

## SUPPLEMENTARY DATA

### Participating Centers.

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\*Indicates clinical centers that participate in both DirecNet and TrialNet; other clinical centers do not participate in DirecNet.

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### **The Type 1 Diabetes TrialNet Study Group:**

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**Supplementary Table 1: Baseline Characteristics<sup>a</sup>.**

	<b>Intensive Treatment Group (N=48)</b>	<b>Usual Care Group (N=20)</b>
<b>Age (years)</b>		
6-<9	5 (10%)	0
9-<12	20 (42%)	6 (30%)
12-<15	15 (31%)	8 (40%)
15-<18	6 (13%)	5 (25%)
18-<46	2 (4%)	1 (5%)
<i>mean ± SD</i>	12.7 ± 4.7	14.7 ± 7.6
<i>range</i>	7.8 to 37.7	9.8 to 45.7
<b>Gender: Female N(%)</b>	17 (35%)	7 (35%)
<b>Race/Ethnicity N(%)</b>		
White	42 (91%)	18 (95%)
Black	1 (2%)	0
Hispanic or Latino	2 (4%)	1 (5%)
More than one race	1 (2%)	0
<b>Parent education<sup>b</sup> N(%)</b>		
≤12	4 (9%)	4 (21%)
Associate	6 (13%)	4 (21%)
Bachelors	10 (22%)	6 (32%)
Masters	17 (37%)	3 (16%)
Professional	9 (20%)	2 (11%)
<b>DKA at Diagnosis N(%)</b>	14 (29%)	6 (30%)
<b>BMI percentile<sup>c</sup></b>		
<20%	15 (33%)	3 (16%)
20-<60%	15 (33%)	9 (47%)
≥60%	16 (35%)	7 (37%)
<i>median (25<sup>th</sup>, 75<sup>th</sup> percentiles)</i>	41% (14%, 70%)	46% (24%, 74%)
<b>C-peptide AUC (pmol/mL)</b>		
<0.15	13 (27%)	3 (17%)
0.15-<0.25	13 (27%)	6 (33%)
0.25-<0.40	13 (27%)	4 (22%)
≥0.40	9 (19%)	5 (28%)
<i>median (25<sup>th</sup>, 75<sup>th</sup> percentiles)</i>	0.24 (0.15, 0.38)	0.27 (0.20, 0.44)
<b>Initial Glucose (mg/dL) mean ± SD</b>	501 ± 193	535 ± 235
<b>HbA1c<sup>d</sup> (%)</b>		
5.0-<8.0% (31-<64 mmol/mol)	2 (4%)	1 (5%)
8.0-<10.0% (64-<86 mmol/mol)	10 (21%)	6 (30%)
10.0-<13.0% (86-<119 mmol/mol)	19 (40%)	7 (35%)
≥13.0% (≥119 mmol/mol)	17 (35%)	6 (30%)

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<i>mean ± SD (%)</i>	11.8 ± 2.4	11.2 ± 2.6
<i>mean ± SD (mmol/mol)</i>	(105 ± 27)	(99 ± 28)
<i>range (%)</i>	6.8 to 16.4	5.8 to 15.9
<i>range (mmol/mol)</i>	(51 to 156)	(40 to 150)
<b>Time to randomization (days)</b>		
<i>mean ± SD</i>	2.9 ± 1.6	3.0 ± 1.7
<i>range</i>	0 to 6	1 to 6

a – Missing data: race/ethnicity-2 in intensive group and 1 in usual care group; education level-2 in the intensive group and 1 in the usual care group; MMTT C-peptide -2 in usual care group.

b – Parent education does not include the 3 participants  $\geq 18$  years old

c – BMI percentile for subjects <18 years of age was calculated based on 2000 CDC pediatric growth chart data (29) and was adjusted for age and gender. 3 participants  $\geq 18$  years old were excluded: 2 were in the intensive group (one with BMI 24.9 kg/m<sup>2</sup>, one with BMI 18.8 kg/m<sup>2</sup>), and 1 was in the control group (BMI=25.7 kg/m<sup>2</sup>).

d – 1 participant had missing central lab A1c at enrollment, which is imputed with local A1c.

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**Supplementary Table 2.** Study data by visit.

