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Is the difference real, is the difference relevant: the minimal detectable and clinically important changes in the Montreal Cognitive Assessment

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ABSTRACT

Background and aims: The Montreal Cognitive Assessment (MoCA) is a widely used instrument for assessing cognitive function in stroke survivors. To interpret changes in MoCA scores accurately, it is crucial to consider the minimal detectable change (MDC) and minimal clinically important difference (MCID). The aim was to establish the MDC and MCID of the MoCA within 6 months after stroke.

Methods: This cohort study analysed data from the EFFECTS trial. The MoCA was administered at baseline and at 6-month follow-up. The MDC was calculated as the upper limit of the 95 % confidence interval of the standard error of the MoCA mean. The MCID was determined using anchor-based and distribution methods. The visual analogue recovery scale of the Stroke Impact Scale (SIS [primary anchor]) and Euro Quality of Life-5 Dimensions index (EQ-5D [confirmatory anchor]) were used as anchors. The distribution-based method, the Cohen benchmark effect size was chosen.

Results: In total, 1131 (mean age [SD], 71 [10.6] years) participants were included. The mean (SD) MoCA scores at admission and 6-month follow-up were 22 (5.2) and 25 (4.2), respectively. The MDC of the MoCA was 5.1 points. The anchor method yielded the MCIDs 2 and 1.6 points for SIS and EQ-5D, respectively. Using the distribution method, the MCID for the MoCA was 1 point.

Conclusions: Even a small change in MoCA scores can be important for stroke survivors; however, larger differences are required to ensure that any difference in MoCA values is a true change and is not related to the inherent variation in the test. Due to small sample sizes, the results of the anchor analysis need to be interpreted with caution.

Introduction

Cognitive impairment is common after a stroke [1,2]. At 3 months, at least one in four patients with stroke have demonstrable cognitive issues, which often persist for $\geq$ 6 months [2,3]. Cognitive issues are consistently described as the outcome of greatest concern for stroke [2, 4]. Therefore, international guidelines emphasise the use of cognitive assessment during hospitalisation and follow-up visits, as well as incorporating cognition as a key outcome measure in clinical stroke trials [5–7].

One commonly utilised tool in both clinical and research stroke

settings is the Montreal Cognitive Assessment (MoCA) [8]. The MoCA has features that make it suitable for use in stroke research, including its short administration time and proven validity in stroke, and is recommended by several stroke societies [9]. However, to employ the MoCA as an endpoint measure in clinical trials, it is important to establish the minimal detectable change (MDC) and minimal clinically important difference (MCID). The MDC can be defined as the smallest change in a score beyond the measurement error of an assessment instrument [10]. The MCID is the smallest change in the score that is meaningful for a patient [11]. Previous studies have looked at MCID using a stroke cohort of 65 stroke survivors 20 months after stroke and in a cohort of 175

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individuals in the first year after aneurysmal subarachnoid haemorrhage [12,13].

The lack of specific data regarding the interpretation of cognitive improvement and treatment effectiveness poses a significant challenge for healthcare professionals and researchers. This knowledge gap hinders the accurate assessment of treatment efficacy and affects the ability to make informed decisions regarding patient care. Furthermore, the lack of understanding impedes the planning of clinical trials focusing on cognition as an outcome [3].

Studies with cognitive function as an outcome are common [14]. Many of these studies recruit in the acute stroke period and so an understanding of the properties of cognitive scores in this time window is important. This study aimed to establish the MDC and MCID of the MoCA within 6 months after stroke. This study adds to the current knowledge by establishing MCID in a large well-defined stroke cohort in the first months after stroke.

Methods

This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [15]. In addition, our methods were aligned with the accepted best practices in the area [16]. The study protocol has been published in the Research and Development in Sweden database (project number: 279114) https://www.researchweb.org/is/se/sverige/project/279114.

