

The Montreal Cognitive Assessment: Normative Data from a German-Speaking Cohort and Comparison with International Normative Samples

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Abstract.

Background: The Montreal Cognitive Assessment (MoCA) is used to evaluate multiple cognitive domains in elderly individuals. However, it is influenced by demographic characteristics that have yet to be adequately considered.

Objective: The aim of our study was to investigate the effects of age, education, and sex on the MoCA total score and to provide demographically adjusted normative values for a German-speaking population.

Methods: Subjects were recruited from a registry of healthy volunteers. Cognitive health was defined using the Mini-Mental State Examination (score $\geq 27/30$ points) and the Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Assessment Battery (total score ≥ 85.9 points). Participants were assessed with the German version of the MoCA. Normative values were developed based on regression analysis. Covariates were chosen using the Predicted Residual Sums of Squares approach.

Results: The final sample consisted of 283 participants (155 women, 128 men; mean (SD) age = 73.8 (5.2) years; education = 13.6 (2.9) years). Thirty-one percent of participants scored below the original cut-off ($< 26/30$ points). The MoCA total score was best predicted by a regression model with age, education, and sex as covariates. Older age, lower education, and male sex were associated with a lower MoCA total score ($p < 0.001$).

Conclusion: We developed a formula to provide demographically adjusted standard scores for the MoCA in a German-speaking population. A comparison with other MoCA normative studies revealed considerable differences with respect to selection of volunteers and methods used to establish normative data.

Keywords: Elderly individuals, healthy participants, mild cognitive impairment, Montreal Cognitive Assessment, regression analysis

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INTRODUCTION

Due to the demographical development, age-related diseases will drastically increase over the next decades. Today, 46.7 million people are suffering from dementia worldwide—a number that is estimated to nearly triple by 2050 and reach 131.5 million cases [1]. To face this healthcare challenge, early and accurate identification of cognitive impairment is crucial. Mild cognitive impairment (MCI) may represent a stage along the clinical continuum of Alzheimer's disease (AD), and currently there are no drugs proven effective for this disease stage [2]. However, implementing off-label pharmacological treatment might be beneficial in certain patients; non-pharmacological interventions should be initiated; behavioral or psychiatric symptoms common in MCI may be treated; and there is time to consider important life choices when a patient is still able to do so [2]. Additionally, future pharmacological interventions against AD mainly target patients in an incipient disease stage [3], and about 10% of the causes of cognitive impairment are reversible [4].

The early detection of cognitive decline requires a tool that is short, easy to administer and interpret, and has high diagnostic accuracy. Currently, a widely used instrument is the Mini-Mental State Examination (MMSE) [5]. However, the MMSE sensitivity is poor when identifying individuals with MCI [6–8], and it lacks meaningful assessment of executive functions [9]. The Montreal Cognitive Assessment (MoCA) [6] has been developed to address these weaknesses. It has demonstrated better diagnostic accuracy in patients with MCI [10, 11], has less ceiling effect [11], and a higher test-retest-reliability [10]. In addition, the MoCA better captures the cognitive domains proposed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [12]. Accordingly, previous research has demonstrated good practical utility of the MoCA as a diagnostic tool in various diseases affecting cognition [13].

Yet, the implementation of the MoCA has some limitations. First, the proposed cut-off score of 26 out of 30 points [6] has been criticized for being too conservative. A recent review found that MoCA specificity was 60% or lower when applying this cut-off score [14], thus, bearing a high risk of false-positive classifications. Second, possible demographic effects on cognitive performance are not well addressed in the original MoCA, which only includes a basic correction for education (+1 point for

individuals with ≤ 12 years of education). However, it has been shown that age and—less consistently—sex may influence MoCA scores [13, 15–28]. Finally, the MoCA performance may vary across different cultures and languages [25]. Accordingly, normative values for the MoCA have been established in several countries [13, 15–28]. The results show great variability; most importantly there are substantial differences regarding the empirically derived MoCA cut-off scores [13, 15–28]. Consequently, a general cut-off for all populations might not be suitable, and diagnostic accuracy may be improved when a cut-off score is based on culture-specific and demographically adjusted normative values.

To our knowledge, normative values for the German version of the MoCA have not yet been established. The aim of our study was to evaluate the effects of age, education, and sex on the MoCA and to create demographically adjusted norms for the German version. This report also provides a comparison of normative data from other international samples.

MATERIALS AND METHODS

Participants

Ethical approval for the study (N° EKNZ 2016-00393) was provided by the *Ethikkommission Nordwest- und Zentralschweiz (EKNZ)* on April 26, 2016. The study was performed in respect of the most recent version of the Declaration of Helsinki and was registered on ClinicalTrials.gov (NCT03246269).

Participants were recruited from an existing Registry of Individuals Interested to Participate in Research established by the Memory Clinic, University Center for Medicine of Aging, Felix Platter Hospital in Basel, Switzerland. The detailed study flow chart is shown in Fig. 1. The registry was established in 2013 with approval from the local ethics committee (N° EKBB 280/12). Individuals were informed about the registry and the possibility to sign-up by means of newspaper advertisements, television interviews, and public scientific lectures. Each time a study with normal control subjects was initiated at the Memory Clinic, potential participants with the required demographic characteristics (age, education, sex) were identified from the registry and invited to provide information about their medical history by completing a detailed medical questionnaire (see Supplementary Figure 1 for an English translation of the medical questionnaire). At the beginning of the current study in December 2016, the registry

consisted of 2,162 individuals. Seven-hundred and ninety-four had previously provided their medical history and were considered during the recruitment process of this study. Four-hundred and eighty-seven individuals remained eligible for telephone screening after applying inclusion and exclusion criteria (see below). During the telephone screening, a further assessment of exclusion criteria was performed, and 153 subjects were excluded. Thus, 334 individuals were assessed between December 2016 and April 2017, and the data of 283 subjects were included in the final analysis (see study flow chart for details).

