Smarta insulinpennor och -hättor

Johan Jendle

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Utveckling av insulinpennor och uppkoppling

Connected pens / Smartpen systems / Smartcaps

NovoPen 6 / NovoPen Echo Plus

Novo Nordisk insulin
1 E / 0,5 E bolus o/e basinsulin
Kompatibel med flera appar
Glooko + samtliga CGM utom Medtronics
3 års garanti/5 års funktion

InPen System

Novo Nordisk, Lilly insulin
0,5 E bolus insulin
Specifik app (kalkylator etc)
Glooko via Apple Health App
1 års garanti/funktion

Mallaya insulin hätta

Novo Nordisk, Lilly, Sanofi insulin
Motsvarande som vald penna
Specifik app
Roche plattform i Frankrike
2 års garanti

Mallaya

De flesta individer som använder insulinpennor använder idag förfyllda flergångspennor

Några studieresultat finns inte avseende Mallaya men Biocorp har knutit ett flertal olika partners inkluderat Novo Nordisk och Sanofi

Nedladdning sker via Glooko

Smart insulin caps	SoloSmart Button	Tempo Smart Button	Dialoq
Picture			
Firm	Sanofi	Lilly	Novo Nordisk
Fits on	Solostar	Tempopen	FlexTouch
Approval	CE-label	CE- an FDA-label	
Dedicated app	yes: Mallya app	yes	no
Sends data to	Gluci-Check & RDCP, YourLoops?	MySugr, RDCP, Glooko, MyDiabby, Welldoc, Dexcom	MySugr, Glooko, Libreview
Battery	Rechargeable via USB	1 year warranty	?

NovoPen® 6 / NovoPen Echo® Plus
Smart insulin injection device

Connectivity

- Dose log (time & dose) with 800 dosing events
- Near Field Communication (NFC) using open standards*

Basic features

- 60/30 units max dose
- 1/0,5 unit dose increment
- 5 years lifetime
- No battery exchange or recharge

Dose setting display

- Easy to use, easy to read

Memory Function

- Last insulin dose and time

NovoPen 6 och NovoPen EchoPlus

diasend®
Glooko AB

FreeStyle LibreLink
Abbott

mySugr®
mySugr® GmbH

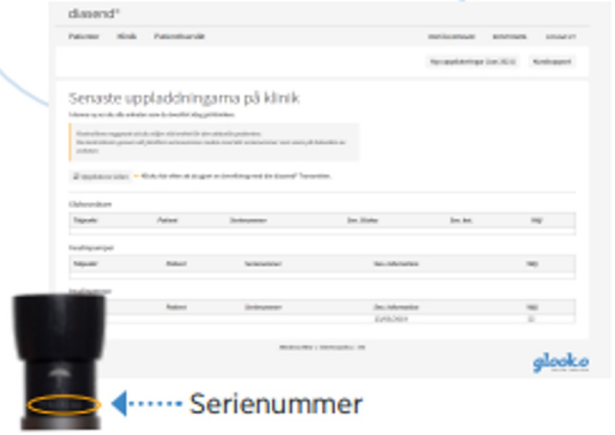
G6®
Dexcom

1. LADDA UPP DATA

- Se till att Glooko® Transmitter är påslagen och redo att ladda upp.
- Se till att pennans doseringsknapp är helt intryckt och att dosräknaren står på noll.
- Placera den smarta insulinpennan i ringen på ovansidan av Glooko® Transmitter. Uppladdningen startar automatiskt.
- Uppladdningen är klar när displayen är grön.
- Logga in på ditt diasend®-konto för att titta på datan.

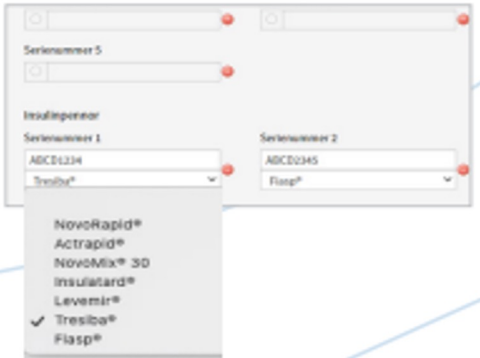
2. KOPPLA EN PENNA TILL EN PATIENT

- Gå till vyn "Senaste uppladdningarna på klinik" och markera den pennan du vill registrera.
- Du identifierar rätt penna med hjälp av dess serienummer, som du kan se när doserings-kolven är helt utdragen (se bild).
- Serienumret börjar alltid med PEN och endast tecknen efter PEN visas i diasend®.



3. VÄLJ INSULIN

När en penna registreras måste det insulin som används i pennan anges. Varje patient kan registrera upp till fyra pennor.



NovoPen 6 och NovoPen EchoPlus

diasend®
Glooko AB

FreeStyle LibreLink
Abbott

mySugr®
mySugr® GmbH

G6®
Dexcom

SÅ HÄR LADDAR DU UPP DATA FRÅN DIN SMARTA INSULINPENNA

1. Du behöver en telefon med NFC-chip för att ladda upp data från en smart insulinpenna.
2. Se till att doseringsknappen är helt intryckt och att dosräknaren står på noll.
3. Starta diasend® Mobile App och logga in. Appen finns att ladda ner från AppStore (iOS) och Google Play (Android).
4. Håll insulinpennan mot telefonens NFC-chip. Överföringen av data startar automatiskt. När överföringen är klar hörs ett kort pling.

5.

Första gången du laddar upp en penna kommer du att bli ombedd att välja vilket insulin pennan ska användas till.

Rapporter visar dina insulindoser över en tidslinje.

Du kan också se ett cirkeldiagram över dina insulin-doser i samma vy.

INPEN

InPen

Share data from multiple InPens to the same app

Connects to the app via Bluetooth®

Available in two colours:
Blue: compatible with Novo Nordisk NovoRapid®, 3 ml cartridges (300 units)
Grey: compatible with Lilly Humalog® 3 ml cartridges (300 units)

Monitors insulin temperature

Battery lasts a full year with no need to charge

Hu
tra

:s of Eli Lilly and Company. Fiasp®, Novorapid® and Novo Nordisk Insulin Aspart are registered

InPen system

Ett data-drivet diabetes management system, Smart Insulin Pen SIP* teknologi, glukossensor och en app.

InPen

Bigfoot Unity (FDA men ej CE-godkänd)

*SIP Session Initiation Protocol

Ilkowitz J, Wissing V, Gallagher MP. Pediatric Smart Insulin Pen Use: The Next Best Thing. JDST. 2021:19322968211041362.

InPen system

Endast för bolusinsulin, flera tillverkare (Novo, Lilly, Sanofi)

Flertal påminnelser: missad dos, glukoskontroll, byte av ampull, insulin temperatur, lågt batteri

Bolus kalkulator / aktivt insulin

Koppling till CGM system (Dexcom och Medtronic) och Glooko möjligt via Apple Health App

Basala rapporter i applikation (Companion)

Gildon BW. InPen Smart Insulin Pen System: Product Review and User Experience. Diabetes Spectr. 2018 Nov;31(4):354-358

Vanligt med missad bolus dos (CSII)

Missad bolus dos <1 per vecka;
- medel HbA1c 8.0%

Missad bolus dos ≥1 per vecka;
- medel HbA1c 8.8%

38% missade >15% av bolus doserna dagen före

Variationen i HbA1c kan förklaras av frekvensen bolusdoser

› Pediatrics. 2004 Mar;113(3 Pt 1):e221-4. doi: 10.1542/peds.113.3.e221.

Missed insulin meal boluses and elevated hemoglobin A1c levels in children receiving insulin pump therapy

Jonathan Burdick [1], H Peter Chase, Robert H Slover, Kerry Knievel, Laura Scrimgeour, Aristides K Maniatis, Georgeanna J Klingensmith

› Pediatr Diabetes. 2009 Apr;10(2):142-8. doi: 10.1111/j.1399-5448.2008.00462.x. Epub 2008 Oct 24.

Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes

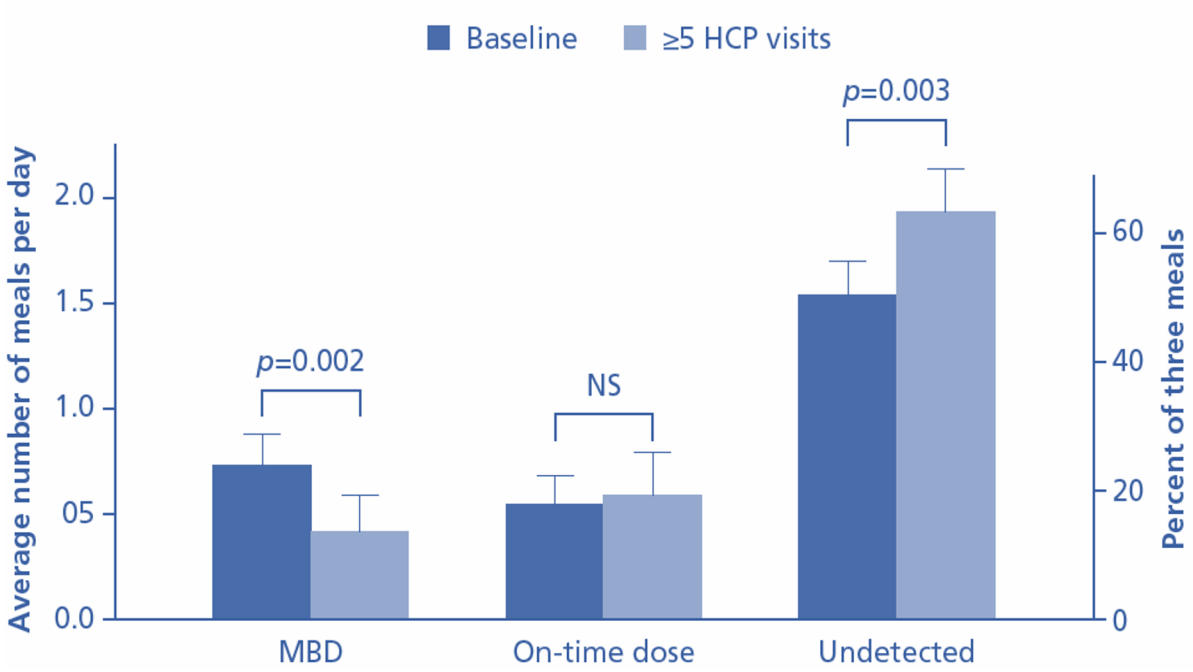
Anna Lindholm Olinder [1], Anna Kernell, Bibbi Smide

