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# The Accuracy of the GlucoWatch® G2™ Biographer in Children with Type 1 Diabetes: Results of the Diabetes Research in Children Network (DirecNet) Accuracy Study*

**The Diabetes Research in Children Network (DirecNet) Study Group**†

## Abstract

**Objective—**To assess the accuracy of the GlucoWatch® G2™ Biographer (GW2B) in children and adolescents with type 1 diabetes mellitus (T1DM).

**Research Design and Methods—**During a 24-hour clinical research center stay, 89 children and adolescents with T1DM (aged 3.5 to 17.7 years) wore 174 GW2Bs and had frequent serum glucose determinations during the day and night and during insulin-induced hypoglycemia and meal-induced hyperglycemia, resulting in 3,672 GW2B-reference glucose pairs.

**Results—**The median relative absolute difference between the GW2B and reference glucose values was 16% ($25^{th}$, $75^{th}$ percentiles = 7%, 29%). The proposed ISO criteria were met for 60% of sensor values. Accuracy was better at higher serum glucose levels than low glucose levels. Accuracy degraded slightly as the sensor aged. Time of day, subject age, gender, or body mass index did not impact GW2B accuracy. There were no cases of serious skin reactions.

**Conclusion—**Although the accuracy of this generation of sensor does not approach that of current home glucose meters, the majority of sensor glucose values are within 20% of the serum glucose. This level of accuracy may be sufficient for detecting trends and modifying diabetes management. Further longitudinal outpatient studies are needed to assess the utility of the GW2B as a management tool to improve glycemic control and decrease the incidence of severe hypoglycemia in children with diabetes.

The Diabetes Research in Children Network (DirecNet) is a NIH-funded collaborative study group that consists of five clinical centers, a coordinating center, a central laboratory, and representatives from NICHD and NIDDK. The major objective of DirecNet is to critically evaluate the clinical usefulness of current and future glucose sensor devices in youth with T1DM. As a prelude to conducting clinical trials to evaluate use of glucose sensors as management tools for children and adolescents with diabetes, the DirecNet Accuracy Study was developed to independently assess the performance of the GlucoWatch Automatic Glucose Biographer (“GWB”; Cygnus Inc. Redwood City, CA) and the Continuous Glucose Monitoring System (“CGMS™”; Medtronic MiniMed, Northridge, CA) in children from 1 to <18 years of age.

The purpose of this paper is to report our findings with respect to the accuracy of the second generation GlucoWatch Automatic Glucose Biographer, the GlucoWatch® G2™ Biographer

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†A listing of the DirecNet Study Group appears in the Appendix.

LifeScan, Milpitas, CA, provided the One Touch® Ultra® Blood Glucose Monitoring Systems and the blood glucose test strips.

The GlucoWatch® G2™ Biographer were purchased from Cygnus, Inc. at a discounted price.

(Cygnus, Inc., "GW2B") in children with T1DM. The GWB adheres to the skin of an extremity via an adhesive pad that incorporates two hydrogel discs, each the size of a dime. The device sends a small current through the discs to pull cations, particularly sodium, through the skin; glucose is present in the fluid that accompanies the ion flow. During a 10-minute cycle, the glucose in the interstitial fluid is then measured. Compared with the first generation GWB, the software of the GW2B model allows for a 2-hour instead of a 3-hour warm up and provides glucose readings every 10 minutes instead of every 20 minutes. The displayed glucose value represents the average of the glucose values from the current and the previous 10-minute cycles. The reported glucose value lags behind the blood glucose level by about 17.5 minutes. The maximum sensor life from the time of initiation is 15 hours. Alarms for high and low glucose levels can be set by the user.

The study was designed to examine sensor accuracy during acute hyper- and hypoglycemia, as well as during spontaneous fluctuations in glucose levels over 24 hours, in comparison with frequent serum glucose values measured in a central laboratory. Results of companion studies with the CGMS™ are reported separately.[1]

## Methods

### Subjects

**Consent Procedures—**The DirecNet Data and Safety Monitoring Board and the Institutional Review Boards at each of the DirecNet centers approved the study protocol, consent form and assent form. A parent or guardian gave written consent and patients 7 years of age or older gave written assent prior to the performance of any study procedures.

