Peak torque, rate of torque development and average torque of isometric ankle and elbow contractions show excellent test–retest reliability

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**Background:** Peak Torque (PT), Rate of Torque Development (RTD) and Average Torque (AT) over a single contraction assess the three components of muscle function during isometric contractions. Surprisingly, AT has never been reported or its reliability confirmed.

**Objectives:** This study aims to establish protocol reliability for ankle dorsiflexion and elbow extension isometric muscle function (PT, RTD, AT) in healthy participants using the Biodex System 3 Dynamometer.

**Methods:** Twelve participants (6 male, 6 female, mean age 39.8 ± 16.0 years) performed four maximal isometric contractions on two occasions. Intraclass Correlation Coefficient (ICC), Typical Error (TE) and Coefficient of Variation (CV) for PT, RTD and AT were reported.

**Results:** The ICC for all strength parameters varied from 0.98–0.92. TE for ankle dorsiflexion PT was 1.38 Nm, RTD 7.43 Nm/s and AT 1.33 Nm, CV varied from 6.26% to 11.72%. For elbow extension, TE was 3.36 Nm for PT, 14.87 Nm/s for RTD and 3.03 Nm for AT, CV varied from 5.97% to 18.46%.

**Conclusion:** Maximal isometric ankle dorsiflexion and elbow extension PT, RTD and AT can be evaluated with excellent reliability when following the described protocol. This testing procedure, including the application of AT, can be confidently applied in research, exercise or clinical settings.

**Keywords:** Reliability; strength testing; Biodex system 3; ankle dorsiflexion; elbow extension.
Introduction

Muscular strength is defined as the production of maximal contractile force against a resistance in a single contraction. To ensure regular functionality of the human body, muscle strength is a paramount requirement. Joint torque produced by muscle strength contributes to normal movement and athletic performance, assists in joint stability and posture control during activities of daily living and plays a vital role in the maintenance of functional independence during the aging process.2,3

The measurement of maximal muscular strength (Peak Torque (PT)) is often used to determine physical condition and the effects of training or rehabilitation programs.4 However, from a functional perspective, the ability to generate torque quickly (Rate of Torque Development (RTD)) and to maintain torque (work/Average Torque (AT) over a single contraction) may be more important than being able to generate high maximal force. Although PT is the universal standard parameter used to measure strength, changes in RTD, Work or AT over a single contraction may represent the most important adaptations occurring from training or rehabilitation.5,6

A comprehensive muscle function assessment should include all three parameters.6,7

First introduced as a device for muscle strength measurement in 1967 by Thistle et al.,8 isokinetic dynamometry is the gold standard for assessing muscular functionality among athletic populations as well as populations engaging in rehabilitation programs.9

The application of isokinetic dynamometry for assessing muscular functionality in research and clinical practice requires testing procedures of high reliability, which refers to consistent reproduction of results when tests are performed multiple times under similar conditions.10 Drouin et al.11 report excellent “mechanical reliability” (Intraclass Correlation Coefficient (ICC) 0.99) for the Biodex System 3 when using force applied by a weight on the dynamometer arm. However, potential for repeatability error increases when applying test protocols with live subjects. Numerous studies have investigated protocol reliability with excellent results (ICC > 0.75), primarily assessing in an isokinetic mode and focusing on knee extension or flexion.12–15 However, isometric mode is regarded as a safer and more appropriate mode for maximal strength testing, particularly in populations who have restricted range of motion or are unable to comply with isokinetic procedures.16 Currently, isometric reliability remains underexplored. Studies include PT and RTD only, AT was not yet investigated.17,18 PT represents the maximum torque produced at a single point of contraction.19–22 RTD measures explosive muscular strength, which is key during movement performances characterized by reduced contraction times such as sprinting or boxing.23–25 In the older or clinical population, RTD can be an indicator for the risk of falls.6 AT over a single isometric contraction can replace the commonly used isokinetic parameter work.5 Work represents the capability to generate muscle torque throughout the full range of movement22,26; this parameter cannot be applied during isometric contractions as there is no movement or distance achieved. In isometric contractions, AT over a single contraction represents the comparable capacity to maintain torque throughout the contraction time interval,5 which is an important factor when performing activities of daily living. Daily tasks generally do not require maximal strength output, but the uphold of a lower torque over a period of time, e.g., lifting a glass of water to drink, putting the washing on the washing line, etc. The ability to sustain a given level of torque production over time is the most precise indicator of functional muscle rehabilitation. It is possible for tested muscle groups to reach rehabilitation standards for maximal muscle strength without regaining the ability to sustain this standard over time; PT often returns to normal before AT or Work.7 Considering the importance of this strength parameter for the evaluation of rehabilitation programs and the appropriateness of isometric strength testing regarding safety and limited range of motion for patients, it is surprising that AT over a single contraction was never before reported during strength evaluation or its reliability established. Furthermore, other human joint actions such as ankle dorsiflexion and elbow extension have been investigated less frequently. Ankle dorsiflexion is a vital movement during the gait cycle and balance control27,28; likewise, elbow extension represents a movement of everyday function such as reaching.29 The reliability of both movements has been investigated in an isometric mode in highly homogeneous populations, i.e., older women (mean age 73.3 ± 4.7) or elite swimmers.17,18 These studies report excellent reliability (ICC 0.86–0.97) for isometric ankle dorsiflexion and elbow extension PT and RTD only.
To date, no study has assessed the test–retest reliability of all three most important parameters for muscle function (PT, RTD, AT) for isometric ankle dorsiflexion and isometric elbow extension using the Biodex System 3.

