Protocol X9001263

A Low-Interventional Study to Record Gait and Physical Activity Using ActiGraph Devices in Children Ages 3-17.

Statistical Analysis Plan (SAP)

Version: **3**

Date: 01 Sep 2023

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1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 11 August 2021	Original	N/A	N/A
2 03 May 2022	Original	Keeping consistency with study data and programming needs	1. Removed the "years of education" in 3.4 since it is not relevant 2. Removed "The variables will be averaged over 20 mins of total activity." in Section 3.1.1 in-lab activities data, as this data will be averaged per activity block (~7mins). 3. Removed "step length" in Section 3.1.1.1/2 and 3.2 to include only common endpoints across devices. 4. Remove "colored by sex" in 6.1 and 6.3.2 since gender is not relevant. 5. In table 5, refine the list of the physical activity metrics to better match what is used in DTS 6. Added "First and last day will be removed for this analysis as we do not expect whole 24 hours of data." in 6.2.3 which is reasonable due to the nature of data collection. 7. Changed "90% CI" to "95% CI" for mixed effects models listed in 6.1, 6.2.6, and 6.3.2 to make it consistent with the general method. 8. Added the sentence that describes how to sum up in the individual wear comfort questionnaire in 6.2.4 as a clarification.

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3 01 Sep 2023	Amendment 1 10 Apr 2023	Changes due to additional study cohort for addition of new device (Panaromic Bracelet, Cohort B)	1. Incorporated study design, additional devices, and other changes according to Protocol Amendment 1 for Cohort B 2. Added objectives and endpoints for Cohort B 3. Added Statistical Analysis Methods for Cohort B

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study X9001263. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

Text taken directly from the protocol is ***italized***.

Assessing the appropriate levels of physical activity is a challenge in healthcare currently. Physical inactivity is linked to 10% of premature mortality and is the fourth leading cause of death globally.[1] The benefit of physical activity in children is well defined: obesity prevention,[2,3] reduction of cardiovascular risk factors,[4,5] normal growth and development,[6,7] depression prevention,[8] reduction in risk of chronic diseases, health-related quality of life.[9] The American guideline recommends 60 minutes per day of moderate-to-vigorous physical activity.[10] However, there is a lack of standardized measures of gait and physical activity, and more accurate measures are needed.

There is a significant growth and interest in wearable accelerometry devices that can measure various gait and activity metrics. The ActiGraph device has been investigated in several studies involving children age from 2 to 18.[11-17] Despite this growing interest, only a few studies have focused their objective on assessing the feasibility of implementing these types of devices.[18,19] Also, little is known about how children and parents accept the devices and perceive their usability and comfort.

The rationale for this study is to compare gait quality metrics collected using the ActiGraph devices, APDM devices and GAITRite® walkway, during in-lab sessions (in the PfIRe Lab). APDM and GAITRite® walkway are used as reference comparators. GAITRite® is a pressure-sensitive walkway, which records gait metrics. APDM is a set of 6 devices that collect gait metrics. Both devices are used during in-lab assessments, but the deployment of these devices at home is impractical and not feasible. Hence the needed validation study of the ActiGraph device to measure for gait metrics continuously in a home environment.

In addition to the ActiGraph device studied in Cohort A, Cohort B of the study aims to evaluate the feasabilty of the Panoramic Bracelet and associated algorithms such as SleepPy and GaitPy compared to the GENEActiv device and to evaluate the comfort and wearability of the

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Panoramic Bracelet. The results of this study will enable the use of novel devices in future clinical trials measuring scratch and sleep.

This study will generate compliance data and recruitment data to derisk future clinical protocols, and potentially enable the use of wearable devices in pediatric research studies. Device data from this study can be used for sample size estimates in future digital studies involving pediatric populations.

2.1. Study Objectives

2.1.1. COHORT A: ActiGraph Device

2.1.1.1. Primary Objective

To compare gait quality metrics collected using ActiGraph devices, APDM devices and GAITRite® walkway, during in-lab sessions.

2.1.1.2. Secondary Objectives

1. *To assess the feasibility of recruiting pediatric participants to conduct a wearable device study.*
2. *To assess the ability of pediatric participants to perform a battery of lab-based tasks.*
3. *To assess the compliance in wearing the ActiGraph devices at home.*
4. *To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph and APDM devices during in-lab sessions.*
5. *To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph devices during the at-home monitoring period.*
6. *To evaluate the effect of floor surface (carpet vs. tile) on gait metrics collected using ActiGraph and APDM devices.*

2.1.1.3. Exploratory Objectives

1. *To investigate the feasibility of using a daily activity diary to provide context in pediatric physical activity data collected by ActiGraph devices at home in pediatric participants.*
2. *To compare gait speed collected using the SIMI® system and GAITRite® walkway, during in-lab sessions.*

2.1.2. COHORT B: Panoramic Bracelet Device

2.1.2.1. Primary Objective

1. *Evaluate the Panoramic Bracelet device and associated algorithms in the quantification of physical activity (eg sleep), scratch, and wear time, as compared to another accelerometry device (GENEActiv) during the at-home period.*

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2. *To evaluate the participant's or caregiver's perception of wearability and comfort of Panoramic Bracelet device during the at home monitoring period.*

2.1.2.2. Secondary Objectives

1. *To assess the compliance in wearing the Panoramic Bracelet device at home.*

2. *To compare gait quality metrics collected using Panoramic Bracelet devices, APDM devices and GAITRite® walkway, during in-lab sessions.*

2.1.2.3. Exploratory Objectives

1. *To evaluate the participant's or caregiver's perception of wearability and comfort of Panoramic Bracelet device in-lab sessions.*

2. *To evaluate the effect of floor surface (carpet vs tile) on gait metrics collected using Panoramic Bracelet and APDM devices.*

2.2. Study Design

This is a non-randomized, single site, low-interventional study to compare gait quality metrics collected using the ActiGraph devices, APDM devices and GAITRite® walkway, during in-lab sessions (in the PfIRe Lab). There will be approximately 39 participants in Cohort A and 39 participants in Cohort B divided equally into 3 independent age groups based on the schematic detailed below:

- *Group 1: 3 years to 5 years old inclusive;*
- *Group 2: 6 years to 11 years old inclusive;*
- *Group 3: 12 years to 17 years old inclusive.*

Participant's assignment to a group will be determined by the age at the time the informed consent is signed. Participants will be recruited into age groups in parallel. Recruitment will stop in a group when there are at least 13 completers in that group. Participants who drop out for reasons other than safety before completion of the study may be replaced.