NP6 Signifikant minskning av missade bolus doser

From baseline to after ≥5 HCP visits:

- MBD **decreases by 43.1%** from 0.74 to 0.42 per day (*p*=0.002, n=81)
- This means more actual meals are dosed

- Undetected meals increases - probably because well-dosed meals show less variation in the CGM signal

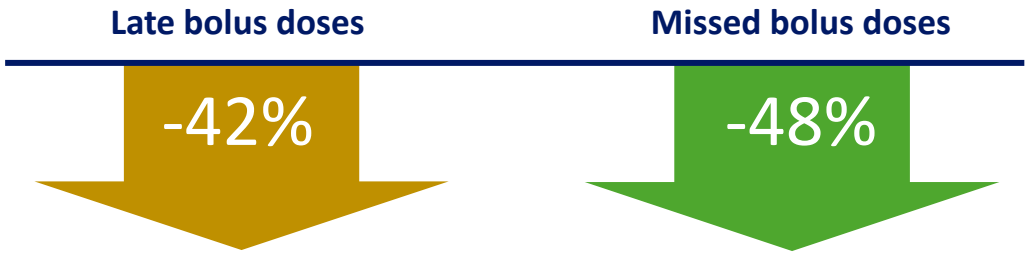


Adolfsson P et al. Diabetes Technol Ther 2020; doi:10.1089/dia.2019.0411

NP6 Distribution av bolus doser och effekten av sent givna doser vad gäller glukossvängningar

At follow-up, there were fewer late doses or missed bolus doses per day than at baseline.

	Baseline	Follow-up	
	Number per day, mean (95% CI)		p value
Late bolus doses	0.32 (0.26, 0.39)	0.18 (0.13, 0.27)	0.005
Missed bolus doses	0.49 (0.41, 0.57)	0.26 (0.19, 0.35)	<0.0001



Late bolus doses were associated with increased glycaemic variability throughout the day.

Glycaemic measure	Change per 10-minute later bolus injection, mean (95% CI)	p value
TIR, %	−0.19 (−0.43, 0.05)	0.13
TBR L1, %	0.03 (−0.03, 0.08)	0.36
TBR L2, %	0.05 (−0.01, 0.10)	0.11
TAR, %	0.09 (−0.16, 0.34)	0.49
Mean glucose concentration, mmol/L / mg/dL	0.03 (0.01, 0.06) / 0.62 (0.11, 1.13)	0.02
%CV, %	0.47 (0.33, 0.61)	<0.0001

Jendle J, et al. Presented at the American Diabetes Association 80th Scientific Sessions Virtual Meeting, June 12–16, 2020.

Basal injection patterns

Figure A

- Greater variability in basal injection timing was observed in adults than in children
- Among both adults and children, there were patients who administered basal doses late at night or in the early hours of the morning

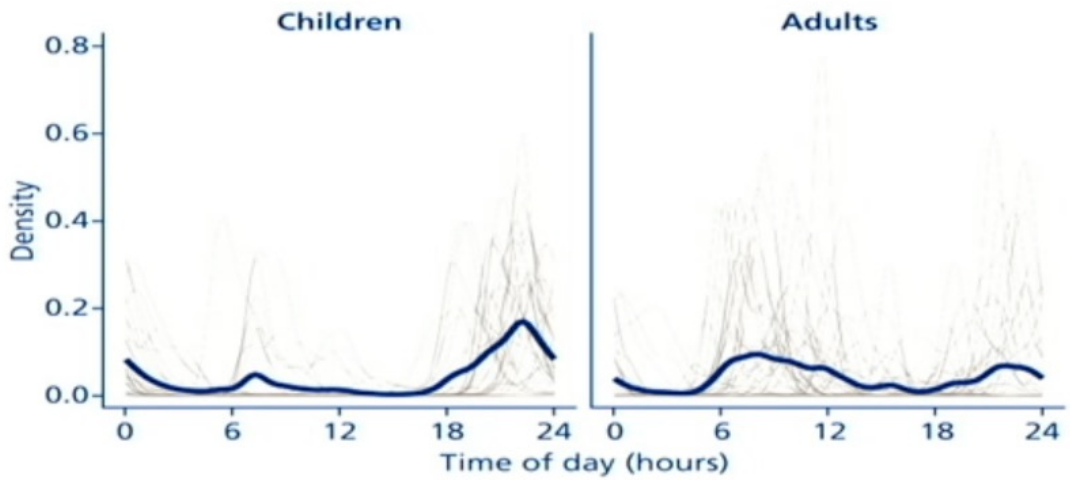


Figure B

The flexibility that degludec provides was clearly required by some adults and children with T1D

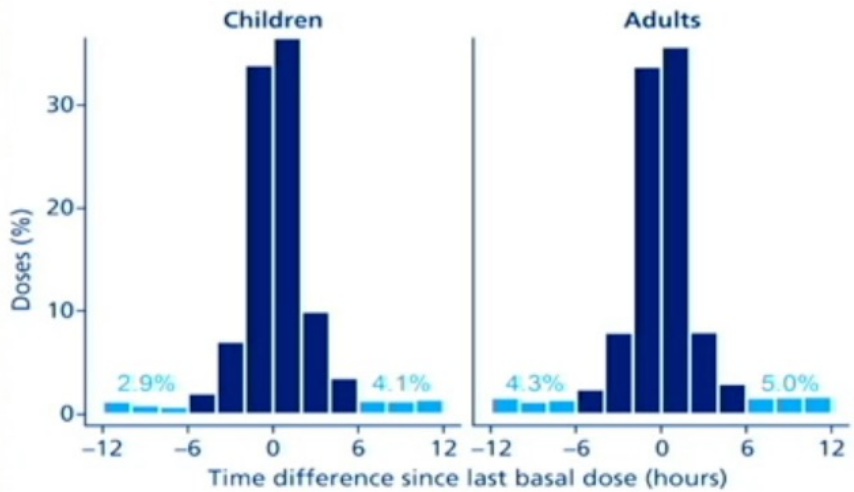
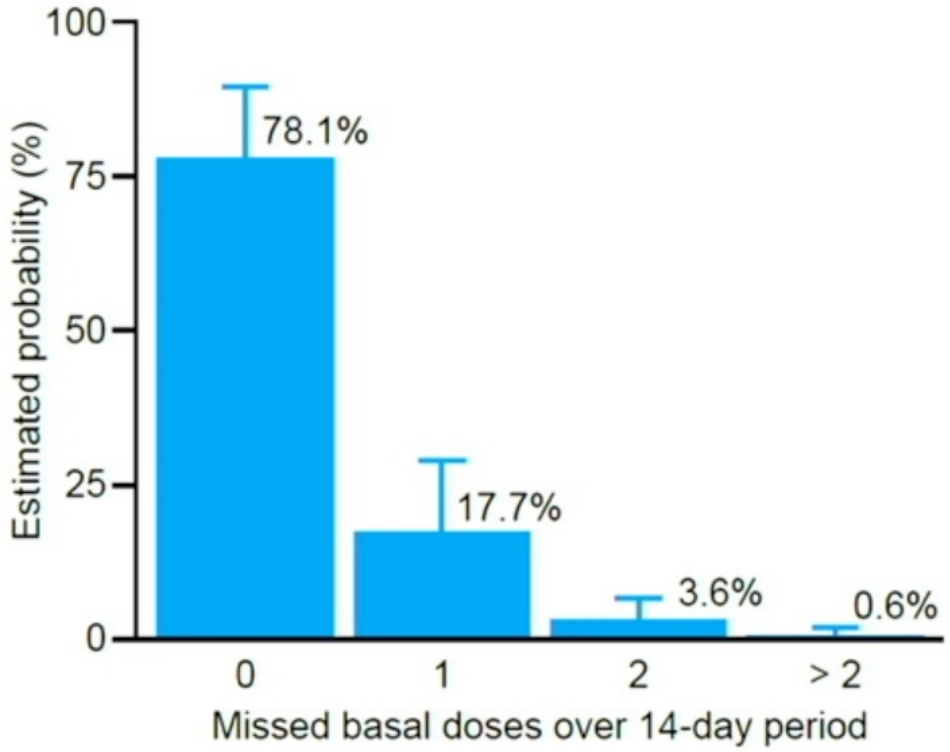


Fig A: Plots are kernel density distributions over the day for each patient, based on all days with basal injections (primarily, insulin degludec). Injections are weighted by dose taken relative to total daily dose. Blue lines indicate the overall average. Number of patients: 35 children and 45 adults; 17,869 injection days
Fig B: Histograms present the clock-time difference between two consecutive insulin degludec doses. All basal injections in the study period are considered, but the injections within one hour of a previous injection are considered part of the same dosing. Number of patients: 35 children and 41 adults. Number of doses: 11,511 in children and 7740 in adults
Cümine S-B, et al. Presented at the American Diabetes Association 80th Scientific Sessions virtual Meeting, June 12–16, 2020. Poster 988-P

Effekter av missade basaldoser



The probability that an average patient missed at least one basal insulin dose during a 14-day period was estimated to be 22% (95% CI: 10%–40%). CI, confidence interval.

diabetes

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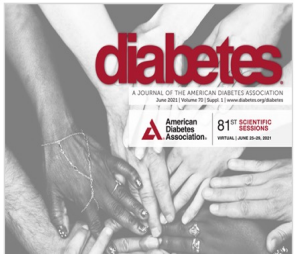
Volume 70, Issue Supplement_1
1 June 2021



P: CLINICAL THERAPEUTICS / NEW TECHNOLOGY—INSULINS | JUNE 01 2021

727-P: The Association between Missed Basal Insulin Injections and Glycemic Control in Adults with Type 1 Diabetes Mellitus FREE

