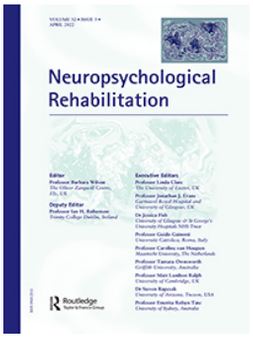

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Remote administration of BICAMS measures and the Trail-Making Test to assess cognitive impairment in multiple sclerosis

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ABSTRACT

Reliable remote cognitive testing could provide a safer assessment of cognitive impairment in multiple sclerosis (MS) during the COVID-19 pandemic and thereafter. Here we aimed to investigate the reliability and feasibility of administering Brief International Cognitive Assessment for MS (BICAMS) and the Trail-Making Test (TMT) to people with MS online. Between-group differences on BICAMS and the TMT were examined in a sample of 68 participants. Group 1 ($N = 34$) was tested in-person pre-pandemic. Group 2 was tested remotely. Within-group differences for in-person and virtual administrations were examined for Group 1. No significant differences between virtual and in-person administrations of the CVLT-II and SDMT were detected. BVMT-R scores were significantly higher for virtual administrations ($M = 20.59$, $SD = 6.65$) compared to in-person administrations ($M = 16.35$, $SD = 6.05$), possibly indicating inter-rater differences. Strong positive correlations were found for in-person and virtual scores within Group 1 on the CVLT-II ($r = .84$), SDMT ($r = .85$), TMT-A ($r = .88$), TMT-B ($r = .76$) and BVMT-R ($r = .72$). No significant differences between in-person and remote administrations of CVLT-II and SDMT in people living with MS were detected. Recommendations for future studies employing the TMT and BVMT-R online are provided.

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SWAT; Study-within-a-trial; Cognitive assessment; Remote testing; Multiple sclerosis

Introduction

Cognitive impairment in multiple sclerosis (MS) is reported to have prevalence rates between 40% and 65% (Amato et al., 2006; DiGiuseppe et al., 2018; Lovera

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& Kovner, 2012). Frequently impaired domains include information-processing speed, working memory, verbal and visual memory, verbal fluency and executive functions (Rao et al., 1991, may 1). Cognitive impairment can considerably impact a person's functioning and quality of life (Pierson & Griffith, 2006), and has been associated with difficulties in managing home and self-care, impaired social functioning, lower life satisfaction and decreased employability (Kalmar et al., 2008). Research in the field of memory rehabilitation in MS has, however, started to show promising results for memory rehabilitation interventions in improving outcomes in memory functioning and quality of life (Taylor et al., 2021).

The Coronavirus disease 2019 (COVID-19) pandemic has had a profound impact on conducting research with human populations, particularly with individuals living with auto-immune diseases such as MS. In-person research trials have been disrupted worldwide, resulting in new challenges for researchers (Goldsack et al., 2020), with possible long-term impacts on the execution of research (Sohrabi et al., 2021, january 12). A recent study revealed that 83% of respondents with MS reported strict self-isolation during the pandemic (Moss et al., 2020) and may be at high risk of refraining from seeking medical attention if having a relapse (Alnajashi & Jabbad, 2020).

Ensuring pre-COVID-19 levels of healthcare has been a challenge for medical professionals working with people with MS (Morrison et al., 2021; Sastre-Garriga et al., 2020). A recent survey, conducted on behalf of the *European Committee for Treatment and Research in Multiple Sclerosis* revealed telemedicine to be the primary or exclusive method of clinical management for 92% of responding neurologists (Portaccio et al., 2021, march 25). Moreover, telemedicine was reported to be a newly activated care strategy for 73% of those respondents. With the development of new telehealth strategies in both MS-related research and healthcare, the investigation into the reliability of an online assessment is warranted.

With respect to cognitive assessment in MS, there is the potential for reliable measures to be administered remotely, which would potentially reduce risk and anxiety regarding contracting the virus during the pandemic and thereafter. Regardless of the pandemic, travel to medical centres can be stress-inducing, particularly for those with reduced mobility, bladder issues, fatigue or visual deficits. Such difficulties may also be compounded by cognitive impairment and resulting stress and anxiety can thus impact on obtaining a reliable reading of cognitive ability. Reliable virtual testing could provide safer and more convenient care for MS patients; provide more accessible means of identification of patients with early signs of cognitive impairment; as well as facilitating participation in large-scale studies.

The current study-within-a-trial (SWAT) occurs within a host trial investigating the feasibility of a novel therapy, the Cognitive Occupation-Based programme for people with Multiple Sclerosis (COB-MS) (Dwyer et al., 2020;

Hynes & Forwell, 2019; Reilly & Hynes, 2018), which provides holistic cognitive rehabilitation in MS through an individualized intervention, measured by and taught through an occupational participation perspective. Pre-pandemic, the host trial's protocol stipulated the administration of cognitive assessments to participants in their homes, with intervention sessions taking place in community centres. The arrival of COVID-19 in Ireland brought the project to a halt, as in-person testing became unsafe due to the risk of spreading the virus. Testing resumed *virtually* via the videoconference platform Zoom for Healthcare (Zoom Video Communications Inc, 2016), following a six-month delay that included renewed ethical approval for an online adaptation of the project (Galway Clinical REC reference 2231, updated approval 3rd September 2020, and NUI Galway REC 19-Oct-10, updated approval 16th September 2020).

With respect to the host trial's outcome measures, the Brief International Cognitive Assessment for MS (BICAMS) (Langdon et al., 2012) recommends the California Verbal Learning Test, Second Edition (CVLT-II) (Woods et al., 2006), the Symbol Digits Modalities Test (SDMT) (Smith, 1982) and the Brief Visuospatial Memory Test-Revised (BVMT-R) (Benedict, 1997) as a battery of cognitive assessments in MS. The Trail-Making Test (TMT) (Reitan & Wolfson, 1992) is also a widely used measure of processing speed, visual scanning and divided attention in MS (Bowie & Harvey, 2006). Previous studies have found that the SDMT and CVLT-II yield indistinguishable results when delivered remotely with samples matched on demographic and disease quality variables (Barcellos et al., 2018; Barcellos et al., 2021).