Study design and sample

Data were prospectively collected from the Efficacy of Fluoxetine—a Randomised Controlled Trial in Stroke (EFFECTS), a multicentre, placebo-controlled, double-blind randomised clinical trial that included 1500 stroke survivors from 35 stroke centres and rehabilitation units across Sweden between October 2014 and June 2019. Detailed information on EFFECTS has been reported elsewhere [17]. EFFECTS included stroke survivors aged $\geq$ 18 years and diagnosed with ischaemic or haemorrhagic stroke within 2–15 days after stroke (International Classification of Diseases codes: I61, non-traumatic intracerebral haemorrhage; I63, cerebral infarction; and I64, stroke, not specified as haemorrhage or infarction). The MoCA data were registered at baseline and 6-month follow-up. The EFFECTS trial was neutral in terms of the primary outcome [17]. This large and robust dataset informed other secondary analyses of stroke assessment [18].

Ethics

This study was approved by the Medical Ethics Committee of Stockholm (Ref. 2013/1265-31/2) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all stroke survivors.

Clinical measures and procedures

Cognitive function was assessed using the Swedish translation of the MoCA (version 7.1) at inclusion and 6 months. The score range on MoCA is 0–30 points, with a higher score indicating better cognitive function and a threshold of $\geq$ 26 indicating a normal cognitive function [19]. A standard deviation (SD) > 0.2 point on MoCA is considered an MCID [20]. The effects of stroke were evaluated using the Swedish translation of the Stroke Impact Scale (SIS, version 3.0), which was assessed 6 months after stroke [21]. A self-reported 10–15 % recovery rate on the visual analogue scale (VAS) of the SIS was considered an MCID [21]. The VAS of the SIS was used for primary anchor analysis. Health-related quality of life after stroke was evaluated using the Swedish translation of the Euro Quality of Life-5 Dimensions (EQ-5D) [22]. A 0.1 change in the EQ-5D index indicates an MCID [22]. The EQ-5D was used for confirmatory anchor analysis. Correlation thresholds between anchor

and MOCA score change was set at 0.3 [23].

Stroke severity was assessed before randomisation in EFFECTS within 2–15 days after stroke. The National Institutes of Health Stroke Scale (NIHSS) was used [24]. $A \leq 3$ points on the NIHSS was classified as mild stroke [24]. Age was categorised into three groups: 18–65, 66–79, and $\geq$ 80 years. Previous transient ischaemic attack (TIA) or stroke was defined as the presence of one or both conditions. Reperfusion therapy was defined as thrombolysis, thrombectomy, or both.

The baseline and 6-month follow-up data were collected via face-to-face interviews with EFFECTS personnel at individual centres. All the assessors received specific training according to local standards.

Statistics

Complete MoCA scores without an extra point for low educational level were used for all analyses. This to make it easier to interpret mathematical comparisons between MoCA scores and not to create skewed means in the anchor groups. Independent samples t-tests (interval and ratio variables) and chi-squared tests (ordinal or nominal variables) were used to compare age, stroke severity, and sex between included and excluded stroke survivors, that is, those with missing MoCA data.

The MDC was calculated as follows (Fig. 1) [21,25].

MDC is the upper boundary of the 95 % confidence interval of the standard error of the mean. Pooled SDs were calculated using the intraclass correlation coefficient (ICC) as a measure of test–retest reliability. The ICC was calculated for absolute agreement in a mixed-effects model using baseline and follow-up MoCA scores. As is standard practice, stroke survivors with MoCA score changes $\geq$ ± 2 SD were excluded to minimise the impact of outliers [21]. Sub group analysis was performed, including all MoCA data.

The MCID was calculated using anchor-based and distribution-based methods [23,25]. Distribution methods rely on descriptive statistics, assuming the minimal change is within a certain spectrum of the distribution. Anchor methods rely on the correlation between an anchor variable and the variable of interest; thus, individuals with the smallest yet significant change in the anchor variable are assumed to have a change of the same magnitude in the variable of interest. We chose to explore both methods since, to the best of our knowledge, no method has been clearly proven superior. For the anchor, we used both a 10–15 % change in the visual analogue recovery scale in the SIS [21] and a 0.1 change in the EQ-5D index [22]. Thus, the mean MoCA score change for the anchor individuals was equal to that of the MCID. Spearman's correlation was used to test the association between anchor variable changes and MoCA score changes.

