The Hachinski Ischemic Scale and cognition: the influence of ethnicity

LEIGH A. JOHNSON1,2, BLAIR CUSHING3, GEOFFREY ROHLFING3, MELISSA EDWARDS4, HEDIEH DAVENLOO1, DARRIN D’AGOSTINO1, JAMES R. HALL2,5, SID E. O’BRYANT1,2

1Department of Internal Medicine, University of North Texas Health Sciences Center, Fort Worth, TX, USA
2Institute for Aging & Alzheimer’s Disease Research, University of North Texas Health Sciences Center, Fort Worth, TX, USA
3Texas College of Osteopathic Medicine, University of North Texas Health Sciences Center, Fort Worth, TX, USA
4Department of Psychology, University of North Texas, Denton, TX, USA
5Department of Psychiatry and Neuroscience, University of North Texas Health Sciences Center, Fort Worth, TX, USA

Address correspondence to: L. Johnson, University of North Texas Health Science Center, 3500 Camp Bowie Boulevard, Fort Worth, TX 76107, USA. Tel: (+1) 817 7352965; Fax: (+1) 817 7350628. Email: leigh.johnson@unthsc.edu

Abstract

Objective: cardiovascular burden is considered a risk factor for the development of cognitive dysfunction and dementia. While this link is well established in the literature, implementing this work in primary care settings remains a challenge. The goal of this study is to examine the utility of the Hachinski Ischemic Scale (HIS) in identifying cognitive dysfunction and diagnosis of mild cognitive impairment (MCI) in an ethnically diverse sample.

Methods: data were analysed on 517 participants (211 Mexican Americans and 306 non-Hispanic Whites) recruited from Project FRONTIER, a study of rural health. Neuropsychological measures were utilised to assess for cognitive functioning.

Results: among non-Hispanic Whites, HIS scores were significantly related to poorer performance on tasks of global cognition \(B (SE) = -0.13 (0.06), P = 0.02\), immediate memory \(B (SE) = -0.85 (0.26), P < 0.001\), attention \(B (SE) = -1.6 (0.36), P < 0.001\) and executive functioning \(B (SE) = 0.46 (0.12), P < 0.001\), and significantly predicted diagnosis of MCI [odds ratio (OR) = 1.4; 95% confidence interval (CI) = 1.2–1.6]. For Mexican Americans, HIS scores were significantly related to immediate memory \(B (SE) = -0.78 (0.28), P = 0.01\), attention \(B (SE) = -0.74 (0.36), P = 0.04\) and executive functioning \(B (SE) = 0.37 (0.14), P = 0.01\); however, HIS scores were not significantly related to diagnosis of MCI in Mexican Americans (OR = 1.2, 95% CI = 0.96–1.4, \(P = 0.116\)).

Conclusion: HIS scores were related to cognitive functioning; however, these results differed by ethnicity. It is possible that these findings indicate that vascular factors may increase risk for MCI among non-Hispanic Whites but not for Mexican Americans. These findings are consistent with past research that suggests risk factors for MCI may differ by ethnicity.

Keywords: Hachinski Ischemic Scale, Mexican American, Cognition, Ethnic differences, Older people

Background

The population of the United States is rapidly ageing. Hispanic elders, of whom 70% are Mexican Americans, make up the fastest growing segment of this ageing population. By 2050, Hispanics over the age of 65 will triple [1], and the rates of dementia, are expected to grow sixfold [2]. Previous research has suggested that Mexican Americans are diagnosed at more advanced stages of AD, and at younger ages than non-Hispanics [3]. Additionally, Mexican Americans experience higher levels of cardiovascular burden from conditions that are considered to be modifiable risk factors for AD [4]. Thus, the increased prevalence of diseases such as diabetes, obesity, hypertension and high cholesterol may put Mexican Americans at greater risk for developing dementia [5,6].

The relationship between cardiovascular risk factors and cognitive decline has been well documented. Research has repeatedly demonstrated that diabetics in particular are more likely to experience cognitive decline or develop dementia [7–9]. Studies on the association between hypertension and cognitive decline have shown an increased prevalence of impaired neurocognitive function in those with uncontrolled blood pressure [7, 9–13]. High cholesterol has also been...
shown to be predictive of the onset of cognitive decline in later life [9, 14]. Elders who were obese in middle-age were more likely to develop cognitive impairments [9, 15].