To our knowledge, no research to date has investigated the reliability of remote administration of the traditional BVMT-R or the TMT in MS patients. Furthermore, previous studies examining remote CVLT-II delivery only address performance on trials 1–5 and have neither reported on potential differences between short- and long-delay trials nor on recognition trials. Thus, the current SWAT aims to investigate the: reliability of administering BICAMS and the TMT to MS patients online; the feasibility of delivering both the TMT and, the third component of BICAMS, the BVMT-R online; and to replicate and extend previous research on the reliability of remote administration of the CVLT and SDMT (Barcellos et al., 2018; Barcellos et al., 2021), by comparing in-person and virtual test scores.

Method

Design

Due to the pandemic, we were unable to counterbalance in-person and virtual administrations between groups. Therefore, a within- and between- group design was employed. Between-group differences on the CVLT-II, SDMT, BVMT-R and TMT were examined in participants who received in-person

testing prior to the pandemic (Group 1) and participants who were not tested prior to the pandemic, but who received virtual testing only (Group 2). Within-group differences were also investigated for Group 1, where scores obtained at in-person assessments were compared within the same group with scores obtained virtually six months later when the project resumed online. Risk of practice effects between in-person and virtual administrations for Group 1 were minimized given the six-month delay between testing sessions.

Sample

Participants were recruited to the main trial via poster advertisements in neurology, community and primary care clinics around the Republic of Ireland, as well as through local radio stations, local and national newspapers, social media and the MS Ireland website. Participants who were 18 years or older, fluent in English, residents of Republic of Ireland with no other neurological history and not experiencing an active relapse were deemed eligible for the study. Participants who were excluded from the main trial were those with cognitive impairment that may affect reliable participation or capacity to give informed consent; or those who were incarcerated or institutionalized.

The SWAT sample ($N = 68$) consisted of two groups. Group 1 (34 participants; 11 males, 23 females) received in-person testing prior to the pandemic and, again six months later through virtual means when the study resumed online. Notably, three participants who received in-person testing as part of Group 1, dropped out of the study due to other commitments and were not tested virtually at the second time point. Group 2 consisted of 34 participants who received virtual testing only – randomly selected from the 110 participants taking part in the host trial (10 males, 24 females).

Measures

The Brief International Cognitive Assessment for MS (BICAMS) (Langdon et al., 2012) recommends a battery of assessments for measuring cognitive impairment in MS, based on an expert consensus of neurologists and neuropsychologists with in-depth clinical and research experience. BICAMS includes the Symbol Digits Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II) and the Brief Visuospatial Memory Test-Revised (BVMT-R), and has been shown to be a good predictor of functional performance in MS (Goverover et al., 2016).

Symbol Digits Modalities Test

Symbol Digits Modalities Test (SDMT) (Smith, 1982) is a test of processing speed and has been shown to be the strongest predictor of future cognitive

impairment in MS. Participants are required to match the correct number corresponding to a symbol in a given key. The test has excellent test-retest reliability ($r = .97$) for individuals with MS (Benedict, 2005). The written version of the SDMT was used for in-person testing, whereas the oral version of the SDMT was used online. The written version was not used for online administration as participants would have been able to alter the sheet or complete the sheet following the online session before sending back the assessment booklet.

California Verbal Learning Test-II

The California Verbal Learning Test-II (CVLT-II) (Woods et al., 2006) is a test of verbal memory and consists of five consecutive trials in which a 16-word list is read aloud to the participant. The participant is asked to recall as many words as possible on a given trial. The list contains four categories of four words and these words are arranged randomly in the list. Participants are also asked to recall as many words as possible after a 20-min delay for long-delay trials. The CVLT-II has an inter-rater reliability of .80–.96 (Delis, 2000). In five cases where internet connection was unstable during remote testing, the CVLT-II was administered via phone call instead of over Zoom to ensure that participants could clearly listen to the words being read out without distraction, and so that the responses could be accurately recorded by the researcher.

Brief Visuospatial Memory Test – Revised

The Brief Visuospatial Memory Test – Revised (BVMT-R) (Benedict, 1997) consists of three consecutive trials in which the participant is presented with a 2×3 stimulus array of abstract geometric figures for 10 s. The participant is required to accurately draw the figures in their correct location on the page. Participants must also recall the display after a 20-minute interval. Following the delay trial, participants must identify the six figures that were previously shown in the presence of six distractor stimuli. The BVMT-R is shown to have 0.96–0.97 inter-rater reliability (Benedict, 1997). For virtual testing, stimuli were presented via Microsoft PowerPoint to ensure constancy of the images. Blank response sheets were posted out prior to testing, which were clearly labelled by trial, and presented on thick paper (100 g bond inside and 250 g cover) to ensure that indentations from previous trials did not influence performance on subsequent trials. Participants were kindly asked to refrain from turning back to previous trials to help them remember the geometrical figures they had previously drawn. Following the direct recall trial, participants were instructed to seal their responses in an envelope provided by the researchers to prevent any changes being made after the testing session.

Trail-Making Test

The Trail-Making Test (TMT) (Reitan & Wolfson, 1992) consists of two parts – Part A and Part B. Part A assesses visual scanning and motor skills and involves

joining encircled numbers from 1 to 25, as quickly as possible. Part B is a measure of cognitive flexibility and task-switching as the participant is requested to join numbers and letters in alternating order (1-A-2-B). Both parts must be completed within 5 min. The TMT has excellent construct validity with the Wechsler Adult Intelligence Scale-III (Sánchez-Cubillo et al., 2009; Wechsler, n.d.) and excellent inter-rater reliability (Bowie & Harvey, 2006). The written version of the TMT was administered during both in-person and virtual sessions, as some authors have suggested there is a limited clinical utility for the oral TMT-A (Ruchinskas, 2003).

For online sessions, participants received test sheets prior to the Zoom meeting by post and completed Parts A and B in the virtual presence of the researcher whereby performance was timed during the Zoom session. Test sheets were unsealed in the presence of the researcher. Participants were requested to position their devices so that the research assistant could monitor their progress over the camera and provide feedback whenever an error occurred. However, for some participants (e.g., mobile phone users) this was not always possible. In such cases, if a trail was not correctly completed, the data was removed from the analysis.

Multiple Sclerosis Neuropsychological Questionnaire

Multiple Sclerosis Neuropsychological Questionnaire (MSNQ) (Benedict et al., 2003) is a self-report screening measure for cognitive impairment in MS. The MSNQ includes 15 items that are designed to assess cognitive functioning during daily activities in people living with MS, regarding various domains, including attention, processing speed and memory. Scores >22 are indicative of cognitive impairment in MS. MSNQ has been shown to have good test-retest reliability (.90) and good internal consistency (cronbach's $\alpha = .94$). MSNQ scores were assessed to provide a comparison of self-reported cognitive difficulties between groups.

