Continuous Glucose Monitoring and Insulin Delivery Devices

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Disclosures

Dualities of Interest:

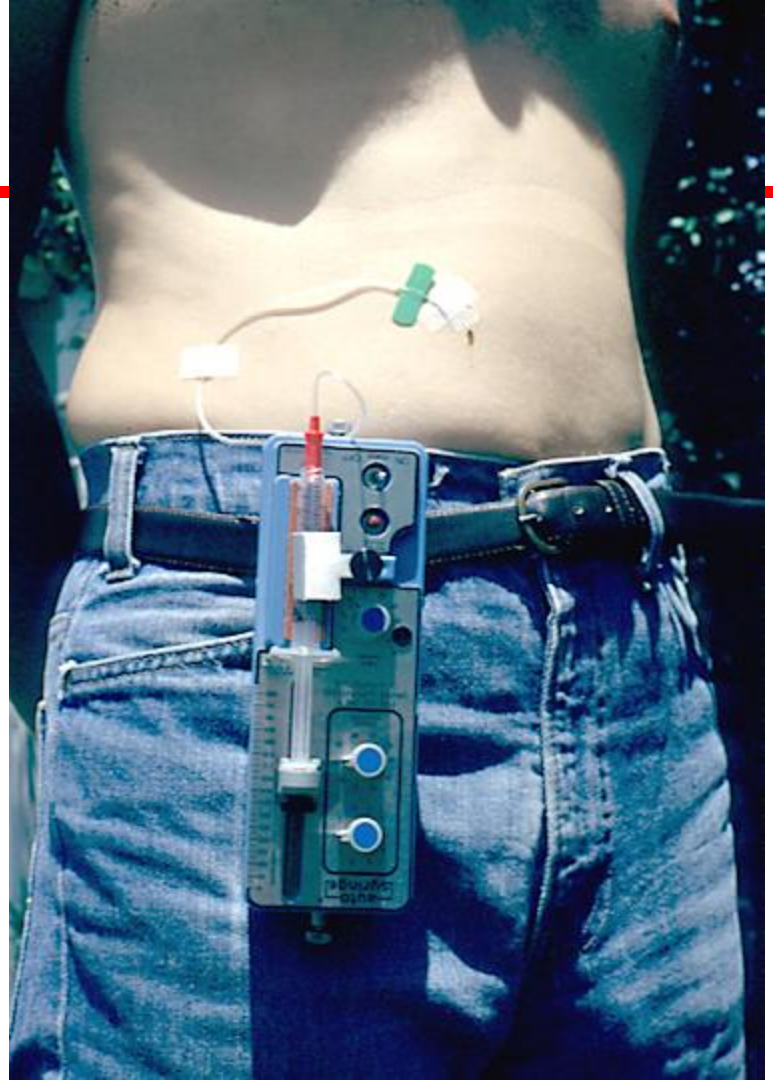
Jay Skyler has acted as an advisor to Adocia, Applied Therapeutics, Astra-Zeneca, Boehringer-Ingelheim, DalCor, Dance Biopharm, Diavacs, Duologics, Elcelyx, Eli Lilly, Esperion, Geneuro, Ideal Life, Immunomolecular Therapeutics, Intarcia, Intrexon/ActoBio, Kamada, Merck, Orgenesis, Sanofi, Servier, Tolerion, vTv, Valeritas, Viacyte, and Zafgen.

He has research funding from NIH, JDRF, and DRIF.

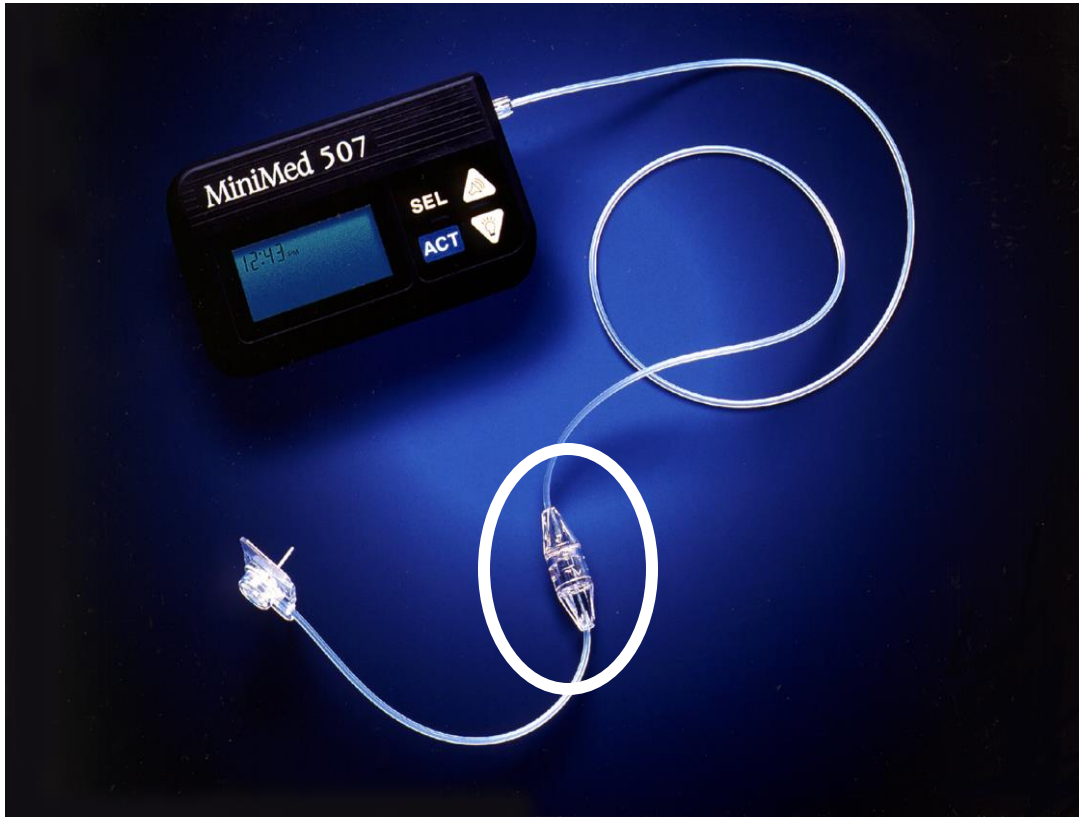
He chairs the Strategic Advisory Board of the EU INNODIA consortium.

He is a member of the board of directors of Dexcom, Intarcia, and Moerae Matrix. He previously was on the board of directors of MiniMed.

Insulin Delivery Devices

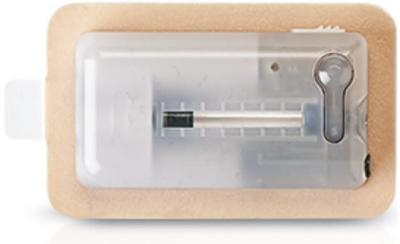


Continuous Subcutaneous Insulin Infusion (CSII)



Continuous Subcutaneous Insulin Infusion (CSII)

Current Insulin Delivery Systems



Companion inPen

Mean HbA1c by Age & Insulin Delivery Method

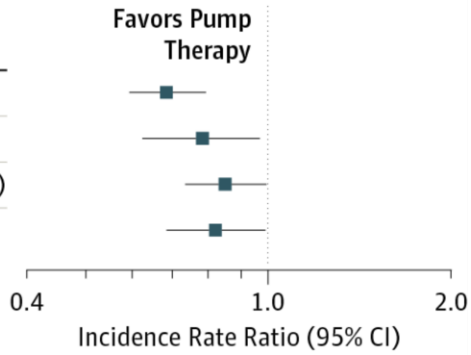
	1.5 to 5 yrs.	6 to 10 yrs.	11 to 15 yrs.	16 to 19 yrs.
Injection therapy Glycated hemoglobin, % (95% CI)	7.36 (7.13-7.59)	7.52 (7.45-7.59)	8.18 (8.14-8.23)	8.48 (8.44-8.53)
Pump therapy Glycated hemoglobin, % (95% CI)	7.38 (7.15-7.60)	7.40 (7.32-7.47)	8.02 (7.97-8.07)	8.29 (8.25-8.33)
Between-group difference (95% CI)	0.02 (-0.30 to 0.34)	-0.12 (-0.22 to -0.03)	-0.16 (-0.23 to -0.10)	-0.19 (-0.25 to -0.13)
P value	.91	.02	< .001	< .001

Karges et al. **JAMA** 2017;318:1358-1366

Severe Hypoglycemia & DKA by Insulin Delivery Method

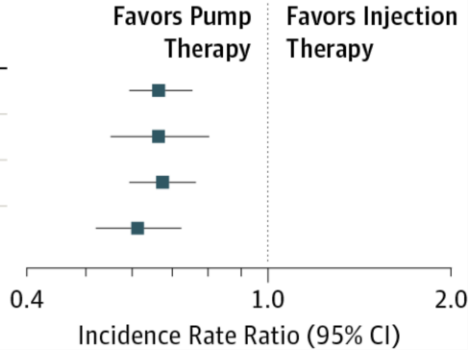
A Matched cohort

	Incidence Rate Ratio (95% CI)
Severe hypoglycemia	0.68 (0.59-0.79)
Hypoglycemic coma	0.78 (0.62-0.97)
Diabetic ketoacidosis	0.85 (0.73-0.995)
Severe ketoacidosis	0.82 (0.68-0.99)



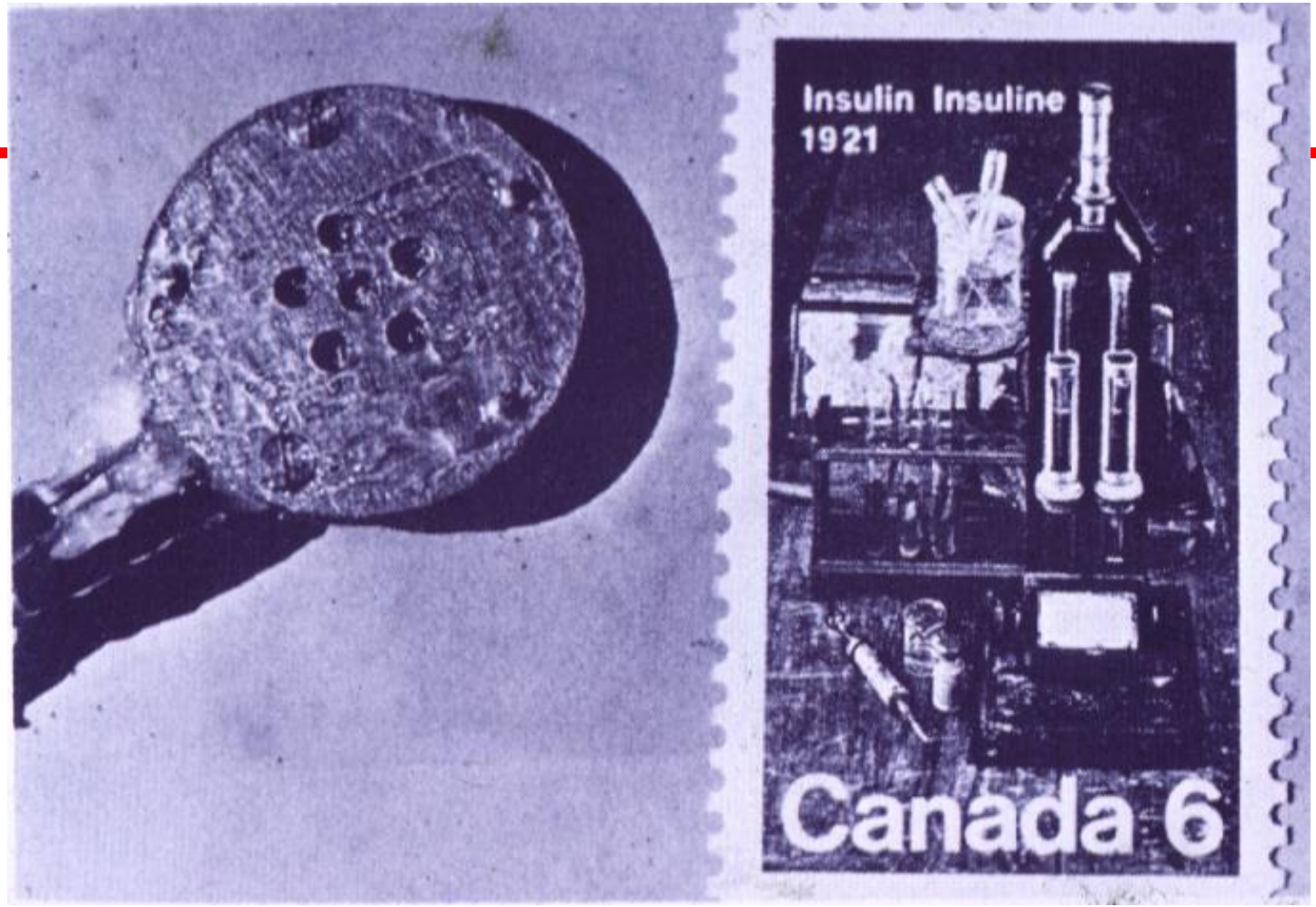
B Entire cohort

	Incidence Rate Ratio (95% CI)
Severe hypoglycemia	0.66 (0.59-0.75)
Hypoglycemic coma	0.66 (0.55-0.80)
Diabetic ketoacidosis	0.67 (0.59-0.76)
Severe ketoacidosis	0.61 (0.52-0.72)



Karges et al. **JAMA** 2017;318:1358-1366

Continuous Glucose Monitoring


Insulin Insuline
1921
Canada 6

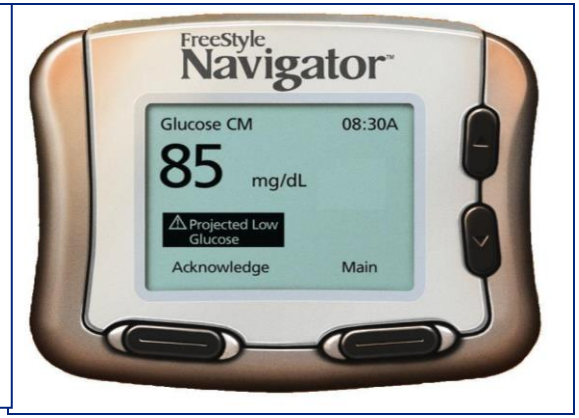
Implantable Glucose Sensor

Continuous Glucose Monitoring System (CGMS)

Guardian Telemetered Glucose Monitoring System

DexCom Seven Plus
Continuous Glucose Monitor

CGM Sensors Circa 2008



The NEW ENGLAND JOURNAL of MEDICINE

Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes

The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group

New England Journal of Medicine 2008: 359: 1464-1476

JDRF RT-CGM Randomized Controlled Trial

Subjects

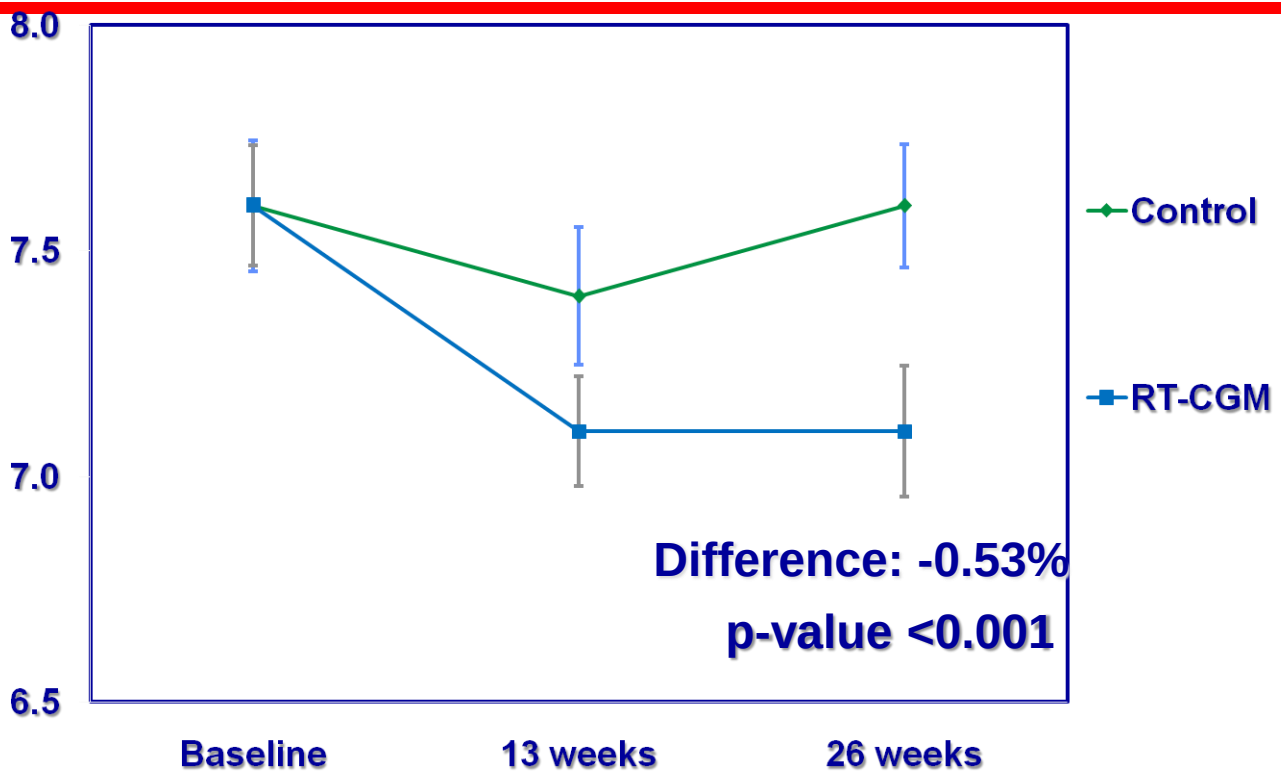
- n = 322
- 3 cohorts by age: 8-14, 14-24, ≥ 25 yrs old
- A1c 7.0% - 10.0%
- CSII (79.5%) or MDI (20.5%)
- SMBG mean 6.4 tests per day

Treatment Groups

- Real-time CGM + SMBG group
  - Abbott, DexCom or Medtronic RT Sensors
- SMBG control group

New Engl J Med 2008: 359: 1464-1476

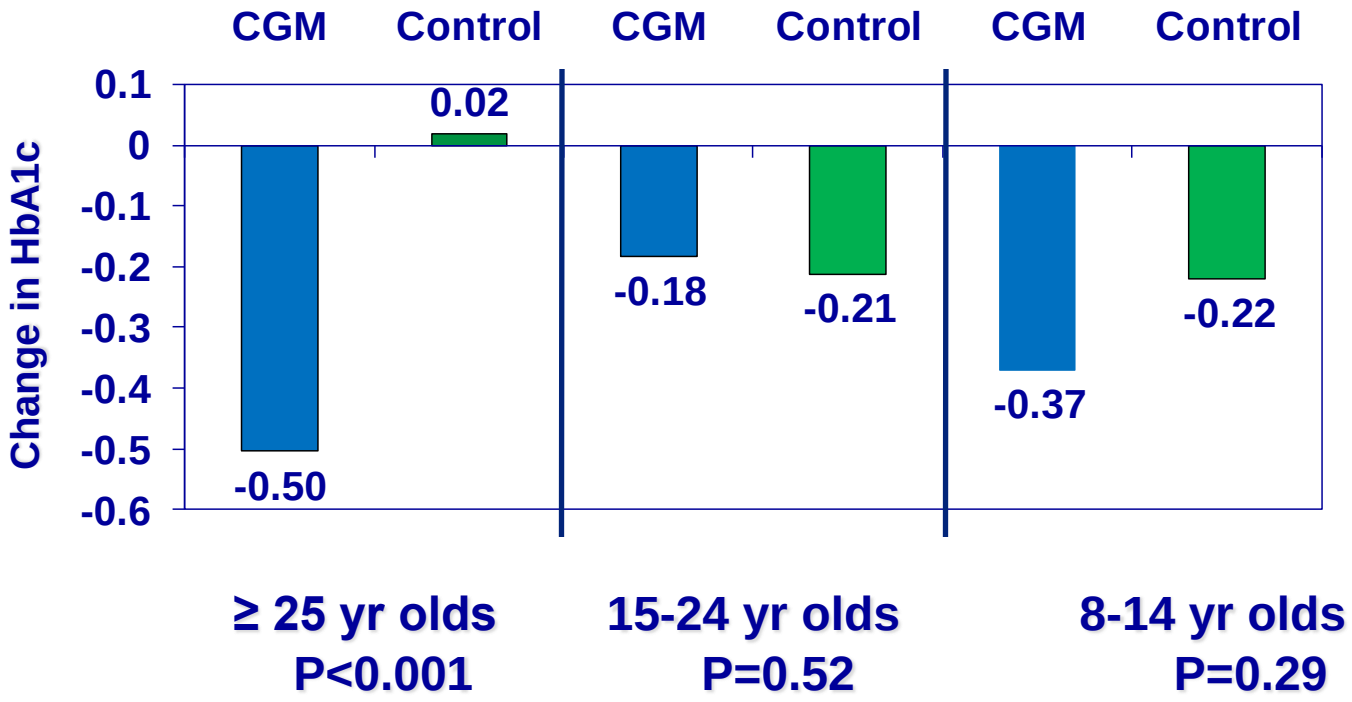
Cohort Starting with A1c 7.0-10.0%
Changes in A1c in ≥25 yr olds



*Error bars stand for 95% CI.