	Baseline		2 weeks		6 weeks		3 months		6 months		9 months		12 months	
	Intensive	Standard	Intensive	Standard	Intensive	Standard	Intensive	Standard	Intensive	Standard	Intensive	Standard	Intensive	Standard
	N=48	N=18	N=44	N=18	N=47	N=17	N=47	N=17	N=47	N=17	N=46	N=17	N=47	N=20
<b>C-peptide AUC</b> (pmol/mL) <i>geometric mean</i> (95% C.I.) <sup>a</sup>	0.29 (0.23, 0.35)	0.35 (0.23, 0.49)	0.49 (0.42, 0.55)	0.60 (0.43, 0.80)	0.65 (0.58, 0.73)	0.80 (0.64, 0.99)	0.67 (0.58, 0.75)	0.83 (0.63, 1.06)	0.57 (0.50, 0.65)	0.71 (0.50, 0.95)	0.50 (0.42, 0.59)	0.61 (0.41, 0.84)	0.43 (0.34, 0.52)	0.52 (0.32, 0.75)
	N=48	N=20	NA	NA	N=48	N=16	N=48	N=18	N=48	N=17	N=47	N=17	N=48	N=20
HbA1c(%) <sup>b</sup> <i>mean ± SD</i>	11.8±2.4	11.2±2.6	NA	NA	7.7±0.9	7.9±1.0	6.0±0.5	6.4±0.7	6.4±0.8	6.6±0.9	7.0±1.2	6.8±0.9	7.4±1.2	7.3±1.1
HbA1c (mmol/mol) <i>mean ± SD</i>	105±27	99±28	NA	NA	60±10	63±11	42±6	46±8	46±9	48±10	53±13	51±10	57±13	57±12
CGM Data <i>median</i>	N=26	N=18	N=47	NA	N=47	NA	N=45	N=14	N=44	N=15	N=45	N=15	N=31	N=15
Mean Glucose (mg/dL)	208	167	118	NA	124	NA	131	124	141	126	161	165	150	152
71-180 mg/dL	41%	63%	89%	NA	87%	NA	85%	83%	78%	88%	68%	64%	69%	70%
<70 mg/dL	0.0%	0.3%	3.5%	NA	1.8%	NA	2.5%	0.9%	2.1%	2.8%	1.3%	1.2%	2.5%	0.7%
>180 mg/dL	59%	33%	6%	NA	7%,	NA	12%	6%	16%	9%	29%	28%	27%	22%
CV <sup>c</sup>	31%	32%	28%	NA	28%	NA	31%	31%	32%	30%	33%	31%	35%	35%
	NA	NA	N=48	N=18	N=48	N=17	N=48	N=18	N=48	N=17	N=48	N=17	N=48	N=20
TDI <sup>d</sup> (U/kg/day)	NA	NA	0.7±0.3	0.5±0.3	0.5±0.2	0.4±0.3	0.5±0.2	0.4±0.4	0.5±0.2	0.4±0.3	0.6±0.2	0.4±0.3	0.6±0.2	0.6±0.3
	N=46	N=19	N=46	N=17	N=46	N=16	N=46	N=17	N=46	N=16	N=46	N=16	N=46	N=19
BMI percentile <sup>e</sup>	41%	46%	59%	51%	59%	54%	59%	59%	57%	49%	56%	49%	58%	62%

a – Geometric mean (95% C.I.) calculated from an inverse transformation as described in Methods.

b – HbA1c not measured at 2 weeks. The 6-week value is based on a local HbA1c measurement, other times are central laboratory results.

c – Coefficient of variation = SD/mean, expressed as a percentage.

d – TDI = Total daily insulin.

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e – BMI percentile was calculated for subjects <18 years of age based on 2000 CDC pediatric growth chart data (29) and was adjusted for age and gender. 3 participants  $\geq 18$  years old were excluded: 2 were in the intensive group (one with BMI 24.9 kg/m<sup>2</sup>, one with BMI 18.8 kg/m<sup>2</sup>), and 1 was in the control group (BMI=25.7 kg/m<sup>2</sup>).

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**Supplementary Table 3.** Subgroup analyses.

