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RESEARCH ARTICLE

# REVISED Social engagement after stroke – is it relevant to cognitive function? A cross-sectional analysis of UK Biobank data [version 2; peer review: 2 approved]

Bogna A. Drozdowska [1], Carlos A. Celis-Morales [1], Donald M. Lyall[2], Terence J. Quinn [1]

[1]Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Lanarkshire, G12 8QQ, UK
[2]Institute of Health and Wellbeing, University of Glasgow, Glasgow, Lanarkshire, G12 8QQ, UK

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## Abstract

**Background:** Findings from studies in older adult populations suggest that measures of social engagement may be associated with health outcomes, including cognitive function. Plausibly the magnitude and direction of this association may differ in stroke. The disabling nature of stroke increases the likelihood of social isolation and stroke survivors are at high risk of cognitive decline. We assessed the association between social engagement and cognitive function in a sample of stroke survivors.
**Methods:** We included available data from stroke survivors in the UK Biobank (N=8776; age range: 40-72; 57.4% male). In a series of regression models, we assessed cross-sectional associations between proxies of social engagement (frequency of family/friend visits, satisfaction with relationships, loneliness, opportunities to confide in someone, participation in social activities) and performance on domain specific cognitive tasks: reaction time, verbal-numerical reasoning, visual memory and prospective memory. We adjusted for demographics, health-, lifestyle-, and stroke-related factors. Accounting for multiple testing, we set our significance threshold at p<0.003.
**Results:** After adjusting for covariates, we found independent associations between faster reaction times and monthly family visits as compared to no visit (standardised beta=-0.32, 99.7% CI: -0.61 to -0.03, N=4,930); slower reaction times and religious group participation (standardised beta=0.25, 99.7% CI 0.07 to 0.44, N=4,938); and poorer performance on both verbal-numerical reasoning and prospective memory tasks with loneliness (standardised beta=-0.19, 99.7% CI: -0.34 to -0.03, N=2,074; odds ratio=0.66, 99.7% CI: 0.46 to 0.94, N=2,188; respectively). In models where all proxies of social engagement were combined, no associations remained significant.
**Conclusions:** We found limited task-specific associations between cognitive performance and proxies of social engagement, with only loneliness related to two tasks. Further studies are necessary to confirm

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1 **Katharina S. Sunnerhagen**, University of Gothenburg, Gothenburg, Sweden

2 **Christian Hakulinen**, University of Helsinki, Helsinki, Finland

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and improve our understanding of these relationships and investigate the potential to target psychosocial factors to support cognitive function in stroke survivors.

**Keywords**
Social engagement, Loneliness, Cognition, Stroke, UK Biobank

**Corresponding author:** Bogna A. Drozdowska (b.drozdowska.1@research.gla.ac.uk)

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**REVISED** **Amendments from Version 1**

In the revised version of our article, we note issues around use of bespoke cognitive tasks and discuss the observed association between religious activity and cognitive performance. We have also included additional information on deriving the 'disability' variable, used as a covariate in our fully-adjusted models. Further, we have aimed to simplify the presentation of our results by combining all Tables with descriptive statistics, combining Figures for outcomes used in linear regression models, and removing information on unstandardised coefficients and exact p-values from Tables with model results. Significance of associations is indicated by confidence intervals, changed from 95% to 99.7%, to match the set p-value threshold of 0.003

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## Lay summary

Having good relationships, feeling supported and participating in group activities may be good for your health. On the other hand, people who are isolated and lonely are more likely to suffer from illness. Some studies have shown a link between a poor social life and problems with memory. People living with stroke are likely to have both social and memory problems.

A stroke can cause issues with walking or communicating that prevent socialising. Strokes can also cause problems with memory and thinking. We wanted to find out whether there is a link between stroke survivors' social life and their memory and thinking skills.

We used data from the UK Biobank. This is a database that has collected health information on over 500,000 people in the United Kingdom. People who volunteered to give information to UK Biobank completed questionnaires on their social life and completed memory and thinking tests.

UK Biobank includes information on 8,700 people living with stroke. To look at their social life, we included information on: relationships and visits from family and friends, loneliness and social activities. We compared these to the person's scores on four different memory and thinking tests. We also considered things that could influence both social life and memory, for example age, health conditions and drinking alcohol.

We found that people who visited family and friends had quicker reactions than people with no visits. We also found that lonely people had poorer scores on two different memory and thinking tests.

Our study suggests that social life may be related to memory and thinking following a stroke. We now need to see if the same is true in other groups of stroke survivors. Things can be done to improve a person social life following a stroke and it would be interesting to test whether such activities prevented memory and thinking problems.

## Introduction

Over 40 years ago, Cassel[1] and Cobb[2] published two influential reviews discussing the association between social engagement, health and well-being. Since then, a good body of evidence has been accumulated, suggesting a potential relationship between aspects of social isolation (the opposite of social engagement) and mortality, morbidity and disability[3–9]. As well as physical health, a relationship between perceived social isolation and cognitive decline has also been described[10–12]. The potential importance of social isolation has been recognised by policy makers. For example, in 2018, a United Kingdom government press release announced a planned £20 million investment to help socially isolated and lonely people by the end of 2020.

While there is general agreement on the importance of social engagement, there is inconsistency in how the concept is defined and measured. Three domains of interest are typically distinguished[13]: social networks, relating to the structure, composition and content of an individual's interpersonal ties[14–16]; social support, relating to the level of emotional and instrumental resources available to an individual[9,17]; and social participation, relating to involvement in activities with a social element[13,18,19]. Another important distinction is made between objective measures of social engagement (e.g. how often do you visit your friends) and subjective measures (e.g. feeling lonely)[20–22].

There are many putative pathways through which social engagement may impact physical and cognitive health[23]. Much of the literature supports an explanation based on stress, impacting health either directly or indirectly[24]. In relation to the former, it has been argued that perceived social isolation evokes a physiological stress response. As a chronic state, it is hypothesised to lead to dysregulation of the endocrine, immune, and cardiovascular systems, and neurodegeneration[23,25,26]. The indirect pathway is associated with stress triggering unhealthy behaviours, such as excessive alcohol consumption[24,27–30]. Unravelling the true nature of these associations is doubtless challenging, particularly in the context of cognition. Age, deprivation, illness, disability and low mood are all examples of factors that may be simultaneously affecting both social engagement and cognitive function, which can result in identifying spurious associations between the two[31,32].