NEDA RAJAMAND EKBERG; NIELS V. HARTVIG; ANNE KAAS; JONAS MOLLER; ANN-CHARLOTTE M. MÅRDBY; PETER ADOLFSSON

Check for updates

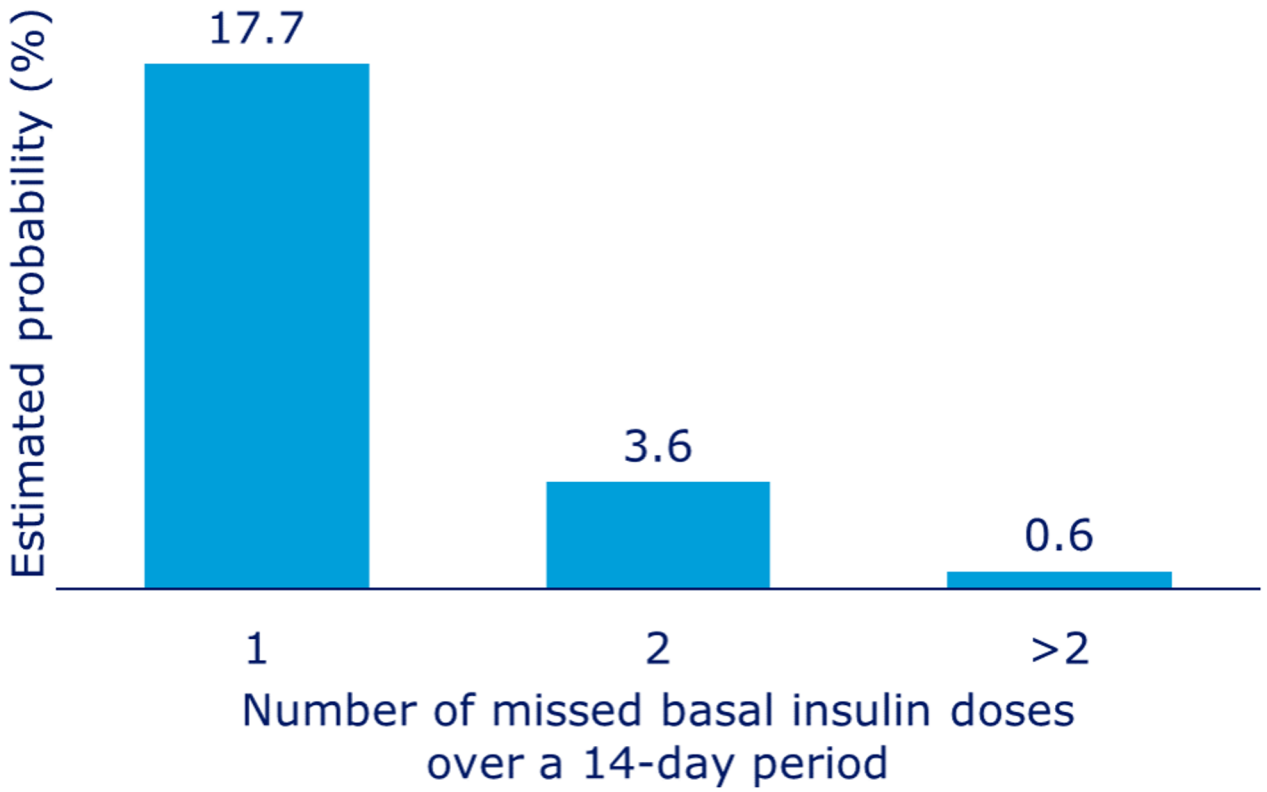
Diabetes 2021;70(Supplement_1):727-P
https://doi.org/10.2337/db21-727-P

The estimated probability that an average patient missed at least one basal insulin dose during a 14-day period was 22% (95% CI: 10%;40%)

	Est. change per missed basal injection (95% CI)	p-value
TIRange	−2.61% (−4.11; −1.11)	<0.001

Basinsulin följsamhet

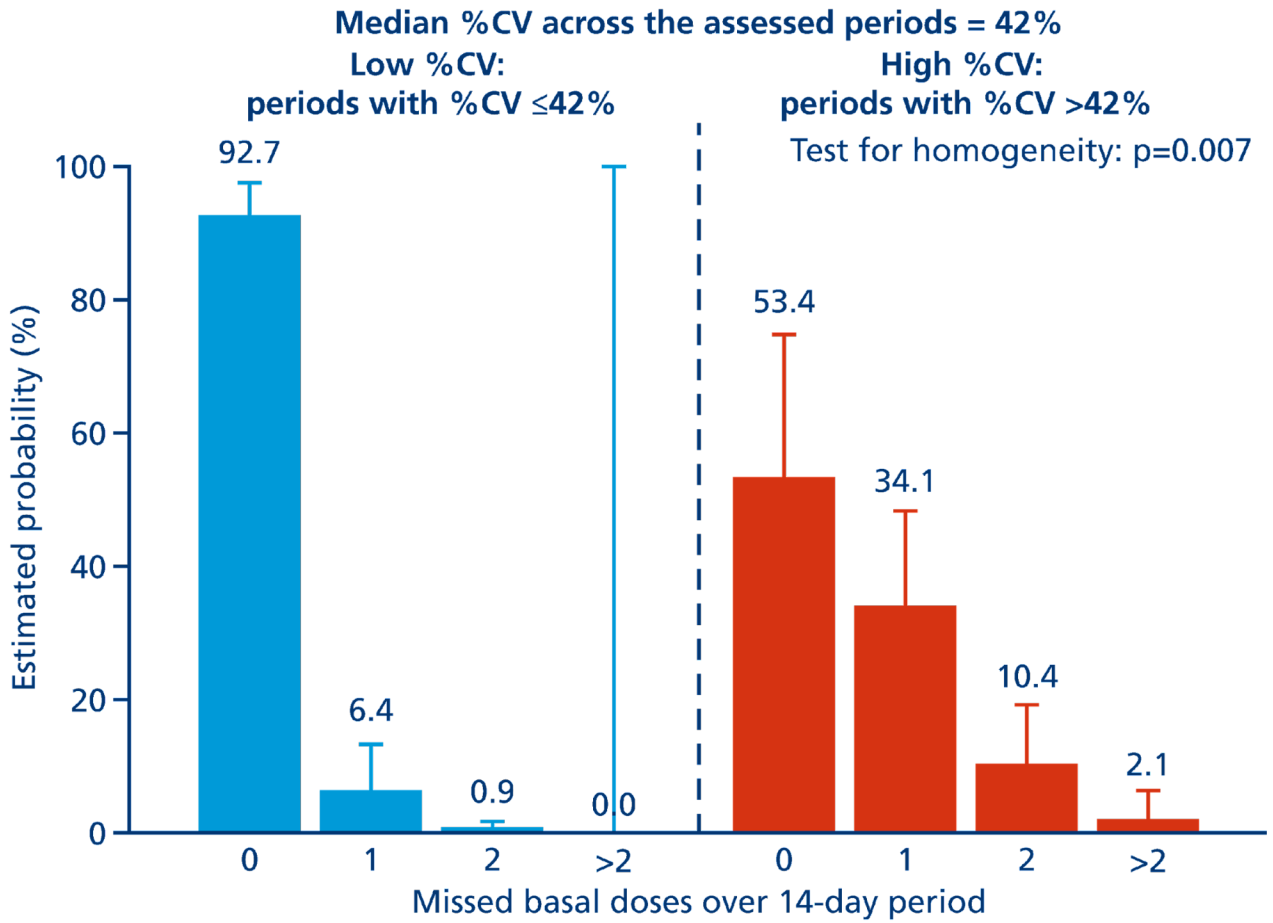
<u>Tendens till missade basaldoser:</u>



Estimerad sannolikhet att missa minst en basaldos under närmaste 14 dagarna var 22% (95% CI: 10%;40%)

Ekberg NR et al. Poster 727-P presented at the 81st Scientific Sessions of the American Diabetes Association (ADA), June 25–29, 2021, virtual

Basinsulin följsamhet



Större glukosvariabilitet hos de som missade basaldos

Ekberg NR et al. Poster 727-P presented at the 81st Scientific Sessions of the American Diabetes Association (ADA), June 25–29, 2021, virtual

Sammanfattning studier basinsulin variabilitet

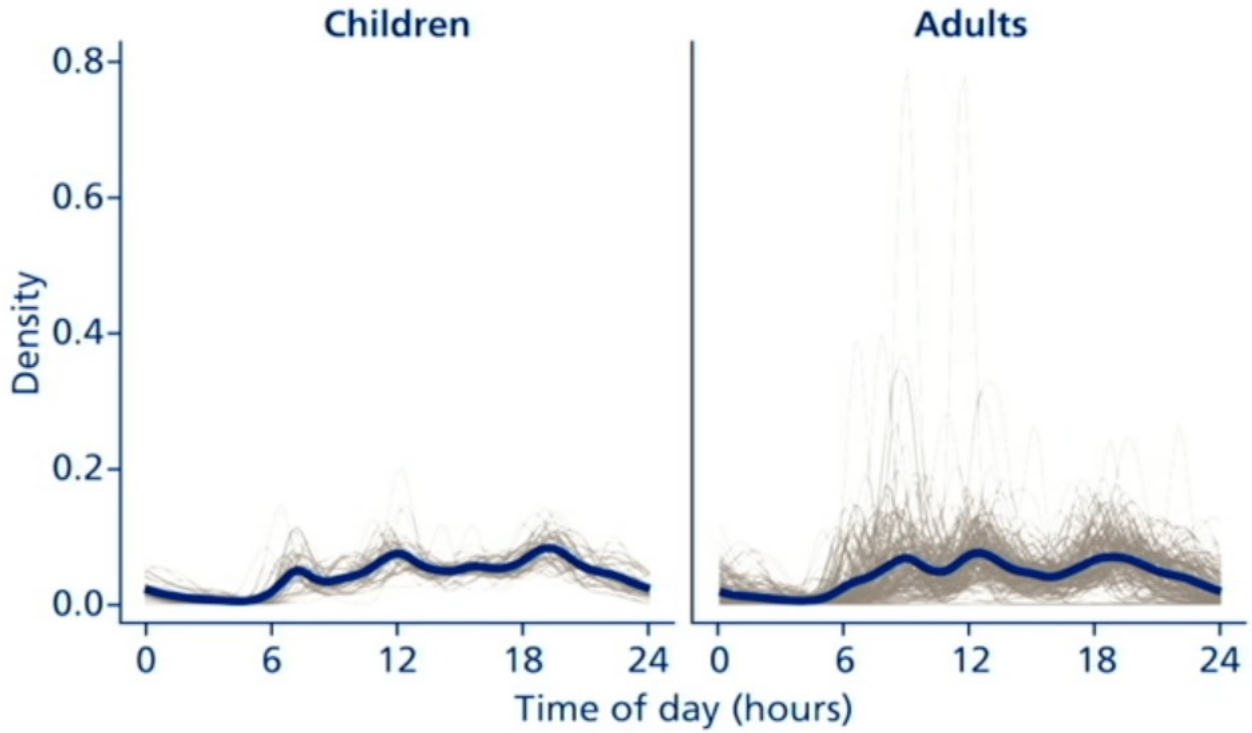
- 22% risk att individer med MDI behandling missar minst 1 basaldos under en 14 dagars period

