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Validity of the Spanish Version of the Quick Mild Cognitive Impairment Screen (Q*mci*-S)

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Abstract

Introduction: Accurate, short, cognitive screening instruments are important for identifying mild cognitive impairment (MCI) and dementia including Alzheimer's disease. The Quick Mild Cognitive Impairment (Q*mci*) screen, given its brevity, may be useful in this setting but it has not been validated in Spanish. Here, we compared the diagnostic accuracy of the Spanish version (Q*mci*-S) to the Montreal Cognitive Assessment (MoCA).

Methods: Patients aged ≥55 years were recruited from six Primary Care Teams in Barcelona, Spain, between 2018-2019. Dementia, MCI and normal cognition (NC) were classified following neuropsychological testing, independent of the Q*mci*-S and MoCA scores. Diagnostic accuracy was determined by the area under receiver operating characteristic curves (AUC), adjusted for age and education.

Results: In total, 337 patients were included, mean 77.9 years, standard deviation (SD) ±6.9. Most were female (57.3%). The intraclass correlation coefficient for the Q*mci*-S was excellent (0.98). The Q*mci*-S had good to excellent diagnostic accuracy for separating NC from MCI and dementia (AUC 0.91) and was statistically greater than the MoCA (AUC 0.86), p=0.029. Accuracy was similar for differentiating NC from MCI and MCI from dementia. The Q*mci*-S had a shorter administer time, mean 8.6 (±3.2) vs 12.75 (SD ±5.5) minutes, respectively, p<0.001.

Conclusions: The newly-developed Q*mci*-S screen showed excellent criterion, construct and concurrent validity versus the widely-used MoCA and had statistically similar, good to excellent, diagnostic accuracy for cognitive impairment. Its significantly shorter administration time suggests it may be the better screen in a Spanish speaking population in primary care, though further research is required.

Key words: Dementia, Mild cognitive impairment, Primary care, Diagnostic test accuracy, Spanish, Cognitive screen

Introduction

Life expectancy is increasing, and with it, the number of people living with cognitive impairment is predicted to double every 20 years reaching 115.4 million by 2050.[1] Recent studies suggest that up to 40% of cases of dementia are related to modifiable risk factors.[2] If these can be addressed, a reduction in the incidence of dementia could be achieved.[3-5] The recent development of disease modifying therapies likewise underscores the need for an early and accurate diagnosis.[6,7] These developments emphasize the ability to screen for mild cognitive impairment (MCI), a prodromal stage before the onset of dementia and to separate those with MCI from normal cognition (NC) to identify those who will benefit from further investigations.[8] Early diagnosis also allows patients and families to initiate advanced care planning,[9] as well as to focus on preventive strategies.

In primary care, due to time constraints, it is important to use short cognitive screening instruments (CSI) with good to excellent diagnostic accuracy for detecting MCI when patients present with cognitive complaints. Disparities in cognitive screening outcomes often arise due to differences in literacy, educational attainment, and language exposure, which can lead to misclassification or underdiagnosis.[10,11] Hence, there is also a need for CSIs to reflect these disparities as well as cultural context.[11] Currently, relatively few CSIs are widely validated for MCI.[12] In Spain, the Mini-mental State Examination (MMSE)[13,14] and the Montreal Cognitive Assessment (MoCA)[15] are used to identify cognitive impairment but the MMSE has poor sensitivity[16] and the MoCA relatively low specificity for MCI.[17] The Quick Mild Cognitive Impairment (Q*mci*) screen was developed to detect MCI,[18] acknowledging the well-established time-accuracy trade-off.[19] It is brief, taking approximately five minutes to complete and has higher sensitivity than the MMSE and greater specificity than the MoCA.[20] The Q*mci* screen is composed of six subtests,[21] orientation, five-word registration, a clock drawing test, delayed recall, verbal fluency (categorial) and logical memory (immediate verbal recall of a story) and has been validated in multiple languages including Chinese,[22] Japanese,[23] Italian,[24] Dutch,[25] and Turkish.[26] However, it has not yet been validated in Spanish and like many short CSIs,[27] infrequently in community samples.[28] To date, it has not been validated in primary care. Hence, the aim of this study is to translate, adapt and validate the Spanish version of the Q*mci* screen (Q*mci*-S) in a large primary care population in Spain and to compare its sensitivity and specificity with the Spanish version of the MoCA in this setting.

