

Investigating measurement equivalence of smartphone sensor-based assessments: A remote, digital, bring-your-own-device study

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Abstract

Background: Floodlight Open is a global, open-access, fully remote, digital-only study designed to understand the drivers and barriers in deployment and persistence of use of a smartphone app for measuring functional impairment in a naturalistic setting and broad study population.

Objective: To assess measurement equivalence properties of the Floodlight Open app across operating system (OS) platforms, OS versions and smartphone device models.

Methods: Floodlight Open enrolled adult participants with and without self-declared multiple sclerosis (MS). The study utilized the Floodlight Open app, a “bring-your-own-device” (BYOD) solution that remotely measured MS-related functional ability via smartphone sensor-based active tests. Measurement equivalence was assessed in all evaluable participants by comparing the performance on the six active tests (i.e., tests requiring active input from the user) included in the app across OS platforms (iOS vs Android), OS versions (iOS versions 11–15 and separately Android versions 8–10 [comparing each OS version with the other two OS versions pooled together]), and device models (comparing each device model with all remaining device models pooled together). The tests in scope were: Information Processing Speed (IPS), IPS Digit–Digit (IPS DD, measuring reaction speed), Pinching Test (PT), Static Balance Test (SBT), U-Turn Test (UTT) and Two-Minute Walk Test (2MWT). Group differences were assessed by permutation test for the mean difference after adjusting for age, sex and self-declared MS disease status.

Results: Overall, 1,976 participants using 206 different device models were included in the analysis. Differences in test performance between subgroups were very small or small, with percent differences generally being $\geq 5\%$ on the IPS, IPS DD, UTT, and 2MWT; $<20\%$ on the PT; and $<30\%$ on the SBT). No statistical significant differences were observed between OS platforms other than the PT ($P<.001$). Similarly, differences across iOS or across Android versions were non-significant after correcting for multiple comparison using false discovery rate correction (all adjusted $P>.05$). Comparing the different device models revealed a statistically significant difference only on the PT for 4/17 models (adjusted $P=<.001-.03$).

Conclusions: Consistent with the hypothesis that smartphone sensor-based measurements obtained with different devices are equivalent, this study showed no evidence for a systematic lack of measurement equivalence across OS platforms, OS versions and device models on six active tests included in the Floodlight Open app. These results are compatible with the use of smartphone-based tests in a BYOD setting but more formal tests of equivalence would be needed.

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Original Manuscript

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Abstract

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Results: Overall, 1,976 participants using 206 different device models were included in the analysis. Differences in test performance between subgroups were very small or small, with percent differences generally being $\leq 5\%$ on the IPS, IPS DD, UTT, and 2MWT; $< 20\%$ on the PT; and $< 30\%$ on the SBT). No statistical significant differences were observed between OS platforms other than the PT ($P < .001$). Similarly, differences across iOS or across Android versions were non-significant after correcting for multiple comparison using false discovery rate correction (all adjusted $P > .05$). Comparing the different device models revealed a statistically significant difference only on the PT for 4/17 models (adjusted $P = < .001 - .03$).

Conclusion: Consistent with the hypothesis that smartphone sensor-based measurements obtained with different devices are equivalent, this study showed no evidence for a systematic lack of measurement equivalence across OS platforms, OS versions and device models on six active tests included in the Floodlight Open app. These results are compatible with the use of smartphone-based tests in a BYOD setting but more formal tests of equivalence would be needed.

Keywords:

Floodlight Open; multiple sclerosis; smartphone; sensors; mobile phone; wearable electronic devices; digital health; equivalence; device equivalence; cognition; gait; upper extremity function; hand motor function; balance; digital biomarker; variability

Abbreviations

2MWT: Two-Minute Walk Test

BYOD: Bring-Your-Own Device

IMU: Inertial measurement unit

IPS: Information Process Speed

IPS DD: Information Process Speed Digit–Digit

MS: Multiple sclerosis

OS: Operating System

PT: Pinching Test

PwMS: People with multiple sclerosis

SBT: Static Balance Test

UTT: U-Turn Test

Introduction

Multiple sclerosis (MS) is a chronic, demyelinating autoimmune disease of the central nervous system, which can manifest in functional impairment in cognitive and motor abilities, and the subsequent accumulation of disability over time [1]. The number of people affected by MS is increasing globally with recent figures estimating over 2.8 million cases worldwide [2]. While assessments of functional ability can inform medical decisions and interventions that can ultimately reduce the risk of relapses and slow down the rate of disease progression, their utility has been limited by their infrequent use and reliance on patient recall [3-5]. An objective and more frequent assessment could provide a more detailed picture of the evolution of the disease.

To address this unmet need, smartphone sensor-based tests, or remote digital assessment technologies, are increasingly being studied for assessing functional ability in people with MS (PwMS) [6-14]. Typically, such tests can be remotely and frequently performed in the patient's home environment without supervision by a healthcare professional [10, 12, 15, 16]. Furthermore, the use of wearable or embedded sensors allows many different aspects of functional ability to be characterized and objectively quantified [12, 13, 17, 18]. Thus, they provide more granular and more detailed information than captured with the single scores of traditional standard clinical assessments such as the Nine-Hole Peg Test, oral Symbol Digit Modalities Test, or the Timed 25-Foot Walk [19-21]. Ultimately, the goal of digital remote assessment tools in MS is to help uncover insidious disease progression [22-24] and allow timely and appropriate medical intervention, which could lead to better treatment outcomes.

While restricting remote digital assessment technologies to a specific device or a single OS platform can offer a simpler integration of hardware and software [12, 13, 25], it may limit their uptake [26]. Bring-your-own-device (BYOD) solutions, by comparison, can help increase the access to remote digital technologies (i.e., reaching more users) by taking into account the differences in market share of iOS and Android devices across geographies [27]. BYOD solutions are also less affected by the unfamiliarity associated with novel tools, speak to the patients' preference of using their own device rather than using and carrying an additional device with them, and potentially improve the user experience [26, 28, 29]. Furthermore, they are associated with fewer logistical challenges and, as a result, are more cost effective to deploy in clinical trials [30, 31]. However, measurement equivalence across different device models must be first established before a BYOD solution can be

successfully deployed [11, 32].

The Floodlight Open app assesses MS-related functional ability through smartphone sensor-based “active” tests (i.e., assessments that require active input from the user) and was specifically developed for use in a BYOD setting [33]. It was deployed in Floodlight Open, an global, open-access, digital-only study that was designed to understand the drivers and barriers in deployment and persistence of use of a smartphone app in a naturalistic setting and broad study population [33]. Previously it was shown that the Floodlight Open app can differentiate and discriminate between MS participants and non-MS participants [33, 34]. Using data from this study, we sought here to establish the properties of measurement equivalence on three separate levels: operating system (OS) platforms, OS versions, and device models.

Methods

Study design and participants

Floodlight Open was run in 17 countries, and data were collected between April 23, 2018 and April 26, 2023. The study design and the Floodlight Open app have been previously described [33]. As a fully remote, digital-only study, Floodlight Open did not involve supervision by healthcare professionals. Adult participants aged ≥ 18 years with or without self-declared MS living in one of the participating countries could enroll by providing full electronic (e-) consent and downloading the Floodlight Open app on their own smartphone device. After providing their e-consent, participants received a token, or activation code, via email with which they could unlock the functionalities of the app. Participants were excluded from the analyses if they did not complete at least one valid active test or had missing device information.

Ethical considerations

The protocol, the informed consent forms, data protection and treatment measures, any information given to the participants, and relevant supporting information were reviewed and approved by local institutional review boards (IRB) or ethics committees (EC) before the study was initiated, as applicable, in accordance with each country's regulatory requirements. Further details on the IRB and EC approvals are described in a previous report [33].

Floodlight smartphone sensor-based active tests

The Floodlight Open app was designed to remotely measure, in a naturalistic setting, functional ability in cognition, hand motor function, gait and balance, mobility, and mood through smartphone-based active tests, passively collected life-space measurements, and patient-reported outcomes. The individual tests have been previously described [33]. It supports all devices running iOS version 11.x or later or Android version 7.x or later, which were commonly available at the time the app was launched. The iOS version was first released on April 22, 2018 and the Android version on July 17, 2019.

