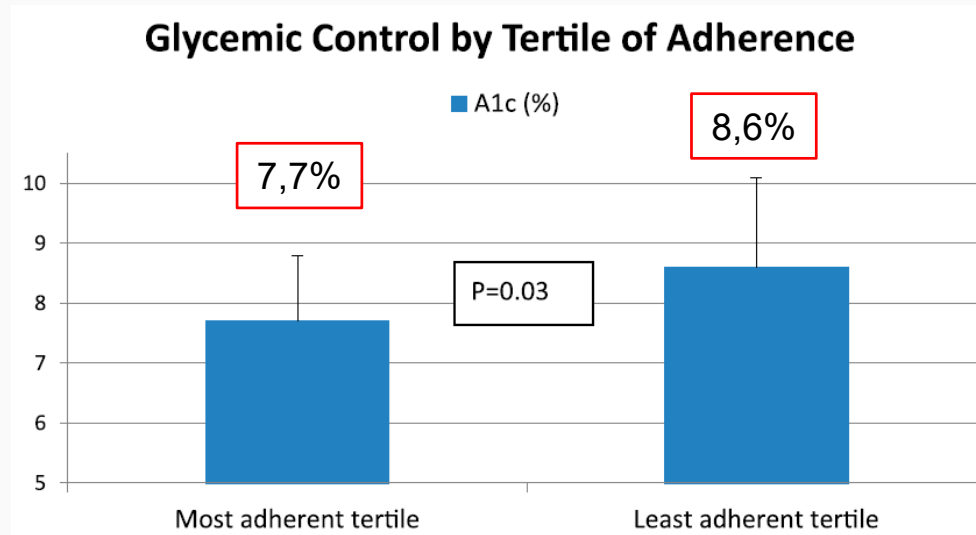
Missed basal insulin doses – Glycemic control – T1DM

Sweden
T1DM on CGM
n=32
Novopen 6, basal insulin (n=32)
Novopen 6, bolus insulin (n=28)
14 days
Prospective observational study

Sweden
T1DM on CGM
n=32
Novopen 6, basal insulin (n=32)
Novopen 6, bolus insulin (n=28)
14 days
Prospective observational study

Meals detection
GRID (Glucose Rate Increase Detector) algorithm:
CGM signal was ≥130 mg/dL and the rate-of-change was ≥95 mg/dL/hour) for the last two consecutive readings,
or
≥90mg/dL/hour for two of the last three readings.

Missed bolus dose (MBD):
without bolus injection
+60 minutes from the
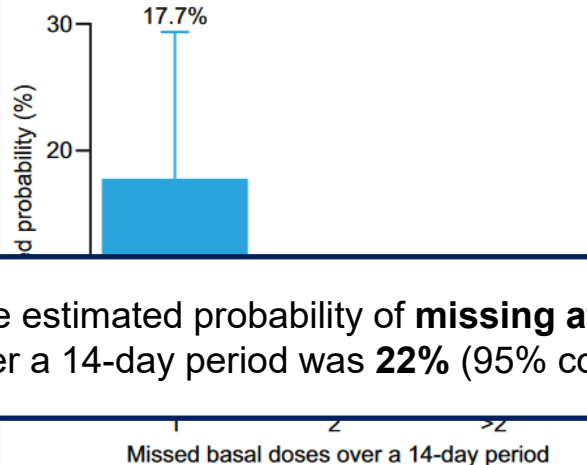
The estimated probability of **missing at least one basal insulin dose** over a 14-day period was **22%** (95% confidence interval: 10%-40%)

Missed basal doses over a 14-day period

17.7%

Missed basal insulin doses – Glycemic control – T1DM

Glycemic parameters	Estimated mean change per missed basal insulin injection (95% CI)	P	Estimated mean change per missed bolus insulin injection (95% CI)	P
TIR, %	−2.63 (−4.41, −0.71)	.005	−0.25 (−0.44, −0.07)	.008
TAR L1, %	0.34 (−0.71, 1.34)	.520	−0.03 (−0.14, 0.07)	.525
TAR L2, %	2.91 (0.99, 4.73)	.002	0.26 (0.07, 0.45)	.008
TBR L1, %	−0.28 (−0.65, 0.11)	.154	0.00 (−0.03, 0.04)	.808
TBR L2, %	−0.29 (−0.78, 0.22)	.256	0.02 (−0.04, 0.06)	.556
Mean glucose, mmol/L	0.44 (0.19, 0.69)	<.001	0.02 (−0.00, 0.05)	.085
%CV, %	−0.09 (−1.08, 0.95)	.855	0.19 (0.09, 0.29)	<.001
GMI, %	0.19 (0.08, 0.30)	<.001	0.01 (−0.00, 0.02)	.085

Ekberg et al.   Diabetes Sci Technol. 2022 Jul. doi: 10.1177/19322968221104142

Συμμόρφωση στην ινσουλινοθεραπεία
Χρόνος bolus για κάλυψη γεύματος
(bolus timing)

Time of bolus - Real world data

USA, UK, Germany
n = 906
adults with T1D (39%) and T2D (61%) treated with insulin therapy
Mean age: T1D 37 years, T2D 47 years

bolus dosing

before meals 57.0%
after meals 18.9%
with meals 12.7%
at varying times (11.5%)

	Bolus dose timing			
	before (n=516)	with (n=115)	after (n=171)	
Experienced out-of-range BG in past week[1]				
Hypoglycemia[2] n(%)	56	73	69	**
postprandial hypoglycemia (low BG after eating) n(%)	28	52	51	**
Hyperglycemia[3] n(%)	71	84	71	*
postprandial hyperglycemia (high BG after eating) n(%)	59	74	65	*