The relationship between social isolation and stroke is also complex. Social isolation has been reported as a risk factor for stroke[33,34], while the disabling nature of stroke can increase the likelihood of social isolation in stroke survivors[35–38]. Social isolation may influence all aspects of the stroke pathway[26,39]. Studies on rodent models of stroke suggest increased stroke severity, reduced recovery and increased mortality in socially isolated animals[40,41]. Observational data in humans also support an association between social isolation and loneliness, stroke incidence and post-stroke adverse outcome events[42]. Noteworthy, however, results from a recent large population-based study indicated that the observed increase in risk can in most part be explained by conventional risk factors, such as obesity or smoking[43].

In the context of functional recovery, two studies found that patients with high levels of social support progressively improved over time, whereas patients with low support (ultimately) deteriorated[44,45]. If social engagement is associated with physical recovery following stroke, an association with cognitive recovery seems plausible. There are some data supporting this link, for example in one study (N = 272) baseline social ties and emotional support were independent predictors of better performance on a cognitive summary score at six months, while emotional support was further associated with greater improvement from baseline to follow-up[46]. When individual tasks were considered, social ties were associated with immediate and delayed recall of a 10-word list, while emotional support was associated with immediate recall only. However, no significant relationships were found for tasks assessing attention, language and executive function, nor for performance on the Mini Mental State Examination (MMSE).

Cumulative findings from studies involving animal models, non-stroke populations and stroke survivors indicate that social engagement may be relevant to post-stroke cognitive function. More evidence is however needed to confirm this hypothesis and improve our understanding of the relationship between the two. Compared to other potentially modifiable risk factors, social isolation seems to have been omitted from studies on risks, prognosis and interventions for post-stroke cognitive decline[47–53].

We conducted an observational study to investigate the associations between social engagement and cognitive function in stroke survivors. We aimed to include proxies that would reflect both the objective and subjective aspects of social engagement. Given the results of the described study investigating cognitive outcomes in a sample of stroke survivors, we further assumed that associations may differ depending on what cognitive function is being assessed. As many variables may be relevant to both social isolation and poorer cognitive function, we ensured that our analyses accounted for plausible confounders.

## Methods

We used anonymised, individual participant level data held in the UK Biobank. The UK Biobank project is overseen by the NHS National Research Ethics Service (approval letter dated 17th June 2011, Ref 11/NW/0382) and has received ethical approval from the Community Health Index Advisory Group (approved 7th December 2006, application number 06-007). This research was conducted under application no. 17689. In reporting our study, we followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[54].

### Study setting and participants

The UK Biobank includes data on over 502,500 participants. Baseline assessments took place between 2006 and 2010, across 22 centres in the United Kingdom. During the study visit participants answered questions regarding sociodemographic, health, mood and lifestyle factors, completed cognitive tasks, and had a range of physical measurements taken. A full description of UK biobank has been presented previously[55].

We focused on baseline data from participants who self-reported a history of stroke or transient ischaemic attack (TIA) (data field 20002). We included TIA on the basis of similar risk factors for cognitive decline as stroke[56], and reports of longer-term cognitive sequalae[57]. Information on medical conditions was obtained during a two-stage process. Firstly, during a touch-screen questionnaire, participants were asked whether they had a history of one or more illnesses, including stroke. Responses were subsequently confirmed during a verbal interview with a trained nurse. In cases where the participant was uncertain of the type of condition they had had, they were asked to describe the illness, so that the nurse could assist in defining it. If the interview revealed an erroneous indication of a certain condition, the initial response could be amended.

We found one item from the cerebrovascular disease category corresponding to a history of transient ischaemic attack (code 1082). We also considered four items from this category to identify subjects with a history of stroke, including an indication of ‘stroke’ (code 1081), ‘ischaemic stroke’ (code 1583), ‘subarachnoid haemorrhage’ (code 1086), or ‘brain haemorrhage’ (code 1491). We excluded participants who reported the occurrence of the cerebrovascular event before the age of 18.

### Measures

***Proxies of social engagement***. We selected six variables reflecting both objective and subjective aspects of social engagement, assuming different degrees of overlap between these aspects. This included: frequency of family and/or friend visits (made and received), satisfaction with family relationships, satisfaction with friendships, frequency of opportunities to confide in someone, loneliness, and participation in social activities. We grouped responses relating to frequency of interactions into four categories: never, once every few months to once a month, one to four times a week, and daily or almost daily. We dichotomised satisfaction with relationship into “satisfied” and “not satisfied”. Similarly, experience of loneliness was dichotomised into “lonely” and “not lonely”. We distinguished seven categories related to participation in social activities: reporting no engagement in social activities, attending a sports club or gym, going to a pub or a social club, participation in a religious group, attending an adult education class, other group activity, engagement in multiple group activities.

***Measures of cognitive performance***. We chose four baseline (2006–2010) cognitive tasks as outcome measures in our analyses: reaction time, verbal-numerical reasoning (referred to as ‘Fluid Intelligence’ in the UK Biobank), visual memory (referred to as ‘Pairs matching’) and prospective memory. Reasoning and prospective memory were added at a later stage of recruitment and so have lower sample sizes[58].

The reaction time task (data field 20023) included 12 rounds (4 training rounds, 8 trials) of card-matching, based on the game ‘Snap’. Participants were presented with two cards at a time and asked to press a button as quickly as possible when the pair was identical. Performance on the task was measured as the average response time across eight trial rounds in milliseconds. Times under 50ms and over 2000ms were excluded.

The verbal-numerical reasoning task (data field 20016) involved answering 13 multiple choice logic/reasoning-type questions, with a 2-minute time limit. Performance was measured as the unweighted sum of correctly-answered questions, with a maximum of 13 points.

In the visual memory task (data field 399) participants were presented with a set of matching pairs of cards and requested to memorise their positions. The cards were then turned over, and the subjects asked to select matching pairs in as few attempts as possible. The task included rounds with three and six pairs of cards, with performance measured as the number of errors in each round. For our analysis we only used results from the six-pair round, as it was less likely for participants to have zero errors, avoiding a ceiling effect.

For the prospective memory task (data field 20018), an initial instruction was given early in the cognitive testing section. Participant were informed that at a later stage they will be shown four coloured shapes and asked to touch a blue square. Instead, however, they are to touch an orange circle. Originally, performance was grouped into three categories: incorrect response/task skipped, correct on first attempt, correct on second attempt. We however dichotomised performance based on whether participants correctly responded on their first attempt or not.

All cognitive tasks were performed using a touchscreen. Additional information on cognitive testing in the UK Biobank can be found in the online Data Showcase under the ‘Cognitive function’ category (category ID: 100026). Previous publications have described the cognitive data from the UK Biobank resource, as well as Cronbach’s alpha values for reliability of the reaction time and reasoning tasks[59–61].