The distribution-based method chosen for this study was the Cohen benchmark effect size method, selected for its provision of a standardized metric that aids in interpreting the magnitude of observed changes [20]. We chose an effect size of 0.20 to equate to the MCID for this study [20]. Previous studies have advocated for the use of 0.50 SD as an optimal benchmark but this is mainly designed for patient reported outcomes on a 7-point Likert Scale [26]. Since MoCA has a higher score range and cannot be considered solely "patient reported" 0.20 may better represent a distribution MCID. A subgroup analysis was performed by calculating the MCID values in the subgroups based on stroke severity, age, previous TIA/stroke, and reperfusion treatment.

Results

Of the 1500 stroke survivors at baseline, 1131 were included in this study. The reasons for exclusion are presented in Fig. 2. Compared with included stroke survivors, excluded individuals were significantly older (mean [± SD], 71 [10.6] vs. 73 [11.4]; $p = 0.008$); had more severe stroke, as assessed using the NIHSS (mean [± SD], 4.0 [3.4] vs. 6.0 [4.8]; $p = 0.001$); and had a higher proportion of females (n [%], 416 [36.8] vs. 159 [43.0]; $p = 0.03$).

$$MDC = \left(SDpooled \; x \; \sqrt{1 - ICC}\right) x \left(1.96 \; x \; \sqrt{2}\right)$$

$$where, \; SDpooled = \sqrt{\frac{SD_{baseline}{}^2 + SD_{follow-up}{}^2}{2}}$$

Fig. 1. Equation for the calculation of minimal detectable change (MDC). Abbreviations: SD, standard deviation; ICC, intraclass correlation coefficient.

Eligible for inclusion, n = 1500

EFFECTS study population

Died before 6-month follow-up

n = 31

MoCA not performed at baseline or 6 months

n = 322

Incomplete MoCA scores

n = 16

Included:

Patients with complete MoCA scores at baseline and 6 months
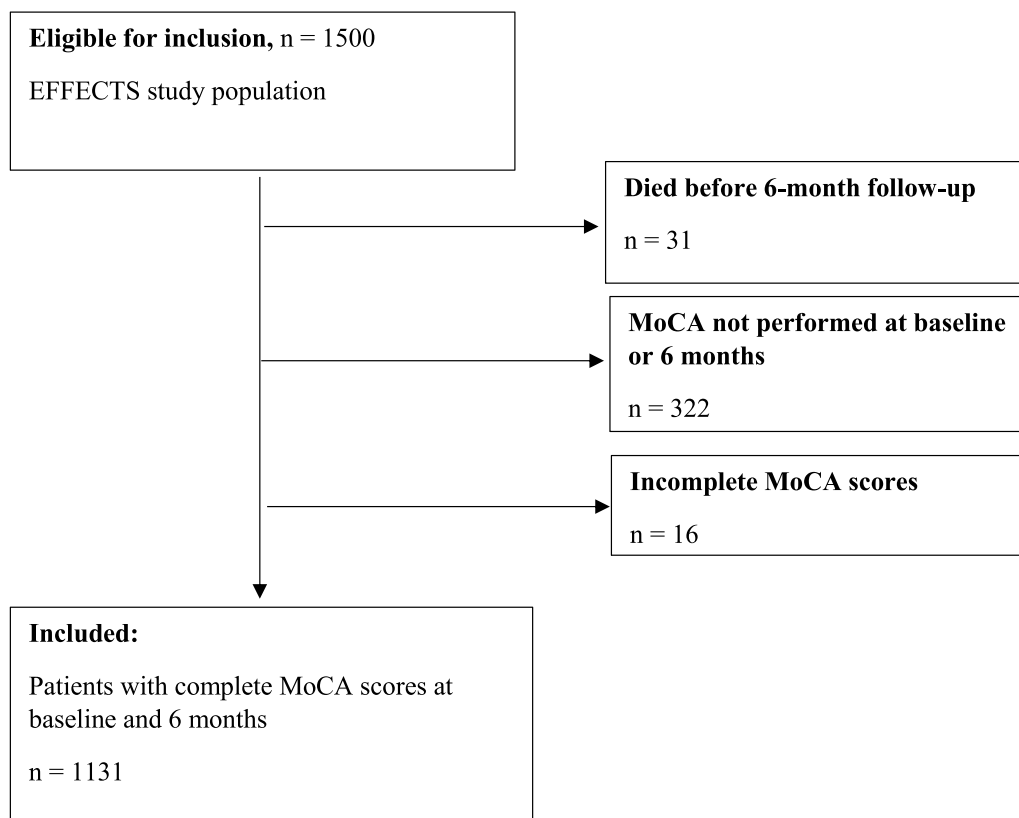
n = 1131