Procedure

Participants were contacted via telephone to arrange a session where a research assistant visited them at their homes prior to the COVID-19 pandemic (Group 1) or via Zoom (Group 2). In-person assessments and the subsequent online assessments were conducted by different research assistants.

For both in-person and virtual assessments, participants were asked to sit where they had a surface on which they could comfortably write. Assessment material, including paper to draw or write, was provided by the research assistant on the day of the assessment for in-person sessions. For virtual sessions, test sheets were bound into testing booklets and sent by post prior to the meeting for virtual sessions clearly marked, "Do not open", to prevent any exposure to

SDMT and TMT test sheets prior to testing, along with documentation providing tips and guidelines for using Zoom. Participants were requested to open the sealed envelopes which contained the test booklets on camera in the presence of the research assistant. Although oral SDMT was administered for online assessments, test sheets were included in the booklet to participants prior to Zoom sessions to ensure that all participants had access to the test in A4 format, regardless of the device that they used to take part in the study. For virtual sessions, participants were advised to be seated in an area of strong internet connection. Assessments were presented to all participants in the same order for both in-person and virtual administrations. The assessments started with trials 1–3 of the BVMT-R, followed by the CVLT-II immediate and short-delay trials, the TMT, the SDMT, the BVMT-R long-delay and then finally, the CVLT-II long-delay trials. Participants were offered breaks as needed throughout the assessment period. The breaks were essential for the needs of the cohort given common difficulties with physical and cognitive fatigue, and a recommendation of the host trial's *Public and Patient Involvement* panel. The breaks were timed in a way that did not interfere with the required delays of assessments such as the CVLT-II.

Sound and visual checks were performed at the beginning of each virtual meeting. Any possible background distractions were addressed at the beginning of the session to minimize the risk of interruptions during testing. BVMT-R stimuli were presented via PowerPoint presentation. TMT and SDMT were also delivered using PowerPoint as a visual aid to facilitate the participants' understanding of the task. Some participants had difficulty identifying key areas on test sheets (e.g., double line to indicate the end of practice boxes on SDMT; the number "1" starting point on TMT). In such cases, a visible red mouse cursor was used during administration to point out certain aspects of the tests on the PowerPoint slides for any participants who may have had visual or attentional difficulties, at the recommendation of the host trial's *Public and Patient Involvement* panel.

Data analysis

Independent samples *t*-tests were conducted to examine between-group differences in Group 1 and Group 2 scores on the CVLT-II; SDMT; and the BVMT-R. Completion times for the TMT were positively skewed, thus violating assumptions for the use of parametric tests. Mann–Whitney *U* tests were conducted to examine between-group differences for TMT Part A and Part B completion times.

Paired-samples *t*-tests were used to examine within-group differences in Group 1 for in-person and online assessments of the CVLT-II; SDMT and BVMT-R. Non-parametric Wilcoxon tests were used to assess within-group differences on the TMT-A and TMT-B for Group 1. Correlations for in-person and

virtual administrations within Group 1 are reported. Bland Altman plots were constructed to assess the level of agreement between in-person and virtual assessments for Group 1.

In-person and virtual assessments were administered by different research assistants (EB and FR respectively). Due to the retrospective nature of the study, it was impossible to control for inter-rater differences. To address this issue, between-group differences between Group 1 virtual scores and Group 2 scores are reported to serve as a comparison in cases where differences between in-person and virtual scores may be attributed to differences in rater scoring.

A supplementary analysis was conducted to investigate differences in performance between laptop and phone users for virtual sessions. As participants were tested by means of their own technological devices, screen size varied across participants, which may have impacted performance, particularly in the measuring of visuospatial memory using the BVMT-R (see Appendix).

Results

Descriptive statistics for demographic variables (age; number of years since diagnosis of MS; and years in education) are presented in Table 1. Date of MS diagnosis was not reported for five participants in Group 1 and Group 2. No significant differences were found between groups for age, duration of MS, years in education or MSNQ scores. Frequencies for MS subtype are also presented in Table 1. A chi-square test of independence revealed no significant differences in the frequencies of relapsing-remitting MS and progressive disease subtypes between groups.

California Verbal Learning Test-II

No significant differences were found regarding total recall scores on the CVLT-II between Group 1 and Group 2. There were no significant within-subjects

Table 1. Demographic variables for Group 1 and Group 2.

	Group 1		Group 2	
	M	SD	*M*	SD
Age (years)	48.59	8.96	47.56	9.90
Duration of MS (years; $N = 29$)	11.66	7.51	12.57	8.56
Education (years)	16.03	3.74	16.35	2.41
MSNQ	33.88	6.03	34.47	8.38
Disease Subtype	*N*		*N*	
Relapsing-remitting (*N*)	22		25	
Primary progressive (*N*)	6		3	
Secondary progressive (*N*)	5		5	
Progressive relapsing (*N*)	1		0	
Unknown	0		1	

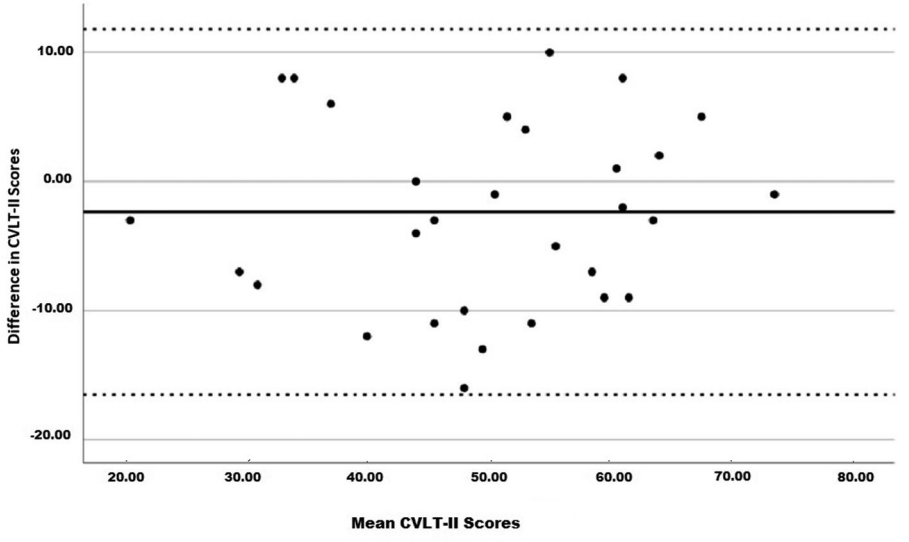

Figure 1. Bland–Altman plot demonstrating differences and means of CVLT-II total recall scores between in-person testing and remote testing.