***Covariates***. Based on previous research, we identified factors associated with both social engagement and cognition that could act as confounders (i.e. lead to a potentially spurious association)[31,32]. Firstly, we considered demographics: age (in years), sex, educational attainment, and the Townsend deprivation index score. We dichotomised education according to whether or not participants reported attainment of a college or university degree. The Townsend deprivation index is a measure of material deprivation based on rates of unemployment, car and home ownership, and household overcrowding in a given population[62]. Each participant was assigned a deprivation index score at recruitment, corresponding to the output area covering their postcode, based on a preceding national census. Negative values indicate relative affluence, while positive values indicate material deprivation.

Secondly, we included factors related to general health status and functioning: self-reported walking pace (three categories: brisk, steady/average, or slow), disability (dichotomised into present or not present), subjective health rating (excellent, good, fair or poor) and body mass index (BMI; continuous measure). Information on disability was derived from responses to a question on employment status (data field 6142). In answer to this questionnaire item, participants were able to select multiple response options, one of which was “unable to work because of sickness or disability”. We considered an activity-limiting disability to be present if this response was selected on its own or in conjunction with another option, for example “retired” or “unemployed”.

We further considered the presence of specific conditions that have been associated with vascular dementia and poorer cognitive outcomes in stroke populations[63–65]: high blood pressure, diabetes, and atrial fibrillation. In relation to mental health, we assumed a relevant association of depression with both social engagement and cognition. We identified participants with a history of depressive episodes applying a method used in a previous UK Biobank-based study, combining responses that jointly indicated experiencing a period of feeling down, depressed, disinterested or unenthusiastic for at least two weeks, and seeking professional help[66].

Another category of covariates included lifestyle factors: frequency of alcohol intake (never/special occasions only, one to three times a month, one to four times a week, or daily/almost daily) and smoking (never, previous or current). These were treated as ordinal variables.

Finally, we included two variables relating to the index stroke event: type of cerebrovascular event (stroke or TIA) and the time between the most recent stroke/TIA and baseline assessment, measured in one-year increments.

### Statistical analysis

To correct for a positive skew in reaction time and visual memory data, we used a natural log transformation. As in the case of the visual memory task there was a possible score of 0 (no errors), we preceded the transformation by adding the value of 1 to all task results. We performed data transformations using IBM SPSS Statistics V.24.

We conducted a series of regression models to investigate the associations between proxies of social engagement and performance on cognitive tasks. We used linear regression analysis for three outcomes – reaction time, reasoning and visual memory, and logistic regression for prospective memory. We conducted three types of models focusing on individual proxies of social engagement, differing in terms of the number of covariates included. Unadjusted models did not control for any potential confounders. In partially-adjusted models we included variables related to demographics: age, sex, education and deprivation score. In the fully adjusted models, we additionally accounted for health-, lifestyle- and stroke-related factors. Finally, we conducted complete models combining all proxies of social engagement and potential confounders (for each cognitive outcome). Total sample sizes varied by model and cognitive task.

To describe and graphically present associations with log reaction time, verbal-numerical reasoning scores and log errors on the visual memory task we used standardised betas. For associations with performance on the prospective memory task we reported odds ratios (OR). Accounting for multiple testing, we accepted differences as significant at $p < 0.003$. We performed all analyses using STATA version 14.2 statistical software (StataCorp LLC).

## Results

We identified 8,776 participants with stroke or TIA. Table 1 presents descriptive statistics for demographics, health, lifestyle- and stroke-related factors; the distribution among

**Table 1. Descriptive statistics for study sample.**

| Variables | |
|---|---|
| Demographics | |
| Age, years | |
| Mean (SD) | 60.9 (6.7) |
| Sex | |
| Male | 5041/8776 (57.4%) |
| Degree-level education | 1877/8569 (21.9%) |
| Missing data | 207 |
| Townsend deprivation score (higher: more deprived) | |
| Mean (SD) | -0.53 (3.4) |
| Missing data | 10 |
| Health-related factors | |
| Walking pace | |
| Brisk | 1844/8484 (21.7%) |
| Steady, average | 4209/8484 (49.6%) |
| Slow | 2431/8484 (28.7%) |
| Missing data | 292 |
| Disability | 1527/8731 (17.5%) |
| Missing data | 45 |
| Subjective health rating | |
| Excellent | 369/8670 (4.3%) |
| Good | 3407/8670 (39.3%) |
| Fair | 3281/8670 (37.8%) |
| Poor | 1613/8670 (18.6%) |
| Missing data | 106 |
| BMI | |
| Mean (SD) | 28.9 (5.2) |
| Missing data | 132 |
| Comorbidities | |
| Hypertension | 4966/8776 (56.6%) |
| Diabetes | 1197/8776 (13.6%) |
| Atrial fibrillation | 256/8776 (2.9%) |
| History of depressive episodes | 667/5834 (11.4%) |
| Missing data | 2942 |
| Lifestyle factors | |
| Alcohol intake frequency | |
| Never/Special occasions only | 2558/8749 (29.2%) |
| Monthly | 945/8749 (10.8% |
| Weekly | 3551/8749 (40.6%) |
| Daily/almost daily | 1695/8749 (19.3%) |
| Missing data | 27 |
| Smoking status | |
| Never | 3655/8698 (42.0%) |
| Previous | 3703/8698 (42.6%) |
| Current | 1340/8698 (15.4%) |
| Missing data | 78 |
| Stroke-related factors | |
| Type of cerebrovascular event | |
| Stroke | 7158/8776 (81.6%) |
| Transient ischaemic attack | 1618/8776 (18.4%) |
| Time from stroke/TIA to baseline assessment, years | |
| Mean (SD) | 7.5 (7.2) |
| Missing data | 558 |
| Proxies of social engagement | |
| Frequency of family and/or friend visits | |
| Never | 287/8615 (3.3%) |
| Every few months to monthly | 1502/8615 (17.4%) |
| Every week | 5505/8615 (63.9%) |
| Daily/almost daily | 1321/8615 (15.3%) |
| Missing data | 161 (1.8%) |
| Satisfaction with family relationships | |
| Unsatisfied | 245/2919 (8.4%) |
| Satisfied | 2674/2919 (91.6%) |
| Missing data | 5857 (66.7%) |
| Satisfaction with friendships | |
| Unsatisfied | 119/2905 (4.1%) |
| Satisfied | 2786/2905 (95.9%) |
| Missing data | 5871 (66.9%) |
| Loneliness | |
| Lonely | 2143/8592 (24.9%) |
| Not lonely | 6449/8592 (75.1%) |
| Missing data | 184 (2.1%) |
| Frequency of opportunities to confide in someone | |
| Never | 1686/8397 (20.1%) |
| Every few months to monthly | 999/8397 (11.9%) |
| Every week | 1570/8397 (18.7%) |
| Daily/almost daily | 4142/8397 (49.3%) |
| Missing data | 379 (4.3%) |
| Type of social activity participated in | |
| None | 2997/8716 (34.4%) |
| Sports club/gym | 740/8716 (8.5%) |
| Pub/social club | 1467/8716 (16.8%) |
| Religious group | 625/8716 (7.2%) |
| Adult education class | 157/8716 (1.8%) |
| Other group activity | 843/8716 (9.7%) |
| Multiple group activities | 1887/8716 (21.6%) |
| Missing data | 60 (0.7%) |
| Cognitive tasks | |
| Reaction time, milliseconds | |
| Mean (SD) | 611.9 (151.5) |
| Missing data | 202 |
| Verbal-numerical reasoning, points (range 0 to 13) | |
| Mean (SD) | 5.4 (2.1) |
| Missing data | 6052 |
| Visual memory, errors | |
| Mean (SD) | 4.5 (3.7) |
| Missing data | 75 |
| Prospective memory | |
| Correct response on first attempt | 1934/2939 (65.8%) |
| Missing data | 5837 |