**Eligibility Criteria and Assessment—**To be eligible for the study the subject had to have 1) age between 1 and 18 years, 2) clinical diagnosis of type 1 diabetes mellitus of ≥1 year duration, 3) for subjects over 2 years of age, body mass index (BMI) between the 5$^{th}$ and 95$^{th}$ percentile for age and gender,[2] 4) weight ≥12.0 kg if <7 years of age and ≥16.0 kg if ≥7 years of age, 5) a normal hematocrit, 6) no current use of glucocorticoids, 7) no skin or other medical disorders that would affect completion of the study, and 8) no history of seizures other than those attributable to either hypoglycemia or high fever. Eligibility was assessed by medical history, physical examination and hematocrit measurement. HbA1c was measured locally with the DCA®2000+ (Bayer Diagnostics, Tarrytown, NY).

### Study Procedures

Following admission to each center's clinical research center (CRC), a GW2B sensor was placed and, after two hours, calibrated by study staff from a glucose measurement obtained using the One Touch® Ultra® Meter ("Ultra"; Lifescan, Milpitas, CA). Between 0 and 9 hours after calibration of the GW2B, a second GW2B sensor was placed such that there would be a minimum of two hours of overlap between the two GW2Bs. Additional sensor pads were used so that at least one GW2B was functioning for the 24 hours of serum glucose measurements. Although the GW2B requires only a single calibration value following the 2-hour warm-up period, for some patients additional calibration values were subsequently entered. The clock time of each GW2B was synchronized with the clock used to document the time of the blood draws. Prior to hospital discharge and at a follow-up visit three to five days following discharge, the skin was formally assessed in the area where each GW2B was worn. Both erythema and edema were evaluated and scored using a 0 to 4 modified Draize scale.[3]

An indwelling intravenous catheter was inserted into an arm vein in order to obtain samples for serum glucose determinations by a central laboratory. In each subject, blood samples were obtained every 60 minutes during the day (7:00 AM to 9:00 PM) and every 30 minutes during

the night (9:30 PM to 6:30 AM). Subjects of sufficient weight to accommodate extra blood sampling also underwent a meal-induced hyperglycemia test and, if they were ≥7 years of age, an insulin-induced hypoglycemia test (see details below). Additional blood samples were obtained when the sensors were calibrated or if there were symptoms of hypoglycemia.

**Meal-induced Hyperglycemia Test Procedures—**The aim of this test was to assess sensor function during a rapid physiologic rise in serum glucose. To ensure the safety of subjects, and since the GW2B does not quantify glucose values that are >400 mg/dL, short-acting insulin was given subcutaneously if the pre-test blood glucose level was ≥250 mg/dL, and the start of the test was delayed until the blood glucose fell to <250 mg/dL. At the start of the study, each subject ingested a high carbohydrate drink containing 1.75 gm of carbohydrate per kg body weight up to a maximum of 75 grams. Blood samples for serum glucose determinations were obtained every 5 minutes for 60 minutes after the subject finished the drink.

**Insulin-induced Hypoglycemia Test Procedures—**The purpose of this test was to assess sensor function during an acute fall in blood glucose levels to the mildly hypoglycemic range. If the pre-test blood glucose was <80 mg/dL, juice or other carbohydrate was given orally to raise the blood glucose above this level before starting the test.

For the test, 0.05–0.10 units per kg body weight of regular insulin was given by intravenous bolus injection. After 30 minutes, a second dose could be given if the target glucose (<55 mg/dL) had not been achieved. Blood samples for serum glucose determinations were obtained every 5 minutes during the test for up to 90 minutes. Bedside glucose monitoring for safety was performed at the same intervals. For subjects who did not reach a glucose level below 80 mg/dL, the test ended after 90 minutes. For the subjects whose glucose decreased below 80 mg/dL, the test continued until the glucose level was above 80 mg/dL. Oral or intravenous glucose was given at investigator discretion if the blood glucose fell below 55 mg/dL.