- Missade bolusdoser noterades i snitt 0,49 respektive 0,74 tillfällen per dag – men reducerades till 0,26 respektive 0,42 tillfällen per dag efter användning CGM + Smartpen

- Sent given bolusdos noterades i snitt 0,32 tillfällen per dag – men reducerades till 0,18 tillfällen per dag efter användning CGM + Smartpen

Bolus injection patterns

- There was substantial variation in bolus injection patterns, both across patients and between children and adults
- The injection patterns were more varied across adults than for children

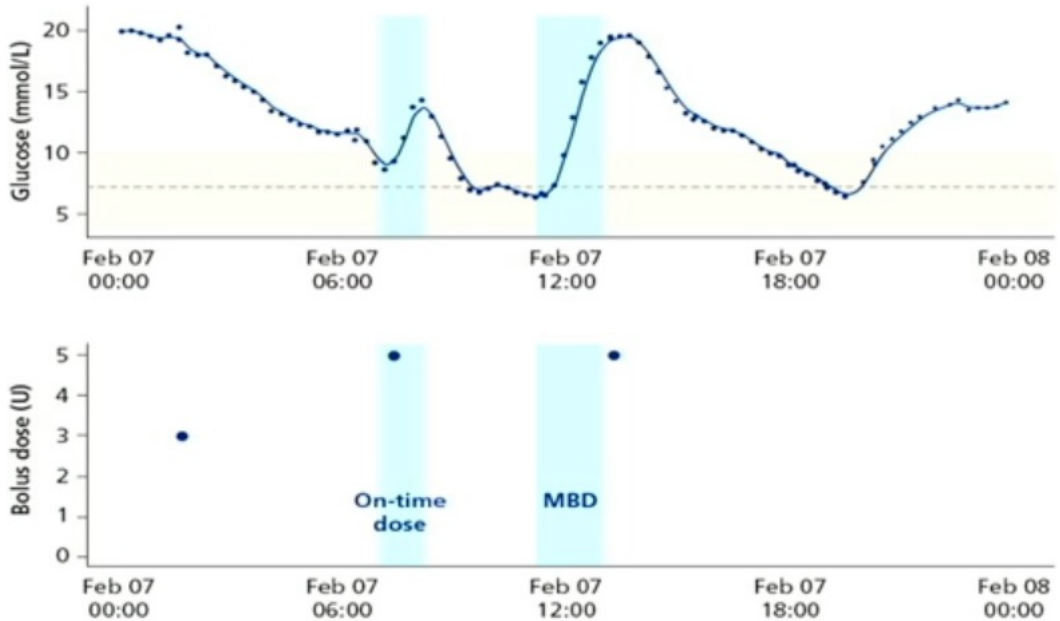


Plots are kernel density distributions over the day for each patient, based on all days with bolus injections (primarily insulin aspart). Injections are weighted by dose taken relative to total daily dose. Blue lines indicate the overall average. Number of patients: 47 children and 159 adults; 38,678 injection days.
Cătrina S-B, et al. Presented at the American Diabetes Association 80th Scientific Sessions Virtual Meeting, June 12–16, 2020. Poster 989-P

Introducing Missed Bolus Doses (MBD)

Meals detected in CGM signal by Glucose Rate Increase Detector

- Clinically validated algorithm[1] used for detecting meals
- Bolus dose 15 min before to 60 min after meal start is considered On-time
- Missed bolus dose (MBD) if not on-time



Example of a day with 2 meals detected[2]

The solid dark blue line represents the CGM signal and the light blue shaded areas each represent a detected meal. The grey, dashed line represents a glucose level of 7.2 mmol/L and the grey shaded area represents a target glycaemic range of 3.9–10 mmol/L. Meals are detected when the CGM signal is ≥7.2 mmol/L and increases steeply over 30–45 minutes. A bolus dose within 15 minutes before to 60 minutes after a meal starts is considered "on-time", whereas a dose outside of this time window is considered a MBD. Blue dots represent the dose/injection.

1 Harvey RA, Dassau E, Zisser H, Seborg DE and Doyle FJ (2014) Design of the Glucose Rate Increase Detector: A Meal Detection Module for the Health Monitoring System. JDST 8(2), 307—320. Meals detected where CGM≥7.2 mmol/L (130 mg/dL), Gradient ≥5.3 mmol/L/hour (1.6 mg/dL/min) for 2 consecutive readings (30 mins) or ≥5.0 mmol/L/min (1.5 mg/dL/min) for 3 readings (45 mins).

2 Patient ID: 7d323bf9b739a12f05b10a33aef843fa, male aged 30 at baseline

https://sciencehub.novonordisk.com/attd2022/Jendle.html?cid=qr-0443819431

Influence of bolus injection dosing frequency and smart pen engagement on glycaemic control in patients with type 1 diabetes

Jarl Hellman,[1] Niels Væver Hartvig,[2] Anne Kaas,[2] Jonas Bech Møller,[2] Mads Reinholdt Sørensen[2] and Johan Jendle[3]

