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Normative performance of healthy older individuals on the Modified Mini-Mental State (3MS) examination according to ethno-racial group, gender, age, and education level

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Abstract

Objective: To present normative performance data on the Modified Mini-Mental State (3MS) examination for healthy community-dwelling older individuals according to gender, age, education level, and ethno-racial group.

Method: More than 19,000 generally healthy older men and women without a diagnosis of dementia were recruited from the general population in Australia and the U.S. for the ASPirin in Reducing Events in the Elderly (ASPREE) study. The 3MS exam was administered as part of the baseline screening and individuals scoring above 77 were eligible to participate.

Results: The sample comprised 16,360 Australian whites, 1080 U.S. whites, 895 African-Americans and 316 Hispanic/Latinos. The median age of participants was 74 years (range 65–98), with an average of 12 years of education and 56% were female. Increasing age and fewer years of completed education were associated with lower scores on the 3MS. Women scored higher than men in most age and education categories. Differences across ethno-racial groups were found.

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With factor analysis, four factors were identified which accounted for 35% of the between-person variance in 3MS scores for white Australians.

Conclusions: This large cohort of older individuals provides some of the most comprehensive 3MS normative data to be generated for whites (Australian and U.S.), Hispanic/Latinos and African-Americans, by age, gender, and educational attainment. These findings will serve as important reference standards for monitoring cognitive function in generally healthy older individuals, becoming increasingly important as this fraction of the population increases.

Keywords

Word; aging; cognition; dementia; Modified Mini-Mental Status examination (3MS); normative data

Introduction

With the increase in life expectancy the proportion of individuals who reach the age of 70 and in relatively good health is rapidly growing (Roser, 2017). Cognitive impairment remains an important concern for many older individuals, and cognitive decline is predictive of dementia risk (Prince et al., 2015). A better understanding of cognitive performance in the healthy older population who are free from dementia and other significant health conditions is needed.

The Mini-Mental State examination (MMSE) (Folstein, Folstein, & McHugh, 1975) is the most commonly used measure to assess global cognitive function in older individuals (Shulman et al., 2006). It has objective scoring and is often used as an initial screening tool for cognitive impairment and dementia (Tsoi, Chan, Hirai, Wong, & Kwok, 2015). However, the limitations of the MMSE are well recognized. These include the focus on only a few cognitive domains, the limited number of items and range of scores, and vulnerability to strong ceiling effects (Devenney & Hodges, 2017; Naugle & Kawczak, 1989).

The Modified Mini-Mental State (3MS) examination was developed to overcome some of these limitations (Teng & Chui, 1987). It incorporates four additional test items to assess other areas of cognitive function, including semantic fluency and delayed memory, and offers a wider range of scores. The 3MS has been shown to have good inter-rater and retest reliability and validity, which is superior to that of the MMSE, as well as having high specificity and sensitivity (McDowell, Kristjansson, Hill, & Hebert, 1997; Teng, Chui, & Gong, 1990; Tombaugh, 2005). The 3MS may be especially useful in assessing cognitive function in individuals without dementia or major cognitive impairment as it is less susceptible to ceiling effects (Chapman et al., 2016). Evaluating such individuals will become increasingly relevant as the population ages and more people remain cognitively intact into later life. This is also important for clinical trials that recruit older individuals without dementia.

Establishing a reference of normative cognitive function in the healthy older population is therefore important and could permit the more widespread use of the 3MS in general clinical practice. Prior studies provide some indication that 3MS scores vary according to age and

education level (Bravo & Hebert, 1997; Tschanz et al., 2002), as well as possibly gender (Brown, Schinka, Mortimer, & Graves, 2003; Tschanz et al., 2002), although other studies have reported no gender differences (Jones et al., 2002; Tombaugh, McDowell, Kristjansson, & Hubley, 1996). The majority of studies to date however, provide 3MS scores within strata defined by either age groups or education levels, but rarely both. Further, most research has focused on predominantly white or mixed populations, with minority populations underrepresented in studies of later life cognitive function. It also remains unclear whether demographic factors influence 3MS scores in a more homogenous population of healthy older individuals without dementia.

This paper provides high-quality normative data across the range of age, gender, and education levels in community-dwelling older individuals without dementia and other major health conditions, taking into account ethno-racial differences. The baseline scores on the 3MS from the ASPREE (ASPirin in Reducing Events in the Elderly) participants are described according to gender, age, education level, and ethno-racial categories (white, African-American, and Hispanic/Latino). The large size of the ASPREE study provides some of the most extensive cognitive normative data available for the 3MS in the generally healthy older population. Finally, we also report on the results of factor analysis to explore the underlying constructs of the 3MS.

Materials and methods

Participants

Full details regarding the sampling procedure and study design of ASPREE have been published previously (ASPREE, 2013; McNeil et al., 2017). In brief, ASPREE is a randomized double-blinded placebo-controlled clinical trial to determine the risks and benefits of low-dose aspirin (100 mg daily) for an average of 5 years when used in the primary prevention setting for older people. This paper describes baseline 3MS data from ASPREE participants.

Recruitment took place from 2010 to 2014. In Australia, recruitment occurred through primary care physicians (general practice, GPs) across rural, regional, and metropolitan centers in the South Eastern region of Australia (four States and one Territory). In the U.S., recruitment of participants from the community occurred through academic and clinical trial centers. A specific goal in the U.S. was to recruit at least 50% from U.S. minority groups, and these individuals were eligible to participate if they were aged 65 years and over. This is due to their survival disadvantage and higher burden of diseases for which aspirin was indicated (e.g. CVD)

ASPREE is being conducted in accordance with the Declaration of Helsinki 1964 as revised in 2008, the NHMRC Guidelines on Human Experimentation, the federal patient privacy (HIPAA) law and ICH-GCP guidelines and the International Conference of Harmonization Guidelines for Good Clinical Practice. ASPREE also follows the Code of Federal Regulations as it relates to areas of clinical research. The overall management and conduct of the trial is the responsibility of the ASPREE Steering Committee.

Inclusion and exclusion criteria

Participants were eligible for inclusion in ASPREE if they were aged 70 years or over (or 65 years and over for U.S. African-American and Hispanic/Latino minority groups), able to provide informed consent and capable of attending the GP/clinic for a study visit. The age differential between U.S. minority groups and other participants was permitted given the evidence that the former populations have a higher burden of disease and increased mortality rates. Full details regarding the inclusion and exclusion criteria have been published previously (ASPREE, 2013; McNeil et al., 2017). Key exclusion criteria were diagnosed dementia, or a score of <78 on the Modified Mini-Mental State (3MS) examination, established cardiovascular disease (e.g. atrial fibrillation, congestive heart failure) or previous cardiovascular event (e.g. myocardial infarction, stroke, transient ischemic attack), uncontrolled hypertension (systolic blood pressures ≥ 180 mmHg and / or a diastolic blood pressure ≥ 105 mmHg), severe physical activity limitations (severe difficulty or inability to perform at least one of the six Katz basic Activities of Daily Living (ADLs)), high risk of bleeding, anemia, current continuous use of antithrombotic medications or aspirin, or contraindication/allergy to aspirin. GPs/primary care physicians also needed to agree to the participant's involvement, and to state that they were free of any chronic illnesses likely to cause death within five years. Given these exclusion criteria, the sample could be considered to be generally healthy.

Assessments

At recruitment, participants underwent two in-person baseline visits within 4 weeks of each other to determine eligibility and complete baseline assessments, including detailed questionnaires, neurocognitive tests, and physical measures. The 3MS (detailed further below) was administered concurrently with the 10-item Center for Epidemiological Studies Depression scale (CES-D-10) (Mohebbi et al., 2018; Radloff, 1977), given that depression can confound performance on this test. Individuals scoring below 78 on the 3MS but with a high depression score (CES-D-10 > 7) were reassessed with the 3MS and CES-D-10 three months later. These individuals were still eligible to participate if their subsequent 3MS score was ≥78, regardless of depression status. The cut-point of 77/78 was chosen to ensure high sensitivity to screen for participants with dementia (Bland & Newman, 2001).