This study hypothesizes excellent protocol reliability when measuring maximal isometric ankle dorsiflexion and elbow extension strength in healthy non-athletic participants using the Biodex System 3 Isokinetic Dynamometer, with particular focus on the currently unexplored parameter AT over a single contraction. Furthermore, we set out to develop novel recommendations that ensure excellent reliability when assessing isometric PT, RTD and AT using the Biodex System 3 Isokinetic Dynamometer with the Biodex advantage software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA).

Methods

Design

This study followed a cross-sectional study of repeated measures for test–retest reliability. Each participant was familiarized in a separate session prior to the main testing at two time points. The same investigators conducted all tests and performed the verbal cueing in a consistent manner for all sessions and participants.

Participants

Twelve participants (Table 1), 6 male and 6 female (age 39.8 ± 16.0 years) (mean ± SD), height 1.68 ± 0.09 m, weight 74.1 ± 11.1 Kg) were recruited for this study. Both genders were recruited as previous studies using the Biodex System 3 for isometric strength use the same protocol for both males and females.30,31

Subjects were included if they (1) were aged between 18 and 65 years, (2) did not participate in strenuous exercise for 48 h prior to testing and (3) were in good health with no reported musculoskeletal dysfunction or surgical intervention in the tested limb within the last 12 months. Subjects were excluded if they (1) suffered from cardiovascular, respiratory or neurological impairments that would prevent physical strengthening activity or if they (2) were pregnant. The Health Science and Physiology Ethics Committee, Department of Life Science, Institute of Technology Sligo granted ethical approval, all participants provided written informed consent according to the Declaration of Helsinki.

Equipment

All tests were conducted on the Biodex System 3 Pro Isokinetic Dynamometer with the Biodex advantage software version 3.45 (Biodex Medical Systems, Inc., Shirley, New York, USA). The standard Biodex ankle unit attachment with limb support and the Biodex Velcro straps were used for ankle dorsiflexion (Fig. 1). The standard shoulder/elbow unit

![Fig. 1. Participant positioning for ankle dorsiflexion.](Image)
attachment with limb support was used for elbow extension (Fig. 2). Before testing each subject, the system was calibrated according to the procedure in the Biodex System 3 manual.32

**Participant positioning**

Ankle dorsiflexion

Participants were positioned in stocking feet on the adjustable chair with the right leg elevated. The right foot was placed on the ankle unit footplate and the right knee was supported by the standard limb support, both were tightly secured with the Velcro straps provided (Fig. 1). Maximal isometric ankle dorsiflexion strength was assessed at the ankle joint angle of 10° plantarflexion (anatomical reference of 0° was set with the tibia perpendicular to the sole of the foot), 120° knee flexion33 and 75° hip flexion.32 The axis of rotation was aligned with the body of talus, fibular malleolus, and through the tibial malleolus. The hip and knee angle were adjusted by changing the distance between the chair and the footplate and by altering the height of the knee support.