Tamborlane et al. Curr Med Res Opin. 2017 Apr;33(4):639

*p<0.05, **p<0.001

Time of bolus - Real world data
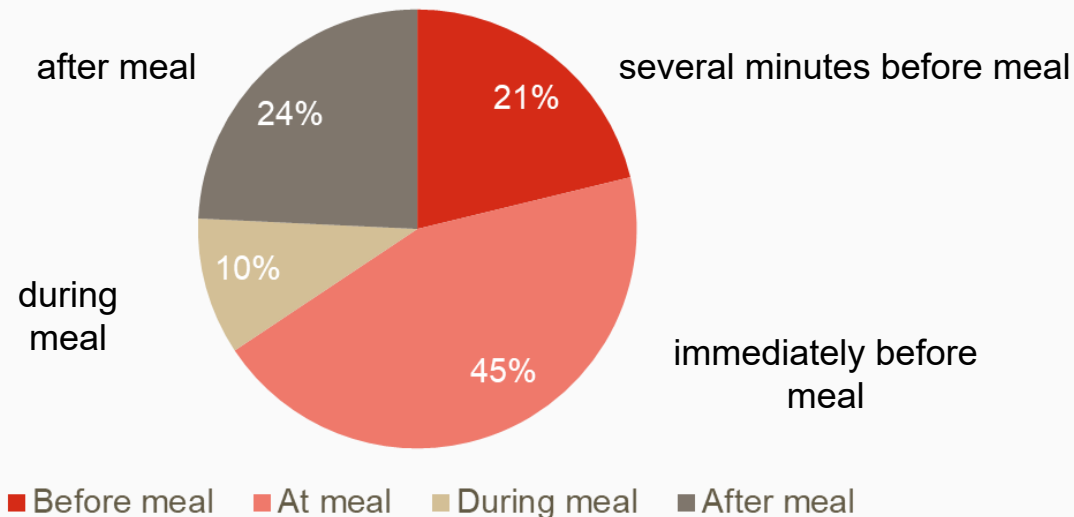
T1D Exchange clinic registry (USA)
n = 4768
age <26 years

HbA1c
Bolus before meal: 8,4%
Bolus during or after meal: 8,8%

p<0,001

Time of Mealtime Insulin Injection[1]

after meal

several minutes before meal

during meal

immediately before meal

21%

45%

10%

24%

■ Before meal   ■ At meal   ■ During meal   ■ After meal

Datye et al. J Diabetes Sci Technol. 2018 Mar;12(2):349

Time of bolus - Real world data

North and South America, Europe
n = 1483
T2D treated with insulin therapy
Mean age: 52 years

bolus insulin:

before meals 58% (n = 864)
(pre-meal cohort)

during or after meals 24% (n=354%)
(post-meal cohort)

before, during, or after meals 18%
(n=265) (mixed cohort).

Pre-meal cohort (N=864): 7% | 15% | 24% | 13% | 29% | 12%

Post-meal cohort (N=354): 8% | 16% | 19% | 10% | 40% | 7%

Legend: ■ 5.9% or less ■ 6.0%-6.9% ■ 7.0%-7.9% ■ 8.0%-8.9% ■ 9.0% or higher ■ Don't know

Schaper et al. Diabetes Ther (2017) 8:1319
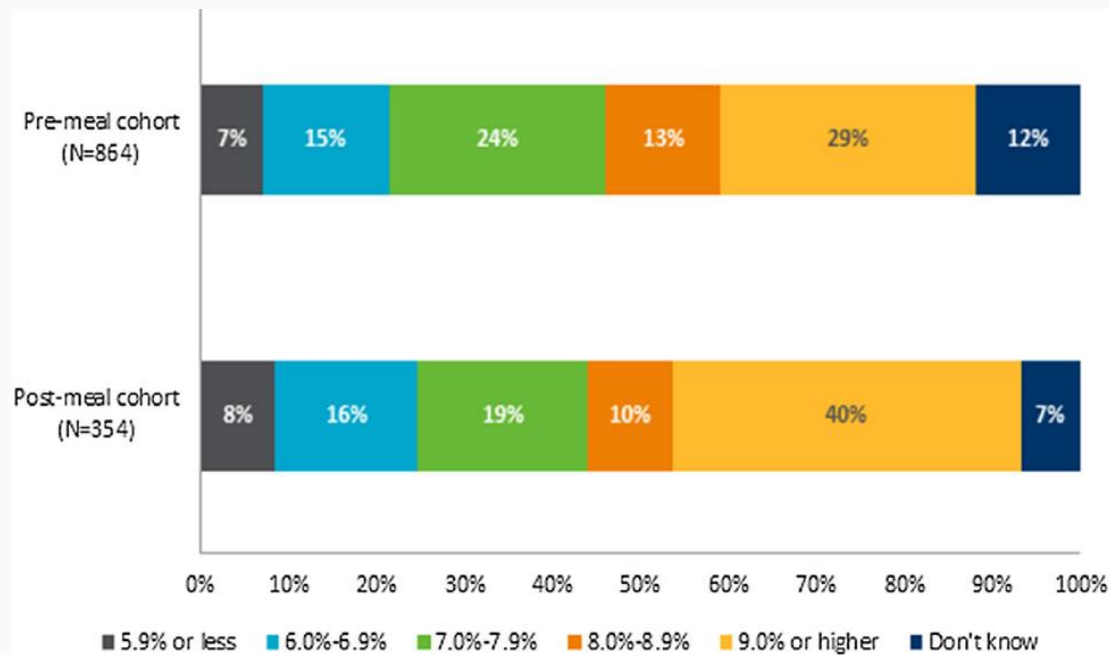
Time of bolus - Real world data