During the recruitment process, a stratification of sex (female and male) and age (groups: 65–69, 70–74, 75–79, and >79 years) was applied to obtain age groups with at least 20 women and 20 men each. The aim was to include only cognitively healthy individuals by applying the following criteria. Inclusion criteria were: 1) age ≥ 65 years, 2) education ≥ 7 years, 3) fluent German-speaking, and 4) provided written informed consent. Subjects who met one of the following criteria were excluded: 1) cognitive impairment (i.e., MMSE $< 27/30$ and/or Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Assessment Battery (CERAD-NAB) < 85.89 [29], any diagnosis of cognitive impairment), 2) diagnosis and/or symptoms of depression (i.e., Geriatric Depression Scale (GDS; [30]) $> 5/15$), 3) severe sensory or motor impairment interfering with cognitive testing, 4) serious somatic disease, 5) any disease or events affecting the central nervous system, 6) cerebrovascular disease, 7) current medication with psychoactive drugs except for benzodiazepines, and 8) participation in a cognitive study within the last 3 months (to avoid practice effects).

Procedures

After obtaining written informed consent, the medical history provided in the medical questionnaire was updated. Then, study eligibility was further assessed with the German versions of the MMSE [5] and the 15-item GDS questionnaire [30]. After completing these screening procedures, all subjects were assessed with the MoCA. The German version of the CERAD-NAB was administered at the end of the assessment to avoid possible interference effects with the MoCA. The MMSE was neither included in this CERAD-NAB version nor used to calculate the CERAD-NAB total score [29]. Subjects meeting any exclusion criteria were omitted from the main

statistical analysis only after all assessments took place. One out of four psychology master students who were specifically trained for the study examinations carried out the assessments. All assessments took place on one day during 1-2 hours and were held in a quiet room with subjects seated at a table.

We used the official German translation of the MoCA (Version 7, November 2004; <http://www.mocatest.org>). The cognitive domains assessed are: 1) "Visuospatial/Executive", 2) "Naming", 3) "Memory", 4) "Attention", 5) "Language", 6) "Abstraction", 7) "Delayed Recall", and 8) "Orientation". The original version provides an extra point for individuals with lower education (i.e., ≤ 12 years). Since we aimed at diligently correcting for education, we used the uncorrected MoCA total score in our calculations.

Statistical analysis

The effect of age, education, and sex on the MoCA total score was calculated using regression analysis. Twenty different general linear models were tested to adjust for the covariates age, education, and sex. A complete model search between a minimal and a maximal model was performed [31]. The models included the quantitative covariates, the quantitative covariates' squares, and their interactions with sex (see Supplementary Table 1 for details).

The MoCA total score was transformed using a cubic transformation to achieve normality and homoscedasticity of the residuals. The initial 20 regression models were then recalculated with the transformed score, and the best model was selected. The best model was defined as the model with the minimum Predicted Residual Sum of Squares (PRESS) statistic. This is a leave-one-out cross-validation with $PRESS = \sum (y_i - \hat{y}_i^{(-i)})^2$ where $\hat{y}_i^{(-i)}$ estimates the i th response from a model that was estimated without this observation [31]. A smaller PRESS statistic indicates a higher predictive power of the corresponding model. The same model was selected before and after transformation, which corroborates the robustness of the method. In a last step, we checked for heterogeneity of variance of the residuals. The formula for the demographically corrected standard scores (z-scores) is based on the final regression model. Normative values were then calculated using the z-score formula.

Sex differences in the MoCA total score were analyzed using the Mann-Whitney U-Test. Spearman's rank correlation for non-parametric data was