The measurement equivalence properties were studied on six active tests, including the Information Processing Speed (IPS), IPS Digit–Digit (IPS DD), Pinching Test (PT), Static Balance Test (SBT), U-Turn Test (UTT) and 2-Minute Walk Test (2MWT) (Table 1). These active tests could be

performed up to once daily (PT, SB, UTT, 2MWT) or up to once weekly (IPS, IPS DD).



Table 1. Active tests included in the analysis.

Functional Domain	Active Test	Sensors Used	Test Schedule	Test Feature to Assess Test Performance	Quality Control Flags		
					Test invalid if characterized by	marked if	Criterion
Cognition	IPS	Touchscreen	Weekly	Number of correct responses, n	'Play-to-quit' attempt	●	Response selected independently of symbol to be matched [15]
Cognition	IPS Digit-Digit Test	Touchscreen	Weekly	Number of correct responses, n	'Play-to-quit' attempt	●	Response selected independently of symbol to be matched
Hand motor function	PT	Touchscreen	Daily	Number of pinches, n	'Play-to-quit' attempt	●	No gestures recorded by the touch screen (no screen interaction)[15]
Gait and balance	SBT	Accelerometer	Daily	Sway path, m/s ²	'Play-to-quit' attempt	●	Phone is kept on the table [15] ● Steps recorded during the test [15]
Gait and balance	UTT	Accelerometer, Gyroscope	Daily	Turn speed, rad/s	'Play-to-quit' attempt	●	Phone is kept on the table [15] ● Main orientation of the phone is stable for ≤90% of the time
Gait and balance	2MWT	Accelerometer	Daily	Number of steps, n	'Play-to-quit' attempt	Insufficient data	
						●	Number of turns ≤ 3
						●	Turn angle is either ≥270 or ≤90 degrees
Gait and balance	2MWT	Accelerometer	Daily	Number of steps, n	'Play-to-quit' attempt	●	Test duration is ≤40 s
						●	Phone is kept on the table [15]
Insufficient data						●	Test duration ≤105 sec

2MWT, Two-Minute Walk Test; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit-Digit; PT, Pinching Test; SBT, Static Balance Test; UTT, U-Turn Test.

The IPS measures cognitive function and instructed participants to match as many symbols to digits as possible within 90 seconds according to a symbol-digit key provided at the top end of the

smartphone display. To account for the visuomotor component involved in this substitution task, participants were additionally asked to match digits to digits instead during the 30-second IPS DD. The PT evaluated the ability to perform upper extremity function tasks. The goal was to pinch, or squeeze, as many tomato shapes as possible within 30 seconds. After each pinched tomato shape, a new shape appeared at a different location on the smartphone display. Gait and balance was assessed with three different active tests. The SBT instructed participants to stand as still as possible for 30 seconds with both feet on the ground and with the eyes open. The UTT prompted participants to perform at least five U-turns on an even ground four meters apart within 60 seconds, and thus assesses both gait and dynamic balance. By comparison, the 2MWT assessed gait during straight walking without turning on an even ground for two minutes. For both the UTT and 2MWT, study participants were instructed to walk as fast as possible but safely; use of assistive devices and/or orthotics was permitted as needed and recorded.

The raw sensor data (touchscreen, accelerometer and gyroscope data) were encrypted and transferred wirelessly to a secure central database server that is controlled and maintained by the study initiator, F. Hoffmann-La Roche Ltd. Subsequently, the raw sensor data were used to compute pre-defined test features that characterize the participant's performance on the individual active tests. These features include the number of correct responses on the IPS and IPS DD, the number of successful pinches on the PT [15], sway path on the SBT [15], the average turn speed on the UTT [15] and the number of steps on the 2MWT.

Data processing and statistical analysis

Two data processing steps were implemented to reduce any potential bias introduced by poor sampling frequency of the embedded sensors or by non-accordant test execution. The second data processing step, however, was not available for the Draw a Shape Test; consequently, this active test is not included in the analyses presented here.

In a first data processing step, any active test recorded with either a low sampling frequency (sampling frequency ≤ 33 Hz) or an unstable sampling frequency (sampling frequency temporarily dropped ≤ 33 Hz) was identified and subsequently excluded from the analyses since low or unstable sampling frequency can negatively affect sensor-based measurements [35]. The minimum sampling frequency was set at 33 Hz for all sensor types as this is the lowest sampling frequency to reliably assess gait [36]. Most currently available commercial smartphone devices support this sampling

frequency. Next, any active test that was not executed according to the test's instructions was disregarded as they were considered invalid. Such non-accordant tests were retrospectively identified with quality control flags, which were derived from the raw sensor data and provide objective information on how the test was executed. Different quality control flags were defined for each of the active tests (Table 1). These quality control flags identified, without any input from an observer, individual tests that were either characterized by 'play-to-quit' behavior or insufficient data. 'Play-to-quit' behavior captures instances where the participant did not intend to perform the test according to the instructions provided and wanted to skip the test instead (e.g., the same response is selected in fast succession irrespective of the symbol shown during the IPS or IPS-DD; no touch screen interaction during the Pinching Test). The insufficient data criterion was introduced to ensure the extraction of meaningful gait features, which is particularly important when comparing smaller subgroups that are more sensitive to noise. According to this criterion, only gait tests with a sufficient number of steps or turns were kept for further analyses.

Measurement equivalence signifies that the measurements obtained from two groups stem from the same distribution, ie, the two groups are equivalent to each other. This was studied separately for each of the six active tests in both MS and non-MS participants using the Floodlight feature values, i.e., measurements of test performance, derived from the raw sensor data (raw accelerometer, gyroscope, and/ or touchscreen data). Since the study duration was not fixed, the first valid test execution (i.e. the first valid IPS, IPS DD, PT, SBT, UTT, and 2MWT) of each participant was used to assess measurement equivalence in order to maximize the number of participants available for analysis and to compare like with like. A test run was considered completed if the participants performed all active tests except the 2MWT in a single session in a pre-defined, fixed sequence. As the 2MWT was self-administered independently from this sequence, the first valid 2MWT of each participant was used to study the equivalence on this active test.

Feature values derived from the raw sensor data (i.e., raw accelerometer, gyroscope, and/or touchscreen data collected while the participants were performing the active tests) were adjusted for age, sex, and self-declared disease status ('MS' and 'Non-MS') with a robust linear model to account for differences in these covariates (function `rlm{}` included in the python statsmodel package v. 0.13.5). Next, subgroups were defined in four separate categories: OS platform (i.e., iOS and Android), iOS version (i.e., iOS versions 11, 12, 13, 14 and 15), Android version (Android version 8, 9, and 10), and device model. To minimize potential issues with small sample sizes but also allow for

as many different subgroups (e.g., device models) as possible to be included in the analysis, only subgroups with at least 20 participants were included.

To study measurement equivalence, each subgroup (e.g., iOS 12) was subsequently compared against their respective reference group. This reference group consisted of all remaining subgroups of the same category pooled together. For example, the reference group for iOS 12 is iOS 11, 13, 14 and 15 pooled together. The null hypothesis was that the distribution of the subgroup—eg, iOS 12—is identical to the distribution of its respective reference group. Differences in the means between the subgroup under study and its reference group was tested for statistical significance through permutation testing [37, 38]. This test was chosen as it is a non-parametric test that requires only minimal model assumptions and additionally is robust. It does not assume a normal distribution and is also robust with regard to unbalanced datasets such as ours and to outliers. To perform the permutation test, the overall population (in the example above, all iOS devices) was randomly sampled to generate two permuted groups whose sample size was identical to the subgroup under study (eg, iOS 12) and its reference group (eg, iOS 11, 13, 14, and 15 pooled together), respectively. This was repeated 10,000 times, resulting in 10,000 permutations, and hence 10,000 mean differences. The reported p-value is defined as the proportion of permutations that resulted in a mean difference between the two permuted groups that is larger than the real observed mean difference between the subgroup and its reference group. Both unadjusted and adjusted *P*-values (adjusted for multiple comparison with false discovery rate correction using the Benjamini-Hochberg method) are reported.