The study is composed of (see Figure 1):

1. *A visit at the PfIRe Lab (Visit 1, Day 1), during which participant eligibility will be confirmed, consent and assent will be obtained. Participants will perform in-lab gait and activities monitoring procedures. During all these activities, participants will wear or interact with the following devices:*

    a. *Wearable devices (ActiGraph for Cohort A), (Panoramic Bracelet device and GENEActiv for Cohort B);*

    b. *GAITRite® Electronic Walkway;*

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c. *Ambulatory Parkinson's Disease Monitoring System (APDM);*

d. *Camera based SIMI® system.*

GAITRite® walkway, APDM will be used as reference comparators. For Cohort B of the protocol the aim is to use GENEActiv as a comparator device to Panoramic Bracelet during the at-home collection period. The in-lab gait and activity monitoring will be video recorded from multiple angles with multiple cameras (camera – based SIMI® system), this will be used to provide contextual information of each portion of the tasks and procedures that may be used by the reviewer when analyzing and interpreting the sensor data. As a tertiary/exploratory objective, gait speed recorded by the SIMI® system against the gait speed collected by GAITRite® walkway will be validated.

The devices and activities in the study are listed in

Table 3 and

Table 3.

Table 2. List of Devices Used in the Study

Device	Information	Algorithms
GAITRite gait mat, model *classic*, 20ft	https://www.gaitrite.com/gait-analysis-walkways	GAITRite/PKMAS
APDM System, Version 2	https://www.apdm.com/wearable-sensors/	APDM
ActiGraph CentrePoint Insight Watch	https://www.actigraphcorp.com/cpiw/	ActiGraph, SKDH (gait, sit-2-stand, activity, sleep)
GENEActiv	https://activinsights.com/technology/geneactiv/	GENEActiv, SleepPy, ScratchPy, SKDH (wear, sleep, activity)
Panoramic Bracelet device	https://www.panoramicdigitalhealth.com/	SleepPy, ScratchPy, SKDH (wear, sleep, activity, gait)

Table 3. Schedule of Activities and Devices Used in Each Activity

Activity	Devices
Walk at natural speed	GAITRite, APDM (6 sensor-set), Actigraph Lumbar (Cohort A), Panoramic Bracelet (Cohort B)

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Walk at slow and fast speed (self-paced)	GAITRite, APDM (6 sensor-set), Actigraph Lumbar (Cohort A), Panoramic Bracelet (Cohort B)
Walk on tile and carpet at natural speed	APDM (6 sensor-set), Actigraph Lumbar, Actigraph Wrist (Cohort A), Panoramic Bracelet (Cohort B)
In-lab Simulated Activities	APDM (6 sensor-set), Actigraph Lumbar, Actigraph Wrist (Cohort A), Panoramic Bracelet (Cohort B)
Free 10 minute walk (only Cohort B)	APDM (6 sensor-set), Panoramic Bracelet

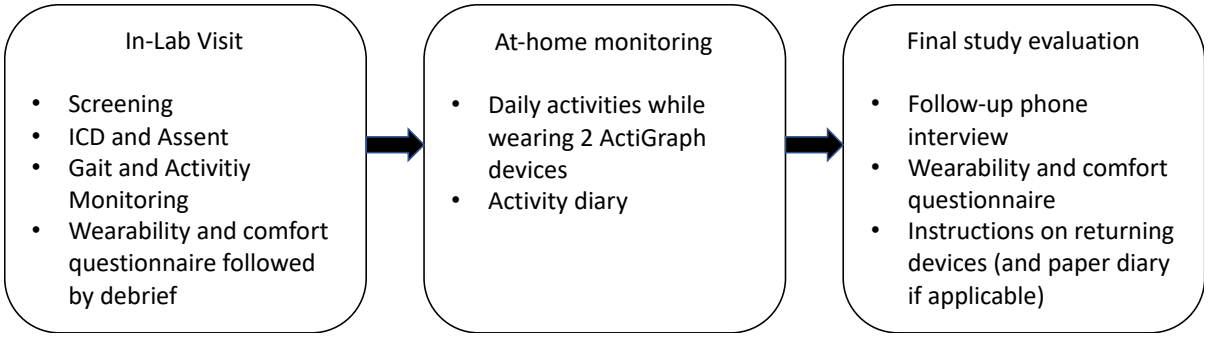
2. *At-home monitoring for approximately 2 weeks (from Day 1 to Day 15 + 3 days) during which participants will wear the devices under the study. Complete a daily activity diary Day 2 to Day 15 (Only Cohort A). Complete activity and sleep diary for Cohort B on Day 2 to day 15.*

3. *Cohort B Only: At-home monitoring day 7+2 Wearability/comfort questionnaire for Panoramic Bracelet device and instruct participant to start wearing the GENEActiv device from Day 7 to end of study. Daily activity and sleep diary.*

4. *For Cohort A Only: A telephone follow-up interview at the end of the 2 weeks at-home monitoring period (Day 15 + 3 days) with administration of the Wearability/comfort questionnaire. For Cohort B follow up call to remind participants to take off devices and mail back. In addition to an end of study phone call for Cohort B.*