Mexican Americans are twice as likely to be diagnosed with diabetes as compared with non-Hispanic Whites, with more than a third considered obese. Furthermore, Hispanic women are 20% more likely to die of a stroke than non-Hispanic women [16]. Despite the fact that Mexican Americans have higher levels of cardiovascular burden, there is a dearth of literature examining the relationship between cardiovascular burden and cognitive dysfunction in this population.

In addition to the gap in literature, there is also a need for assessment tools that can be readily utilised in a primary care setting to identify individuals at risk for cognitive decline related to cardiovascular burden. The Hachinski Ischemic Scale (HIS) is a brief clinical tool that can be used to identify patients with vascular dementia [17]. A multitude of studies have demonstrated the validity of HIS in identifying vascular dementia [18]. However, little research has examined the correlation between HIS and measures of cognitive functioning. Paul and colleagues [19] found that HIS scores correlated with a decline in verbal learning in patients with evidence of cortical stroke. The primary goal of this study was to evaluate the relation between HIS and measures of cognition (global cognition, specific cognitive domains and executive functioning). Additionally, we wanted to examine the utility of the HIS in predicting a diagnosis of mild cognitive impairment (MCI). Little is known about the utility of the HIS in ethnically diverse samples [18]. One of the unique aspects of the current study is the use of the HIS in a community based, ethnically diverse (half Mexican American and half non-Hispanic) sample. It was hypothesised that the HIS would prove to be a more predictive tool for diagnosing MCI in Mexican Americans as a result of the increased cardiovascular burden in this population.

Methods

Participants and procedures

A total of 517 participants (211 Mexican Americans and 306 non-Hispanic Whites) age 40 and above were recruited from Project FRONTIER, a study of rural health [20]. Project FRONTIER utilises a community-based participatory research (CBPR) approach. CBPR involves partnering communities with scientific groups to conduct studies of human disease. Prior work from this study has demonstrated the comparability of the recruited cohort to that of the eligible population [21]. Inclusion criteria were (i) age 40 and above and (ii) residing in one of the three counties included in the study.

All participants signed an informed consent document and the study is conducted under an Institutional Review Board approved protocol. Participants underwent an examination that included a medical evaluation (including the HIS), neuropsychological testing, blood draw and an interview according to a standardised protocol. Diagnosis for MCI was assigned according to standardised Mayo criteria [21], which utilises both subjective cognitive complaints and objective cognitive assessments that support cognitive deficits above that seen within the normal ageing population. The Mayo criteria states that ‘in general’ patients diagnosed with MCI score −1.5 standard deviations below the mean on standardised testing. Our team has generated normative data for the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) for both English- and Spanish-speaking individuals (manuscript in preparation), and these norms were utilised for the Hispanic participants. The norms provided by the manual were utilised for non-Hispanic Whites. In order to ensure no ethnic biases towards MCI diagnoses were emerging, the cohort data were evaluated regularly with our recent work demonstrating that prevalence rates of MCI among our cohort were comparable between Hispanics and non-Hispanics [22]. Normal controls were those who performed within normal psychometric limits.

Materials

Hachinski Ischemic Scale

HIS was originally developed to establish a relationship between cerebral blood flow and dementia. Patients scoring 7 or greater are classified as having ‘multi-infarct dementia’, and patients scoring ≤5 are classified as having ‘primary degenerative dementia’. [17] Researchers have recognised the utility of the HIS as a tool to differentiate ischemic forms of dementia from AD cases. The HIS possesses good psychometric properties [18, 23] and has been shown to have strong inter-rater reliability [24].

Mini Mental Status Exam

The Mini Mental Status Exam (MMSE) [25] was used to provide a brief assessment of global cognition. The MMSE is the most widely used cognitive screening tools and possesses good psychometric properties [26].