Material and Methods

Translation and Adaption

Translation of the Q*mci* screen into Spanish was performed using a forward-backward translation method.[29,30] Initially, the original version was translated to Spanish by two different professionals, a health professional with a high level of proficiency in English and a professional English translator, whose primary language in both cases was Spanish. After this, consensus on the translation was obtained to ensure semantic and conceptual equivalence, and an expert panel of Spanish health professionals later reviewed it for cultural relevance and appropriateness. A completed version of the Q*mci*-S was then obtained. Next, two professional native English language-speaking translators, without knowledge of the concepts behind the screening tool, performed the back-translation. The back-translation was then reviewed by the original developers of the Q*mci* screen in the University College, Cork, in Ireland approved the final version. The Q*mci*-S was pre-tested on 20 patients with presumed NC in one primary care centre before it was used in this study to assess their

ability to comprehend it and acceptability, allowing refinement before study use; these reported no difficulty understanding. This multi-step process ensured the adapted instrument, maintained validity and cultural relevance consistent with International Test Commission Guidelines standards.[31]

Like the original English version, the Q*mci*-S consists of six subtests assessing six cognitive areas: orientation (country, year, month, day, and date with two points for each correct answer), word registration (five words with three alternative versions available with one point for immediate recall of each), a clock drawing test (with a maximum of 15 points - 12 per correct number, two for the hands and one point for the correct placement of the pivot), five word delayed recall (four points per correct word recalled to a maximum of 20), verbal fluency (semantic memory testing composed of category recall within one minute with three alternative versions available to a total score of 20 points with 0.5 points per item named) and logical memory (immediate verbal recall of one of three short stories to a maximum of 30 points; 2 points per key word recalled). The total score ranges from 0 (severe cognitive impairment) to 100 (no impairment). Previous validated alternative versions of the verbal fluency and logical memory stories were used in random sequence to minimize learning effects if patients had previously been tested.[32] The Q*mci*-S screen is presented in Appendix 1.

Data collection and sample

Test-retest reliability (TRT) was assessed using a test-retest approach for a subsample of patients selected by simple randomisation, participated reliability testing by completing the Q*mci*-S on two separate occasions within three weeks. Validity was assessed by comparing the Q*mci*-S to the Spanish version of the MoCA,[15] collected on the same day, to an independent neuropsychological assessment as a gold standard. The sample size calculation was based on an expected accuracy difference (Δ) in area under the curve (AUC) of 0.04 found in other studies to differentiate between NC and CI (MCI and dementia) groups,[20] resulting in a minimum sample of 250-300 individuals in total.[33] Diagnostic accuracy testing was carried out between 2018-2019 including patients aged 55 years or older recruited by primary health care nurses or general practitioners from consecutive patients attending six primary health care centres in Barcelona, Spain. Patients under 55 years of age, unable to communicate verbally in Spanish or with communication problems that could interfere with testing (e.g. expressive dysphasia and other neurological disorders such as motor neuron disease, semantic aphasia, Lewy Body and Parkinson's disease), as well as those with active serious psychiatric disorders including uncontrolled Schizophrenia, bipolar affective disorder and active depression, defined by a score of 5 or more on the Geriatric Depression Scale,[34] were excluded. Those bilingual in Catalan, commonly spoken in Barcelona were included, while those unable to speak Spanish were excluded.

The Q*mci*-S and MoCA were administered alternately in a random sequence by trained physicians and primary care nurses to all patients. Each patient underwent a comprehensive geriatric assessment and neuropsychological evaluation to determine the diagnostic classification. Using this information and without any prior knowledge of the results of the CSIs, a physician-led multi-disciplinary team including a neuropsychologist confirmed whether the patients had NC, MCI or dementia. Patients were classified using the Clinical Dementia Rating (CDR) scale, a global assessment incorporating memory, orientation and functional and self- care aspects.[35,36] Dementia was based upon DSM-V criteria as a major neurocognitive disorder (NCD). MCI was based on the principle proposed by Petersen's.[37] Components of the neuropsychological battery included the MMSE,[13,14] the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-cog),[38] examining memory, language and

praxis with higher scores indicating greater cognitive impairment,[38] the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Battery testing attention, language, visuospatial/constructive skills and immediate and delayed memory with lower scores suggesting greater cognitive deficits,[39] the Controlled Oral Word Association Test of verbal fluency with lower scores reflecting poorer cognitive performance,[40] the Trail Making Test to assess attention, mental flexibility and visuospatial ability.[41] In addition, affective, functional, mobility, quality of life and social assessments were carried out. Demographic data (age and sex, education, and living arrangements), health services use, co-morbidities and eFragicap Frailty Index (FI),[42] a validated index including 36 deficits from electronic health records, were also collected. Patients were followed for five years, to the end of 2023, to investigate the predictive validity of the CSIs for the incidence of a new diagnoses of cognitive impairment, and healthcare outcomes including rates of institutionalisation or death were also recorded. Data were obtained from primary care clinical health records. Ethical approval was obtained in advance from the IDIAPJGol Clinical Research Ethics Committee (Date:15.03.2017, P17/081).