difference for Group 1, with in-person scores significantly correlated with virtual scores after a 6-month interval ($r = .84$, $p < .001$). A Bland Altman plot was constructed to assess the level of agreement between in-person and virtual assessment techniques (see Figure 1). A linear regression investigating the relationship between mean scores and differences between the two measures was non-significant, suggesting no proportional bias between the two forms of administration. No significant differences were found between Group 1 and Group 2 on performance on short-delay trials, long-delay trials and recognition trials. Table 2 reports the breakdown of the mean and standard deviations across group 1 (virtual and in-person) and group 2 (virtual) for each sub-test. Correlations can be seen in Figure 2 scatterplot, which indicates that there is a strong positive correlation between both forms of administration, though more participants sit below the line of equality. An independent samples *t*-test revealed no significant differences between virtual administrations for Group 1 and Group 2.

Symbol Digits Modalities Test

No significant difference was found between Group 1 and Group 2 on SDMT scores. There was no significant within-subject differences for Group 1, with written SDMT scores for Group 1 strongly correlated with oral SDMT scores administered at virtual testing after a 6-month interval ($r = .85$, $p < .001$). Table 2 reports the mean and standard deviations across the groups. A Bland Altman plot was constructed to assess the level of agreement

Table 2. Descriptive statistics for CVLT-II, SDMT, TMT, BVMT-R, TMT (A and B).

	Group 1 ($n = 34$; in-person)		Group 2 ($n = 34$; virtual)		Group 1 ($n = 31$, virtual)	
	M	SD	*M*	SD	*M*	SD
CVLT-II						
Total recall	50.74	12.20	53.02	11.98	48.84	13.09
Short-delay free recall	9.82	3.72	10.35	3.49	9.84	4.00
Short-delay cued recall	11.21	3.23	11.68	3.08	11.52	3.60
Long-delay free recall	10.44	3.66	11.12	4.33	10.35	4.26
Long-delay cued recall	11.68	3.01	11.53	3.50	11.48	3.20
Recognition hits	14.56	2.06	14.65	1.82	14.68	1.96
False alarms	3.65	5.09	2.09	2.69	3.45	3.38
SDMT	40.45	13.52	46.67	12.10	41.5	13.19
BVMT-R						
Total recall	16.35	6.05	20.59	6.65	18.61	7.47
Learning	3.68	1.74	3.50	1.78	3.39	2.14
Long-delay recall	6.32	2.85	7.98	2.70	7.16	3.12
Recognition hits	5.15	1.21	5.06	1.15	5.55	.89
False alarms	.21	.73	.11	.41	.23	.72
	Median	Min–max	Median	Min–max	Median	Min–max
TMT A (s)	32.15	21.10–112.45	30.66	10.37–64.96	28.57	18.36–90.90
TMT B (s)	59.23	35.52–153.02	56.59	24.63–159.33	54.10	24.63–159.33

between in-person (written) and virtual (oral) assessments for the SDMT (see Figure 3). A linear regression investigating the relationship between mean scores and differences revealed no proportional bias, indicating a good level of agreement in written and oral SDMT scores within Group 1. An independent samples *t*-test revealed no significant differences between SDMT scores on virtual administrations for Group 1 and Group 2. A strong positive correlation can be seen on SDMT scores for in-person testing (written) and remote (oral) testing after a 6-month interval within Group 1 in Figure 4.

Brief Visuospatial Memory Test – Revised

A statistically significant difference was detected between in-person (Group 1) and virtual administration (Group 2) of the BVMT-R, $t(66) = -2.75$, $p = .008$. Total recall scores tended to be higher for virtual testing ($M = 20.59$, SD = 6.65) compared to in-person testing ($M = 16.35$, SD = 6.05; see Figure 5). No significant differences were found in learning scores, or in hits and false alarms in recognition trials between groups. No significant difference was detected between virtual scores for Group 1 and Group 2. The mean scores for each sub-test along with the standard deviation are reported in Table 2. A Bland Altman plot was constructed for means and differences for in-person and virtual administrations of the BVMT-R total recall scores (see Figure 6). A linear regression investigating the relationship between mean

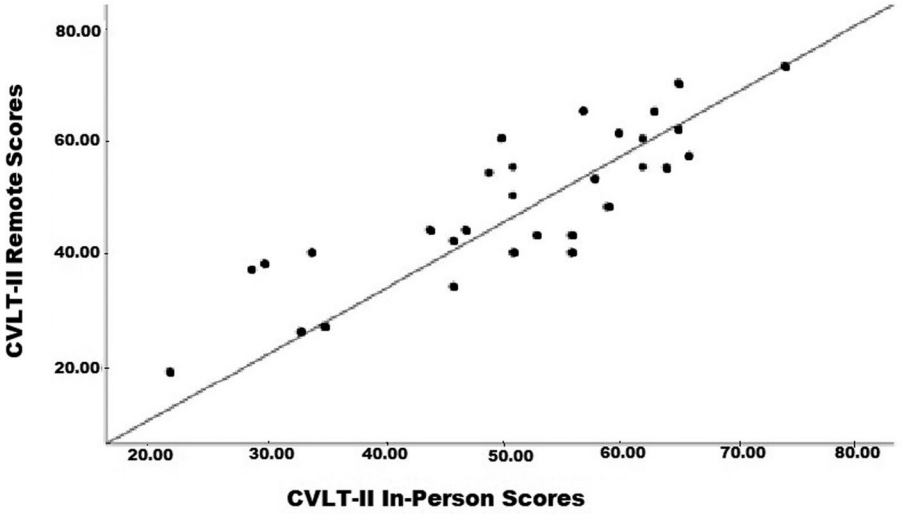

Figure 2. Scatter plot of in-person and remote testing CVLT-II for Group 1.