Additional reported metrics include the 95% confidence intervals (CI) of expected mean differences under the assumption of the null hypothesis, which were derived from the permutation test; the absolute difference and percent difference in the observed mean scores (mean feature values) between each subgroup and their respective reference group; the standard deviation of each subgroup and its reference group; as well as the effect size of these differences (Cohen's *D*) are reported (very small effect size: $D=0.01$; small effect size: $D=0.2$; medium effect size: $D=0.5$; large effect size: $D=0.8$ [39, 40]).

To corroborate the findings, a sensitivity analysis was run, which used the median as the test statistic difference (instead of the mean difference) of the permutation test.

In a separate analysis, smartphones were compared against tablets to evaluate the impact of screen size on measurement equivalence. Differences between smartphones and tablets were assessed for statistical significance with the Mann-Whitney U Test.

Data availability

For up-to-date details on Roche's Global Policy on Sharing of Clinical Study Information and how to request access to related clinical study documents, see here: https://go.roche.com/data_sharing. Request for the data underlying this publication requires a detailed, hypothesis-driven, statistical analysis plan that is collaboratively developed by the requestor and company subject matter experts. Such requests should be directed to dbm.datarequest@roche.com for consideration. Anonymized records for individual patients across more than one data source external to Roche cannot, and should not, be linked due to a potential increase in risk of patient re-identification.

Results

Smartphone data were available for 2,010 participants aged ≥ 18 years. Of these, 34 (1.7%) participants were excluded from the analyses due to low or unstable sampling frequency, resulting in 1,976 evaluable participants using 206 different, or unique, device models (1,614 participants with iOS devices and 362 participants with Android devices). Details on the participant, the devices they used, and their demographics are provided in Figure 1 and Table 2.

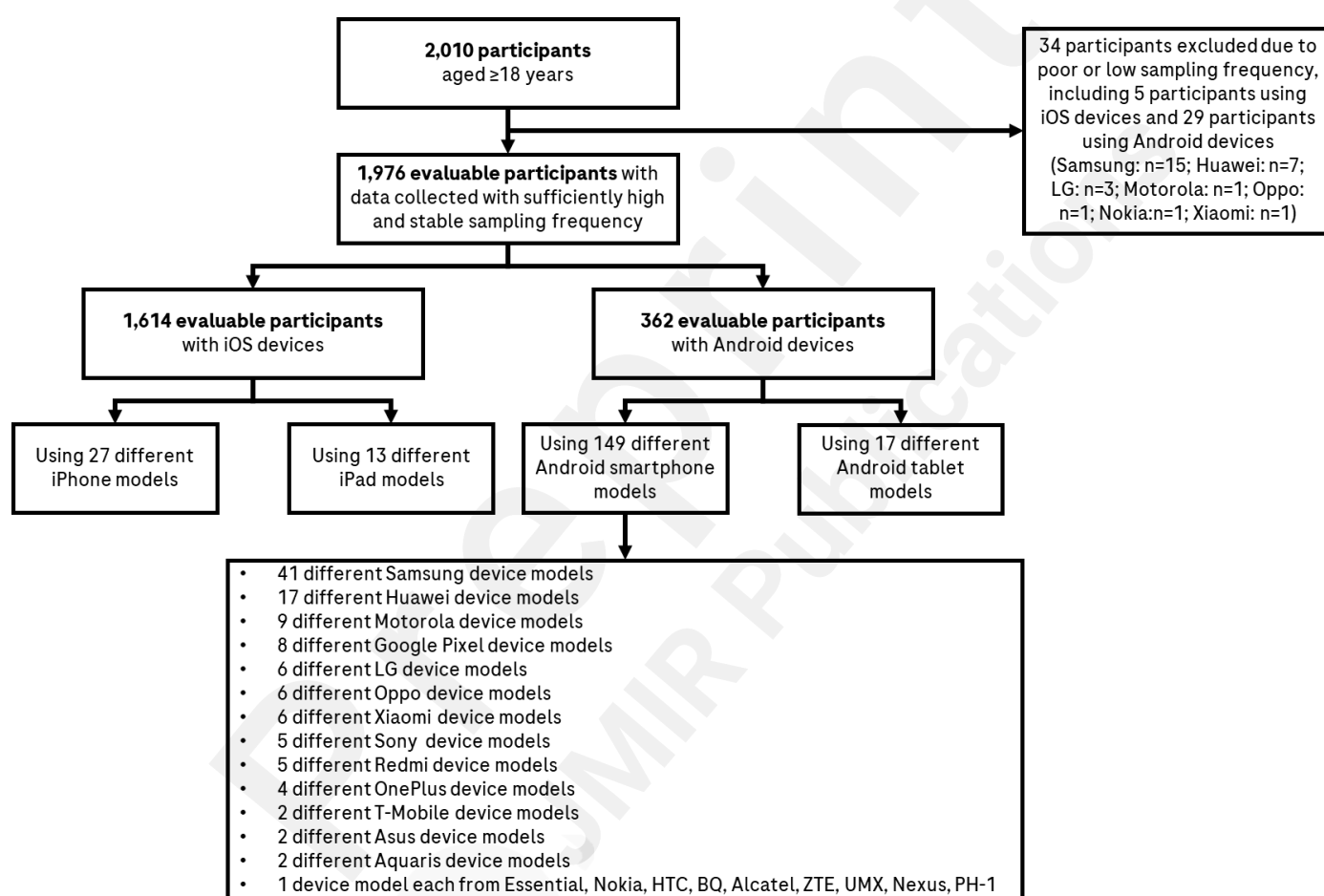


Figure 1. Participant deposition and the devices they used.

Table 2. Baseline demographics and disease characteristics.

Variable		All (n=1,976)	MS (n=1,140)	Non-MS (n=836)
Age, years, mean (SD)		43.1 (12.5)	45.5 (12.0)	39.8 (12.4)
Female, n (%)		1,243 (62.9)	838 (73.5)	405 (48.4)
Participants with iOS devices, n (%)		1,614 (81.7)	879 (77.1)	735 (87.9)
Active tests	IPS, correct responses, n, mean (SD)	43.8 (11.9)	43.2 (10.7)	45.0 (13.7)
	IPS DD, correct responses, n, mean (SD)	17.9 (3.6)	17.7 (3.4)	18.3 (4.0)
	PT, successful pinches, n, mean (SD)	30.8 (13.5)	28.1 (13.0)	34.6 (13.5)
	SBT, sway path, m/s ² , mean (SD)	21.8 (21.9)	22.7 (22.0)	20.5 (21.6)
	UTT, turn speed, rad/s, mean (SD)	1.40 (0.35)	1.37 (0.34)	1.43 (0.37)
	2MWT, steps, n, mean (SD)	190.2 (38.2)	191.2 (38.1)	187.8 (38.2)

2MWT, Two-Minute Walk Test; IQR, interquartile range; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit–Digit; MS, multiple sclerosis; PT, Pinching Test; SBT, Static Balance Test; UTT, U-Turn Test.

Quality checks

Devices running iOS devices were less prone to low or unstable sampling frequency than Android devices, although the overall number of participants that were excluded for failing to meet the sampling frequency requirements was small: In total, five participants with iOS devices and 29 with Android devices (15 with Samsung, 7 with Huawei, three with LG and one each with Motorola, Oppo, Nokia and Xiaomi devices) were excluded. Of all tests performed during the study, 95.9% (91,002/94,925 tests) were recorded with a sufficiently high and stable sampling frequency.

Across the entire study duration, the proportion of active tests executed in accordance with the test instructions, i.e., which passed the criteria defined by the quality control flags, varied from approximately 61.9% to 99.1% (IPS: 92.1%; IPS DD: 95%; PT: 99.1%; SBT: 87.9%; UTT: 61.9%; 2MWT: 84.0%). However, no participant was excluded from the analysis for failing to meet these criteria as each participant performed at least one entire test run in accordance with the provided instructions (for each participant, the first valid test from each active test was used for the measurement equivalence analysis). Nonetheless, this highlights that large observational remote assessment studies such as Floodlight Open require checks that provide objective measures for assessing data quality and accordance with the test instructions of self-administered assessments [15].

