



University of California San Francisco

## CGM Use In Children With Type 2 Diabetes

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## Disclosures

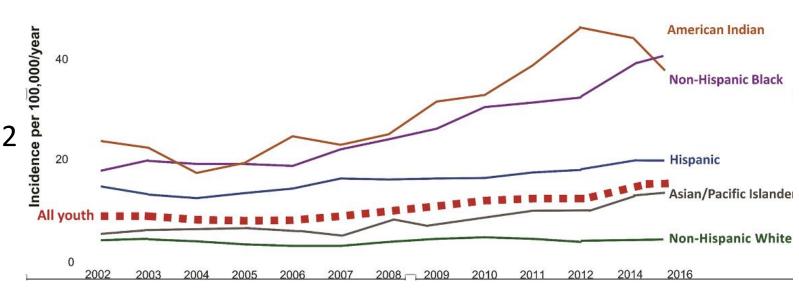
COMPANY / NAME	HONORARIA / EXPENSE	CONSULTING / ADVISORY BOARD	FUNDED RESEARCH
MEDTRONIC		<	<
MANNKIND			$\checkmark$
Abbot			<
NIH			$\checkmark$
JDRF			<
TANDEM DIABETES CARE		<	
YPSOMED		<	
INSULET	<		
SEQUEL		<	
JAEB		<	
DIABETES CENTER BERNE		<	

## Outlines

- What do we know about CGM use in adults with Type 2 Diabetes?
- What do we know about CGM use in youth with Type 2 Diabetes?
- UCSF clinical trials in children with Type 2 Diabetes
- Future directions?

## Epidemiology of Type 2 Diabetes (T2D) in Children

- Incidence of Type 2 Diabetes in Children: awakening epidemic
- Across all racial and ethnic groups, the prevalence of type 2 diabetes increased with age
- Aggressive disease course with increased risk of complications compared to adults with T2D and youth with type 1 diabetes (T1D)