Fig. 2. Flowchart of study participants.

From the 1131 stroke survivors, 89 % ($n = 1006$) had ischaemic stroke. The mean MoCA scores at admission and 6-month follow-up were 22 (SD, 5.2) and 25 (SD, 4.2) points, respectively (Table 1).

The minimal detectable change of the Montreal Cognitive Assessment

The ICC analysis was based on 1030 stroke survivors who met the criteria of having a MoCA score change $\leq \pm 2$ SD. The ICC was 0.9, indicating good test–retest reliability. The MDC was 5.1 MoCA points.

Sensitivity analysis, including all MoCA data ($n = 1131$), yielded an MDC of 6.7 MoCA points, with an ICC of 0.7.

Minimal clinically important difference of the MoCA

Correlation coefficients between MoCA score change and anchors were 0.1 for SIS VAS scale and –0.1 for EQ-5D index change. The MCID values obtained through the anchor method were 2.0 (95 % CI 0.49 to 4.49 [$n = 13$ with 10 - 15% recovery]) for the SIS anchor and 1.6 (95 % CI 0.30 to 2.92 [$n = 23$ with 0.1 change]) for the EQ-5D anchor. The MCID value of the MoCA determined using the distribution method was 1.0 based on a SD of 5.19 for a mean MoCA score of 22.43 (95 % CI 22.13 to 22.73, $n = 1131$).

Subgroup analyses

There was a 1-point higher MCID value for stroke survivors with a previous stroke or TIA for both anchor methods, Table 2. There was no difference in those who received reperfusion treatment using the distribution method; however, a 1.5-point smaller MCID value was obtained using the EQ-5D anchor. The MCID values differed by age group according to the distribution method (Table 2). Stroke survivors aged 66–79 years had a 1-point higher MCID compared with younger stroke survivors using the EQ-5D anchor. There was no difference in the MCID between stroke survivors with or without a previous stroke or TIA using the distribution method.

Discussion

We aimed to establish the MDC and MCID of the MoCA within 6 months of stroke by analysing data from a large sample of stroke survivors. The MDC was 5.1 points, indicating that the change exceeds the measurement error. The MCID values varied depending on the method and anchor used, ranging from 1.0 to 2.0 points.

A difference between the MDC and MCID values indicates that there is a range of score changes that are statistically significant but not

Table 1
Characteristics of study sample, $n = 1131$.

	Baseline characteristics	Six-month follow-up	Missing data n (%)
Age, years			
Mean ($\pm$ SD)	71.0 (10.6)		
Median (Q1–Q3)	72 (65–78)		
Min–max	21–95		
Sex, female, n (%)	416 (37)		
Previous stroke or TIA, n (%)	193 (17)		
Race, n (%)			
Asian	3(0.3)		
Black	4 (0.4)		
White	1119 (99)		
Others	5 (0.4)		
Marital status, n (%)			19 (1.7)
Single	391 (35)		
Partner	721 (64)		
Employment, n (%)			14 (1)
Full time	250 (22)		
Part time	54 (5)		
Unemployed/retired	813 (72)		
Diabetes, n (%)	219 (19)		2 (0.2)
Coronary heart disease, n (%)	182 (16)		4 (0.4)
Stroke severity at baseline, NIHSS			
Mean ($\pm$ SD)	4.0 (3.4)		
Median (Q1–Q3)	3 (2–5)		
Min–max	0–20		
Reperfusion treatment, n (%)	252 (22)		
Stroke type, n (%)			
Ischaemic stroke	1006 (89)		
Haemorrhagic stroke	125 (11)		
Montreal cognitive assessment			
Mean ($\pm$ SD)	22.0 (5.2)	25.0 (4.2)	
Median (Q1–Q3)	24 (20–26)	26 (23–28)	
Min–max	0–30	2–30	
Normal cognition, ≥ 26 points, n (%)	374 (33)	580 (51)	
SIS recovery scale			
Mean ($\pm$ SD)		69 (22.7)	
Median (Q1–Q3)		75 (50–90)	
Min–max		0–100	
EQ-5D index			
Mean ($\pm$ SD)	0.5 (0.3)	0.7 (0.3)	
Median (Q1–Q3)	0.6 (0.2–0.8)	0.7 (0.6–0.8)	
Min–max	–0.4–1.0	–0.3–1.0	

