

SUPPLEMENTARY DATA

Supplementary Table 1. Eligibility and Exclusion Criteria

Eligibility Criteria

- 1) Clinical diagnosis of type 1 diabetes and using daily insulin therapy for at least one year and an insulin infusion pump for at least 6 months
The diagnosis of type 1 diabetes is based on the investigator's judgment; C peptide level and antibody determinations were not required.
- 2) Age 3 to 14 years
- 3) Glycated hemoglobin level $\leq 8.5\%$ (69 mmol/mol)
 - Measured with DCA2000 or equivalent device for assessing eligibility
 - Based on an analysis of the JDRF CGM RCT dataset²⁰, participants higher than 8.5% (69 mmol/mol) are not expected to meet the minimum amount of nocturnal hypoglycemia (at least one night with a CGM glucose value ≤ 60 mg/dL or at least three different nights with a sensor glucose value ≤ 70 mg/dL).
 - Glycated hemoglobin measurements performed as part of usual clinical care within 2 weeks prior to obtaining informed consent for participation in the trial may be used.
- 4) Availability of internet access for periodic upload of study data

Exclusion Criteria

- 1) Diabetic ketoacidosis in the past 3 months
- 2) Hypoglycemic seizure or loss of consciousness in the past 6 months
- 3) History of seizure disorder (except for hypoglycemic seizure)
- 4) History of any heart disease including coronary artery disease, heart failure, or arrhythmias
- 5) Cystic fibrosis
- 6) Current use of oral/inhaled glucocorticoids, beta-blockers or other medications, which in the judgment of the investigator would be a contraindication to participation in the study.
- 7) History of ongoing renal disease (other than microalbuminuria). Creatinine level to have been obtained within the last year if participant has diabetes of >10 years duration. If creatinine is > 1.5 mg/dL (0.08 mmol/L), the participant is excluded.
- 8) Medical or psychiatric condition that in the judgment of the investigator might interfere with the completion of the protocol such as:
 - Inpatient psychiatric treatment in the past 6 months
 - Uncontrolled adrenal disorder
 - Abuse of alcohol
- 9) Pregnancy
If female and sexually active, must agree to use a form of contraception to prevent pregnancy while a participant in the study. A negative serum pregnancy test will be required for all premenopausal women who are not surgically sterile. Participants who become pregnant will be discontinued from the study.
- 10) Liver disease as defined by an ALT greater than 3 times the upper limit of normal