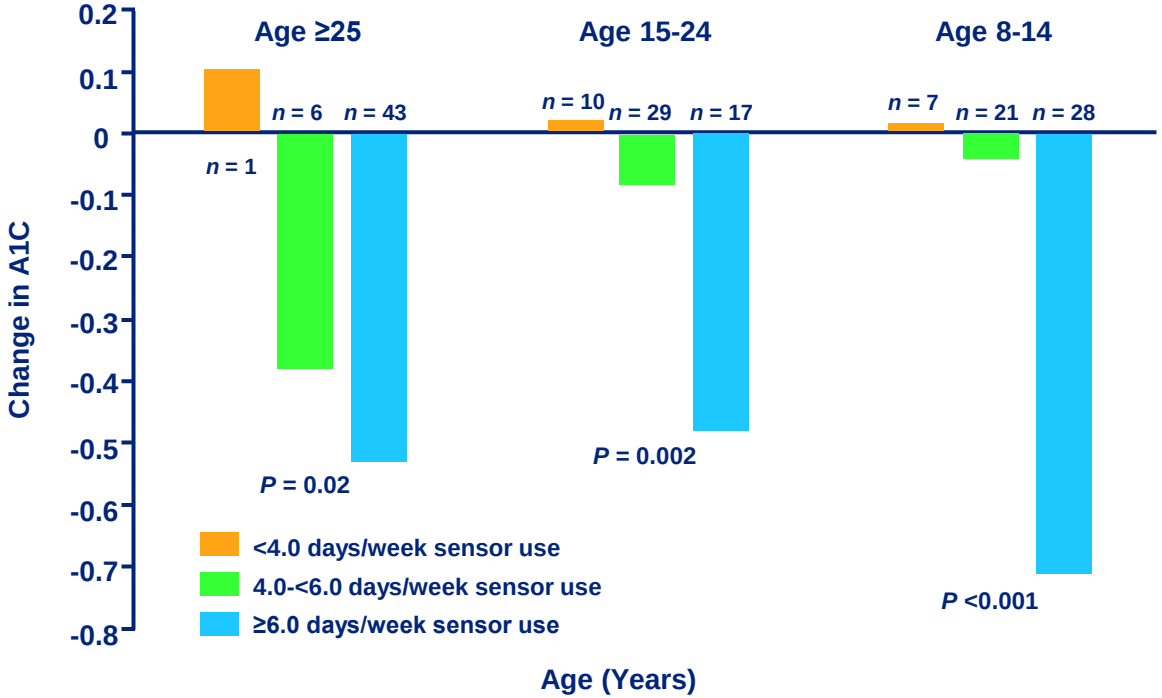
New Engl J Med 2008: 359: 1464-1476

Change in A1c from Baseline to 26 Weeks in ≥7.0% HbA1c Cohort



New Engl J Med 2008: 359: 1464-1476

Change in A1C by Sensor Use



Diabetes Care. 2009;32:1947-5193.

Current Glucose Monitoring Systems

Dexcom G6

- 10 day wear
- No calibrations
- iOs and Android compatible for smartphones and smart watches
- System contains:
  - G6 app
  - G6 transmitter
  - G6 receiver
  - G6 sensors (3 pack)
- Patients age 2 and above

“Followers” May Take Advantage of Remote Monitoring

Apple Watch Display

Dexcom G6 Mobile. If you have type 1 or type 2 diabetes, you can now test your glucose levels at a glance.

Current Glucose Monitoring Systems

Medtronic Guardian Connect

- 7 day wear
- Calibrate ≥2 times daily
- System contains:
  - Guardian sensor 3
  - Rechargable transmitter
  - Guardian connect to CareLink
  - Sugar IQ App
- For patients ages 14-75

Current Glucose Monitoring Systems

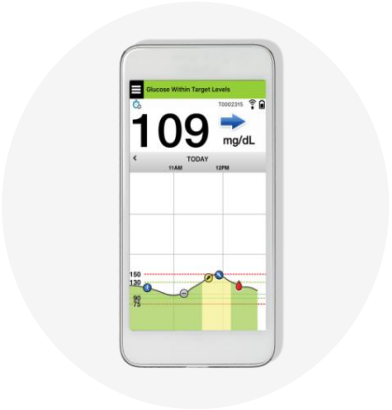
Eversense Implantable CGM System

Sensor

Fully implanted
Small size
Up to 90 days

Smart Transmitter

On-body vibe alerts
Removable/Rechargeable
Gentle adhesive



Mobile App

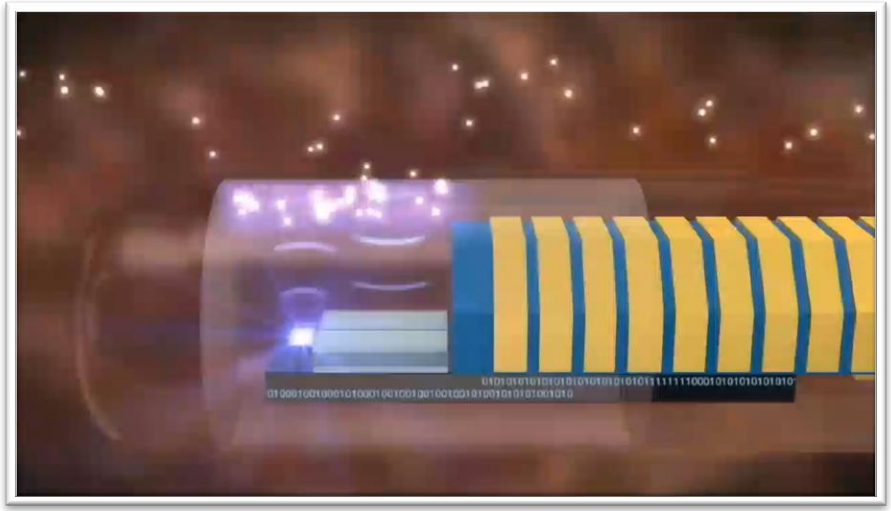
Real-time readings every 5 mins
Trends, alerts w/ predictive alerts

Current Glucose Monitoring Systems

Eversense Implantable CGM System

Sensor Powered by Transmitter

Fluorescence with Glucose Binding

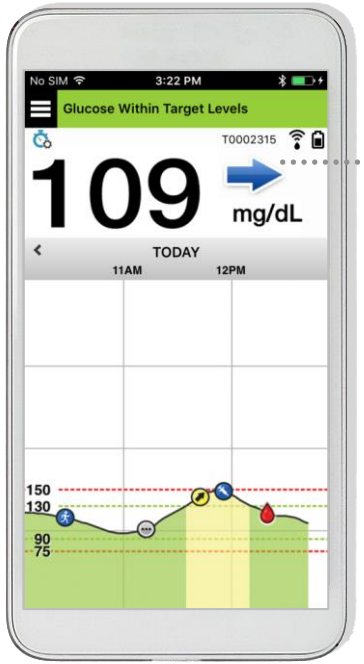


Current Glucose Monitoring Systems

Eversense Implantable CGM System

Current glucose reading

Trend arrow



Trend graph

High glucose alert (top red line)

High glucose target level (top green line)

Low glucose target level (bottom green line)

Low glucose alert (bottom red line)

Current Glucose Monitoring Systems

Libre Flash Glucose Monitoring

- 14 day wear
- No calibration
- No alarms
- Records data q 15 min (8hr)
- Don’t rely on readings for first 12 hours
- “Scan” to see glucose levels
  - 8-hour look-back with graph

Flash Glucose Monitoring vs Continuous Glucose Monitoring

Feature	FGM	CGM
Alarms	-	+
Duration	10-14 days	7-10 days
Calibration	-	+ ≥2 times daily (Guardian) + 2 times daily (Eversense) + (G6 optional)
Data Transfer	Requires “scan”	Passive

Operator's Manual

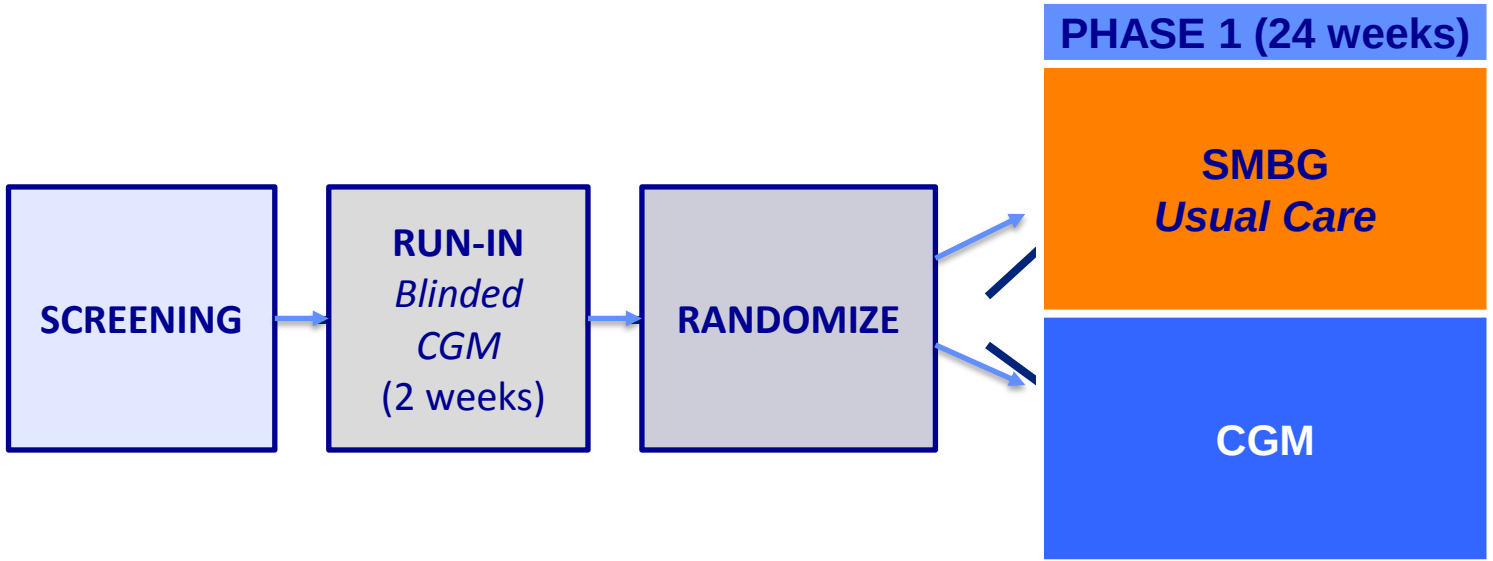
IMPORTANT: The device may inaccurately indicate hypoglycemia. The results of the clinical study conducted for this device showed that 40% of the time when the device indicated that user sensor glucose values were at or below 60 mg/dL, user glucose values were actually in the range of 81-160 mg/dL. Therefore, interpretation of the FreeStyle Libre Pro Flash Glucose Monitoring System readings should only be based on the trends and patterns analyzed through time using the reports available per the intended use.

Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections
The DIAMOND Randomized Clinical Trial

Roy W. Beck, MD, PhD; Tonya Riddlesworth, PhD; Katrina Ruedy, MSPH; Andrew Ahmann, MD; Richard Bergenstal, MD; Stacie Haller, RD, LD, CDE; Craig Kollman, PhD; Davida Kruger, MSN, APN-BC; Janet B. McGill, MD; William Polonsky, PhD; Elena Toschi, MD; Howard Wolpert, MD; David Price, MD; for the DIAMOND Study Group

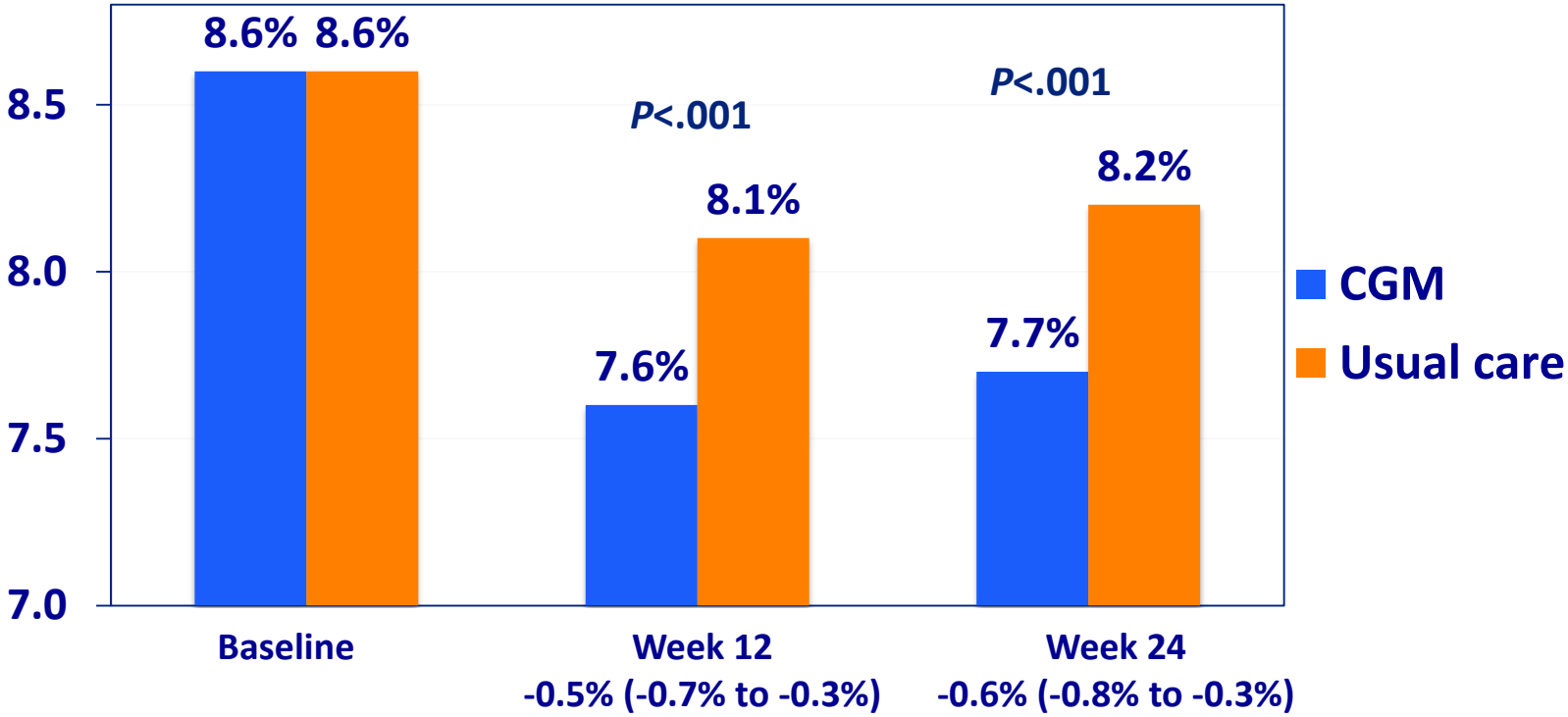
JAMA 2017; 317:371-378

DIaMonD Study Design – Phase 1: The First RCT Specifically Looking at the Clinical Efficacy of MDI + CGM



Beck et al. JAMA. 2017;317:371-378

A1c Differences – CMG vs SMBG
The DIaMonD Randomized Controlled Trial



Beck et al. JAMA. 2017;317:371-378

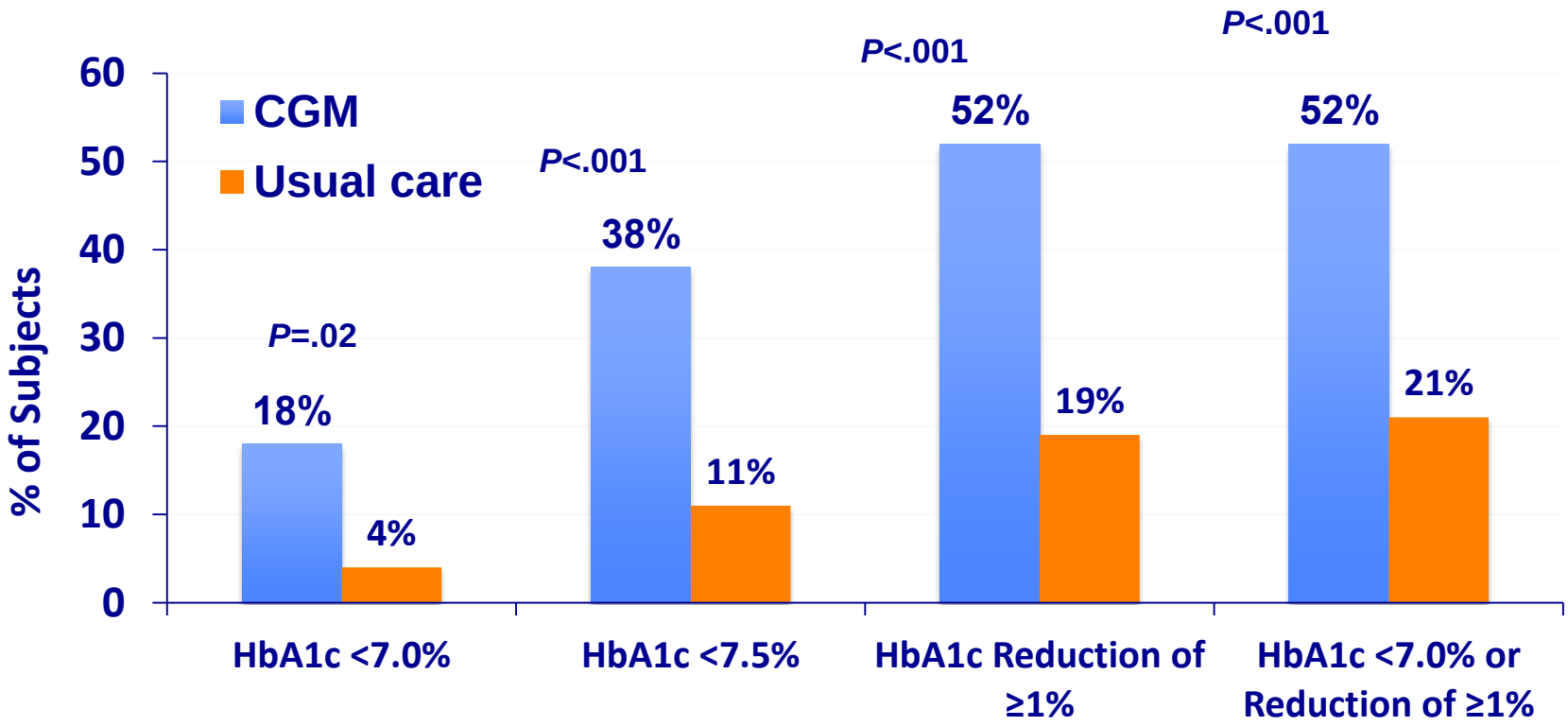
CGM Usage: Majority of MDI Patients Wore CGM ≥6 Days/Week

	Week 4 Visit (N=105)	Week 12 Visit (N=103)	Week 24 Visit (N=102)
Mean CGM usage, days/week	6.9	6.8	6.7
0 days/week	0%	1%	2%
≥6 days/week	94%	96%	89%
Mean % of CGM readings captured	95%	93%	90%

All data reflect the 28 days prior to each visit.