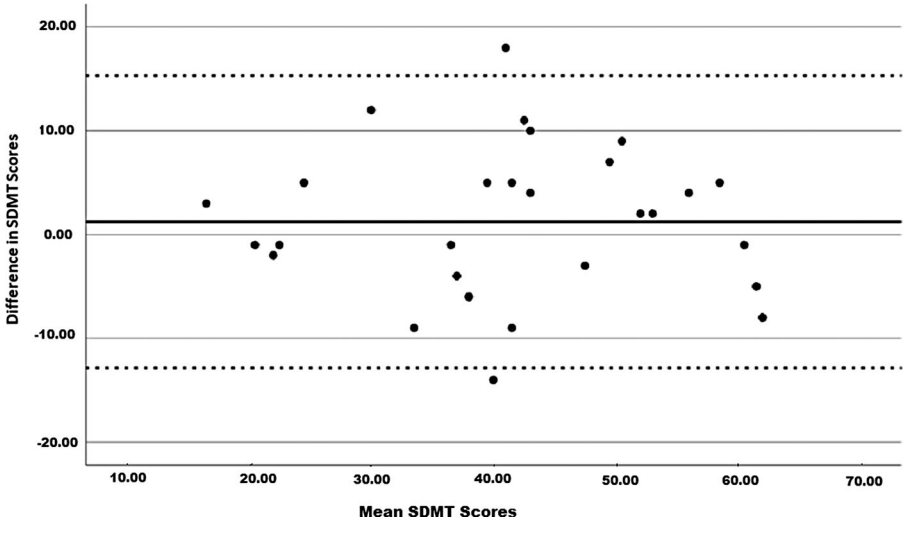

Figure 3. Bland Altman plot demonstrating differences and means of SDMT written (in-person) and virtual (oral) scores.

scores and differences was non-significant, suggesting a good level of agreement in in-person and virtual administrations of the BVMT-R within Group 1. In-person and virtual scores were strongly correlated for Group 1 after a six-month interval ($r = .72$, $p < .001$; see Figure 7). Scores tended to be higher for virtual administrations within Group 1, although this did not achieve statistical significance.

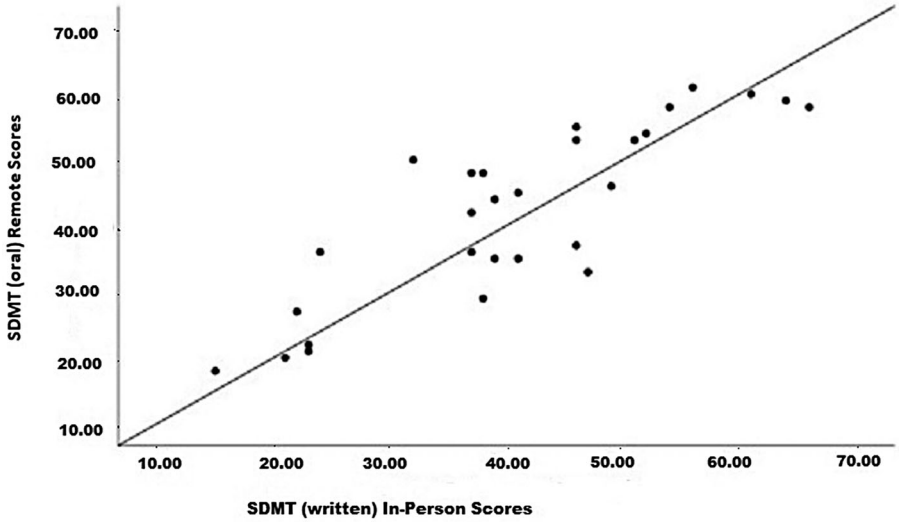

Figure 4. Scatter plot of in-person and remote testing SDMT for Group 1.

Trail-Making Test

Distributions of TMT-A and TMT-B completion times were positively skewed across Group 1 (in-person and virtual administrations) and Group 2. Therefore, non-parametric Mann–Whitney *U* tests and Wilcoxon tests were used to investigate between- and within-group differences respectively. Medians and ranges are reported in Table 2 for both version A and version B.

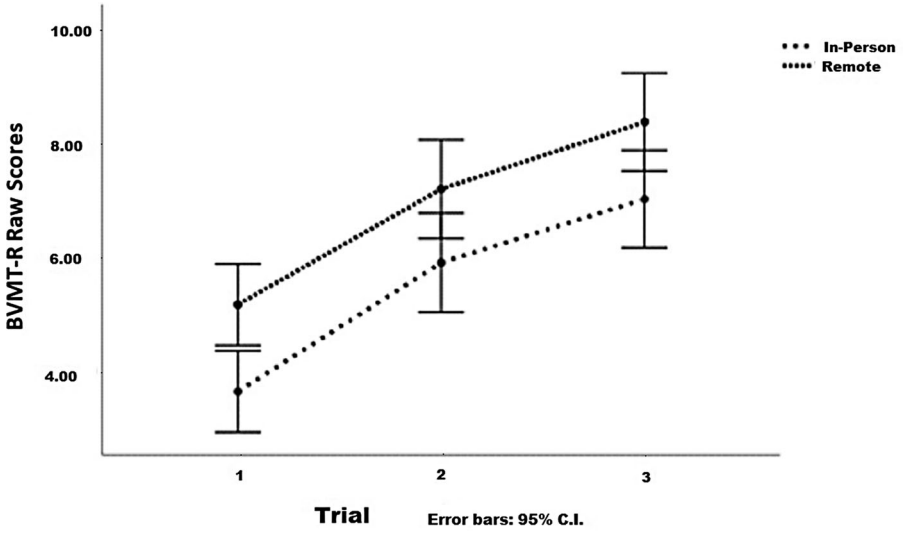

Figure 5. Difference in Group 1 (in-person) and Group 2 (virtual) on total recall score between in-person and remote testing on BVMT-R.

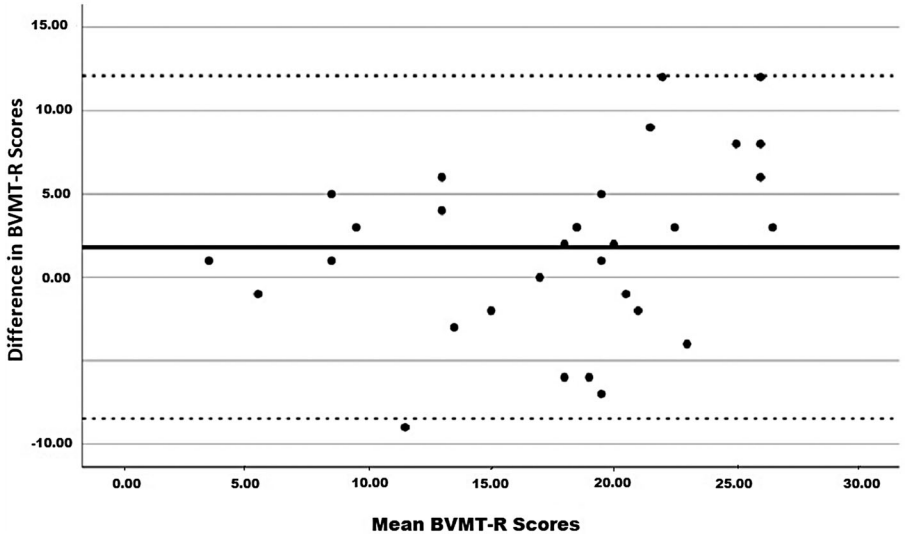

Figure 6. Group 1 Bland–Altman plot for total recall scores for in-person and virtual administrations on the BVMT-R.