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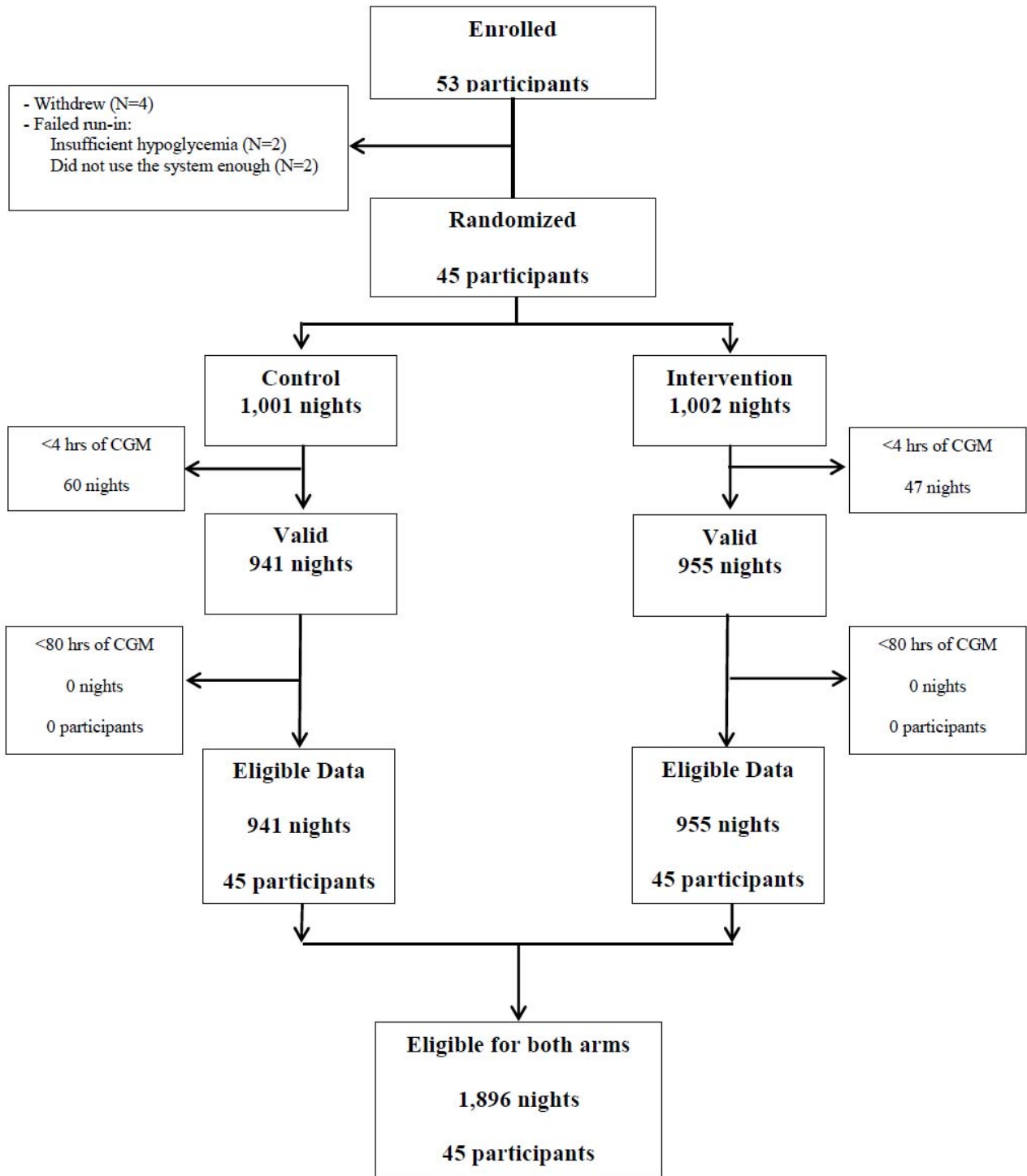
Supplementary Table 2. Participant Characteristics at Enrollment – medians (IQR) or n (%)

| Characteristic | Participants 11-14 Years of Age (N=45) | Participants 4-10 Years of Age (N=37) |
|-------------------------------|---|--|
| Age (yrs) | 13 (11, 13) | 8 (6, 9) |
| <i>Range</i> | 11 to 14 | 4 to 10 |
| Male | 25 (56%) | 17 (46%) |
| Race | | |
| White non-Hispanic | 43 (96%) | 35 (95%) |
| Hispanic | 1 (2%) | 2 (5%) |
| Asian | 1 (2%) | 0 |
| Diabetes duration (yr) | 6 (3, 9) | 3 (2, 5) |
| Body-mass index percentile * | 69 (44, 82) | 69 (51, 82) |
| HbA1c (%) | 7.7 (7.3, 8.2) | 7.8 (7.5, 8.0) |
| HbA1c (mmol/mol) | 61 (56, 66) | 62 (58, 64) |
| Daily insulin dose (U/kg/day) | 0.83 (0.72, 0.96) | 0.76 (0.69, 0.86) |

* Body-mass index percentiles adjusted for age and gender were computed using the 2000 CDC population growth chart data (Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC growth charts: United States. *Adv Data* 2000:1-27).