Figure 1. Study Outline

Cohort A



Cohort B

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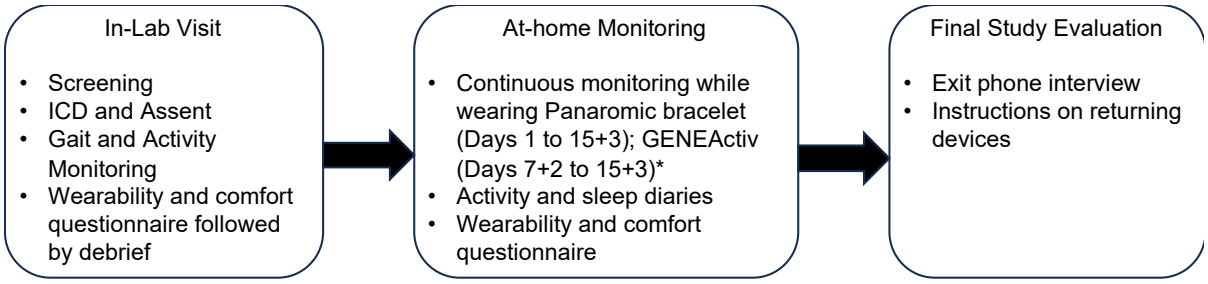

** The position of the GENEActiv device and the Panoramic Bracelet device closeness to the wrist* (i.e., proximity of the device) *will be balanced per age group. Approximately half the participants in each age group will wear the Panoramic Bracelet device proximal to the wrist and the GENEactiv device more distal to the wrist and vice versa*

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

Cohort A: Actigraph Device

This section contains a list of digital endpoints derived during in-lab activities related to the study primary objective in Cohort A: i.e., *to compare gait quality metrics collected using ActiGraph devices, APDM devices and GAITRite® walkway, during in-lab sessions.*

3.1.1. In-Lab Activities

Each variable will be summarized as mean (or median depending on the distribution) over the activity duration. The in-lab simulated activities will last approximately 20 mins and be performed in two sets as detailed in the protocol (7 mins of activity, 5 mins of break, 7 mins of activity).

3.1.1.1. Walk at Natural, Slow and Fast Speed Tasks:

<u>GAITRite Walkway, APDM, Actigraph Lumbar:</u>

- Double support (sec)
- Single limb support (sec)
- Stance time (sec)
- Swing time (sec)
- Stride length (meters)
- Step duration (sec)

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- Cadence (steps/min)
- Gait speed (meters/sec)
- Steps (steps)
- Stride duration (sec)

The gait parameters for GAITRite and APDM will be derived from their manufacturer's algorithms (GAITRite[20] and/or PKMAS[21], APDM: Mobility Lab[22]). The gait parameters from the Actigraph sensor on the lumbar location will be derived by in-house built gaitPy algorithm[23].

3.1.1.2. In-lab Simulated Activities

APDM, Actigraph Lumbar:

- Double support (sec)
- Single limb support (sec)
- Stance time (sec)
- Swing time (sec)
- Stride length (meters)
- Step duration (sec)
- Cadence (steps/min)
- Gait speed (meters/sec)
- Steps (steps)
- Stride duration (sec)

The gait parameters for APDM will be derived from the manufacturer's algorithm[22]. The gait parameters from the Actigraph sensor on the lumbar location will be derived by in-house built gaitPy algorithm[23].

Actigraph Wrist:

- Total number of steps (#)

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The number of steps will be derived from the manufacturer's default algorithm[24]. We will extract the total number of steps over the activity periods in the epoch data file.

Cohort B: Panoramic Bracelet Device

This section contains a list of digital endpoints related to the study primary objective in Cohort B: i.e. *Evaluate the Panoramic Bracelet device and associated algorithms in the quantification of physical activity (eg sleep), scratch, and wear time, as compared to another accelerometry device (GENEActiv) during the at-home period.*

The position of the GENEActiv device and the Panoramic Bracelet device closeness to the wrist (i.e., proximity of the device) will be balanced per age group. Approximately half the participants in each age group will wear the Panoramic Bracelet device proximal to the wrist and the GENEactiv device more distal to the wrist and vice versa

3.1.2. Sleep, Scratch and Wear Time

Each variable will be summarized daily or nightly, as appropriate.

3.1.2.1. Sleep Parameters

- Total sleep opportunity (min)
- Total sleep time (min)
- Percent time asleep (%)
- Number of wake bouts (no.)
- Sleep onset latency (min)
- Wake after sleep onset (min)

The sleep-related parameters for GeneActive and Panoramic Bracelet will be derived by the SleepPy[25] algorithm.

3.1.2.2. Scratch Parameters

- Total scratch duration (min.)
- Total scratch episodes (no.)

The scratch-related parameters for GENEActiv and Panoramic Bracelet will be derived by the ScratchPy[26] algorithm.

3.1.2.3. Wear Time Parameters

- Number of available hours (h) or minutes (min)
- Number of hours (h) or minutes (min) of wear
- Number of wear hours (h) or minutes (min) while awake

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The wear time parameters for GENEActiv and Panoramic Bracelet will be derived by the in-house built SKDH package[27].

3.1.3. Wearability and Comfort Questionnaire

At-home Panoramic Bracelet device wearability/comfort questionnaire responses from the at-home monitoring period will be summarized.