Modified Mini-Mental State (3MS) examination

The 3MS is a reliable and valid instrument that is relatively short and easy to administer (Cullen, O'Neill, Evans, Coen, & Lawlor, 2007). It consists of 34 questions over 15 items (maximum scores from 3 to 10), and the total scores range from 0 to 100, with higher scores indicating better cognitive function (Teng & Chui, 1987). The 3MS provides a brief assessment of a number of cognitive domains including attention, verbal recall, expressive language, verbal fluency, visual construction and reasoning. It was developed as an extension of the MMSE with additional items and a broader range of scores for most items. This contrasts with many items on the MMSE which are scored as either correct (1) or incorrect (0) responses and the maximum score is only 30 points (Folstein et al., 1975).

Staff training and monitoring

Administration of the 3MS assessments were strictly monitored to ensure consistency from all staff members. Training of staff in Australia was undertaken by a neurologist study investigator and staff were re-accredited annually during the baseline period. In the U.S., site staff were trained by qualified Coordinating Center staff supervised by a neurologist study investigator with site staff re-accredited annually throughout the study. The development of detailed scoring guidelines for the 3MS, was overseen by the ASPREE Chair of the Dementia Adjudication Committee, and staff reviewed (both in the administration as well as the scoring of the 3MS) annually, for the duration of the study, to ensure procedural adherence and high quality data collection.

Demographic characteristics

A wide range of demographic, health and lifestyle information was available on all participants. Factors considered in this analysis included gender (male or female), age at randomization (years), which was treated as a categorical variable defined as: 65–69 years (U.S. minorities only), 70–74 years, 75–79 years, 80+ years, and education level (ranging from less than 9 years attained to more than 16 years). Self-identified ethno-racial groups included Hispanics/Latinos, non-Hispanic whites, Aboriginal or Torres Strait Islanders, Asians, African-Americans, and American Indians. Based on the small numbers within some of these groups, some individuals were excluded and other demographic groups were combined for these 3MS analyses.

Statistical analysis

Summary statistics were calculated for all participants and within strata. Given the skewed distribution of 3MS scores, the median and interquartile range (IQR) were used as the summary statistics, and the mean and standard deviation are reported for direct comparison with prior studies. Scores were compared between groups defined by gender, age, education, or ethno-racial categories using the Kruskal-Wallis rank test, where appropriate. Linear regression analysis was used to determine which demographic factors were most predictive of total 3MS scores within separate ethno-racial groups. Two-way interaction terms between age group, education group and/or gender were investigated in the models. Standard regression model assumptions of homogeneity of variance and approximately normal distribution of the residuals were examined.

An exploratory factor analysis was conducted in the Australian white population using the 15 items from the 3MS to identify possible underlying constructs. This analysis was not performed for the three U.S. groups given the smaller size of these groups, which increases the likelihood of poor-factor analysis solutions (MacCallum, Widaman, Preacher, & Hong, 2001). We used both orthogonal and oblique rotation to assess the inter-factor correlation structure. Multiple criteria were used to decide on the final number of factors, including the scree plot, Kaiser criterion with eigenvalues >1, and interpretation of the result. Stata version 14.1 (StataCorp, College Station, U.S.A.) was used for all statistical analyses.

Results

Demographic characteristics of the study population

From a total of 19,114 recruited to the ASPREE study, one participant was excluded from this analysis for not providing information on gender and one for not reporting ethnicity. A further two participants were excluded as they were subsequently found to be ineligible due to 3MS scores below the 78 cut-off pre-specified at inclusion (with scores of 72 and 76).

As shown in Figure 1, the remaining sample included 16,701 participants in Australia and 2409 in the U.S. Within each country, individuals were categorized according to their reported ethno-racial groups. In Australia, the number of non-whites was particularly low (n = 341), with a number of individuals reporting mixed ethnicity and only eight individuals self-identified as Aboriginal or Torres Strait Islander. In the U.S., the largest single group was whites (45%), with a substantial proportion of African-Americans and Hispanic/Latinos. Only 53 individuals were not in one of these three groups. Given our pre-specified decision to stratify all analyses by ethno-racial group, the groups with few participants (non-shaded boxes in Figure 1) were not considered further in the analyses described here. In addition, we also excluded 57 participants from the current analysis who had completed the 3MS in Spanish (all others having completed the test in English). All of these participants self-identified as Hispanic, reducing this group from 373 to 316.

The sample included in the analysis was 18,659 participants, which is 97.9% of the overall ASPREE participants (McNeil et al., 2017). Over half of the participants were female (56.6%).

At randomization, individuals ranged in age from 65 to 98 years (median 74, mean 75). U.S. African-Americans and Hispanic/Latino participants (both median 70 years, IQR 67–74 years) were younger than white participants from the U.S. (median 75 years, IQR 72–79 years) and from Australia (median 74 years, IQR 72–79 years). This corresponds to the study design (McNeil et al., 2017).

The number of years of completed education was grouped into one of five categories and as a binary variable (0–12,>12 years). Significant differences (X^2 = 1700, p < 0.0001) in the proportion of individuals who had completed more than 12 years of education were observed across the ethno-racial groups: 38.6% white Australians, 81.3% white U.S., 68.2% African-American U.S. and 35.7% Hispanic/Latino U.S.

Figure 2 shows the overall distribution of test scores on the 3MS, and Figure 3 for each ethno-racial group. As can be seen, the distribution of scores was skewed and defined by upper and lower limits, which corresponds to the maximum possible score on the 3MS (100) and the minimum score for eligibility into the ASPREE study (78), respectively. For both the Australian and U.S. whites, there is a long tail for the lower 3MS scores, suggesting that the cut-off of >77 has had little influence on the overall distribution of scores. However, this is not the case for U.S. African-American and Hispanic/Latino groups.

3MS scores according to demographic characteristics

A graphical display of 3MS scores across ethno-racial groups is shown in Figure 4. The U.S. whites had higher 3MS scores, while the Hispanic/Latinos in this population had slightly lower scores (X^2 = 447.6, d.f.3, $p < 0.0001$). The 3MS summary statistics for the overall population and by social demographic characteristics are shown in Table 1. Females performed slightly better than males (X^2 = 348.6, d.f.1, $p = 0.0001$), and 3MS scores increased with education level (X^2 = 1023.8, d.f.1, $p = 0.0001$). As expected, older age groups had lower 3MS scores (X^2 = 447.6, d.f.3, $p = 0.0001$), with the exception of the 65–69 age group. This anomaly is likely to be due to the different ethno-racial characteristics of this group, which included only U.S. African-Americans and Hispanic/Latinos.

For all subsequent analyses, we considered ethno-racial groups separately and provide percentiles according to gender, age and education level given the skewed distribution. The 3MS scores obtained from the Australian whites are shown in Table 2 and Figure 5. The 3MS scores are provided separately for males and females, and according to three age groups and five educational categories. In all cases, 3MS scores declined with age, increased with higher levels of education and were higher in women than men. The decline with increasing age was most noticeable for women with higher levels of education. Supplementary Table 1 provides the percentile scores for 3MS scores for females and males for these three age groups and according to two levels of education (0–12yrs and >12 years). These groups were generated to ensure adequate numbers of individuals within each sub-category, while retaining the effect of these demographic characteristics on 3MS scores. This education grouping is also consistent with that for the U.S. populations (as described below).