Measurement equivalence

The measurement equivalence analysis was assessed after adjusting for age, sex and self-reported

disease status. Overall, results show no indication that any of the six active tests are associated with a systematic measurement non-equivalence. The findings were consistent across OS platforms, OS versions, and device models, although the findings for the device models were more variable given the smaller subgroups. The effect sizes of the difference between subgroups were mostly very small (effect size <0.20) or small (effect size <0.5). For each observed subgroup, the mean differences were considerably smaller than one standard deviation of the respective reference group, and most mean differences were within the 95% CI obtained from the permutation test (Tables 3–5; Supplementary Table S1).

When comparing iOS devices with Android devices, percent differences of adjusted test scores between iOS devices and Android devices were $<5\%$ on the IPS, IPS DD, SBT, UTT, and 2MWT, and $\leq 10\%$ on the PT (Table 3). Permutation testing revealed a statistically significant, but small difference between iOS and Android on the PT (percent difference: 8.0%, effect size: 0.24, $P < .001$; Figure 2; Table 3).

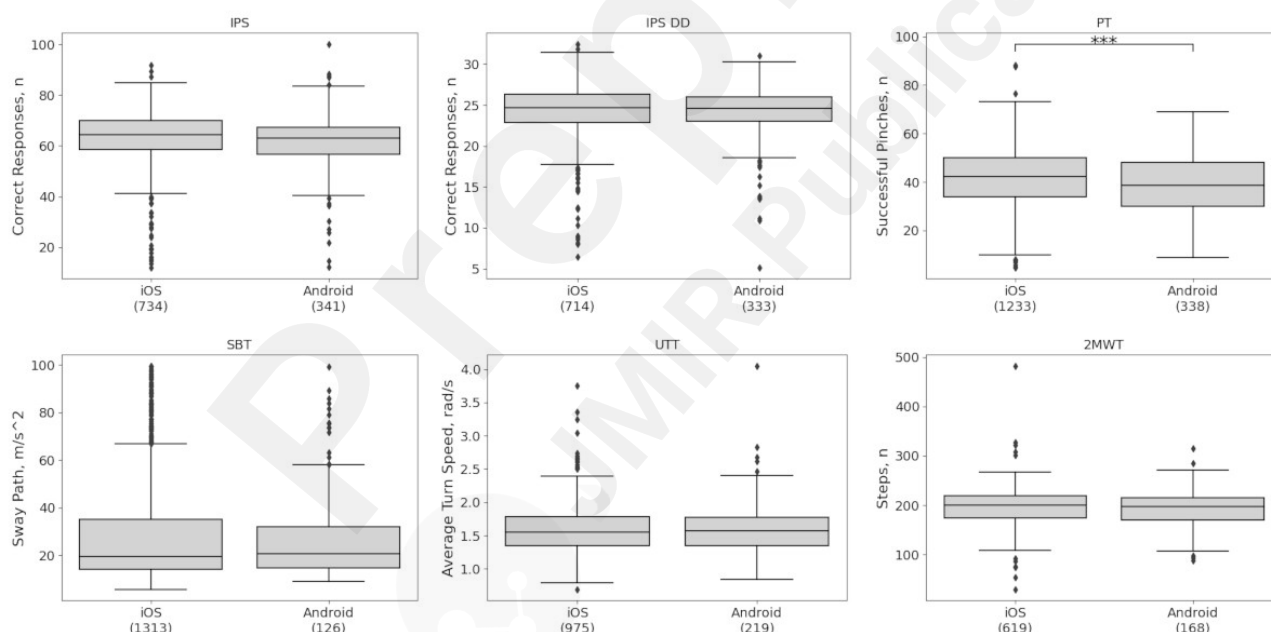


Figure 2. Measurement equivalence by OS platform. Permutation testing showed no evidence of a systematic lack of equivalence between the two OS platforms iOS and Android. A small but statistically significant difference was only observed on the PT. Differences between groups as well as effect sizes are provided in Table 3. Brackets indicate the sample size. *** $P < .001$. 2MWT, Two-Minute Walk Test; IQR, interquartile range; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit-Digit; PT, Pinching Test; SBT, Static Balance Test; UTT, U-Turn Test.

Table 3. Absolute and percent mean differences across OS platforms (iOS vs Android).

Active test	iOS			Android			Mean difference from Android devices			Permutation test	
	n	Mean	SD	n	Mean	SD	Absolute difference	Percent difference	Effect size		<i>P</i> unadjusted
IPS, correct responses, n	734	63.1	11.2	341	61.8	10.3	1.3	2.1	0.12	0.0, 1.6	.07
IPS DD, correct responses, n	714	24.3	3.4	333	24.2	3.1	0.1	0.5	0.04	0.0, 0.5	.60
PT, successful pinches, n	1233	41.5	12.7	338	38.4	12.1	3.1	8.0	0.24	0.0, 1.7	<0.001
SBT, sway path, m/s ²	1313	28.2	20.7	126	28.4	20.8	0.2	0.7	0.01	0.1, 4.3	.92
UTT, turn speed, rad/s	975	1.59	0.34	219	1.59	0.37	0.01	0.4	0.02	0.00, 0.06	.80
2MWT, steps, n	619	195.9	38.0	168	191.9	38.2	4.0	2.1	0.11	0.1, 7.5	.23

Entries highlighted in bold are statistically significant ($P < .05$).

2MWT, Two-Minute Walk Test; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit–Digit; PT, Pinching Test; SBT, Static Balance Test; SD, standard deviation; UTT, U-Turn Test.

Similar results were observed when comparing the five iOS versions 11, 12, 13, 14 and 15 (Figure 3A). Across all five iOS versions, the percent differences were mostly $<5\%$ on the IPS and IPS DD, PT, UTT, and 2MWT, with only iOS 15 showing percent differences greater than 5% on the IPS (percent difference: 5.3%) and IPS DD (percent difference: 5.2%) (Table 4). Larger differences were observed on the SBT, with percent differences ranging from 1.3% to 18.3%. Permutation testing revealed statistically significant differences only for iOS 12 on the IPS (percent difference: 3.0%, effect size: 0.17, P unadjusted = .02) and IPS DD (percent difference: 2.5%, effect size: 0.19, P unadjusted = .01). However, the observed mean differences of 1.9 (IPS) and 0.6 (IPS DD) correct responses were within the 95% CI obtained from the permutation test (IPS: [0.0, 1.9]; IPS DD: [0.0, 0.6]), and these differences were no longer statistically significant after correcting for multiple comparisons (P adjusted = .11 and .07, respectively). Differences of similar magnitude were observed when comparing Android versions 8, 9 and 10 (Figure 3B). Across these OS versions, percent differences were mostly $\leq 5\%$ on the IPS, IPS DD, PT (only Android 8 showed a larger percent difference of 5.1%), UTT and 2MWT; and $<30\%$ on the SBT (Table 5). None of these differences reached statistical significance (all P unadjusted = .06–.96, all P adjusted = .19–.96).