Statistical Analysis

Data were analysed using SPSS version 23.0 (IBM, Chicago, IL, USA) and R version 3.5.1 (R Core Team). Test-re-test reliability were determined using the intraclass correlation coefficient (ICC). A value 0-0.3 indicate poor reliability, 0.3-0.5 fair, 0.5-0.75 moderate, (≥0.75) strong, with values of >0.90 approaching 1.0 reflecting near excellent to perfect correlation.[43] Construct validity of Q*mci*-S vs MoCA and MMSE was assessed with the Pearson correlation coefficient scored from -1.0 to 1.0. Scores of -1.0 and 1.0 reflect perfect linear correlation with scores between suggesting weak to strong (≥0.7) correlation.[44] Differences in Q*mci*-S and MoCA scores between cognitive groups were tested using one-way analysis of variance. The diagnostic accuracy of the instruments was analysed from the area under the curve (AUC) of receiver operating characteristic (ROC) curves. Binary logistic and linear regression was used to adjust ROC curve analysis for the effects of age and education. Differences between AUCs were calculated using the DeLong approach.[45] The optimal cut-off score for each instrument was calculated from the ROC curves using the maximal accuracy approach. Binary logistic regression was also used to generate odds ratios (OR) to assess the predictive accuracy for the before-mentioned outcome measures at follow-up.

Results

In total, 377 participants from six primary care teams were available. After exclusion of those with missing data, 337 were included. Of these, 57.3% were female and the sample had a mean age of 77.9, standard deviation (SD) ±6.9 years. A large proportion of the sample had low levels of education attainment with only 23.1% having completed secondary or third-level education. In all, 163 (48.4%) had NC, 107 (31.8%) had MCI and 67 (19.9%) had a major NCD i.e. dementia. The group with dementia was older than the MCI and NC groups (mean age 81.0 vs. 77.7 and 76.7 respectively, $p<0.001$) and had a higher proportion of women. The mean MMSE score for the sample was 25.7 (SD ±3.5) with a median CDR score was 0.5. There were high levels of multi-morbidity and frailty with a mean FI score of 0.23 (SD ±0.11). Q*mci*-S scores were significantly lower with higher levels of frailty; mean of 56 for patients identified as fit, 49 for those with mild frailty, 48 for moderate frailty and 43 for patients with severe frailty ($p<0.001$). Additional demographic and clinical data are summarised in Table 1.

Reliability

The ICC score was 0.98, 95% confidence intervals (CI): 0.95-0.99. Construct validity was assessed by correlating the Q*mci*-S screen with the MoCA (r=0.76; p<0.001) and with MMSE (r=0.73; p<0.001), showing strong correlation. Criterion validity was assessed by examining the Q*mci*-S subtests. TRT was performed on 21 individuals; 11 had NC, 4 MCI, and 6 had a diagnosis of dementia. Of these, 86% were female, their mean age was 80 ±10.7 years and most (62%) had <8 years education.

Table 1. Demographic and clinical data by cognitive groups, comparing those with normal cognition (NC), mild cognitive impairment (MCI) and dementia (Major NCD).