	N <sup>a</sup>	Baseline C-peptide AUC		N <sup>a</sup>	12 month C-peptide AUC	
		Intensive Mean (95% C.I.) <sup>b</sup>	Standard Mean (95% C.I.) <sup>b</sup>		Intensive Mean (95% C.I.) <sup>b</sup>	Standard Mean (95% C.I.) <sup>b</sup>
<b>Overall Intent to Treat Analysis</b>	48/18	0.29 (0.23, 0.35)	0.35 (0.23, 0.49)	47/20	0.43 (0.34, 0.52)	0.52 (0.32, 0.75)
<b>Per Protocol Analysis</b>	22/13	0.32 (0.23, 0.42)	0.34 (0.21, 0.47)	22/15	0.54 (0.39, 0.71)	0.43 (0.23, 0.66)
<b>Age</b>						
7-<12 years	25/4	0.27 (0.18, 0.37)	0.21 (0.12, 0.32)	24/6	0.32 (0.22, 0.43)	0.33 (0.08, 0.63)
≥12 years	23/14	0.31 (0.23, 0.38)	0.39 (0.23, 0.57)	23/14	0.55 (0.41, 0.71)	0.61 (0.33, 0.94)
<b>Gender</b>						
Female	17/6	0.35 (0.23, 0.49)	0.49 (0.11, 1.02)	17/7	0.52 (0.33, 0.74)	0.74 (0.18, 1.56)
Male	31/12			30/13		
<b>DKA at diagnosis</b>						
Yes	14/5	0.21 (0.17, 0.26)	0.20 (0.09, 0.31)	14/6	0.34 (0.19, 0.51)	0.52 (0.18, 0.95)
No	34/13	0.32 (0.24, 0.40)	0.41 (0.25, 0.60)	33/14	0.47 (0.36, 0.59)	0.52 (0.25, 0.84)
<b>Baseline lab HbA1c<sup>c</sup></b>						
<10.0% (<86 mmol/mol)	12/7	0.50 (0.32, 0.71)	0.56 (0.25, 0.94)	12/7	0.57 (0.33, 0.86)	0.66 (0.17, 1.36)
≥10.0% (≥86 mmol/mol)	36/11	0.22 (0.19, 0.26)	0.23 (0.17, 0.29)	35/13	0.38 (0.29, 0.48)	0.44 (0.24, 0.69)
<b>Baseline C-peptide at 90 min (pmol/mL)</b>						
<0.30	26/9	0.16 (0.14, 0.18)	0.19 (0.15, 0.23)	25/9	0.31 (0.22, 0.41)	0.37 (0.16, 0.61)
≥0.30	22/9	0.46 (0.37, 0.56)	0.54 (0.32, 0.79)	22/9	0.57 (0.42, 0.74)	0.72 (0.31, 1.25)

a - # participants: Intensive/Standard

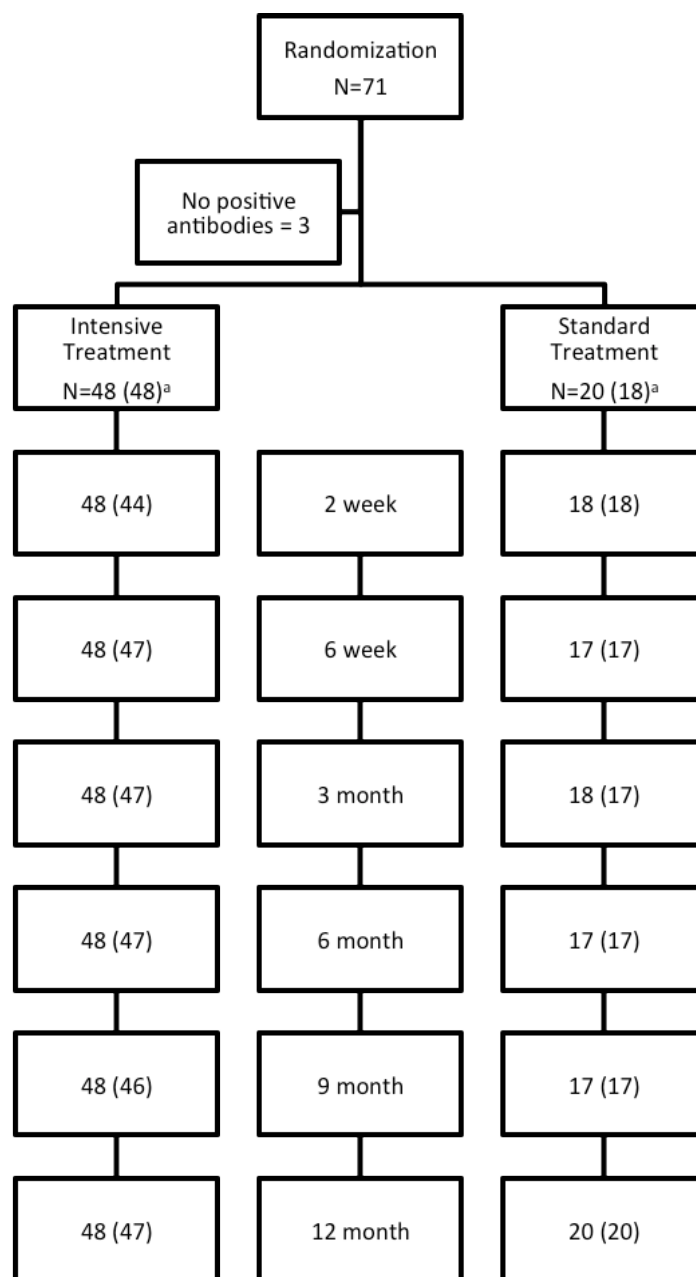
b- Geometric mean (95% C.I.) as defined in Methods.