**Serum Glucose Determinations—**Blood samples for determination of serum glucose levels ("reference" glucose values) were obtained through the indwelling catheter after at least 1.3 ml of blood was drawn through the line to clear it of saline. A 0.3 ml sample was then obtained in a CAPIJECT® gel barrier blood collection tube and allowed to clot at room temperature for 20 minutes. The sample was then separated in a centrifuge and frozen at −20° C to − 80 °C until shipped in insulated boxes on dry ice to the DirecNet Central Biochemistry Laboratory at the University of Minnesota. Glucose levels were measured on these samples using a hexokinase enzymatic method, which has been suggested as the reference method for measuring glucose.[4, 5]

**Statistical Methods:** The underlying principle in the sample size estimations was to determine the number of subjects required for a prespecified width of a two-sided 95% confidence interval for each measure of accuracy. We estimated that with a sample size of 30 subjects and the projected number of reference-sensor matched glucose values, a 95% confidence interval half-width would be approximately 0.02 for the proportion of paired points in the modified Clarke (or consensus) error grid zones A + B[6] and 0.03 for the mean relative absolute difference based on the number of expected paired sensor-reference serum glucose values. In order to be able to assess accuracy separately in three age groups (1.0 to <7.0 years old, 7.0 to <12.0 years old, and 12.0 to <18.0 years old), a target sample size of 90 was selected, with 30 planned for each age group.

For the accuracy analyses, after accounting for a lag between the sensor reading and blood glucose of 17.5 minutes, the GW2B glucose measurements were matched to reference measurements from blood samples drawn within ±5 minutes (i.e., 17.5 ± 5 minutes) of the

sensor reading for all reference glucose values except for those obtained during the tests inducing hyperglycemia and hypoglycemia for which the matching was performed on ± 2.5 minutes (i.e., 17.5 ± 2.5 minutes). The lag time is the midpoint of the 15 to 20 minute lag time proposed by the company.[7] Most of the lag is related to the time required for sampling of the interstitial fluid and measurement of the glucose. For each matched pair, the following were computed: difference (sensor value minus reference value), absolute difference (absolute value of difference), relative difference (difference divided by reference value, multiplied by 100 to convert proportion to percentage), and relative absolute difference (absolute difference divided by reference value, multiplied by 100 to convert proportion to percentage, referred to as "RAD"). Each pair was also evaluated to determine whether it met the proposed International Organisation for Standardisation (ISO) criteria (for reference glucose value ≤75 mg/dL, GW2B value within ± 15 mg/dL and for reference glucose value >75 mg/dL, GW2B value within ± 20%, hereafter referred to as the "ISO criteria").[8] Summary statistics (e.g., mean and median) were computed by pooling all paired values; in order to account for the within-subject correlation, 95% confidence intervals were constructed by initially computing a mean for each subject and then basing the confidence interval on a variance estimate across subjects.

Pearson correlation coefficients were computed using two methods. The first method was a simple pooling of data points without adjustment for subject effects. The second method was to calculate a Pearson correlation separately for each subject and then take a weighted average across subjects. Only correlations obtained with the first method are presented; correlations obtained with the second method were consistently slightly lower than those obtained with the first method. Modified (consensus) error grids[6] were constructed based on the published algorithms. For the evaluation of variation among sensors, only sensors with at least 10 matched pairs (sensor and reference glucose values) were included. The median RAD and percentage of values meeting the ISO criteria were calculated separately for each sensor. Results are displayed in terms of the cumulative distribution for both RAD and ISO criteria. Analyses showed no meaningful differences across the clinical centers (data not shown).

Differences in accuracy among subgroups were evaluated by comparing ranks for RAD and comparing percentages meeting the ISO criteria. The percentage of GW2B skips was compared according to the age of the sensor.