Variable	**Total** (n=337)	**NC** (n=163)	**MCI** (n=107)	**Dementia** (n=67)	**P value**
Age, mean (SD*)	77.9 (6.8)	76.8 (7.4)	77.8 (5.8)	81.0 (6.0)	<0.001
Biological Sex (% female)	193 (57.3)	88 (54.0)	59 (55.1)	46 (68.7)	0.11
Education (%)					
Illiterate	4 (1.2)	1 (0.6)	2 (1.9)	1 (1.5)	0.09
Primary incomplete	150 (44.5)	68 (41.7)	48 (44.9)	34 (50.7)	
Primary completed	98 (29.1)	40 (24.5)	37 (34.6)	21 (31.3)	
Secondary completed	54 (16.0)	32 (16.9)	13 (12.1)	9 (13.4)	
Tertiary completed	31 (7.1)	22 (13.5)	7 (6.5)	2 (3.0)	
Marital status (%)					
Married	214 (63.5)	104 (63.8)	70 (65.4)	40 (59.7)	0.47
Single	15 (4.5)	6 (3.7)	5 (4.7)	4 (6.0)	
Divorced	20 (5.9)	13 (8.0)	6 (5.6)	1 (1.5)	
Widow	88 (26.1)	40 (24.5)	26 (24.3)	22 (32.8)	
Living arrangements (%)					
Lives alone	90 (26.9)	49 (30.1)	27 (25.2)	14 (20.9)	0.24
Couple	193 (57.3)	92 (56.4)	65 (60.7)	36 (53.7)	
Family	52 (15.4)	22 (13.5)	14 (13.1)	16 (23.9)	
Carer	2 (0.6)	0 (0.0)	1 (0.9)	1 (1.5)	
Lifestyle (%)					
Social services use (any)	108 (32.0)	43 (26.4)	31 (29.0)	34 (50.7)	0.001
Hospitalisation (<1 year)	101 (30.0)	45 (27.6)	35 (32.7)	21 (31.3)	0.64
Smoking	20 (5.9)	12 (7.4)	7 (6.5)	1 (1.5)	0.01
Alcohol	83 (24.6)	50 (30.7)	22 (20.6)	11 (16.4)	0.04
Exercise (% sedentary)	30 (9.3)	12 (7.8)	5 (4.8)	13 (19.7)	0.008
Co-morbidity (%)					
Stroke	50 (14.8)	19 (11.7)	16 (15.0)	15 (22.4)	0.12
Ischemic Heart disease	47 (13.9)	21 (12.9)	12 (11.2)	14 (20.9)	0.17
Heart failure	25 (7.4)	11 (6.7)	6 (5.6)	8 (11.9)	0.27
Diabetes mellitus	116 (34.4)	56 (34.4)	39 (36.4)	21 (31.3)	0.79
Hypertension	230 (68.2)	112 (68.7)	74 (69.2)	44 (65.7)	0.87
Hearing impairment	79 (23.4)	40 (24.5)	23 (21.5)	16 (23.9)	0.84
Visual impairment	182 (54.0)	84 (51.5)	59 (55.1)	39 (58.2)	0.63
Neuropsychological Battery, mean (SD)					
ADAS-Cog	12.2 (5.9)	8.1 (2.5)	13.0 (2.7)	21.0 (5.4)	<0.001

RBANS	143.8 (41)	173.3 (31.1)	130.0 (20.2)	94.4 (24.1)	<0.001
MMSE	25.7 (3.5)	27.9 (1.8)	25.2 (2.3)	21.0 (3.3)	<0.001
COWAT	38.1 (17)	47.6 (15.6)	33.0 (12.8)	23.3 (11.2)	<0.001
CDR-SB	0.36 (0.39)	0 (0)	0.5 (0)	1.0 (0)	<0.001
Prescription Medications, mean number (SD)	7.8 (4.6)	7.1 (4.0)	8.0 (5.2)	9.3 (4.6)	0.004
Frailty Index score, mean (SD)	0.23 (0.11)	0.20 (0.10)	0.23 (0.11)	0.29 (0.12)	<0.001

ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive Subscale; CDR-SB = Clinical Dementia Rating scale Sum of Boxes; COWAT = Controlled Oral Word Association Test; MMSE = Mini-Mental State Examination; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; *standard deviation

Table 2 presents the results according to the cognitive status of the individuals based on the gold-standard evaluation. The NC group had a mean Q*mci*-S screen score of 61/100 (SD ±11.56) compared to 45/100 (SD ±10.9) for the MCI group and 32/100 (SD ±10.7) for those with dementia. The Q*mci*-S screen was statistically significantly faster to administer than the MoCA, mean 8.6 (SD ±3.2) vs 12.75 (SD ±5.5) minutes, respectively, p<0.001. Administration times by diagnostic category are presented in Table 2.

Table 2. The Spanish version of the Quick Mild Cognitive Impairment (Q*mci*-S) screen (total and subtest scores) versus Montreal Cognitive Assessment (MoCA) scores by cognitive status, comparing those with normal cognition (NC), mild cognitive impairment (MCI) and dementia (Major NCD) including administration times. (*SD = Standard Deviation)