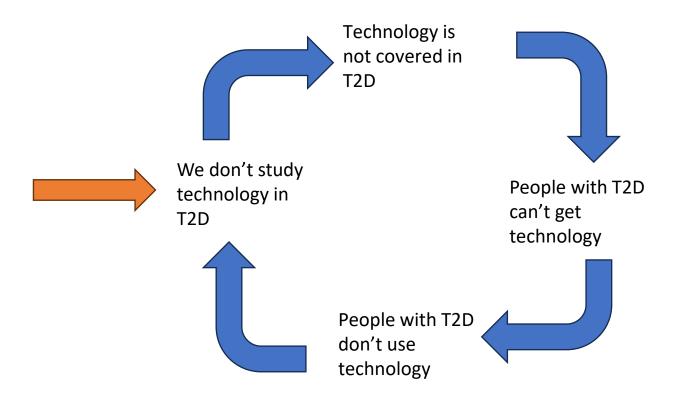


Perng, Diabetes Care, 2023 Lawrence, JM, JAMA, 2021 Today Study, NEJM, 2021

### Professional Society Guidelines

Organization	Clinical guideline	Recommendation for people with T2D	
CGM			
Endocrine Society 2018 [64]	Advances in Glucose Monitoring and Automated Insulin Delivery Systems: Supplement to Guidelines in 2016	Short-term intermittent CGM in people with T2D who have HbA1c>7%	
AACE 2021 [65]	Use of Advanced Technology in the Management of Persons with Diabetes Mellitus	CGM strongly recommended for all persons with diabe- tes treated with MDI (3 or more injections per day) or insulin pump CGM is recommended for individuals with problematic hypoglycemia Pregnant women treated with MDI CGM may be recommended for individuals with T2D who are treated with less intensive insulin therapy	
AACE 2022 [66]	Diabetes Mellitus Comprehensive Care Plan	All persons using insulin should use CGM CGM is recommended for persons with T2D who are treated with insulin therapy or have high risk for hypoglycemia	
ADA 2023 [67••]	Standards of Care	Adults using multiple daily injections (MDI) or con- tinuous subcutaneous insulin infusion (CSII) Adults with diabetes on basal insulin Periodic use of CGM	
AACE 2023 [68••]	T2D Algorithm	In people with T2D on basal insulin, CGM is associ- ated with increased time-in-range, improved HbA1c, and decreased hypoglycemia Diagnostic or professional CGM can be used for new T2D diagnosis and for those with hypoglycemia	
Connected pens			
AACE 2021 [65]	Use of Advanced Technology in the Management of Persons with Diabetes Mellitus	Connected pens may be recommended for all persons with diabetes treated with MDI or on insulin pump therapy	
ADA 2023 [67••]	Standards of Care	Connected insulin pens can be helpful Insulin dose calculator or decision support systems may be helpful for titrating doses	
Insulin pump or AIDs			
Endocrine Society 2018 [64]	Advances in Glucose Monitoring and Automated Insulin Delivery Systems: Supplement to Guidelines in 2016	Suggest CSII in people with T2D who have poor glycemic control despite intensive insulin therapy, oral agents, other injectable therapy and lifestyle modifications	
AACE 2021 [65]	Use of Advanced Technology in the Management of Persons with Diabetes Mellitus	Insulin pump with CGM or SAP is recommended for persons with diabetes treated with MDI who prefer not to use AIDs	
ADA 2023 [67••]	Standards of Care	Insulin pump therapy should be offered to youth and adults capable of using the device safely	

## History of Technology (CSII, CGM, AID) for T2D



Courtesy of Gregory Forlenza, MD.

## **Glucose Dysregulation**

- The dawn phenomenon
- Postprandial Glucose excursion
- Risk of hypoglycemia
- Glycemic variability

## CGM use

- Can retrospectively review data to make lifestyle changes or medication adjustments.
- Could be a personal tool for behavior modification in T2D.
- Teenagers enjoy using technology

# Effectiveness of CGM in adults with Type 2 Diabetes



## Key studies in CGM and T2 Diabetes

Author (year)	Type of study	Number of participants	Treatment	Participant age (years) at study start	Glycaemic status (HbA <sub>1c</sub> (%)) at study start	CGM sensor	Study Period
Riveline et al. (2022) <sup>135</sup>	Retrospective	41,027	Any	18–99	_	FreeStyle Libre	2 years
Guerci et al. (2023) <sup>65</sup>	Retrospective	5,933	Basal insulin	18–99	_	FreeStyle Libre	2 years
Ajjan et al. (2023) <sup>196</sup>	RCT	141	Insulin or sulfonylurea	Adults with AMI		FreeStyle Libre	90 days
Chesser et al. (2022) <sup>81</sup>	Single-arm interventional	9	Any	13–21	Mean 11.9	Dexcom G6	12 weeks
Aronson et al. (2023) <sup>110</sup>	RCT	116	Non-insulin	≥18	Mean 8.6	FreeStyle Libre	16 weeks
Manfredo et al. (2023) <sup>155</sup>	Prospective interventional	41	Insulin	Median 16.2 (youth)	Mean 10.3	Dexcom G6	10 days
Chang et al. (2023) <sup>156</sup>	Crossover RCT	9	Insulin	15–19	Mean 11.5	Dexcom G6	3 months