categories of social engagement proxies; and a summary of performance on cognitive tasks. For unadjusted models, sample sizes ranged from 2,617 to 8,648, for partially adjusted models from 2,580 to 8,520, and for fully adjusted models from 2,040 to 5,034. Below we present results from all conducted models according to investigated outcome measure.

### Reaction times

In unadjusted models, we found that faster reaction times were associated with monthly and weekly family/friend visits and participation in sports, while slower reaction times were associated with loneliness and participation in a religious group activity. After adjusting for demographics, associations with monthly family visits and sports were no longer significant. In fully adjusted models, we found only two proxies of social engagement to be significant predictors of performance: reaction times were significantly faster for monthly family/friend visits (standardised beta = -0.318, 99.7% CI: -0.608 to -0.029, p < 0.003) and slower for engagement in religious group activities (standardised beta = 0.254, 99.7% CI: 0.066 to 0.442, p < 0.001). Finally, we observed no significant associations between any proxies of social engagement and reaction time in the complete model (Figure 1A). We found that neither satisfaction with friendships nor opportunity to confide in someone predicted reaction time in any of the models. We presented complete results from all models investigating associations with reaction time in Table 2.

### Verbal-numerical reasoning

In unadjusted models, we found that better verbal-numerical reasoning task scores were associated with engaging in multiple

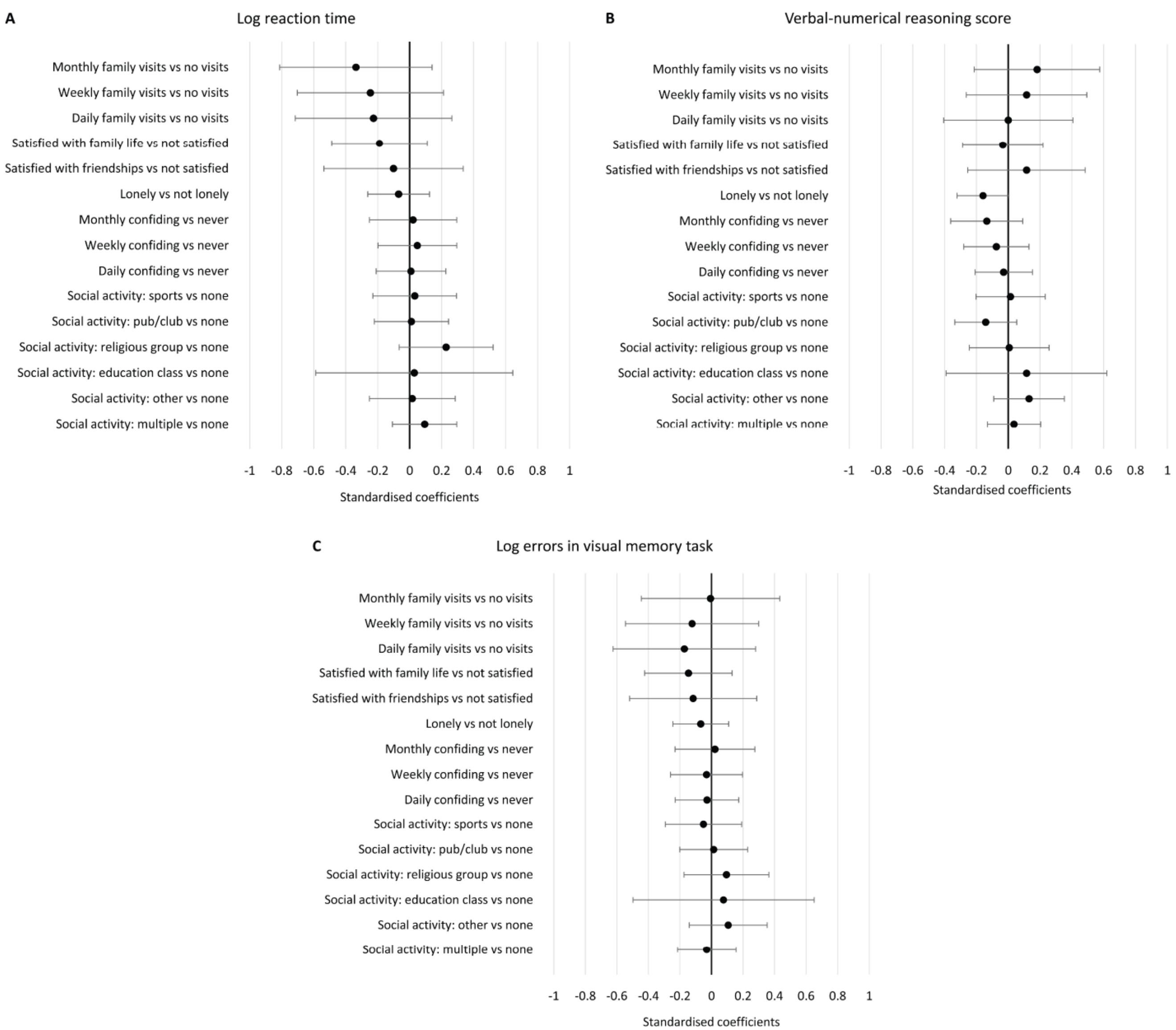


**Figure 1.** Associations between proxies of social engagement and log reaction time (**A**), verbal-numerical reasoning task scores (**B**) and log errors in the visual memory task (**C**) in complete models, with 99.7% confidence intervals.