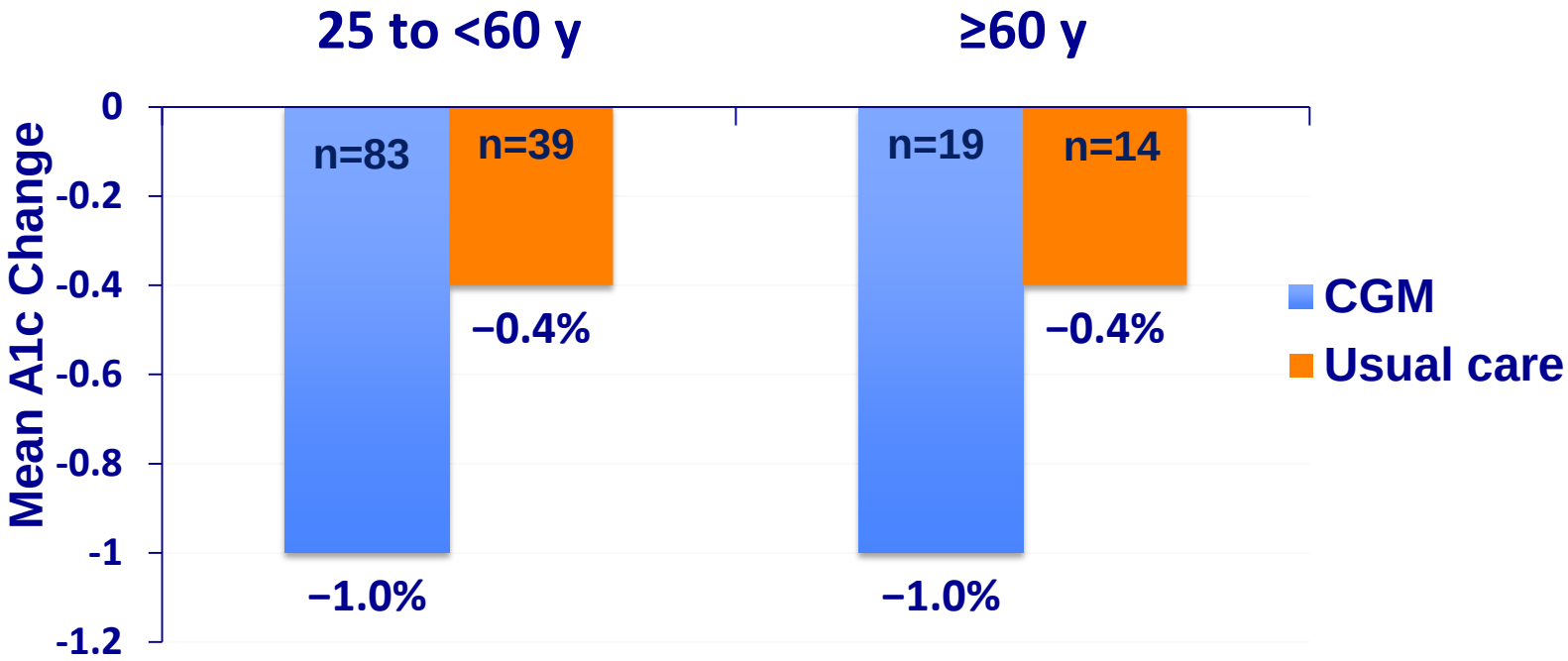
Beck et al. JAMA. 2017;317:371-378

At 6 Months, 52% of Subjects Reaching Goal A1c or Reduced A1c by 1%



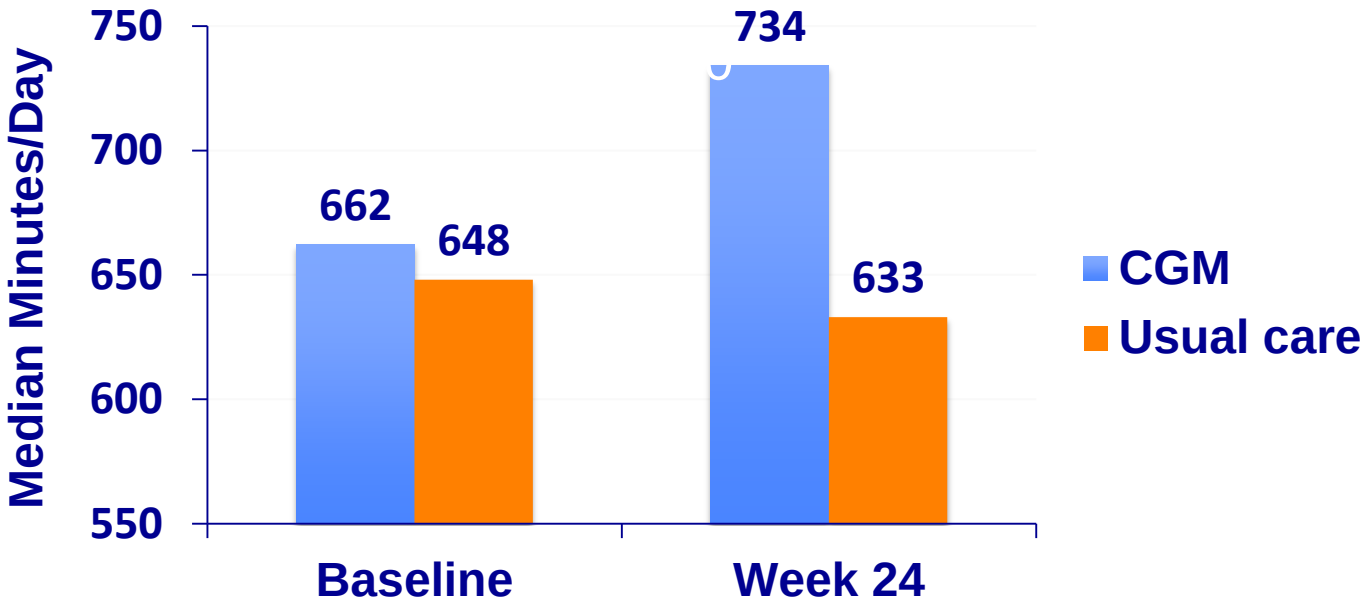
Beck et al. JAMA. 2017;317:371-378

A1c Reduction with MDI Subjects Did Not Differ Among Adult age groups



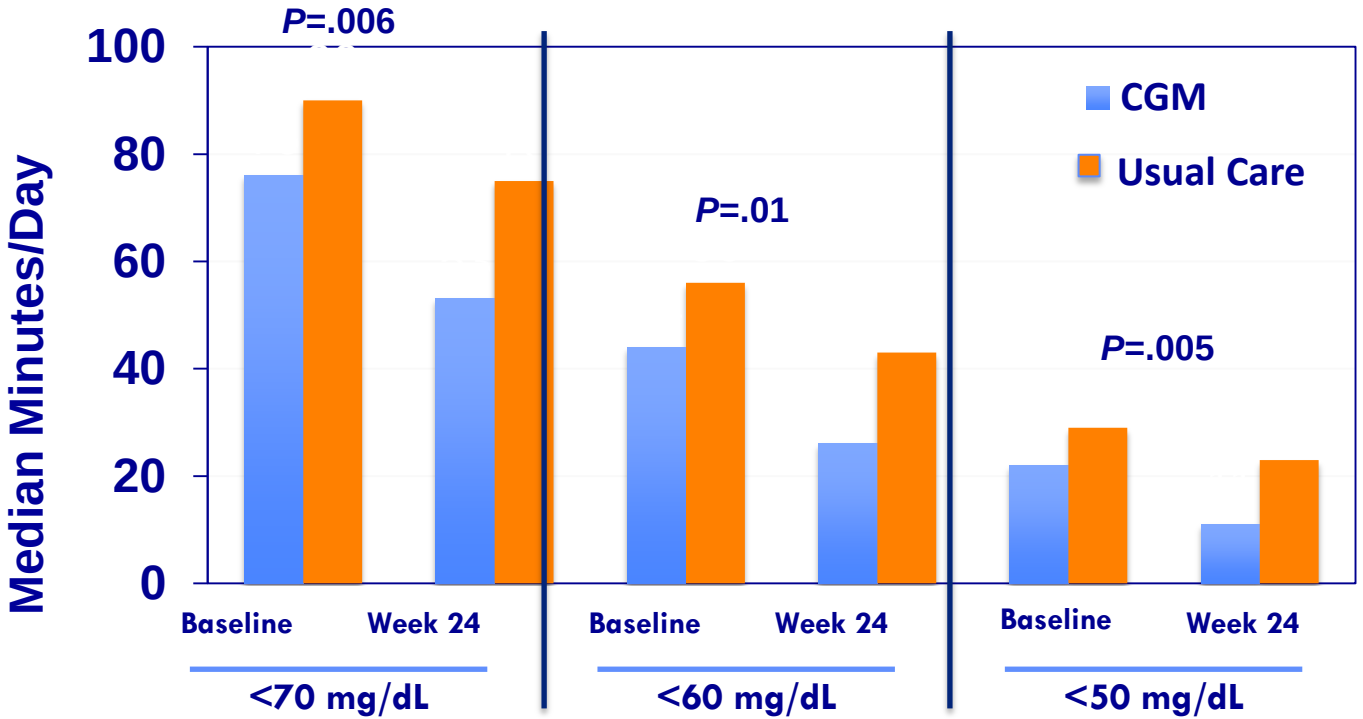
Beck et al. JAMA. 2017;317:371-378

Time-in-Range 70-180 mg/dL Increased



Beck et al. JAMA. 2017;317:371-378

Hypoglycemia Decreased Across All Low Levels



Beck et al. JAMA. 2017;317:371-378

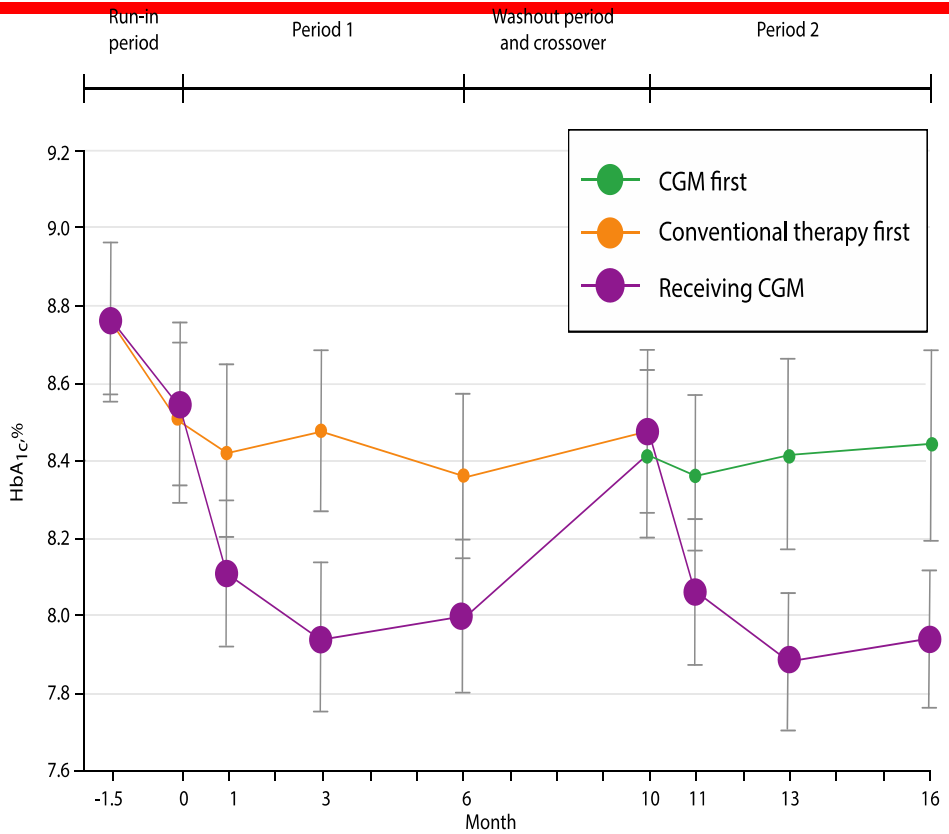
Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections

The GOLD Randomized Clinical Trial

Marcus Lind, MD, PhD; William Polonsky, PhD; Irl B. Hirsch, MD; Tim Heise, MD; Jan Bolinder, MD, PhD; Sofia Dahlqvist; Erik Schwarz, MD, PhD; Arndís Finna Ólafsdóttir, RN; Anders Frid, MD, PhD; Hans Wedel, PhD; Elsa Ahlén, MD; Thomas Nyström, MD, PhD; Jarl Hellman, MD

JAMA 2017; 317:379-387

CGM vs SMBG for Glycemic Control in Adults with T1D on MDI - The GOLD Randomized Clinical Trial



Baseline A1C Reduction with CGM vs MDI: 0.8%

Between Group A1C Reduction with SMBG + MDI vs CGM + MDI: 0.4%

More severe hypoglycemia in SMBG + MDI group (12 events vs. 1 event)

88% of time CGM worn throughout the study

Lind et al. JAMA. 2017;317:379-387.

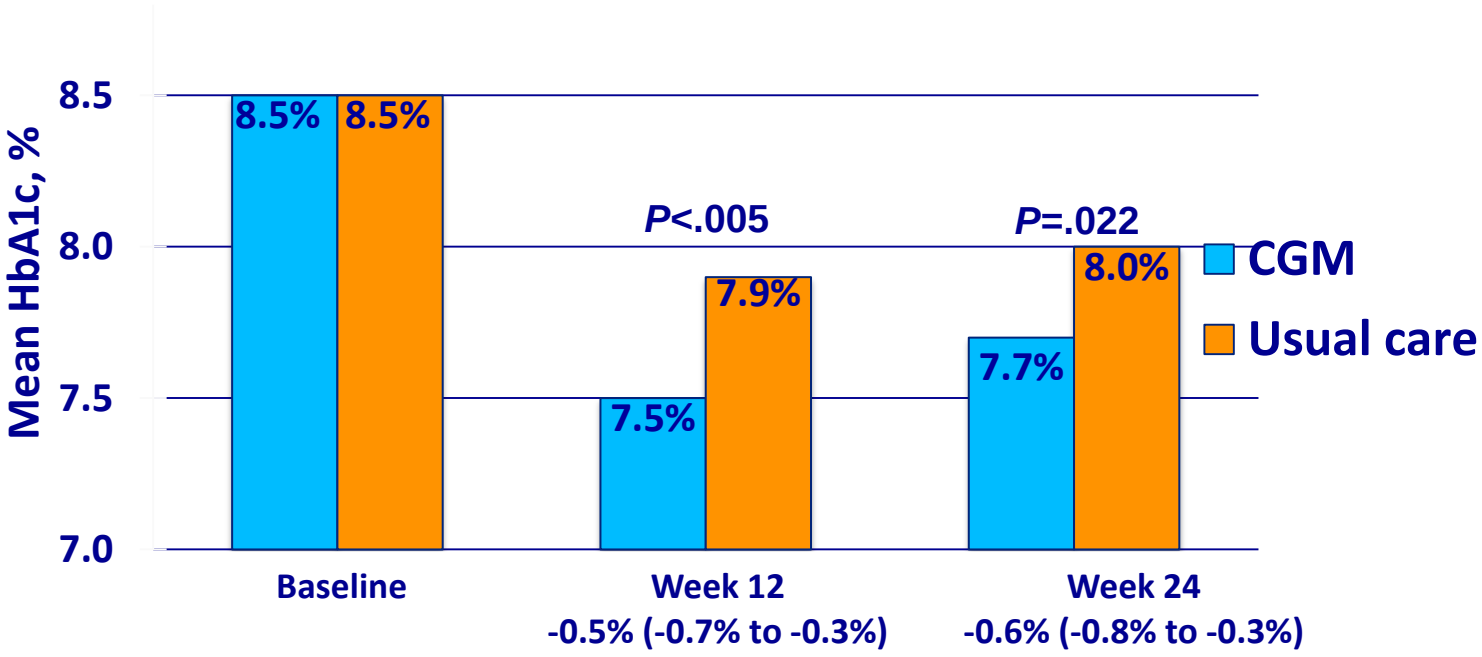
Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections

A Randomized Trial

Roy W. Beck, MD, PhD; Tonya D. Riddlesworth, PhD; Katrina Ruedy, MSPH; Andrew Ahmann, MD; Stacie Haller, RD, LD, CDE; Davida Kruger, MSN, APN-BC; Janet B. McGill, MD; William Polonsky, PhD; David Price, MD; Stephen Aronoff, MD; Ronnie Aronson, MD; Elena Toschi, MD; Craig Kollman, PhD; and Richard Bergenstal, MD; for the DIAMOND Study Group*

Annals of Internal Medicine 2017; 167:365-374

DIaMonD T2D Study:
HbA1c Treatment Group Differences



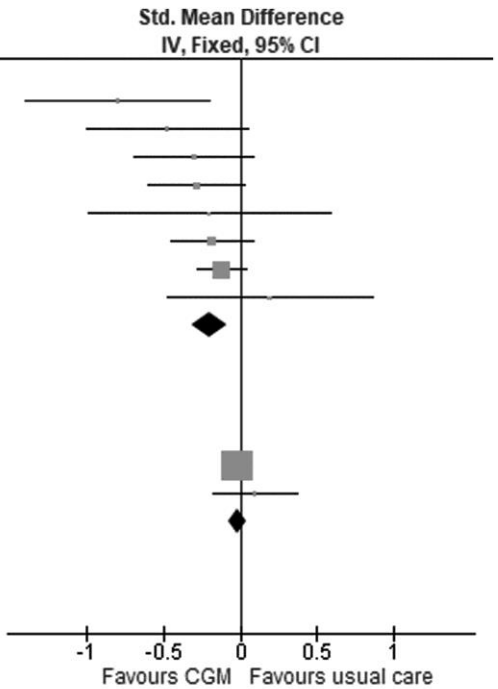
Bergenstal et al **Ann Int Med** 2017; 167:365-374

Glucose Monitoring in Type 2 Diabetes

All Trials

Study or Subgroup	CGM Mean	CGM SD	CGM Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.1.2 RT-CGM and P-CGM								
Allen 2008	-1.16	1.04	21	-0.32	1.02	25	3.5%	-0.80 [-1.41, -0.20]
Yoo 2008	-1.1	1.56	29	-0.4	1.3	28	4.6%	-0.48 [-1.01, 0.05]
Ehrhardt 2011	-1	1.64	50	-0.5	1.63	50	8.2%	-0.30 [-0.70, 0.09]
Beck 2017	-0.8	0.92	77	-0.5	1.14	75	12.4%	-0.29 [-0.61, 0.03]
Cosson 2009	-0.63	1.44	11	-0.31	1.55	14	2.0%	-0.21 [-1.00, 0.59]
Kim 2014	-0.6	1.86	65	-0.2	2.26	301	17.6%	-0.18 [-0.45, 0.09]
Kesavadev 2017	-0.5	1.66	296	-0.3	1.56	296	48.9%	-0.12 [-0.29, 0.04]
Sato 2016	0	1.77	17	-0.3	1.2	17	2.8%	0.19 [-0.48, 0.87]
Subtotal (95% CI)			**566**			**806**	**100.0%**	**-0.20 [-0.31, -0.09]**
Heterogeneity: $Chi^2 = 7.63$, df = 7 (P = 0.37); $I^2 = 8\%$								
Test for overall effect: Z = 3.51 (P = 0.0004)								
1.1.3 FGM								
Anjana 2017	-0.9	11.17	2339	-0.7	8.69	2339	95.9%	-0.02 [-0.08, 0.04]
Haak 2017	-0.28	1.3	149	-0.41	1.5	75	4.1%	0.09 [-0.18, 0.37]
Subtotal (95% CI)			**2488**			**2414**	**100.0%**	**-0.02 [-0.07, 0.04]**
Heterogeneity: $Chi^2 = 0.63$, df = 1 (P = 0.43); $I^2 = 0\%$								
Test for overall effect: Z = 0.53 (P = 0.59)								

Test for subgroup differences: $Chi^2 = 8.44$, df = 1 (P = 0.004), $I^2 = 88.1\%$

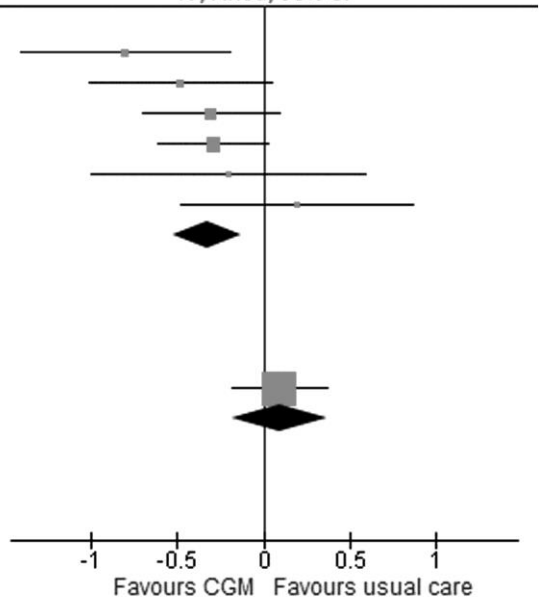


Park & Le. **Diabetes Technology & Therapeutics** 2018;20:613-621

Glucose Monitoring in Type 2 Diabetes

RCTs Only

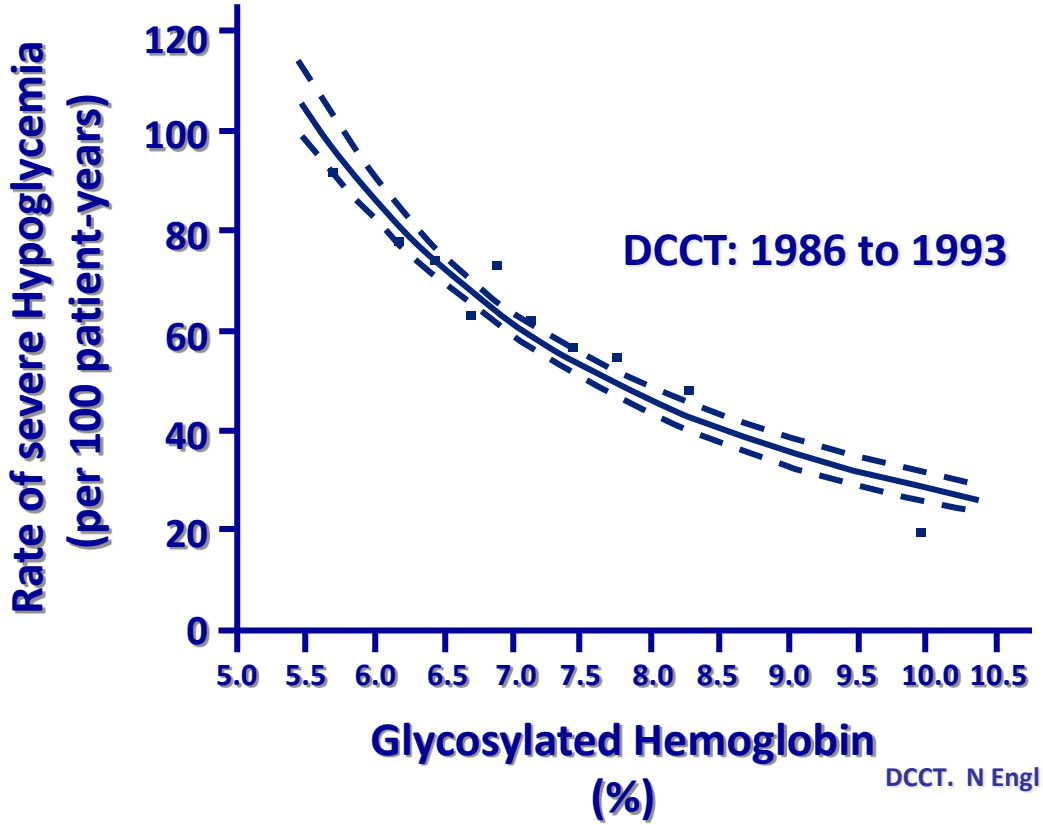
Study or Subgroup	CGM Mean	CGM SD	CGM Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.2.2 RT-CGM and P-CGM								
Allen 2008	-1.16	1.04	21	-0.32	1.02	25	10.4%	-0.80 [-1.41, -0.20]
Yoo 2008	-1.1	1.56	29	-0.4	1.3	28	13.7%	-0.48 [-1.01, 0.05]
Ehrhardt 2011	-1	1.64	50	-0.5	1.63	50	24.4%	-0.30 [-0.70, 0.09]
Beck 2017	-0.8	0.92	77	-0.5	1.14	75	37.2%	-0.29 [-0.61, 0.03]
Cosson 2009	-0.63	1.44	11	-0.31	1.55	14	6.1%	-0.21 [-1.00, 0.59]
Sato 2016	0	1.77	17	-0.3	1.2	17	8.4%	0.19 [-0.48, 0.87]
Subtotal (95% CI)			**205**			**209**	**100.0%**	**-0.33 [-0.52, -0.13]**
Heterogeneity: Chi² = 5.15, df = 5 (P = 0.40); I² = 3%								
Test for overall effect: Z = 3.28 (P = 0.001)								
1.2.3 FGM								
Haak 2017	-0.28	1.3	149	-0.41	1.5	75	100.0%	0.09 [-0.18, 0.37]
Subtotal (95% CI)			**149**			**75**	**100.0%**	**0.09 [-0.18, 0.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.67 (P = 0.50)								
Test for subgroup differences: Chi² = 5.92, df = 1 (P = 0.02), I² = 83.1%								