MMAS-8 components	Pre-meal cohort (N = 864)	Post-meal cohort (N = 354)
Sometimes forget to take insulin	32%	53%***
Had days not taking insulin in the past 2 weeks	20%	39%***
Forget to bring insulin when leave home	25%	34%**
Did take all insulin the day before the questionnaire	88%	77%***
Difficulty remembering to take all insulin (never)	55%	35%***
Cut back or stop taking insulin	17%	32%***
Stop taking insulin when symptoms controlled	17%	31%***
Feel hassled about sticking to treatment plan	44%	55%**

Schaper et al. Diabetes Ther (2017) 8:1319

Σωστός υπολογισμός bolus
(bolus calculation)

Σωστός υπολογισμός bolus (bolus calculation)

Η δυναμική προσαρμογή της ινσουλινοθεραπείας είναι απαραίτητο συστατικό στη θεραπεία του τύπου 1 διαβήτη

ADA Standards of care 2023
ΕΔΕ Κατευθυντήριες οδηγίες 2023

Δυναμική προσαρμογή της ινσουλινοθεραπείας → βελτίωση γλυκαιμικού ελέγχου

Αναλογία ινσουλίνης/ γρ. υδατανθράκων ή ισοδύναμο (Insulin to Carbohydrate Ratio, ICR)

Παράγοντας ευαισθησίας ινσουλίνης
    (Insulin Sensitivity Factor, ISF)

Στόχοι Σχ (BG targets)

↓ μεταγευματικής υπεργλυκαιμίας

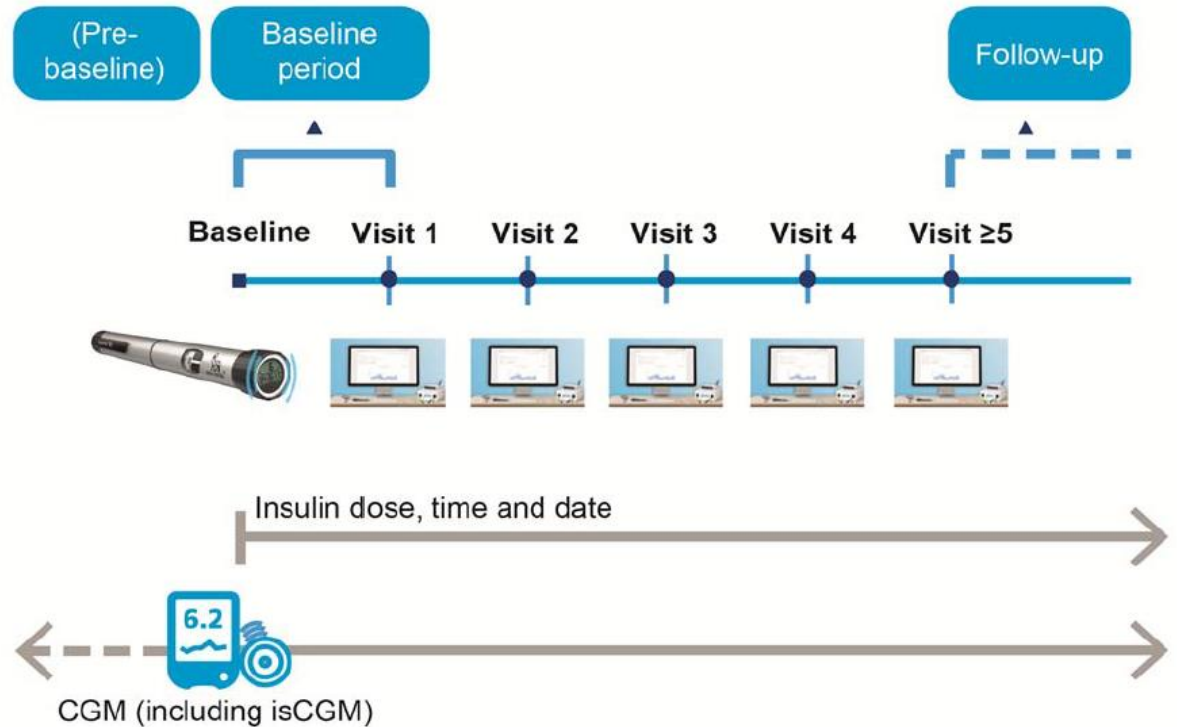↓ μεταγευματικής υπογλυκαιμίας

Δεδομένα από κλινικές μελέτες

12 Swedish diabetes clinics
T1DM on CGM
n=94
Prospective observational study

mean time between visits: 71 days

Meals detection
GRID (Glucose Rate Increase Detector) algorithm:
CGM signal was ≥130 mg/dL and the rate-of-change was ≥95 mg/dL/hour) for the last two consecutive readings,
or
≥90mg/dL/hour for two of the last three readings.