**Table 2. Associations between proxies of social engagement and log reaction time.**

| | Model | | | |
|---|---|---|---|---|
| **Variable** | **Unadjusted Std. beta (99.7% CI)** | **Partially adjusted Std. beta (99.7% CI)** | **Fully adjusted Std. beta (99.7% CI)** | **Complete Std. beta (99.7% CI)** |
| **Family/friend visits (never)*** | | | | |
| Monthly | -0.281** (-0.502, -0.059) | -0.222 (-0.442, -0.002) | -0.318** (-0.608, -0.029) | -0.336 (-0.813, 0.140) |
| Weekly | -0.254** (-0.463, -0.046) | -0.232** (-0.440, -0.025) | -0.263 (-0.539, 0.013) | -0.246 (-0.703, 0.212) |
| Daily | -0.136 (-0.360, -0.088) | -0.151 (-0.374, (0.072) | -0.225 (-0.520, 0.070) | -0.226 (-0.716, 0.264) |
| Sample size | 8,426 | 8,303 | 4,930 | 2,029 |
| **Family satisfaction (not satisfied)*** | | | | |
| Satisfied | -0.218 (-0.447, 0.011) | -0.259** (-0.486, -0.032) | -0.205 (-0.480, 0.070) | -0.189 (-0.487, 0.110) |
| Sample size | 2,842 | 2,794 | 2,172 | 2,029 |
| **Friendship satisfaction (not satisfied)*** | | | | |
| Satisfied | -0.046 (-0.365, 0.273) | -0.110 (-0.424, 0.205) | -0.156 (-0.561, 0.249) | -0.101 (-0.537, 0.335) |
| Sample size | 2,829 | 2,783 | 2,164 | 2,029 |
| **Loneliness (not lonely)*** | | | | |
| Lonely | 0.121** (0.036, 0.207) | 0.100** (0.014, 0.187) | 0.025 (-0.097, 0.148) | -0.069 (-0.262, 0.124) |
| Sample size | 8,404 | 8,212 | 4,876 | 2,029 |
| **Confiding in someone (never)*** | | | | |
| Monthly | 0.087 (-0.049, 0.224) | 0.098 (-0.037, 0.234) | 0.131 (-0.040, 0.302) | 0.021 (-0.252, 0.295) |
| Weekly | 0.011 (-0.109, 0.130) | 0.022 (-0.097, 0.142) | 0.057 (-0.094, 0.207) | 0.048 (-0.198, 0.295) |
| Daily | -0.026 (-0.125, 0.073) | -0.003 (-0.102, 0.095) | 0.028 (-0.094, 0.150) | 0.008 (-0.210, 0.226) |
| Sample size | 8,218 | 8,034 | 4,779 | 2,029 |
| **Social activities (none)*** | | | | |
| Sports | -0.166** (-0.306, -0.026) | -0.101 (-0.240, 0.038) | 0.008 (-0.158, 0.174) | 0.032 (-0.230, 0.293) |
| Pub/social club | 0.032 (-0.078, 0.141) | 0.013 (-0.096, 0.122) | 0.021 (-0.117, 0.159) | 0.011 (-0.221, 0.243) |
| Religious group | 0.296** (0.146, 0.447) | 0.256** (0.107, 0.406) | 0.254** (0.066, 0.442) | 0.228 (-0.066, 0.522) |
| Adult education | 0.099 (-0.180, 0.378) | 0.149 (-0.127, 0.426) | -0.024 (-0.390, 0.342) | 0.029 (-0.588, 0.645) |
| Other | 0.058 (-0.075, 0.191) | 0.040 (-0.092, 0.172) | -0.030 (-0.196, 0.135) | 0.016 (-0.252, 0.285) |
| Multiple | -0.020 (-0.120, 0.080) | -0.013 (-0.113, 0.087) | 0.072 (-0.053, 0.197) | 0.094 (-0.108, 0.295) |
| Sample size | 8,526 | 8,336 | 4,938 | 2,029 |

Std., Standardised *reference category **significant at $p < 0.003$

Covariates included in partially adjusted models: age, sex, education and deprivation score. Covariates included in fully adjusted models: age, sex, education, deprivation score, walking pace, disability, subjective health rating, BMI, comorbidities, history of depressive episodes, alcohol intake frequency, smoking status, type of cerebrovascular event and time from stroke/TIA to baseline assessment. Complete models included all covariates from fully adjusted models as well as all proxies of social engagement.

social activities, while worse scores were associated with reported loneliness. After adjusting for demographics, only the association with reported loneliness remained significant. We obtained similar results in the fully adjusted model, where loneliness was associated with significantly worse scores (standardised beta = -0.185, 99.7% CI: -0.339 to -0.032, $p < 0.001$). However, after combining all proxies of social engagement in the complete model this association was no longer significant, although close to our set threshold ($p = 0.004$) (Figure 1B). We found no significant associations between verbal-numerical reasoning scores and family/friend visits, satisfaction with relationships and frequency of opportunities to confide in someone in any of the models. We presented complete results from all verbal-numerical reasoning models in Table 3.

### Visual memory

We did not find the log number of errors in the visual memory task to be associated with any proxy of social engagement at $p < 0.003$. Table 4 includes results from all analyses focusing on visual memory task performance. Associations with variables of interest in the complete model are presented in Figure 1C.

### Prospective memory

In all models focusing on individual proxies of social engagement, our results indicated that loneliness was the only significant predictor of performance on the prospective memory task. For the fully adjusted model, with reported loneliness odds of a correct response on the first attempt were lower by 33.9% (OR = 0.661, 99.7% CI: 0.463 to 0.943, $p < 0.003$). However, in the complete model we found the association with loneliness to be no longer significant (Figure 2). We presented complete results for prospective memory models in Table 5.

## Discussion

We have found some evidence of an association between measures of social engagement and cognition. However, magnitude of association was often modest, there was no consistency of effect across our chosen exposures or outcomes and most of the associations became non-significant when corrected for potential confounders.

The most consistent association demonstrated with our measure of cognitive function was with loneliness. Our results in this stroke-survivor population are broadly aligned with research investigating these associations in the general population[67]. Longitudinal studies of older adults have reported that loneliness was associated with an increased risk of cognitive decline, increased rate of cognitive decline and increased risk of incident dementia[68,69].

The inconsistent associations between our social engagement proxies and cognition could, in part, be a factor of how outcomes were measured. Overall, the UK Biobank cognitive assessment is relatively brief, and some differences in levels of cognitive function that would be identified using a more comprehensive psychometric tool may have been missed. Moreover, most studies in older adults have assessed global cognition, while in our study we had domain specific data. Some of these domains may be better measures of pathological cognition than others. For example, in the previously described study investigating cognitive outcomes in stroke survivors, there was a significant association between social ties and emotional support, and a cognitive summary score[46]. Yet when individual tasks were considered, only performance on one out of seven, namely word recall, was predicted by social factors.