The data obtained for the U.S. white, African-American and Hispanic/Latino participants are shown in Table 3 and visually presented in Figures 6 and 7. Given the smaller numbers of U.S. participants when considering gender, age, and education groups, education attainment was grouped into two categories; lower and higher number of years (0–12 and >12 years), and age also divided into two categories (65–69 years and ≥70 years). All sub-categories are represented by a minimum of 20 participants, with Hispanic/Latino males aged 60–69 years and with over 12 years of education the group with the smallest representation (n = 23). Similar patterns in the U.S. white population were observed to those seen in the Australian whites, with age, education, and gender effects; although these varied across categories. In the U.S. minority groups however, differences in 3MS scores according to education level were much more noticeable, but males and females had very similar scores. Supplementary Tables 2–4 provide simple reference tables with percentile scores for the 3MS in each ethno-racial category.

Linear regression models

A standard linear regression analysis was performed to determine the contribution of gender, age, and education level to 3MS scores within each ethno-racial group (Tables 4 and 5). This analysis further supports the data in the summary tables, with female gender, decreasing age and increasing education all associated with higher 3MS scores in whites (both Australian and US). In the U.S. minority populations, decreasing age was also associated with better 3MS scores, and increasing education level was strongly associated with better test scores.

Noticeably, however there was no significant difference in 3MS scores according to gender in either the African-American or Hispanic/Latino population. There was no strong evidence that gender, education or age group was an effect modifier in these models, and therefore further stratified regression models were not performed.

Factor structure of the 3MS

Summary statistics were calculated for each of the 15-items and for the total score on the 3MS in the overall sample (Table 6). On a number of the items, participants scored very highly, with over 90% achieving full scores. The majority of errors were made on the first recall and the similarities tasks. Other tasks with a moderate number of errors were semantic fluency (four-legged animals), the repetition task, pentagon copying and the second recall. Only 3.75% of the population scored full marks (100) on the overall 3MS. Normative data on these selected tasks will be the subject of a future manuscript.

The exploratory factor analysis using data gathered from Australian whites (by far the largest group in this study) indicated a four or five factor solution with eigenvalues of at least one (Supplementary Table 5). Based on these values, in combination with the scree plot (Supplementary Figure 1) and the interpretation of the alternative five factor solution, a four-factor solution was deemed most appropriate and fulfilled the Kaiser criterion (eigenvalues >1). These four factors explained a total of 34.4% of the variation. The factor loadings for the orthogonal and oblique rotations were very similar (Supplementary Tables 6 and 7) and the inter-factor correlation matrix for the oblique rotation indicated the factors were independent, with very weak correlations (ranging from $r = 0.06$ to 0.19). This supports the use of the principal axis method with a varimax orthogonal rotation to extract the non-correlated components (Supplementary Tables 7). In interpreting the rotated factor pattern, an item was said to load on a given component if the factor loading was .40 or greater for that component. Based on the pattern of loadings, the factors were labeled as verbal episodic memory (2 items), language and executive function (5 items), psychomotor speed & working memory (2 items) and orientation & visual construction (3 items). Four-legged animals loaded most strongly on factor 2 (0.38), although it fell short of the cut-off. Temporal orientation and registration had low factor loadings (<0.30) on all four factors.

Discussion

The 3MS is a general screening tool for cognitive function, and has been adapted to overcome several of the limitations with the widely used MMSE. The 3MS is simple and easy to use in large population settings. This study provides some of the most substantial normative data for the 3MS, according to gender, age, and educational level and across ethnic-racial groups (whites, African-Americans and Hispanic/Latinos). Our sample was a healthy older community-dwelling population free of dementia (according to clinical history and 3MS cut point) and cardiovascular disease, and thus our data may not be reflective of all older individuals. These norms were derived in a community cohort and the inclusion criteria was only based on the 3MS score. It is thus possible that there is an admixture of mild cognitive disorders included.

The proportion of healthy individuals aged 65+ around the world is expected to grow, and to date, these individuals have received less attention in studies of cognitive screening tools (Cullen et al., 2007). Establishing normative data for the 3MS scale in healthy older individuals will be informative for future clinical trials and could enable the more widespread use of this scale in general population screening. There have been a few previous studies, the majority involving North American white populations, which provide normative data for the 3MS in individuals without dementia; however, no study as large as the one described here. Our results also suggest that while there are similarities across the countries, there would also be some risks in applying U.S. (or North American) norms to other populations. This is even the case for Australia where the same language is spoken and which could be considered culturally similar.

The 3MS is considered a valid and reliable tool for assessing cognitive function, and covers a broader range of cognitive domains than the majority of screening tools (Cullen et al., 2007). The key domains assessed are thought to include attention/working memory, verbal recall, expressive language, verbal fluency, visual construction and reasoning (Cullen et al., 2007). Our factor analysis of the 3MS indicated a 4 component solution for the 15-items in Australian whites, although the first two factors, labeled as verbal episodic memory and executive function/language, accounted for the majority of the variance in scoring. Interestingly, these are two cognitive domains which decline with age and where poor performance has been linked to Alzheimer's dementia (Chen et al., 2001; Dickerson, Sperling, Hyman, Albert, & Blacker, 2007).

Our results indicate that 3MS scores vary by age and education level. Ethnic differences were found, which suggests the need to consider cultural bias in the 3MS. There are a number of possible reasons for these differences, but there is good evidence to indicate that the lack of availability of quality education (for similar years of education) is an important factor driving racial differences in cognitive function between older whites and African-Americans in the U.S. {Carvalho, 2015 #234}. The linear regression models also indicated that the strength of association between education and gender with 3MS differed across ethno-racial groups, while associations with age were similar. In African-Americans, more than 12 years of education, compared with fewer years, was associated with a 2.8 point higher 3MS score, when gender and age were kept constant. In comparison, the higher education level in the U.S. whites was associated with a 1.9 point increase in 3MS score, while in Hispanic/Latinos it was 4 points higher, indicating that education level had a greater influence on 3MS scores in this sample. We also observed significant but clinically small differences in 3MS scores between female and male participants, across the different categories of education level and age for white U.S. and Australians. This is despite the higher levels of education attainment in white male (43.9% > 12 years) compared with white female (39.2% > 12 years) participants. In the linear regression analysis, this corresponded to an average 1.4 points lower score on the 3MS in white males compared to females, when education and age were held constant. While clinically this is a small effect size, it is of a similar order to that of age in the white samples, and only marginally smaller than the effect size with education. No gender differences were evident in the U.S. minority groups.

The Canadian Study of Health and Aging involved 7754 individuals without dementia aged 65+ years who were recruited predominantly from the community, and administered the 3MS in either English (81%) or French (Bravo & Hebert, 1997). Individuals scoring 77 or lower on the 3MS and those who did not undergo further cognitive evaluation, were excluded. No information on the ethno-racial mix of the population was given. Normative data was reported for five age groups and four education levels, and 3MS scores decreased with age and fewer years of education. The authors did not report separate norms for gender but stated that gender had a smaller effect. A prior publication on a smaller sub-sample (n = 406) from this study also indicated no association between 3MS scores and gender (Tombaugh et al., 1996).

A similar pattern of scores and associations has also been reported in the Charlotte County Healthy Aging Study in the U.S., which involved 393 community-dwelling primarily white (98.2%) individuals aged 60–85 years (Jones et al., 2002). Associations with 3MS scores were reported for age, education, and gender. However, the last effect was said to be small and gender was thus combined for the normative tables. Furthermore, given the small sample size, education-stratified data could not be given and instead, score adjustments based on age were provided.

Other studies have reported that females perform significantly better on the 3MS than males (Bassuk & Murphy, 2003; Tschanz et al., 2002), but the small size of the samples has likely prohibited reporting of gender-specific normative data. Education level may also influence the association between both age (Bravo & Hebert, 1997) and gender with, for example, stronger gender associations with 3MS at lower levels of education (Tschanz et al., 2002). However, we found no evidence of interactions in our analysis (data not shown).

In one of the few studies of 3MS scores in older non-white community populations, Brown et al. (2003) provided normative data for 238 U.S. African-Americans aged 60–84 years, examining performance and the influence of demographic characteristics. They found that age had a moderately large effect on 3MS scores, and associations with both gender and education level were also reported, both overall and within age strata.