Executive Interview

The Executive Interview (EXIT25) [27] is a well-validated global measure of executive control that covers a range of tasks including sequencing, fluency, analogous sentence repetition, thematic perception, automatic behaviours, go-no-go, and others. EXIT25 scores are significantly related with other validated measures of executive functioning [27].

Repeatable Battery for the Assessment of Neuropsychological Status

RBANS [28] was used to assess cognitive functioning. It has extensive normative data [28] and yields good psychometric properties [29]. The results yield five subscales: immediate memory, visuospatial/constructional, language, attention and delayed memory [28].
Results

Demographic characteristics of the sample can be found on Table 1. Mexican American participants were roughly 55 years old and had an average of 7.5 years of education. The non-Hispanic White participants were 65 years old and had 13 years of education. Thirty-two of the Mexican American participants were diagnosed with MCI and 42 of the non-Hispanic White. The medical diagnoses of the cohort were as follows: diabetes presence—non-Hispanic White = 22%, Mexican American = 40%; hypertension presence—non-Hispanic White = 58%, Mexican American = 59%; dyslipidaemia—non-Hispanic White = 63%, Mexican American = 57%; hypothyroidism—non-Hispanic White = 22%, Mexican American = 10%; tobacco dependence—non-Hispanic White = 11%, Mexican American = 11%; possible alcohol use problems—non-Hispanic White = 4%, Mexican American = 4%.

Regression analyses were conducted to examine the influence of HIS scores on several measures of cognition: MMSE, RBANS and EXIT25 (see Table 2). Age, education and language of administration were entered into the model as covariates. The results indicated that HIS scores were significantly negatively related to both immediate memory and attention RBANS subscales and positively associated with delayed memory [RBANS Attention Index B (SE) = 1.4, P = 0.01] and Mexican Americans [B (SE) = −0.85 (0.26), P < 0.001; B (SE) = −1.6 (0.36), P < 0.001] and Mexican Americans [B (SE) = −0.78 (0.28), P = 0.01; B (SE) = −0.74 (0.36), P = 0.04]. Finally, we used linear regressions to examine the relationship between HIS scores and executive functioning, EXIT25. Higher HIS scores were related to significantly poorer executive functioning scores among non-Hispanic Whites [B (SE) = 0.46 (0.12), P < 0.001] and Mexican Americans [B (SE) = 0.37 (0.14), P = 0.01].

Additional regression analyses were conducted, which excluded MCI cases, to examine the influence of HIS scores on cognition within a sample of individuals without cognitive deficits. Age, education and language of administration were entered into the model as covariates. The results indicated that HIS scores were significantly related to functional status [clinical dementia rating (CDR) total] for non-Hispanic Whites [B (SE) = 0.08 (0.01), P < 0.001] and Mexican Americans [B (SE) = 0.11 (0.02), P < 0.001]. Analyses also supported that for non-Hispanic Whites, HIS scores were significantly negatively associated with executive functioning [EXIT25 B (SE) = 0.39 (0.13), P = 0.003], attention [RBANS Attention Index B (SE) = −1.32 (0.43), P = 0.002] and positively associated with delayed memory [RBANS Delayed Memory Index B (SE) = 0.63 (0.30), P = 0.03] for non-Hispanic Whites and also for Mexican Americans [RBANS Delayed Memory Index B (SE) = 0.79 (0.28), P = 0.007] (see Table 3).

Logistic regression modelling was used to examine the utility of the HIS in predicting a diagnosis of MCI. Age, education, test language, gender and HIS scores were entered into the model. The results indicated that HIS scores successful predicted MCI status for non-Hispanic White participants only [odds ratio (OR) = 1.4; 95% confidence interval (CI) = 1.2–1.6, P = 0.01]. For Mexican Americans, HIS scores did not significantly predict a diagnosis of MCI (OR = 1.2; 95% CI = 0.96–1.4, P = 0.116).