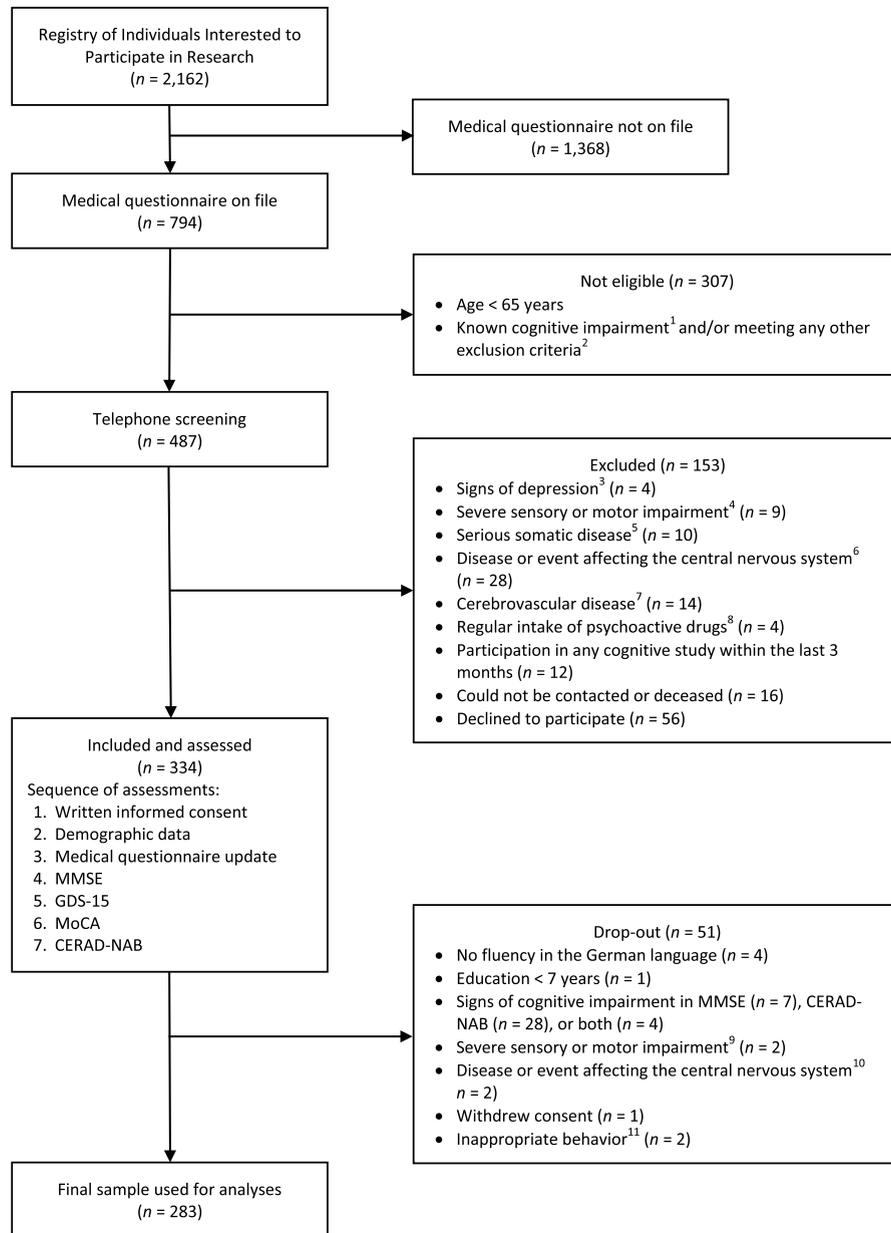


Fig. 1. Study flow chart. ¹Based on neuropsychological test results in previous studies and/or individuals with any diagnosis of cognitive impairment. ²Based on information provided in the medical questionnaire. ³Signs of depression: reported symptoms of depression and/or current diagnosis of depression and/or current psychotherapy for depression. ⁴Severe sensory or motor impairment: any visual or auditory impairment not correctable with (reading) glasses or hearing aids; motor impairment of the upper extremity (e.g., essential tremor, paresis, dyskinesia). ⁵Serious somatic disease (i.e., current chemo- or radiotherapy; severe cardiac, pulmonary, renal, gastrointestinal, or endocrine disease interfering with everyday functioning). ⁶Disease or event affecting the central nervous system (i.e., meningitis, encephalitis, severe traumatic brain injury with loss of consciousness >5 minutes, intoxication with neurotoxic substances, prior intracranial neurosurgery, general anesthesia within the last three months, previous or current substance addiction (drugs, alcohol, medication)). ⁷Cerebrovascular disease (i.e., stroke, transient ischemic attack). ⁸Regular intake of psychoactive drugs (i.e., for treatment of schizophrenia, bipolar disorder, obsessive compulsive disorder, personality disorder; substance-induced mental disorder). ⁹Macular degeneration ($n = 1$), hearing impairment interfering with cognitive testing ($n = 1$). ¹⁰Suspected Parkinson's disease ($n = 1$), general anesthesia within the last three months ($n = 1$). ¹¹Subject was verbally offensive towards test administrator ($n = 1$); subject deliberately made mistakes during cognitive testing ($n = 1$). CERAD-NAB, Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Assessment Battery; GDS-15, Geriatric Depression Scale (15 items; no subject scored >5/15 points); MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

Table 1
Demographic characteristics

Age group	<i>n</i>	Age, y	Women, %	Education ¹ , y	GDS-15 total score	CERAD-NAB total score	MMSE total score	MoCA total score
65–69	68	67.6 (1.4)	61.8	13.2 (2.7)	0.3 (0.8)	97.9 (5.5)	29.4 (0.9)	26.6 (2.6)
70–74	102	72.2 (1.3)	56.9	14.0 (2.9)	0.4 (0.7)	98.6 (5.2)	29.4 (0.7)	26.4 (2.4)
75–79	68	76.5 (1.4)	50.0	13.7 (3.2)	0.3 (0.6)	99.5 (5.9)	29.3 (0.9)	25.8 (2.5)
>79	45	82.6 (2.4)	46.7	13.3 (2.8)	0.4 (0.7)	99.0 (6.5)	28.9 (1.0)	25.1 (2.4)
Total	283	73.8 (5.2)	54.8	13.6 (2.9)	0.4 (0.7)	98.7 (5.7)	29.2 (0.9)	26.1 (2.5)

Data are presented as mean (SD). ¹Years of education was defined as the total number of years in school plus any professional education (not counting years needed to repeat). The maximum education was set at 20 years. In case of multiple specialized educations, only the longest one was counted. CERAD-NAB, Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological Assessment Battery; GDS-15, Geriatric Depression Scale (15 items); MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; y = years.

used to investigate the associations between the MoCA, the CERAD-NAB, and the MMSE total scores. Kendall's Tau for non-parametric data was used to test the associations between the demographic variables and the MoCA subdomains. Raw scores (i.e., not demographically corrected) were used in all analyses.

The required sample size was 171 participants. This allows the estimation of the 5th and the 95th percentile with no more than 2% deviation. Ten additional subjects were included per predictor variable (age, sex, education, and three expected interactions) to account for adjustments in the regression models. Thus, the minimum required sample size was 231 to account for all the predictor variables in the regression model [32].