The Women's Health Initiative Memory Study (WHIMS) of women aged 65–80 years in the U.S. included 6,490 whites, 536 African-American, and 181 Hispanic/Latino women (Rapp, Espeland, Hogan, Jones, & Dugan, 2003). The composition of minority groups is similar, although it represents a smaller proportion of their overall sample (12%), compared to our ASPREE U.S. population (53%). They excluded individuals based on self-reported dementia or cognitive impairment and the overall scores for the three U.S. populations were very similar to ours. Ethno-racial differences observed in our study were also similar to those from the WHIMS, with whites scoring higher overall on the 3MS than African-Americans and Hispanics. The differences observed between Australian and U.S. whites in education level for older individuals of this generation have been reported previously (Tunny, 2006), and are unlikely to be driven to a major extent by the differences in recruitment strategies between the two countries (i.e. U.S. recruitment occurred through academic and clinical trial centers, while Australians were recruited through primary care physicians).

A couple of previous studies have also investigated the factor structure of the 3MS, and reported either a four or five factor solution, although the loading of items on each of the factors has differed. The first study, by Abraham et al., identified a 5-factor solution in a population of 892 nursing home residents aged 71–92 years, which accounted for 59% of the variance (Abraham et al., 1993). A similarly higher percentage of the variance was explained by the four factor solution in a small study of 94 psychiatric outpatients (aged 63–93 years) with the French version of the 3MS (Cappeliez et al., 1996). Our findings, are however, more in line with those of Rapp et al., 2003; which was also based on a healthy population recruited for a clinical trial (WHIMS) (Rapp et al., 2003). Their population, which only included females, had a similar ethnic mix, with a majority of whites, but also African-Americans and Hispanics. While Rapp identified a five factor solution through their formal tests, they deemed that four factors were more appropriate, and this accounted for 37% of the variance. The exact loading of items on each of the components was slightly different from those of Australian whites in ASPREE; for example, verbal semantic fluency four-legged animals loaded on their first component ‘verbal memory, whereas in our study it did not load strongly on any component. In concordance with our finding though, they identified the same ‘Orientation & Visuo-construction’ factor as we did, with the same three items, and they also found that the temporal orientation item did not load on any of the factors. This could be explained by the very small variance in scores on this item in healthy populations. Indeed, despite a range of scores from 0 to 15, only 0.73% of participants scored less than 13 on this test. In the nursing home study, this item loaded on the orientation factors (Abraham et al., 1993).

Limitations and strengths

The ASPREE pospulation is representative of a generally healthy older population more highly educated than the general population and without overt clinical disease. Individuals were without a diagnosis of dementia and had 3MS scores above 77. This will limit the generaliz-ability of these normative data. The distribution of 3MS scores in this population is constrained by both floor and ceiling effects, which has resulted in the exclusion of individuals without dementia but with lower 3MS scores. This influenced the sample selection of minority participants, but appeared to have little effect in our study for the white population (as observed in Figure 2). Another limitation is the low representation of certain ethno-racial groups, including Aboriginal and Torres Strait Islanders, Native Americans and Asians, for whom we were not able to provide meaningful normative data. We were also limited in the extent to which we could sub-divide participants across age and education groups for the U.S. individuals, particularly those from the minority populations, as well as being unable to perform reliable exploratory factor analysis on these groups. However, our sample is considerably larger than most previous studies, indicating that the data will make a significant contribution to existing information. A further strength of the study is the recruitment of individuals across a number of sites in South Eastern Australia and the United States, which includes many individuals from not only metropolitan districts, but also regional and rural areas. The size of the population has permitted us to provide reference ranges stratified by ethno-racial group, gender, age and educational categories, unlike any

previous study utilizing the 3MS. It has also enabled us to investigate the factor structure of the 3MS in white Australians.

Conclusion

In summary, using data gathered at baseline from a large community-based clinical trial, our study reports 3MS scores for self-identified Australian and U.S. whites, U.S. African-Americans, and U.S. Hispanic/Latinos, by age, gender, and education level. We have shown in ASPREE that despite a relatively select and generally healthy population, differences were observed in 3MS scores according to demographic characteristics, which is in line with associations reported previously. This information should provide a very useful reference for both clinicians and researchers and important information for future clinical trials, especially those involving healthy individuals without dementia. It should be noted however, that these normative data have been derived in a community cohort that were not screened to be 'cognitively healthy' and thus it is possible that an admixture of mild cognitive disorders is included. This needs to be considered when clinicians are using this data, if the goal is to screen out mild cognitive disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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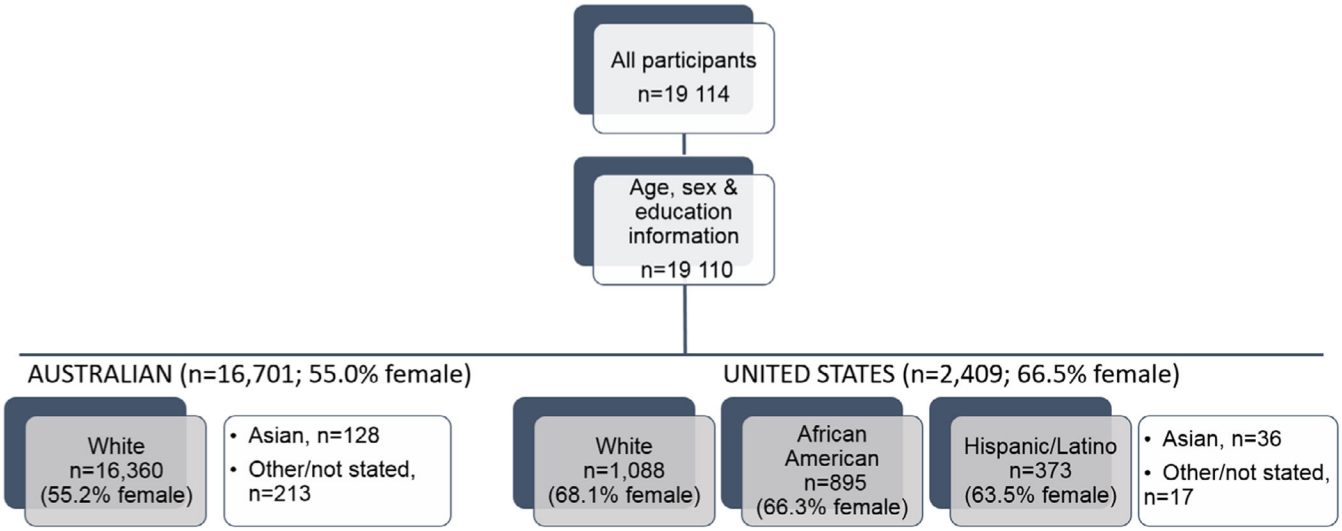

Figure 1. Participants recruited in ASPREE across groups defined by country, ethnicity, and race. 3MS: Modified Mini-Mental State examination.

Note: the two groups on the left are Australian participants and the four groups on the right are U.S. participants. Groups without shading could not be included in ethno-racial stratified analyses due to the small numbers.