Discussion

Cardiovascular burden is considered a risk factor for the development of cognitive dysfunction as well as for dementia, hypertension, diabetes, high cholesterol and obesity [7, 9, 10]. In the present study, the HIS score was significantly related to poorer global cognition among non-Hispanic Whites, but

Table 1. Demographics split by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Mexican American (n = 211)</th>
<th>Non-Hispanic Whites (n = 306)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>62</td>
<td>94</td>
</tr>
<tr>
<td>Female</td>
<td>149</td>
<td>212</td>
</tr>
<tr>
<td>MCI diagnosis</td>
<td>32</td>
<td>42</td>
</tr>
<tr>
<td>Age</td>
<td>55.5 (SD = 9.9)</td>
<td>65.4 (SD = 12.6)</td>
</tr>
<tr>
<td>Range</td>
<td>40–86</td>
<td>40–96</td>
</tr>
<tr>
<td>Education</td>
<td>7.5 (SD = 4.1)</td>
<td>13.3 (SD = 2.7)</td>
</tr>
<tr>
<td>Range</td>
<td>0–18</td>
<td>2–20</td>
</tr>
<tr>
<td>MMSE</td>
<td>26.7 (SD = 3.0)</td>
<td>28.4 (SD = 1.9)</td>
</tr>
<tr>
<td>Range</td>
<td>14–30</td>
<td>12–30</td>
</tr>
<tr>
<td>Hachinski</td>
<td>1.9 (SD = 2.0)</td>
<td>1.9 (SD = 1.9)</td>
</tr>
<tr>
<td>Range</td>
<td>0–14</td>
<td>0–11</td>
</tr>
<tr>
<td>EXIT25</td>
<td>8.0 (SD = 4.6)</td>
<td>6.5 (SD = 4.4)</td>
</tr>
<tr>
<td>Range</td>
<td>1–21</td>
<td>0–23</td>
</tr>
<tr>
<td>RBANS immediate memory</td>
<td>39.9 (SD = 8.8)</td>
<td>41.6 (SD = 9.5)</td>
</tr>
<tr>
<td>Range</td>
<td>14–57</td>
<td>5–61</td>
</tr>
<tr>
<td>RBANS visuospatial</td>
<td>27.9 (SD = 6.2)</td>
<td>29.9 (SD = 5.9)</td>
</tr>
<tr>
<td>Range</td>
<td>0–30</td>
<td>0–40</td>
</tr>
<tr>
<td>RBANS language</td>
<td>25.6 (SD = 4.9)</td>
<td>28.3 (SD = 5.3)</td>
</tr>
<tr>
<td>Range</td>
<td>11–38</td>
<td>8–42</td>
</tr>
<tr>
<td>RBANS attention</td>
<td>42.1 (SD = 16.3)</td>
<td>50.2 (SD = 15.2)</td>
</tr>
<tr>
<td>Range</td>
<td>9–85</td>
<td>11–100</td>
</tr>
<tr>
<td>RBANS delayed memory</td>
<td>35.1 (SD = 8.8)</td>
<td>35.7 (SD = 9.1)</td>
</tr>
<tr>
<td>Range</td>
<td>14–54</td>
<td>10–60</td>
</tr>
</tbody>
</table>

Table 2. HIS impact on cognitive functioning split by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Mexican American (B (SE))</th>
<th>Non-Hispanic White (B (SE))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P-value</td>
<td>P-value</td>
</tr>
<tr>
<td>MMSE</td>
<td>1.16 (0.09)</td>
<td>−1.3 (0.06)</td>
</tr>
<tr>
<td>Immediate memory</td>
<td>−0.78 (0.28)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Attention</td>
<td>−0.74 (0.36)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Delayed memory</td>
<td>0.37 (0.29)</td>
<td>0.19</td>
</tr>
<tr>
<td>Language</td>
<td>−0.24 (0.16)</td>
<td>0.13</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>−0.04 (0.22)</td>
<td>0.87</td>
</tr>
<tr>
<td>EXIT25</td>
<td>0.37 (0.14)</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

Covariates include age, education and language of administration. *Significance at P < 0.05. B, unstandardised regression coefficient; SE, standard error.
controls split by ethnicity