Correlated observations from the same subject were handled by bootstrapping the confidence intervals and statistical comparisons, randomly resampling subjects with replacement. RAD values were converted to ranks within each bootstrap sample. Results were verified using a second technique to account for within subject correlation. A summary statistic was calculated separately for each subject and inferences were then based on the across subject variation. The two methods produced similar results, those from the bootstrap technique are shown in this paper. In all statistical tests, sensor age, subject age, BMI percentile, and blood glucose level were treated as continuous variables.

For evaluating precision between two simultaneous GW2B measured glucose values, sensor values were matched within 5 minutes of each other. The absolute difference, RAD and Pearson correlations were calculated on these pairs.

## Results

Between May 31 and November 21, 2002, 97 subjects were admitted to the clinical centers' CRCs for the study. One subject withdrew before GW2B use was initiated. In two subjects, both African Americans, GW2B initiation was unsuccessful due to a high voltage error messages, and in five subjects, GW2B use was initiated but the subject withdrew shortly after admission (in no cases was the subject's withdrawal related to sensor use). The age of the 89

subjects remaining for analysis ranged from 3.5 to 17.7 (mean 9.9) years; 49% were female and 87% Caucasian (Table 1).

## Sensor Accuracy

There were 3,672 GW2B-reference paired glucose values: 2,653 for the hour/half-hour blood draws, 482 for the insulin-induced hypoglycemia test, 417 for the meal-induced hyperglycemia test, and 120 at other times. The number of paired glucose values averaged 41 ± 15 per subject (median= 43, interquartile range= 32 to 51, range= 8 to 75).

The median difference between glucose sensor and reference glucose levels was 3 mg/dL and the mean difference was 2.2 mg/dL (not significantly different than 0 mg/dL) (Table 2), indicating that the sensor did not systematically under or over estimate glucose values. On the other hand, the median RAD was 16% for the 3,672-paired GW2B-reference glucose values (Table 2). The Pearson correlation between the paired GW2B and reference glucose values was 0.86 and the ISO criteria were met for 60% of sensor values. Sixty-seven percent of sensor values were within zone A of the modified error grid and 97% were within zones A + B.

GW2B accuracy showed no meaningful variation according to time of day, subject age, gender, or BMI (Table 3). Results did not vary according to whether the sensor pad was placed on the upper or lower arm or the inner or outer aspect; there were too few sensor pads placed on the leg to statistically compare arm versus leg accuracy. Accuracy degraded slightly as the sensor pad aged (Table 3). Accuracy (based on the RAD and percentage of values meeting ISO criteria) was better at higher serum glucose levels than low glucose levels ($P < 0.001$ for both RAD and ISO criteria, Table 3). When the analyses were limited to the sensor pads with only a single calibration value, the median RAD was 17%, and 57% of the sensor values met ISO criteria.

Accuracy was computed separately for each sensor pad. Among the 171 sensor pads with at least 10 paired sensor-reference values, 26% had a median RAD <10% whereas 13% had a median RAD ≥30% (Table 4). For 27% of the sensor pads, ISO criteria were met for at least 80% of the sensor glucose values whereas for 30% of the sensor pads, ISO criteria were met for less than 50% of the sensor glucose values.

## Precision

During the time periods when the subjects were wearing two GW2Bs, there were 2,815 pairs of sensor values. The Pearson correlation of the paired sensor values was 0.85, but only 64% of values were within 20% of each other. Accuracy was higher for duration-concordant than duration-discordant pairs (as defined in Table 5; P= 0.003 for RAD and P= 0.005 for percentage of paired values within 20% of each other).

## Sensor Function

Sensor calibration was successful on the first attempt for 269 (94%) of the 285 sensors (excluding the times when calibration could not be completed because the blood glucose was out of range: >279 or <41mg/dL) and successful on a subsequent attempt for 5 of the other 16 sensors. There were 11 instances in which the sensor could not be calibrated.

Among the 113 calibrated sensors that were not removed early for logistical reasons (such as at the time of study completion), the sensor functioned for its full life span (≥14.5 hours from initiation) in 92 (81%), 10.0 to <14.5 hours in 3 (3%), 6.0 to <10.0 hours in 7 (6%), and <6.0 hours in 11 (10%).