Abbreviations: SD, standard deviation; Q1–Q3, first quartile and third quartile; Min–max, minimum and maximum values; TIA, transient ischaemic attack; NIHSS, National Institutes of Health Stroke Scale; EQ-5D, Euro Quality of Life-5 Dimensions.

Table 2
Subgroup analysis on minimal clinically important difference of Montreal Cognitive Assessment.

Subgroups		MoCA MCID values (No. of patients)		
		Anchor SIS	Anchor EQ-5D	Distribution
NIHSS (n [%])	≤ 3 (621 [55])	1.0 (2)	2.0 (17)	0.9 (621)
	≥ 4 (510 [45])	2.6 (11)	0.5 (6)	1.1 (510)
Age (n [%])	18–65 (280 [25])	–	1.3 (6)	1.1 (280)
	66–79 (645 [57])	2.7 (9)	2.3 (13)	1.0 (645)
	> 80 (206 [18])	0.5 (4)	0.3 (4)	1.0 (206)
Previous stroke/TIA (n [%])	Yes (193 [17])	2.5 (4)	2.3 (4)	1.1 (193)
	No (936 [83])	1.8 (9)	1.5 (19)	1.0 (936)
Reperfusion treatment (n [%])*	Yes (228 [23])	0.6 (1)	0.5 (4)	0.9 (228)
	No (778 [77])	1.7 (12)	2.1 (19)	1.0 (778)

Results from anchor subgroups that have fewer than 5 participants should be interpreted with caution. Abbreviations: NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischaemic attack; SIS, Stroke Impact Scale; EQ-5D, Euro Quality of Life-5 Dimensions.
*Only participants with ischaemic stroke.

clinically meaningful, or vice versa [27]. The differences between the MDC and MCID values of the MoCA have important clinical and scientific implications [25]. From a clinical perspective, a change of ≥ 1 to 2 points in a patient's MoCA score may be considered important by the patient or clinician, although larger changes may be required to definitively demonstrate significant differences. Our results suggest that the MoCA may not be an ideal outcome measure for studies evaluating the effectiveness of interventions for cognitive impairment, as subtle improvements or deteriorations in cognitive function that are important to stroke survivors may be 'lost' in test -retest variability.

Our results are similar in magnitude to the MDC values reported for individuals with dementia. In a study by Lee et al. [28] including 60 individuals, an MDC of 4.71 points was reported. However, other values have been reported. For example, in a study by Feeney et al. [29] involving 130 individuals, an MDC value of 3 points was reported for the MoCA. This observed disparity may stem from divergent participant cohorts. In our cohort of stroke patients, the mean MoCA score increased

from 22 to 25. It is possible that MoCA scores were unstable during the study period, potentially leading to a larger MDC. However, the measurement of outcomes at 6 months is common in stroke research and thus it is informative to visualize the MoCA-score MDC in that time-interval in stroke survivors. The study by Feeney et al. [29] was based on community-dwelling middle-aged and older adults without severe cognitive impairment. This highlight that descriptions of MDC are sensitive to the populations studied and that we should not extrapolate data from other conditions to stroke research.