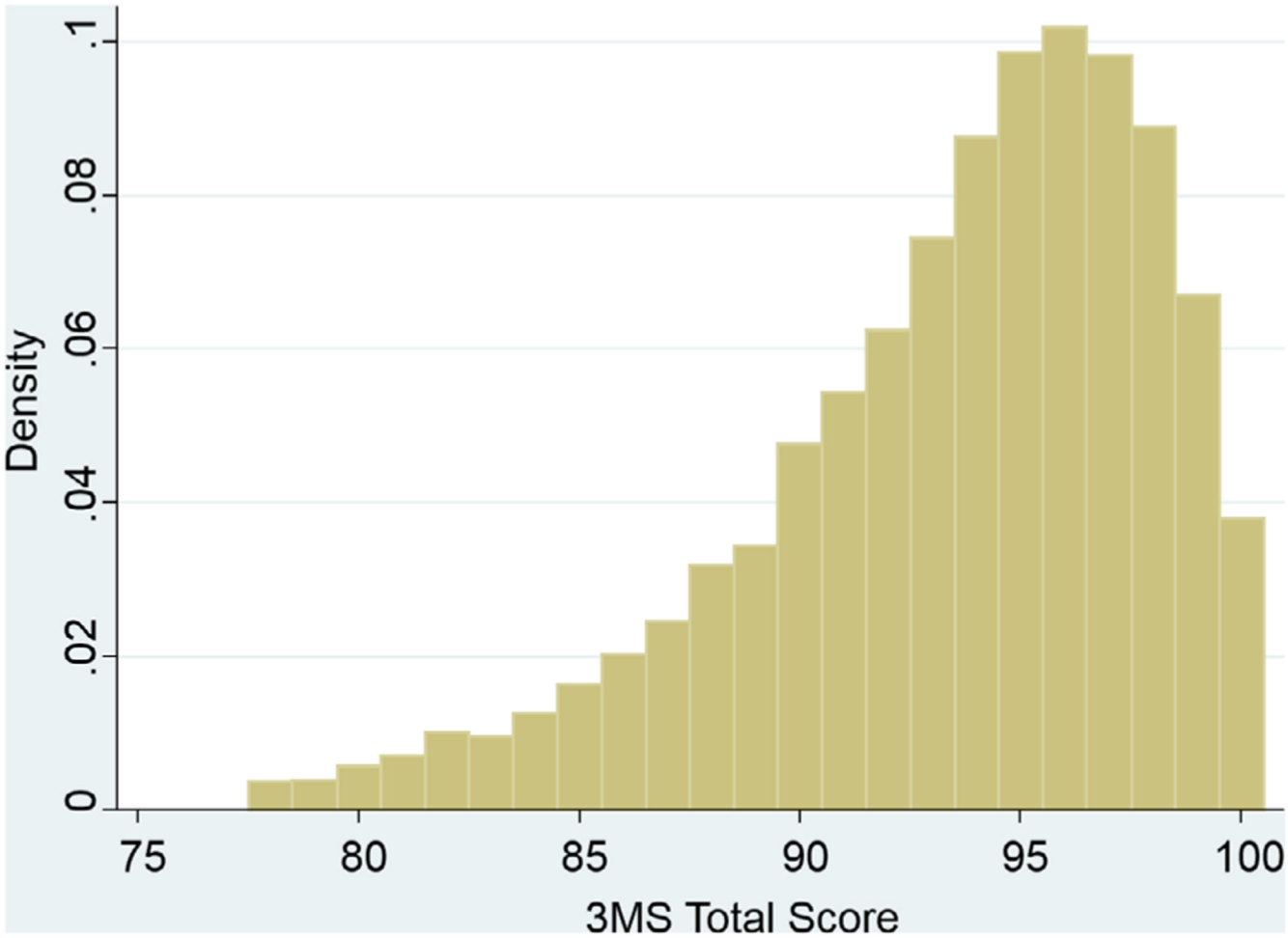

Figure 2.
The distribution of total 3MS scores across all ASPREE participants included in this study (n = 18,659). 3MS: Modified Mini-Mental State examination.

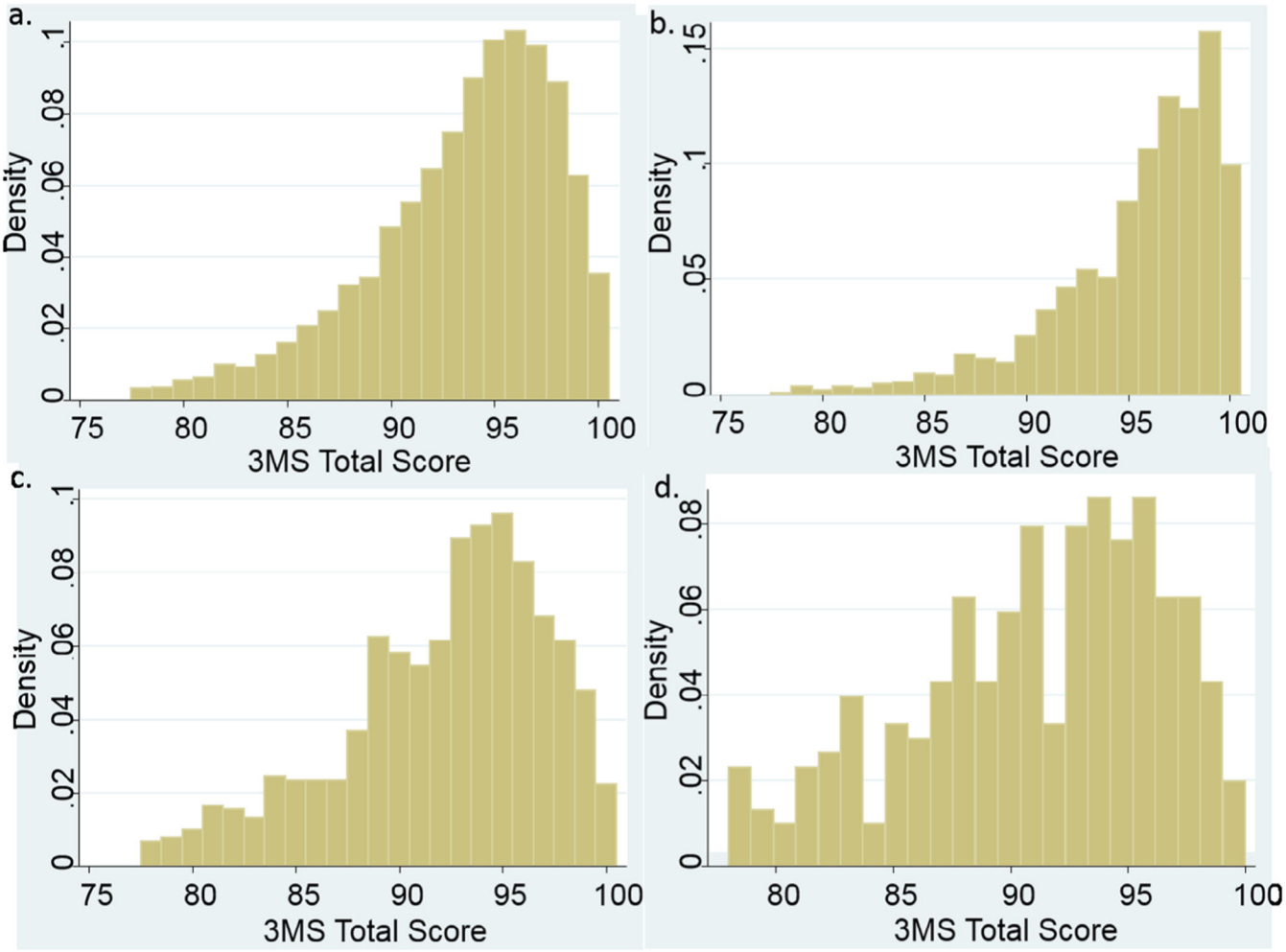

Figure 3.

The distribution of total Modified Mini-Mental State (3MS) examination scores across participants within each ethno-racial category. (a). white Australians (n = 16,360); (b). white U.S. (n = 1,088); (c). African-American U.S. (n = 895); (d). Hispanic/Latino U.S. (n = 316).