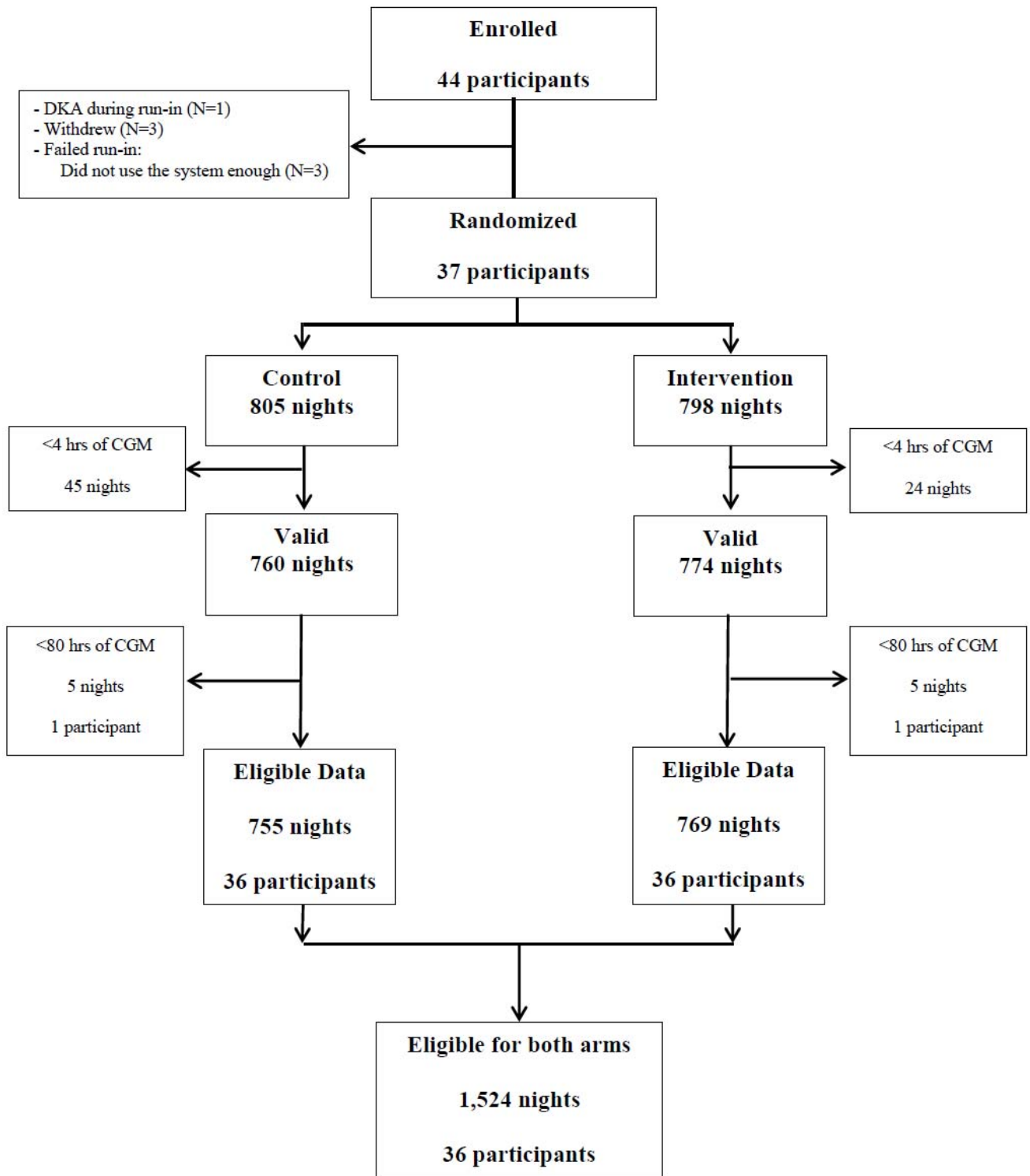
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Supplementary Figure 3A. Among Participants 11-14 Years of Age, Study Flowchart



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Supplementary Figure 3B. Among Participants 4-10 Years of Age, Study Flowchart



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Supplementary Table 4. Number of Nights Required to Complete 42 Nights

| | Participants 11-14 Years of Age | Participants 4-10 Years of Age |
|--|--|---|
| # participants enrolled | 45 | 37 |
| # participants with at least 80hr of CGM in each arm | 45 (100%) | 36 (97%) |
| # participants completing 42 nights. | 44 (98%) | 34 (92%) |
| # nights to complete study | | |
| Median (<i>IQR</i>) | 59 (52, 69) | 63 (54, 71) |
| 42-47 nights | 2 (5%) | 1 (3%) |
| 48-53 nights | 11 (25%) | 6 (18%) |
| 54-59 nights | 9 (20%) | 7 (21%) |
| 60-65 nights | 6 (14%) | 6 (18%) |
| 66-70 nights | 6 (14%) | 5 (15%) |
| ≥71 nights | 10 (23%) | 9 (26%) |
| # nights skipped <i>median (IQR)</i> | 15 (9, 25) | 18 (11, 25) |
| # nights with <4 hours of CGM data <i>median (IQR)</i> | 1 (1, 3) | 1 (0, 2) |