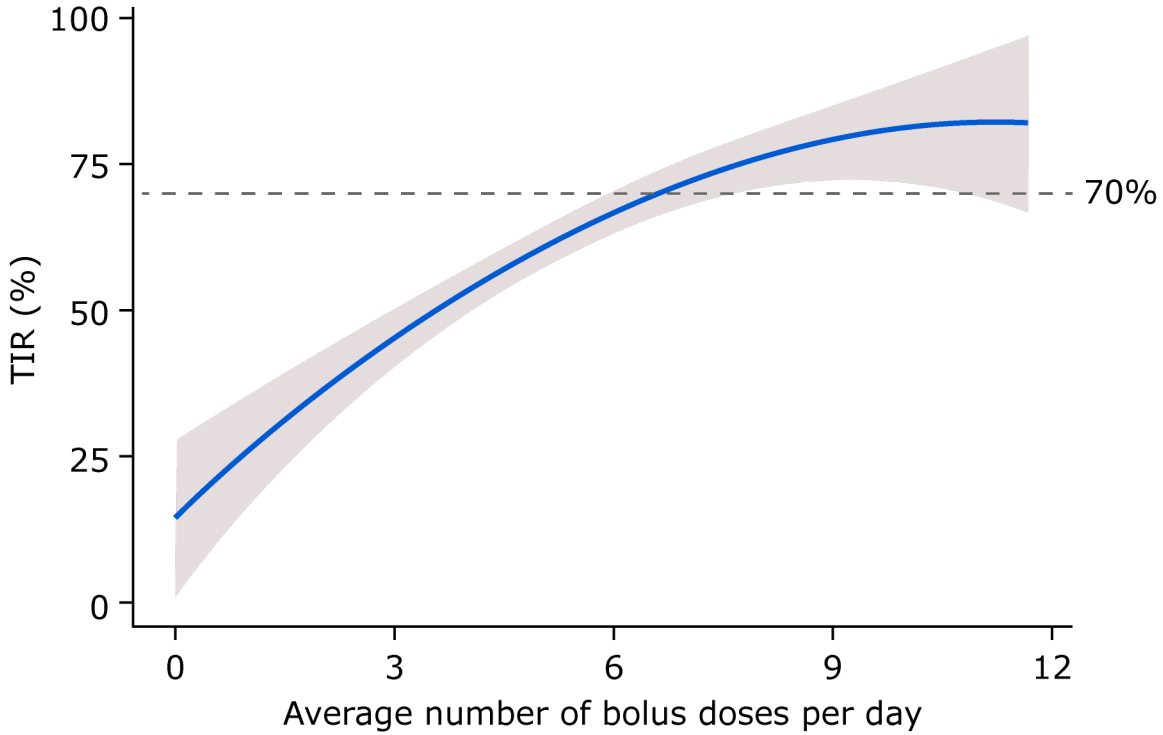
[1]Uppsala University, Uppsala, Sweden

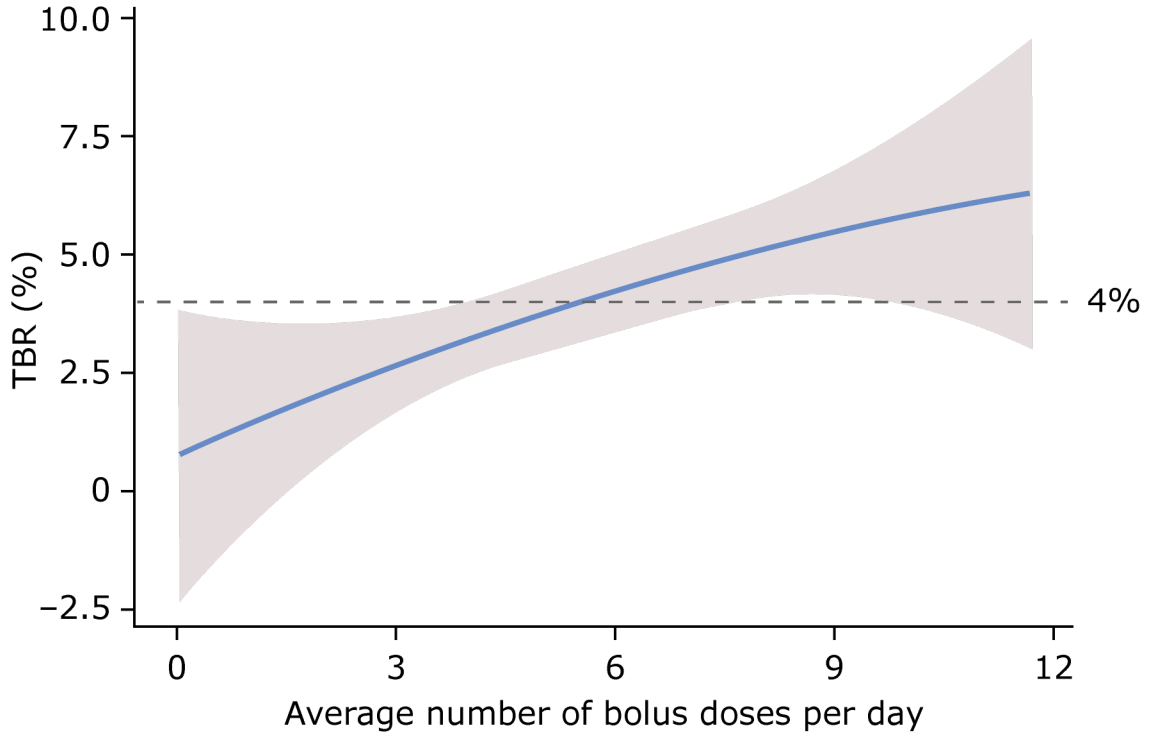
[2]Novo Nordisk A/S, Søborg, Denmark

[3]Örebro University, Örebro, Sweden

Advanced Technologies & Treatments for Diabetes, 27–30 April 2022, Barcelona, Spain and online

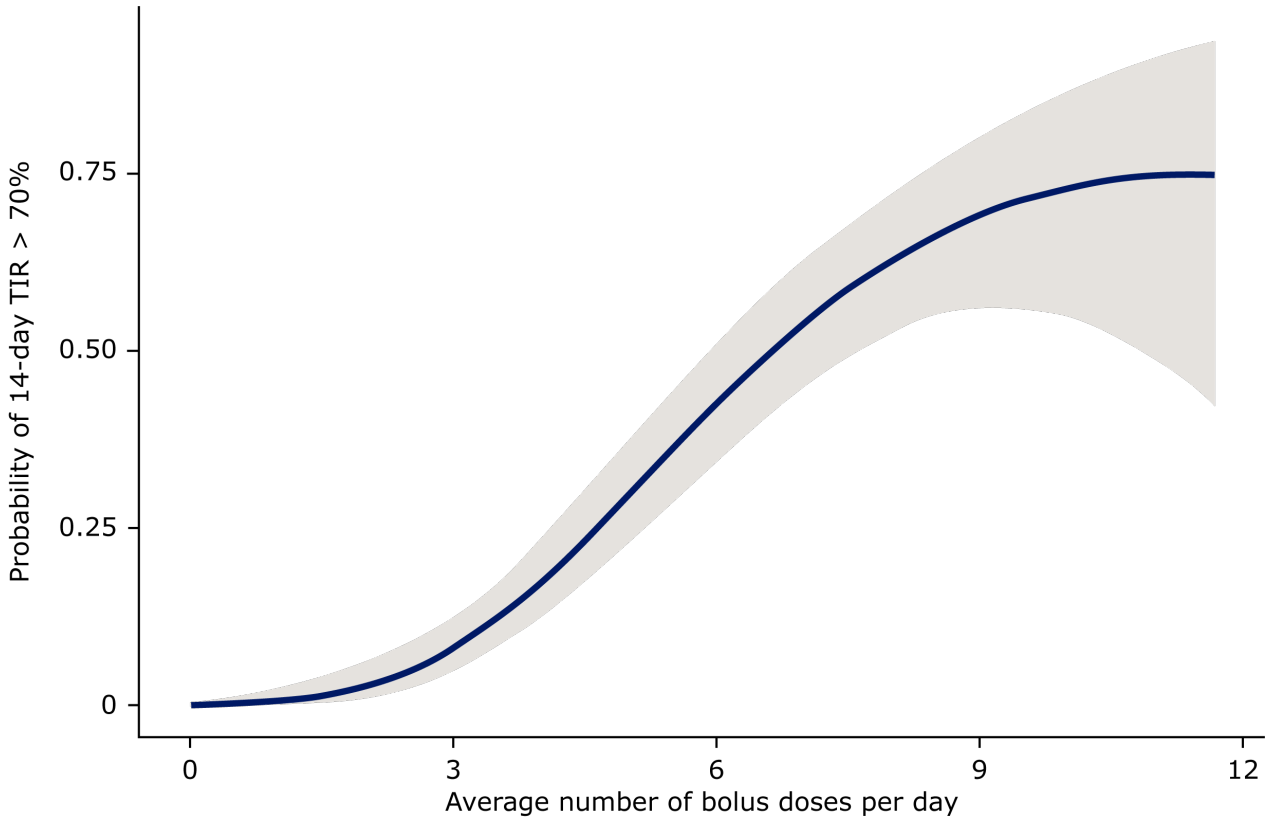
Antalet bolus doser är associerat med TIR* och TBR**





Based on estimated least-squares mean with 95% CIs. Effects were averaged with equal weights over factors other than number of bolus doses. The grey shading represents 95% CI values. Dashed lines indicate thresholds for glycaemic targets recommended by the American Diabetes Association for many non-pregnant adults.[1] N = 224 patients; 11 467 calendar days.
*$p < 0.0001$; **$p = 0.0021$.
CI, confidence intervals; TBR, time below range (< 3.9 mmol/L [< 70 mg/dL]); TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]).
1. American Diabetes Association Professional Practice Committee. *Diabetes Care* 2022;45(Suppl 1):S83–96.

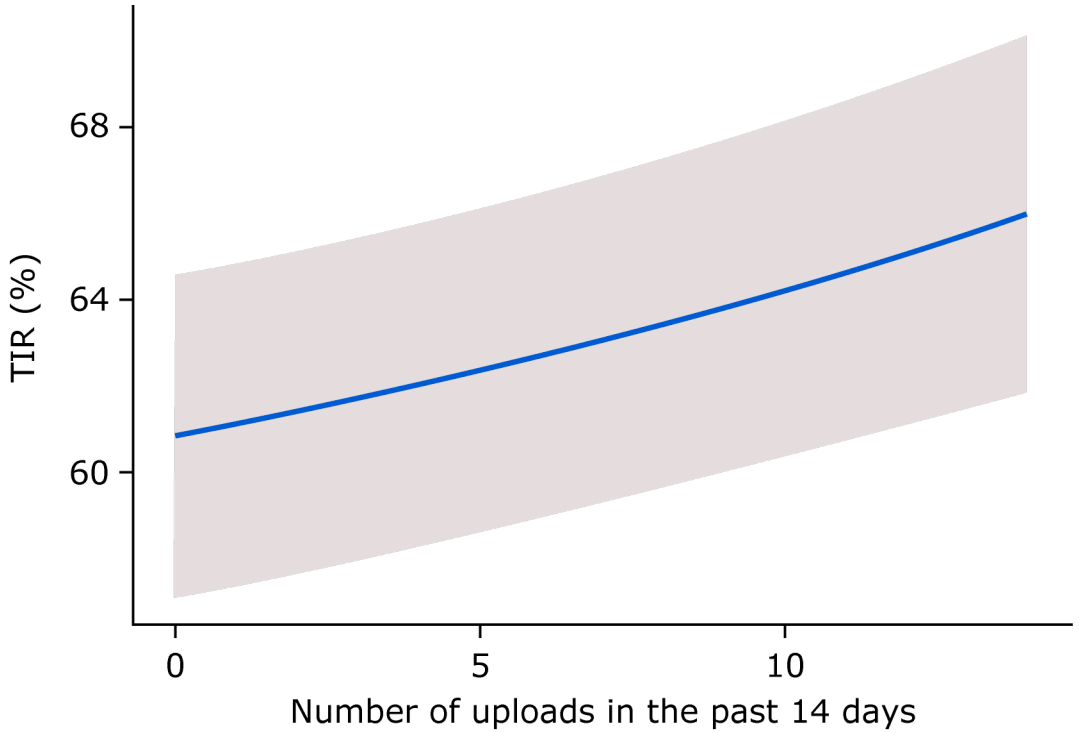
Sannolikheten att nå högre TIR än 70% vid T!D

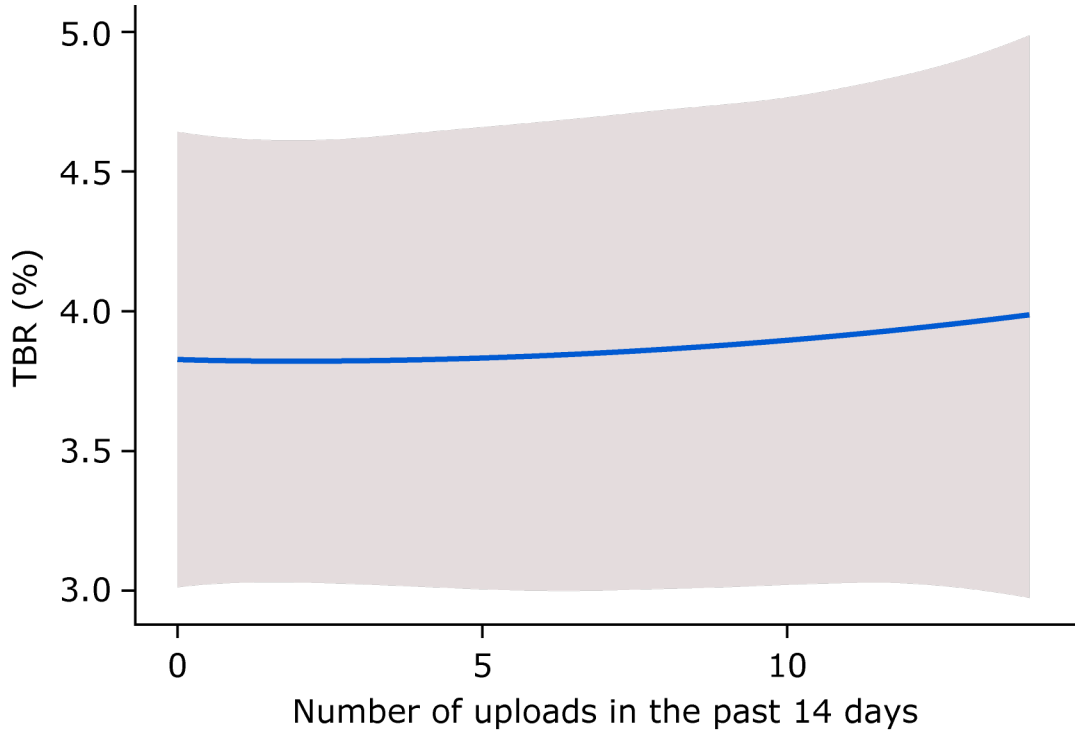


Patients with an average of **three daily bolus doses** have an **8.1%** (95% CI: 4.9–12.6%) chance of reaching the target of **more than 70% TIR**