Table 3. HIS impact on cognitive functioning among normal controls split by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Mexican American</th>
<th>Non-Hispanic White</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( B ) (SE)</td>
<td>( P )-value</td>
</tr>
<tr>
<td>MMSE</td>
<td>-0.01 (0.08)</td>
<td>0.84</td>
</tr>
<tr>
<td>CDR total</td>
<td>0.11 (0.02)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Immediate memory</td>
<td>-0.12 (0.24)</td>
<td>0.62</td>
</tr>
<tr>
<td>Attention</td>
<td>-0.01 (0.38)</td>
<td>0.98</td>
</tr>
<tr>
<td>Visual spatial</td>
<td>-0.03 (0.24)</td>
<td>0.89</td>
</tr>
<tr>
<td>Delayed memory</td>
<td>0.79 (0.28)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Language</td>
<td>0.08 (0.16)</td>
<td>0.57</td>
</tr>
<tr>
<td>EXIT25</td>
<td>0.11 (0.14)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Covariates include age, education and language of administration. *Significance at \( P < 0.05 \). B, unstandardised regression coefficient; SE, standard error; CDR, clinical dementia rating.

not among Mexican Americans. However, higher HIS scores were consistently related to poorer scores in immediate memory, attention and executive functioning among both non-Hispanics Whites and Mexican Americans. It is possible that subtle neurological changes related to subcortical and frontal vasculature associated with the HIS are responsible for these findings. This study also highlighted a significant difference in reported education for non-Hispanic Whites and Mexican Americans, with Mexican Americans reporting significantly lower education. This may have indirectly impacted the discrepancy seen in MCI diagnosis between the ethnic groups. Our prior work has demonstrated that Mexican Americans are likely to present with cognitive deficits at younger ages [22, 30]. Level of education may provide a protective factor, thereby the greater the educational attainment the lower the probability for obtaining an MCI diagnosis once the sufficient level of education is attained. However, in our recent work, education was not significantly related to MCI diagnosis among Mexican Americans [22]. This may be due to the non-linear impact of education on cognition and the lack of a protective effect due to this ethnic group not reaching sufficient educational attainment to receive the protective benefit.

As the HIS is the most commonly used screening tool of its kind, we sought to examine its role in predicting MCI. We hypothesised that the HIS would predict MCI diagnosis better among Mexican Americans than non-Hispanic Whites, due to the fact that Mexican Americans experience higher levels of cardiovascular/metabolic burden when compared with non-Hispanic Whites. In the present study, the HIS significantly predicted cognitive impairment for non-Hispanic Whites. However, the results did not support our hypothesis that the HIS would be a better predictor among Mexican Americans. This leads to the notion that vascular factors may play a more prominent role in MCI among non-Hispanic Whites while metabolic factors may play a more predominant role in MCI among Mexican Americans.

While cardiovascular and metabolic factors have been associated with MCI, results have not always been consistent [31, 32] and the risk associated with these various factors (including APOE ε4 genotype) have been shown to vary by age, gender and ethnicity [22, 33–36]. In fact, this notion has been indirectly proposed by prior work has shown (i) diabetes and the metabolic syndrome to be more common among Mexican Americans and (ii) the suggestion by others that diabetes and metabolic factors (i.e. metabolic syndrome) may be a key driving factor for AD among this ethnic group [37, 38]. In our recent work, the presence/absence of metabolic factors showed a trend towards being a significant risk factor for MCI among Mexican Americans, but not among non-Hispanics, which was consistent across independent cohorts [22]. We previously proposed the notion of a metabolic endophenotype of Alzheimer’s disease among Mexican Americans based on biological profiles [39]. In that study, the overall profile was heavily weighted towards metabolic markers as compared with our prior work showing a biological profile of AD among non-Hispanics that is largely weighted towards inflammatory and vascular factors [40–42], which lead us to propose the notion of an inflammatory endophenotype of AD among non-Hispanic Whites [40, 43]. In fact, the top ranking serum biomarker in the AD profile among Mexican Americans was fatty acid-binding protein (FABP). FABPs are implicated in diabetes, obesity, insulin resistance and the metabolic syndrome. Other markers in the biomarker profile of AD among Mexican Americans have also been associated with metabolic conditions including CD40 [44], glucagon-like peptide 1 [45], pancreatic polypeptide [46], β2-microglobulin [47], insulin-like-growth factor [48], peptide YY [49], insulin and TSH [50]. Therefore, when combined, our data suggest the notion of a vascular/inflammatory endophenotype among non-Hispanic Whites [43] and have now provided evidence for a metabolic endophenotype of MCI/AD among Mexican Americans using clinical measures along with biological profiles.