Missed bolus dose (MBD):
were meals without bolus injection within -15 and +60 minutes from the start of a meal

NovoPen® 6 − T1DM
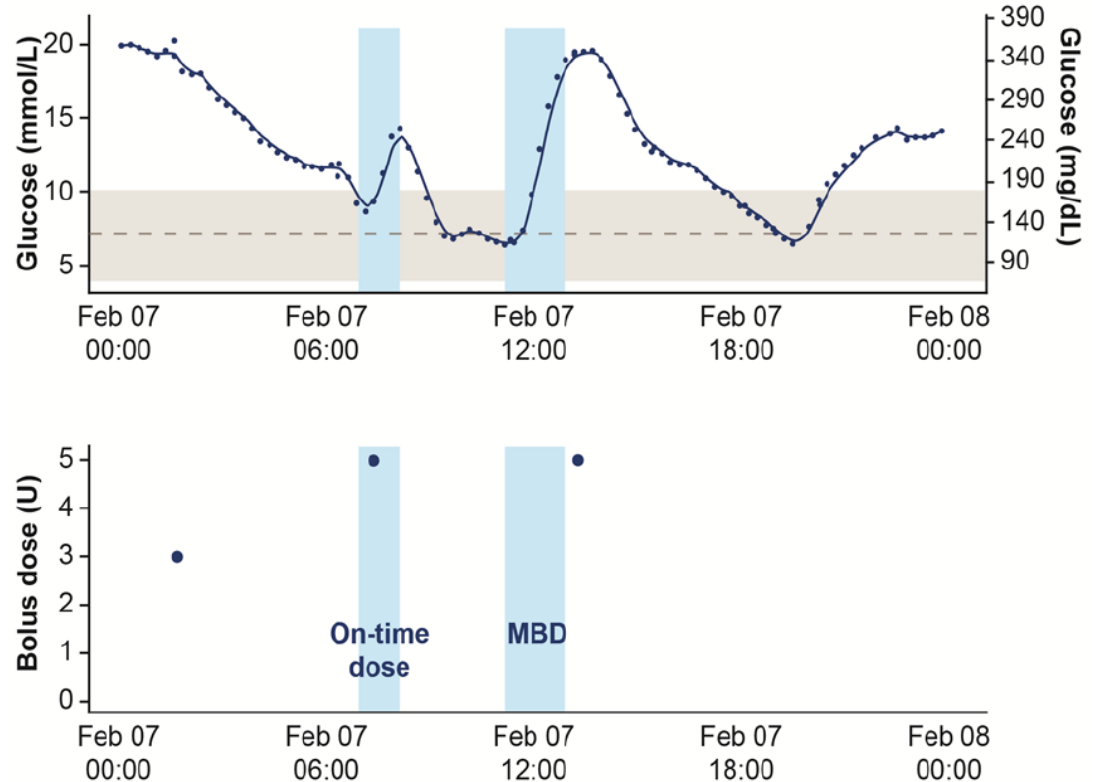
baseline to follow-up period

TIR   ↑ 1.9 hours/day; p<0.001

TAR   ↓ 1.8 hours/day; p<0.003

L1 hypo   ↔

L2 hypo   ↓ 0.3 hours/day; p<0.005

use of a connected pen might help to facilitate more **informed dialogs between HCPs and people with T1D**

Missed bolus dose (MBD): ↓ 43% (p=0.002)

decrease from 25% to 14% based on the assumption that participants had three main meals/day.

P: CLINICAL THERAPEUTICS/NEW TECHNOLOGY—INSULIN DELIVERY SYSTEMS | JUNE 01 2020

975-P: Effect of Late Bolus Injections on Glycemic Variability Studied by Connected Pens ⊘

Jendle et al Diabetes 2020;69(Supplement_1):975-P

12 Swedish diabetes clinics
T1DM on CGM
n=96

late-bolus dose:
bolus dose given **60-120 minutes**
after the estimated start of the meal

mean number of late-bolus doses

Baseline:	0.32 per day
Smart pen follow up:	0.18 per day

↓ 42% ($p = 0.005$).

A significant correlation between the **timing of the bolus** dose and the **coefficient of variation (CV) of the CGM** signal was found
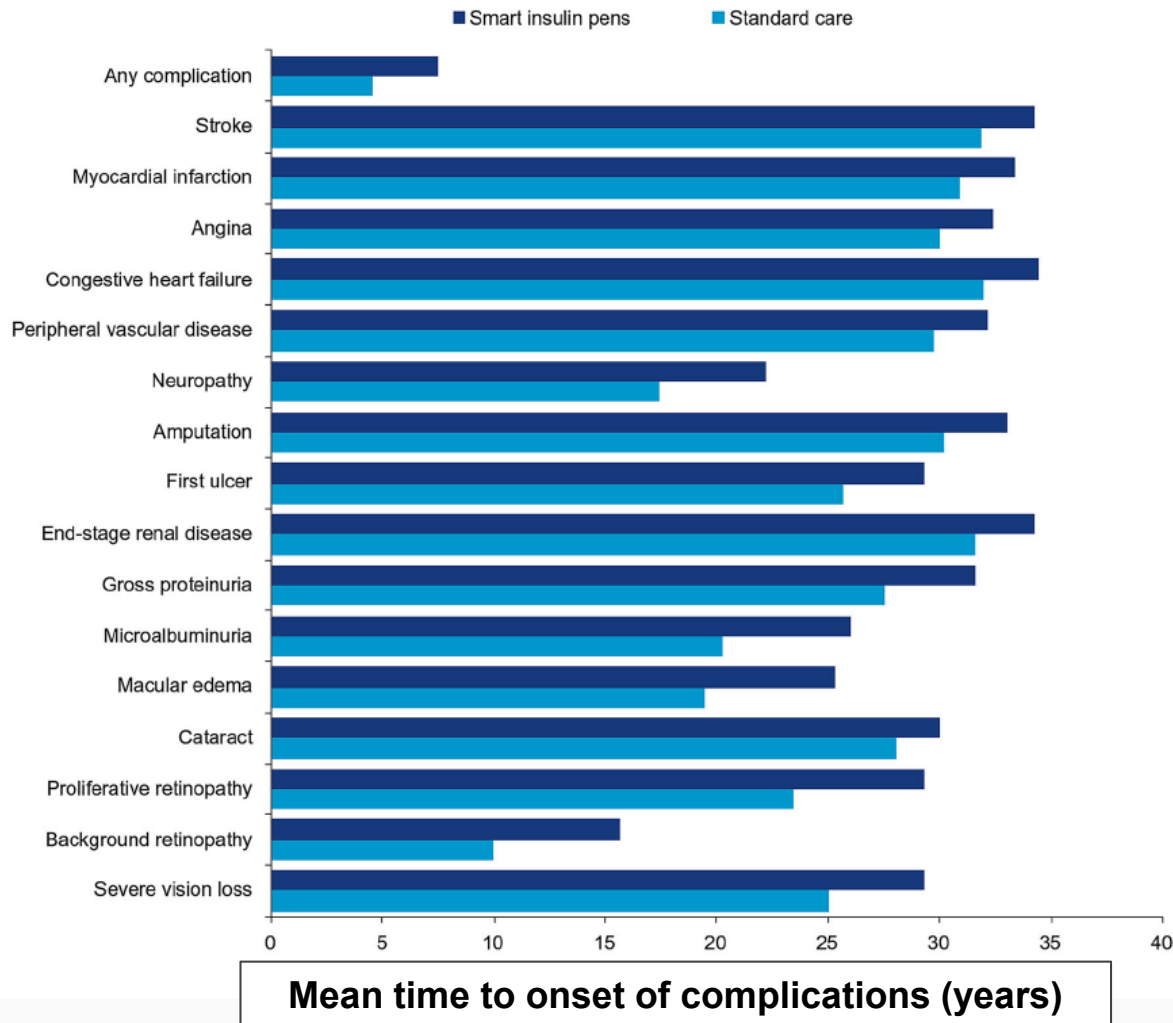
each 10-minute delay of the bolus dose was associated with an increase of 0.5% CV ($p < 0.0001$) on average.