In our study we similarly found an association between a subjective proxy of social engagement (loneliness) and a memory-based task. There is also some evidence from non-stroke populations that supports our observation of loneliness independently predicting performance on the verbal-numerical reasoning and prospective memory tasks. A longitudinal study of middle-aged and older North American adults showed that perceived social support had a positive association with executive function (employed in reasoning and problem-solving tasks[70,71]) and word recall[72]. Regarding predictors of reaction time, on the other hand, evidence seems to be overall inconclusive, with some studies supporting our findings[73,74] and others – not[72,75]. In this context, perhaps most surprising is the observed association between religious activity and slower reaction times, with many existing reports suggesting a positive relationship between religious engagement and cognition (ref). An accurate interpretation of this discrepancy seems however to exceed the scope of our analysis, with potentially multiple factors contributing to the obtained results. For example, this may include the used measures of cognitive performance and religious involvement, uncontrolled relevant variables and residual confounding from included covariates (demographics, health status).

Performance on the visual memory task was the only outcome not associated with any measure of social engagement. This may potentially be related to relatively low immediate test-retest stability reported for the task[61]. There were also other analyses where existing studies would have suggested an association that we did not observe in our data. For example, we did not find any significant results for social activities such as sports or adult education, where relevance to cognitive function seems relatively well-documented[76–80].

There are a number of possible explanations for this lack of expected associations. It is possible that the relationship between social engagement and cognition differs in stroke-survivors compared to other populations. There are plausible examples, such as that stroke-related motor impairments may confound reaction time measures. The cross-sectional nature of our data may also be in part responsible, as we are unable to investigate predictors of cognitive decline or changes in associations across the life-course. The complexity of associations between social engagement and cognition may further exceed the limits of regression analysis, with some variables potentially mediating the effect of others[67]. Moreover, our finding that associations with cognitive outcomes were no longer significant when all proxies of social engagement were included in one, fully adjusted model, may suggest model overfitting.

We acknowledge several limitations in our approach. The cognitive assessment conducted for the UK Biobank involved

**Table 3. Associations between proxies of social engagement and verbal-numerical reasoning scores.**

| Variable | Model | | | |
|---|---|---|---|---|
| | Unadjusted Std. beta (99.7% CI) | Partially adjusted Std. beta (99.7% CI) | Fully adjusted Std. beta (99.7% CI) | Complete Std. beta (99.7% CI) |
| **Family/friend visits (never)*** | | | | |
| Monthly | 0.176 (-0.157, 0.510) | 0.151 (-0.171, 0.474) | 0.177 (-0.187, 0.541) | 0.181 (-0.214, 0.575) |
| Weekly | 0.151 (-0.163, 0.464) | 0.113 (-0.191, 0.417) | 0.132 (-0.214, 0.477) | 0.115 (-0.264, 0.494) |
| Daily | -0.018 (-0.356, 0.320) | -0.004 (-0.332, 0.323) | 0.008 (-0.365, 0.381) | 0.000 (-0.406, 0.407) |
| Sample size | 2,705 | 2,666 | 2,096 | 1,947 |
| **Family satisfaction (not satisfied)*** | | | | |
| Satisfied | 0.129 (-0.072, 0.329) | 0.109 (-0.084, 0.302) | 0.052 (-0.184, 0.287) | -0.034 (-0.287, 0.218) |
| Sample size | 2,674 | 2,635 | 2,078 | 1,947 |
| **Friendship satisfaction (not satisfied)*** | | | | |
| Satisfied | 0.158 (-0.122, 0.438) | 0.158 (-0.109, 0.425) | 0.096 (-0.251, 0.443) | 0.115 (-0.255, 0.484) |
| Sample size | 2,667 | 2,628 | 2,073 | 1,947 |
| **Loneliness (not lonely)*** | | | | |
| Lonely | -0.296** (-0.425, -0.167) | -0.183** (-0.310, -0.055) | -0.185** (-0.339, -0.032) | -0.159 (-0.322, 0.004) |
| Sample size | 2,675 | 2,636 | 2,074 | 1,947 |
| **Confiding in someone (never)*** | | | | |
| Monthly | -0.044 (-0.248, 0.160) | -0.108 (-0.305, 0.088) | -0.110 (-0.330, 0.110) | -0.135 (-0.362, 0.091) |
| Weekly | 0.006 (-0.175, 0.187) | -0.017 (-0.192, 0.159) | -0.025 (-0.223, 0.172) | -0.075 (-0.280, 0.130) |
| Daily | 0.035 (-0.122, 0.192) | -0.001 (-0.153, 0.150) | 0.013 (-0.157, 0.184) | -0.029 (-0.209, 0.152) |
| Sample size | 2,617 | 2,580 | 2,039 | 1,947 |
| **Social activities (none)*** | | | | |
| Sports | 0.182 (-0.022, 0.386) | 0.067 (-0.129, 0.263) | 0.028 (-0.184, 0.240) | 0.014 (-0.203, 0.232) |
| Pub/social club | -0.083 (-0.252, 0.085) | -0.041 (-0.205, 0.123) | -0.122 (-0.311, 0.067) | -0.142 (-0.336, 0.053) |
| Religious group | -0.029 (-0.255, 0.196) | -0.059 (-0.277, 0.158) | -0.033 (-0.277, 0.211) | 0.006 (-0.245, 0.257) |
| Adult education | 0.032 (-0.421, 0.486) | -0.004 (-0.436, 0.428) | 0.071 (-0.401, 0.544) | 0.115 (-0.391, 0.620) |
| Other | 0.113 (-0.091, 0.317) | 0.113 (-0.084, 0.310) | 0.107 (-0.111, 0.324) | 0.131 (-0.091, 0.353) |
| Multiple | 0.257** (0.108, 0.406) | 0.141 (-0.004, 0.286) | 0.035 (-0.128, 0.198) | 0.036 (-0.131, 0.204) |
| Sample size | 2,707 | 2,667 | 2,097 | 1,947 |

Std., Standardised *reference category **significant at $p < 0.003$

Covariates included in partially adjusted models: age, sex, education and deprivation score. Covariates included in fully adjusted models: age, sex, education, deprivation score, walking pace, disability, subjective health rating, BMI, comorbidities, history of depressive episodes, alcohol intake frequency, smoking status, type of cerebrovascular event and time from stroke/TIA to baseline assessment. Complete models included all covariates from fully adjusted models as well as all proxies of social engagement.