3.2. Secondary Endpoints

Table 4. Secondary Objectives and Endpoints (Cohort A)

Secondary Objective(s):	Secondary Endpoint(s):
• *To assess the feasibility of recruiting pediatric participants to conduct a wearable device study.*	• Recruitment data listed by age group: (a) Number of participants contacted (b) Number of participants screened (c) Number of participants enrolled over time (d) Time taken (number of days) to enroll approximately 13 participants per group
• *To assess the ability of pediatric participants to perform a battery of lab-based tasks.*	• Total number of participants able to perform each of the 7 tasks • Number of participants per age group able to perform each of the 7 tasks • Percentage of tasks completed (from a total of 7 tasks)
• *To assess the compliance in wearing the ActiGraph devices at home.*	• Number of hours per day wearing the lumbar and wrist devices • Number of days with more than 10 hours of wear time for lumbar device • Number of days with more than 18 hours of wear time for wrist device
• *To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph and APDM devices during in-lab sessions.*	• Wearability/Comfort Questionnaire for APDM device and for Actigraph lumbar and wrist device separately (All questions are on a 5-point Likert scale) • Cognitive Debrief of Wearability/Comfort Questionnaire

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• *To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph devices during the at-home monitoring period.*	• Wearability/Comfort Questionnaire for Actigraph lumbar and wrist device separately (All questions are on a 5-point Likert scale)
• *To evaluate the effect of floor surface (carpet vs. tile) on gait metrics collected using ActiGraph and APDM devices.*	Actigraph Lumbar and APDM: • Double support (sec) • Single limb support (sec) • Stance time (sec) • Swing time (sec) • Stride length (meters) • Step duration (sec) • Cadence (steps/min) • Gait speed (meters/sec) • Steps (steps) • Stride duration (sec) The gait parameters for APDM will be derived from the manufacturer's algorithm[22]. The gait parameters from the Actigraph sensor on the lumbar location will be derived by in-house built gaitPy algorithm[23].

Table 5 Secondary Objectives and Endpoints (Cohort B)

• *To assess the compliance in wearing the Panoramic Bracelet device at home.*	**Panoramic Bracelet (Days 1-7)** • Number of available hours (h) or minutes (min) • Number of hours (h) or minutes (min) of wear • Number of wear hours (h) or minutes (min) while awake
• *To compare gait quality metrics collected using Panoramic Bracelet devices, APDM devices and GAITRite® walkway, during in-lab sessions.*	• **GAITRite Walkway, APDM & Panaromic Bracelet devices** • Double support (sec) • Single limb support (sec) • Stance time (sec)

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	• Swing time (sec) • Stride length (meters) • Step duration (sec) • Cadence (steps/min) • Gait speed (meters/sec) • Steps (steps) • Stride duration (sec) The gait parameters for GAITRite and APDM will be derived from their manufacturer's algorithms (GAITRite[20] and/or PKMAS[21], APDM: Mobility Lab[22]). The gait parameters from the Paranomic Bracelet devices will be derived by in-house built SKDH gait algorithm[27].

3.3. Exploratory Endpoints

Table 6. Exploratory Objectives and Endpoints (Cohort A)

• *To investigate the feasibility of using a daily activity diary to provide context in pediatric physical activity data collected by ActiGraph devices at home in pediatric participants.*	**ActiGraph Physical Activity Endpoints from Wrist** • Light Activity Time (min) • Moderate Activity Time (min) • Vigorous Activity Time (min) • Sedentary Activity Time (min) • Non Sedentary Physical Activity (min) • Moderate to Vigorous Physical Activity (MVPA, min) • Calories (kcal) • Total Activity Count for Axis X, Y, and Z • Total Vector Magnitude These parameters will be derived from the manufacturer's algorithms. • **Activity Diary** 1. Sickness or events preventing normal physical activity: Yes/No 2. Sport or very active physical activities: Yes/No

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	3. Length of time of sports or very active physical activities: <30 min, 30 min – 1 hr, > 1 hr
• *To compare gait speed collected using the SIMI® system and GAITRite® walkway, during in-lab sessions.*	• Gait speed measured by SIMI® system[28] • Gait speed measured by GAITRite® walkway[20] derived during natural, slow and fast speed walk tasks

Table 7 Exploratory Objectives and Endpoints (Cohort B)

• *To evaluate the participant's or caregiver's perception of wearability and comfort of Panoramic Bracelet device in-lab sessions.*	In-lab Wearability/Comfort Questionnaire for Panoramic Bracelet (wrist and lumbar) from Visit 1 (Day 1).
• *To evaluate the effect of floor surface (carpet vs tile) on gait metrics collected using Panoramic Bracelet and APDM devices.*	Panoramic Bracelet and APDM: • Double support (sec) • Single limb support (sec) • Stance time (sec) • Swing time (sec) • Stride length (meters) • Step duration (sec) • Cadence (steps/min) • Gait speed (meters/sec) • Steps (steps) • Stride duration (sec) The gait parameters for APDM will be derived from the manufacturer's algorithm[22]. The gait parameters from the Panoramic Bracelet devices will be derived by in-house built SKDH gait algorithm[27].

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3.4. Other Endpoints

Participant demographics and other information will be recorded for each subject: age, sex, height, weight, race, ethnicity and handedness (using the Edinburgh Handedness Inventory (EHI)-short form).

3.5. Baseline Variables

Due to the nature of the study design, no baseline variables are defined.

Demographic variables (Section 3.4), floor type (carpet, tile), proximity of the device (Cohort B, Panoramic closer to wrist vs GENEActiv closer to wrist), and devices (GAITRite, APDM, Actigraph, GENEActiv, Panoramic Bracelet) may be adjusted as covariates in the statistical models.

3.6. Safety Endpoints

An adverse event (*AE) is defined as any untoward medical occurrence and can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease, whether or not related to the participant's participation in the study.*

Any AE that occurs from the time the participant consents to the clinical research through and including 12 hours after completion of the qualifying procedure* will *be recorded.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database and classifications will be documented per standard operating procedures.