## CGM led to modest but statistically significant declines in HbA1c, with little heterogeneity in the results.

CGM Type and Reference	Follow-up N	Treatment Mean (SD) N	Control Mean (SD)				MD (95% CI)	% Weight
Real Time								
Yoo et al. 2008	12 weeks 29	8.00 (1.20) 28	8.30 (1.10)		*		-0.30 (-0.90,	0.30) 1.87
Cosson et al. 2009	12 weeks 11	-0.63 (0.34) 14	-0.31 (0.29)			_	-0.32 (-0.57,	-0.07)10.52
Ehrhardt et al. 2011	12 weeks 50	-1.00 (1.10) 50	-0.50 (0.80)	_	•	-	-0.50 (-0.88,	-0.12) 4.70
Yeoh et al. 2016	12 weeks 14	8.80 (1.80) 16	9.10 (1.10) —		•		-0.30 (-1.39,	0.79) 0.57
Price et al. 2021	12 weeks 44	-0.50 (0.90) 23	-0.30 (0.70)				-0.20 (-0.59,	0.19) 4.37
Bergenstal et al. 2022	16 weeks 59	-1.12 (1.10) 55	-0.82 (0.90)		•	<u> </u>	-0.30 (-0.67,	0.07) 4.93
Beck et al. 2017	24 weeks 79	-0.80 (0.67) 79	-0.50 (0.91)			—	-0.30 (-0.55,	-0.05)10.80
Isaacson et al. 2022	24 weeks 50	-0.63 (1.14) 49	-0.23 (0.61)			—	-0.40 (-0.76,	-0.04) 5.13
Martens et al. 2021	32 weeks 105	-1.10 (1.50) 51	-0.60 (1.20)		•	<u> </u>	-0.50 (-0.94,	-0.06) 3.50
Subgroup, DL+HKSJ ( $\tau^2 = 0.000$ )	441	365			$\langle \rangle$		-0.34 (-0.48,	-0.20)46.39
(l <sup>2</sup> = 0.0%, p = 0.981)								
Flash								
Yaron et al. 2019	10 weeks 51	-0.82 (0.84) 43	-0.33 (0.78)	-	•		-0.49 (-0.82,	-0.16) 6.21
Haak et al. 2017	24 weeks 149	8.37 (0.83) 75	8.34 (1.14)			•	0.03 (-0.26, 0	0.32) 7.91
Ajjan et al. 2019	24 weeks 49	8.20 (0.90) 52	8.70 (1.20)		•	-	-0.50 (-0.91,	-0.09) 3.93
Wada et al. 2019	24 weeks 41	-0.46 (0.43) 35	-0.17 (0.23)			-	-0.29 (-0.44,	-0.14)28.90
Furler et al. 2020	24 weeks 115	8.10 (1.08) 106	8.60 (1.30)		•		-0.50 (-0.82,	-0.18) 6.66
Subgroup, DL+HKSJ ( $\tau^2 = 0.023$ ) ( $I^2 = 54.0\%$ , p = 0.069)	405	311				>	-0.33 (-0.61,	-0.05)53.61
Heterogeneity between groups: p	= 0.907							
Overall, DL+HKSJ ( $\tau^2 = 0.000$ )	846	676			$\diamond$		-0.32 (-0.41,	-0.23)00.00
(l <sup>2</sup> = 0.0%, p = 0.623)					÷			
				 _1	І –.5	l I 0 .5	1	
					Favors CGM	Favors SMBG		
				HbA1c	(%)			

Fourteen RCTs assessing CGM were included with 825 patients in 9 RCTs using rt-CGM and 822 in 5 RCTs using FGM