Park & Le. **Diabetes Technology & Therapeutics** 2018;20:613-621

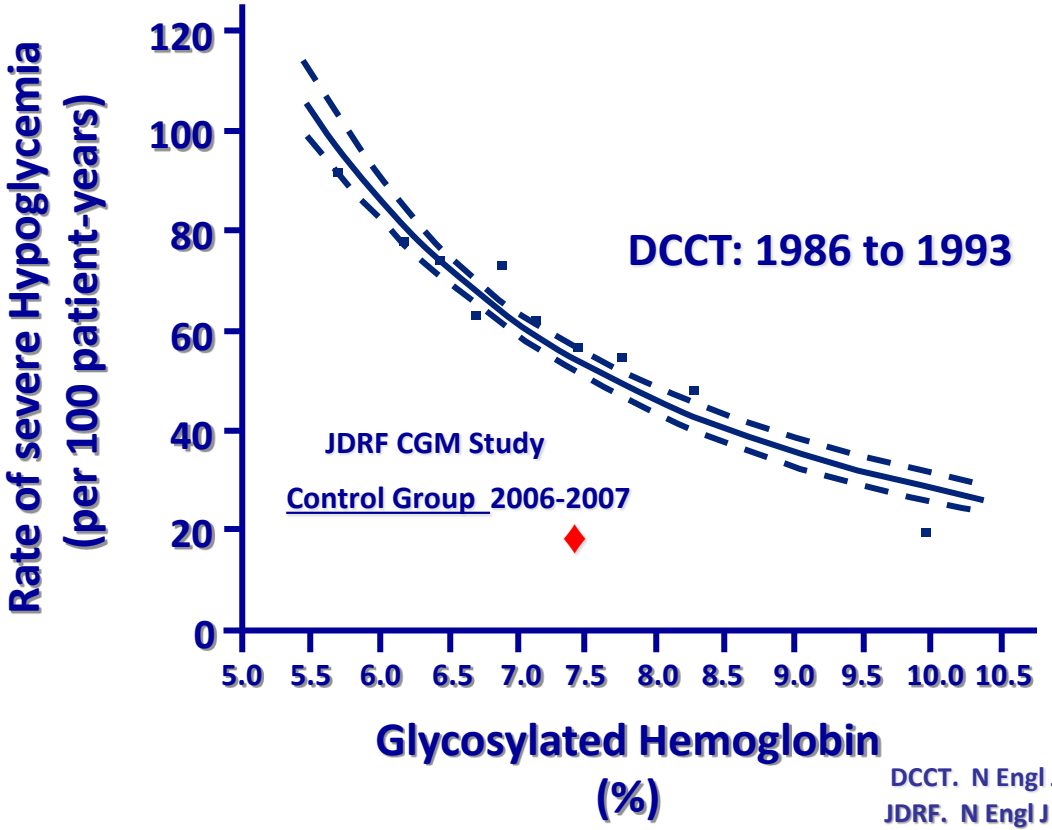
A1c and Hypoglycemia Risk

DCCT: Absolute Risk of Severe Hypoglycemia by Mean A1c



DCCT. N Engl J Med 1993;329:977-86

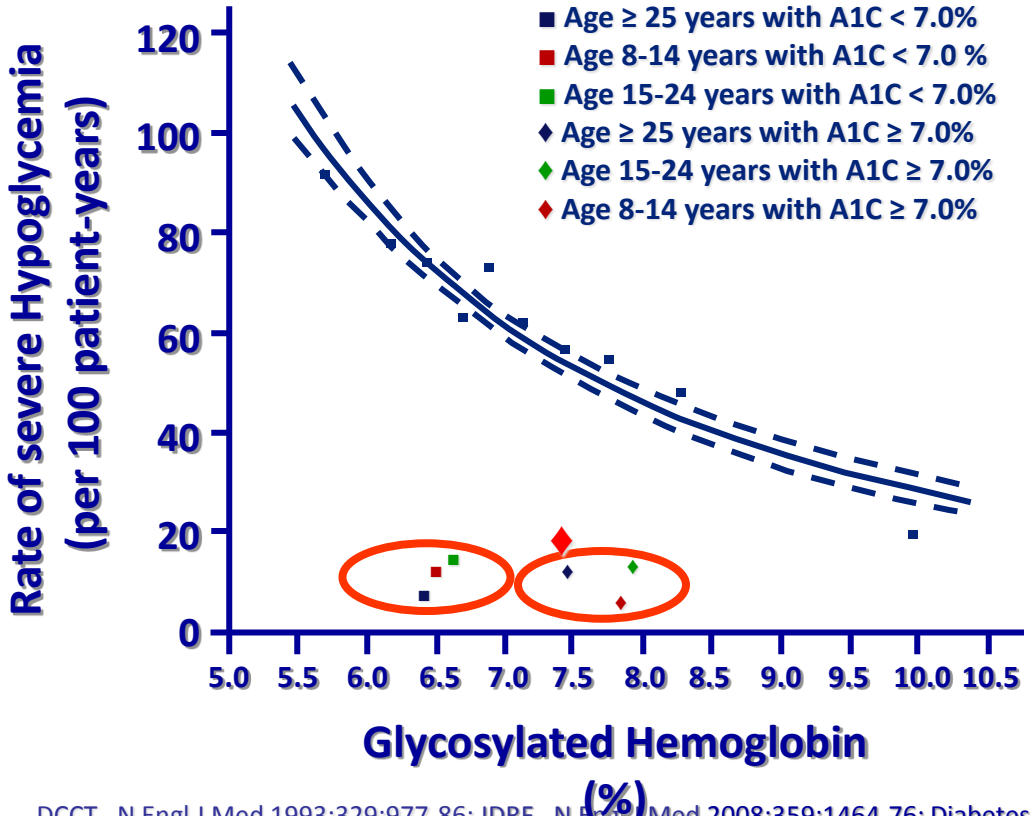
Two Eras of Diabetes Management



DCCT. N Engl J Med 1993;329:977-86

JDRF. N Engl J Med 2008;359:1464-76

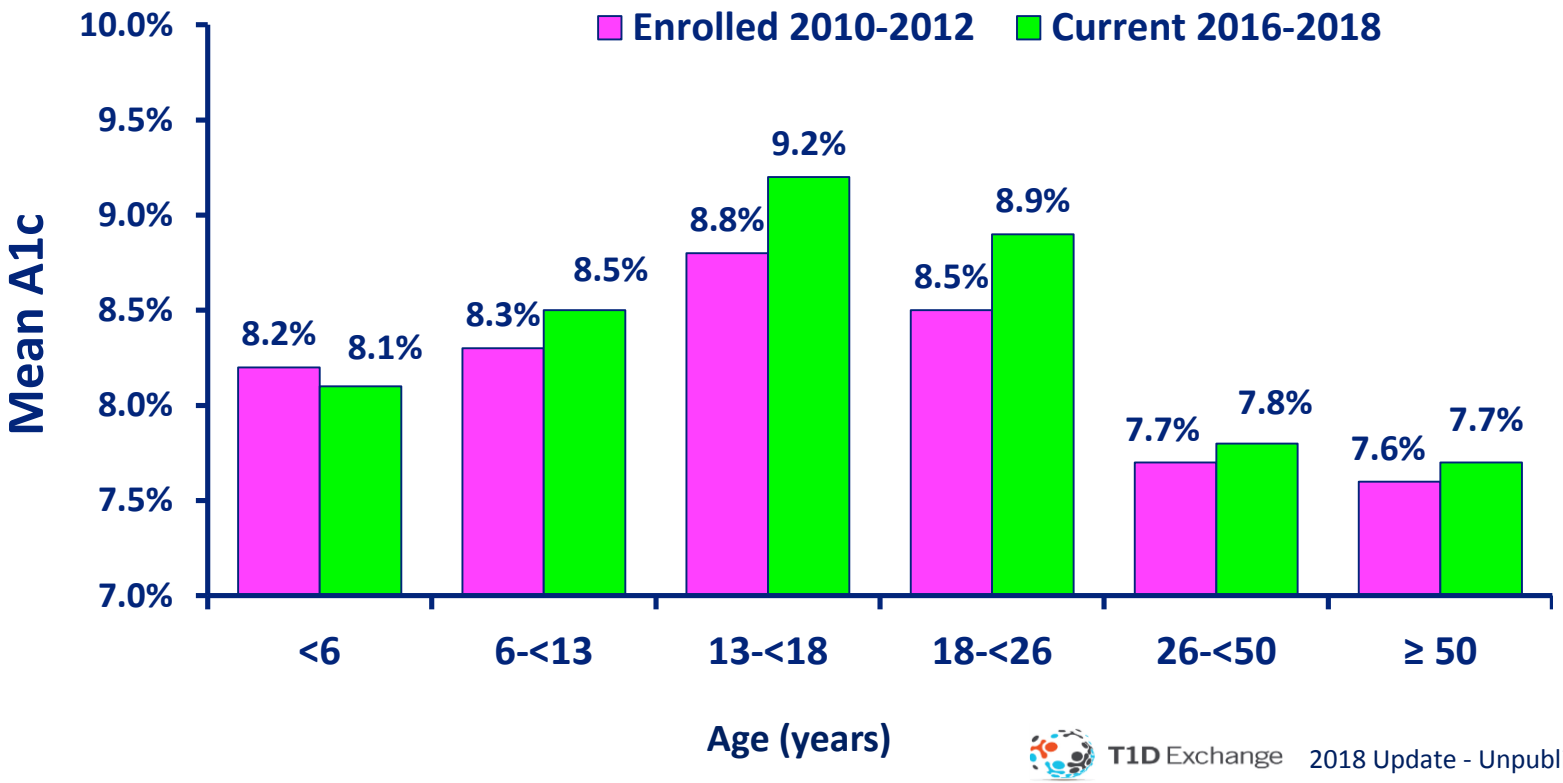
Impact of Continuous Glucose Monitoring on Rate of Severe Hypoglycemia Compared to DCCT



DCCT. N Engl J Med 1993;329:977-86; JDRF. N Engl J Med 2008;359:1464-76; Diabetes Care 2009: 32:1378-1383

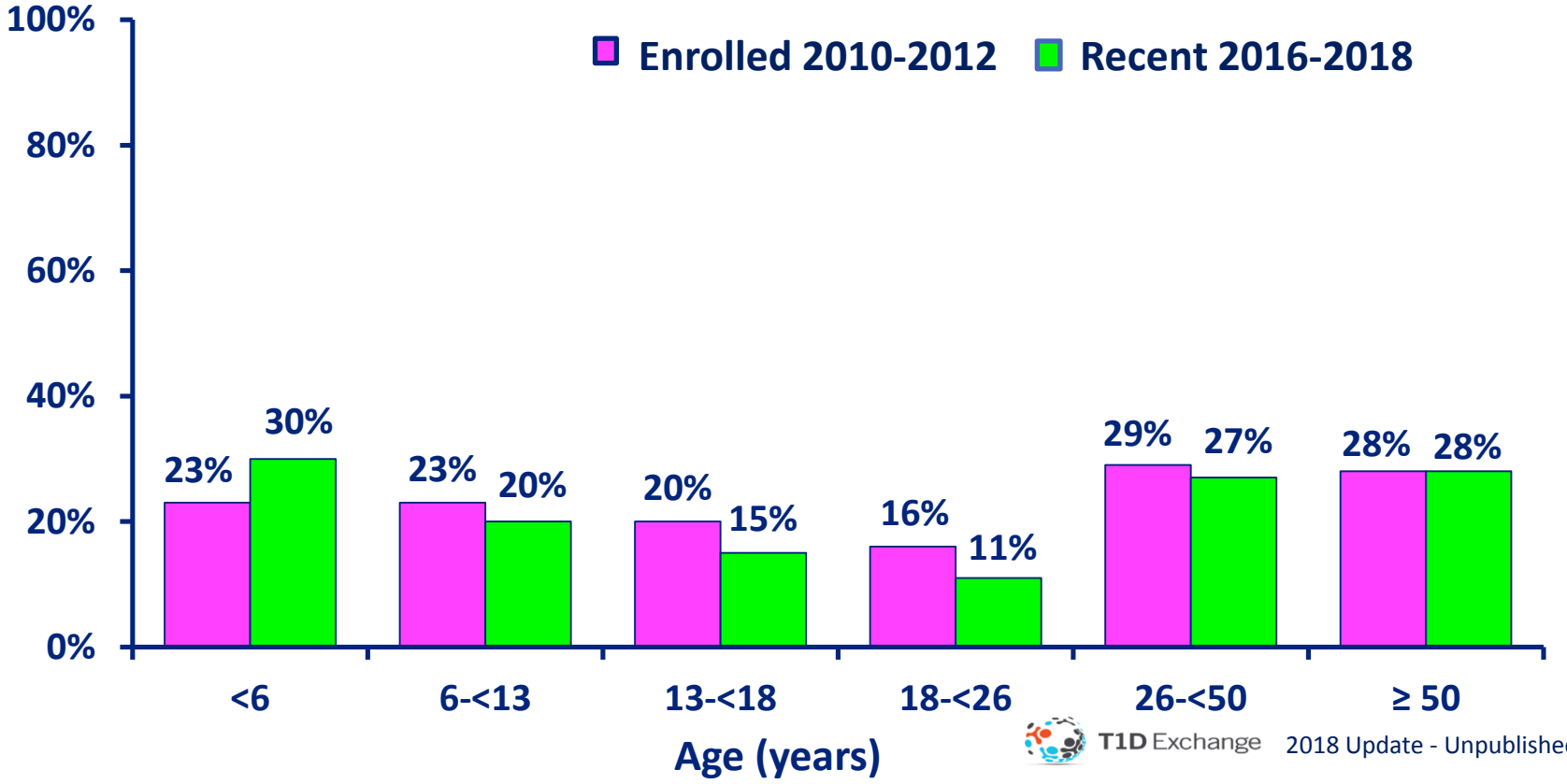
Type 1 Diabetes Exchange

A1c by Age and Time Period



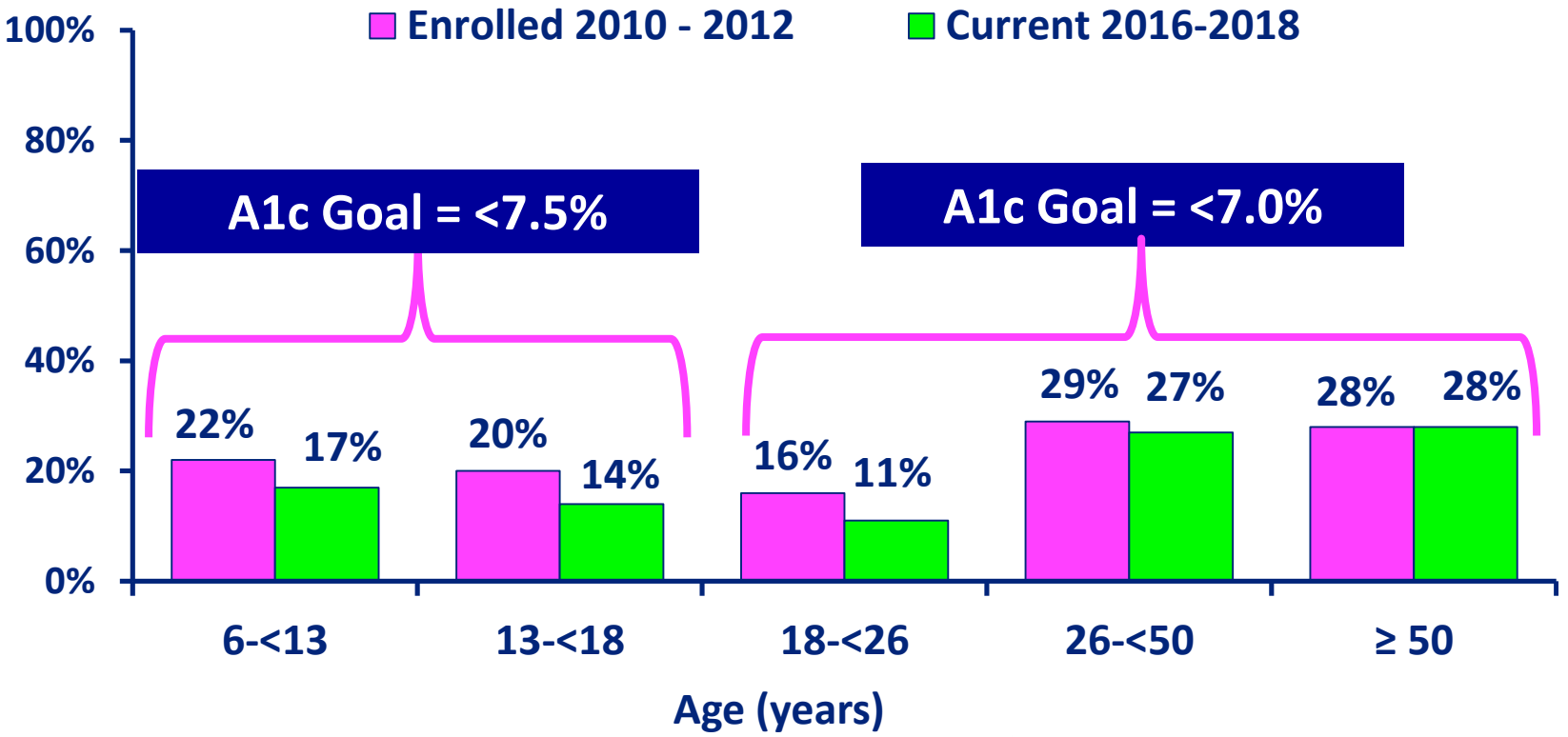
T1D Exchange 2018 Update - Unpublished

Proportion of Participants Achieving Target A1c of ≤7%



T1D Exchange 2018 Update - Unpublished

Only A Small Percentage of T1D Patients Achieve Target A1c Levels



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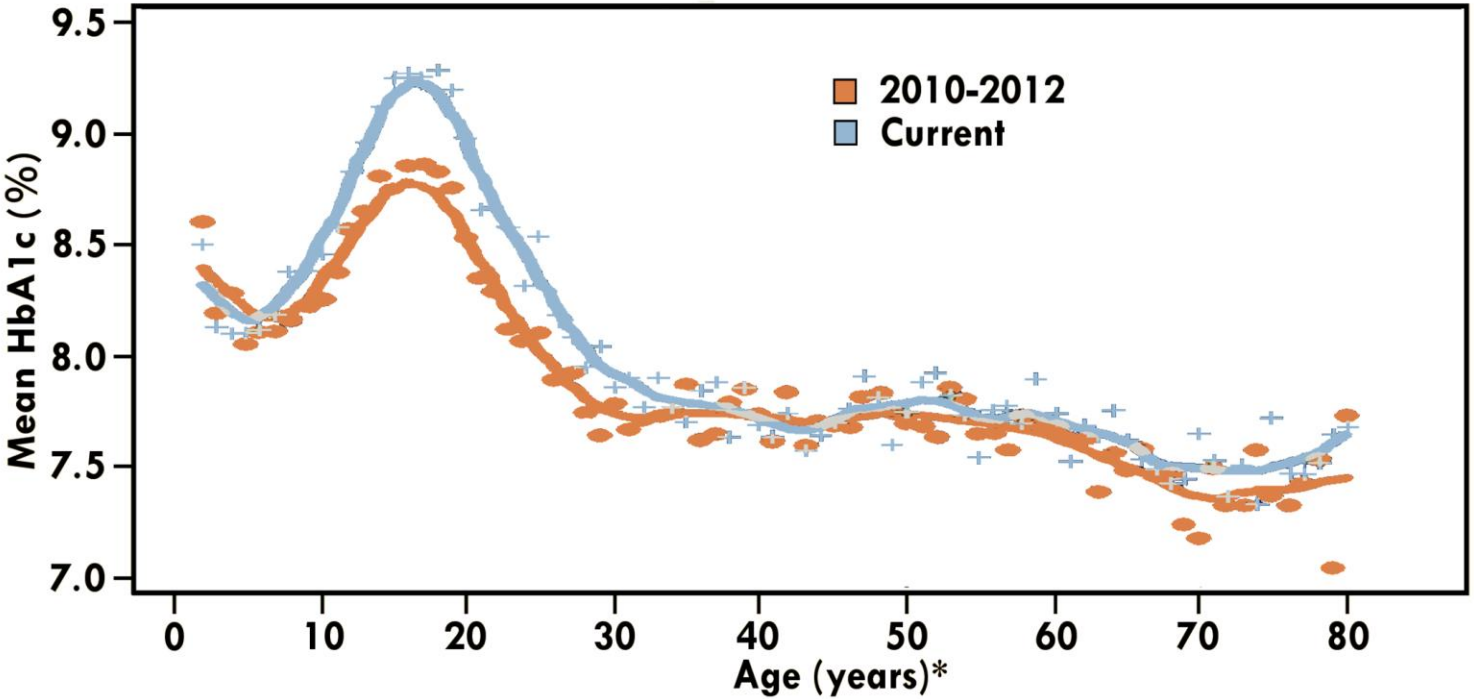
A1c by Age