Elbow extension

Participants were positioned on the adjustable chair with their right upper arm supported by the standard limb support (Fig. 2). Maximal isometric elbow extension strength was assessed at 85° elbow flexion (angle of most force production),34 where 0° refers to full elbow extension, the shoulder joint was positioned at 45° shoulder flexion.29 The axis of rotation was aligned with the center of the trochlea and the capitulum, bisecting the longitudinal axis of the shaft of the humerus. Participants were instructed to hold the handle of the elbow/shoulder attachment with a closed grip. A 5 cm space was consistently kept between the attachment and the anatomical axis of rotation; elbow and wrist joints were aligned with the wrist in neutral position by adjusting the chair, the dynamometer and the length of the arm/shoulder attachment. The shoulder angle was achieved by altering the height of the limb support.

All joint angles were measured with a hand-held goniometer; range of motion measurement followed the Biodex procedure.

Participant positioning, i.e., chair height, dynamometer height, attachment length, etc., was recorded during familiarization to ensure consistent set-up for all testing sessions.

**Test-protocol**

All testings were performed on the Biodex System 3 Isokinetic Dynamometer in the Health Science & Physiology Laboratory. The protocol was performed at three time points: **Familiarization** (pre-test), **Test 1** (> 48 h post familiarization) and **Test 2** (at least 7 days post-test 1). For all participants, laboratory conditions were consistent and all testings were conducted on the right side only to facilitate data collection.35

During all sessions, the lower limb was warmed up first and ankle dorsiflexion was assessed, the upper limb was then warmed up and elbow extension was assessed. The warm-up consisted of 3 min of leg/arm cycling performed at a level of perceived exertion of 10–12 on the Borg scale36 and 1 set of 5 repetitions of unilateral, submaximal (perceived 50% of MVC), isometric contractions held for 5 s, separated by 5 s of rest.37 Following the warm-up, maximal isometric strength was assessed using 4 maximal isometric contractions held for 5 s, separated by 45 s of rest.38 Participants were blinded to the number of repetitions being recorded to avoid “saving energy” for later contractions.

Verbal cues given by the investigator were consistent for all participants during all sessions. For each contraction, participants were instructed to pull their toes towards their shin as “hard and as fast as possible” for ankle dorsiflexion assessment and to push their fist towards the ground as “hard and as fast as possible” for elbow extension assessment. Each participant was asked to give maximal strength each time and not to hold back.
The starting sign given by the investigator was a count down from 3, 2, 1 followed by “go”. During the 5 s contractions, the principal investigator would loudly encourage the participant by using the verbal cues “go, go, go, keep going, keep going, keep going and rest”.

**Data analysis**

From each set of four contractions, assessors identified the contraction with (1) the highest PT in Nm, (2) the highest RTD in Nm/s within the first 0.20 s of a single contraction, and (3) the highest AT in Nm of a single contraction. The time of contraction onset was identified manually (gold standard), defined as the last trough before a sharp rise. Contractions were excluded if the participant performed an early contraction or counter movement before contraction onset. Counter movement refers to the lengthening of a muscle prior to contraction, resulting in a greater strength output and is indicated by a downward deviation of more than 10% of baseline torque in the resting position.

**Statistical analyses**

Data were analyzed using the statistical package for social sciences (SPSS) for Windows (Version X, Chicago, IL, USA). Mean PT, RTD and AT were compared using a paired sample t-test. The (ICC_{2,1}) was used to calculate relative reliability. The first subscript number represents the “model” and the second subscript number signifies the “form”. Model 2 was chosen as the appropriate model when each subject is measured by each assessor, and assessors are considered representatives of a larger population of similar assessors. Form 1 represents the use of a single score, in contrast to the use of a mean of multiple assessors’ scores. As a statistical measure of absolute reliability, Typical Error (TE) and the Coefficient of Variation (CV) were calculated. These values represent the expected random variability in measurement between two assessment time points.

TE is expressed in the measurement unit it refers to calculated as

$$TE = \frac{SD_1}{\sqrt{2}},$$

where SD_1 is the standard deviation of the differences between the two measurements.

CV is expressed as a percentage score. For a sample of individuals, it is recommended to calculate a mean CV from individual CVs.

$$CV = 100 \times \frac{SD_2}{\text{mean}},$$

where SD_2 and the mean are calculated from the data of each individual.

**Results**

For ankle dorsiflexion, 5 out of 96 (5.2%) contractions were excluded, for elbow extension, 21 out of 96 (21.8%) were excluded.