Cost-Effectiveness Analysis – T1DM - Sweden

Adolfsson et al, Sweden, T1DM → TIR ↑ 1.9 hours/day; p<0.001

T1DM: Smart pen vs Standard care,
simulated cohort based on Swedish National Diabetes Register

Jendle et al Diabetes Ther (2021) 12:373

Mean time to onset of complications (years)

Legend: Smart insulin pens / Standard care

Partial visible text (right side, obscured):
...Sweden
...s/day; p<0.001
...etes Register

Sweden

Smart insulin pens ■ Standard care

Direct and Indirect cost

Mean time to onset of complications (years)

	Smart insulin pens	Standard care
Combined costs	1,541,648	2,039,643
Indirect costs	906,049	1,279,774
Direct costs	635,599	759,869

Jendle et al Diabetes Ther (2021) 12:373
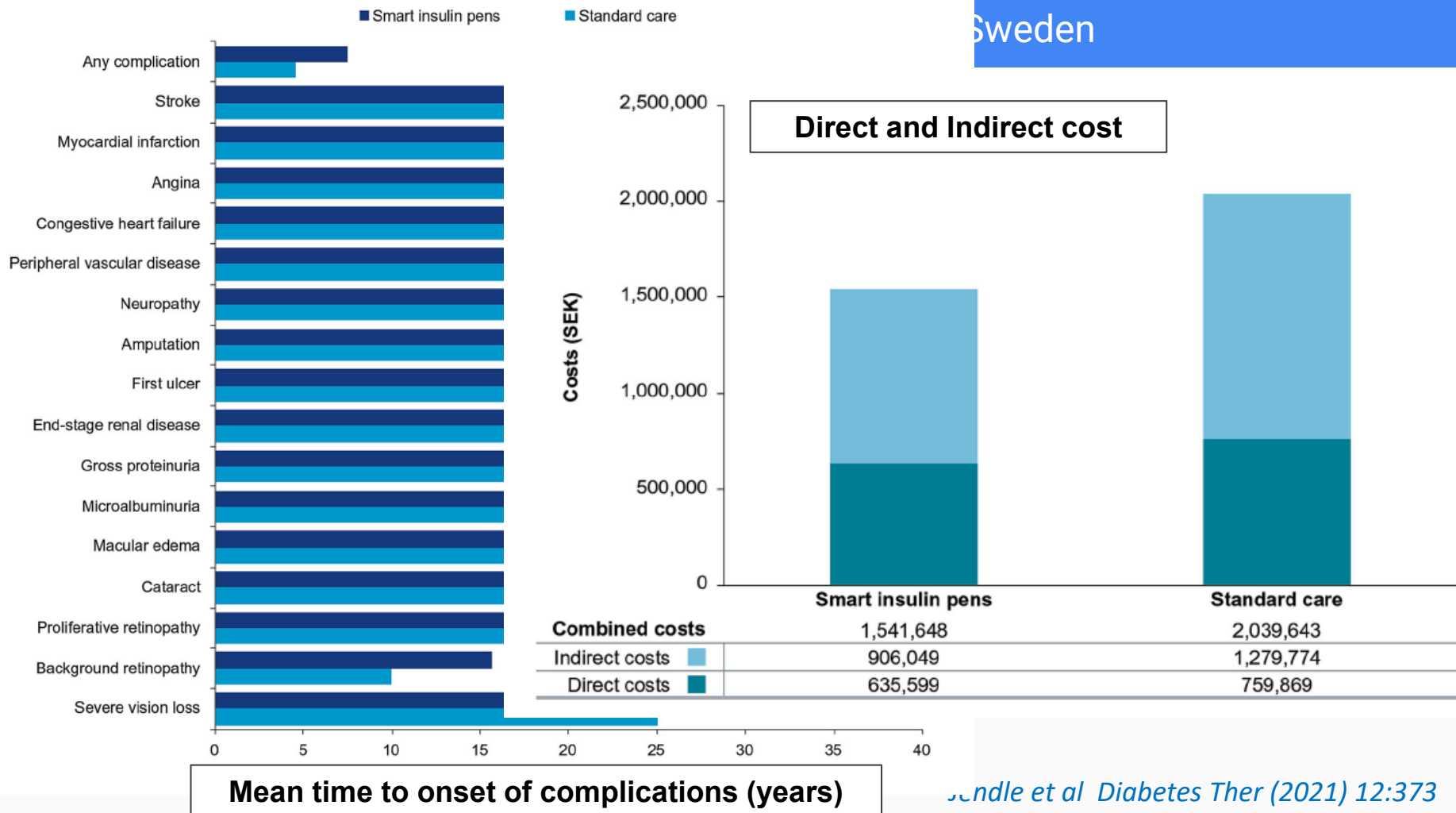
Smart insulin pen cap (Insulclock) – T1DM