In our study, the MCID values of the MoCA test exhibited disparities between the distribution- and anchor-based methods. The distribution method yielded a lower MCID value than the anchor method, which may indicate that the distribution method is more sensitive in detecting small changes in cognitive function than the anchor method. The reason for the disparities between the two methods is plausibly related to the different assumptions and criteria they use and the variability of the anchors and the populations they are applied to [27,25]. Distribution-based methods use statistical criteria to determine the minimal change that can be detected beyond the error, whereas anchor-based methods use patient-reported outcomes or other indicators to determine the minimal change associated with the change [27].

In our study, the anchor method yielded slightly higher MCID values for the SIS than for the EQ-5D. The SIS anchor, a stroke-specific measure of health status, yielded a higher MCID value than the EQ-5D anchor, a generic measure of health-related quality of life. We can assume that some anchors may not reflect the true change in cognitive function or that some populations may have different thresholds for perceiving improvement or worsening [27]. The correlation between the anchor variable and the MoCA score change failed to reach the 0.3 threshold. This could be attributed to the limited sample sizes in the anchor groups (SIS $n = 13$ and EQ-5D $n = 23$). While Reiki et al. [23] propose a correlation range of 0.30–0.35 as adequate for establishing a satisfactory relationship between an anchor and a Patient-Reported Outcome change score, they also recognize that alternative thresholds may be appropriate when extra data is accessible. Our results suggest that the SIS anchor is more specific for capturing changes in cognitive function related to stroke, whereas the EQ-5D anchor may be influenced by other factors,

such as physical or mental health. Hence, we recommend using values based on the SIS anchor, namely, 2.0 MoCA points.

In contrast, the anchor-based MCID values were fairly consistent with an MCID ranging from 1 to 2 MoCA points [12,13]. However, these results may not be directly comparable because of variations in the study cohorts, follow-up periods, and anchor thresholds. Wu et al. [12] assessed the MCID in 65 patients with stroke, whereas Wong et al. [13] examined 175 patients with subarachnoid haemorrhage. Wu et al. [12] found that the MCID of the MoCA was 2.15, with a mean of 12 months after stroke, which is in the same range as that reported by Wong et al. However, unlike Wu et al., Wong et al. measured the MCID of the MoCA at two different time points after stroke. They found MCIDs of MoCA of 2.0 and 1.1 at 3 and 12 months after stroke, respectively [13]. The Distribution MCID was similar to the results obtained by Wu et al. after adjusting their MCID (SD x 0.5 = 2.15) to our threshold value of 0.2 (SD x 0.2 = 0.86) [26]. Distribution MCID value was also 1 point smaller than the results by Wong et al. [12,13]. The use of a small effect size threshold for MCID in conjunction with the relatively narrow range of MoCA scores of the EFFECTS population may have produced a deflated distribution MCID value smaller than that of a more cognitively diverse stroke cohort [30]. This may have implications for generalisability. Several other methods for deriving the MCID values have been used. Opinion-based methods use expert opinions (clinicians or patients) to define the MCID and add a qualitative aspect to the MCID that the anchor and distribution methods lack [31].

In the sub group analysis, the distribution method yielded similar MCID values for all subgroups. For stroke severity, the anchor-based methods yielded a 1.5 MoCA point difference between mild stroke (NIHSS $\leq$ 3) and severe stroke (NIHSS $\geq$ 4). However, these were inconsistent between our anchors, and subgroup samples were small. Notably, the feasibility of the MoCA tends to decline with increasing stroke severity [32]. Hence, these stroke survivors are at a high risk of being excluded from MoCA testing and have a greater need for cognitive evaluation because of a higher risk of post-stroke dementia [33]. Both anchor methods yielded a 2-point lower MCID value for stroke survivors aged > 80 years. Stroke survivors with previous stroke or TIA had a 1-point higher MCID value than those without previous cerebrovascular incidents, which reflects that these stroke survivors are more likely to have worse functional outcomes and that cognition is of less importance to overall disability. The results from the sensitivity analysis of the anchor groups should be interpreted with caution due to the small number of participants in some of the subgroups. Despite this limitation, retaining these results was important because they underscore the necessity for future research on a larger scale. These initial findings can help identify areas of interest for more detailed investigations, thus serving as an important foundation for subsequent studies.