Cognitive Screen	**NC** Mean (±SD)	**MCI** Mean (±SD)	**Dementia** Mean (±SD)	**p-value**
Q*mci*-S Total	60.63 (11.6)	44.94 (10.9)	31.72 (10.7)	<0.001
Q*mci*-S Orientation	9.88 (0.4)	9.08 (1.6)	7.21 (2.4)	<0.001
Q*mci*-S Registration	4.44 (0.7)	4.03 (0.9)	3.25 (1.0)	<0.001
Q*mci*-S Clock Drawing Test	12.36 (3.9)	9.27 (5.1)	6.94 (5.3)	<0.001
Q*mci*-S Delayed Recall	13.09 (5.7)	8.06 (5.6)	3.96 (5.2)	<0.001
Q*mci*-S Verbal Fluency	8.44 (2.7)	6.43 (2.1)	4.78 (1.6)	<0.001
Q*mci*-S Logical Memory	12.34 (4.9)	8.07 (3.9)	5.58 (3.9)	<0.001
Q*mci*-S Administration Time	7.8 (2.5)	9.02 (3.4)	9.8 (3.9)	<0.001
MoCA Total	22.9 (3.6)	18.23 (4.1)	14.31 (4.0)	<0.001
MoCA Administration Time	11.7 (4.1)	12.8 (4.3)	15.1 (4.9)	<0.001

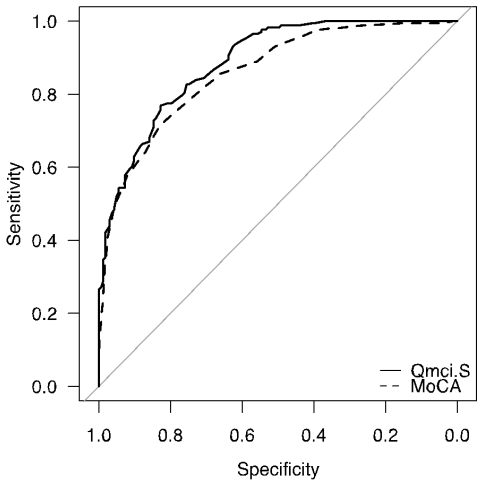
Comparing their ability to distinguish NC from MCI, the Q*mci*-S had similar accuracy to the MoCA (AUC 0.83, 95% CI: 0.79-0.88 compared to 0.80, 95% CI: 0.75-0.85, respectively p>0.05). The Q*mci*-S also had similar accuracy in differentiating MCI from dementia (AUC 0.81, 95% CI: 0.74-0.87 compared to AUC of 0.76, 95% CI: 0.68-0.83 for the MoCA, p>0.05) (Table 3). These were unchanged after adjustment for age and education. The corresponding ROC curves are presented in Figure 1.

Table 3. Diagnostic accuracy, based on area under the curve (AUC) with 95% confidence intervals (CI), of the Spanish version of the Quick Mild Cognitive Impairment (Q*mci*-S screen) and Montreal Cognitive Assessment (MoCA) comparing those with normal cognition (NC), mild cognitive impairment (MCI) and dementia (Major NCD). (*For age and education)

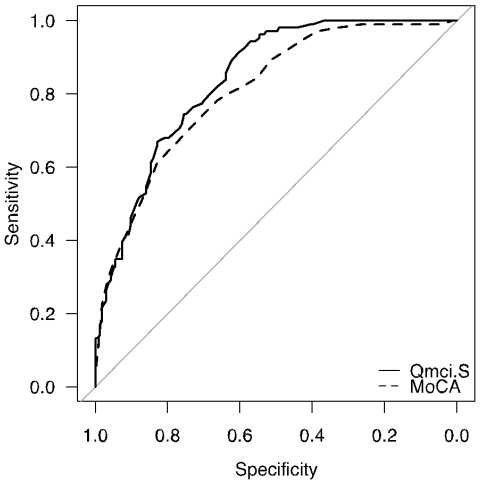
Diagnostic Comparison	**Q*mci*-S** AUC (95% CI)	**MoCA** AUC (95% CI)	**p-value**

NC vs MCI			
Unadjusted	0.834 (0.787-0.880)	0.802 (0.750-0.854)	0.214
Adjusted*	0.862 (0.818-0.905)	0.813 (0.760-0.866)	0.077
NC vs cognitive impairment (MCI and dementia)			
Unadjusted	0.883 (0.849-0.917)	0.855 (0.815-0.894)	0.129
Adjusted*	0.905 (0.874-0.936)	0.862 (0.823-0.900)	**0.029**
MCI vs Dementia			
Unadjusted	0.808 (0.741-0.874)	0.756 (0.683-0.829)	0.164
Adjusted*	0.818 (0.754-0.881)	0.767 (0.695-0.840)	0.161