Population	Description
Full Analysis Set (FAS)	All participants who have a signed and dated informed consent document, have assented to the study and are enrolled in the study. *Qualified male or female participants aged 3 to 17 years old inclusive. Qualified is defined as no significant health problems that would impair the completion of the physical activity tasks, does not carry any diagnosis of developmental delay and/or significant co-morbid medical conditions as determined by a medically qualified individual during medical history review with LAR and participant. Children who are ambulatory.*

5. GENERAL METHODOLOGY AND CONVENTIONS

The primary analysis will be performed after database lock.

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5.1. General Methods

Data will be summarized using descriptive statistics (number of subjects (n), mean, median, standard deviation (SD), minimum and maximum, as appropriate) for continuous (or near continuous) variables, and using frequency and percentages for discrete variables. The temporal data may be summarized over activity task during in-lab activities and over days for at-home monitoring.

Cohort A:

The comparisons between devices (e.g. APDM vs Actigraph) will be investigated with Mixed Model Repeated Measures (MMRM), ANOVA or a non-parametric equivalent (Kruskal-Wallis, Friedman tests). Necessary covariates will be included such as demographic variables such as age and gender, and floor type. Pairwise comparisons will be performed with paired t-tests or their non-parametric equivalent (Wilcoxon Signed-rank test). If visual inspection of the data suggests that a transformation of the endpoints should be performed, this will be applied as appropriate prior to analysis and documented in the final report as required.

P-values will be generated where appropriate and any p-value < 0.05 will be considered statistically significant. If multiple p-values are generated, an experiment wise significance threshold will also be provided for context using methods such as family wise error rate (FWER) and/or false discovery rate (FDR) control. P-values will be rounded to 3 decimal places and therefore presented as 0.xxx; P-values smaller than 0.001 will be reported as '<0.001'.

Agreement between two measurements will be assessed by the intra-class correlation coefficient (ICC, type 2 way random effects, absolute agreement), according to the following benchmarks: ICC ≤ 0.4 indicates 'poor', 0.4 to 0.59 'moderate', 0.6 to 0.74 'good', and 0.75 to 1 'excellent' agreement[29]. In addition, Bland–Altman plots and 95% limits of agreement (average difference ± 1.96 standard deviation of the difference) will be used to visualize and quantify differences between endpoints derived from the reference devices and comparator device (Actigraph).

Cohort B:

The comparisons between devices (e.g. GENEActiv vs Panoramic Bracelet) will be investigated with mixed effect models. Necessary covariates will be included such as demographic variables such as age, gender, proximity of the device and floor type. Pairwise comparisons will also be performed with paired t-tests or their non-parametric equivalent (Wilcoxon Signed-rank test). Mean absolute percent error between the comparator and reference metrics will be computed and Bland-Altman plots and 95% limits of agreement will be used to assess the bias. The endpoints might be log transformed using log(x+1).

To assess the relationship of endpoints between devices, Deming regression will be used. Deming regression takes into account the variations from the multiple measures on both test devices and traditional methods. The slope and intercept from model fitting and their 95% CI

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will be reported. The ratio of variances of the two devices will also be calculated. Weighted Deming and Passing-Bablok regression may also be used if deemed appropriate.

P-values will be generated where appropriate and any p-value < 0.05 will be considered statistically significant. If multiple p-values are generated, an experiment wise significance threshold might be provided for context using methods such as family wise error rate (FWER) and/or false discovery rate (FDR) control. P-values will be rounded to 3 decimal places and therefore presented as 0.xxx; P-values smaller than 0.001 will be reported as '<0.001'.

Agreement between two measurements will be assessed by the intra-class correlation coefficient (ICC, type 2 way random effects, absolute agreement), according to the same benchmarks used in Cohort A. The ICC will be computed and compared between each pair of endpoints, using mean/median/25% & 75% quantiles across daily records.

5.2. Methods to Manage Missing Data

All summaries and analyses will be based on observed data and missing data imputation is not planned.

6. ANALYSES AND SUMMARIES

6.1. Primary Objective (Cohort A): To compare gait quality metrics collected using ActiGraph devices, APDM devices and GAITRite® walkway, during in-lab sessions.

The list of common device data and comparisons are listed in Table 8. We will compare the common endpoints derived from Actigraph worn on the lumbar position (test device) with respect to GAITRite and APDM.

Table 8. Specific Endpoints and Analyses for Primary Objective (Cohort A)

Task	Devices	Measurements/comparisons
In-lab walk at natural speed	**Reference:** GAITRite, APDM (Mobility Lab) **Comparator:** Actigraph Lumbar (gaitPy)	Common gait metrics* (Comparison across devices)
In-lab walk at slow and fast speed (self-paced)	**Reference:** GAITRite, APDM (Mobility Lab), **Comparator:** Actigraph Lumbar (gaitPy)	Common gait metrics* (Comparison across devices)
In-lab Simulated Activities	**Reference:** APDM (free living method) **Comparator:** Actigraph Lumbar (gaitPy)	Common gait metrics* (Comparison across devices)
In-lab Simulated Activities	**Reference:** APDM (free living method) **Comparator:** Actigraph Wrist, Actigraph Lumbar (gaitPy)	Number of Steps (Comparison across devices)

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* Common gait metrics between devices are Double Support Time, Single Limb Support Time, Stance Time, Swing Time, Step Duration, Stride Duration, Stride Length, Gait Speed, and Cadence, as in Section 3.1.1.1 and 3.1.1.2.