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Supplementary Table 5. Additional Efficacy and Safety Secondary Outcomes*

| | Participants 11-14 Years of Age (N=45) | | | Participants 4-10 Years of Age (N=36†) | | |
|---|--|---------------------|---------|--|---------------------|---------|
| | Control Nights | Intervention Nights | P-value | Control Nights | Intervention Nights | P-value |
| | 941 | 955 | | 755 | 769 | |
| Hypoglycemia Outcomes | | | | | | |
| % of nights with glucose level <70 mg/dL for a cumulative duration of | | | | | | |
| > 30min | 31% | 23% | <0.001 | 26% | 18% | <0.001 |
| > 60min | 26% | 17% | <0.001 | 19% | 12% | <0.001 |
| > 120min | 18% | 9% | <0.001 | 12% | 6% | <0.001 |
| > 180min | 13% | 5% | <0.001 | 6% | 3% | 0.002 |
| % of nights with glucose level <60 mg/dL for a cumulative duration of | | | | | | |
| > 30min | 21% | 14% | <0.001 | 16% | 10% | <0.001 |
| > 60min | 15% | 9% | <0.001 | 10% | 6% | 0.005 |
| > 120min | 11% | 4% | <0.001 | 6% | 3% | 0.002 |
| > 180min | 7% | 2% | <0.001 | 3% | 1% | 0.002 |
| % of nights with events of glucose <70 mg/dL continuously‡ for | | | | | | |
| > 10min | 36% | 31% | 0.006 | 32% | 25% | 0.001 |
| > 25min | 32% | 23% | <0.001 | 25% | 18% | <0.001 |
| > 60min | 23% | 14% | <0.001 | 15% | 10% | 0.003 |
| > 120min | 14% | 7% | <0.001 | 8% | 4% | <0.001 |

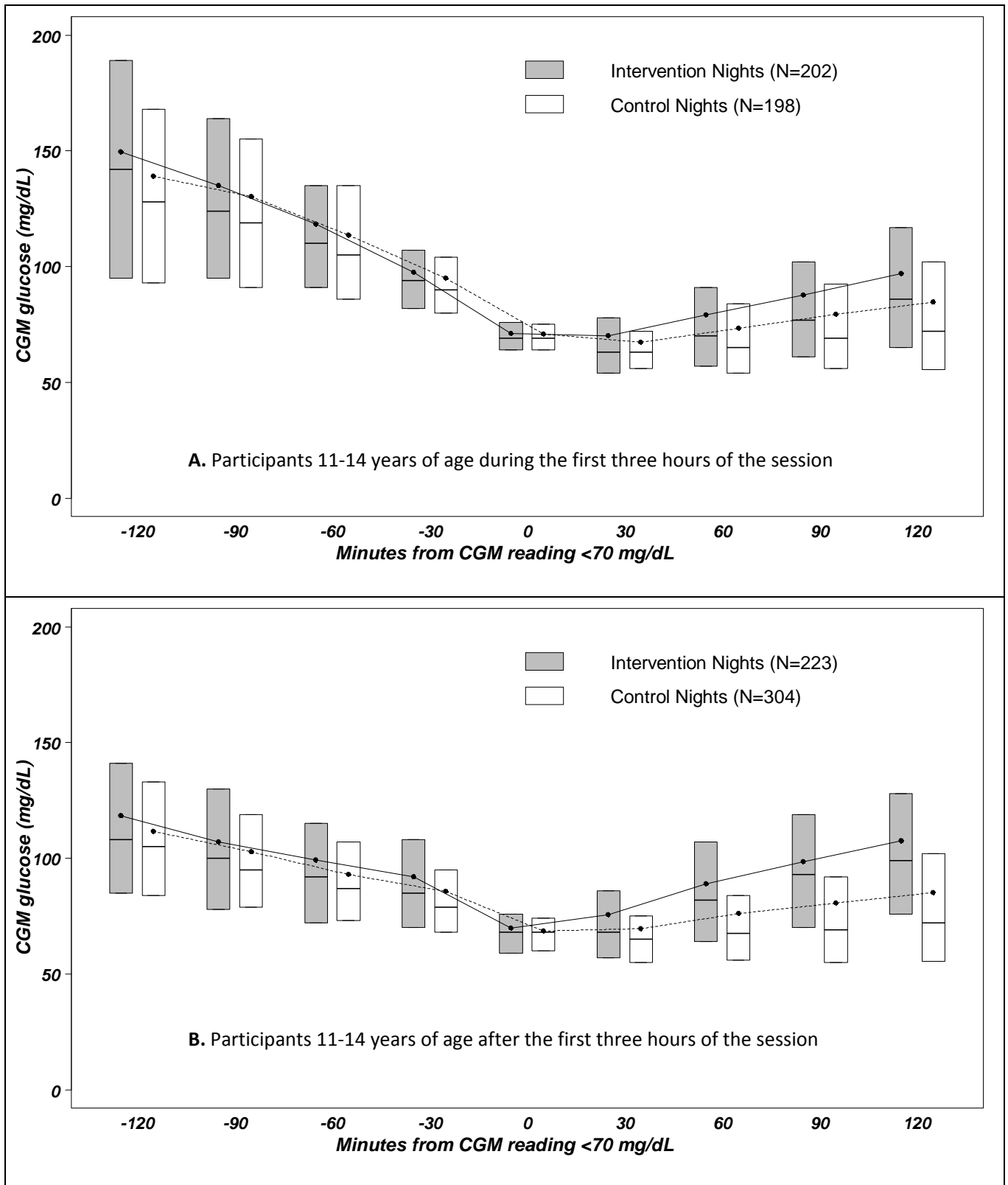
*Glucose results from CGM unless specified as blood glucose.