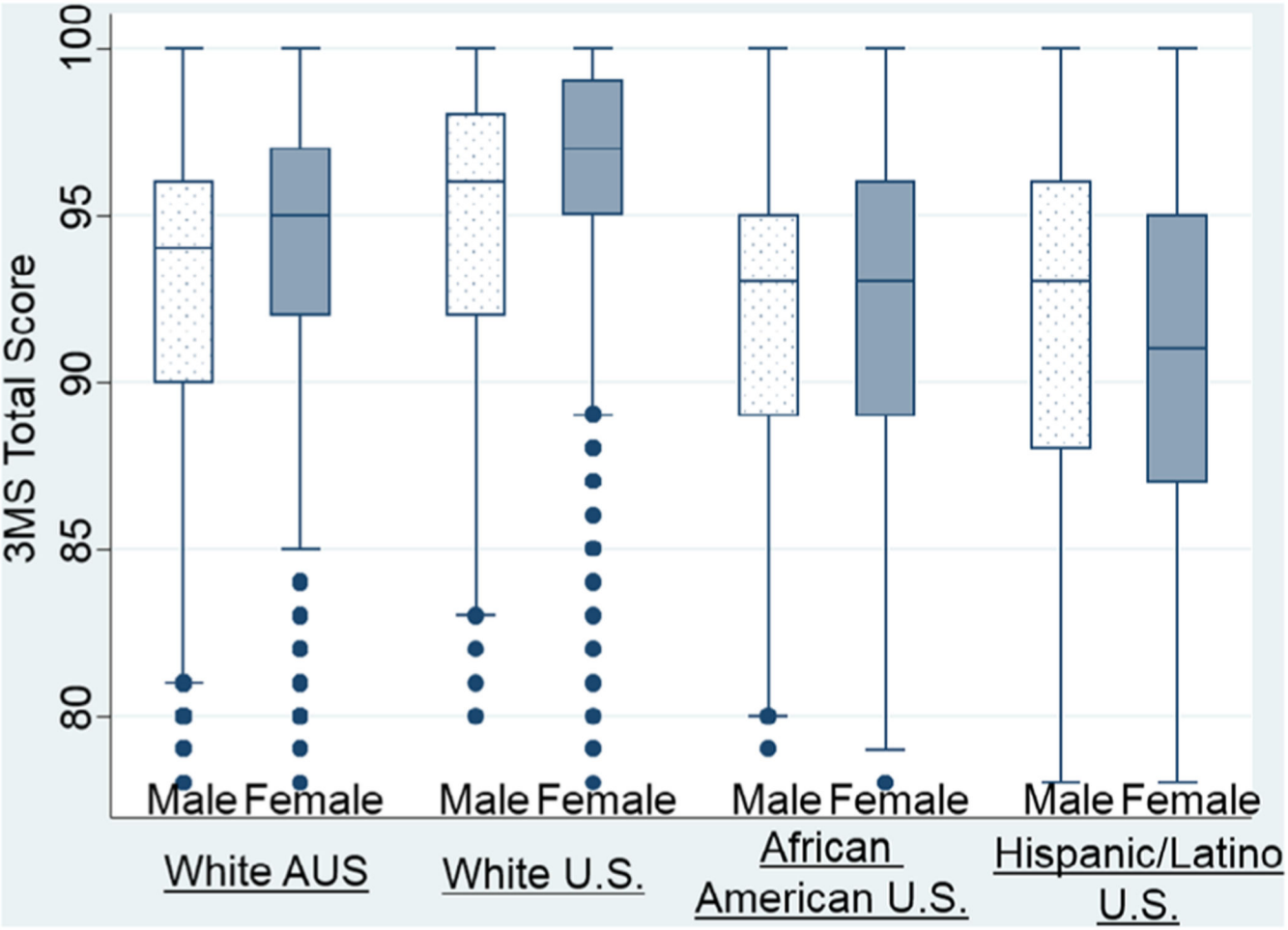

Figure 4.

The distribution of total Modified Mini-Mental State (3MS) examination scores across ethno-racial categories and according to gender (n = 18,659). The box represents the interquartile range (IQR, 25–75% percentile) and the horizontal line the median. The whiskers extend to +/−1.5*IQR and the dots represent outlying observations (≥1 participants) that are above or below these limits for 75 and 25% percentiles, respectively.

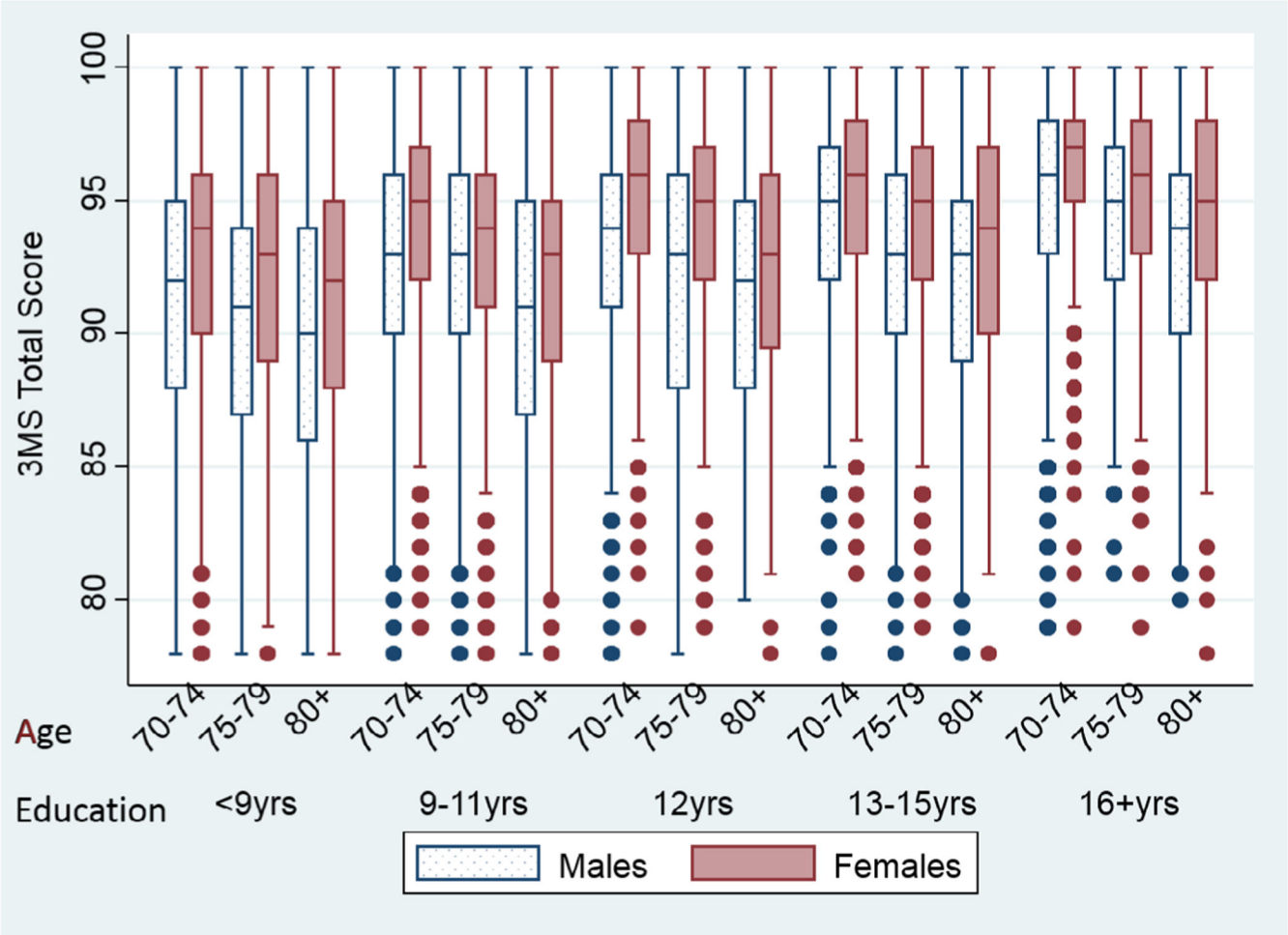

Figure 5.