Individual results for each strength parameter for Tests 1 and 2 are given in Table 2. The means,

| Table 2. Individual results for PT, RTD and AT for each test. |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Subject ID      | PT (Nm) Test 1  | PT (Nm) Test 2  | RTD (Nm/s) Test 1 | RTD (Nm/s) Test 2 | AT (Nm) Test 1 | AT (Nm) Test 2 | PT (Nm) Test 1 | PT (Nm) Test 2  | RTD (Nm/s) Test 1 | RTD (Nm/s) Test 2 | Elbow Extension |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 1               | 22.6            | 23.6            | 51.5            | 62.5            | 19.28           | 19.53           | 23.7            | 24.1            | 47.5            | 21.5            | 20.29           | 19.15           |
| 2               | 37.8            | 43.5            | 163.5           | 196.0           | 35.36           | 40.48           | 81.6            | 94.8            | 194.0           | 249.0           | 66.08           | 80.96           |
| 3               | 43.9            | 45.2            | 214.0           | 215.0           | 40.10           | 41.70           | 67.7            | 80.7            | 234.5           | 169.5           | 61.00           | 61.16           |
| 4               | 21.3            | 25.4            | 101.5           | 122.0           | 18.59           | 23.08           | 29.7            | 28.6            | 105.5           | 94.0            | 25.60           | 23.49           |
| 5               | 27.7            | 26.6            | 125.0           | 114.5           | 22.78           | 24.04           | 45.0            | 41.5            | 147.0           | 81.5            | 36.35           | 34.55           |
| 6               | 25.9            | 25.2            | 118.0           | 104.5           | 23.86           | 22.90           | 35.9            | 33.0            | 148.0           | 126.0           | 33.43           | 29.10           |
| 7               | 21.7            | 21.7            | 61.5            | 89.5            | 20.18           | 20.17           | 31.9            | 33.4            | 80.5            | 97.5            | 29.11           | 28.37           |
| 8               | 19.7            | 14.4            | 86.0            | 58.5            | 18.09           | 13.52           | 24.4            | 25.6            | 70.5            | 76.5            | 21.76           | 23.94           |
| 9               | 24.3            | 22.0            | 100.5           | 85.0            | 22.73           | 18.82           | 70.2            | 58.7            | 193.0           | 218.5           | 61.22           | 52.20           |
| 10              | 44.7            | 44.3            | 199.5           | 214.0           | 42.38           | 41.48           | 65.8            | 61.4            | 223.5           | 214.0           | 57.74           | 57.14           |
| 11              | 33.1            | 36.9            | 147.0           | 178.5           | 29.80           | 29.50           | 68.7            | 72.5            | 123.5           | 156.5           | 60.23           | 57.66           |
| 12              | 27.5            | 25.4            | 116.0           | 112.0           | 24.73           | 22.68           | 37.0            | 33.9            | 74.0            | 55.5            | 34.61           | 30.05           |
standard deviations and reliability values for PT, RTD and AT are presented in Table 3. There were no significant differences between tests 1 and 2 for all measures for both ankle dorsiflexion and elbow extension \((p > 0.05)\).

### Reliability analysis

Relative reliability (ICC) was excellent\(^5\) for ankle dorsiflexion (PT 0.98, RTD 0.96, AT 0.98) and for elbow extension (PT 0.98, RTD 0.92, AT 0.98).

TE for ankle dorsiflexion PT was 1.38 Nm, RTD 7.43 Nm/s and AT 1.33 Nm, CV was 6.26% for PT, 11.72% for RTD and 6.44% for AT.

For elbow extension, TE was 3.36 Nm for PT, 14.87 Nm/s for RTD and 3.03 Nm for AT, CV was 6.05% for PT, 18.46% for RTD and 5.97% for AT.