# CGM led to a mean difference (MD) in HbA1c of -3.43 mmol/mol (-0.31%)p<0.00001

		CGM		s	MBG			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
1.2.1 Insulin yes									
Martens (2021) [28]	-12	16.4	116	-6.56	13.1	59	7.5%	-5.44 [-9.92, -0.96]	
Yaron (2019) [25]	-8.96	9.18	53	-3.61	8.52	48	11.6%	-5.35 [-8.80, -1.90]	
Beck (2017) [22]	-8.74	10.1	77	-5.46	12.5	75	10.7%	-3.28 [-6.90, 0.34]	
Haak (2017) [23] Subtotal (95% CI)	-3.06	14.2	149 395	-4.48	16.4	75 257	7.9% 37.6%	1.42 [-2.94, 5.78] -3.27 [-6.22, -0.31]	→ <sup>1</sup>
Heterogeneity: Tau <sup>2</sup> = 5	.01: Chi <sup>2</sup>	= 6.73	3. df = 3	3 (P = 0	.08): l <sup>a</sup>	= 55%			-
Test for overall effect: Z				- (	,,				
1.2.2 Insulin no									
Moon (2023) [32]	-6.56	7.65	15	0	12	15	3.2%	-6.56 [-13.76, 0.64]	+
Price (2021) [29]	-5.46	9.84	44	-3.28	7.65	23	8.1%	-2.18 [-6.45, 2.09]	
Wada (2020) [24]	-5.03	5.14	48	-1.86	7.76	45	16.8%	-3.17 [-5.86, -0.48]	
Subtotal (95% CI)			107			83	28.1%	-3.22 [-5.39, -1.05]	◆
Heterogeneity: Tau <sup>2</sup> = 0	.00; Chi <sup>2</sup>	<sup>2</sup> = 1.0	6, df = 2	2 (P = 0	.59); l²	= 0%			
Test for overall effect: Z	= 2.91 (	P = 0.0	004)						
1.2.3 Insulin or other g	lucose	loweri	ng me	dicatior	1				
Ajjan (2023) [21]	-5.36	21.3	55	-9.95	26.5	55	2.1%	4.59 [-4.40, 13.58]	
Bergenstal (2022) [26]	-12.2	12	59	-8.96	9.84	55	9.0%	-3.24 [-7.26, 0.78]	
Vigersky (2012) [30]	-8.74	16.4	50	-2.19	14.2	50	4.4%	-6.55 [-12.56, -0.54]	
Cosson (2009) [27]	-6.89	3.72	11	-3.39	3.17	14	16.3%	-3.50 [-6.25, -0.75]	
Yoo (2008) [31]	-12	17.1	29	-4.37	14.2	28	2.5%	-7.63 [-15.78, 0.52]	
Subtotal (95% CI)			204			202	34.3%	-3.65 [-6.14, -1.15]	•
Heterogeneity: Tau <sup>2</sup> = 1				4 (P = 0	.28); l²	= 21%			
Test for overall effect: Z	= 2.87 (	P = 0.0	004)						
Total (95% CI)			706			542	100.0%	-3.43 [-4.75, -2.11]	•
Heterogeneity: Tau <sup>2</sup> = 0	.80; Chi <sup>2</sup>	<sup>i</sup> = 12.1	95, df =	11 (P =	= 0.30)	;  2 = 15	5%		-20 -10 0 10 20
Test for overall effect: Z		-	,						Favours CGM Favours SMBG
Test for subgroup different	ences: C	hi² = 0	.07, df	= 2 (P =	0.97)	, I <sup>2</sup> = 0%	%		

#### 12 RCTs comprising 1248 participants.

eight investigating rtCGM and four isCGM. Compared with SMBG, CGM use (rtCGM or isCGM)

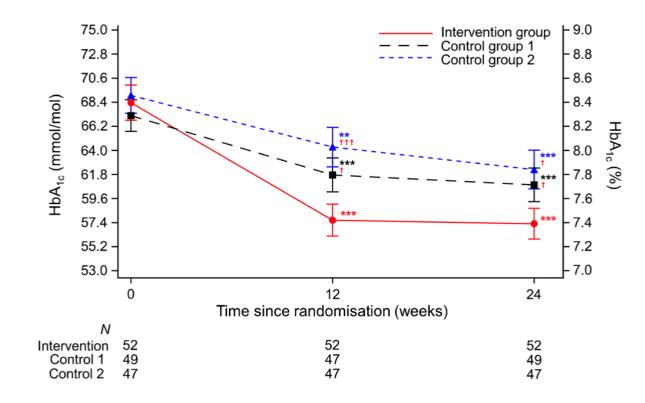
## CGM decreases HbA<sub>1c</sub> (-0.37, p < 0.001)