While our study provides valuable insights, it is important to acknowledge the limitations associated with the low correlation between the MoCA score and the anchor variables, which may reflect the restricted number of participants demonstrating minimal clinically significant changes in the anchor variables. These factors may have influenced the interpretation of our findings and should be considered when generalizing the results. The discrepancy between the MCID and MDC should also be taken into consideration. A perceived meaningful change in cognitive function by the patient may not be statistically significant, indicating that it might not genuinely reflect a cognitive shift beyond measurement error. This limitation could be due to the inherent variability of the MoCA. Conversely, results derived from anchor methods, which capture patients' perspectives, faced challenges due to the limited number of patients meeting the established MCID thresholds. This limitation could affect the comparability among the various methods employed to ascertain MCID. Describing MDC in the acute phase of stroke is valuable, as several trials, including trials of cognitive interventions, are conducted in the acute phase. However, cognition is dynamic after a stroke, especially early after stroke onset. This can explain the trend for improvement of MoCA scores in our study sample

and, consequently, the large MDC values in the context of substantial temporal variation in scores. Hence, our MDC data may not be applicable to patients with stroke who are later in stroke recovery, where cognition may be more stable. The study cohort was large, well-defined, and consisted of participants with a verified stroke. The participants were heterogeneous in terms of age, stroke severity, stroke type, and post-stroke cognitive function. However, data were taken from an intervention study using fluoxetine and despite the trial was neutral in terms of primary functional outcome, there was a difference in rate of patients with diagnosis of depression between treated and non-treated groups. This might have had an impact in the present analysis since we are talking about measures of self-reported quality of life. This might have introduced a bias. Moreover, several patients experienced mild stroke. Although our sample is representative of the Swedish stroke population in terms of stoke severity [34], the generalisability of our study results to other stroke populations may be limited. All assessment instruments used in the study were valid and reliable for use in patients with stroke; [21,22,35] however, they can have various sensitivities to capture changes. Hence, there is a divergence in the MCID values of MoCA regarding the distribution and anchor-based methods. Different methods and assessments were used to calculate the MCID. However, the results should be interpreted with caution, as an MCID that is less than the MDC may be questioned for its reliability, as it lies within the bounds of measurement error of the patient-reported outcome measure.

To conclude, the MDC value of the MoCA test suggests that a change of > 5 points in the MoCA score is likely to reflect a true change in cognitive function rather than a measurement error. The MCID values of the MoCA suggest that a change of at least 1 point in the MoCA score is likely to be perceived as meaningful by stroke survivors or associated with changes in health-related quality of life. Hence, small changes in the MoCA score can potentially have clinically relevant benefits for stroke survivors; however, more studies are required to validate our results. Due to the small sample sizes in our anchor groups the results may be due to chance and must be interpreted with caution. Further, the MCID analysis needs to be replicated with larger number of participants in the anchor groups to validate the SIS and EQ-5D as anchors. Incorporating qualitative aspects into the MCID estimation is likely to further increase the accuracy of the MCID value. The results of our study may have implications for sample size in studies that aim to use the MoCA as an outcome measure.

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Nothing to declare.

Data availability

According to Swedish regulations (https://etikprovning.se/for-fors kare/ansvar/), the data for this study cannot be publicly shared, for ethical and legal reasons. Researchers can request access to the data by emailing the chief investigator Erik Lundström at erik.lund-strom@neuro.uu.se.

CRediT authorship contribution statement

Elias Lindvall: Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis. **Tamar Abzhandadze:** Writing – review & editing, Writing – original draft, Validation, Funding acquisition, Conceptualization. **Terence J. Quinn:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Katharina S. Sunnerhagen:** Writing – review & editing, Supervision, Funding acquisition, Data curation, Conceptualization. **Erik Lundström:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Data curation.

Declaration of competing interest

The authors have no conflicting interests to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cccb.2024.100222.

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