Based on estimated least-squares mean with 95% CIs. The grey shading represents 95% CI values. Effects were averaged with equal weights over factors other than number of bolus doses. A standard deviation of 17.7% of TIR was assumed. N = 224 patients; 11 467 calendar days. The mean number of daily faster aspart doses among the 224 patients was five.
CI, confidence interval; faster aspart, fast-acting insulin aspart; T1D, type 1 diabetes; TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]).

Ju fler nedladdningar som görs är associerat med bättre TIR*, men inte med TBR**





Days with daily uploads conducted during the previous 14 days had 5% more TIR than those with no uploads conducted during the previous 14 days

Plots of estimated model effects. Estimated least-squares mean with 95% CIs. The grey shading represents 95% CI values. Effects were averaged with equal weights over factors other than number of uploads. N = 224 patients; 11 467 calendar days.
*$p < 0.0001$; **$p = 0.90$.
CI, confidence interval; TBR, time below range (< 3.9 mmol/L [< 70 mg/dL]); TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]).

DIABETES, OBESITY AND METABOLISM
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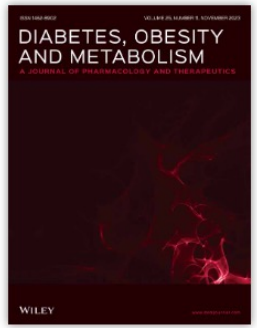


Early View

Online Version of Record before inclusion in an issue

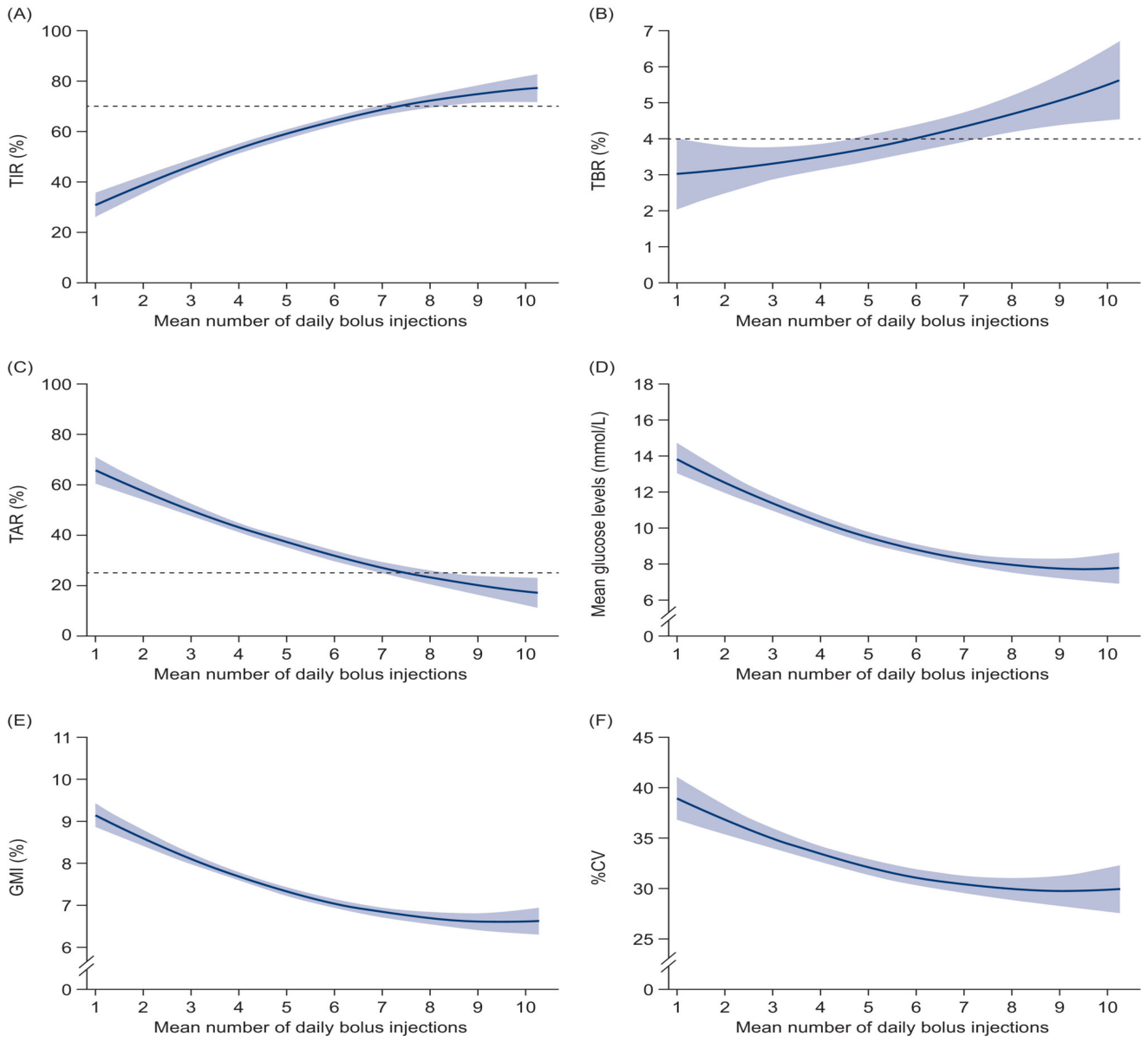
ORIGINAL ARTICLE | Open Access

Associations of bolus insulin injection frequency and smart pen engagement with glycaemic control in people living with type 1 diabetes

Jarl Hellman MD, Niels Væver Hartvig PhD, Anne Kaas MD, Jonas Bech Møller PhD, Mads Reinholdt Sørensen PhD, Johan Jendle MD

First published: 05 November 2023 | https://doi.org/10.1111/dom.15316

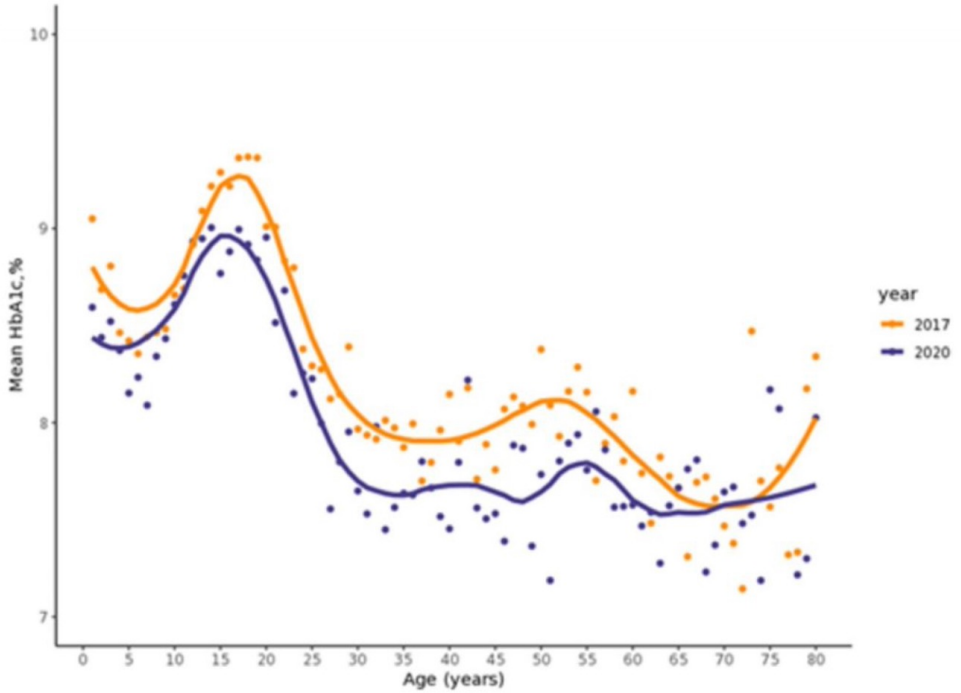
Association av bolus frekvens, användande av smarta insulinpennor och glukoskontroll vid T1D