Smart insulin pen cap (Insulclock)
Spain
T1DM uncontrolled
n=16
Randomized Trial: active vs masked
4weeks

masked FreeStyle Libre Pro CGM device (professional use)

Meals detection
GRID (Glucose Rate Increase Detector) algorithm

Late meal bolus (mistimed): insulin **≥30 min** after a glucose rise
Missed dose: no iinsulin **≥2 h** after a glucose rise

Insuclock (vs masked)

mean daily blood glucose:	-27 mg/dL	P < 0.013
SD:	-14,4 mg/dL	P = 0.003
TIR:	+7%	P = 0.038
TAR:	-12,5%	P = 0.0026
number of missed insulin doses / month:	-3,9	P = 0.14
number of mistimed insulin doses / month:	-5,4	P = 0.032
Insulin Treatment Satisfaction Questionnaire (ITSQ)	↑	

Smart insulin pen cap (Insulclock) – T1DM
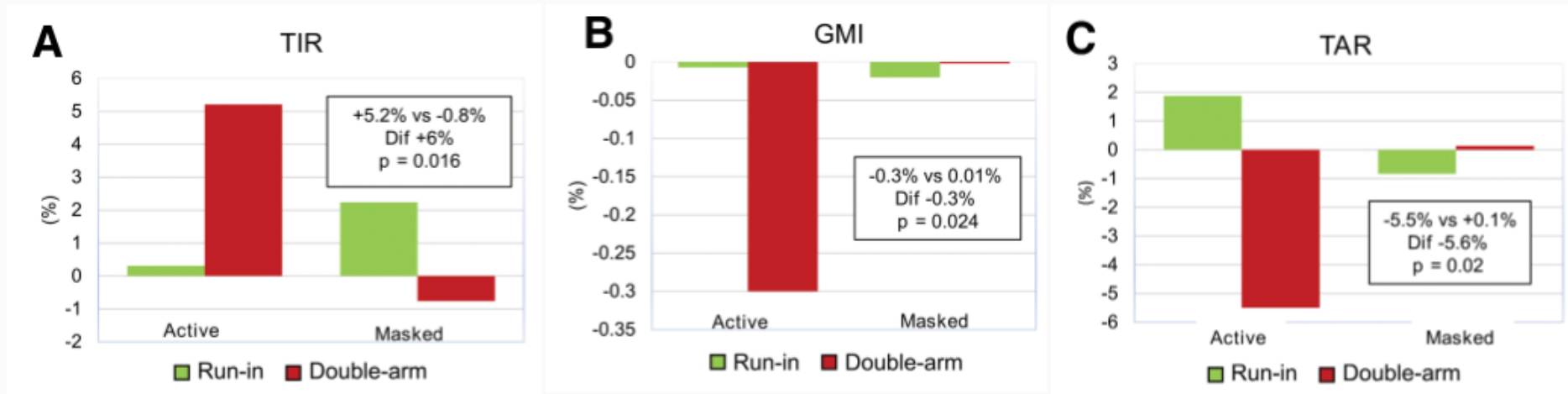
Smart insulin pen cap (Insulclock)
Spain
T1DM on Freestyle Libre 2
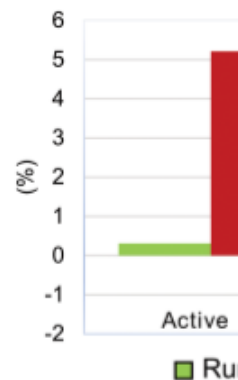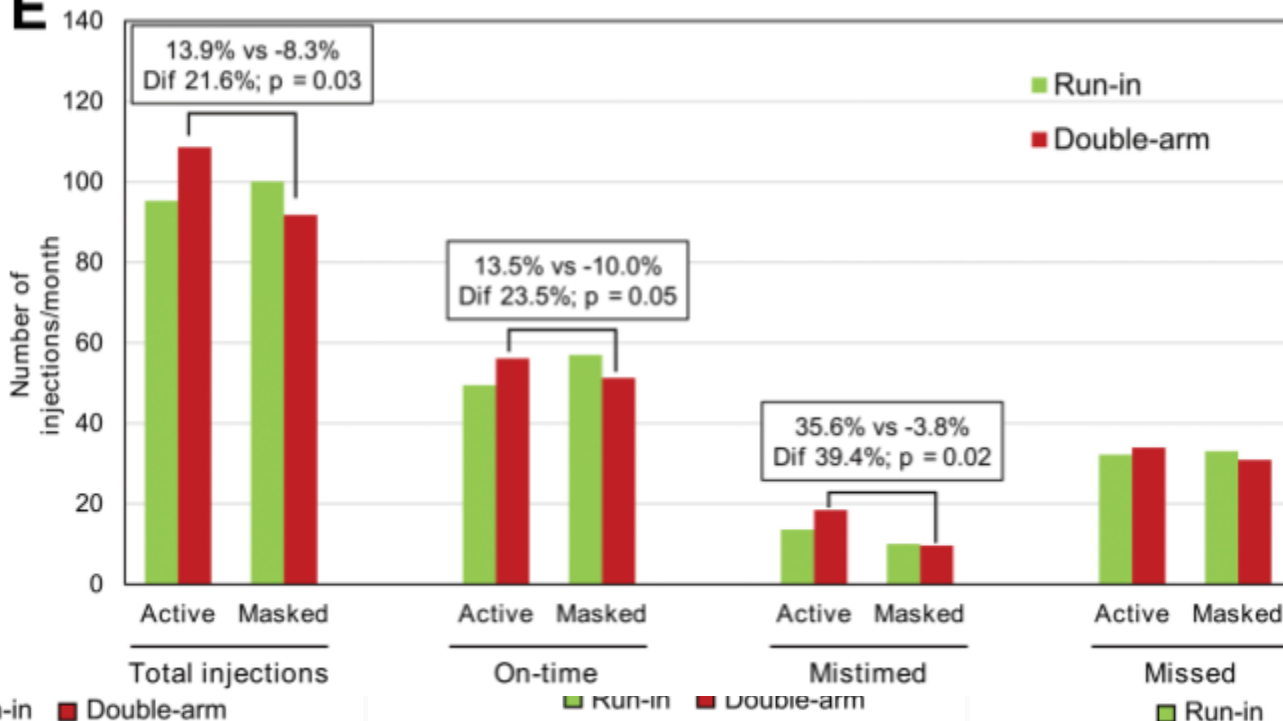**n=55**
Randomized Control Study
6 weeks active vs masked