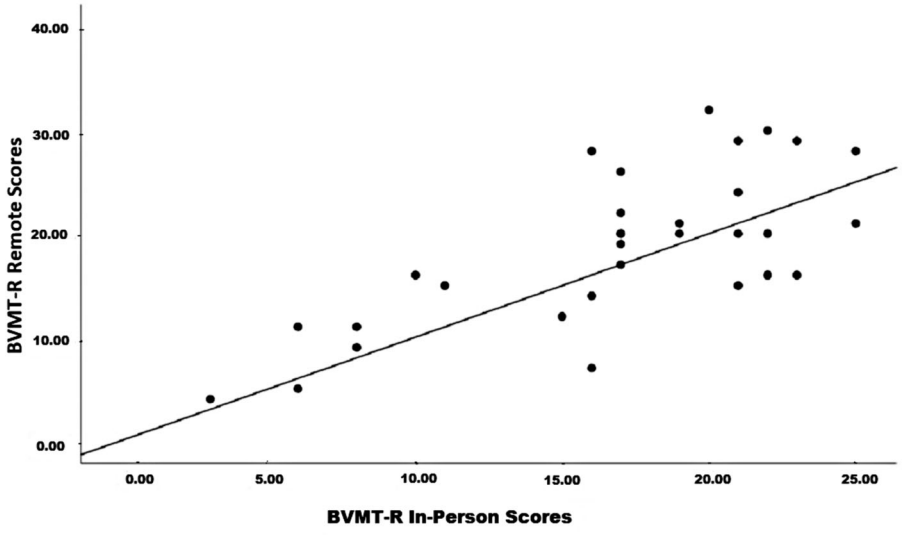

Figure 7. Scatter plot of in-person and remote testing BVMT-R for Group 1.

A Mann–Whitney U test found no significant differences between Groups 1 and 2 on completion times for TMT-A. To test within-group differences, three outliers were removed from the analysis and one participant failed to complete the trail within the specified time. A Wilcoxon signed-rank test showed a significant difference between in-person and virtual administration of the TMT-A for Group 1 ($z = -2.74$, $p = .006$), where the median virtual completion time

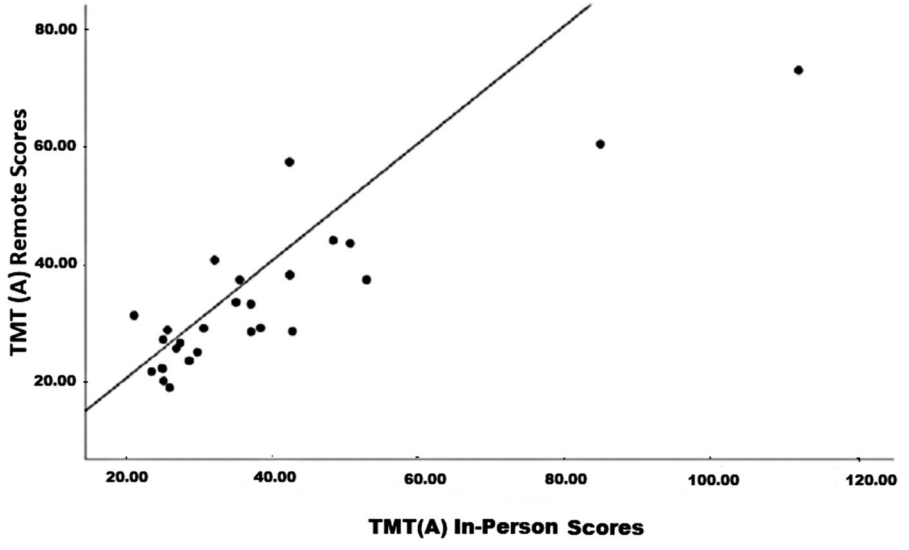

Figure 8. Scatter plot of in-person and remote testing TMT-A for Group 1.

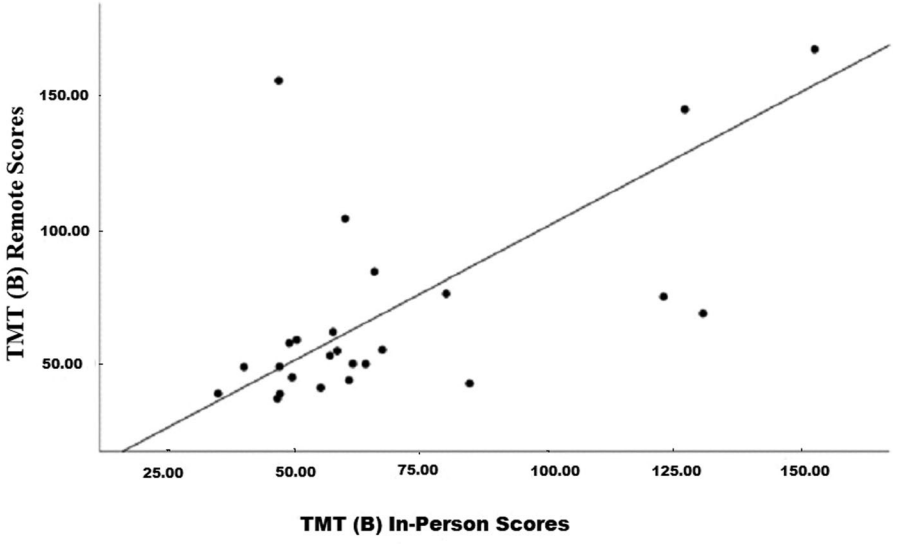

Figure 9. Scatter plot of in-person and remote testing TMT-B for Group 1.

(28.57 s) was significantly faster than the median in-person completion time (32.15 s). Scores were strongly correlated ($r = .88$, $p < .001$, see Figure 8).