Among the 14,224 possible sensor glucose measurements between the time of calibration and the shut off, removal of the sensor or end of study, 2,369 (17%) were skipped. Skipped readings occurred more frequently early in sensor life than later in sensor life (sensor life 0 to <6.0 hours= 20% skips of 5,308 possible values, 6.0 to <10.0 hours= 17% of 4,921, and ≥10.0 hours= 12% of 3,995; P< 0.001).

### Adverse Effects

There were no cases of a serious skin reaction from the GW2B. At the time of hospital discharge, the maximum score for any subject was 5 (3 subjects) on the scale of 0 to 8, with a score of 6 representing a reportable adverse event. Four percent of subjects had a maximum score (maximum at any skin site where a GW2B was worn) of 0, 71% a maximum score ≤2, 90% a maximum score ≤3, and 97% a maximum score ≤4.

## Discussion

The data presented here represent the most comprehensive assessment of the accuracy of the GWB to date. Since the appropriate set of accuracy measures to evaluate near continuous glucose monitoring remains to be developed, the approach that was taken in this report, as well as in previous GWB studies, is similar to that utilized to assess the accuracy of blood glucose meters. However, it should be recognized that these methods might not adequately capture the time dimension of glucose sensor data with respect to glucose trend (slope) information or glucose pattern detection across the day. We have focused the analyses on reporting the median relative absolute difference, which we prefer to the mean because it is less affected by outliers, and the percentage of values meeting ISO criteria, which we believe to be more clinically relevant than either the percentage of values in error grid zones A+B or the correlation coefficient. In our view, the latter two measures can give a false sense of the level of accuracy. Using traditional accuracy metrics, the GW2B performed as well in the children and adolescents in this study as has been reported for older diabetic patients. When all of the data were analyzed together, the median relative absolute error of 16% and the correlation coefficient of 0.86 are quite similar to those reported in studies of adults (mean RAD 15.6% to 21.3%[9–11]) and in one study of children (mean RAD 21% to 22%).[12] Overall, the GW2Bs functioned well. Almost all of the sensor pads could be calibrated, most on the first attempt, and most of the sensor pads functioned for their full life span. Our skipped reading rate of 17% is similar to what has been reported in the literature. In controlled settings, skipped reading rates have been reported to be 8% to 17%[7, 9, 10, 12] and in the home setting 24% to 32%.[13] Anecdotally, study personnel who have used both versions of the GWB found the second generation GW2B, with its 2-hour (versus 3-hour for the first generation GWB) calibration time point and its ability to be recalibrated following skipped readings, to be advantageous compared with the first generation GWB. The sensor pads were well tolerated by the patients and there were no serious skin reactions. Our results should be interpreted in the context of the study design in which data were collected in a controlled, inpatient environment. Since sweating can cause skipped readings, a higher skipped rate might be expected when the device is used in an outpatient rather than in our inpatient setting in which the children had limited activity.

The relatively large sample size of subjects and paired glucose levels allowed us to examine factors that might favorably or unfavorably influence the accuracy of the device in children. Accuracy decreased slightly as the sensor aged over its 15-hour lifespan, but it did not vary by the subject age, gender, or BMI or by placement site on the arm. Accuracy was similar during daytime and nighttime hours.

We purposely attempted to vary the glucose across the wide range commonly experienced among children and adolescents with T1DM. As the first continuous monitoring sensor to

report estimated glucose concentrations in near real time, an important potential use of the GW2B will be as a sentinel for hypoglycemia and hyperglycemia detection. As might be expected, the accuracy did vary by glucose level. The GW2B performed best when glucose levels were elevated, with median relative absolute differences when compared with the reference glucose values ranging between 13–14% when glucose levels were >120 mg/dL. Thus, sensor values in the hyperglycemic range may be of considerable value in adjusting bolus and basal insulin doses in youngsters with elevated HbA1c levels. On the other hand, the median RAD rose to 18% for reference glucose levels between 71 and 120mg/dL and to 38% for reference glucose levels ≤70 mg/dL.