All statistical analyses were performed using R, version 3.4.1 (R Foundation, Vienna, Austria) and RStudio Desktop (RStudio, Boston, MA, USA). Data are presented as mean (SD), unless stated otherwise.

RESULTS

Descriptive analysis

Two hundred and eighty-three cognitively healthy individuals (155 women, 128 men) were included in the final analysis. Participants' mean age was 73.8 (5.2) years, ranging from 65 to 91 years. Education was 13.6 (2.9) years, ranging from 7 to 20 years. The MoCA total score was 26.1 (2.5) points, and the MMSE total score was 29.2 (0.9) points. Detailed demographics are shown in Table 1. Medical history and current medications of all subjects were assessed based on the medical questionnaire and are displayed in Table 2.

The MoCA total scores ranged from 15 to 30 points when corrected for education [6]. Their distribution is shown in Fig. 2. Eighty-eight of the 283 subjects (31.1%) scored below the cut-off

score of <26/30 points. The mean MoCA total score was higher for women than for men (26.3 (2.4) versus 25.7 (2.6) points, $p=0.042$). The rates of subjects with the maximum scores in subdomains were: "Visuospatial/Executive" = 50.2%, "Naming" = 99.3%, "Attention" = 76.0%, "Language" = 52.7%, "Abstraction" = 56.9%, "Delayed Recall" = 29.7%, and "Orientation" = 93.3%. The MoCA total score showed a moderate positive correlation with the CERAD-NAB total score ($r_s=0.45$, $p<0.001$) and a weak positive correlation with the MMSE total score ($r_s=0.20$, $p<0.001$). A weak positive correlation was also observed between MMSE and CERAD-NAB total scores ($r_s=0.23$, $p<0.001$). There were no missing values in any of the analyses.

Demographic influences on the MoCA total score

The MoCA total score was best predicted by a regression model with age, education, and sex (adjusted $R^2=0.12$, $F=14.2$, $p<0.001$), explaining 12% of the variance. In the regression analysis, increasing age ($p<0.001$), less education ($p<0.001$), and male sex ($p=0.003$) were associated with a lower MoCA total score. The t-values indicate that this effect is strongest for education ($t=4.99$), followed by age ($t=-3.41$), and sex ($t=3.02$). The associations between the MoCA total score and demographic characteristics are shown in Fig. 3. An analysis of the influence of demographic variables on the MoCA subdomains is presented in Supplementary Table 2.

Z-score calculation

The z-scores are based on the formula: $z=(\text{transformed score} - \text{expected score}) / \text{residual standard deviation}$. A nearly normal distribution of the residuals was achieved using a cubic transformation of the raw MoCA total score. The formula for

Table 2
Medical history and current medications

Age group	<i>n</i>	History of head trauma ¹	Prior general anesthesia ²	Prior diagnosis of major depression ³	Prior psychiatric hospitalization ⁴	Regular alcohol consumption ⁵	Oral anticoagulants/antiplatelet drugs	Anti-hypertensive drugs	Statins	Oral antidiabetic drugs
65–69	68	5 (7.4)	59 (86.8)	3 (4.4)	1 (1.5)	45 (66.2)	5 (7.4)	20 (29.4)	14 (20.6)	4 (5.9)
70–74	102	11 (10.8)	85 (83.3)	7 (6.9)	3 (2.9)	61 (59.8)	13 (12.7)	36 (35.3)	14 (13.7)	6 (5.9)
75–79	68	5 (7.4)	56 (82.4)	0 (0)	1 (1.5)	49 (72.1)	17 (25.0)	31 (45.6)	18 (26.5)	1 (1.5)
>79	45	4 (8.9)	39 (86.7)	1 (2.2)	0 (0)	26 (57.8)	19 (42.2)	25 (55.6)	14 (31.1)	3 (6.7)
Total	283	25 (8.8)	239 (84.5)	11 (3.9)	5 (1.7)	181 (64.0)	54 (19.1)	112 (39.6)	60 (21.2)	14 (4.9)

Data are presented as *n* (%). ¹Mild head trauma with or without loss of consciousness <5 minutes. ²General anesthesia at least three months prior to study participation. ³No current diagnosis of major depression and/or current psychotherapy for major depression. ⁴Due to psychiatric diseases that occurred in the past (e.g., major depression). ⁵Participants answering the question: “Do you drink alcohol regularly?” with: “yes”.

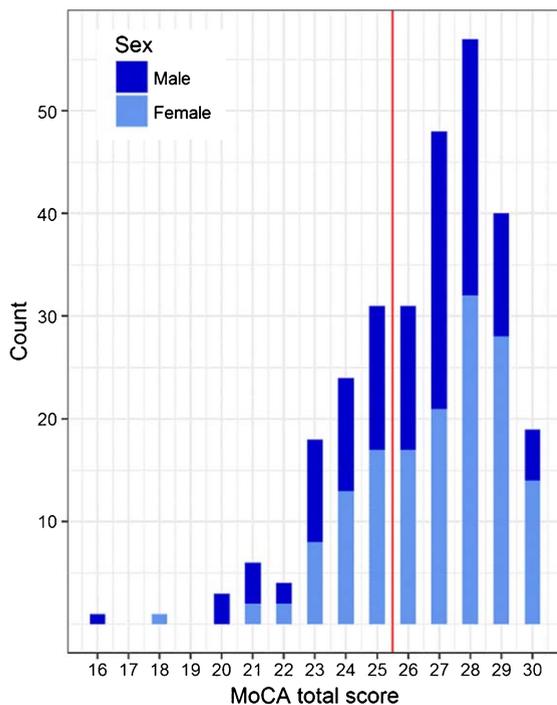


Fig. 2. Distribution of corrected MoCA total scores. The line indicates the originally proposed MoCA cut-off (26/30 points). In our study, 88 subjects (31.1%) scored below this cut-off.