†One participant with 5 intervention nights and 5 control nights was excluded for <80 hours of CGM glucose data.

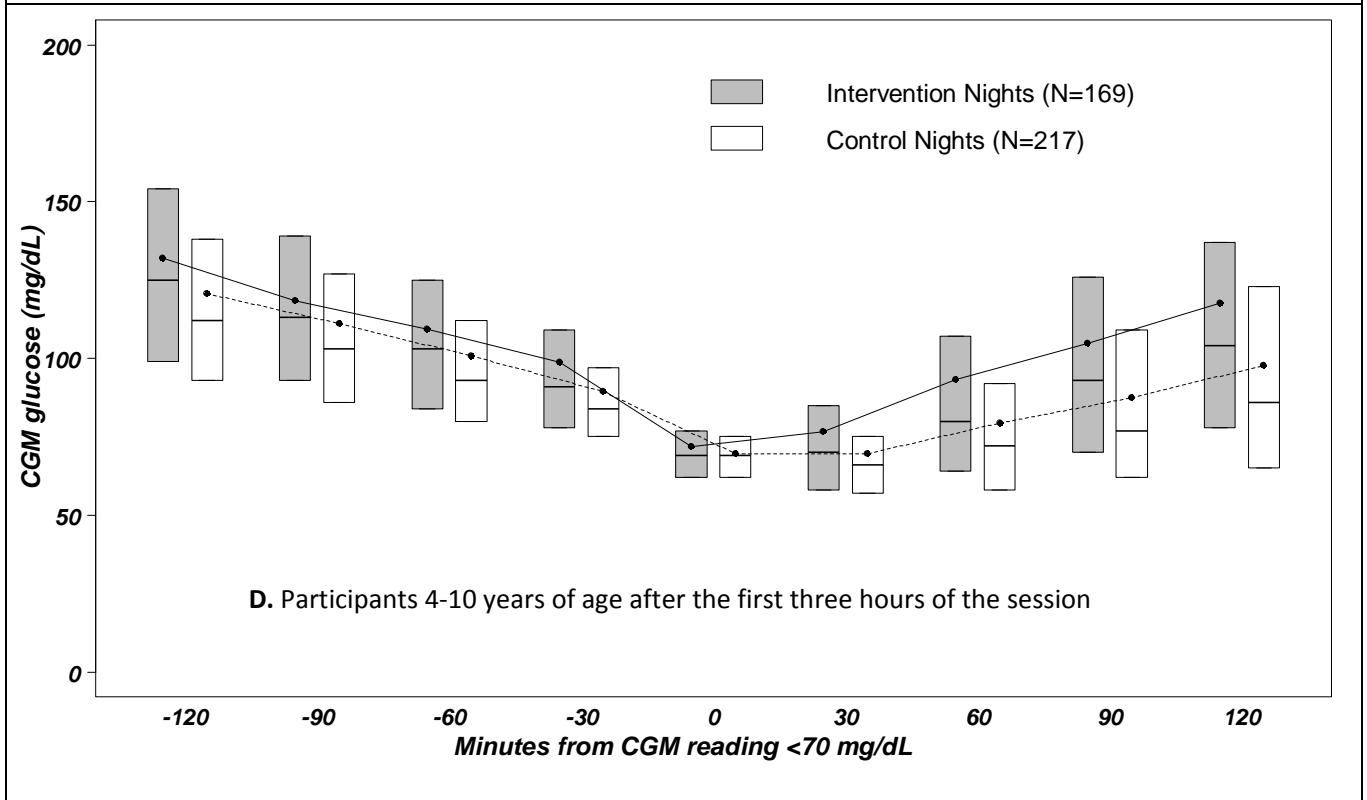
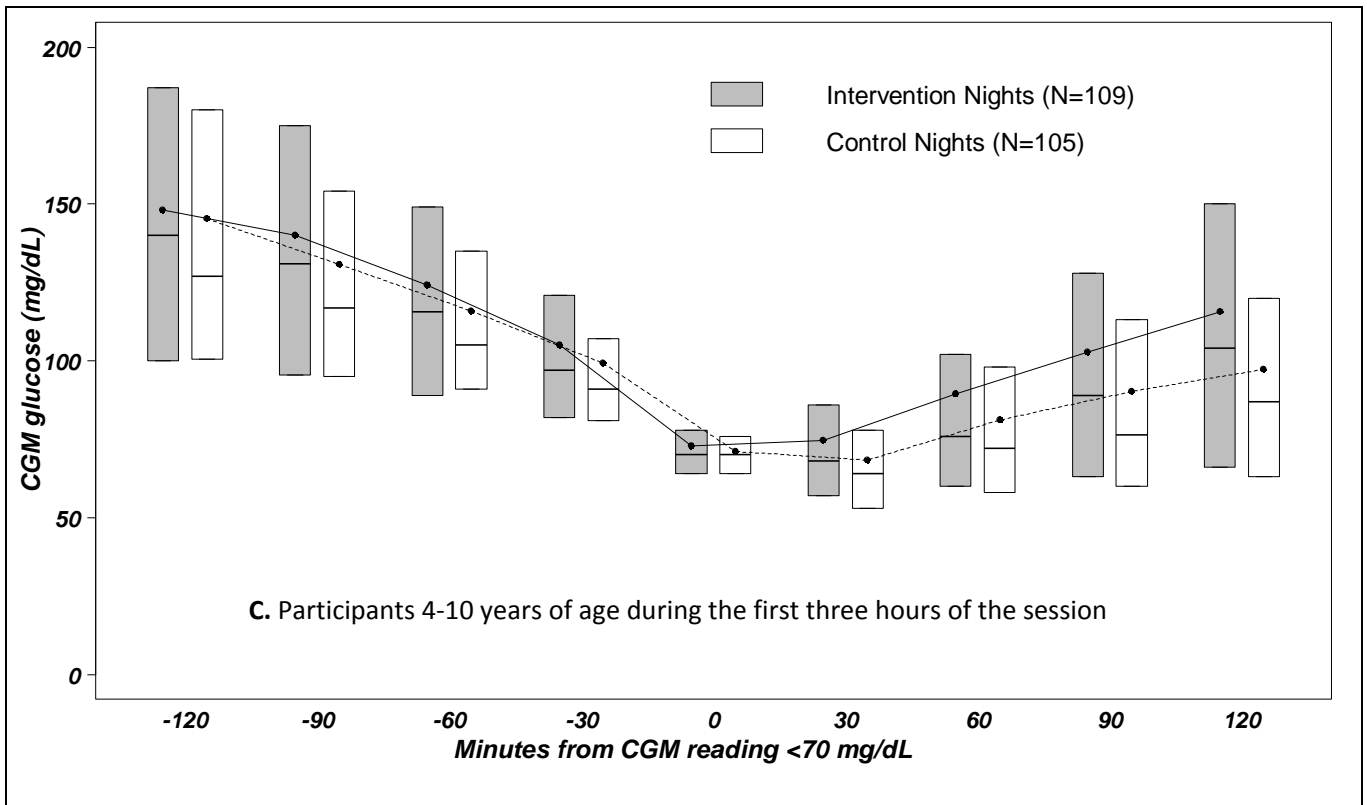
‡Hypoglycemia event assessment based on continuous CGM values below threshold was added to statistical analysis plan post hoc

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Supplementary Figure 6. Mean Glucose hours before and 2 hours after Occurrences of CGM Glucose <70 mg/dL.