The accuracy of this early generation of direct reporting glucose sensors is reminiscent of the early generations of glucose meters, which were less accurate than the currently available glucose meters. Using the newly proposed ISO criteria (±15 mg/dL for glucose levels ≤75 mg/dL and ±20% for glucose levels >75 mg/dL) for accuracy of home glucose meters, the 1,741 glucose values of the Ultra meter used in our study (from venous samples) met these criteria 96% of the time compared with only 60% for the GW2B sensor glucose values. In the current study, 67% of GW2B levels were in modified error grid zone A whereas 98% of Ultra meter measurements in this study fell into zone A.

In summary, our results are similar to those reported in studies conducted by Cygnus, Inc. We found the GW2B to be more accurate during periods of hyperglycemia than hypoglycemia. The accuracy of this generation of the sensor does not approach the accuracy of current home glucose meters. However, the majority of sensor glucose values are within 20% of the serum glucose. This level of accuracy may be sufficient for detecting trends and modifying diabetes management. One study of 40 children with T1DM demonstrated that use of the GWB lowered HbA1c compared with usual care.[13] We are currently conducting a larger longitudinal outpatient study to assess the utility of the GW2B as a management tool to improve glycemic control and decrease the incidence of severe hypoglycemia in children with diabetes.

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## References

1. The Diabetes Research in Children Network (DirecNet) Study Group. The accuracy of the CGMS in children with type 1 diabetes: results of the Diabetes Research in Children Network (DirecNet) accuracy study. Diabetes Technol Ther. 2003In Press
2. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. BMI-for-age charts, 2 to 20 years, LMS parameters and selected smoothed BMI percentiles, by sex and age. 2000 [Accessed March 2003]. Available from http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm
3. Draize, JH. The Appraisal of Chemicals in Food, Drugs, and Cosmetics, Dermal Toxicity. Association of food and drug officials of the United States; Topeka, Kansas: 1965. p. 45-59.
4. Neese, J.; Duncan, P.; Bayse, D.; Robinson, M.; Cooper, T.; Stewart, C. Development and evaluation of a hexokinase/glucose-6-phosphate dehydrogenase procedure for use as a national reference method. HEW Publication No. (CDC). Atlanta: Centers for Disease Control; 1976. p. 77-8330.
5. Passey RB, Gillum RL, Fuller JB, Urry FM, Giles ML. Evaluation and comparison of 10 glucose methods and the reference method recommended in the proposed product class standard (1974). Clin Chem 1977;23(1):131–9. [PubMed: 832363]

6. Parkes JL, Slatin SL, Pardo S, Ginsberg BH. A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. Diabetes Care 2000;23(8):1143–8. [PubMed: 10937512]

7. Potts RO, Tamada JA, Tierney MJ. Glucose monitoring by reverse iontophoresis. Diabetes Metab Res 2002;18(Suppl 1):S49–53.

8. International Organisation for Standardisation. ISO/TC 212/WG3.Draft International Standard ISO/DIS 15197. Geneva, Switzerland: 2001. Requirements for in vitro blood glucose monitoring systems for self-testing in managing diabetes mellitus.

9. Tamada JA, Garg SK, Jovanovic L, Pitzer KR, Fermi SJ, Potts RO. the Cygnus Research Team. Noninvasive glucose monitoring: comprehensive clinical results. JAMA 1999;282(19):1839–44. [PubMed: 10573275]

10. Garg SK, Potts RO, Ackerman NR, Fermi SJ, Tamada JA, Chase HP. Correlation of fingerstick blood glucose measurements with GlucoWatch Biographer glucose results in young subjects with type 1 diabetes. Diabetes Care 1999;22(10):1708–14. [PubMed: 10526740]

11. Tierney MJ, Tamada JA, Potts RO, Eastman RC, Pitzer KR, Ackerman NR, Fermi SJ. The GlucoWatch Biographer: a frequent, automatic and noninvasive glucose monitor. Ann Med 2000;32:632–41. [PubMed: 11209971]