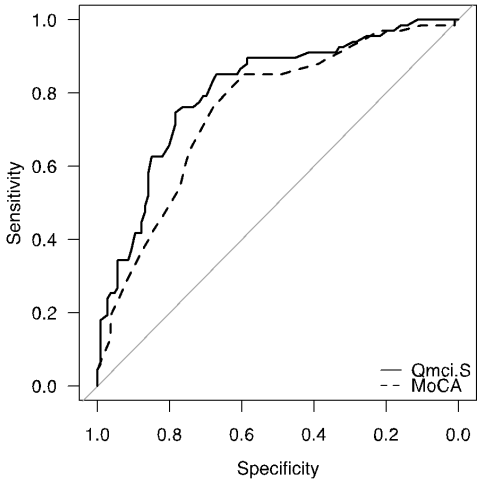
Figure 1a-c. Receiver operating characteristic curves comparing the Spanish version of the Quick Mild Cognitive Impairment (Q*mc*i-S) screen and Montreal Cognitive Assessment (MoCA) in their ability to differentiate (a) those with normal cognition (NC) and cognitive impairment including mild cognitive impairment (MCI) and dementia (Major NCD), (b) NC and MCI and (c) MCI and dementia (Major NCD).



a.



b.



c.

Table 4. Diagnostic properties of the Q*mci*-S screen by age and education level, including cut-offs, diagnostic accuracy based on the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV) and negative values (NPV) to differentiate between normal cognition (NC) and cognitive impairment (CI) including mild cognitive impairment (MCI) and dementia (Major NCD).

Comparison	Q*mci*-S Cut-off Value	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
NC vs MCI						
Overall	59	0.834	90.7	60.1	59.9	90.7
Age <76 >8y education	62	0.904	91.3	82.7	70.0	95.6
Age <76 <8y education	43	0.866	64.3	100	100	76.2
Age >75 >8y education	58	0.934	88.2	88.1	85.7	90.2
Age >75 <8y education	46	0.756	66.7	71.7	61.5	76.0
NC vs CI (MCI & Dementia)						
Overall	50	0.883	76.4	82.8	82.6	76.7
Age <76 >8y education	62	0.922	93.5	82.7	76.3	95.6
Age <76 <8y education	43	0.901	73.7	100	100	76.2
Age >75 >8y education	58	0.958	93.1	88.1	91.5	90.2
Age >75 <8y education	42	0.839	69.7	84.9	85.2	69.2
MCI vs Dementia						
Overall	40	0.808	79.1	70.1	62.4	84.3
Age <76 >8y education	42	0.813	62.5	95.7	83.3	88.0
Age <76 <8y education	37	0.871	100	85.7	71.4	100
Age >75 >8y education	41	0.806	83.3	73.5	69.0	86.2
Age >75 <8y education	37	0.788	83.3	66.7	67.6	82.8

Outcome data for patients were available at five years follow-up. In all, 143/344 (41.6%) had received a new diagnosis of cognitive impairment (MCI or dementia), 38/375 (10.1%) were institutionalized in a nursing home, and 85/375 (22.7%) had died. Table 5 shows the OR with 95% CI for specific outcomes. The Q*mci*-S was significantly associated with a new diagnosis of cognitive impairment (OR 1.07), institutionalisation (OR 1.03) and death (1.04) at five years. Taking a fixed cut-off on the Q*mci*-S, such as that typically used for dementia i.e. <50/100,[18] the OR increased to 2.47 (95% CI: 1.4-4.3) for mortality, to 2.62 (95% CI: 1.2-5.7) for institutionalisation and 4.2 (2.6-6.7) for incident cognitive impairment (all p values <0.001).

Table 5. Multiple logistic regression modelling with odds ratio (OR) and 95% confidence intervals (CI) comparing outcomes according to the Spanish version of the Quick Mild Cognitive Impairment (Q*mci*-S) screen scores, age and sex.

Variables	Incident Cognitive Impairment (OR 95%)	Institutionalisation	Death	Combined outcome
Q*mci*-S (Higher scores)	0.94 (0.92-0.95)	0.97 (0.95-0.99)	0.97 (0.95-0.98)	0.94 (0.93-0.96)
Age (Older age in years)	1.00 (0.96-1.04)	1.05 (0.99-1.12)	1.11 (1.06-1.17)	1.06 (1.02-1.10)

Sex (Female)	1.47 (0.90-2.42)	1.39 (0.66-2.90)	0.29 (0.17-0.52)	0.86 (0.54-1.38)

Discussion

The study is the first to validate the Spanish version of the Quick Mild Cognitive Impairment screen, a brief screening tool for cognitive impairment, in comparison with the well-established MoCA. The results show that the Q*mci*-S has good to excellent diagnostic accuracy in differentiating MCI from normal cognition and dementia, which was mainly statistically similar but with significantly faster administration times than the Spanish version of the MoCA. It also confirms its utility, reliability and accuracy in primary care settings among a large sample of Spanish-speaking older adults. The results of this validation study re-affirms the results of other adaptations and translations of the original Q*mci* screen across a broad range of different languages, settings and study populations,[20–24,46,47] with similar ability to discriminate between normal cognition, MCI and dementia. This paper includes a large sample of older adults attending six large primary care teams with a robust diagnosis supported by a complete and independent neuropsychological and detailed functional assessment including the 36-item eFragicap FI.