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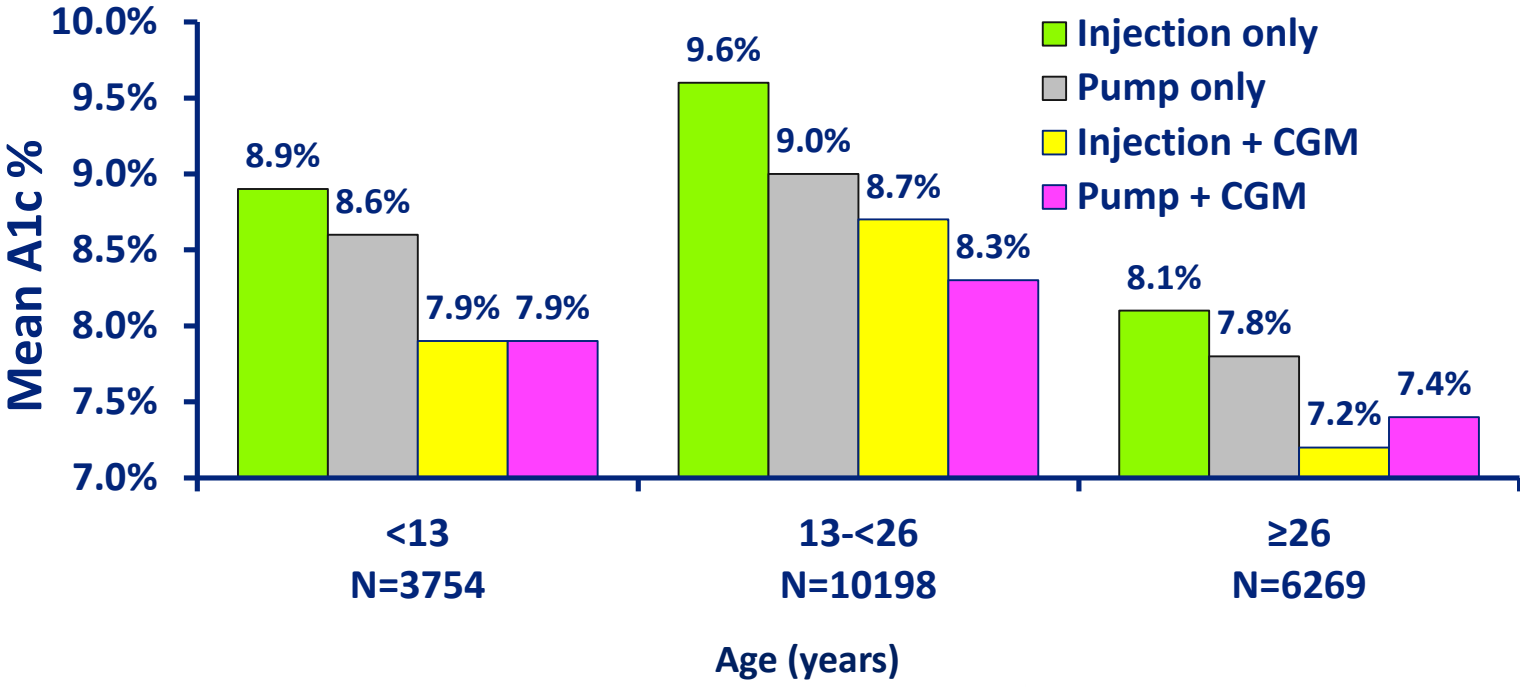
A1c by Insulin Delivery Method and CGM Use



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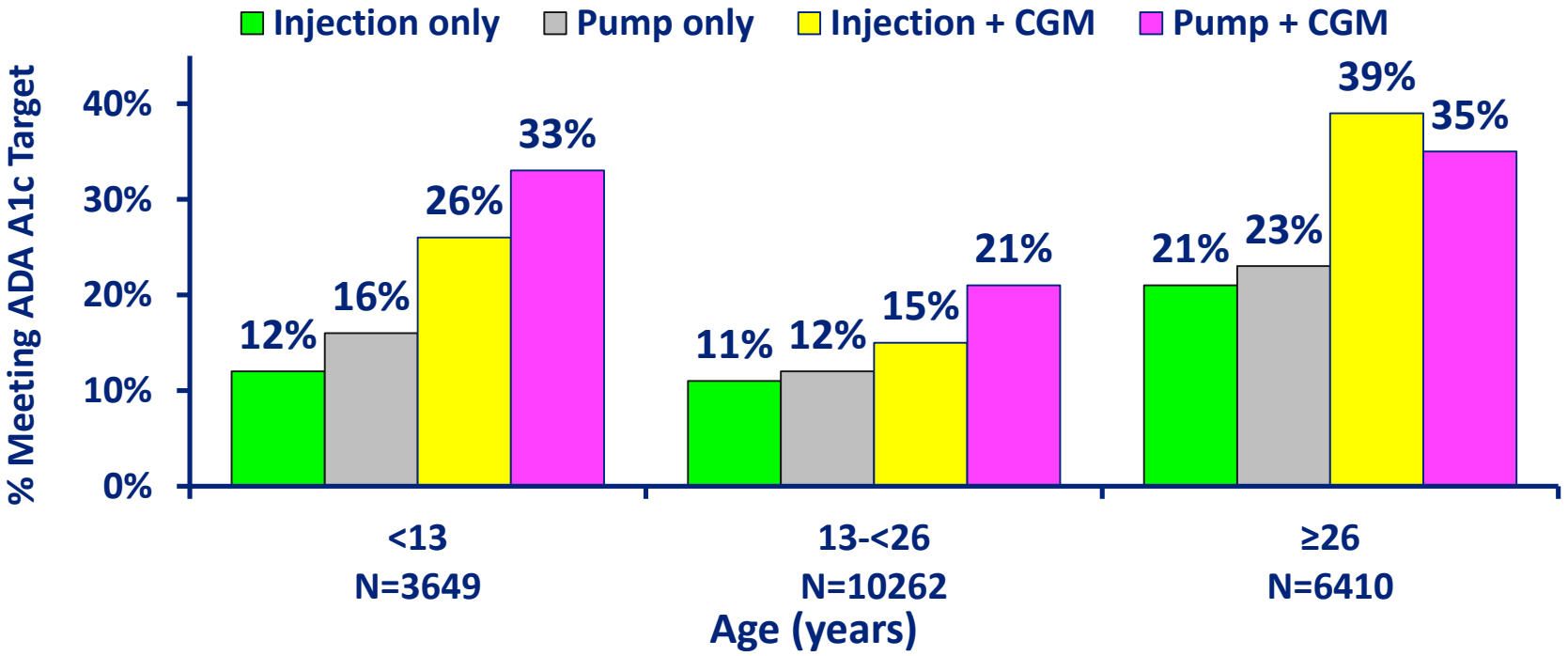
% Meeting A1c ADA Target by Insulin Delivery Method & CGM Use



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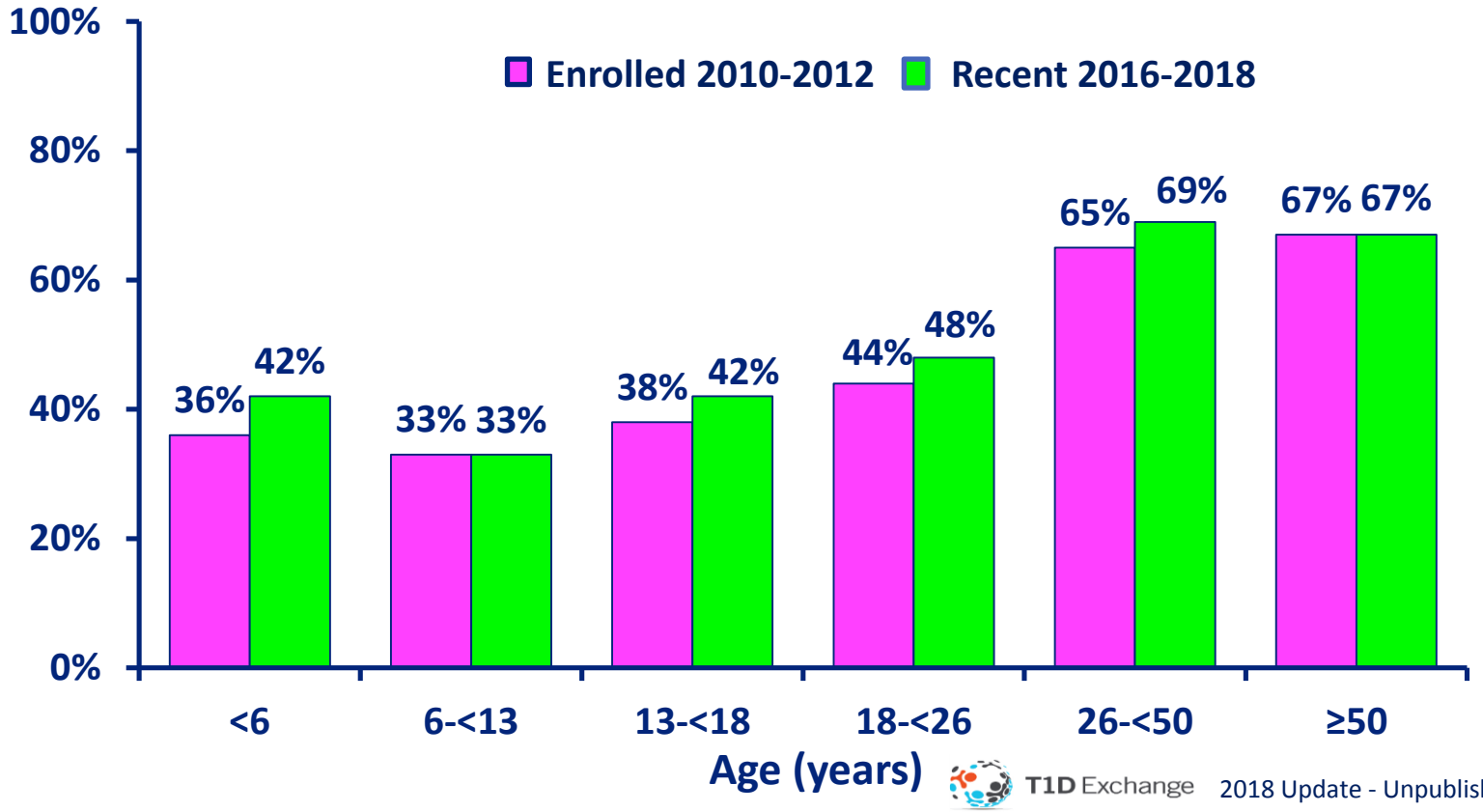
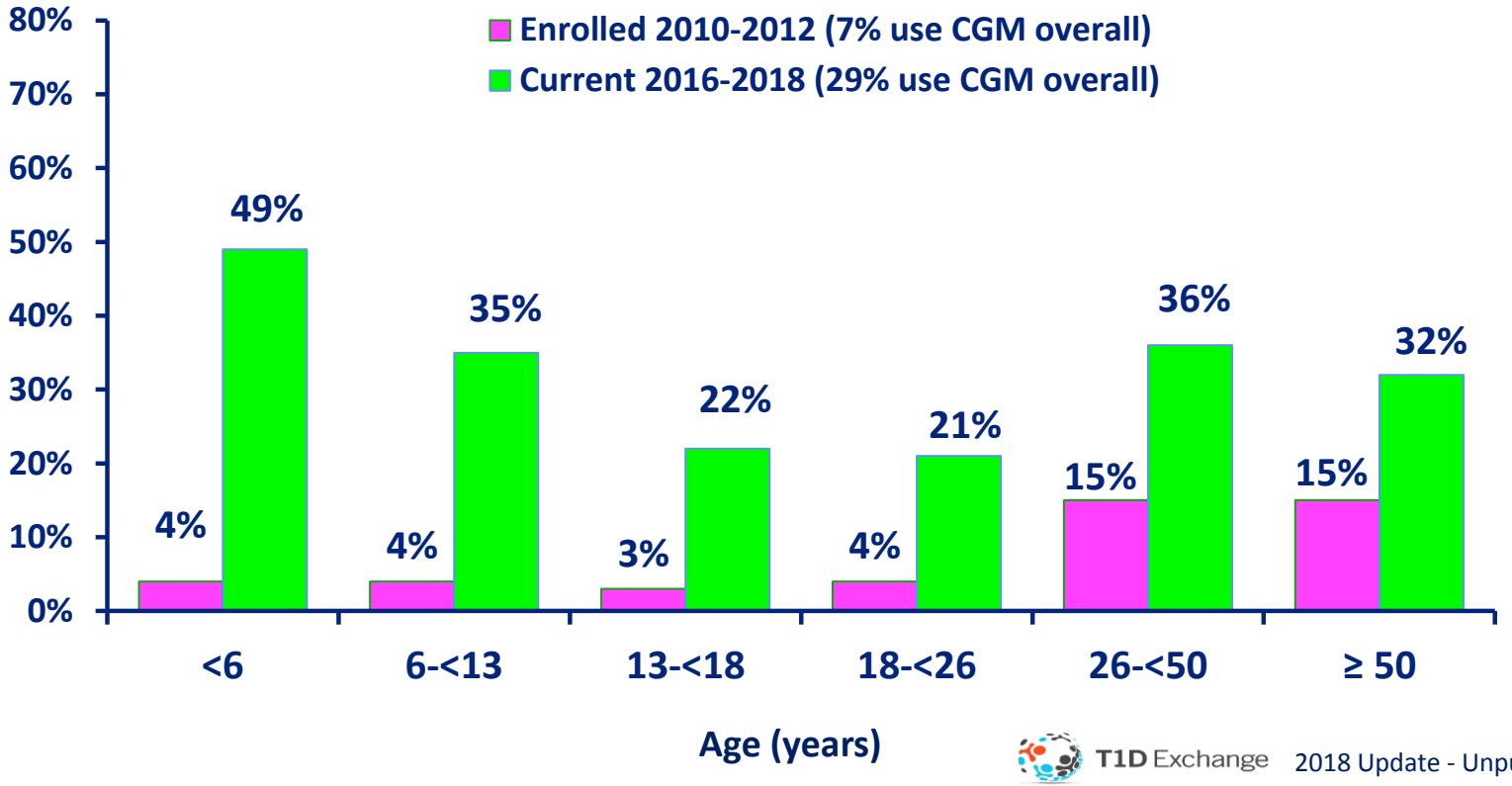
Proportion of Participants Overweight/Obese



T1D Exchange 2018 Update - Unpublished

CGM Use in Type 1 Diabetes Exchange



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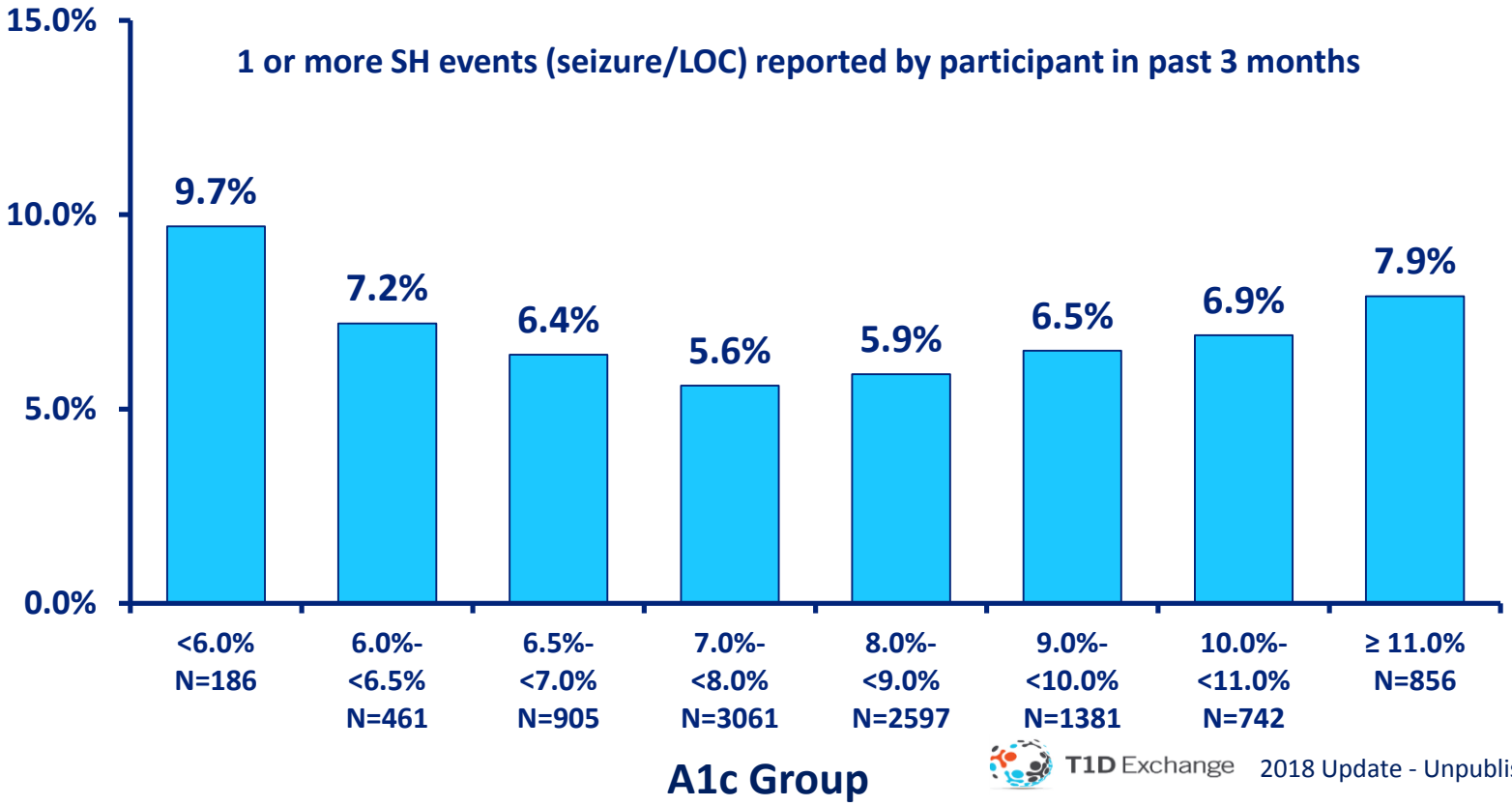
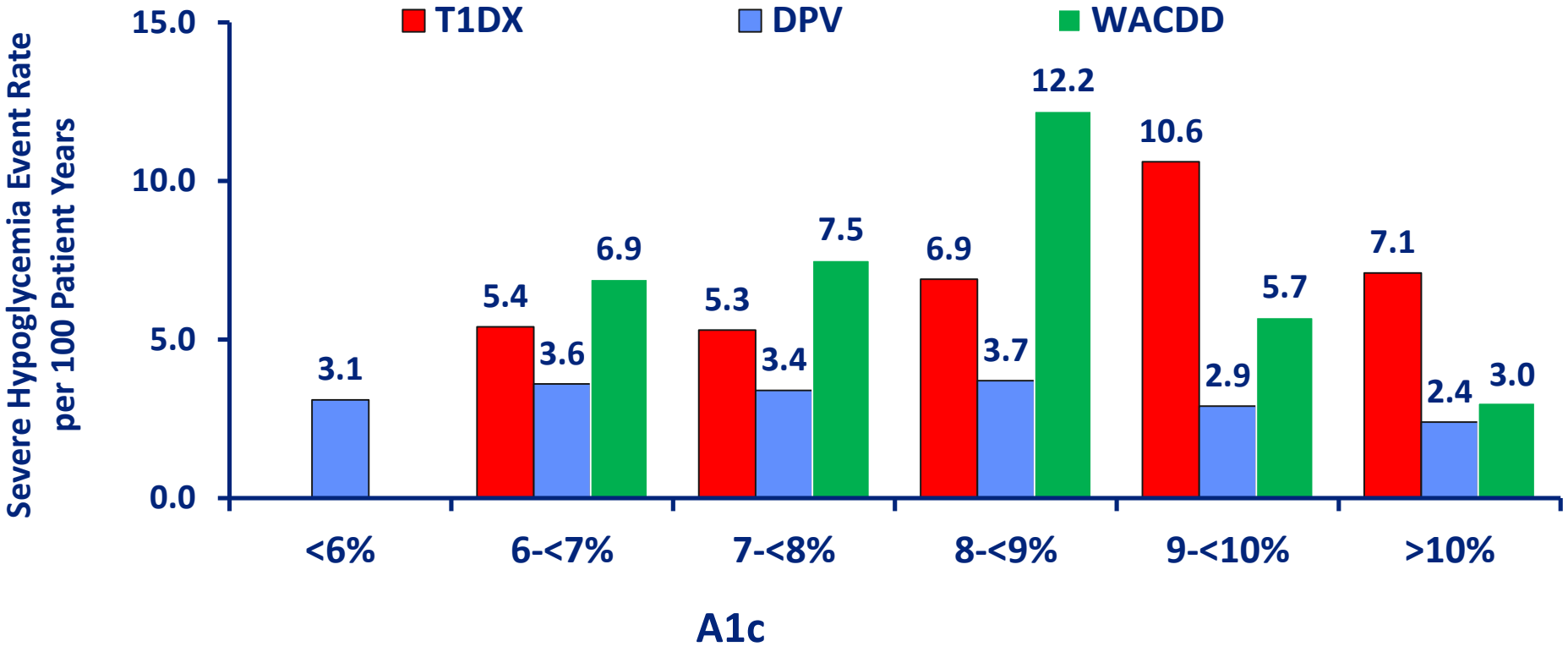
Severe Hypoglycemia in Type 1 Diabetes by A1c