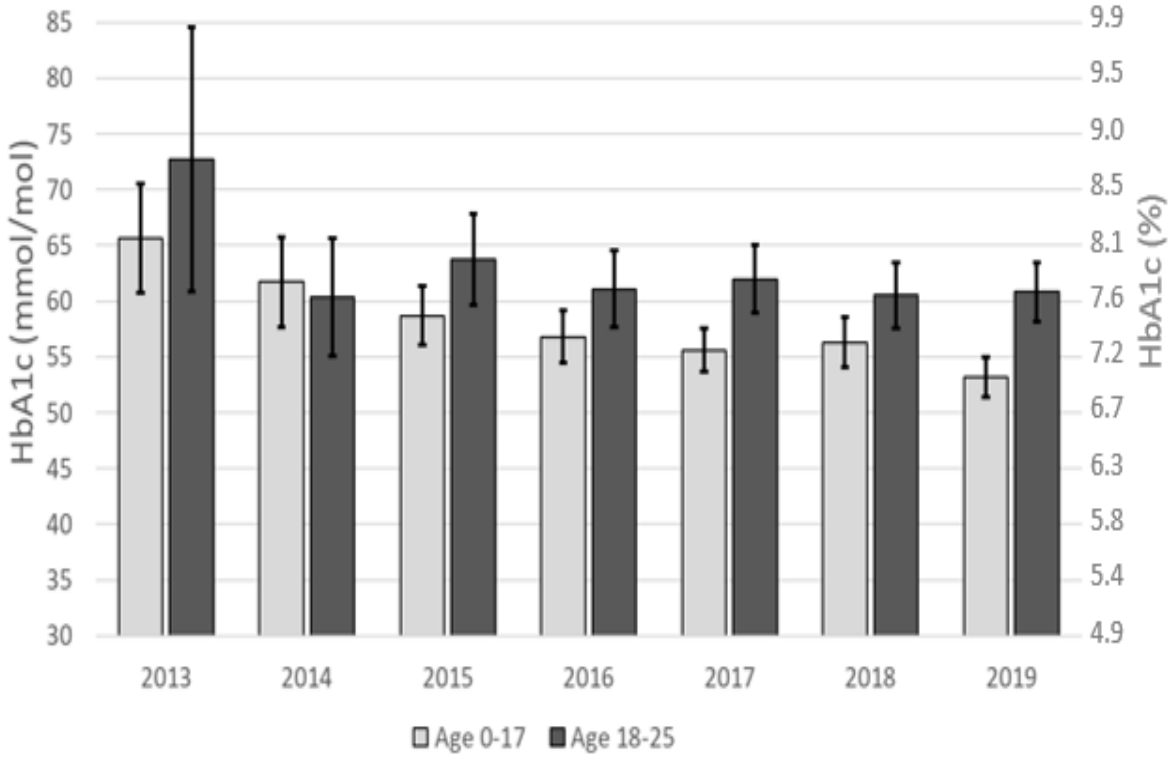


Diabetes Obesity Metabolism, First published: 05 November 2023, DOI: (10.1111/dom.15316)

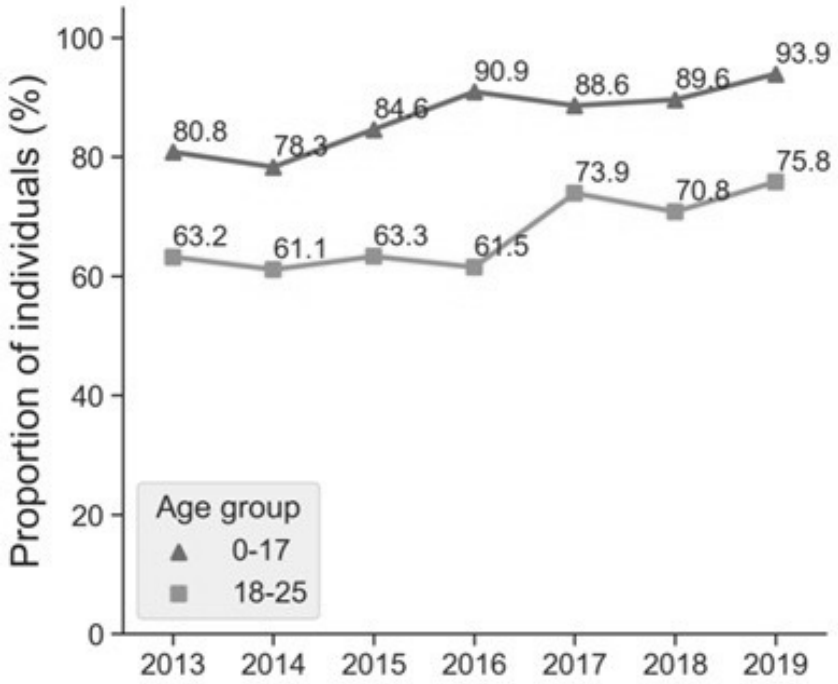
New teens, ATTD 2022 Barcelona, poster 156

Jendle J, Agvall B, Galozy A, Adolfsson P. Better Glycemic Control and Higher Use of Advanced Diabetes Technology in Age Group 0-25 Years in Individuals with Type 1 Diabetes. 2022. JSDT. Doi10.1177/19322968221096423





New teens - bättre för vart år

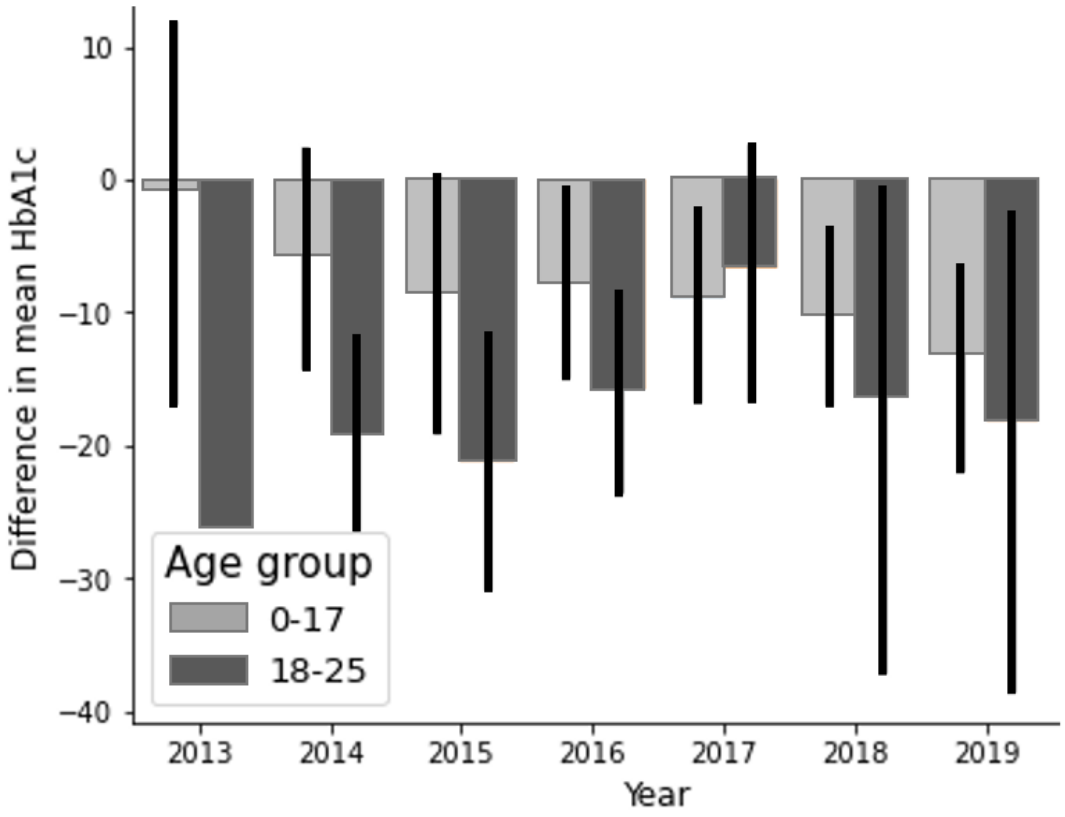


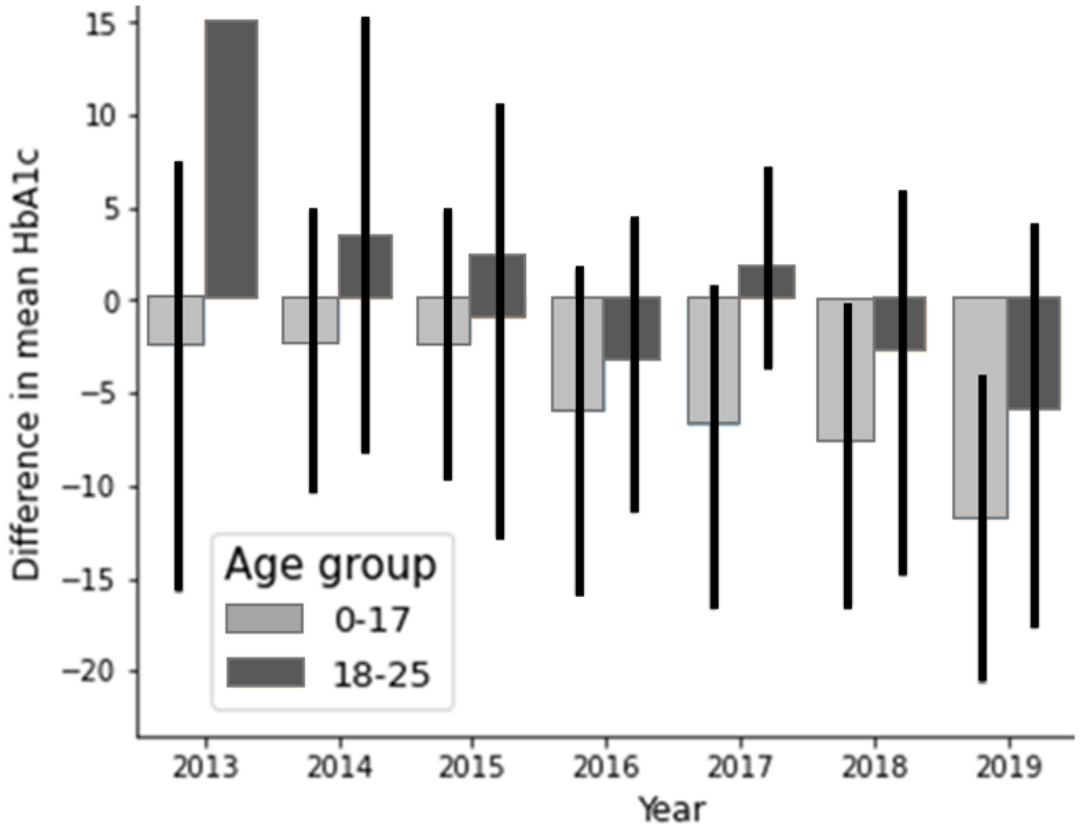
Skillnader barn/unga vuxna

- Fler på rt-CGM
- Fler på CSII och HCL/AID
- Fler och tätare besök HCP

Jendle J, et al. Patterns and Predictors Associated with Long-Term Glycemic Control in Pediatric and Young Adult Patients with Type 1 Diabetes. JSDT. 2023;17(5):1243-1251.