Study		ES	95%	6 CI		Hedge's G
ID	Ν	(hg)	Lower Limit	Upper Limit	Weight	Random Effect Model, 95% CI
1	43	-0.21	-0.84	0.42	5.2%	2.1
2	46	-0.38	-0.97	0.20	5.4%	
3	158	-0.37	-0.69	-0.06	6.8%	
4	88	-0.12	-0.54	0.30	6.3%	
5	25	-0.13	-0.92	0.66	4.4%	
6	100	-0.27	-0.67	0.12	6.4%	
7	267	-1.50	-1.77	-1.23	7.0%	
8	224	0.03	-0.25	0.31	6.9%	
9	156	-0.29	-0.63	0.04	6.7%	
10	34	0.28	-0.40	0.95	4.9%	
11	57	-0.26	-0.78	0.26	5.8%	
12	30	-0.20	-0.92	0.51	4.7%	
13	101	-0.47	-0.87	-0.07	6.4%	
14	93	-1.15	-1.59	-0.71	6.2%	4
15	30	-0.54	-1.27	0.19	4.7%	-2 -1 0 1 2
16	67	-0.09	-0.60	0.41	5.8%	-2 -1 0 1 2 Hedge's g
17	100	-0.27	-0.67	0.12	6.4%	incuge a g
Total	1619	-0.37	-0.63	-0.11	100%	Heterogeneity: Q = 92.35, Q-df = 74.35, I <sup>2</sup> = 82.7%, t <sup>2</sup> = 0.23, (p<0.001)

17 RCT, 1619 patients

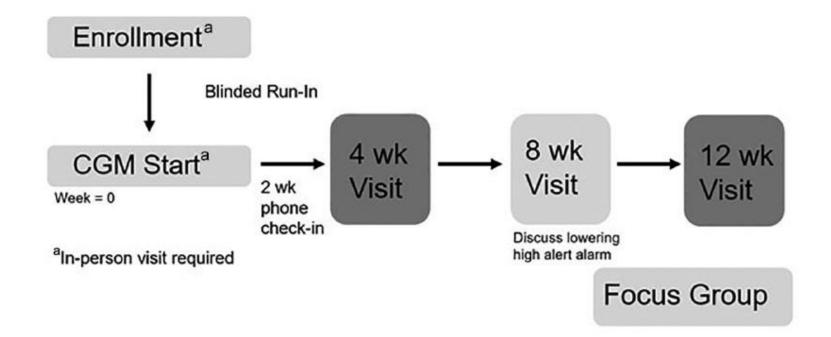
King, Health Care, 2024

# isCGM offers a greater reduction in $HbA_{1c}$ when education on the interpretation of graphical patterns in CGM is provided



24 week randomized openlabel multicenter trial, adults with type 2 diabetes

## Real-Time CGM in Adolescents and Young Adults With Type 2 Diabetes Can Improve Quality of Life (SOY-T2 Study)



Chesser, JDST, 2022

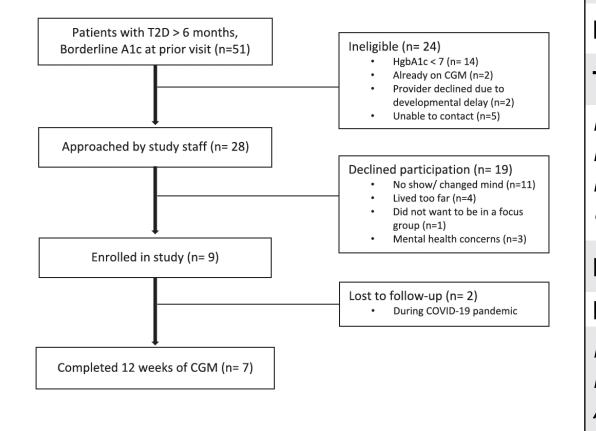
## Population

Participants recruited for UCSF Madison Clinic for Pediatric Diabetes

- Inclusion Criteria:
  - Ages: 13 21 yo
  - T2DM  $\geq$  6 months
  - No diabetes medications added or discontinued in prior 4 weeks
  - HgbA1c > 7.0%
  - All FDA approved medication regimens included (lifestyle alone, metformin, victoza, daily basal insulin, and/or short acting insulin)