The biomarker profile included markers related to inflammation, infection, protease inhibition, iron and oxygen binding and oxidative stress. This concept of a metabolic endophenotype among Mexican Americans is consistent with other biomarker work from our laboratory as a blood-based biomarker profile of AD showed a preponderance of metabolic-related factors that was different from the non-Hispanic AD biomarker profile (O’Bryan et al. manuscripts under review for publication). Therefore, the current group is seeking to identify a metabolic endophenotype of cognitive dysfunction/MCI/AD that incorporates blood-based biomarkers and clinical labs among Mexican Americans.

Detecting early stage cognitive decline can be difficult in primary care settings. Thus, the identification of quick cognitive screeners can greatly aid physicians in detecting patients that should be referred for in depth neuropsychological testing. The HIS is a commonly used diagnostic tool for vascular dementia; however, little is known regarding its utility in assessing cognitive functioning.

There are several limitations to the present study. First, the data are cross sectional, and the sample size is small and...
In this study, the HIS score signified cardiovascular burden is considered a risk factor for cognitive dysfunction. It is possible that these findings indicate that vascular factors may increase risk for MCI among non-Hispanics, whereas metabolic profiles may be more important among Mexican Americans. A follow-up study among an independent cohort, the HABLE study, is ongoing to cross-validate these findings. This study examined the link between HIS scores and detailed neuropsychological test scores and was the first to examine this question among Mexican Americans. These findings suggest that vascular factors may increase risk for MCI among non-Hispanics, whereas metabolic profiles may be more important among Mexican Americans.

Key points

- Cardiovascular burden is considered a risk factor for cognitive dysfunction and diagnoses of dementia (vascular and Alzheimer's disease).
- In this study, the HIS score significantly predicted cognitive impairment for non-Hispanic Whites.
- It is possible that these findings indicate that vascular factors may increase risk for MCI among non-Hispanic Whites but not for Mexican Americans.
- Ethnicity is an important variable when assessing risk for cognitive dysfunction.

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Conflicts of interest

None declared.

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Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References

The very long list of references supporting this review has meant that only the most important references are listed here and are represented by bold type throughout the text. For the full list of references, see Supplementary data available in Age and Ageing online.

Older people’s experiences of therapeutic exercise as part of a falls prevention service: survey findings from England, Wales and Northern Ireland

AMANDA K. BUTTERY1,2, JANET HUSK1, DEREK LOWE1, JONATHAN TREML1,3, NAOMI VASILAKIS1, JACKIE RIGLIN1,4

1Clinical Effectiveness and Evaluation Unit, Royal College of Physicians, London, UK
2Department of Physiotherapy, Guy’s and St Thomas’ NHS Foundation Trust, London, UK
3Geriatric Medicine, Queen Elizabeth Hospital Birmingham, UK
4Falls Prevention Service, Cambridgeshire Community Services NHS Trust, Cambridge, UK

Address correspondence to: J. Husk. Tel: +44 (0) 207 3075 1347; Fax: +44 (0) 20 7487 3988. Email: janet.husk@rcplondon.ac.uk

Abstract

Introduction: falling, and fear of falling, significantly affect older people and their lifestyle resulting in loss of confidence, restriction of activity and deteriorating quality of life. Multi-factorial assessment and active participation in an evidence-based exercise programme are key interventions to prevent and manage falls.

Objective: to examine older people’s experiences of therapeutic exercise as part of a falls prevention service in NHS Trusts in England, Wales and Northern Ireland.

Methods: a cross-sectional survey targeted patients and staff members delivering exercise interventions for reducing falls. A multi-disciplinary group including patient and staff representatives developed a 20-item patient questionnaire and a 12-item staff questionnaire that were distributed to 94 NHS Trusts (113 participating sites within the NHS Trusts) in October 2011.

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Older people’s experiences of therapeutic exercise