Appropriate summaries and plots for each digital endpoint will be produced **per task** (colored by age group, if necessary) as follows:

- Scatter plots of digital metrics from each reference device vs comparator device with corresponding regression line and 95% confidence interval (CI) will be plotted.
- Accuracy of the sensor-derived metrics will be determined by computing the mean difference, mean absolute difference, variation of the difference, the mean percent error, the mean absolute percent error and the effect size between reference device(s) and comparator device metrics.
- Bias will be assessed by Bland-Altman plots and 95% limits of agreement between each reference devices and comparator device. Specifically, the following error measures will be computed: mean difference, lower and upper 95% limit of agreement.
- Intra-class correlation coefficient (ICC) and its lower and upper confidence limits between metrics derived from reference devices and comparator device will be computed.
- For in-lab walk at natural, slow and fast speed tasks, the ICC will be used to compare gait endpoints derived from APDM, GAITRite and Actigraph lumbar sensor.
- The correlation coefficients (Pearson's) between metrics from each reference device and comparator device will be calculated.
- Box and whisker plots of digital metrics from each reference device and comparator device will be plotted.
- Mixed model regression analyses will be used to investigate the effect of device (e.g., GAITRite, APDM, Actigraph), and the interaction between device and task (normal/slow/fast speed walks) on each gait metric. The device, task, and their interaction will be fixed effects, and subject will be entered as random effect. Post-hoc t-tests might be performed between devices. Multiple comparisons, when necessary, will be performed using FDR. Age (or age group) and sex may be used as covariates in the models. The estimates for fixed effect parameters, standard errors, 95% CIs, and p-values, as well as the variance estimates for the random effect will be summarized. Results from all models will be presented in a table. Furthermore, Least Squares Means (LSMeans) together with their 95% CI will be calculated for each of the device-task combination (e.g. LSMean of GAITRite gait speed for normal walk task).

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6.2. Primary Objectives (Cohort B):

6.2.1. To Evaluate the Panoramic Bracelet device and associated algorithms in the quantification of physical activity (eg sleep), scratch, and wear time, as compared to another accelerometry device (GENEActiv) during the at-home period.

The list of common device data and comparisons are listed in Table 9. We will compare endpoints related to wear time, sleep, and scratch between Panoramic Bracelet (comparator) and GENEActiv (reference), during the at home period (~ days 8-15).

Table 9 Specific Endpoints and Analyses for Primary Objective (Cohort B)

	Devices	**Measurements/comparisons**
At-home monitoring (~days 8-15)	**Reference:** GENEActiv **Comparator:** Panaromic Bracelet	Sleep, scratch, and wear time endpoints as listed in Section 3.1.2

Appropriate summaries and plots for each digital endpoint will be produced (colored by age group, if necessary) as follows:

- To model the correlation between endpoints by the Panoramic Bracelet (comparator) and the GENEActiv device (reference), mixed effects model with repeated measures will be used with Panoramic Bracelet endpoints as the response, GENEActiv endpoints, as fixed effects, subject as the random effect. Device proximity (categorical; Panaromic- vs GENEActiv-closer to wrist) and their interaction might be added as fixed effects,. Within the subject (i.e., days) compound symmetry will be considered in the model. If there is no interaction effect, the interaction term will be removed from the model. Subject will be entered as random effect. As a sensitivity analysis, device proximity and the subject nested within the device proximity may be considered as random effects. Age group may be used as covariates in the models. The coefficient estimations for the fixed effects and the corresponding p values and 95% CI will be reported.

- To model the difference between the Panoramic Bracelet endpoints and the GENEActiv device (reference) endpoints, mixed effects with repeated measures model will be used with the difference as the response. Age group and proximity of the device may be used as additional fixed effects in the models. Subject will be entered as random effect. Compound symmetry will be considered to model within subject variability. The estimates for fixed intercept and fixed effect (if available) and the corresponding p values and 95% CI will be reported.

- The Deming regression will be used to assess relationship of endpoints between the comparator and reference devices while taking into account of variations from the multiple measures. The fitted slope, intercept and their corresponding 95% CI will be

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reported. Weighted Deming and Passing-Bablok regression may also be considered if deemed appropriate.

- For each day, accuracy of the sensor-derived metrics will be determined by computing the mean difference, mean absolute difference, variation of the difference, the mean percent error, the mean absolute percent error and the effect size between the Panoramic Bracelet device and GENEActiv (reference) device metrics.

- Box and whisker plots of digital metrics from the Panoramic Bracelet device and GENEActiv device will be plotted for each day.

- Bias, including the mean bias across days and bias from repeated meaures, will be assessed by Bland-Altman plots and 95% limits of agreement between the Panoramic Bracelet device and GENEActiv device. Specifically, the following error measures will be computed: mean difference, lower and upper 95% limit of agreement. For assessing bias from repeated measures, both mean difference and 95% limits will be computed from the mixed effects model described above.

- Intra-class correlation coefficient (ICC) and its lower and upper confidence limits between metrics derived from the Panoramic Bracelet device and GENEActiv device will be computed, for mean/median/25% quantile/75% quantile across daily measures.

- Scatter plots of digital metrics from the Panoramic Bracelet device vs GENEActiv device with corresponding regression line and 95% CI will be plotted. The regression line and the 95% CI will be derived from the previous mixed effects model.

6.2.2. To evaluate the participant's or caregiver's perception of wearability and comfort of Panoramic Bracelet device during the at home monitoring period.

The Wearability/Comfort Questionnaire responses obtained during the at home period (Day 7+2) for the Panoramic Bracelet device will be summarized as frequency and percentages. Bar plots will be provided per question (might be stratified by age group).

Due to the ordinal nature of the responses, a 0 to 4 scale will be assigned to each option (i.e. 0 = strongly disagree, and 4 = strongly agree), except for questions 5 ("The device changes the way I move") and 6 ("The device changes the way I behave") , where the order of the scale should be reversed (i.e. 0 = strongly agree, and 4 = strongly disagree) to be consistent with the ranking of other questions. The total score will be calculated by summing up numeric scales for each individual question, and summarized descriptively.

The Cognitive Debrief of Wearability/Comfort Questionnaire will be summarized as frequency and percentages when appropriate. Participant explanations entered as free text will be provided in a listing.

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6.3. Secondary Objectives (Cohort A)

6.3.1. To assess the feasibility of recruiting pediatric participants to conduct a wearable device study

- The number of participants contacted, screened and enrolled will be summarized overall and by age group. The number of participants enrolled over time (per month) for each group will be calculated and listed. The time (number of days) taken to enroll approximately 13 participants per group will be listed.