Modified Mini-Mental State (3MS) examination scores in Australian whites, according to demographic characteristics (n = 16,360). The box represents the interquartile range (IQR, 25–75% percentile) and the horizontal line the median. The whiskers extend to +/−1.5*IQR and the dots represent outlying observations (≥1 participant) that are above or below these limits for 75 and 25% percentile, respectively.

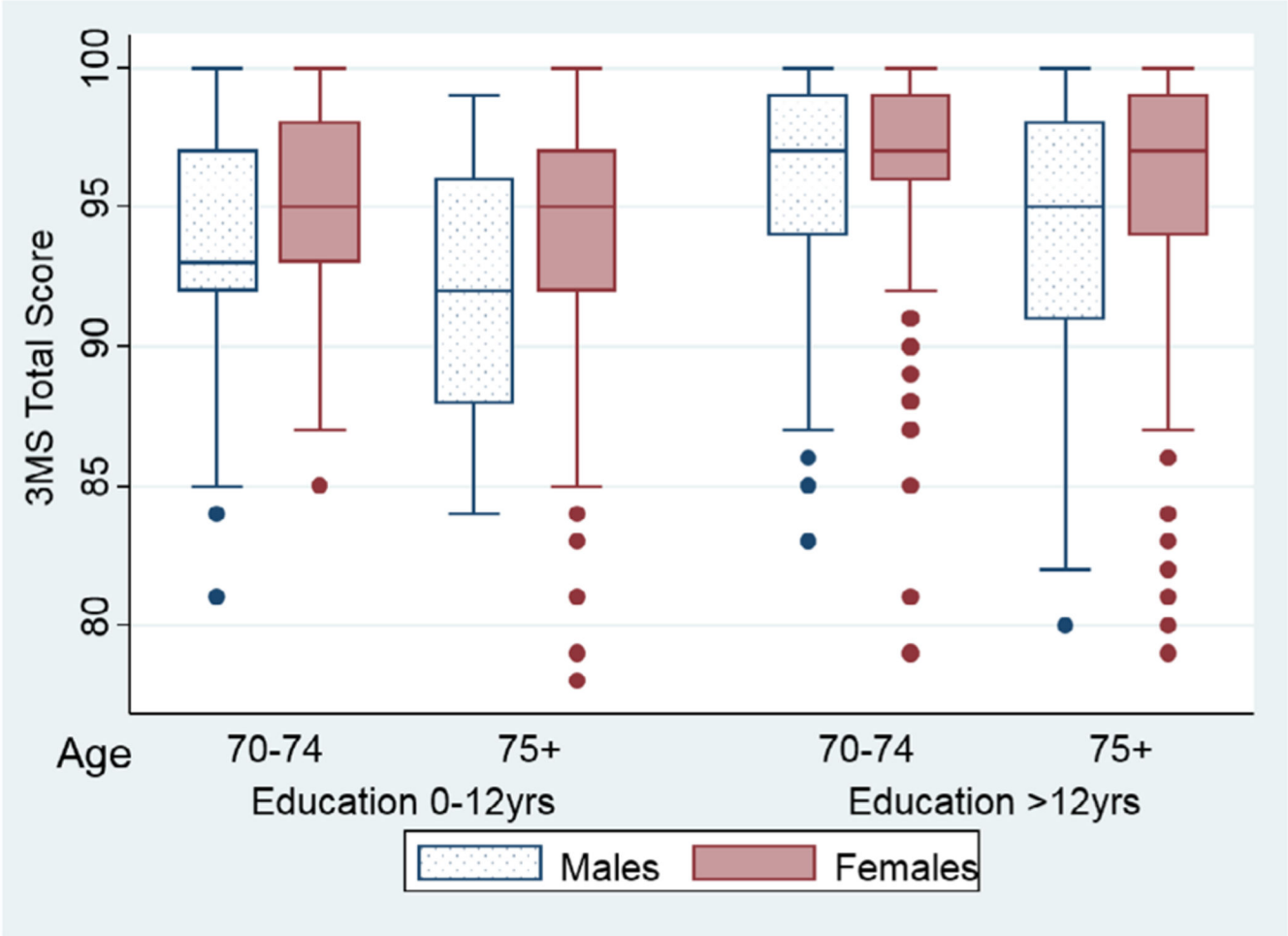

Figure 6.

Modified Mini-Mental state (3MS) examination scores in U.S. whites, according to demographic characteristics (n = 1088). The box represents the interquartile range (IQR, 25–75% percentile) and the horizontal line the median. The whiskers extend to +/−1.5*IQR and the dots represent outlying observations (≥1 participant) that are above or below these limits for 75 and 25% percentile, respectively.

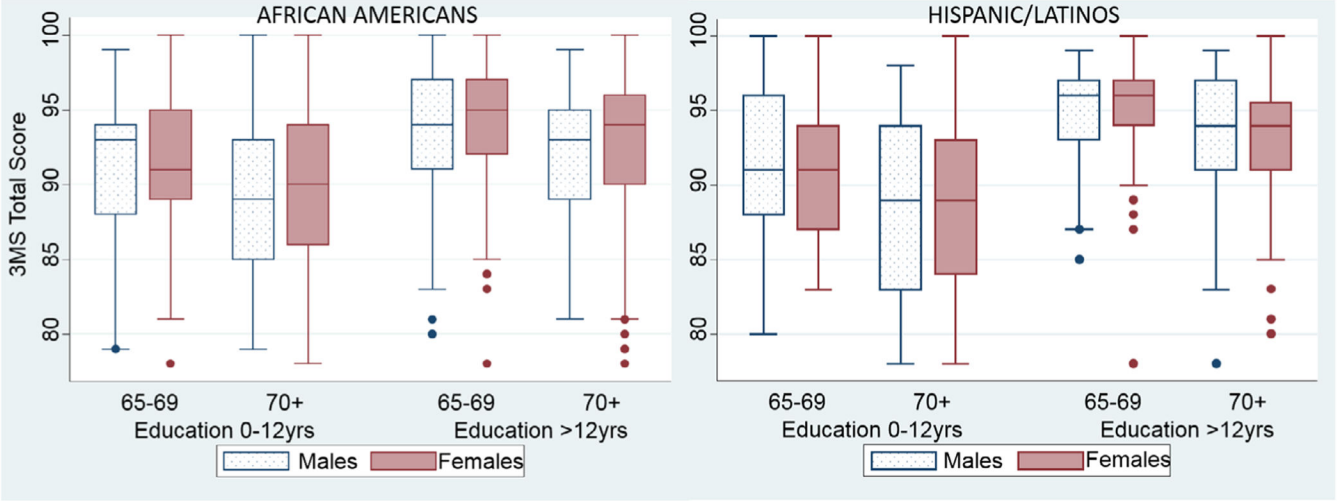

Figure 7.

Modified Mini-Mental state (3MS) examination scores in U.S. African-Americans (n = 895) and Hispanic/Latinos (n = 316), according to demographic characteristics. The box represents the interquartile range (IQR, 25–75% percentile) and the horizontal line the median. The whiskers extend to +/−1.5*IQR and the dots represent outlying observations (≥1 participant) that are above or below these limits for 75 and 25% percentile, respectively.

Table 1.

Summary statistics for the Modified Mini-Mental State (3MS) examination scores according to demographic characteristics.