### Discussion

According to Fleiss,\(^5\) ICCs in the range of 0.5–0.6 = fair, 0.6–0.7 = good and > 0.75 = excellent test–retest reliability. When measuring PT, RTD and AT for maximal isometric ankle dorsiflexion and elbow extension with the described protocol using the Biodex System 3 Isokinetic Dynamometer, this study established that the test–retest reliability was excellent (ICC 0.92–0.98). Excellent reliability implies high precision of measurement and allows confidence when assessing strength changes following exercise or rehabilitation programs.\(^10\) The combination of all three strength parameters offers a comprehensive analysis of muscle function or recovery.\(^7\)

Relative and absolute reliability established in this study is higher than the previously reported values for ankle dorsiflexion and elbow extension.\(^17,18,29,37\) Previous reliability studies for ankle dorsiflexion and elbow extension have reported PT ICC values ranging from 0.80 to 0.97.\(^17,18,29,37\) Contraction mode may be an influencing factor; joint movement during isokinetic testing appears to result in lower reliability values.\(^29,37\) Furthermore, it is important to record participant positioning to ensure exact replication of protocol.\(^18\) It is not surprising that ICC values are slightly lower due to potential positioning difficulties when assessing individuals who suffered a stroke, particularly, if equipment modification is required.\(^29\)

Reliability (ICC, TE and CV) for RTD in this study is generally lower than for PT and AT. Participants were instructed to contract as hard and fast as possible. Although this is a recommended practice, participant’s attention may be more focused on reaching highest peak values, with less emphasis on producing explosive muscular strength.\(^46\) However, RTD ICC values in this study are higher than in the previous similar studies (0.84–0.86).\(^17\) Variability in the methods for obtaining RTD values may be one reason for differing results. In this study, RTD was calculated

### Table 3. Means, standard deviations and reliability measures for PT, RTD and AT.

|                      | PT (Nm) | RTD (Nm·s\(^{-1}\)) | AT (Nm) |
|----------------------|---------|---------------------|---------|
| **Ankle dorsiflexion** |         |                     |         |
| Test 1 \((n = 12)\)  | 29.18 ± 8.73 | 123.67 ± 50.14 | 26.49 ± 8.47 |
| Test 2 \((n = 12)\)  | 29.52 ± 10.25 | 129.33 ± 56.89 | 26.49 ± 9.64 |
| T1–T2 Difference \((p)\) | 0.72 | 0.35 | 1.00 |
| TE                   | 1.38 | 7.43 | 1.33 |
| ICC (95% CI)         | 0.98 (0.91–0.99) | 0.96 (0.88–0.99) | 0.98 (0.92–0.99) |
| CV (%)               | 6.26 ± 6.25 | 11.72 ± 8.27 | 6.44 ± 6.69 |
| **Elbow extension**  |         |                     |         |
| Test 1 \((n = 12)\)  | 48.47 ± 20.83 | 136.79 ± 63.51 | 42.29 ± 17.49 |
| Test 2 \((n = 12)\)  | 49.02 ± 23.80 | 129.99 ± 71.50 | 41.48 ± 19.54 |
| T1–T2 Difference \((p)\) | 0.79 | 0.53 | 0.63 |
| TE                   | 3.36 | 14.87 | 3.03 |
| ICC (95% CI)         | 0.98 (0.92–0.99) | 0.92 (0.74–0.98) | 0.98 (0.92–0.99) |
| CV (%)               | 6.05 ± 3.82 | 18.46 ± 14.78 | 5.97 ± 4.52 |

**Notes:** The highest PT, the highest RTD and the highest AT of the four contractions of each individual in Tests 1 and 2 were used to calculate means, standard deviations and the reliability analyses.
using the manual procedure recommended by Biodex System 3 (initial contraction onset to 0.2 s).\textsuperscript{32} RTD has previously been reported for other time intervals, e.g., 0–50 ms, 0–50\% of PT and 40–80\% of PT.\textsuperscript{17,47} Considering that RTD is an indicator of initial contraction torque,\textsuperscript{23–25} measurements should start at contraction onset. It is worth noting that the Biodex advantage software version 3.45 only allows time intervals of 200 ms when analyzing data using the cursor function, or time intervals of 100 ms when using the “log to file” application. This limits the ability to analyze RTD at shorter time intervals.

To our knowledge, this study is the first to include AT over a single isometric contraction. Our findings suggest that the analysis of AT is highly reliable for ankle dorsiflexion (ICC 0.98) and elbow extension (ICC 0.98) and should therefore be implemented in future isometric strength-testing studies. To assess a participant’s torque generating capacity in all aspects, it is important to include all three of the aforementioned strength parameters, as one parameter alone does not provide a comprehensive insight into muscular function.