New teens, dietistbesök och psykologbesök

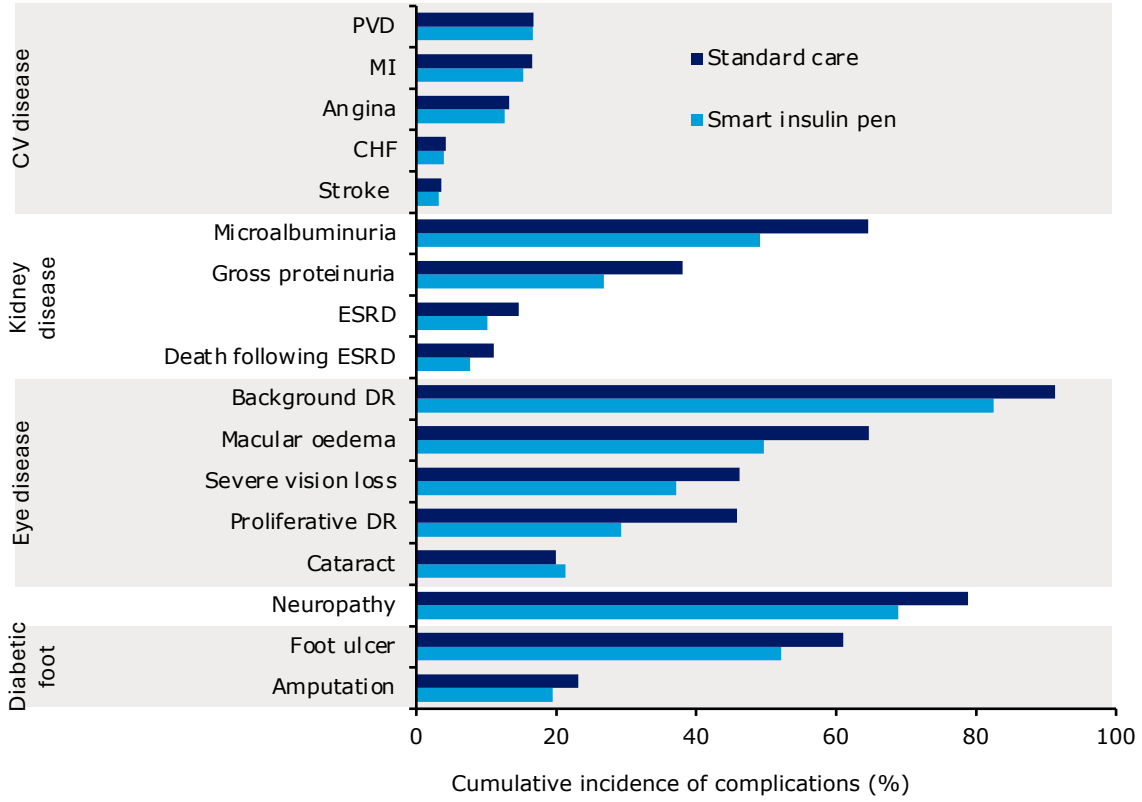




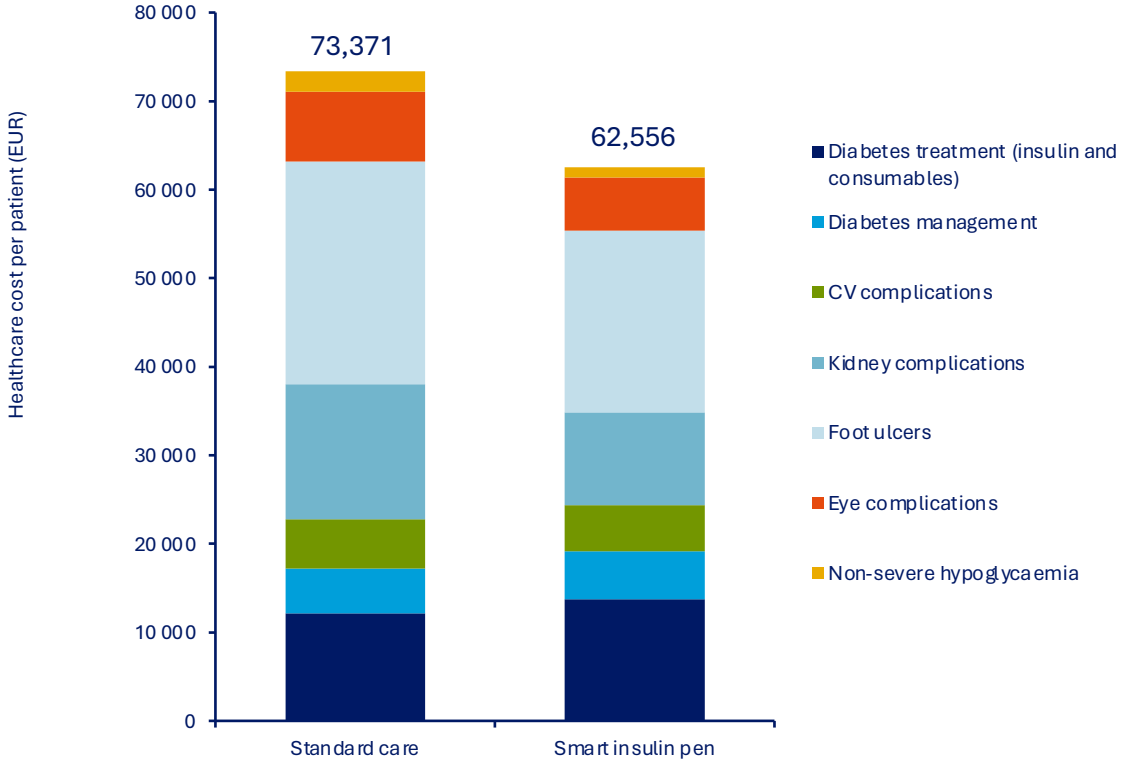
Jendle J, et al. Patterns and Predictors Associated with Long-Term Glycemic Control in Pediatric and Young Adult Patients with Type 1 Diabetes. JSDT. 2023;17(5):1243-1251.

Hälsoekonomi och smarta pennor
Förväntade resultat (livstid)– färre komplikationer och lägre kostnader med smarta pennor

Cumulative incidence of diabetes-related complications



Mean discounted direct healthcare costs per patient



Figures 1 and 2. Differences between arms (standard care and smart insulin pen) were not statistically analysed. Costs projected in Swedish krona were converted to EUR using an exchange rate of 0.091. CHF, congestive heart failure; CV, cardiovascular; DR, diabetic retinopathy; ESRD, end-stage renal disease; EUR, Euro; MI, myocardial infarction; PVD, peripheral vascular disease

Oavsett scenario, smarta insulinpennor är dominanta

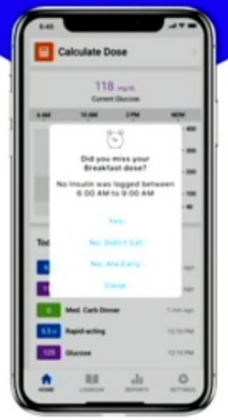
Analysis	Discounted direct costs (EUR)			Discounted quality-adjusted life expectancy (QALYs)			Interpretation
	Standard care	Smart insulin pen	Difference	Standard care	Smart insulin pen	Difference	
Base case	**73,371**	**62,556**	**–10,816**	**13.20**	**14.34**	**1.13**	**Smart insulin pen dominant**
Combined costs (includes direct costs in addition to direct costs)	197,228	151,396	–45,833	13.20	14.34	1.13	Smart insulin pen dominant
3-year time horizon	4007	3687	–319	2.17	2.21	0.04	Smart insulin pen dominant
Baseline HbA_{1c} of 54.1 mmol/mol (7.1%)[1]	43,991	38,978	–5012	15.74	16.49	0.75	Smart insulin pen dominant
HbA_{1c} difference between arms of 4.4 mmol/mol (0.4%)	73,371	66,463	–6908	13.20	14.03	0.83	Smart insulin pen dominant
Biosimilar bolus insulin cost†	72,558	61,467	–11,091	13.20	14.34	1.13	Smart insulin pen dominant

Table 2. Difference and interpretation reported for smart insulin pens – standard care
†Insulin lispro biosimilar Sanofi®. EUR, Euro; QALY, quality-adjusted life-year
1. Nationella Diabetesregistret (NDR). https://www.ndr.nu/#/knappen

Smarta pennor här för att stanna!

Smart MDI system – solutions to remove MDI therapy barriers

Missing insulin doses
Missing two doses per week can lead to an increase in A1C of up to 0.4%.[1]



Insulin dose reminder

Insulin dose calculator

Miscalculating insulin doses
Up to 60% people need help calculating their insulin doses.[2-3]

Insulin stacking
Difficulty to calculate insulin on-board can lead to stacking and hypoglycemia.[4]

Active Insulin Tracking

Shareable insight reports

Lack of MDI data reports
Lack of accurate dosing data is a significant barrier to optimizing glycemic control.[4]

1. Robinson S et al. Missed and mistimed insulin doses in people with diabetes: A systematic literature review. Diab Tech Ther 2021: DOI: 10.1089/dia.2021.0164 .
2. Zaugg, Stephanie D., et al. Diabetes numeracy and blood glucose control: association with type of diabetes and source of care. *Clinical diabetes: a publication of the American Diabetes Association* 32.4 (2014): 152-157.
3. Cavanaugh, Kerri, et al. "Association of numeracy and diabetes control." *Annals of Internal Medicine*. 148.10 (2008): 737-746.
4. Klonoff DC, Kerr D. Smart Pens Will Improve Insulin Therapy. *J Dia Sci & Tech*. 2018;12(3):551-553.

Medtronic

Frågor?