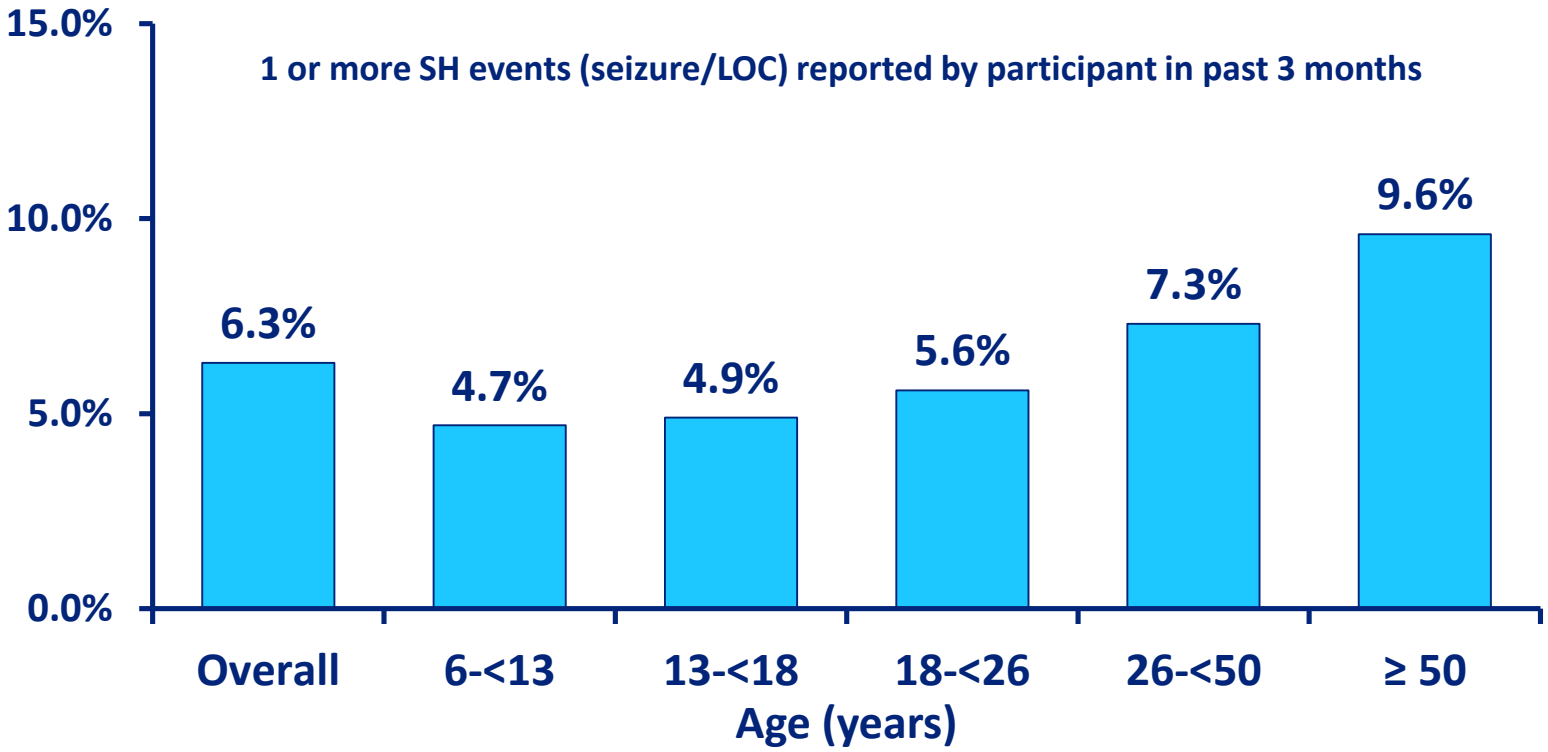


Risk of Severe Hypoglycemia Is Not Associated With A1c



Haynes et al. **Pediatric Diabetes** 2017;18:643–650

Occurrence of Severe Hypoglycemia by Age



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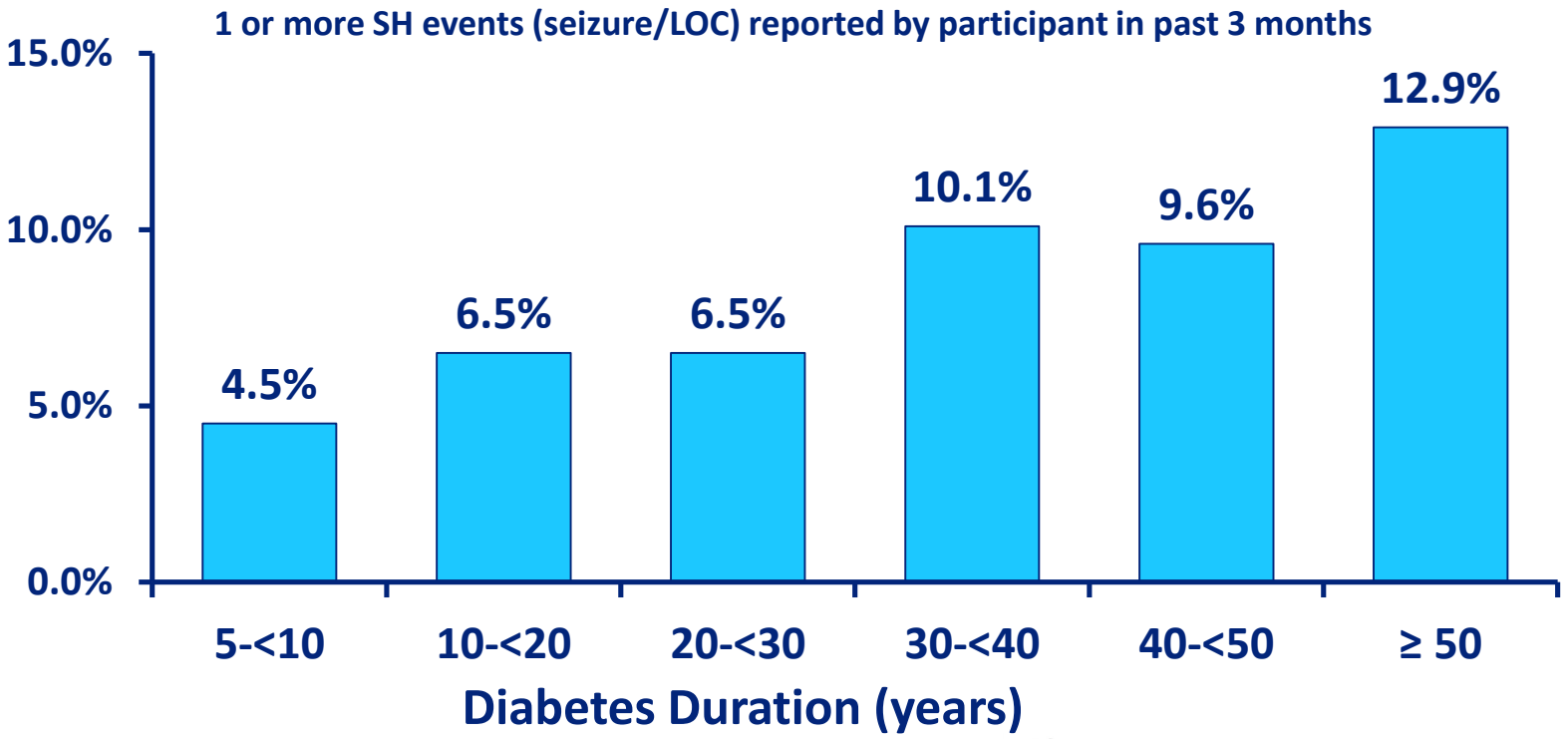
Occurrence of Severe Hypoglycemia by Diabetes Duration



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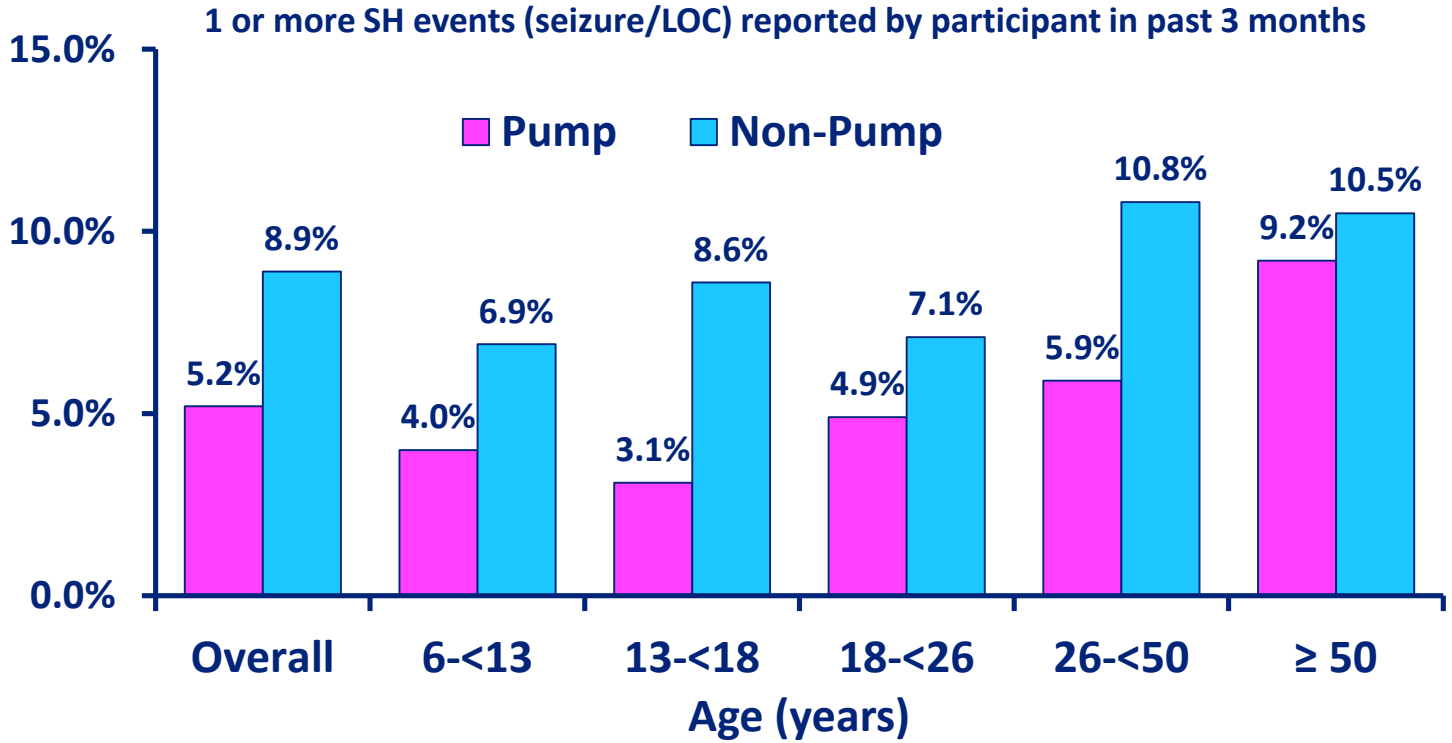
Occurrence of Severe Hypoglycemia by Pump Use Status



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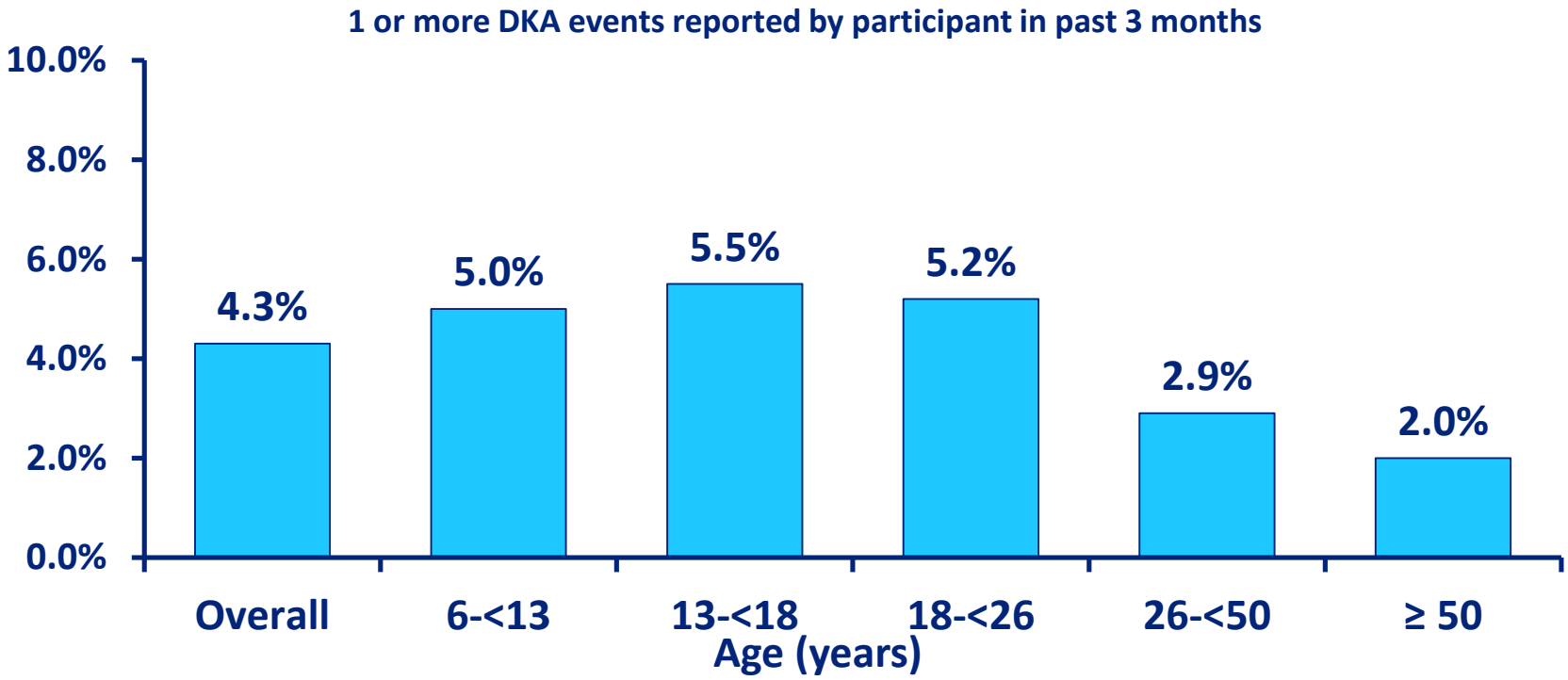
Occurrence of DKA by Age



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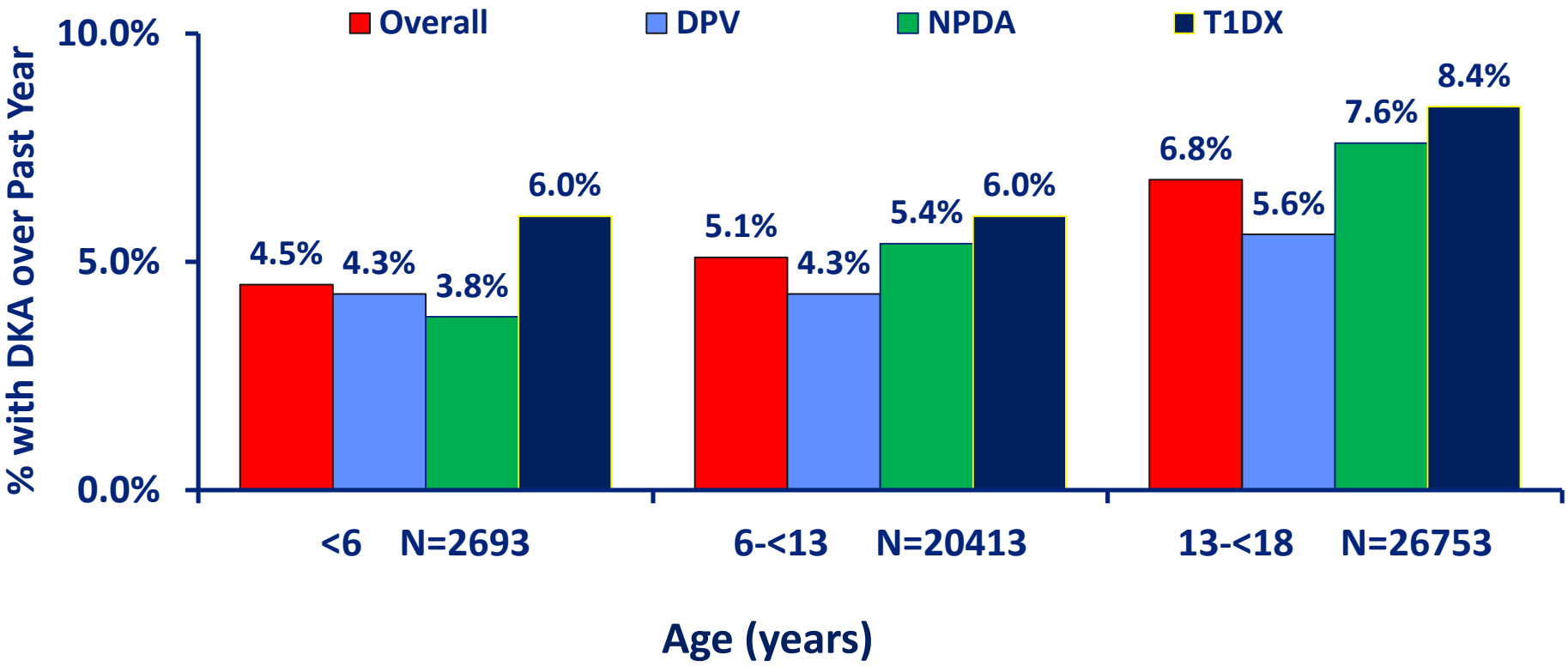
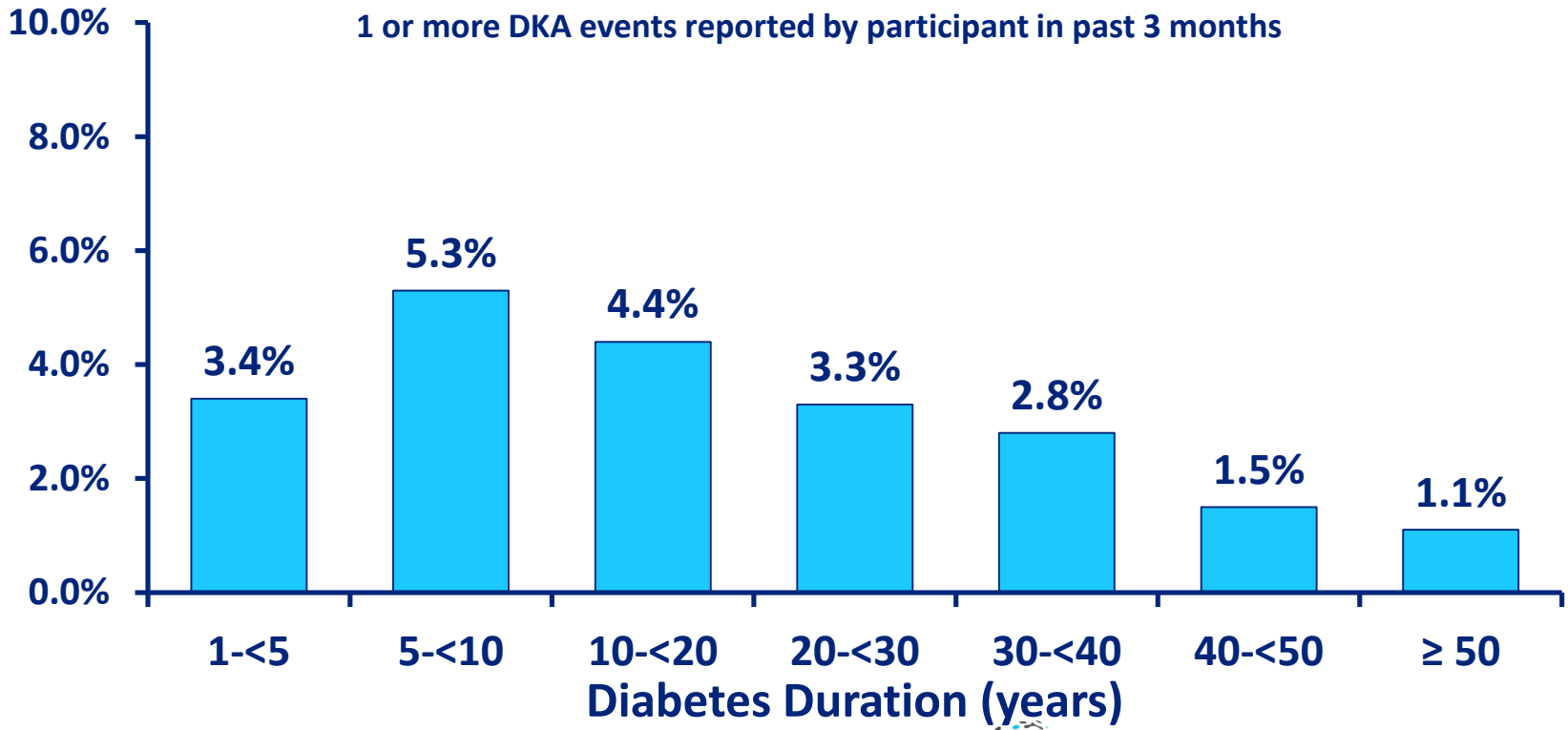
Frequency of Diabetic Ketoacidosis According to Age