- Exclusion Criteria:
  - No personal smart phone
  - Non-English or Spanish speaker

## Consort Diagram



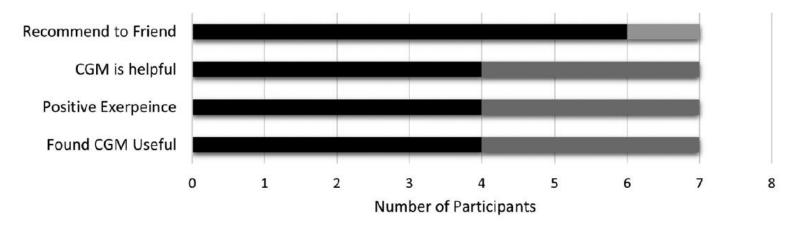
n=9 Median age (years) 19.1 [16.8, 20.5] Female gender 78% **T2D** characteristics Median duration of diabetes (y) 2.5 [1.4, 6.0] Mean baseline A1c (%) 11.9 + 2.8Mean baseline TIR (%)  $16 \pm 14$ Using insulin 67% **Public insurance** 67% **Race and Ethnicity** Hispanic/Latinx 44% Non-Hispanic Black 44% Asian/Pacific Islander 33% Parent with some college 33% education

Recruitment challenges

#### Chesser, JDST, 2022

## Quantitative feedback

#### Use of rt-CGM Quantitative Feedback



■ Very Positive/Strongly Agree ■ Positive/Agree ■ Neutral ■ Negative/Disagree ■ Very Negative/Strongly Disagree

## Focus Group/Feedback

"It was something different. I never thought there was something like that that I could get. I always thought I would have to prick my fingers." "Seeing my numbers made me think about what I was putting in my body."

"It is life changing."

"I worried about everything [at first]. I was so scared to stick myself with the tiny plastic needle. I worked myself up [...] But, it got quicker every time I did it."

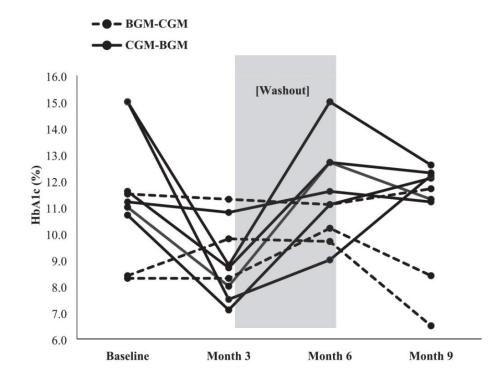
"I want to see my numbers change. I want to make them different."

## CGM is both feasible and acceptable

- All participants reported using the CGM
- There was a significant increase in the PedsQL diabetes score (70-75, P=0.0263)
- On a satisfaction survey (n=7), 100% had a positive experience with CGM, found it easy to use, useful, and desired to continue to use CGM in the future
- 67% self-reported eating fewer meals while using CGM

## **CGM in adolescents with Type 2** Pilot RT cross over

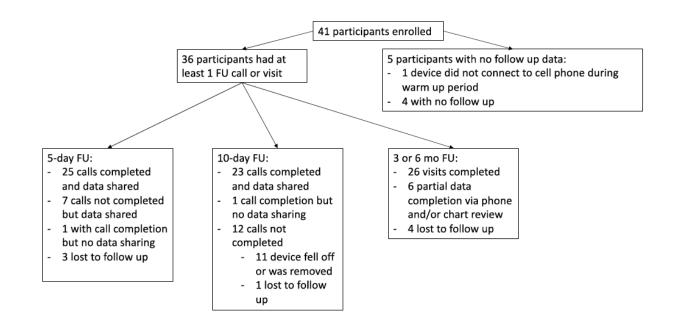
- 9 adolescents, majority Latinx
- Randomzied to Dexcom G6 or BGM followed by 3 months wash out period and then crossed over to the other arm