the demographically corrected z-score was derived from the final regression model. The z-score can be calculated as follows: $z = \text{MoCA total score}^3 - (23816.36 + (-175.821 * \text{age}) + (472.9053 * \text{education}) + (1672.542 * \text{sex})) / 4470.258$. Sex is coded as male = 0 and female = 1. Age and education are entered in integer values (years). We followed the example of Weintraub and colleagues (2017) [33] and will provide a web-based calculation tool (<http://www.mocatest.ch>) to automatically determine

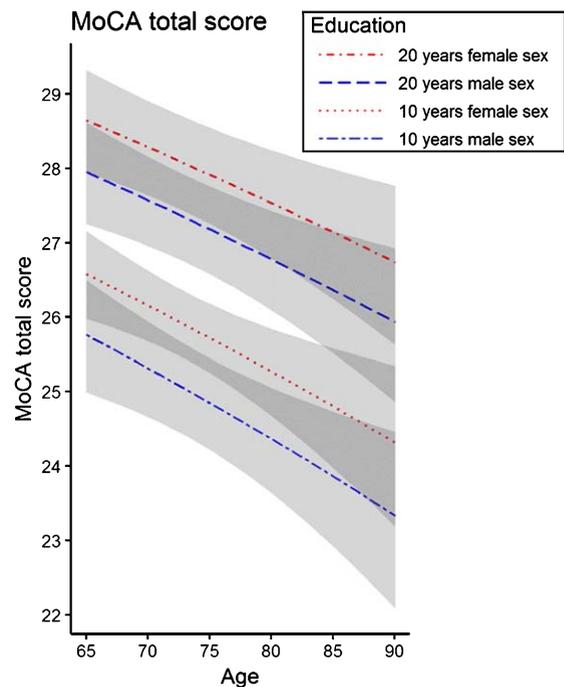


Fig. 3. Association of the MoCA total score with age, education, and sex. Exemplary regression lines are shown for 10 and 20 years of education, respectively. The regression model indicates that the MoCA total score is lower with increasing age and fewer years of education. Overall, female sex was associated with a higher MoCA total score than male sex. The areas in grey represent the 95% confidence intervals.

the z-score by entering the individual demographic data and MoCA total score.

Cut-off scores

Cut-off values were calculated based on the z-score formula (Table 3). The calculation was done separately for women and men for each year of age (65–91) and year of education (7–20). The cut-off

was set at a z-score of ≤ -1.28 (10th percentile) to achieve 90% specificity. The applied percentiles may vary depending on the specific setting (e.g., screening in research or case-finding). We, therefore, chose to establish normative tables for the most common percentiles used. All cut-off score tables (i.e., -1.64 SD (5th percentile), -1 SD (16th percentile), -1.5 SD (7th percentile), and -2 SD (2.5th percentile)) are provided in Supplementary Tables 3–6.

DISCUSSION

Our study provides demographically corrected normative values (z-scores) for the German version of the MoCA. The MoCA total score was influenced by age, education, and sex, which is in line with previous normative studies of the MoCA [13, 19, 28]. Other studies found significant effects of age and education, but not for sex [16–18, 20–27]. While there is a basic adjustment for education in the original version (+1 point for education ≤ 12 years), our analyses provide a more precise correction for this important influencing factor. Moreover, we made necessary adjustments for age and sex, which are lacking in the original version.

Considering these demographic influences will likely improve the diagnostic accuracy of the MoCA. For instance, in our sample of cognitively healthy participants, 88 subjects (31.1%) scored below the originally proposed cut-off score of 26 points [6], even when the bonus point was given for individuals with ≤ 12 years of education. The demographically corrected cut-off values provided in our study may reduce this false-positive rate. For example, a MoCA total score of 23 in an 85-year-old man (hypothetical patient 1) with 8 years of education is considered to be pathological according to the originally recommended cut-off score, even if one point would be added due to education ≤ 12 years. However, his demographically corrected z-score (based on our study) is -0.11 , which is still considered to be within normal limits. In contrast, a MoCA total score of 26 points in a 65-year-old woman (hypothetical patient 2) with 20 years of education is considered to be within normal limits. Yet, her demographically corrected z-score (based on our study) is -1.33 , which is below the 10th percentile and, therefore, pathological. These two examples illustrate that using demographically adjusted normative values lead to a decrease of false-positive (hypothetical patient 1) and false-negative results (hypothetical patient 2), respectively.

In our analysis, 12% of the variance in the MoCA total score was explained by demographic characteristics, while other authors reported an explained variance up to 49% [17]. This discrepancy is likely due to the much larger age range in some studies. Because both age and education influence cognitive performance, the variance increases when age or education ranges are broad. Consequently, including these variables in a regression model will explain more of the variance. When paralleling our findings to a study with a smaller age range [13], results are very comparable ($R^2 = 0.11$).

In our study, the correlation between the MoCA and CERAD-NAB total scores was much higher than the correlation between the MMSE and CERAD-NAB total scores. This suggests that the MoCA assesses cognition in a more comprehensive way compared to the MMSE. Twenty-eight excluded subjects scored below the cut-off on the CERAD-NAB, but still had an MMSE score ≥ 27 points, supporting the notion that the MMSE lacks sensitivity for detection of MCI. In this context, a recent report by Chapman and colleagues [34] indicates that the MMSE might be unsuitable to define eligibility for AD clinical trials. There is a clear need for a cognitive screening tool with high diagnostic accuracy for subject enrollment in AD studies. Future studies may verify whether the MoCA (used with appropriate norms) is more suitable to determine subject selection.