For TMT-B analyses, 12 participants were removed: 6 from Group 1 (2 outliers; 4 incorrectly completed the trail) and 6 from Group 2 (1 outlier; 5 incorrectly completed the task). A Mann–Whitney U Test did not reveal any significant differences between Group 1 and 2. No significant within-subjects difference

was detected for Group 1. A strong positive correlation was also detected for in-person and virtual testing in Group 1 ($r = .76$, $p < .001$, see Figure 9).

Discussion

The results of this SWAT did not reveal any statistically significant differences between in-person and remote administrations of BICAMS measures CVLT-II and SDMT in a sample of participants living with MS. The findings are consistent with previous research (Barcellos et al., 2018; Barcellos et al., 2021) which found SDMT and CVLT-II scores to be indistinguishable when administered in-person and remotely. This SWAT extends these findings by investigating differences between in-person and remote administrations on short- and long-delay trials and recognition trials of the CVLT-II. Similarly, no statistically significant differences were found in these trials.

To our knowledge, this is the first study to have investigated remote administration of the written TMT and BVMT-R in people living with MS. No significant differences were detected between Groups 1 and 2 on TMT-A and TMT-B. A statistically significant difference was found in TMT-A scores within Group 1, where the median virtual completion time was approximately four seconds faster than in-person median completion time. No significant differences were found on Part B within Group 1. Similar rates of attrition were observed for each group in both in-person and virtual groups. Strong positive correlations were found between in-person and virtual administrations of the CVLT-II, SDMT, TMT-A and TMT-B after a six-month interval for Group 1. Bland Altman plots suggest a good level of agreement between in-person and virtual administrations of BICAMS measures.

With regards to the BVMT-R, total recall scores on virtual administrations for Group 2 were found to be significantly higher than scores for in-person testing in Group 1. As personal technological devices were used for online assessments, stimuli size varied across assessments depending on the type of device a participant used. Due to screen size, BVMT-R test stimuli occupied a larger portion of the visual field for laptop users compared to phone users. Stimuli presented on A4 test sheets as per the original BVMT-R test materials used for in-person sessions were larger again. If encoding smaller stimuli enhanced recall scores on the BVMT-R, then this may be detected in scores between phone and laptop users. The supplementary analysis (Appendix) did not reveal any significant differences between device types. However, it should be noted that laptop users tended to be younger than phone-users, which limits the conclusions that can be drawn from this analysis. Furthermore, the small sample size did not allow for the inclusion of other devices such as notebooks or tablets which were used by a smaller portion of participants in the sample. The BVMT-R and SDMT are reported to be the most sensitive assessments in the BICAMS battery (Sumowski et al.,

2018), with the BVMT-R as the most sensitive *memory performance* test, which is recommended as a monitoring tool in standard clinical care (Archibald & Fisk, 2000). Therefore, future studies administering the BVMT-R online should further investigate participants' performance in various environments (e.g., with and without the assessor physically present) using various devices (e.g., tablets, smartphones and laptops) using age-matched samples where possible.

Inter-rater differences may account for the discrepancy in total recall scores on the BVMT-R, as in-person and virtual tests were administered by different research assistants. Due to the retrospective nature of this SWAT in light of the COVID-19 pandemic, inter-rater differences were not accounted for in the design of the study. Support for this perspective comes from the finding that there were no significant differences in learning scores or in the number of hits and false alarms on recognition trials between groups. Furthermore, when scores were analysed for virtual administrations in Group 1 and Group 2, which were carried out by the same researcher, no significant differences were found. Benedict and colleagues (Benedict, 1997) report reliability coefficients for the BVMT-R to be .96–.97 but they also acknowledge the possibility of inflation as raters were trained directly by the author. In the BVMT-R, responses are scored on location and accuracy for each geometrical shape, where interpretation is somewhat left to each corrector's discretion. Previous research on inter-rater reliability found that scores may be inconsistently rated for location, rotation and preservation (Gaines et al., 2008), and other studies reported moderate agreement between raters (Caneda et al., 2018). In this study, the mean scores on virtual assessments were 20.59 (Group 1), and 18.61 (Group 2), which are comparable to those reported in similar samples (21.5) (Spedo et al., 2015), and greater than mean in-person scores for Group 1 (16.35). Inter-rater differences on the BVMT-R could impact large longitudinal studies where more than one rater is employed. Further research is needed to establish whether differences might be attributed to inter-rater differences, type of technology used, or a combination of these factors.

It is important to acknowledge the main limitation of remote assessment, which is the manner in which certain communication is restricted – for example, simply pointing to a specific location on a test page is not feasible online. This can pose difficulties for participants, particularly those with attention or visual deficits. Other methods of presentation are required to ensure task clarity and to reduce stress for participants in this context. Pinpointing specific areas on test sheets using a red marker and providing a visual aid on screen can be beneficial. This is particularly important for tasks that require visual scanning, such as the TMT.

In cases where a participant makes an error on the TMT, it is advisable to provide them with a new sample sheet so that they can begin again, but this is also not feasible with online testing. Despite the potential limitations of

virtual assessment in this context, results suggest that TMT-A completion times were faster for Group 1 when tested virtually six months after being tested in-person. This finding should be interpreted with caution due to high levels of attrition rates and the possibility of practice effects, considering Group 1 completed virtual assessments *after* in-person assessments. With that, no difference was found between in-person Group 1 scores and Group 2 virtual scores. Due to the COVID-19 pandemic, it was not possible to counterbalance conditions as in-person testing was not feasible, although this could be addressed in future research. Many authors have commented on the limited clinical utility of using the oral TMT-A (Bastug et al., 2013; Ruchinskas, 2003). Although further research is needed to establish the reliability of using the TMT remotely, the similar attrition rates between in-person and virtual testing found in this study are promising.

The limitations of the oral version of the TMT-A are not seen with the oral SDMT, which has been found to have strong psychometric properties and clinical utility (Jaywant et al., 2018). Importantly, the written and the oral SDMT, that use the same test form but where verbal responses are given in place of written responses, are strongly correlated in healthy adults (Smith, 1991), and those living with MS (Sandroff et al., 2013). The oral SDMT is used most extensively in the assessment of people with MS (Benedict et al., 2002), possibly due to upper limb difficulties that are seen in this cohort. Although remote assessment is challenging, any differences or otherwise seen in the SDMT groups should not be as a result of the administration of different forms of the SDMT.