Gomez-Peralta et al Diabetes Care. 2023 Jan 1;46(1):206

Smart insulin pen cap (Insulclock) – T1DM

Smart insulin p...
Spain
T1DM on Frees...
n=55
Randomized C...
6 weeks active...

Bolus calculator

Smart pens / insulin caps → Καταγραφή / Υπενθύμιση δόσης

Smart pens / insulin caps → Bolus calculator

Δεν υπάρχουν κλινικές μελέτες που να εξετάζουν το επιπλέον όφελος από τη σύνδεση με υπολογιστή δόσης

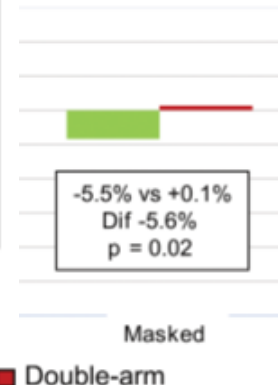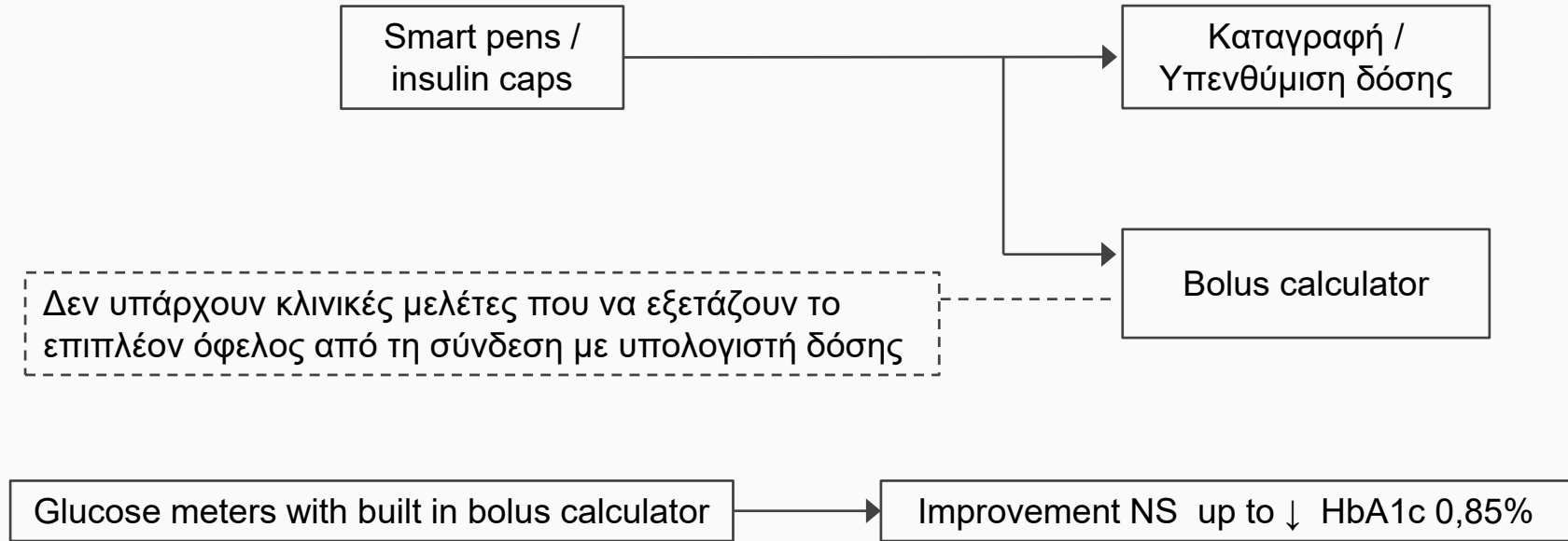Glucose meters with built in bolus calculator → Improvement NS up to ↓ HbA1c 0,85%

Colin et al Diabetes Ther. 2013 Jun;4(1):1
Gonzalez et al Diabetes Technol Ther. 2016 May;18(5):282