## Short term use of CGM >> behavioral modifications

• Participants (n=41) had median age of 16.2 y



- 10-day CGM use did not impact shortterm or long-term glycemic control in youth with T2D
- Most participants reported behavioral changes and wanted to continue using CGM

## Barriers and Facilitators to CGM uptake

- 20 AYAs and 10 parents: 35% used CGM
- Average age 16.5 yo
- 65% female and 55% from minorities background

## Semi structured interview

Lifestyle

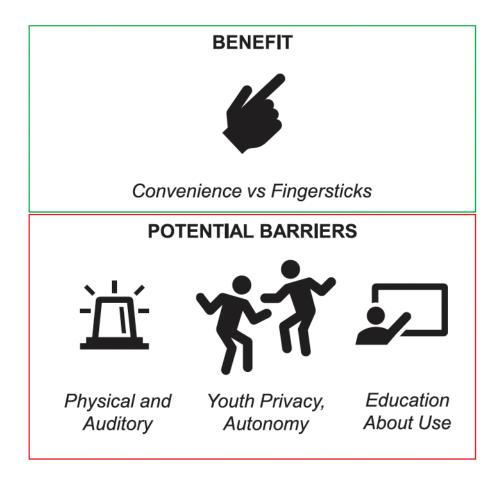
## CGM users

Getting started on CGM Education Diabetes management Opinion What care givers should know

## Non CGM users

Prior knowledge Decision making Education Potential lifestyle changes

## **Benefits vs Barriers**



## Ongoing study at UCSF:

Feasibility Of The Freestyle Libre Continuous Glucose Monitoring System In Youth With Type 2 Diabetes (FREE-CGM)

#### **Objectives:**

 $_{\odot}$  To investigate the acceptability, appropriateness, and feasibility of CGM  $\,$  use in youth with T2D

 $_{\odot}$  To determine the effect size of CGM on glycemic control-related measures in youth with T2D

 $\odot$  To evaluate the effect of CGM use on behavioral and psychosocial outcomes in youth with T2D

## **Study Design**

6-month pilot randomized controlled feasibility study of CGM use compared to standard glucose monitoring

#### **Inclusion criteria**

- Age < 21 years
- Clinical diagnosis of T2D
- Duration of T2D  $\geq$  3 months
- HbA1C ≥ 6.5%
- Stable medication regimen (No medication changes and no change in basal insulin dose by more than 20% in the 2 weeks prior to enrollment)
- Naïve to CGM use
- Has a smart phone compatible with CGM system

## Evidence for AID in Type 2 Diabetes

Table. AID RCTs in T2D									
		Duration of		Target					
Study	System	AID	Control Group	Range	Time in target improvement				
Kumareswaran 2014	Hovorka	24h	Usual Care	70-144	+16% (40 v 24%)				
Thabit 2017	Hovorka	72h	Conventional SQ	100-180	+21.8% (59.8 v 38.1%)				
Bally 2018	Hovorka	up to 15d	Conventional SQ	100-180	+24.3% (65.8 v 41.5%)				
Taleb 2019	Haidar	24h	MDI	72-180	+23% Overnight (100 v 78%)				
Boughton 2021	Hovorka	20d	MDI	100-180	+15.1% (52.8 v 37.7%)				
Peters 2022	OP5	8 wk	MDI	70-180	+15.1% (52.8 v 37.7%)				

## **Future Directions**

- More and larger studies: randomized controlled trials, real-world studies, and studies with patient-reported outcome measures.
- The Cost Effectiveness of Use of CGM in youth with type 2 diabetes (MDI, CSII, basal insulin, no insulin, and prediabetes)
- The correlation between the use of CGM and treatment plan and change in plan
- Correlation with behavioral modifications
- CGM use in new-onset Type 2 Diabetes
- Inpatient use of CGM in Type 2 Diabetes

#### <u>Acknowledgment</u>

- Study participants and their families
- Srinivasan, Shylaja, MD.
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- Wong, Jenise, MD., PhD.
- UCSF Diabetes Technology Research Group