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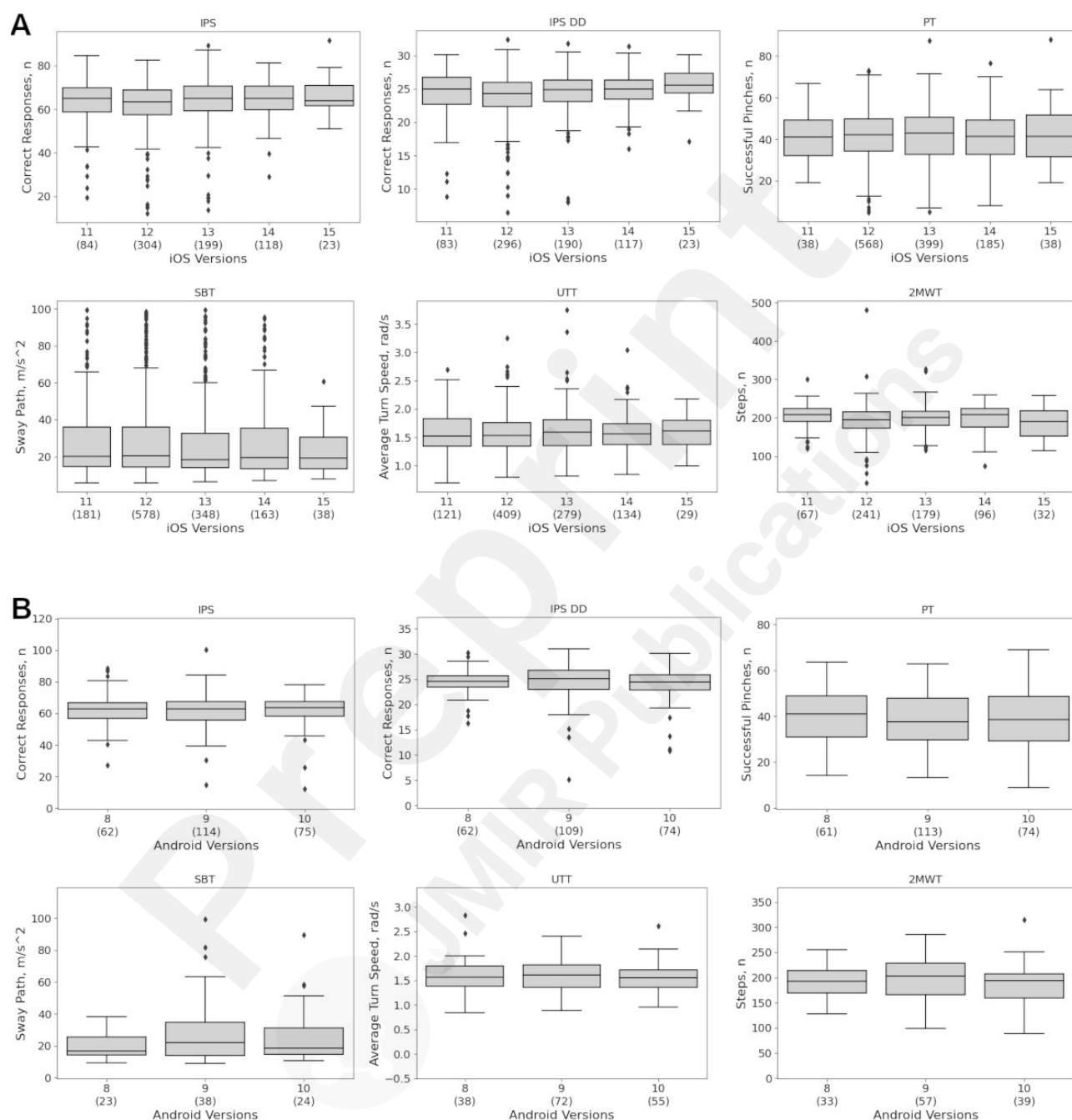


Figure 3. Measurement equivalence by iOS version (A) and Android version (B). Permutation testing revealed no evidence for a systematic lack of equivalence. No statistically significant differences were observed across OS version after correcting for multiple comparison (all P adjusted >0.05). Absolute and percent differences as well as effect sized are provided in Tables 4 and 5. Brackets indicate the sample size. 2MWT, Two-Minute Walk Test; IQR, interquartile range; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit-Digit; PT, Pinching Test; SBT, Static Balance Test; UTT, U-Turn Test.

Table 4. Absolute and percent differences across iOS versions.

Active test	iOS subgroup			Reference group ^a		Mean difference from reference group			Permutation test		
	n	Mean	SD	Mean	SD	Absolute difference	Percent difference	Effect size	95% CI	P unadjusted	P adjusted ^b
iOS 11	84	62.9	12.8	63.1	11.0	0.2	0.4	0.02	0.0, 2.9	.86	.87
iOS 12	304	62.0	11.5	63.9	11.0	1.9	3.0	0.17	0.0, 1.9	.02	.11
iOS 13	199	63.7	11.8	62.9	11.0	0.8	1.2	0.07	0.0, 2.1	.40	.50
iOS 14	118	64.5	8.5	62.8	11.7	1.7	2.7	0.15	0.0, 2.5	.12	.27
iOS 15	23	66.3	9.0	63.0	11.3	3.3	5.3	0.30	0.1, 5.3	.16	.27
iOS 11	83	24.2	3.9	24.3	3.3	0.1	0.5	0.03	0.0, 0.9	.78	.78
iOS 12	296	23.9	3.5	24.5	3.3	0.6	2.5	0.19	0.0, 0.6	.01	.07
iOS 13	190	24.5	3.3	24.2	3.4	0.2	0.9	0.07	0.0, 0.6	.43	.53
iOS 14	117	24.8	2.7	24.2	3.5	0.6	2.4	0.17	0.0, 0.8	.09	.16
iOS 15	23	25.5	3.1	24.2	3.4	1.3	5.2	0.38	0.0, 1.6	.08	.16
iOS 11	38	41.2	11.7	41.5	12.7	0.3	0.7	0.02	0.1, 4.7	.89	.99
iOS 12	568	41.6	12.0	41.3	13.3	0.3	0.7	0.02	0.0, 1.6	.71	.99
iOS 13	399	41.5	13.6	41.5	12.3	0.0	0.0	0.00	0.0, 1.8	.99	.99
iOS 14	185	40.9	12.8	41.6	12.7	0.7	1.7	0.06	0.0, 2.3	.48	.99
iOS 15	38	42.6	15.0	41.4	12.6	1.2	2.9	0.09	0.1, 4.8	.58	.99
iOS 11	181	29.1	21.5	28.1	20.5	1.0	3.7	0.05	0.0, 3.7	.54	.67
iOS 12	578	29.1	21.0	27.5	20.4	1.6	5.7	0.08	0.0, 2.6	.17	.29
iOS 13	348	26.7	20.0	28.7	20.9	2.0	7.1	0.10	0.0, 2.9	.11	.29
iOS 14	163	28.5	21.7	28.2	20.5	0.4	1.3	0.02	0.1, 3.9	.83	.83
iOS 15	38	23.2	12.0	28.3	20.9	5.2	18.3	0.25	0.1, 7.6	.13	.29
iOS 11	121	1.58	0.35	1.59	0.34	0.01	0.4	0.02	0.00, 0.08	.85	1.0
iOS 12	409	1.57	0.33	1.60	0.35	0.03	2.0	0.09	0.00, 0.05	.15	.38
iOS 13	279	1.62	0.38	1.58	0.33	0.04	2.7	0.12	0.00, 0.06	.08	.38
iOS 14	134	1.59	0.31	1.59	0.35	0.00	0.0	0.00	0.00, 0.07	1.0	1.0
iOS 15	29	1.59	0.31	1.59	0.35	0.00	0.2	0.01	0.00, 0.15	.96	1.0
iOS 11	67	204.1	33.7	194.8	38.4	9.3	4.8	0.25	0.2, 10.9	.057	.16
iOS 12	241	192.2	42.1	198.1	35.0	5.9	3.0	0.15	0.1, 7.1	.06	.16
iOS 13	179	197.7	34.1	195.0	39.5	2.6	1.4	0.07	0.1, 7.6	.43	.45
iOS 14	96	198.4	36.1	195.3	38.4	3.1	1.6	0.08	0.1, 9.5	.45	.45
iOS 15	32	186.9	38.7	196.3	38.0	9.4	4.8	0.25	0.2, 15.7	.17	.29

^aThe reference group consists of all other iOS devices pooled together.

^bP-values were adjusted for multiple comparisons with false discovery rate (FDR) correction using the Benjamini-Hochberg method.

2MWT, Two-Minute Walk Test; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit–Digit; PT, Pinching Test; SBT, Static Balance Test; SD, standard deviation; UTT, U-Turn Test.

Table 5. Absolute and percent differences across Android versions.