6.3.2. To assess the ability of pediatric participants to perform a battery of lab-based tasks

The total number of participants able to perform each of the 7 tasks (i.e., walking at natural, slow and fast speeds, tile and carpet walks, 2 sessions of in-lab simulated activities) will be summarized overall and by age group. The number of tasks performed by each participant (out of a total of 7 tasks) will be derived and expressed as a percentage. Descriptive statistics of this percentage across participants will be computed.

6.3.3. To assess the compliance in wearing the ActiGraph devices at home

Compliance information for at-home deployment will be based on wear time derived from both wrist and lumbar-worn ActiGraph device. First and last day will be removed for this analysis as we do not expect whole 24 hours of data.

For the wrist device, for each participant, the (a) *Wrist wear time*: Number of hours per day wearing the wrist device; (b) *Wrist compliant days*: Number of days with more than 18 hours of wrist wear time will be derived. Wear time will be obtained from the manufacturer's default parameter (Wear).

For the lumbar device, for each participant, the (a) *Lumbar wear time*: Number of hours per day wearing the lumbar device; (b) *Lumbar compliant days*: Number of days with more than 10 hours of lumbar wear time will be derived. Wear time will be obtained from the manufacturer's default parameter (Wear).

Summary statistics will be computed for these four endpoints across all participants and by age group. Box and whiskers plots of *wear time per day* (in hours and percentage of the day) across participants will be provided for both wrist and lumbar sensors.

6.3.4. To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph and APDM devices during in-lab sessions

The Wearability/Comfort Questionnaire responses from the in-lab visit (Day 1) for the APDM device and for the Actigraph lumbar and wrist devices will be summarized as frequency and percentages. Bar plots will be provided per question.

Participant responses for Actigraph wrist and lumbar devices will be compared to assess the participants' preference for device location. Due to the ordinal nature of the responses, a 0 to

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4 scale will be assigned to each option (i.e. 0 = strongly disagree, and 4 = strongly agree), except for questions 5 ("The device changes the way I move") and 6 ("The device changes the way I behave") , where the order of the scale should be reversed (i.e. 0 = strongly agree, and 4 = strongly disagree) to be consistent with the ranking of other questions. The total score will be calculated by summing up numeric scales for each individual question. Wilcoxon signed rank test will be used to test the paired difference of total score between wrist and lumbar. A non-significant result would indicate that there is no evidence of a systematic difference between the wearability and comfort of wrist and lumbar locations, while a significant result would indicate the presence of systematic differences between the two locations. Results will be presented in a table.

The Cognitive Debrief of Wearability/Comfort Questionnaire will be summarized as frequency and percentages when appropriate. Participant explanations entered as free text will be provided in a listing.

6.3.5. To evaluate the participant's or caregiver's perception of wearability and comfort of ActiGraph devices during the at -home monitoring period.

The Wearability/Comfort Questionnaire responses obtained during the Final Study Evaluation (Day 15 + 3 days) for the Actigraph lumbar and wrist devices will be summarized as frequency and percentages. Bar plots will be provided per question.

Participant responses for Actigraph wrist and lumbar devices will be compared and presented as described in Section 6.3.4.

6.3.6. To evaluate the effect of floor surface (carpet vs. tile) on gait metrics collected using ActiGraph and APDM devices.

The effect of floor surface will be evaluated on gait metrics extracted from APDM and Actigraph worn on the lumbar position (Section 3.2., Table 4).

The following analyses and plots will be provided (see Table 10):

- Box and whiskers plots of gait parameters by floor type.
- The effect of floor type on gait parameters will be analyzed using paired tests (paired t-test or Wilcoxon Signed-rank test), and the effect size will be computed per device.
- Mixed model regression analyses will be used to investigate the effect of device (APDM vs Actigraph), and device by floor type (carpet vs tile) interaction. The device, floor type, and their interaction will be fixed effects, and subject will be entered as random effect. Post-hoc t-tests might be performed between devices. Multiple comparisons, when necessary, will be performed using FDR. Age (or age group) and sex may be used as covariates in the model. The estimates for fixed effect parameters, standard errors, 95% CIs, and p-values, as well as the variance estimates for the random effect will be summarized. Results from all models will be presented in a table. Furthermore, Least Squares Means (LSMeans) together with their 95% CI will be calculated for each device-floor-type combination.

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Table 10. Specific Endpoints for Secondary Objective (Cohort A): Evaluation of floor surface effect

Task	Devices	Measurements/comparisons
In-lab walk on tile and carpet on natural speed	**Reference:** APDM **Comparator:** Actigraph-lumbar (gaitPy)	Gait metrics (Comparison within and between devices)

6.4. Secondary Objectives (Cohort B)

6.4.1. To assess the compliance in wearing the Panoramic Bracelet device at home.

Compliance information for at-home deployment (~Days 1-7) will be based on wear time parameters (Section 3.1.2.3) derived from the Panoramic Bracelet device. First and last day may be removed for this analysis as we do not expect whole 24 hours of data.

Summary statistics will be computed for the wear endpoints across all participants and by age group. Box and whiskers plots (in hours and percentage of the day) across participants will be provided.

Two definitions of compliant days will be derived: 1) >10 hours of wear time, and 2) >18 hours of wear time per day. The summary statistics will be presented in a table.

6.4.2. To compare gait quality metrics collected using Panoramic Bracelet devices, APDM devices and GAITRite® walkway, during in-lab sessions.

The common endpoints are derived from the Panoramic Bracelet device with respect to GAITRite and APDM. Same analyses plan will be implemented as listed in Section 6.1 Primary Objective (Cohort A).