Maahs et al. **Diabetes Care** 2015;38:1876–1882

Occurrence of DKA by Diabetes Duration



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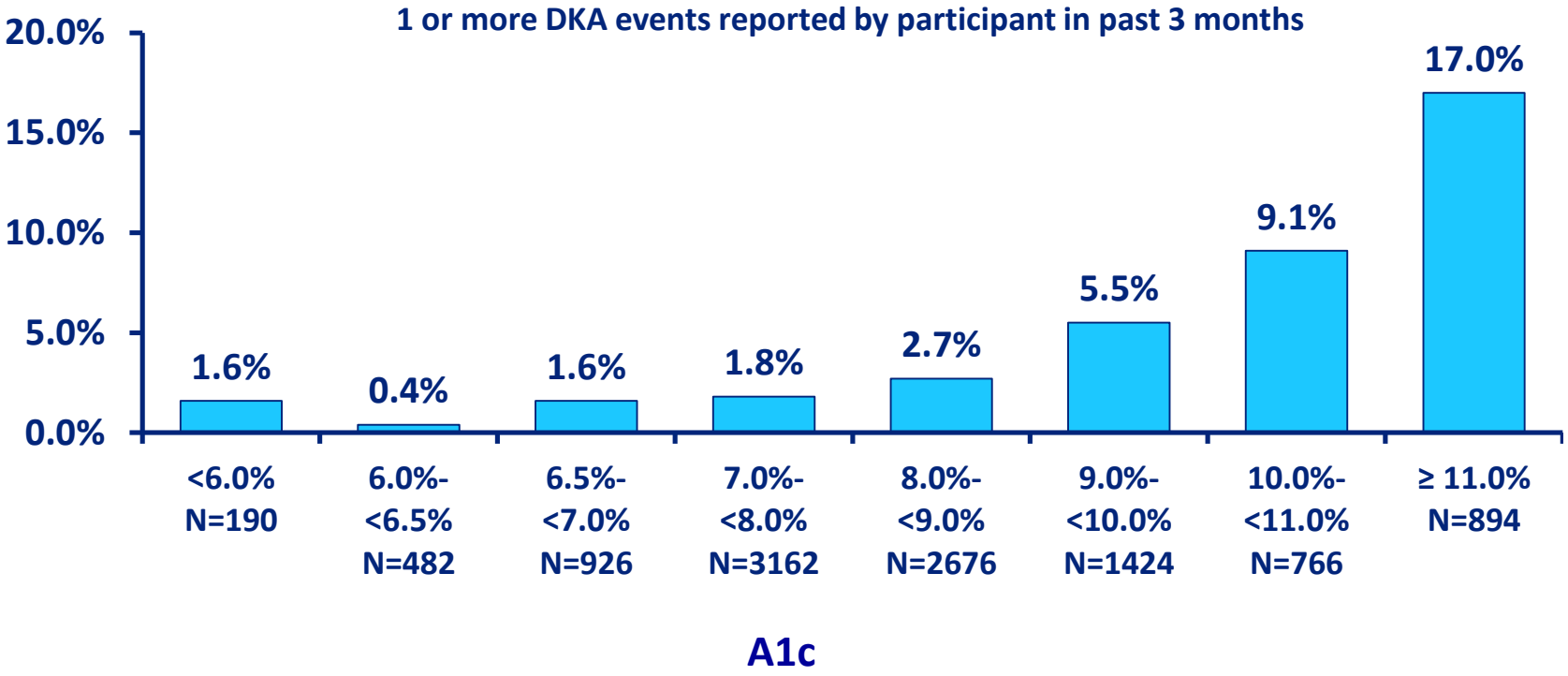
Occurrence of DKA by A1c



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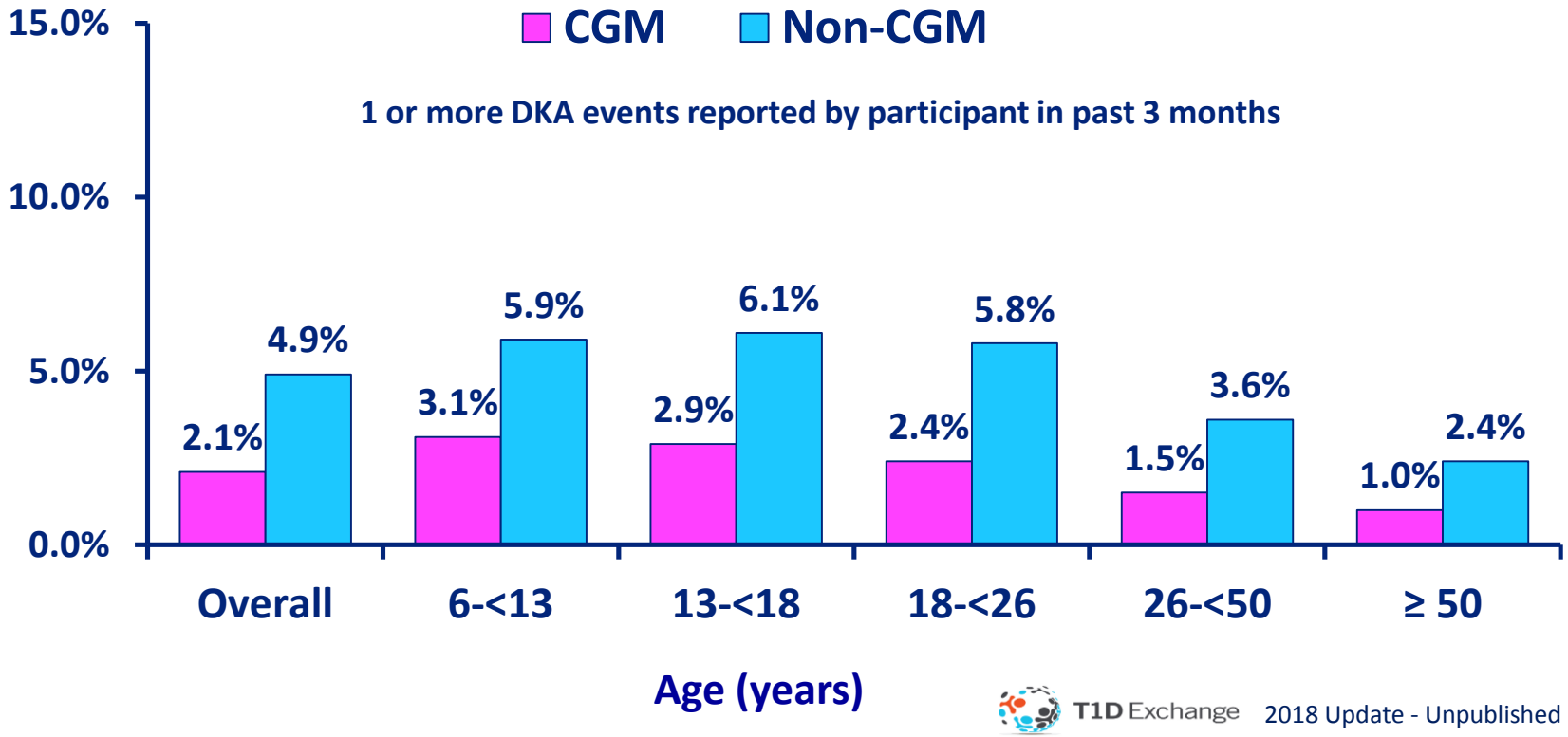
Occurrence of DKA by CGM Use Status



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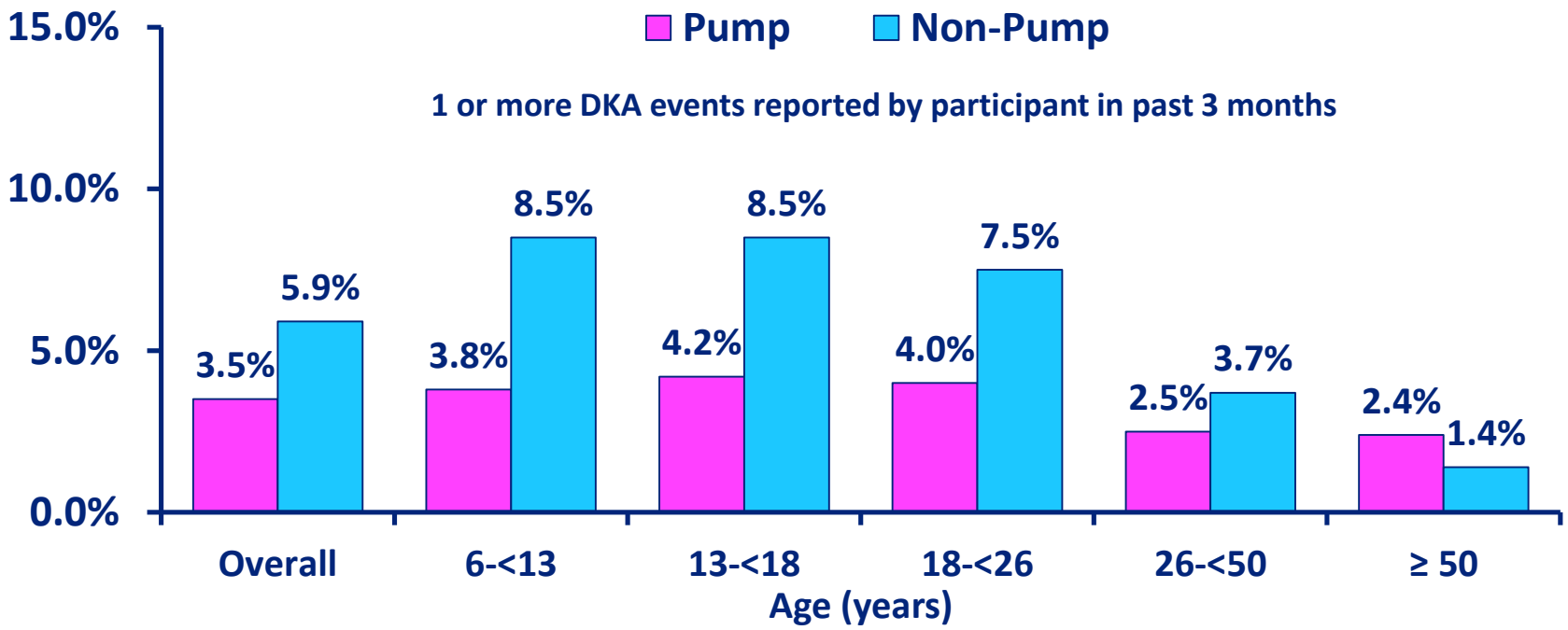
Occurrence of DKA by Pump Use Status



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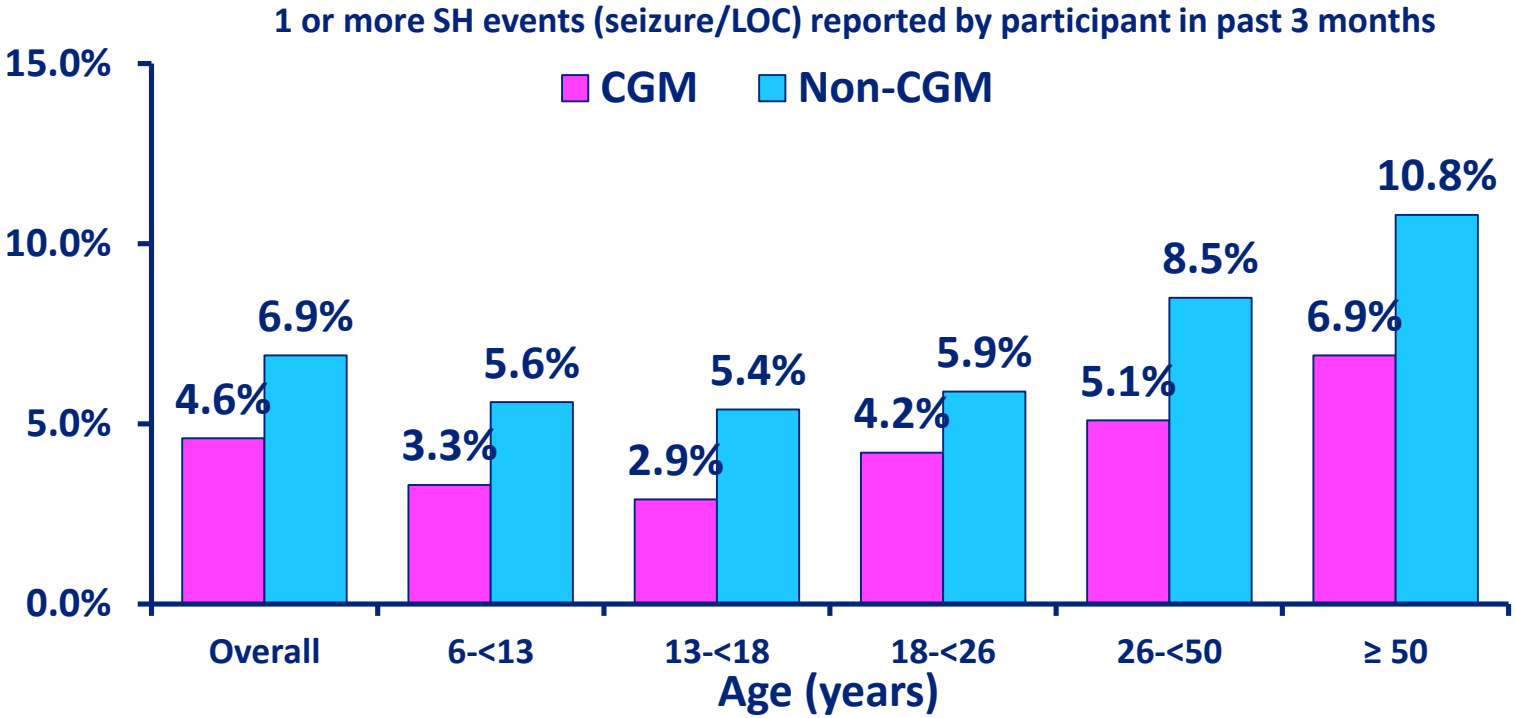
Severe Hypoglycemia by CGM Use



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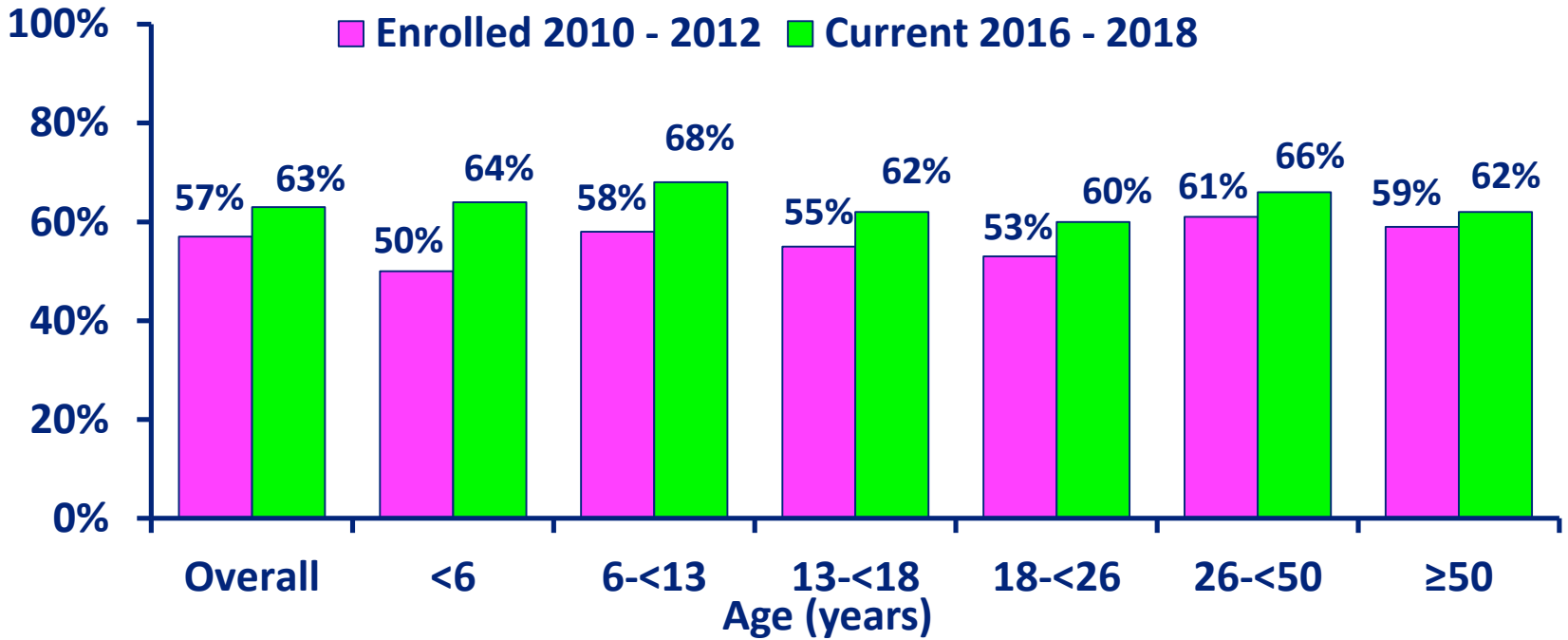
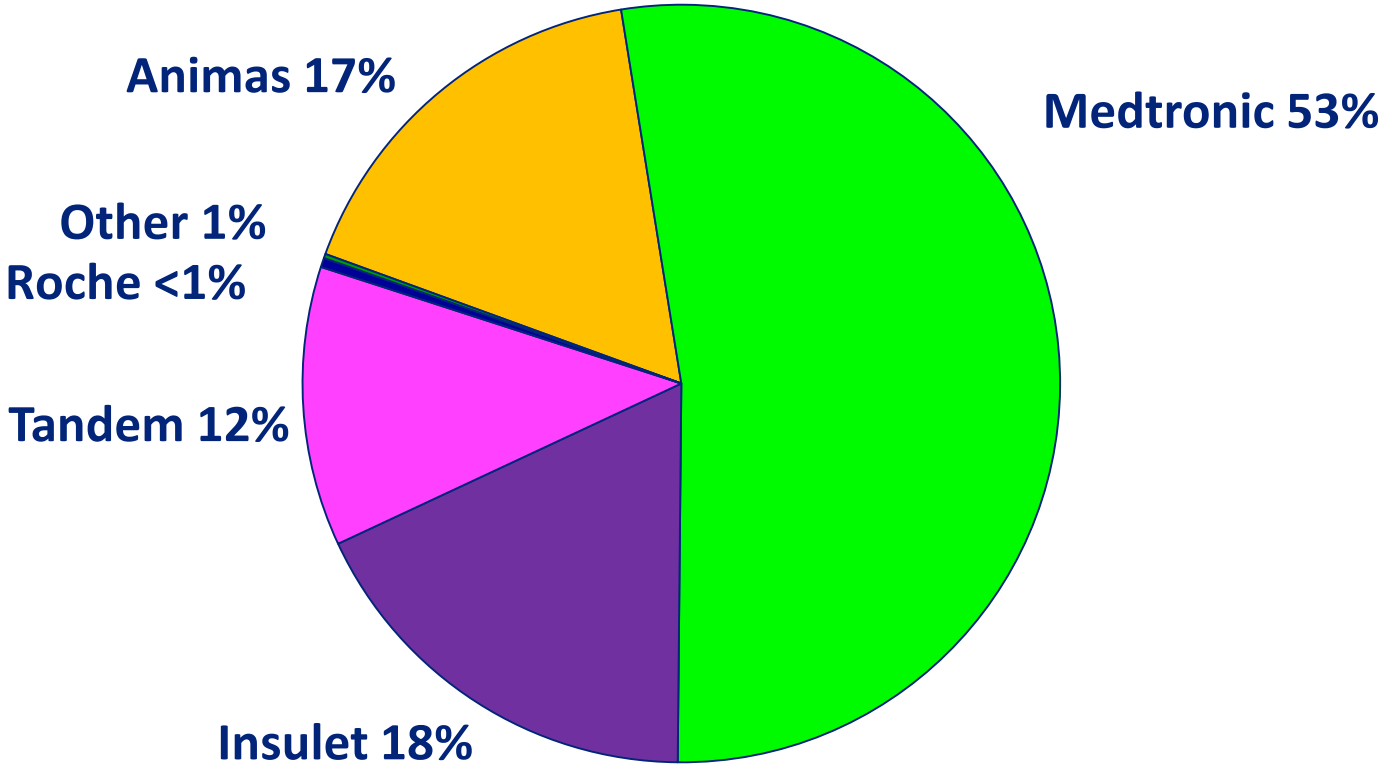
Insulin Pump Use Has Increased Mainly in Youth