12. Eastman RC, Chase HP, Buckingham B, Hathout EH, Fuller-Byk L, Leptien A, Van Wyhe M, Davis TL, Fermi SJ, Pechler H, Sahyun G, Lopatin M, Wang BY, Wei C, Bartkowiak M, Ginsberg BH, Tamada JA, Pitzer KR. Use of the GlucoWatch biographer in children and adolescents with diabetes. Pediatric Diabetes 2002;3:127–134. [PubMed: 15016152]

13. Chase HP, Roberts MD, Wightman C, Klingensmith GJ, Garg S, Van Wyhe M, Desai S, Harper W, Lopatin M, Bartkowiak M, Tamada JA, Eastman RC. Use of the GlucoWatch Biographer in children with type 1 diabetes. Pediatrics 2003;111(4Pt 1):790–4. [PubMed: 12671113]

# Appendix

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**Table 1**

Demographic and Clinical Characteristics of Study Subjects

| | **N= 89** |
|---|---|
| **Gender** Female *N (%)* | 44 (49) |
| **Age** *mean ± SD (years)* | 9.9 ± 4.1 |
| **Race/Ethnicity** *N (%)* | |
| White | 77 (87) |
| Hispanic or Latino | 7 (8) |
| African-American | 2 (2) |
| Other | 3 (3) |
| **Duration of Diabetes by Age Group** *mean ± SD (years)* | |
| All ages | 4.6 ± 3.2 |
| <7 (N= 30) | 3.1 ± 1.0 |
| 7–<12 (N= 28) | 3.7 ± 2.4 |
| 12–<18 (N= 31) | 6.9 ± 3.8 |
| **Insulin Route** *N (%)* | |
| Pump | 39 (44) |
| Injections | 50 (56) |
| **HbA1c** *mean ± SD* | 7.8% ± 1.2% |
| **BMI percentile** *mean ± SD* | 67% ± 23% |

## Table 2

**GW2B Accuracy Summary Statistics**

(N=3,672 paired GW2B-reference glucose values)

| | Mean (95% confidence interval) | Median ($25^{th}$, $75^{th}$ percentiles) |
|---|---|---|
| **Difference** *mg/dL*[*] | 2.2 (−2.0, 6.1) | 3 (−19, 26) |
| **Absolute Difference** *mg/dL*[†] | 30.9 (28.7, 33.2) | 23 (11, 42) |
| **Relative Difference**[‡] | 6% (4%, 9%) | 2% (−12%, 20%) |
| **Relative Absolute Difference**[§] | 22% (20%, 23%) | 16% (7%, 29%) |

[*] Difference is the sensor glucose value minus the reference value.

[†] Absolute Difference is the absolute value of the difference.

[‡] Relative Difference is the difference divided by the reference value (expressed as percentage).

[§] Relative Absolute Difference is the absolute difference divided by the reference value (expressed as percentage).