Comparison with international normative samples

In recent years, several research groups conducted normative studies for the MoCA in different languages. An overview of the existing literature is provided in Table 4. The majority of these reports suggest that the originally proposed MoCA cut-off score of 26 points is too conservative. Nine out of 14 normative studies reported a mean MoCA total score < 26 points in their sample [15–17, 20, 22, 23, 25–27]. In general, studies reported the mean MoCA total score without the one-point correction for education; one study did not mention whether the correction was applied [17]. When applying the bonus point for education, nearly one-third of our sample scored below the cut-off of 26 points. Previous normative studies using the original cut-off score reported false-positive rates of 46% [22] up to 76% [26].

Table 3
Highest MoCA total scores located just below the 10th percentile (z-score ≤ -1.28)

Women													Men																	
Age (y)	Education (y)												Age (y)	Education (y)																
	7	8	9	10	11	12	13	14	15	16	17	18		19	20	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
65	22	22	23	23	23	24	24	24	24	25	25	25	25	26	65	21	21	22	22	22	23	23	23	23	24	24	24	25	25	
66	22	22	23	23	23	24	24	24	24	25	25	25	25	26	66	21	21	22	22	22	23	23	23	24	24	24	24	25	25	
67	22	22	23	23	23	23	24	24	24	24	25	25	25	25	67	21	21	21	22	22	22	23	23	24	24	24	24	25	25	
68	22	22	22	23	23	23	24	24	24	24	25	25	25	25	68	21	21	21	22	22	22	23	23	23	24	24	24	24	24	
69	22	22	22	23	23	23	23	24	24	24	25	25	25	25	69	21	21	21	22	22	22	23	23	23	24	24	24	24	24	
70	22	22	22	23	23	23	23	24	24	24	24	25	25	25	70	20	21	21	21	22	22	22	23	23	24	24	24	24	24	
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72	21	22	22	22	23	23	23	24	24	24	24	24	25	25	72	20	20	21	21	21	22	22	22	23	23	23	24	24	24	
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79	20	21	21	21	22	22	22	23	23	23	23	24	24	24	79	19	19	20	20	21	21	21	22	22	22	23	23	23	24	
80	20	21	21	21	22	22	22	23	23	23	23	24	24	24	80	19	19	20	20	20	21	21	22	22	22	22	23	23	23	
81	20	21	21	21	22	22	22	23	23	23	23	24	24	24	81	19	19	20	20	20	21	21	21	22	22	22	23	23	23	
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84	20	20	20	21	21	22	22	22	23	23	23	23	24	24	84	18	19	19	20	20	20	21	21	21	21	22	22	22	23	23
85	20	20	20	21	21	21	22	22	22	23	23	23	23	24	85	18	19	19	19	20	20	21	21	21	21	22	22	22	22	23
86	19	20	20	21	21	21	22	22	22	23	23	23	23	24	86	18	18	19	19	20	20	21	21	21	21	22	22	22	23	23
87	19	20	20	20	21	21	21	22	22	22	23	23	23	24	87	18	18	19	19	19	20	20	21	21	21	21	22	22	22	23
88	19	20	20	20	21	21	21	22	22	22	23	23	23	23	88	18	18	19	19	19	20	20	20	21	21	21	22	22	22	22
89	19	19	20	20	21	21	21	22	22	22	22	23	23	23	89	17	18	18	19	19	19	20	20	20	21	21	21	22	22	22
90	19	19	20	20	20	21	21	21	22	22	22	23	23	23	90	17	18	18	19	19	19	20	20	20	21	21	21	22	22	22
91	19	19	20	20	20	21	21	21	22	22	22	23	23	23	91	17	18	18	18	19	19	20	20	20	21	21	21	22	22	22

The values correspond to the highest raw scores just below the 10th percentile. For instance, a MoCA total score of 22 points is just below the 10th percentile for a 65-year-old woman with 7 years of education.

Note: The bonus point for individuals with ≤ 12 years of education must not be applied when using this cut-off score table.

There are several explanations for these high false-positive rates and their substantial variation between studies. First, the MoCA total score might be influenced by intercultural and language differences (e.g., socioeconomic or sociodemographic factors, different word lengths originating from translations [20, 21, 26, 35]). One study suggests that ethnicity may influence the MoCA total score [26]. However, this may be explained by disparities in socioeconomic factors (e.g., quality of education) rather than ethnicity itself [35]. Second, there are important differences in sample sizes, ranging from $n = 90$ [6] to $n = 6,283$ [21]. Larger samples may better represent the general population and decrease the risk of sampling errors [35]. Yet, even large studies may have small cell sizes, when distinct subgroups (e.g., age categories) are defined to create norms. Third, not all studies were intended as normative studies, and data may have been collected for other purposes [13, 22–26, 28]. These “samples of convenience” may lack appropriate inclusion/exclusion criteria and standard procedures in MoCA administration, leading to increased variability within samples, especially if data are gathered from multiple centers [35]. Fourth, there are substantial dissimilarities in the demographic characteristics of study participants. Mean

age differs by almost 40 years between the youngest [19] and the oldest sample [22]. Large variances can also be seen in mean education, ranging from 8.2 (4.7) [17] to 14.4 (3.8) [28] years. Considering the effects of these demographic characteristics on the MoCA performance, differences in mean age or education possibly lead to variances in the mean MoCA total score among studies. Finally, normative studies diverge regarding inclusion/exclusion criteria [13, 23, 36]. Cognitive health of participants is of utmost importance in normative studies, particularly if subtle cognitive changes should be detected. In some normative studies, cognition was assessed using methods that might not be sensitive enough to detect subtle cognitive impairment [18, 25, 26]. Other investigators did not screen for cognitive impairment at all [23].