Additionally, Deming regression will be used to assess relatioship of endpoints between the comparator and reference devices while taking into account of variations from the multiple measures. The fitted slope, intercept and their corresponding 95% CI will be reported. Weighted Deming and Passing-Bablok regression may also be considered if deemed appropriate.

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6.5. Exploratory Objective(s) (Cohort A)

6.5.1. To investigate the feasibility of using a daily activity diary to provide context in pediatric physical activity data collected by ActiGraph devices at home in pediatric participants.

MMRMs will be used to examine the association between Actigraph's activity metrics from the wrist sensor and the participants' responses from the daily activity diaries during the at-home monitoring period (Section 3.3, Table 6).

For each of the physical activity metrics, two models will be computed, one to investigate the effect of *Sickness or events preventing normal physical activity* and another to investigate the effect of *Sport* on that activity metric. In one model, *Sickness or events preventing normal physical activity* (yes/no) will be considered as categorical fixed effect and subject as the random effect. In the other model, *Sport* (no, yes > 30 mins, yes 30min - 1hr, yes > 1 hour) will be the categorical fixed effect, with subject as the random effect. Covariates such as age and gender may be utilized in both.

Autoregressive AR(1) variance-covariance structure will be used for the MMRM. The estimate of the coefficient for *Sickness or events preventing normal physical activity* / *Sport*, its standard error, 95% CI, and p-value will be derived. The model results will be presented in a table.

6.5.2. To compare gait speed collected using the SIMI® system and GAITRite® walkway, during in-lab sessions.

Agreement between gait speed computed by GAITRite® (reference device) and SIMI® system (comparator device) will be assessed using the same methods described in Section 6.1.

Appropriate summaries and plots will be produced **per task** (colored by age group, if necessary) as follows:

- Scatter plots of gait speed from GAITRite® and SIMI® system with corresponding regression line and 95% CI will be plotted.
- Accuracy of SIMI®-derived gait speed will be determined by computing the mean difference, mean absolute difference, variation of the difference, the mean percent error, the mean absolute percent error and the effect size between the two devices.
- Bias will be assessed by Bland-Altman plots and 95% limits of agreement. Mean difference, lower and upper 95% limit of agreement will be computed.
- Intra-class correlation coefficient (ICC) and its lower and upper confidence limits between the two gait speeds will be computed.
- The correlation coefficients (Pearson's) between the two gait speed metrics will be calculated.
- Box and whisker plots of gait speed for the two devices will be generated.

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- Mixed model regression analyses will be used to investigate the effect of device (e.g., GAITRite, SIMI), and interaction between device and task (normal/slow/fast walk tasks) on gait speed. The device, task, and their interaction will be fixed effects, and subject will be entered as random effect. Post-hoc t-tests might be performed between devices. Multiple comparisons, when necessary, will be performed using FDR. Age (or age group) and sex may be used as covariates in the models. The estimates for fixed effect parameters, standard errors, 95% CIs, and p-values, as well as the variance estimates for the random effect will be summarized. Results from all models will be presented in a table. Furthermore, Least Sqaures Means (LSMeans) together with their 95% CI will be calculated for each device-task combination (e.g. LSmean of GAITRite normal speed walk task).

6.6. Exploratory Objectives (Cohort B)

6.6.1. To evaluate the participant's or caregiver's perception of wearability and comfort of Panoramic Bracelet device in-lab sessions.

The Wearability/Comfort Questionnaire responses from the in-lab visit (Day 1) for the Panoramic Bracelet (wrist and lumbar) devices will be summarized as frequency and percentages. Bar plots will be provided per question.

Participant responses for Panaromic Bracelet (wrist and lumbar) devices will be compared to assess the participants' preference for device location. Due to the ordinal nature of the responses, a 0 to 4 scale will be assigned to each option (i.e. 0 = strongly disagree, and 4 = strongly agree), except for questions 5 ("The device changes the way I move") and 6 ("The device changes the way I behave") , where the order of the scale should be reversed (i.e. 0 = strongly agree, and 4 = strongly disagree) to be consistent with the ranking of other questions. The total score will be calculated by summing up numeric scales for each individual question. Wilcoxon signed rank test will be used to test the paired difference of total score between wrist and lumbar. A non-significant result would indicate that there is no significant evidence of a systematic difference between the wearability and comfort of wrist and lumbar locations, while a significant result would indicate the presence of systematic differences between the two locations. Results will be presented in a table.

The Cognitive Debrief of Wearability/Comfort Questionnaire will be summarized as frequency and percentages when appropriate. Participant explanations entered as free text will be provided in a listing.

6.6.2. To evaluate the effect of floor surface (carpet vs tile) on gait metrics collected using Panoramic Bracelet and APDM devices.

The effect of floor surface will be evaluated on gait metrics extracted from APDM and Panoramic Bracelet devices (Section 3.3, Table 7). Same analyses plan will be implemented as listed in Section 6.3.6.

6.7. Safety Endpoints

AEs will be summarized and presented in a table.

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7. INTERIM ANALYSIS

No interim analysis is planned.

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9. APPENDICES

Appendix 1. List of Abbreviations

Abbreviation	Term
AE	Adverse Event
ANOVA	Analyses of Variance
APDM	Ambulatory Parkinson's Disease Monitoring
AR	Autoregressive
CI	Confidence Interval
EHI	Edinburgh Handedness Inventory
FAS	Full Analysis Set
FDR	False Discovery Rate
FWER	FamilyWise Error Rate
ICC	Intra-Class Correlation Coefficient
ICD	Informed Consent Document
LS	Least Squares
MMRM	Mixed Model Repeated Measures
MVPA	Moderate to Vigorous Physical Activity
PfIRe Lab	Pfizer Innovation Research Laboratory
PKMAS	ProtoKinetics Movement Analysis Software
SAP	Statistical Analysis Plan
SD	Standard Deviation
SKDH	Sci-kit Digital Health

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