c - Lab HbA1c missing for 1 cases was imputed from DCA HbA1c by site using repeated measures least squares model.



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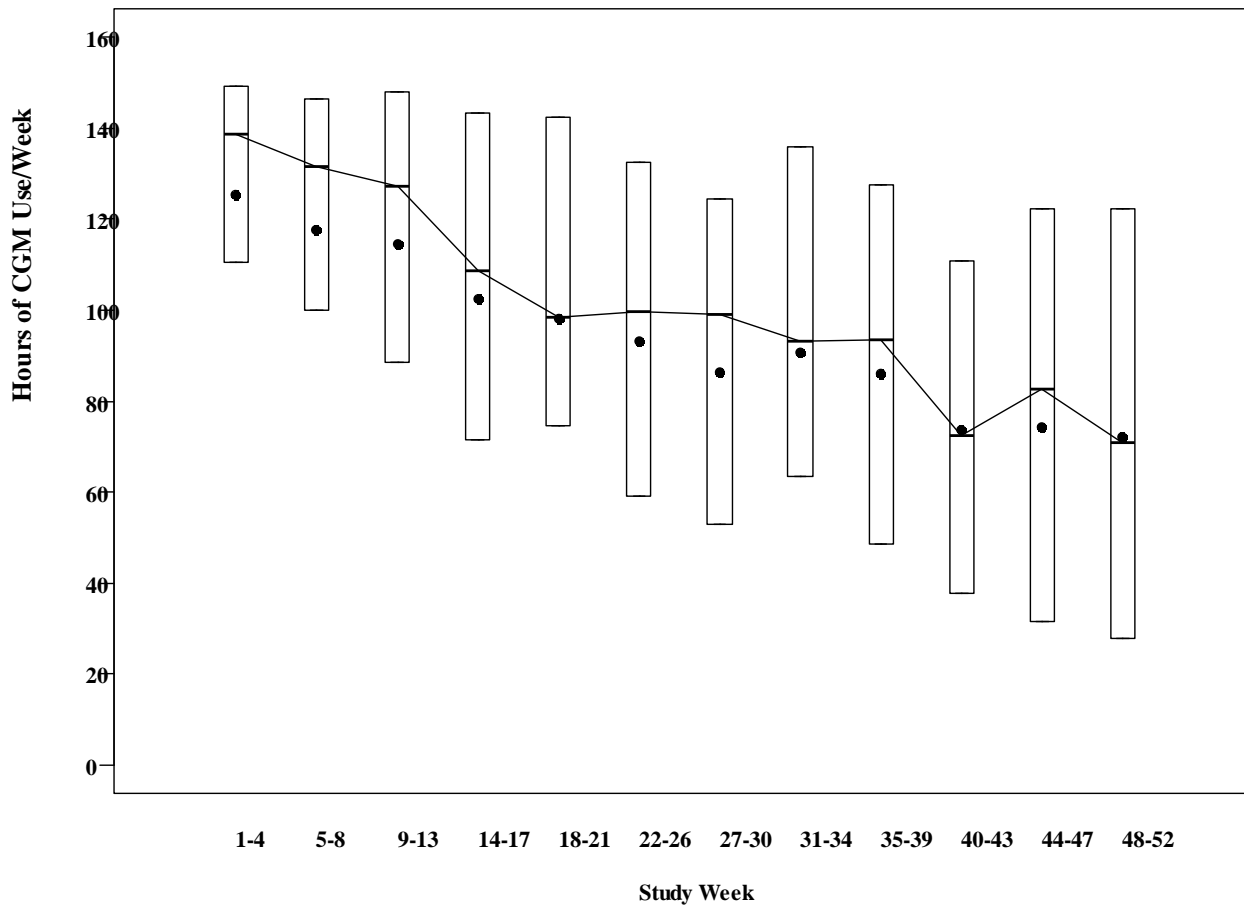
Supplementary Figure 1. Cohort flowchart.



a - Number completed visits (# completed MMTT)