Demographic characteristics	*N*	%	Mean	S.D.	Q1	Median	Q3
3MS all	19110		93.4	4.6	91	94	97
3MS ethno-racial groups	18659		93.5	4.6	91	94	97
Ethno-racial groups							
White Australians	16360	87.7	93.5	4.5	91	94	97
White U.S.	1088	5.8	95.5	4.1	93	97	99
African-American U.S.	895	4.8	92.2	5.0	89	93	96
Hispanic/Latino U.S.	316	1.7	91.2	5.6	88	92	96
Gender							
Female	10,557	56.6	94.0	4.5	92	95	97
Male	8102	43.7	92.8	4.7	90	94	96
Age, years							
65–69 *	537	2.9	93.0	4.6	90	94	96
70–74	10,320	55.3	94.0	4.3	92	95	97
75–79	4911	26.3	93.2	4.6	91	94	97
80–85+	2891	15.5	92.0	5.0	89	93	96
Education level, years							
<9	2926	15.8	91.4	5.0	88	92	95
9–11	5549	29.7	93.0	4.5	90	94	96
12	2256	12.1	93.2	4.7	91	94	97
13–15	3171	17.0	94.0	4.3	92	95	97
16+	4757	25.4	95.1	3.8	93	96	98
<9–12years	10,731	57.5	92.6	4.7	90	94	96
> 12 years	7928	42.5	94.7	4.1	93	96	98

Notes:

* Only included the African-American and Hispanic/Latino U.S. participants.; S.D: standard deviation; Q1: 25th percentile; Q3: 75th percentile. 3MS scores ranged from 78 to 100.

Table 2.

Age, education, and gender specific reference values for Modified Mini-Mental State (3MS*) examination in Australian whites (*n* = 16,360).

	Education <9 years		Education 9–11 years		Education 12 years		Education 13–15 years		Education ≥16 years	
Age, years	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**
70–74	*n* = 775	*n* = 669	*n* = 1,797	*n* = 1,326	*n* = 561	*n* = 445	*n* = 783	*n* = 671	*n* = 1,159	*n* = 1,259
	79, 81, 84, 86, 94	79, 80, 82, 84, 92	82, 84, 86, 89, 95	81, 81, 84, 87, 93	83, 85, 87, 89, 96	79, 80, 84, 86, 94	82, 85, 88, 91, 96	81, 84, 86, 89, 95	86, 88, 90, 92, 97	82, 85, 88, 90, 96
75–79	*n* = 463	*n* = 356	*n* = 893	*n* = 605	*n* = 268	*n* = 199	*n* = 390	*n* = 253	*n* = 462	*n* = 453
	78, 80, 82, 86, 93	78, 79, 81, 83, 91	80, 82, 85, 87, 94	79, 80, 83, 85, 93	80, 80, 85, 89, 95	78, 78, 82, 85, 93	81, 82, 84, 88, 95	78, 80, 83, 86, 93	82, 85, 87, 90, 96	84, 85, 87, 89, 95
80+	*n* = 339	*n* = 239	*n* = 527	*n* = 290	*n* = 176	*n* = 123	*n* = 211	*n* = 186	*n* = 224	*n* = 258
	78, 79, 81, 84, 92	78, 79, 80, 82, 90	78, 79, 82, 85, 93	79, 79, 82, 84, 91	78, 80, 84, 86, 93	80, 80, 82, 85, 92	78, 81, 82, 86, 94	78, 79, 83, 86, 93	80, 82, 87, 89, 95	81, 83, 85, 86, 94

Note:

* Data reported as 1st, 2nd, 5th, 10th & 50th (median) percentiles.

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Table 3.

Age, education, and gender specific reference values for Modified Mini-Mental State (3MS) examination in U.S. whites (n = 1088), African-Americans (n = 895) and Hispanic/Latinos (n = 316).

	Education 0–12 years		Education >12 years	
	Female	**Male**	**Female**	**Male**
U.S. white				
70–74	n = 56	n = 29	n = 273	n = 132
	−, 86, 88, 93, 95	−, −, 85, 92, 93	87, 90, 92, 96, 97	84, 87, 91, 94, 97
75–85+	n = 88	n = 31	n = 324	n = 155
	−, 83, 88, 92, 95	−, −, 86, 88, 92	83, 88, 91, 94, 97	83, 86, 88, 91, 95
U.S. African-American				
65–69	n = 64	n = 54	n = 183	n = 101
	−, 82, 84, 89, 91	−, 80, 82, 88, 93	84, 88, 89, 92, 95	80, 84, 87, 91, 94
70–85+	n = 106	n = 61	n = 240	n = 86
	78, 79, 81, 86, 90	−, 80, 81, 85, 89	80, 83, 85, 90, 94	−, 82, 86, 89, 93
U.S. Hispanic/Latino				
65–69	n = 47	n = 28	n = 37	n = 23
	−, −, 84, 87, 91	−, −, 82, 88, 91	−, −, 88, 93, 96	−, −, 87, 93, 96
70–85+	n = 79	n = 37	n = 32	n = 33
	−, 79, 81, 84, 89	−, −, 78, 83, 89	−, −, 83, 91, 94	−, −, 86, 91, 94

*Due to the smaller number in each cell, data reported are 2nd, 5th, 10th, 25 & 50th (median) percentiles.; When numbers were too small, the percentile is not given and replaced by −.

Table 4.

Linear regression model of the association between demographic characteristics and Modified Mini-Mental State (3MS) examination scores in Australian whites (n = 16,360).

Variable		β	SE	t statistic	p
Gender					
Male	REF				
Female		1.40	0.067	20.8	<0.0001
Age, years					
70–74	REF				
75–79		−0.85	0.078	−10.8	<0.0001
80+		−1.92	0.095	−20.2	<0.0001
Education level, years					
<9	REF				
9–11		1.29	0.099	13.1	<0.0001
12		1.78	0.13	13.8	<0.0001
13–15		2.40	0.12	20.5	<0.0001
16+		3.43	0.11	32.3	<0.0001

Table 5.

linear regression models of the association between demographic characteristics and Modified Mini-Mental state (3MS) examination scores in U.S. participants, stratified by ethno-racial group (n = 2299).

Variable		β	SE	t statistic	p
Whites					
Gender					
Male	REF				
Female		1.39	0.26	5.42	<0.0001
Age, years					
70–74	REF				
75+		−0.92	0.24	−3.83	<0.0001
Education level, years					
≤12	REF				
>12		1.89	0.31	6.20	<0.0001
African-Americans					
Gender					
Male	REF				
Female		0.54	0.34	1.62	0.11
Age, years					
65–69	REF				
70+		−1.68	0.32	−5.29	<0.0001
Education level, year					
≤12	REF				
>12		2.82	0.34	8.30	<0.0001
Hispanic/Latinos					
Gender					
Male	REF				
Female		−0.11	0.59	−0.19	0.85
Age, years					
65–69	REF				
70+		−1.86	0.58	−3.20	0.002
Education level, year					
≤12	REF				
>12		4.03	0.59	6.76	<0.0001

Table 6.

Normative scores for the Modified Mini-Mental State (3MS) examination individual items and total scores in the overall population (n = 18,659).

Item	Mean	S.D	Median	Interquartile range (IQR)	Range	% Proportion scoring full marks
Place & date of birth	4.99	0.10	5	5–5	2–5	99.28
Registration	2.99	0.09	3	3–3	0–3	99.48
Mental reversal	6.81	0.57	7	7–7	0–7	86.33
First recall	7.55	1.52	8	7–9	0–9	**37.08**
Temporal orientation	14.9	0.50	15	15–15	6–15	93.30
Spatial orientation	4.93	0.27	5	5–5	1–5	93.48
Naming	4.92	0.30	5	5–5	1–5	93.54
Four-legged animals	9.14	1.44	10	9–10	0–10	64.26
Similarities	4.40	1.50	5	3–6	0–6	**27.51**
Repetition	4.55	0.71	5	4–5	1–5	65.30
Read and obey	2.95	0.23	3	3–3	0–3	95.99
Writing	4.94	0.34	5	5–5	0–5	96.44
Copying two pentagons	9.41	0.96	10	9–10	0–10	61.70
Three-stage command	2.92	0.29	3	3–3	0–3	92.18
Second recall	8.00	1.58	9	7–9	0–9	60.84
Overall	93.42	4.62	94	91–97	78–100	3.75