**Table 4. Associations between proxies of social engagement and log errors in the visual memory task.**

| Variable | Model | | | |
|---|---|---|---|---|
| | Unadjusted Std. beta (99.7% CI) | Partially adjusted Std. beta (99.7% CI) | Fully adjusted Std. beta (99.7% CI) | Complete Std. beta (99.7% CI) |
| **Family/friend visits (never)*** | | | | |
| Monthly | -0.024 (-0.227, 0.178) | -0.016 (-0.221, 0.188) | -0.082 (-0.358, 0.194) | -0.006 (-0.445, 0.433) |
| Weekly | -0.020 (-0.210, 0.171) | -0.025 (-0.218, 0.168) | -0.132 (-0.395, 0.131) | -0.123 (-0.545, 0.299) |
| Daily | -0.004 (-0.208, 0.201) | -0.006 (-0.213, 0.201) | -0.111 (-0.393, 0.170) | -0.172 (-0.624, 0.280) |
| Sample size | 8,615 | 8,486 | 5,015 | 2,069 |
| **Family satisfaction (not satisfied)*** | | | | |
| Satisfied | -0.107 (-0.317, 0.104) | -0.153 (-0.366, 0.059) | -0.166 (-0.424, 0.091) | -0.146 (-0.424, 0.131) |
| Sample size | 2,919 | 2,867 | 2,217 | 2,069 |
| **Friendship satisfaction (not satisfied)*** | | | | |
| Satisfied | -0.045 (-0.340, 0.250) | -0.099 (-0.395, 0.197) | -0.200 (-0.576, 0.177) | -0.116 (-0.519, 0.287) |
| Sample size | 2,905 | 2,855 | 2,209 | 2,069 |
| **Loneliness (not lonely)*** | | | | |
| Lonely | -0.019 (-0.098, 0.059) | 0.002 (-0.079, 0.083) | 0.029 (-0.088, 0.146) | -0.068 (-0.245, 0.109) |
| Sample size | 8,524 | 8,393 | 4,960 | 2,069 |
| **Confiding in someone (never)*** | | | | |
| Monthly | -0.016 (-0.142, 0.109) | -0.019 (-0.146, 0.107) | 0.005 (-0.159, 0.169) | 0.022 (-0.231, 0.275) |
| Weekly | 0.007 (-0.103, 0.118) | 0.008 (-0.104, 0.120) | -0.024 (-0.168, 0.121) | -0.031 (-0.260, 0.197) |
| Daily | -0.005 (-0.096, 0.086) | -0.011 (-0.103, 0.081) | -0.034 (-0.151, 0.083) | -0.028 (-0.230, 0.173) |
| Sample size | 8,331 | 8,206 | 4,856 | 2,069 |
| **Social activities (none)*** | | | | |
| Sports | 0.030 (-0.099, 0.160) | 0.031 (-0.100, 0.162) | -0.035 (-0.196, 0.125) | -0.051 (-0.293, 0.191) |
| Pub/social club | -0.026 (-0.127, 0.074) | -0.045 (-0.147, 0.058) | -0.068 (-0.201, 0.065) | 0.014 (-0.201, 0.229) |
| Religious group | 0.059 (-0.079, 0.198) | 0.036 (-0.104, 0.175) | 0.066 (-0.113, 0.246) | 0.095 (-0.174, 0.364) |
| Adult education | -0.097 (-0.357, 0.162) | -0.087 (-0.347, 0.173) | -0.038 (-0.390, 0.315) | 0.076 (-0.498, 0.651) |
| Other | 0.037 (-0.086, 0.160) | 0.019 (-0.105, 0.143) | 0.032 (-0.127, 0.191) | 0.106 (-0.141, 0.353) |
| Multiple | 0.011 (-0.082, 0.104) | -0.007 (-0.101, 0.087) | -0.083 (-0.203, 0.038) | -0.030 (-0.215, 0.156) |
| Sample size | 8,648 | 8,520 | 5,023 | 2,069 |

Std., Standardised *reference category **significant at p < 0.003

Covariates included in partially adjusted models: age, sex, education and deprivation score. Covariates included in fully adjusted models: age, sex, education, deprivation score, walking pace, disability, subjective health rating, BMI, comorbidities, history of depressive episodes, alcohol intake frequency, smoking status, type of cerebrovascular event and time from stroke/TIA to baseline assessment. Complete models included all covariates from fully adjusted models as well as all proxies of social engagement.

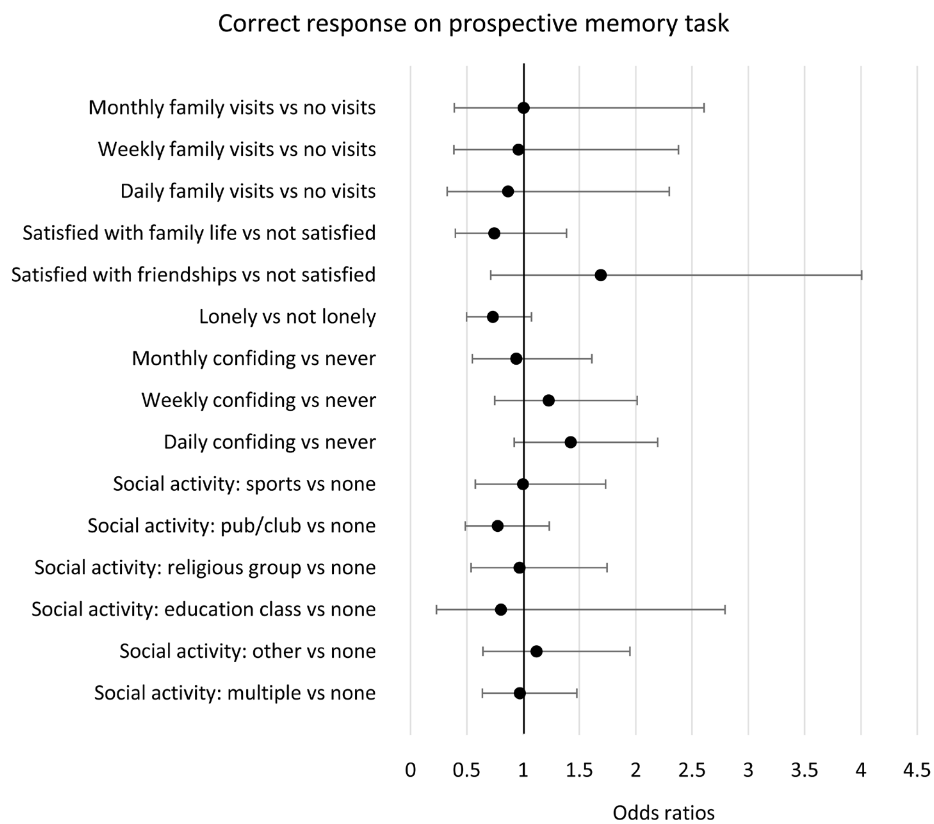


**Figure 2. Associations between proxies of social engagement and a correct response on the prospective memory task in the complete model, with 99.7% confidence intervals.**