## Table 3

GW2B Accuracy Summary Statistics by Various Factors

| | # Paired Data Points | Relative Absolute Difference (*median*) | ISO criteria met* (*percentage*) | P-values† |
|---|---|---|---|---|
| **Overall** | 3,672 | 16% | 60% | |
| **Subject Age** *(years)* | | | | 0.97/0.91 |
| 1 – <7 | 896 | 17% | 59% | |
| 7 – <12 | 1,178 | 15% | 61% | |
| 12 – <18 | 1,598 | 16% | 60% | |
| **Gender** | | | | 0.99/0.70 |
| Female | 1,815 | 16% | 60% | |
| Male | 1,857 | 16% | 61% | |
| **Body Mass Index** | | | | 0.21/0.27 |
| ≤50$^{th}$ percentile | 853 | 15% | 64% | |
| >50$^{th}$ percentile | 2,819 | 16% | 59% | |
| **Time of Day**‡ | | | | 0.56/0.49 |
| Daytime (6:30AM – 10:30PM) | 1,123 | 15% | 63% | |
| Nighttime (11:00PM – 6:00AM) | 1,530 | 16% | 61% | |
| **Sensor Age** (hours) | | | | 0.002/0.006 |
| 0 – <6 | 1,316 | 15% | 63% | |
| 6 – <10 | 1,142 | 15% | 64% | |
| ≥ 10 | 1,214 | 19% | 54% | |
| **GW2B Location**‖ | | | | 0.26/0.22§ |
| Lower Arm | 2,226 | 16% | 59% | |
| Inner | 1,417 | 15% | 61% | |
| Outer | 809 | 18% | 56% | |
| Upper Arm | 1,284 | 15% | 63% | |
| Inner | 268 | 17% | 58% | |
| Outer | 1,016 | 15% | 65% | |
| **Serum Glucose Level** *(mg/dL)* | | | | <0.001/< 0.001 |
| ≤70 | 334 | 38% | 32% | |
| 71–120 | 926 | 18% | 55% | |
| 121–180 | 963 | 14% | 66% | |
| 181–240 | 776 | 14% | 66% | |
| >240 | 673 | 13% | 67% | |
| **Hypoglycemia Test** | 482 | 20% | 52% | 0.007/0.02 |
| **Hyperglycemia Test** | 417 | 15% | 66% | |

*ISO criteria: for reference glucose value ≤75 mg/dL, GW2B value within ±15 mg/dL and for reference glucose value >75 mg/dL. GW2B value within ±20%.

†The first P-value is for RAD and the second P-value is for ISO criteria met.

‡Includes only hourly and half hour reference glucose values.

§Comparing lower arm vs. upper arm.

‖162 pairs from sensor pads placed on leg not included.

**Table 4**

Variation of Accuracy Among GW2B Sensor Pads (N= 171)*

| | % of Sensors |
|---|---|
| Sensor Pads with Median RAD <10% | 26% |
| Sensor Pads with Median RAD <20% | 68% |
| Sensor Pads with Median RAD <30% | 87% |
| Sensor Pads with Median RAD <40% | 97% |
| **Values Meeting ISO Criteria**† | |
| Sensor Pads with ≥90% of Values Meeting ISO Criteria | 8% |
| Sensor Pads with ≥80% of Values Meeting ISO Criteria | 27% |
| Sensor Pads with ≥70% of Values Meeting ISO Criteria | 40% |
| Sensor Pads with ≥60% of Values Meeting ISO Criteria | 57% |
| Sensor Pads with ≥50% of Values Meeting ISO Criteria | 70% |

* Includes only sensors with 10 or more paired reference glucose values.

† ISO criteria: for reference s glucose value ≤75 mg/dL, GW2B value within ±15 mg/dL and for reference glucose value >75 mg/dL, GW2B value within ±20%.

**Table 5**

Precision for Comparison of Two GW2Bs in Simultaneous Use

| | All Pairs | Duration-Concordant Pairs* | Duration-Discordant Pairs* |
|---|---|---|---|
| **# of paired data points** | 2,815 | 873 | 1,942 |
| **Absolute difference** *median mg/dL*† *(25th, 75th percentiles)* | 21 (10, 38) | 18 (8, 34) | 22 (10, 40) |
| **Relative absolute difference** ‡ *median (25th, 75th percentiles)* | 15% (7%, 26%) | 11% (5%, 21%) | 16% (8%, 29%) |
| **Values within 10%** *percentage* | 36% | 46% | 32% |
| **Values within 15%** *percentage* | 51% | 62% | 47% |
| **Values within 20%** *percentage* | 64% | 74% | 59% |
| **Pearson Correlation** | 0.85 | 0.89 | 0.83 |

* Concordant Pair means that the glucose value from each GW2B was from the same sensor period and Discordant Pair means that they were from different periods. Sensor time periods were defined as 0–<6.0 hrs, 6.0–<10.0 hrs, ≥10.0 hrs.

† Absolute Difference is the absolute value of the difference.

‡ Relative Absolute Difference is the absolute value of the relative difference (expressed as percentage).