Though the current SWAT yielded a number of interesting results, there remain a number of limitations that require consideration. The first limitation was the inability to control testing environment, as participants were assessed in their own homes. Although safeguards were implemented to reduce the number of possible distractions during testing, interruptions such as family members, pets and unexpected phone calls were unpredictable. Notably, however, this was largely consistent across groups and reflective of the reality of virtual assessment. With respect to environmental control for virtual assessment, other factors such as stability of internet connectivity and quality of the technological equipment used by participants may have influenced virtual sessions; and, along with factors such as security settings, e-mail alerts or error messages, one's own image or reflection on the screen can both distract participants and impede the building of rapport, the participant's understanding of the task, as well as the researcher's interpretation of responses (Beier et al., 2020). Furthermore, the use of screens may not be suitable for all participants, such as those with visual deficits, optic neuritis or those who may be more susceptible to eye strain. Moreover, due to COVID-19 societal restrictions, many participants had family members engaging in work and/or school from home, which may have led to increased risk of distractions and further strain on bandwidth.

The possibility of practice effects influencing the repeat testing results must be acknowledged as a potential confound. People with MS have been found to benefit from simple exposure to the BICAMS (Walker et al., 2016), regardless of the specific items administered (e.g., regardless of whether an alternative form was used), but importantly the testing periods were much closer together (two-three weeks Walker et al., 2016) than in the current study. We cannot be sure that re-testing would not leave traces, through exposure to the test and learning about testing parameters. Although a minimum of a six-month delay was provided between testing – consistent with recommendations for cognitive assessment in clinical care for people with MS (Daniels et al., 2020) – participants would have been aware of the requirements of the assessments, thus, the second trial may potentially have been easier for them.

When the decision was made to change to virtual administration of the assessments, the team investigated the feasibility and availability of computerized versions of the tests. When looking at alternative online possibilities for outcome measures, ease of use was considered a priority. By moving the outcome measures online, it is recognized that many people uncomfortable with using technology would need to be reassured that an online format would be as easy to use as possible. As such, the search focused on looking for a single platform with all the tests in one place, that participants could easily access, rather than several websites with a single test on each. One option had been the iCAMS (Passell et al., 2019), a validated tablet version of the BICAMS, but this was not readily available in Ireland at the time of administration. Another option that was investigated was the free to use an online platform called Test My Brain (TMB) (Luxton et al., 2014). This platform included similar tests that examine the same cognitive functions – processing speed (SDMT), visual attention and task-switching (TMT) and immediate visual, episodic recall (BVMT). The Digit Symbol Matching (SDMT-equivalent) and TMT appear to be similar to their original tests, requiring participants to use a keyboard/mouse where they would have used a pen and paper in the original. The team decided not to use the TMB platform as the assessments had not been validated on people with MS, they require a relatively high level of computer literacy including dexterity in keyboard and mouse use, floor effects were reported on some measures, and most importantly there were concerns about use and storage of the participant data. For this reason, and in consultation with the Public and Patient Involvement Advisory Panel, the decision was made to use a mixed design where instructions and response sheets were sent by post and the assessments were administered via teleconferencing. With this approach, there is always a risk of exposure to test sheets prior to testing, but the risks of this were minimized as much as possible through strategies described earlier.

Overall, the COVID-19 pandemic has had a global impact on research and healthcare in MS, with increased levels of distress reported in MS populations

(Alschuler et al., 2021). The need for remote assessment has become more urgent with increases in the use of telehealth to accommodate social distancing measures. The findings of this SWAT support the remote use of BICAMS and the TMT in the cognitive assessment for people with MS. Remote testing may be more convenient for those who might find difficulty in travelling to in-person appointments, potentially relieving participants of the stress, fatigue and risk of infection associated with travel to testing centres. It is recommended that future research should further investigate the feasibility and reliability of online cognitive assessment of people living with MS and develop safeguards aimed at reducing online distractions and promoting inclusivity, for example, through developing accessible methods of overcoming potential technical difficulties that can lead to frustration, and influence motivation and adherence to assessments (Luxton et al., 2014).

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Data availability statement

Data will be shared at the Irish Social Science Data Archive (ISSDA) (http://www.ucd.ie/issda/data/) following full analysis and write-up of the host (COB-MS) trial.

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Appendix

Supplementary analysis

A supplementary analysis was conducted to investigate whether the type of device a participant was using for online assessment may have impacted performance on different measures. Participants used their own devices for the virtual test sessions, and therefore the screen size varied across individuals. Some participants viewed test stimuli using their smartphones, whereas others had access to a laptop or PC. Screen size was particularly relevant with regards to the BVMT-R, as test stimuli were presented on screen to measure visual memory.

A cluster sample of 30 phone users and 30 laptop users was selected from the host trial sample (42 females and 18 males; mean age = 47.83 years, SD = 9.65). A significant difference was found for age, where laptop users tended to be younger ($M = 44.97$ years, SD = 9.27) than phone users ($M = 50.70$ years, SD = 9.29), $t(58) = -2.391$, $p = .020$. No significant difference was found in MSNQ scores between groups. Independent samples *t*-tests revealed no significant differences in total recall scores for phone and laptop users on the BVMT-R ($t = 1.65$, $p = .104$). Table A1 shows comparable scores between groups on other BVMT-R indicators. Thus, no evidence was found for the impact of device size on visual memory as measured by the BVMT-R.

No significant differences were found between phone and laptop users on CVLT-II total recall scores, SDMT scores (Table A1) or TMT completion times (Table A2).

Table A1. Descriptive statistics for age, MSNQ and BICAMS scores administered virtually across laptop and smartphone users.

	Laptop		Phone	
	M	SD	*M*	SD
Age	44.97	9.27	50.70	9.29
MSNQ	34.30	6.65	35.37	7.80
CVLT-II Total recall	50.73	10.96	49.60	10.29
BVMT-R				
Total recall	20.87	6.81	18.00	6.65
Learning	3.93	1.91	3.40	1.96
Long-delay Recall	7.9	2.73	7.1	2.56
Recognition Hits	5.4	.97	5.1	.18
False Alarms	.17	.53	.13	.35
SD*MT*	46.43	10.65	41.24	14.20

Table A2. Descriptive statistics for TMT completion times administered virtually across laptop and smartphone users.

	Laptop			Phone		
	Median	Min	Max	Median	Min.	Max.
TMT A (s)	29.78	14.81	60.00	30.02	17.33	82.94
TMT B (s)	55.32	32.04	199.10	58.31	33.61	159.33