Active test	Android subgroup			Reference group ^a		Mean difference from reference group			Permutation Test			
	n	Mean	SD	Mean	SD	Absolute difference	Percent difference	Effect size	95% CI	P unadjusted	P adjusted ^b	
Android 8	62	62.4	11.5	61.8	10.5	0.6	0.9	0.05	0.1, 3.6	.71	.90	
Android 9	114	61.8	10.5	62.1	10.9	0.3	0.5	0.03	0.0, 3.0	.83	.90	
Android 10	75	61.9	10.6	62.0	10.8	0.2	0.3	0.02	0.0, 3.3	.90	.90	
Android 8	62	24.4	2.5	24.2	3.5	0.3	1.1	0.09	0.0, 1.1	.57	.85	
Android 9	109	24.3	3.6	24.2	3.0	0.1	0.3	0.03	0.0, 0.9	.85	.85	
Android 10	74	24.0	3.4	24.3	3.2	0.3	1.4	0.11	0.0, 1.0	.46	.85	
Android 8	61	40.0	12.0	38.1	12.0	1.9	5.1	0.16	0.1, 3.9	.27	.57	
Android 9	113	37.8	11.3	39.2	12.6	1.3	3.4	0.11	0.1, 3.5	.38	.57	
Android 10	74	38.5	13.3	38.6	11.5	0.1	0.3	0.01	0.1, 3.7	.94	.94	
Android 8	23	19.8	7.8	28.2	20.6	8.4	29.8	0.46	0.2, 10.0	.06	.19	
Android 9	38	28.7	21.7	23.8	15.3	4.9	20.6	0.27	0.1, 9.1	.23	.35	
Android 10	24	27.5	19.8	25.3	18.0	2.2	8.7	0.12	0.1, 9.9	.63	.64	
Android 8	38	1.59	0.37	1.59	0.32	0.00	0.2	0.01	0.00, 0.14	.96	.96	
Android 9	72	1.62	0.34	1.57	0.32	0.05	3.1	0.15	0.00, 0.12	.36	.54	
Android 10	55	1.55	0.30	1.60	0.35	0.05	3.2	0.15	0.00, 0.12	.35	.54	
Android 8	33	191.1	33.8	191.8	42.6	0.7	0.4	0.02	0.3, 18.3	.94	.94	
Android 9	57	195.7	41.0	188.3	40.0	7.3	3.9	0.18	0.2, 16.1	.31	.46	
Android 10	39	186.0	45.3	194.0	38.1	7.9	4.1	0.20	0.3, 17.3	.30	.46	

^aThe reference group consists of all other Android devices pooled together.

^bP-values were adjusted for multiple comparisons with false discovery rate (FDR) correction using the Benjamini-Hochberg method. 2MWT, Two-Minute Walk Test; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit-Digit; N/A, data not available due to too small sample size ($n \leq 20$); PT, Pinching Test; SBT, Static Balance Test; SD, standard deviation; UTT, U-Turn Test.

Next, we evaluated whether a device model shows an out-of-distribution performance compared to the null hypothesis of all device models being from the same distribution (Supplementary Table S1; Supplementary Figure S1). Only device models used by at least 20 participants were included in this analysis, resulting in 17 different models being evaluated. Percent differences were mostly $\leq 5\%$ on the IPS, IPS DD, UTT (only the iPhone 7 Plus showed a larger percent

difference of 5.6%) and 2MWT; and <20% on the PT and SBT (Supplementary Table S1). Unadjusted permutation testing revealed that most device models did not show a statistically significant difference (IPS: 12/13 models, IPS DD: all models, PT: 12/16 models, SBT: 12/14 models, UTT: all models, 2MWT: all models). Of note, the statistically significant differences (P unadjusted: <.001–.04) were not associated with any particular device model. After adjusting for multiple comparisons, statistically significant differences were observed only on the PT (iPhone SE: P adjusted=.02; iPhone X Global: P adjusted=.03; iPhone X GSM: P adjusted=<.001; iPhone 11: P adjusted=.03). In all four instances, effect sizes ranged from 0.38 to 0.50, and percent differences from 11.4% to 15.1%. Furthermore, the observed mean differences were outside the 95% CI obtained from the permutation test (Supplementary Table S1).

The sensitivity analysis, which used the median difference rather than the mean difference as the test statistic for the permutation test, revealed similar findings across OS platforms, OS versions, and device models (Supplementary Tables S2–S5).

Screen size had a limited impact on the measurement equivalence properties. No significant differences were observed between smartphones ($n = 1,788$, of which 1,556 (87.0%) were iOS devices) and tablets ($n = 89$, of which 58 (65.2%) were iPads running iOS) on the gait and balance tests (i.e. SBT, UTT and 2MWT, all P =.27–.75). Statistically significant differences with small effect sizes between smartphones and tablets were observed on the IPS (percent difference: 11.9%, effect size: 0.45, P =.001), IPS DD (percent difference: 7.3%, effect size: 0.37, P =.022), and PT (percent difference: effect size: 0.38, 18.1%, P =.002).

Discussion

Principal findings

Ensuring measurement equivalence across different device models is necessary to conduct a new form of large scale, global and cost effective clinical research on digital outcomes in a BYOD setting. In this analysis, no evidence was found for a systematic lack of measurement equivalence across devices for the six smartphone sensor-based active tests considered. The key learnings are summarized in the Panel.

Panel. Key learnings.
• The broad, multinational cohort of 1,976 participants and 206 different device models allowed us to study measurement equivalence in a naturalistic environment, reflective of a real-world setting. • No evidence for the systematic lack of measurement equivalence was found; the features derived from our smartphone-based assessments were by large robust against differences in inertial measurement unit (IMU) sensors, sampling frequency and device latency. • Designing features to be robust against cumulative device latency effects can help with ensuring measurement equivalence across operating system (OS) platforms, OS versions, and device models. • Objective criteria that assess whether a self-administered digital test was taken as instructed and recorded with a sufficiently high and stable sampling frequency can help with evaluating the quality of the data collected in an unsupervised setting and, hence, informing whether the data should be included in further analyses.

Measurement non-equivalence can in theory arise from various sources. For example, differences in inertial measurement unit (IMU) sensors can potentially contribute to differences in measurements obtained with between devices [35]. However, our results suggest that differences IMU sensors did not impact the features derived from our active tests as no statistically significant differences were observed on tests that rely on IMU sensors (i.e., the SBT, UTT, and 2MWT).

Another factor that could contribute to measurement non-equivalence are differences in sampling frequency or sampling frequency heterogeneity [35]. We, therefore, excluded any tests that were recorded with either too low a sampling frequency or with an unstable sampling frequency as the sampling frequency can vary from test execution to execution, even with the same device model. Nonetheless, the sampling frequency requirements were met in most cases even if the computational load was temporarily increased due to the simultaneous activity of other apps installed on the participants' own smartphone devices as it can be expected in a BYOD setting. Of the 2,010 participants considered for the analyses, only 34 participants were excluded from the analysis for the lack of a sufficiently high and stable sample frequency.

A third factor that could impact measurement equivalence is device latency. For touch-screen based tests, it was estimated that latencies associated with displaying a new visual cue on the screen and registering a touch screen input by the user can account for a variance in response time of up to 100 ms, with Android devices tending to show higher latencies than iOS devices [41]. We estimated that such latencies could, in the worst case, account for a difference of up to 3 pinches on the Pinching Test (100ms latency per pinched tomato * an average 30.8 pinched tomatoes during a Pinching Test [see Table 2] = 3.08 seconds latency during a Pinching Test; with approximately 1 pinched tomato per second, this cumulative latency may thus explain a difference of up to 3 successful pinches). This is comparable to the 3.1 fewer successful pinches observed on Android devices than on iOS device. While other factors cannot be ruled out, it is plausible that the difference of 3.1 successful pinches between Android and iOS devices observed in this study could be explained by differences in device latencies. Developing features that are not affected by such cumulative latency effects could improve the measurement equivalence between iOS and Android devices. For the Pinching Test, a possible feature is double touch asynchrony, which was developed for other studies that deployed the Floodlight technology as a measure of finger coordination. It measures the duration of the gap between the first and second finger touching the touch screen. In a previous analysis, it was reliable, correlated with clinician-administered measures of upper extremity impairment and MS-related disability, and differentiated between people with different levels of disability [42]. Unlike the number of successful pinches, this feature is by design not affected by cumulative latency effects as it measures the average time between the first and second finger touching the touch screen during a

single Pinching Test.

Our study also highlighted the need for objective measures of data quality and accordance with the test instructions. Across the six active tests considered, approximately 61.9% through 99.1% of all test attempts were considered valid. Higher proportion of tests passing the QC flags have been previously reported when using less stringent criteria [33]. Ensuring that the tests are executed in accordance with their instructions remains a challenge with fully remote digital health studies which do not involve direct oversight of test performance and feedback mechanisms with the participants. In-clinic visits, for example, could be used to onboard study participants in-person and explain the tests in more detail, and consequently increase the proportion of active tests executed in accordance with the test instructions. In fact, we previously reported for a separate study, which included regular clinic visits, that up to 99% of active test attempts were considered valid [15]. Furthermore, digital health studies that include clinic visits, such as [15], are more likely than fully remote studies to enroll participants who are more motivated. This becomes more noticeable the longer the test duration is and the smaller the subgroups that are compared with each other are. As a result, we implemented in this study additional quality control flags to ensure sufficient evaluable data were collected during the two active tests with the longest test duration, the UTT and 2MWT (Table 1).