In Spain, the most widely-used short cognitive screen is the MMSE,[13] although it has been shown to be inaccurate in differentiating between NC and MCI.[16] More recently, the Spanish version of MoCA has become more popular as it has shown better diagnostic properties than the MMSE in discriminating NC from MCI, albeit with a relatively low specificity and longer administration times.[17] The head-to-head comparison of the Q*mci*-S with the MoCA, presented in this analysis, shows that the two instruments had comparable good to excellent diagnostic accuracy in differentiating NC, MCI and dementia, with AUCs higher than 0.80. The discriminatory ability of both instruments was further improved when adjusted for age and educational level, and in this case the Q*mci*-S was statistically superior to the MoCA in discriminating between NC and cognitive impairment i.e. MCI and dementia (AUC 0.91 versus 0.86, p=0.029) following this adjustment. The Q*mci*-S also had excellent test-retest reliability and a statistically significantly shorter administration time, making it potentially more suitable for use in a setting where visiting time is limited such as in General Practice (primary care). However, other short CSIs have also been validated in Spanish speaking populations including in primary care such as the Memory Impairment Test (T@M) and Eurotest, amongst others, which can also be administered in under 10 minutes and achieve excellent accuracy for cognitive impairment in this setting.[48] Further research comparing these tools and their diagnostic accuracy for MCI, head to head with the Q*mci*-S and more established instruments such as the MoCA ,is now required. Further, the Q*mci*-S should also be compared to the most-widely used screen, the MMSE. Here it could not be assessed as the MMSE was part of the diagnostic standard risking incorporation bias, which would have inflated its accuracy, potentially overestimating its sensitivity and specificity.[49]

The cut-off values of the Q*mci*-S were similar, albeit slightly lower than those reported for the English language version, to distinguish NC from MCI at 59/100 compared to a cut-off of <65/100 in a sample from Ireland.[20] The lower cut-offs were also seen for differentiating NC from CI (50/100) and MCI from suspected dementia (40/100). However, these are similar to other translated versions in other countries. For example, in the Netherlands the cut-off scores were almost identical; the optimal cut-off for separating MCI from NC was 52/100, while for MCI and dementia it was 42/100.[25] Similarly, the Greek version of the Q*mci* screen had a cut-off of 50/100 for cognitive impairment and 43/100 for dementia.[50] These studies

had smaller and more restricted samples than the original validation studies in English, which included over 3,500 patients.[20,21] Cut-off values should be taken with caution for any sample however, and studies with larger populations would be required to determine population-level values for Spanish speakers in Spain i.e. normative values. Compounding this, our sample included the general population attending primary care centres in Barcelona, but may have overrepresented individuals of medium to low socioeconomic status and patients with less education. Furthermore, education levels vary between different cohorts, as the education system has changed over time, with schooling being compulsory until age 14-16 only for the youngest in our sample. Therefore, the age and education cut-off points need larger, and representative samples according to educational levels as well, to show more accurate values. The need to adjust cut-offs has been seen before for the use of the Q*mci* screen in other populations of older people, particularly those in rural communities and in patients with low literacy levels and illiteracy such as in Portugal,[51] where a higher proportion (up to 71%) of these have very low literacy (0-5 years) or are illiterate,[51] compared to only 44.5% with very low literacy and 1.2% illiterate in this cohort. The Q*mci*-S, validated in a diverse primary care population, demonstrates potential for broader public health application, particularly in community settings with limited access to specialist care. Its brevity, reliability, accuracy and ease of use supports equitable, early detection of cognitive impairment across varied populations,[52] though further research is needed to understand if it is adequately cross-culturally adapted.[11]