Cognitive health in normative samples

There are two different methodological approaches to normative studies. One is to rely on a population-based sample to create norms; for the other, a sample of indisputably healthy volunteers is chosen. Both methods bear the risk of inducing bias: while the former is prone to false-negative errors, the latter is prone to false-positive ones [35]. In our study, we

Table 4
Overview of international normative data for the MoCA

Source publication	MoCA language	Study type	n	Age, y	Age range, y	Female, %	Education, y	Exclusion of medical comorbidities ¹	Exclusion of cognitive impairment	Method	Output	Demographic effects	MMSE score	MoCA total score (uncorrected ²)	MoCA total score < 26; % (corrected ²)
Abou-Mrad et al. (2017) [15]	Arabic	NS	164	70.1 (6.9)	60–87	58.5	n. r.	Yes	Yes (DQ)	Frequency analysis, regression models	Base-rates for the 5 th , 10 th , 15 th percentiles, z-scores, regression equation	E (A and S not significant)	28.6 (1.3)	24.2 (2.9)	n. r.
Borland et al. (2017) [13]	Swedish	NS	758	73.1 (5.1)	65–85	62.5	n. r.	Yes	Yes (MMSE < 24 + AQT > 90 s, in some subjects: neuropsychological assessment, brain imaging, CSF analysis)	Regression models, intercept, estimates, RMSE	Percentiles, z-scores, regression equation	A, E, S	27.9 (1.4)	26.0 (2.3)	n. r.
Conti et al. (2015) [16]	Italian	NS	225	70.1 (5.7)	60–80	50.7	9.9 (4.6)	Yes	Yes (adjusted MMSE ≤ 23.8 + adjusted PMT ≤ 6.25)	Regression models	Correction grid for total scores, regression formula	A, E	n. r.	23.3 (3.2)	74*
Freitas et al. (2011) [17]	Portuguese	NS	650	55.8 (15.1)	25–91	62.8	8.2 (4.7)	Yes	Yes (abnormal performance in neuropsychological assessment, CDR)	Regression models	Mean (SD) ± cut-off scores for 1 SD, 1.5 SDs, and 2 SDs below the mean	A, E	28.9 (1.3) ³	24.7 (3.7)*	n. r.
Kenny et al. (2013) [18]	English	NS	5802	63.1 (n. r.)	n. r.	54.7	n. r.	n. r.	Yes (MMSE < 10, diagnosis of dementia, AD or PD)	GAMLSS	Percentiles, mean (SD)	A, E	n. r.	n. r.	n. r.
Konstantopoulos et al. (2016) [19]	Greek	NS	710	46.9 (16.6)	20–85	53.8	13.8 (3.8)	Yes	Yes (some questions of CDR, > 1.5 SDs below the normative values in ≥ 1 neuropsychological tests)	Regression models	Percentiles, mean (SD) for the total and subscores	A, E, S	n. p.	27.2 (1.9)*	n. r.
Kopecek et al. (2017) [20]	Czech	NS	540	75.6 (9.1)	n. r.	54.1	12.7 (3.5)	Yes	Yes (2 SDs below the sample mean in ≥ 2 neuropsychological tests)	Regression models	Percentiles	A, E	27.4 (2.0) ³	24.7 (2.9) ⁵	50
Larouche et al. (2016) [28]	Quebec-French	NS	1019	67.8 (8.8)	n. r.	67.3	14.4 (3.8)	Yes	Yes (neuropsychological assessment in most subjects, self-report in all subjects)	Regression models, PRESS, cross-validation	z-scores, regression equation	A, E, S	n. p.	26.4 (2.7)	n. r.
Lu et al. (2011) [21]	Chinese	VS	6283 (NC)	72.0 (0.8)	65–100	52.1	6.7 (1.1)	Yes	Yes (CDR > 0)	n. r.	Mean (SD)	A, E	26.3 (0.6)	23.8 (0.9)*	48
Malek-Ahmadi et al. (2015) [22]	English	NS	205	84.7 (7.9)	70–99	68.3	n. r.	Yes	Yes (MMSE < 26)	ANOVA	Mean (SD)	A, E	28.9 (1.2)	25.0 (3.1)	46
Narazaki et al. (2013) [23]	Japanese	NS	1977	73.6 (6.2)	65–96	58.7	11.0 (2.5)	Yes	No	Regression models	Mean (SD), median, range	A, E	n. p.	21.8 (3.9)	75
Nasreddine et al. (2005) [6]	French/English	VS	90 (NC)	72.8 (7.0)	n. r.	60.0	13.3 (3.4)	Only in 51 subjects	Yes (neuropsychological assessment)	n. r.	Cut-off score	E	n. r.	26.9 (n. r.)* ⁴	13 ⁵
Pereiro et al. (2017) [24]	Spanish	NS	563	66.4 (11.2)	n. r.	57.2	9.8 (4.8)	Yes	Yes (MMSE > 1.5 SD below the mean of the corresponding age and education group)	Regression coefficient, SD of the residuals	Percentiles, regression equation	A, E	27.9 (2.1)	n. r.	n. r.