Limitations

There are some limitations associated with our study. First, the observational nature of our study in a naturalistic environment implies that confounding factors may have affected the comparisons despite the adjustments we performed. For instance, we could not adjust for disease severity, as this information is not available in this fully remote, digital-only study. This might partially explain the larger percent differences observed in smaller subgroups. However, given the small overall differences among the investigated subgroups, the residual confounding effects are plausibly small. And while statistical tests did not indicate that the measurements obtained across devices are systematically non-equivalent, we cannot rule out that this finding may be due to high variability, different average disease severity or, for some few comparisons, small sample size. A lack of sensitivity of the Floodlight tests, however, can be excluded as a reason for the similarity of the results as these tests have shown ability to differentiate people with multiple sclerosis from

healthy controls or between people with multiple sclerosis with different levels of impairment [15, 42, 43].

Second, the earlier release of the iOS version of the Floodlight Open app has resulted in a larger number of iOS participants compared with Android participants. Furthermore, the larger choice on different Android device models than iOS device models meant that there were fewer participant per Android device model, resulting in an unbalanced dataset for the comparison of measurement equivalence by device model.

Finally, the analyses presented here are retrospective as the study was not purposely designed to assess equivalence or reliability. Ideally, device equivalence studies with purpose-built study designs have each participant perform the active tests multiple times using the same set of devices and assess equivalence across devices using appropriate statistical tests with pre-specified equivalence margins. As an alternative, equivalence can be assessed with bench testing utilizing robots able to cover the range of features values typically observed in the population of interest. Nonetheless, the preliminary findings of our analyses can inform the design of future device equivalence studies and the equivalence margins to assess equivalence.

Comparison with prior work

Recent studies compared smartphone-based measurements of gait, balance or physical activity [44-48], cognitive functioning [49, 50], or sleep [51]. However, these studies typically compared the smartphone-based measurements and measurements obtained with other devices with gold-standard measures such as manual step count [46, 47] or smartphone-based measurements with measurements obtained with other device types [44, 45, 51]. This makes it challenging to separate the potential impact arising from differences in the device or sensor specifications from those arising from differences in the algorithms used to extract the features. A small number of studies assessed device equivalence using the same feature extraction algorithm [35, 49]. For example, van Oirschot et al. [49] investigated their smartphone-based Symbol Digit Modalities Test on devices running either iOS or Android and found no differences between the two OS platforms, which is in line with our findings on the IPS. Additionally, Ena et al. identified a number of features extracted from their smartphone-based mobility tests that showed in a

prospective study reliability across iOS and Android devices [52].

Strengths of this remote, digital only, unsupervised, BYOD study include the comprehensive approach to assess measurement equivalence across different smartphone devices. Unlike other studies, we investigated measurement equivalence on three levels by separately looking at the two OS platforms iOS and Android, different iOS and Android versions, and at device models. The large sample size of 1,976 study participants and the wide range of smartphone device models (n=206) used add to the strength of our study. Finally, we used objective measures to ensure data quality and accordance with test instructions.

Conclusions

In this study, we investigated a key criterion for the deployment of six smartphone sensor-based active tests assessing cognition, hand motor function, and gait and balance in BYOD setting. Using data collected in Floodlight Open, we found no evidence for substantial and consistent lack of measurement equivalence across different OS platforms, OS versions and smartphone device models for features derived from these active tests. These features were largely unaffected by differences in IMU and touchscreen sensors and were also not impacted by the activity of other apps installed on the participants' own smartphone devices as evidenced by the sufficiently high and stable sampling frequency in a vast majority of participants. These findings are compatible with the use of smartphone-based tests in a BYOD setting and will inform future studies with purpose-built study designs that will further investigate the device equivalence properties of smartphone-based assessments.

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Disclosures

LK, LC, FL, AG are employees of F. Hoffmann-La Roche Ltd.

FD: was an employee of F Hoffmann-La Roche Ltd during the completion of the work related to this manuscript. FD is now an employee of Novartis (Basel, Switzerland), which was not in any way associated with this study.

CB was a contractor for F. Hoffmann-La Roche Ltd. during the completion of the work related to this manuscript. CB is now with Limites Medical Research Ltd., which was not in any way associated with this study.

ML is a consultant for F. Hoffmann-La Roche Ltd via Inovigate.

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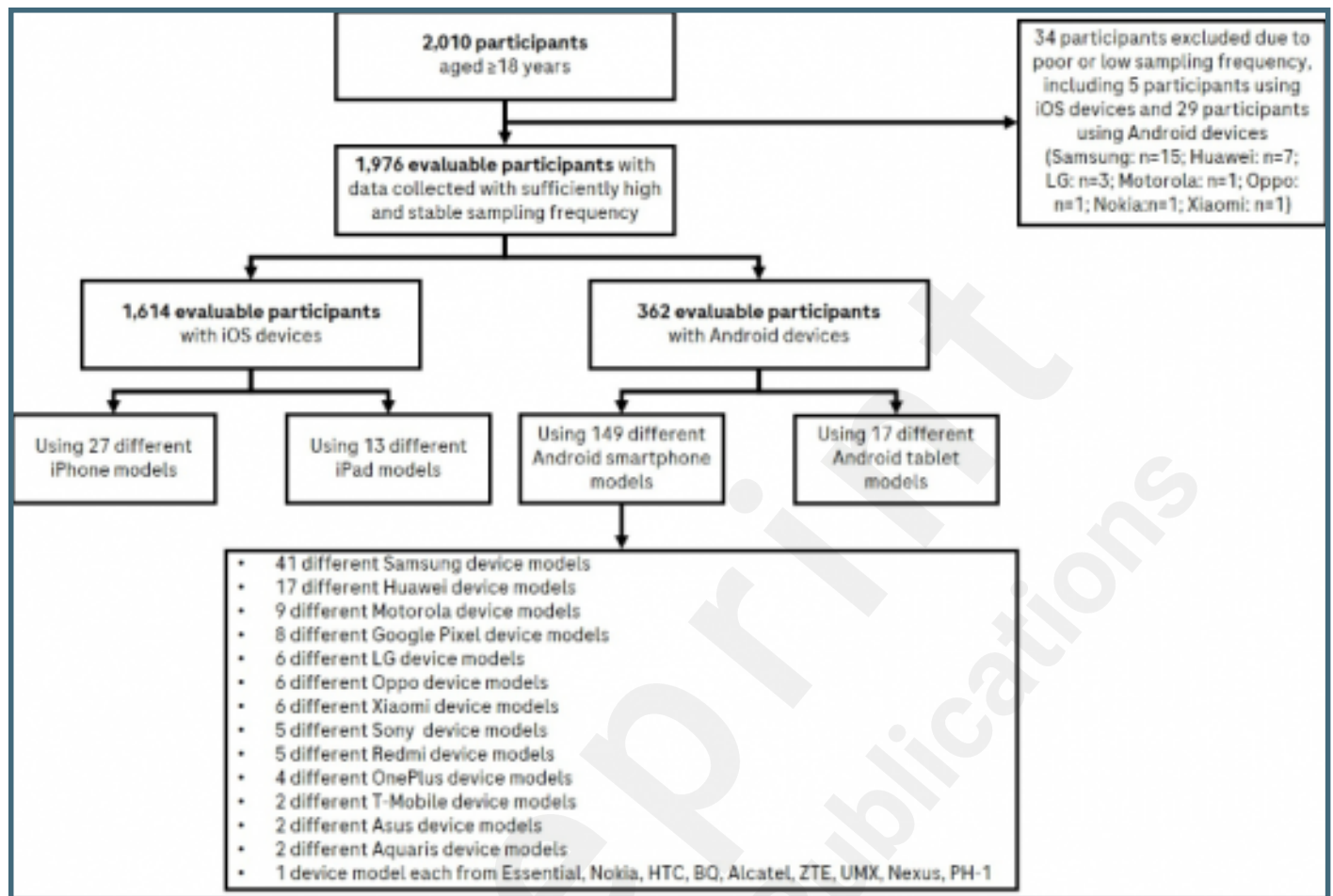
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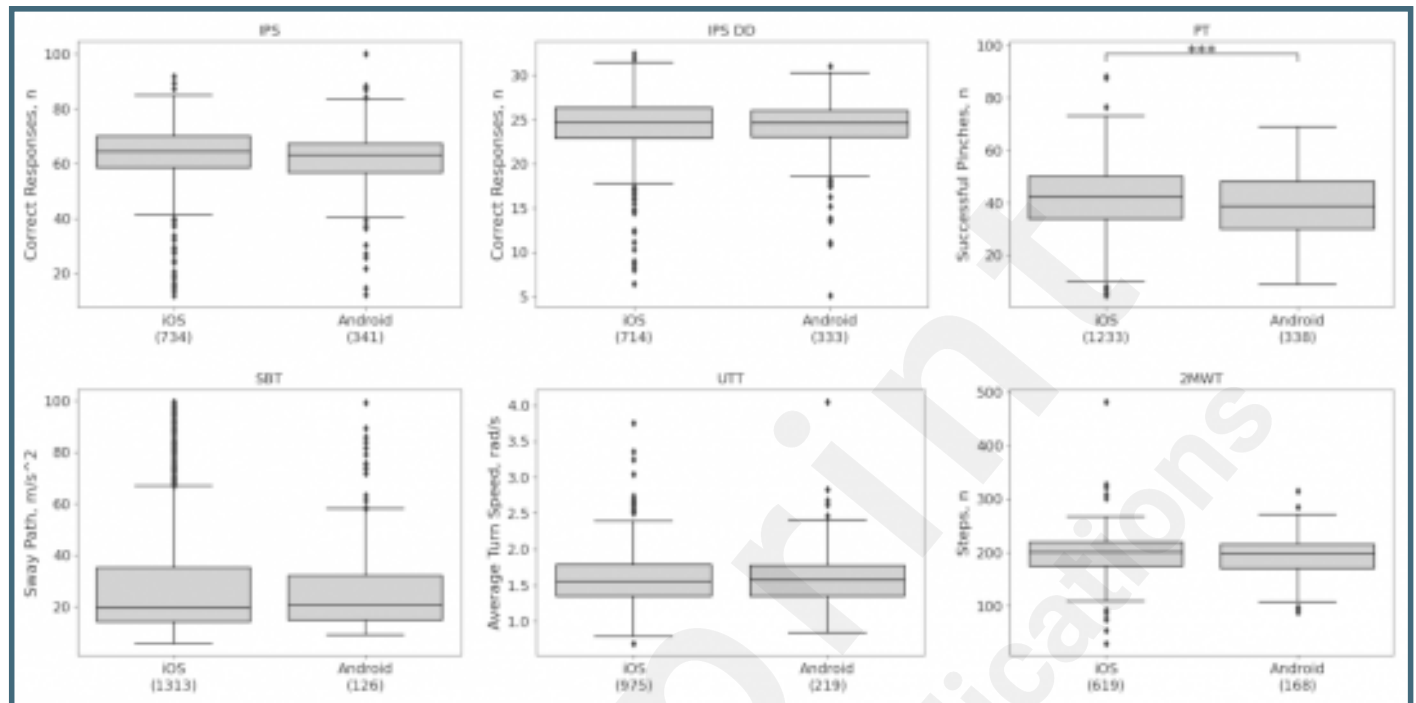
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Supplementary Files