The validation of these instruments in primary care also provides a different perspective to memory clinic samples and includes people with different cognitive levels who present for very different reasons. Some were likely screened opportunistically rather than presenting directly with cognitive complaints. It is a setting where it is very useful to have a rapid screening instrument that allows the early detection of MCI and initial stages of dementia to activate onwards referral and utilisation of appropriate community supports and resources. In primary care, the prevalence of cognitive impairment is lower than in other settings such as memory clinics or geriatric outpatients, and it is important to show that screening with these CSIs is also valid. Relatively few studies have validated these instruments or other short CSIs in primary care and further research such as this adds to the evidence for their use in this setting.[53] The Q*mci*-S scores correlated strongly with the MoCA and MMSE. It also was able to predict incident cognitive impairment in patients without a known history of decline. Further, its association with FI also adds to its construct validity, given the well-established relationship between frailty and cognitive decline are well-established.[54,55] Similarly, the predictive validity of the Q*mci*-S for adverse events such as institutionalisation and death add to its construct validity. Cognitive decline has been shown to be associated with higher rates of institutionalisation.[56,57] Dementia and cognitive impairment as a syndrome, have likewise been associated with increased mortality.[58] Here lower Q*mci*-S scores were associated with increased odds of death, regardless of age and biological sex. However, the ORs for these outcomes were small, albeit statistically significant. This said, the results of a short CSI in a cross-sectional diagnostic accuracy test study would not be expected to show a large association with healthcare outcomes up to five years.

Several limitations should be mentioned. In this study sample, there was a relatively high prevalence of cognitive impairment (51.6%), suggesting over-representation and over-sampling of this group and risk of spectrum bias. In addition, those who were classified as having dementia were mainly mild cases (CDR 1). More advanced stages of dementia would not be the target of primary care screening, and it would also have interfered with

both the performance of the screens and the neuropsychological battery used. While consecutive sampling was attempted, those without cognitive symptoms were less likely to participate and hence this is unlikely to represent the true cross-sectional prevalence of cognitive impairment among patients aged ≥55 years attending primary care centres in Barcelona. Instead, rates of approximately 18.5% among those aged ≥65 years and over 45% in those aged ≥85 years have been reported in this setting in Spain.[59] In this study, we did not consider the category of subjective memory complaints, limiting comparability to other studies that have used this classification. These were included within the normal cognition group with 70% of individuals with normal cognition reporting memory complaints, which are very common as people age and in primary care in Spain,[60] even if these were not the specific reason for a visit, unlike those who attend geriatric or memory clinics consultations where this is the indication. However, as those with self-reported memory complaints are at higher risk of progression to cognitive impairment,[61,62] it is likely that the NC group may have included those with occult cognitive impairment, albeit this would have lower the diagnostic accuracy of the CSIs. In addition, a dedicated a priori sample size calculation was only provided for the comparison between NC and MCI groups. In our study, there were 174 participants with either MCI or dementia. Based on previous literature,[20] the diagnostic accuracy of the Q*mci* screen and MoCA in distinguishing MCI from dementia is high and quite similar (AUC of 0.95 versus 0.91, respectively). Detecting such a small difference (Δ AUC=0.04) using DeLong's method for correlated ROC curves,[45] would require an estimated 250–300 participants to achieve 80% power at α=0.05. Given our current sample size, the study was possibly underpowered for this secondary comparison. The sample size was adequate to power the comparison between NC and MCI, (n=170) the key comparison when examining MCI-specific instruments. Another limitation is that as this study was conducted in primary care, subtyping of MCI and dementia syndromes was incomplete. Most were diagnosed with AD or vascular cognitive impairment based on established criteria as outlined above and atypical syndromes such as movement disorders or those with exaggerated language-predominant disorders including semantic dementias and those with post-stroke expressive dysphasia were excluded. Nevertheless, it means that a comparison of the diagnostic accuracy of the two CSIs was not possible. This is a direction for future research. Finally, while alternative versions of the Q*mci* screen with different subtests were included to minimise potential learning effects, which patients had scored which subtest was not recorded, meaning the effect of this on individual performance could not be assessed. This said, studies suggest that the different versions of verbal fluency and logical memory are equivalent.[32,63]

In conclusion, this study shows that the Q*mci*-S is a reliable and valid short CSI suitable for use in Spanish speaking populations, with good to excellent diagnostic accuracy to differentiate NC from MCI and dementia in a general practice. Though it generally had similar accuracy to the MoCA, its shorter administration time potentially makes it a better instrument in this setting, though larger validation studies would be needed to confirm these findings and to develop normative data for the Q*mci*-S.

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Ethics Statement: To conduct the research, approval was obtained from the IDIAPJGol Clinical Research Ethics Committee (Date:15.03.2017, P17/081).

Conflicts of Interest: Rónán O'Caoimh is an Editorial Board Member of this journal, but was not involved in the peer-review process nor had access to any information regarding its peer-review. Dr O'Caoimh and Prof Molloy are co-copyright holders of the Quick Mild Cognitive Impairment screen. The authors declare no other conflicts of interest.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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