Smart Meters

	Study design	Results
Maurizi et al.	3- to 6-month randomized trial comparing patients using an ABC to a control group 40 consecutive adult type 1 diabetes patients	At 3 months: nonsignificant improvement in HbA1c levels (-0.61%) At 6 months: significant improvement in HbA1c levels (-0.85%; P<0.05)
Garg et al.	1-year open-label, randomized, controlled trial 123 adult type 1 diabetes patients randomized on a 1:1 basis to either an ABC or control group	HbA1c improvement by 0.6% at 12 months (P<0.02) Higher proportion of ABC users achieving HbA1c<7.5% (P<0.01)
Gonzalez et al.	36 weeks, crossover, prospective, randomized, controlled, multicenter study T1DM under MDI treatment (n=51)	Control HbA1c -0.39%; ABC HbA1c -0.52% [P = 0.8]

ABC: automated bolus calculator

Colin et al Diabetes Ther. 2013 Jun;4(1):1
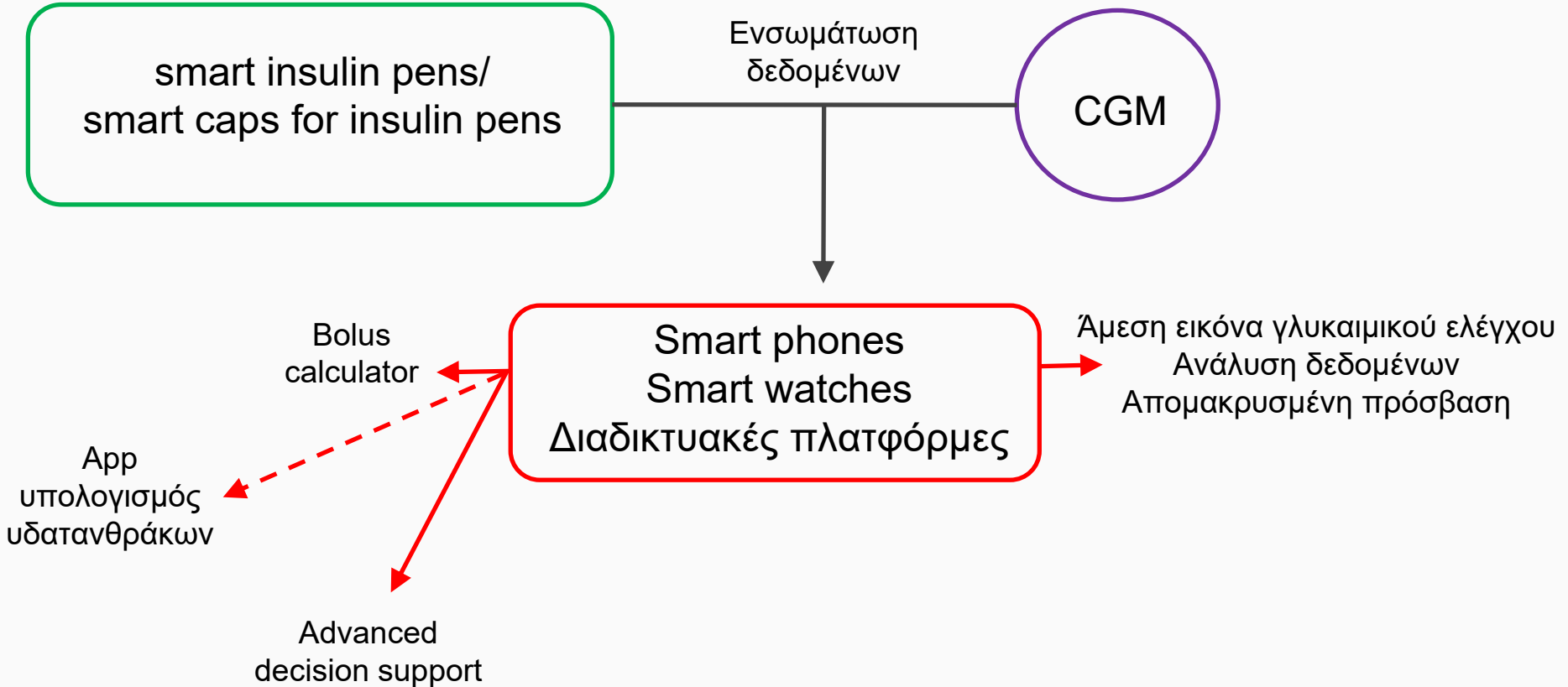Maurizi et al Diabetes Technol Ther. 2011;13:425
Garg et al Diabetes Technol Ther. 2008;10:369
Gonzalez et al Diabetes Technol Ther. 2016 May;18(5):282

ΣΥΝΟΨΗ

- Οι έξυπνες πένες ινσουλίνης (smart insulin pens) και τα έξυπνα καλύμματα για πένες ινσουλίνης (smart caps for insulin pens) αποτελούν ένα δυναμικά αναπτυσσόμενο πεδίο

- Λίγες κλινικές μελέτες με υποσχόμενα αποτελέσματα όσον αφορά στο όφελος από την καλύτερη συμμόρφωση

- Δεν υπάρχουν ακόμη κλινικά στοιχεία για το πιθανό όφελος από τη βοήθεια που μπορούν να προσφέρουν στη δυναμική προσαρμογή της ινσουλινοθεραπείας (bolus calculator)

- Στην πλήρη ανάπτυξη τους τα συστήματα αυτά θα μπορούσαν να προσφέρουν ένα περιβάλλον με πολλά κοινά στοιχεία με αντλία ινσουλίνης

Ευχαριστώ
για την προσοχή σας