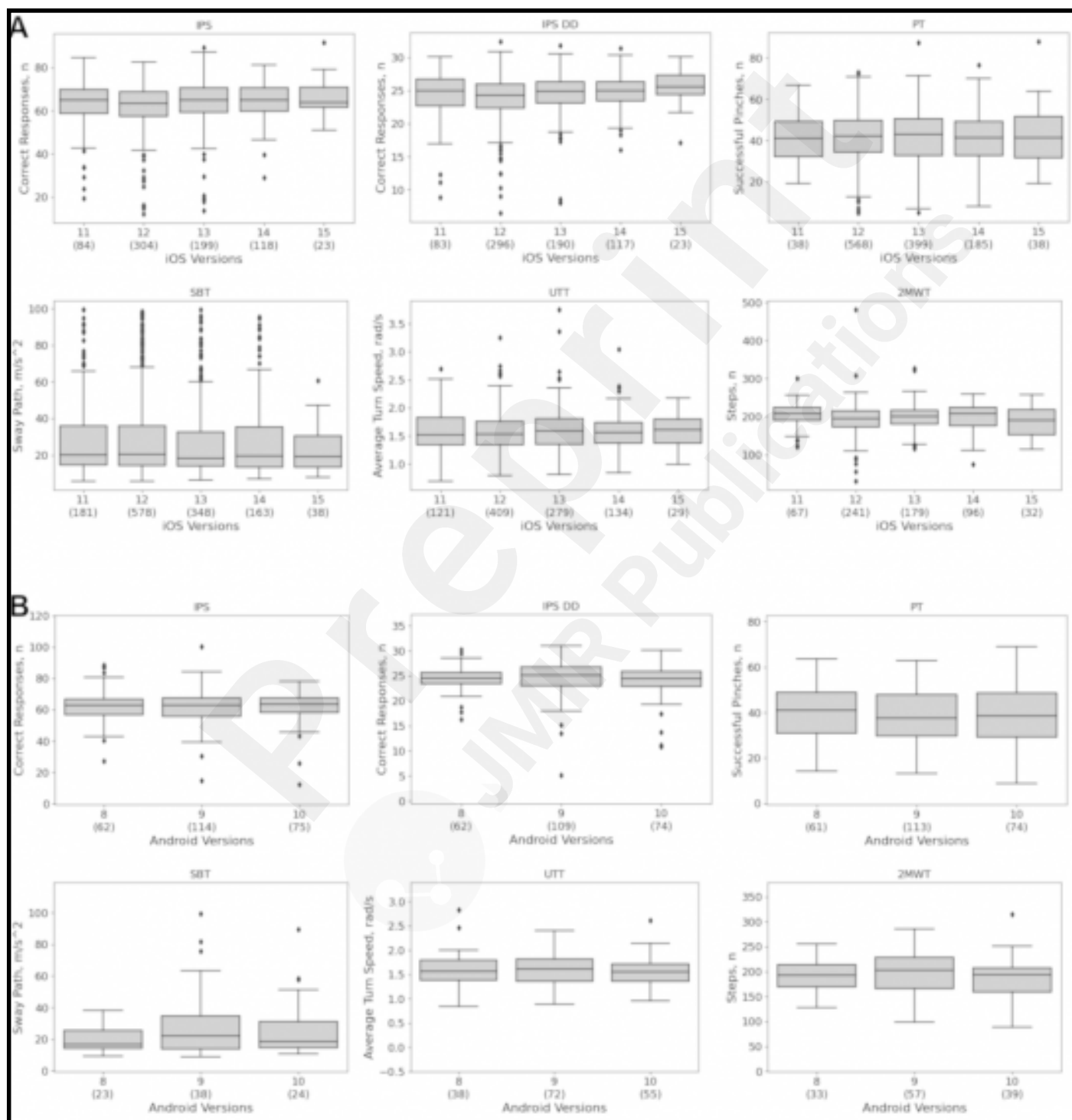
Figures

Participant deposition and the devices they used.





Measurement equivalence by iOS version (A) and Android version (B). Permutation testing revealed no evidence for a systematic lack of equivalence. No statistically significant differences were observed across OS version after correcting for multiple comparison (all P adjusted >0.05). Absolute and percent differences as well as effect sized are provided in Tables 4 and 5. Brackets indicate the sample size. 2MWT, Two-Minute Walk Test; IQR, interquartile range; IPS, Information Processing Speed; IPS DD, Information Processing Speed Digit–Digit; PT, Pinching Test; SBT, Static Balance Test; UTT, U-Turn Test.



Multimedia Appendixes

Supplementary appendix.

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CONSORT (or other) checklists

STROBE checklist.

URL: <http://asset.jmir.pub/assets/388806f3a8f62b918eddb6a22181e7a9.pdf>