In this study, values for TE and CV are lower than the previously reported ones,\textsuperscript{17,37} indicating better test–retest reliability. Differences may be due to the lack of familiarization with the testing equipment and procedure.\textsuperscript{17} A lack of a familiarization session may affect scores of the second testing session due to a learning effect.\textsuperscript{17} Dynamic modes appear to result in lower absolute reliability,\textsuperscript{37} i.e., higher TE and CV values.

Early contractions and counter movements occurred more frequently during elbow extension than ankle dorsiflexion. Observations during testing revealed that more efficient participant positioning could be achieved when performing ankle dorsiflexion compared to elbow extension. During ankle dorsiflexion, all involved joints can be firmly stabilized. In comparison, during elbow extension, the upper arm cannot be firmly strapped to the elbow support due to contraction restriction, potentially resulting in higher technique variability. It may be necessary to address this issue when giving verbal instructions.

Compared to other reliability studies, this study consists of a relatively small sample size ($n = 12$). It is advised to base sample size calculations for reliability studies on the ICC value and width of the confidence interval. The higher the ICC value, and the narrower the width of the confidence interval, the smaller the sample size requirement.\textsuperscript{38,49} Based on the lowest ICC value (0.92) and its widest width of confidence interval (0.24) achieved in this study, the sample size of 12 participants is sufficient when calculated as follows\textsuperscript{50}:

$$k = \frac{8z^2 \left(1-p\right)^2 (1+(n-1)p)^2}{w^2 n (n-1)}$$

where $k$ = number of subjects rated, $n$ = number of tests, $p$ = ICC value, $w$ = width of 95\% confidence interval.

**Recommendations for achieving excellent reliability**

Assessor observation and comparison with previous studies has led to a number of recommendations resulting in excellent reliability when closely followed:

- Familiarization session should take place prior to test 1.
- Subject positioning should be carefully recorded and reproduced at each testing session.
- Participants should be blinded to the number of repetitions being recorded to avoid “saving energy” for later contractions. Each participant should be instructed to give maximal strength each time and not to hold back.
- To ensure accurate curve analysis, the designed protocol should represent the desired number of repetitions as sets consisting of 1 repetition. For example, in this study, 4 sets of 1 repetition was implemented rather than 1 set of 4 repetitions. When recording numerous repetitions per set, strength curves cannot be viewed individually, this may compromise the accuracy of manual analysis.
- To reduce the number of excluded contractions, how to avoid counter movements should be explained to participants and the importance to wait for “go” before contracting should be emphasized.
- Calculation of the novel parameter AT over a single contraction using the Biodex Software: select a specific contraction in the curve analysis program, click on the “log to file” application and save the data as a text document. The text document can then be opened in a spread sheet and calculations performed as normal.
**Limitations**

The inclusion criteria regarding age of participants in this study allowed for a wide age range to be recruited. Participation was voluntary and open to all staff and students of the Institute of Technology. This resulted in high age heterogeneity, which differs from other studies. This study, however, did not aim to assess reliability according to age category and there are no obvious reasons why age in a healthy population should affect reliability. Although the relatively small sample size is sufficient for reliability testing, it does not allow for subgroup analysis, i.e., age categories, sex, dominant versus non-dominant side.

**Conclusion**

This study is the first to establish excellent test–retest reliability for all three strength parameters (PT, RTD and AT) for isometric ankle dorsiflexion and elbow extension for the described protocol using the Biodex System 3 Isokinetic Dynamometer. Furthermore, this study has proven AT to be a reliable strength parameter when testing in an isometric mode. When the aforementioned-recommended procedures are closely followed, this testing protocol can be confidently applied in research, exercise science or clinical populations, in which impairments in ankle dorsiflexion and elbow extension are common.

**Conflicts of Interest**

All contributors are independent authors and there are no conflicts of interest regarding this paper.

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**Author Contributions**

Daniel JC Simpson and Monika Ehrensberger contributed to study design, acquisition of data, analysis and interpretation of data, and writing of the manuscript. Study design, acquisition of data and revision of manuscript were carried out by Christopher Nulty. Joanne Regan contributed to study design, interpretation of data, and revision of manuscript. Patrick Broderick contributed to acquisition of data, and revision of manuscript. Dr. Catherine Blake carried out the analysis and interpretation of data and revision of manuscript. Dr. Kenneth Monaghan contributed to study design, interpretation of data and revision of manuscript.

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