Table 4
(continued)

Rossetti et al. (2011) [25]	English	NS	2653	50.3 (11.2)	18–85	60.0	13.4 (2.5)	Only stroke	Yes (3 yes/no questions regarding subjective cognitive impairment)	Pearson correlation, analysis of variance	Mean (SD)	A, E	n. p.	23.4 (4.0)	62
Rossetti et al. (2017) [26]	English	NS	1118	n. r.	n. r.	n. r.	n. r.	Only stroke	Yes (3 yes/no questions regarding subjective cognitive impairment)	Pearson correlation, independent samples t-test	Mean (SD), median	A, E	n. p.	22.3 (3.9)	76
Santangelo et al. (2015) [27]	Italian	NS	415	56.8 (18.8)	21–95	60.7	11.1 (4.8)	Yes	Yes (MMSE below the demographically corrected cut-off score)	Regression models	Correction grid for total scores, cut-off score	A, E	28.0 (2.4)	22.0 (4.2)	n. r.
Current study	German	NS	283	73.8 (5.2)	65–91	54.8	13.6 (2.9)	Yes	Yes (MMSE < 27 + CERAD total score < 85.89)	Regression models, PRESS	Percentiles, z-scores, regression equation	A, E, S	29.2 (0.9)	26.1 (2.5)	31

Studies are ordered alphabetically. Data are presented as mean (SD), unless stated otherwise.

¹Medical comorbidities (e.g., neurologic, cerebrovascular and/or psychiatric diseases known to affect cognition).

²Studies marked with an asterisk (*) did not indicate if the presented MoCA total score is corrected for education or not.

³Pooled mean (SD).

⁴As reported by Nasreddine and colleagues (2012) [36].

⁵As reported by Abou-Mrad and colleagues (2017) [15], based on the reported specificity of 0.87 by Nasreddine and colleagues (2005) [6].

A, age; AD, Alzheimer's disease; AQT, A Quick Test of Cognitive Speed; ANOVA, analysis of variance; DQ, Dementia Questionnaire; CDR, Clinical Dementia Rating; CSF, cerebrospinal fluid; E, education; GAMLSS, Generalized Additive Models for Location, Shape, and Scale; S, sex; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; n. r., not reported; n. p., not performed; NC, normal controls; NS, normative study; PD, Parkinson's disease; PMT, Prose Memory Test; VS, validation study (with control group); PRESS, Predicted Residual Sum of Squares; RMSE, Root Mean Square Error; SD, standard deviation. y = years.

chose the latter approach and applied stringent criteria to assure cognitive health of the participants. One might argue that such rigorous exclusion criteria may lead to a sample of “supernormal” individuals. However, the population-based approach does not seem appropriate when normative data are collected for an elderly population. Since the incidence and prevalence of MCI increases with age [2], the probability of erroneously including individuals suffering from a cognitive disorder increases as well. Including cognitively impaired individuals in a normative group lowers the reference range for cognitive health, and the distinction between the two groups (MCI versus healthy individuals) will be less clear. Consequently, it is very likely that the sensitivity for the detection of MCI decreases when relying on a population-based approach. Thus, we consider the criteria of indisputable cognitive health as a mandatory prerequisite for normative data.

Strengths and limitations

A regression-based approach yields some important advantages over the traditional norming method (i.e., reference ranges for cells of age and/or education groups). First, in traditional norming the sample is divided into subgroups. This leads to relatively small sample sizes per group, even if the overall sample size is quite large [31]. In contrast, regression-based norming considers the whole sample, and the continuous variables (i.e., age and education) are analyzed in their full range. Second, relying on age and/or education groups to create norms may misrepresent individuals who are situated close to the boundary of a subgroup [28]. Moreover, due to the more or less arbitrarily chosen subgroup boundaries, traditional norming may not properly reflect the natural development of cognitive performance [35]. The regression-based approach, however, considers the overall trend in the data. Third, the regression-based approach allows to simultaneously study multiple covariates and their potential interactions.

We acknowledge some limitations of our study. First, there may be a selection bias as our participants were recruited from an existing registry of individuals interested in taking part in research projects. These individuals may potentially show a greater motivation to perform well in cognitive testing than the average population. Individuals who participated in this study completed the Swiss educational system. Although the educational system in Switzerland is not 100% equal to the educational sys-

tems in other German-speaking countries [37], we believe that the acquired normative data are suitable for German-speaking populations in general. Our norms are intended for the elderly population and cannot be applied to individuals younger than 65 years. Second, cognitive test performance is commonly adjusted for demographic influences. Yet, some authors question if demographic adjustments are appropriate in dementia diagnostics, because age and education are known risk factors for cognitive impairment [23, 35]. O’Connell and Tuokko (2010) found that the overall diagnostic accuracy is comparable for raw versus adjusted scores [38]. While having lower sensitivity, the adjusted scores were shown to have better specificity. As our results show, MoCA performance declines with older age and/or lower education (Table 3). Therefore, when using a simple cut-off, the rate of false-positives may be higher with increasing age and/or lower education. Thus, adjusted scores may be more appropriate if the MoCA is used for diagnostic purposes in elderly individuals.

Our aim was to enhance the sensitivity of the MoCA by excluding any individuals with signs of cognitive impairment. In addition, specificity likely increases when applying a demographic adjustment of the obtained total score. However, the current normative data are not suitable to determine the exact diagnostic accuracy of the German MoCA. This version of the MoCA must first be validated in cognitively impaired patients, which is a follow-up project.

Conclusions

This study provides normative values for the German version of the MoCA. Our findings support the frequent statement that the originally proposed cut-off score may be too conservative. The MoCA performance was influenced by age, education, and—less consistently—by sex in all available studies, including ours. Thus, using demographically adjusted norms will improve the diagnostic accuracy of the MoCA. In addition, we observed a high level of heterogeneity in the methodology of existing normative studies. Therefore, we strongly suggest an international harmonization of guidelines for normative studies to enhance comparability in the future.

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SUPPLEMENTARY MATERIAL

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