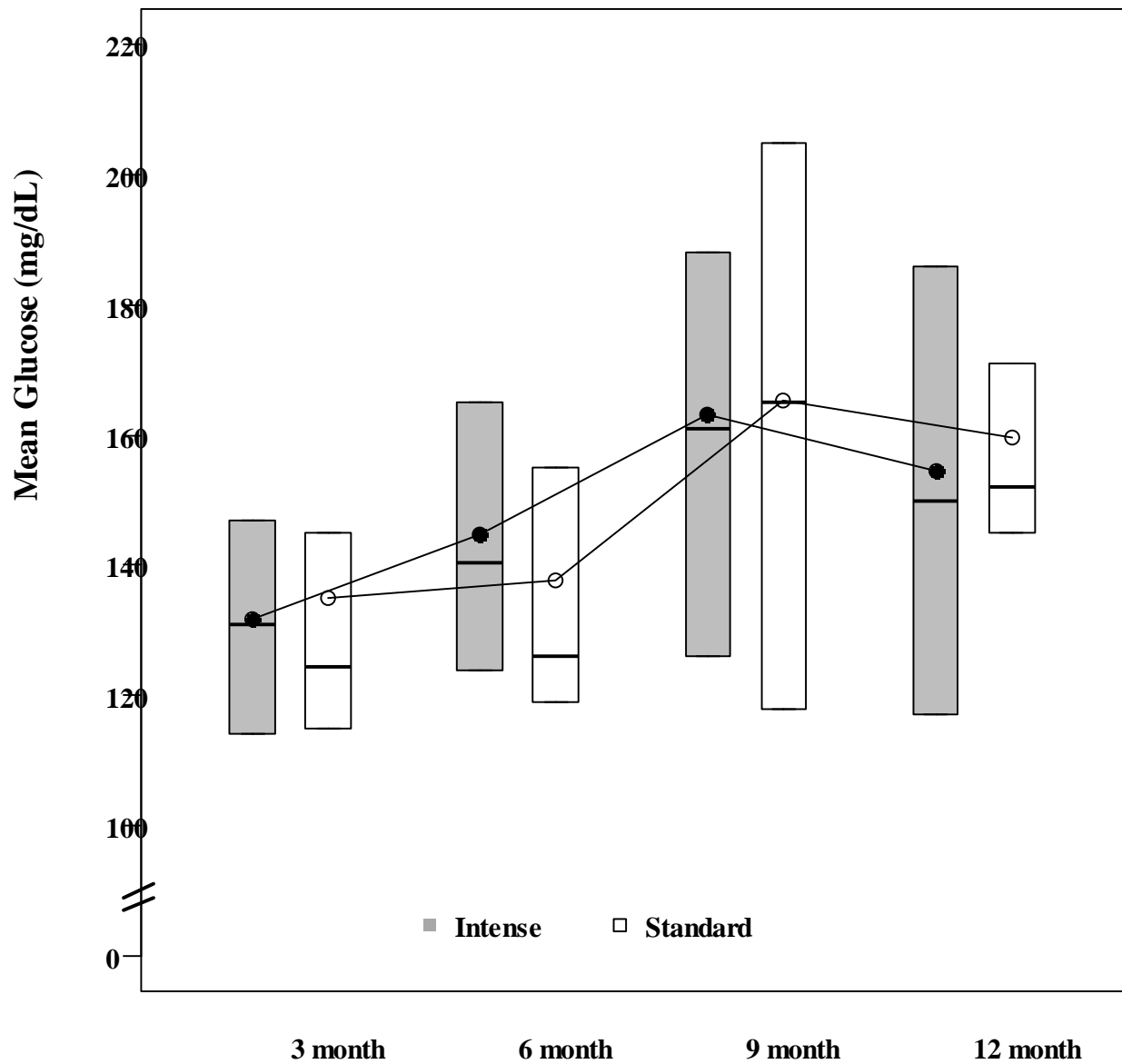
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**Supplementary Figure 2.** Boxplots for sensor use in every 4-week period among intensive treatment group. The bottom and top of each box denote the 25<sup>th</sup> and 75<sup>th</sup> percentiles, the line inside the box denotes the median and the dot is the mean.



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**Supplementary Figure 3.** Mean glucose from CGM data following each visit. The bottom and top of each box denote the 25<sup>th</sup> and 75<sup>th</sup> percentiles, the line inside the box denotes the median and the dot is the mean.



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**Supplementary Figure 4.** Mean of C-peptide AUC compared with TrialNet controls.