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Supplementary Table 7. Application of Algorithm to Control Nights*

| | Age Group | | |
|---|----------------------|-----------|-----------|
| | All | 11-14 | 4-10 |
| # Control Nights overall | 1,696 | 941 | 755 |
| # w/ prediction of CGM glucose <80 mg/dL | 1,148 | 647 | 501 |
| <i>On nights when predicted, did CGM glucose actually drop to <80 mg/dL within 2 hours?</i> | | | |
| | <i>No</i> 548 (48%) | 294 (45%) | 254 (51%) |
| | <i>Yes</i> 600 (52%) | 353 (55%) | 247 (49%) |
| <i>On nights when CGM glucose dropped to <80 mg/dL, time from pump suspension recommendation to CGM glucose <80 mg/dL</i> | | | |
| A) within 30 min | 306 (51%) | 179 (51%) | 127 (51%) |
| B) 30-<60 min | 168 (28%) | 100 (28%) | 68 (28%) |
| C) 60-<120 min | 126 (21%) | 74 (21%) | 52 (21%) |

* The first 15 minutes of the night were ignored because it was possible for the sensor glucose to start out <80 mg/dL.

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Supplementary Table 8. Assessment of Sensor Accuracy

| | | Age Group | | | |
|---------------------------------------|--------------|----------------------------------|---------------------------------------|----------------------------------|---------------------------------------|
| | | 11-14 Years of Age | | 4-10 Years of Age | |
| | | <i>Control</i> <i>N=2,193</i> | <i>Intervention</i> <i>N=2,143</i> | <i>Control</i> <i>N=2,173</i> | <i>Intervention</i> <i>N=2,129</i> |
| Sensor minus Reference Glucose | Mean ± SD | -20.8 ± 40.2 | -20.4 ± 42.7 | -19.2 ± 37.3 | -18.4 ± 39.8 |
| | Median (IQR) | -15.0 (-36.0, 1.0) | -15.0 (-38.0, 3.0) | -15.0 (-37.0, 3.0) | -13.0 (-36.0, 4.0) |
| <i>Reference Meter Glucose</i> | | | | | |
| ≤70 mg/dL | N | 81 | 54 | 117 | 45 |
| | Mean ± SD | -0.5 ± 18.7 | +0.2 ± 18.7 | +2.4 ± 23.2 | +14.8 ± 35.8 |
| | Median (IQR) | -3.0 (-11.0, 7.0) | -2.0 (-15.0, 10.0) | 1.0 (-10.0, 11.0) | 8.0 (-5.0, 18.0) |
| 71-120 mg/dL | N | 578 | 467 | 578 | 489 |
| | Mean ± SD | -12.1 ± 21.5 | -4.3 ± 28.2 | -7.1 ± 23.4 | -3.7 ± 22.4 |
| | Median (IQR) | -12.0 (-24.0, 1.0) | -6.0 (-23.0, 9.0) | -6.0 (-21.0, 6.0) | -3.0 (-17.0, 8.0) |
| 121-180 mg/dL | N | 756 | 768 | 653 | 722 |
| | Mean ± SD | -15.2 ± 30.0 | -15.6 ± 31.9 | -15.7 ± 31.7 | -13.8 ± 32.8 |
| | Median (IQR) | -13.0 (-32.0, 3.0) | -13.0 (-34.0, 2.0) | -14.0 (-34.0, 2.0) | -11.0 (-30.0, 4.0) |
| >180 mg/dL | N | 778 | 854 | 825 | 873 |
| | Mean ± SD | -35.0 ± 54.5 | -34.9 ± 53.0 | -33.5 ± 45.1 | -32.2 ± 47.4 |
| | Median (IQR) | -26.0 (-56.0, -4.0) | -28.0 (-60.0, -1.0) | -30.0 (-57.0, -7.0) | -28.0 (-56.0, -4.0) |