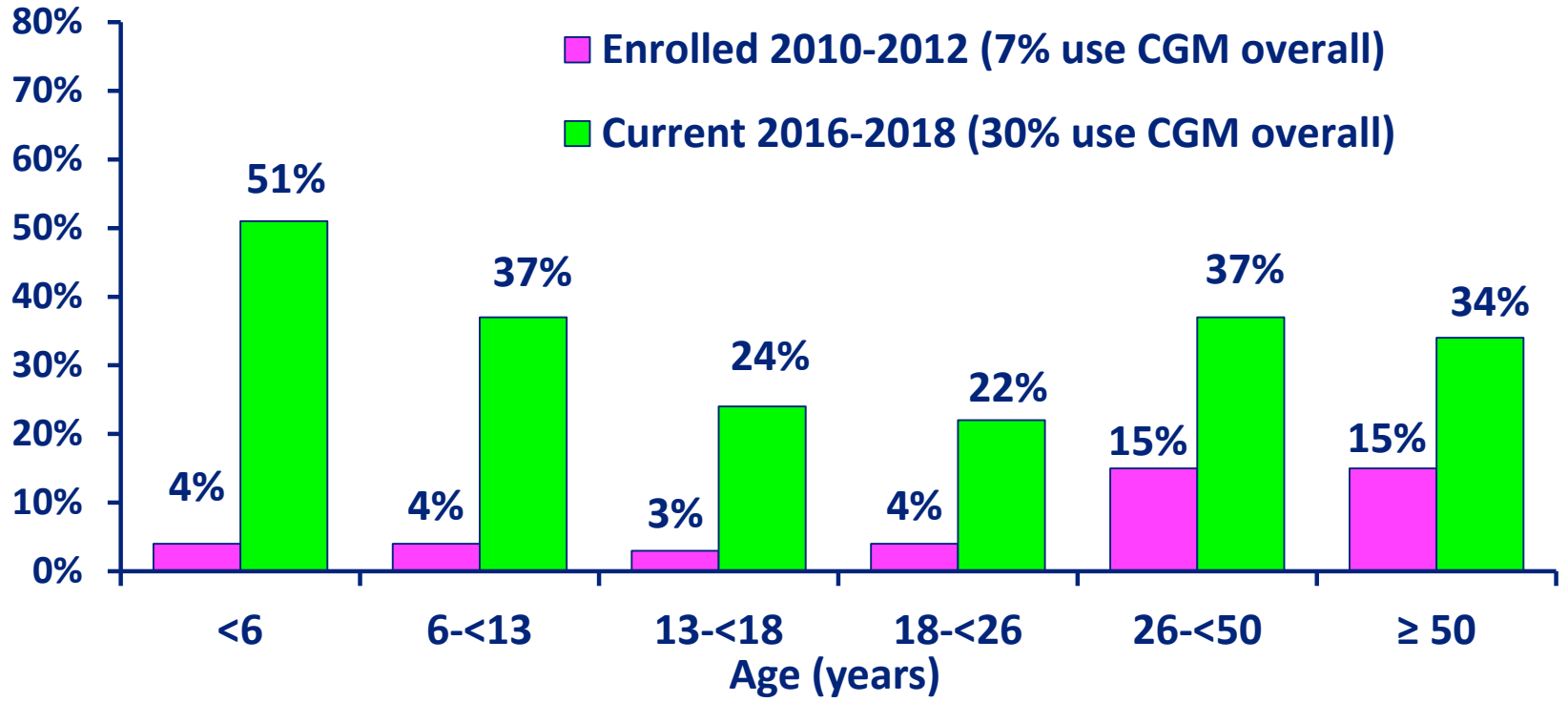
T1D Exchange 2018 Update - Unpublished

Pump Manufacturer



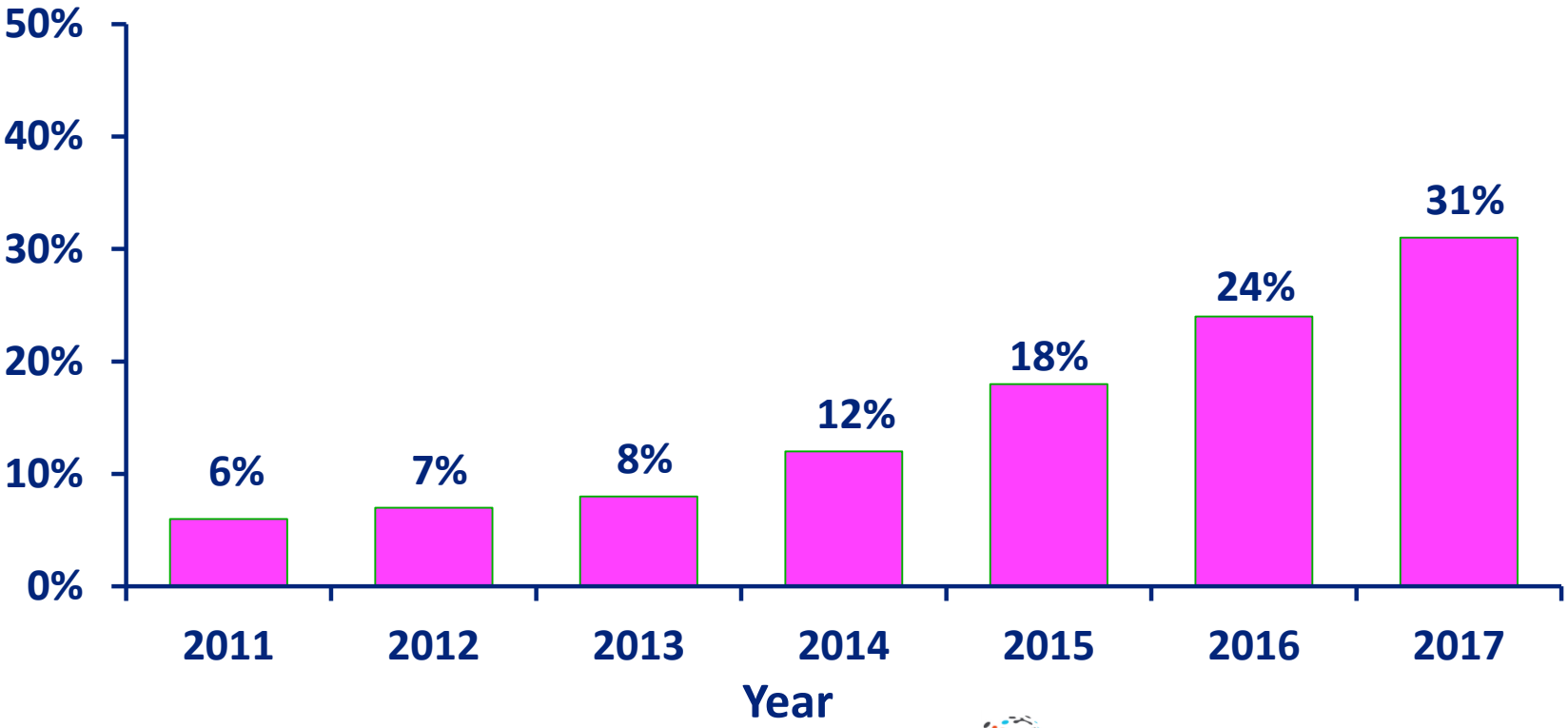
T1D Exchange 2018 Update - Unpublished

CGM Use Has Increased Substantially



T1D Exchange 2018 Update - Unpublished

CGM Use by Year



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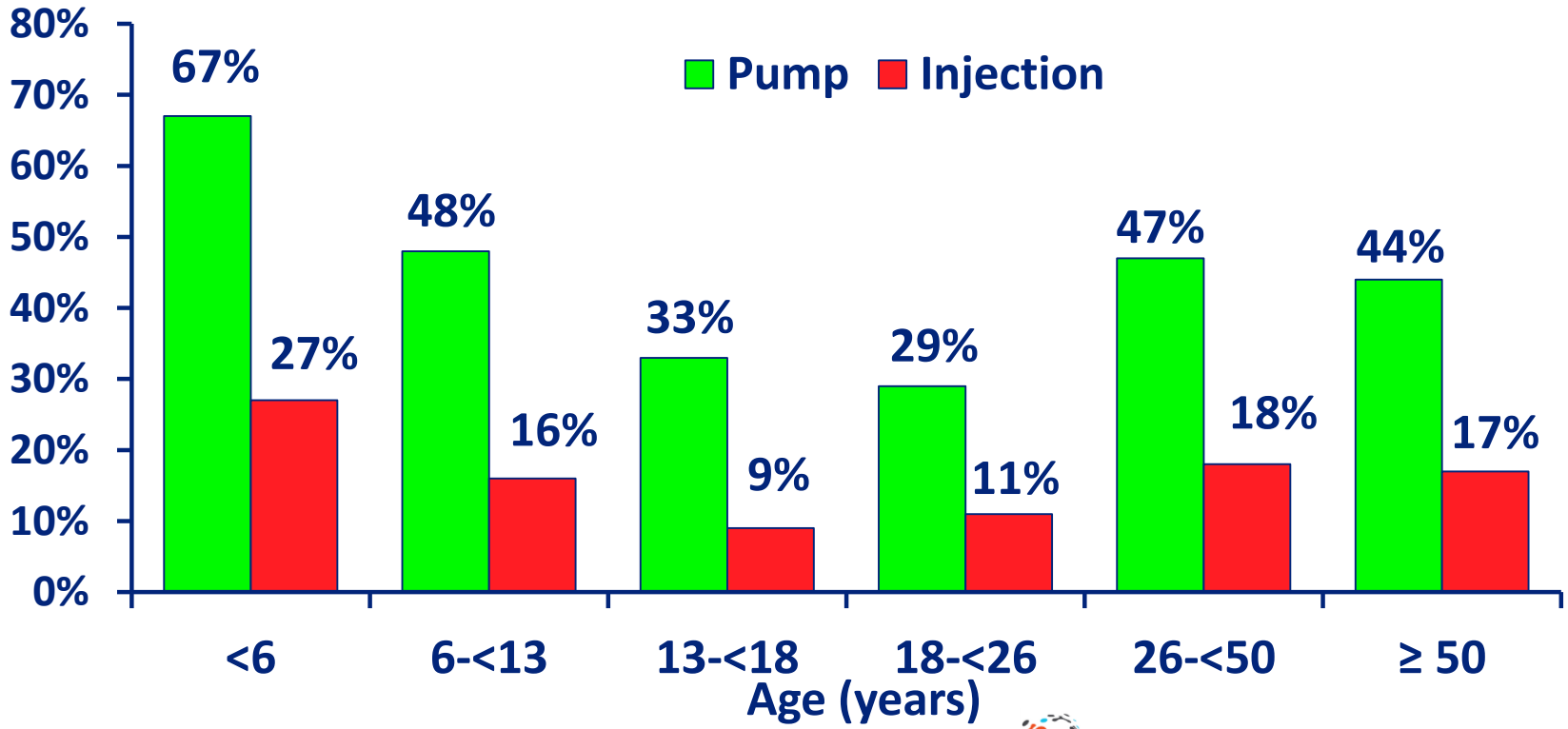
CGM Use by Insulin Delivery Method



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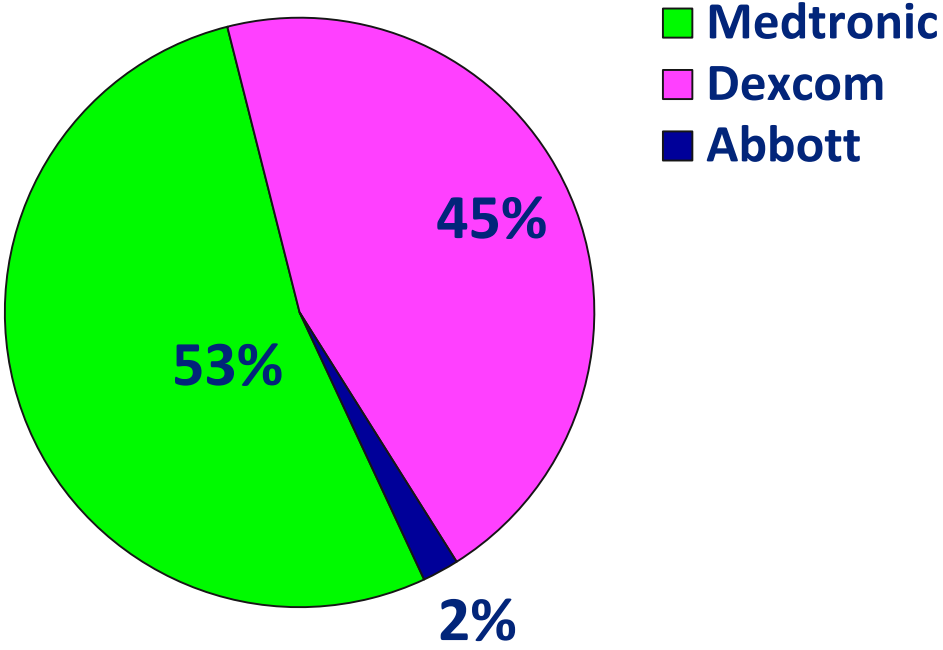
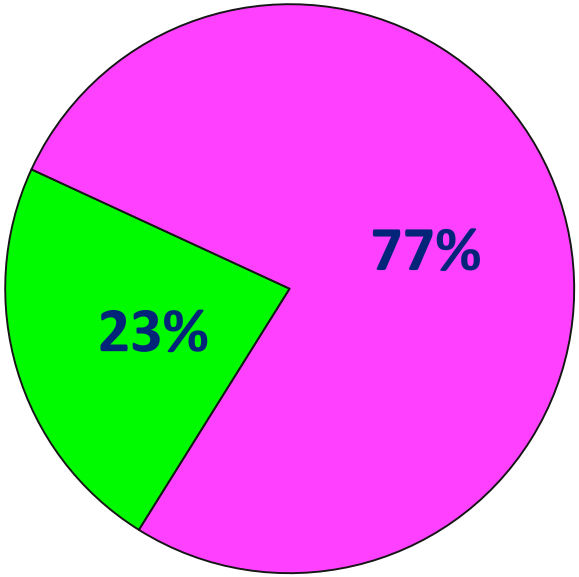
CGM Device Type

Enrolled 2010-2012



Current 2016-2017



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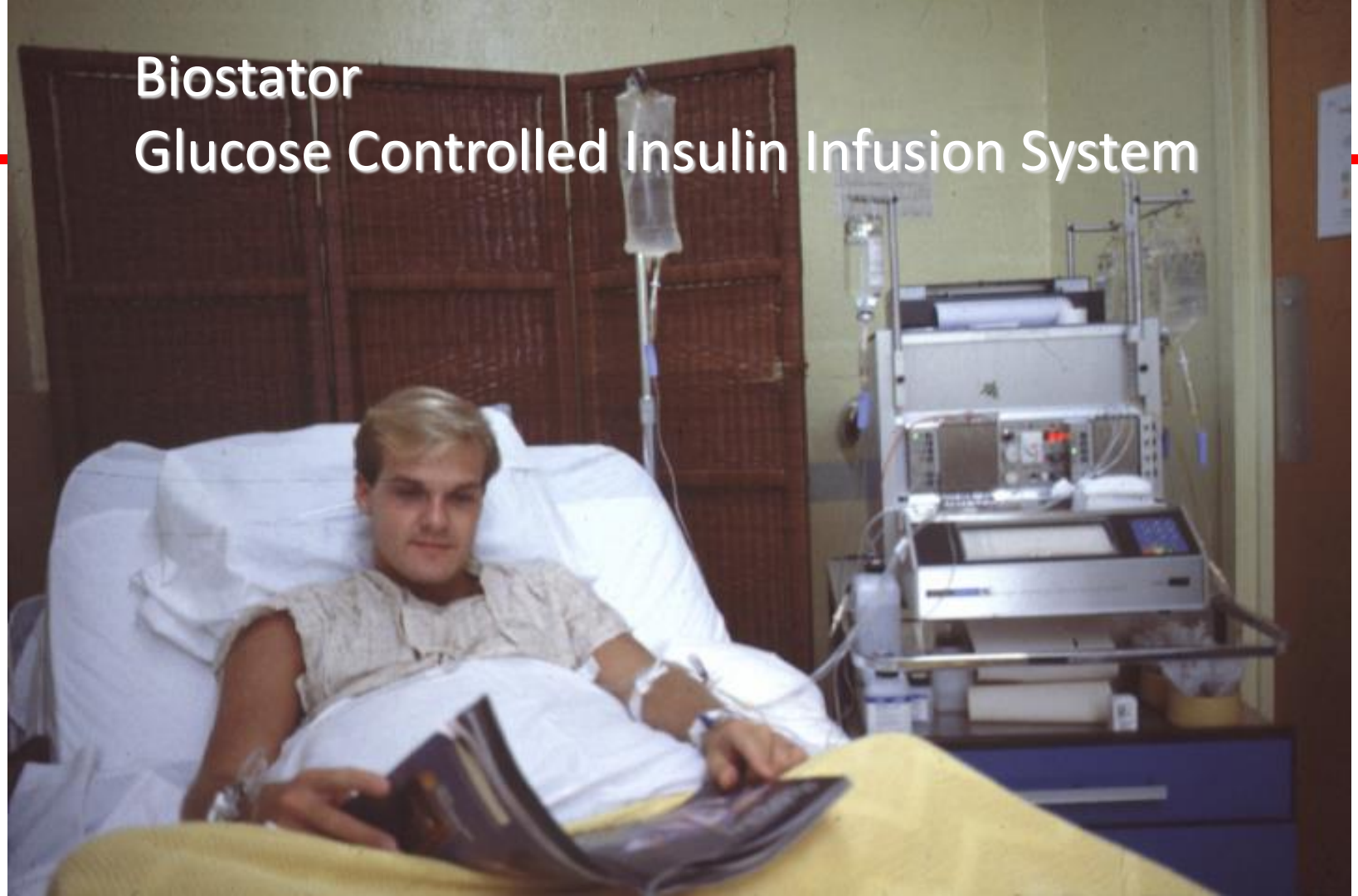
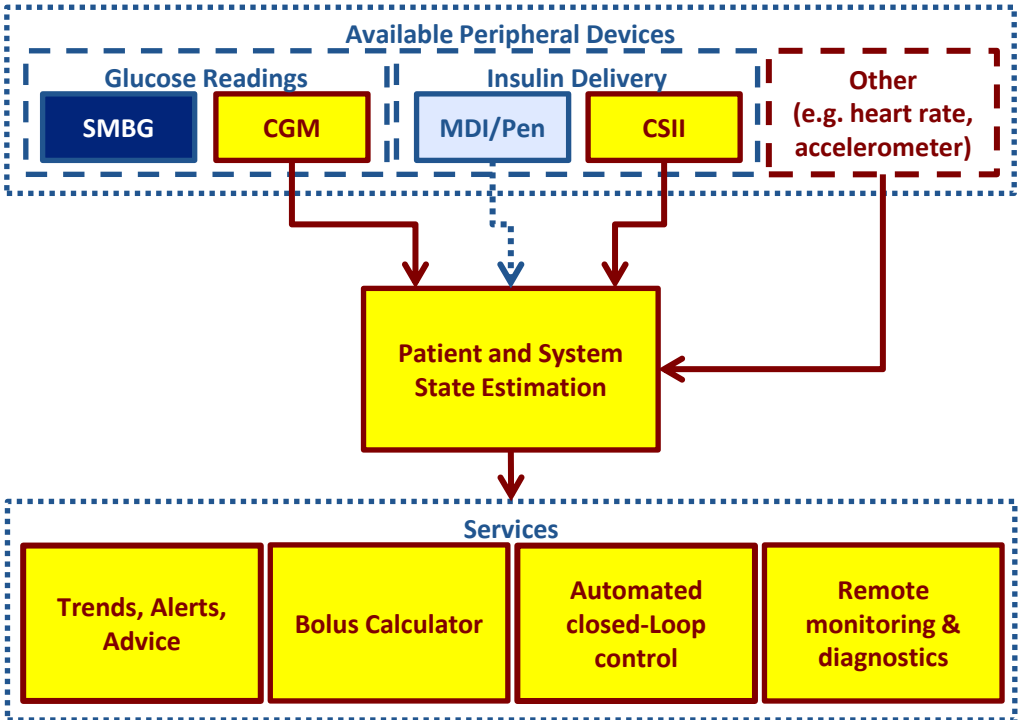
Automated Insulin Delivery


Biostator
Glucose Controlled Insulin Infusion System

Implantable Insulin Pump & External Controller

Devices, Algorithms, and Services of the Artificial Pancreas

Input: Continuous Glucose Monitoring;
Output: Insulin pump



Automated Insulin Delivery Systems in Development

TANDEM DIABETES CARE

typezero

Insulet Corporation

Medtronic MiniMed

βetα βionics

bigfoot BIOMEDICAL

DIY

Multiple Academic Groups


The Future
NEXT EXIT