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| | Age Group | | | | |
|--|--------------|----------------------------------|---------------------------------------|----------------------------------|---------------------------------------|
| | | 11-14 Years of Age | | 4-10 Years of Age | |
| | | <i>Control</i> <i>N=2,193</i> | <i>Intervention</i> <i>N=2,143</i> | <i>Control</i> <i>N=2,173</i> | <i>Intervention</i> <i>N=2,129</i> |
| Relative Absolute Difference [†] | Mean ± SD | 18% ± 16% | 19% ± 17% | 18% ± 17% | 18% ± 19% |
| | Median (IQR) | 14% (7%, 26%) | 15% (6%, 27%) | 14% (7%, 25%) | 13% (6%, 24%) |
| <i>Reference Meter Glucose</i> | | | | | |
| ≤70 mg/dL | N | 81 | 54 | 117 | 45 |
| | Mean ± SD | 22% ± 28% | 24% ± 20% | 23% ± 37% | 40% ± 73% |
| | Median (IQR) | 15% (8%, 28%) | 20% (12%, 31%) | 16% (8%, 28%) | 18% (11%, 33%) |
| 71-120 mg/dL | N | 578 | 467 | 578 | 489 |
| | Mean ± SD | 20% ± 16% | 21% ± 19% | 19% ± 16% | 17% ± 15% |
| | Median (IQR) | 16% (7%, 30%) | 16% (7%, 29%) | 15% (6%, 27%) | 12% (6%, 25%) |
| 121-180 mg/dL | N | 756 | 768 | 653 | 722 |
| | Mean ± SD | 17% ± 15% | 18% ± 15% | 18% ± 16% | 17% ± 16% |
| | Median (IQR) | 13% (6%, 23%) | 13% (6%, 25%) | 14% (7%, 25%) | 13% (6%, 25%) |
| >180 mg/dL | N | 778 | 854 | 825 | 873 |
| | Mean ± SD | 18% ± 16% | 19% ± 17% | 17% ± 14% | 17% ± 15% |
| | Median (IQR) | 13% (6%, 25%) | 15% (6%, 27%) | 14% (7%, 23%) | 14% (7%, 24%) |

[†]Defined as the absolute value of the difference divided by the reference value, expressed as a percentage

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Supplementary Table 9. Sensor Accuracy when Sensor Glucose below 70 mg/dL and a Paired Meter Blood Glucose was Available.

| <i>Reference Meter Glucose</i> | Age Group | | | | | | |
|--------------------------------|------------------------------|----------------------------|--------------------------------|-------------------------------------|----------------------------|--------------------------------|-------------------------------------|
| | <i>Total</i> <i>N=772</i> | 11-14 Years of Age | | | 4-10 Years of Age | | |
| | | <i>All</i> <i>N=417</i> | <i>Control</i> <i>N=260</i> | <i>Intervention</i> <i>N=157</i> | <i>All</i> <i>N=355</i> | <i>Control</i> <i>N=231</i> | <i>Intervention</i> <i>N=124</i> |
| <70 mg/dL | 194 (25%) | 93 (22%) | 55 (21%) | 38 (24%) | 101 (28%) | 77 (33%) | 24 (19%) |
| 70-79 mg/dL | 111 (14%) | 63 (15%) | 45 (17%) | 18 (11%) | 48 (14%) | 36 (16%) | 12 (10%) |
| 80-89 mg/dL | 105 (14%) | 59 (14%) | 45 (17%) | 14 (9%) | 46 (13%) | 27 (12%) | 19 (15%) |
| ≥90 mg/dL | 362 (47%) | 202 (48%) | 115 (44%) | 87 (55%) | 160 (45%) | 91 (39%) | 69 (56%) |

Supplementary Table 10. Among Intervention Nights with Pump Suspensions*, Number of Pump Suspensions and their Duration by Time of Night - median (IQR)

| <i>Age Group</i> | <i>Time of Night</i> [†] | <i># Events</i> | <i>Duration per Event (min)</i> | <i># Nights</i> [‡] | <i>Total Duration (min)</i> |
|------------------|-----------------------------------|-----------------|---------------------------------|------------------------------|-----------------------------|
| 11-14 | Before Midnight | 686 | 13 (5, 29) | 370 | 30 (11, 56) |
| | Midnight to 4:00AM | 1211 | 11 (5, 25) | 439 | 40 (19, 77) |
| | After 4:00AM | 826 | 10 (5, 19) | 364 | 25 (10, 46) |
| | Before Midnight | 476 | 11 (5, 23) | 250 | 21 (10, 45) |
| 4-10 | Midnight to 4:00AM | 752 | 14 (5, 26) | 274 | 45 (20, 80) |
| | After 4:00AM | 676 | 10 (5, 20) | 297 | 27 (14, 54) |

* N=671 and 503 intervention nights with one or more pump suspensions among the 11-14 and 4-10 years of age respectively.

† Based on the when the suspension was initiated.

‡ Number of nights with at least one event starting during the indicated time period.