bespoke tasks, designed to allow brief testing of cognitive performance on a large scale, without the need for examiner supervision. This approach, although having practical advantages, entails that the used tasks cannot be directly compared to standard cognitive measures, routinely employed in research and clinical practice. Moreover, for some variables included in the analyses, over 2/3 of participants had missing data. For the majority of cases, these were not missing data per se, rather certain assessment tasks and questions were added at later stages of UK biobank recruitment. Thus, we assumed that these data may be missing completely at random (in the context of the common observation that there is probably some degree of non-missing at random in terms of participation in the first place given a 5% response rate)[81]. Further, although repeat assessments for the UK Biobank were conducted between 2012 and 2013 (around 20,300 participants), data on variables of interest were available for only a small percentage of our baseline sample (e.g. 290 stroke survivors completed the verbal-numerical reasoning task at follow-up). As these attrition rates may have introduced considerable bias, it did not seem feasible to perform a longitudinal analysis.

As with many UK Biobank based studies, there are also issues around generalisability. Participants in our study were overall younger, highly educated and had lower comorbidity burden than an unselected stroke population (see Sentinal Stroke National Audit Programme (SSNAP) results). Yet the prevalence of both poor social engagement and cognitive issues are likely to be higher in a 'real world' stroke group and the associations observed here may be exacerbated in a dedicated stroke cohort. Another related limitation is that we did not have access to data on stroke-related factors that predict cognitive outcome, such as acute symptoms, acute physiology and most importantly stroke severity[47,63]. We have attempted to partially adjust for the latter by including disability, a potential proxy of stroke severity, among our covariates[82]. Finally, we identified our study participants based on self-report of stroke and TIA, which compared to use of an objective source (e.g. hospital records) increases the risk of both missing relevant cases, as well as including false positives[83].

However, there are also many strengths to our analysis. Our study is one of the few to investigate the relationship between social engagement and cognitive performance in a stroke population – a group at an increased risk of social isolation, cognitive impairment and dementia. Use of UK biobank gave us access to a relatively large sample of stroke survivors, with our population being several times larger than most bespoke stroke cohorts. The wealth of variables included in the UK Biobank resource allowed us to control for the most relevant covariates linked to both

**Table 5. Associations between proxies of social engagement and correct responses on the prospective memory task.**

| Variable | Model: Unadjusted OR (99.7% CI) | Partially adjusted OR (99.7% CI) | Fully adjusted OR (99.7% CI) | Complete OR (99.7% CI) |
|---|---|---|---|---|
| **Family/friend visits (never)*** | | | | |
| Monthly | 0.942 (0.476, 1.864) | 0.869 (0.426, 1.775) | 1.116 (0.473, 2.635) | 1.005 (0.388, 2.607) |
| Weekly | 1.026 (0.540, 1.950) | 0.932 (0.475, 1.829) | 1.111 (0.492, 2.506) | 0.958 (0.385, 2.380) |
| Daily | 0.848 (0.425, 1.693) | 0.817 (0.396, 1.686) | 1.058 (0.441, 2.541) | 0.866 (0.326, 2.298) |
| Sample size | 2,910 | 2,859 | 2,212 | 2,050 |
| **Family satisfaction (not satisfied)*** | | | | |
| Satisfied | 1.093 (0.721, 1.657) | 1.147 (0.746, 1.762) | 0.946 (0.538, 1.666) | 0.743 (0.398, 1.385) |
| Sample size | 2,880 | 2,829 | 2,195 | 2,050 |
| **Friendship satisfaction (not satisfied)*** | | | | |
| Satisfied | 1.328 (0.752, 2.346) | 1.422 (0.793, 2.548) | 1.532 (0.687, 3.416) | 1.690 (0.713, 4.007) |
| Sample size | 2,867 | 2,818 | 2,187 | 2,050 |
| **Loneliness (not lonely)*** | | | | |
| Lonely | 0.690** (0.530, 0.897) | 0.716** (0.542, 0.945) | 0.661** (0.463, 0.943) | 0.731 (0.498, 1.074) |
| Sample size | 2,877 | 2,826 | 2,188 | 2,050 |
| **Confiding in someone (never)*** | | | | |
| Monthly | 0.909 (0.596, 1.387) | 0.822 (0.531, 1.271) | 0.891 (0.535, 1.486) | 0.940 (0.549, 1.610) |
| Weekly | 1.151 (0.787, 1.685) | 1.104 (0.743, 1.640) | 1.175 (0.736, 1.874) | 1.227 (0.748, 2.013) |
| Daily | 1.284 (0.922, 1.788) | 1.203 (0.854, 1.694) | 1.388 (0.928, 2.077) | 1.422 (0.921, 2.195) |
| Sample size | 2,803 | 2,757 | 2,152 | 2,050 |
| **Social activities (none)*** | | | | |
| Sports | 1.166 (0.752, 1.808) | 1.046 (0.665, 1.645) | 1.009 (0.599, 1.699) | 0.999 (0.576, 1.733) |
| Pub/social club | 0.845 (0.597, 1.195) | 0.889 (0.621, 1.274) | 0.792 (0.510, 1.229) | 0.774 (0.486, 1.232) |
| Religious group | 0.806 (0.514, 1.265) | 0.814 (0.512, 1.295) | 0.895 (0.517, 1.551) | 0.968 (0.537, 1.746) |
| Adult education | 0.709 (0.275, 1.825) | 0.656 (0.251, 1.717) | 0.869 (0.280, 2.697) | 0.803 (0.231, 2.793) |
| Other | 1.133 (0.731, 1.756) | 1.125 (0.717, 1.766) | 1.068 (0.631, 1.806) | 1.119 (0.643, 1.949) |
| Multiple | 1.287 (0.933, 1.776) | 1.192 (0.854, 1.662) | 1.017 (0.684, 1.513) | 0.971 (0.638, 1.477) |
| Sample size | 2,914 | 2,862 | 2,214 | 2,050 |

Std., Standardised *reference category **significant at $p < 0.003$

Covariates included in partially adjusted models: age, sex, education and deprivation score. Covariates included in fully adjusted models: age, sex, education, deprivation score, walking pace, disability, subjective health rating, BMI, comorbidities, history of depressive episodes, alcohol intake frequency, smoking status, type of cerebrovascular event and time from stroke/TIA to baseline assessment. Complete models included all covariates from fully adjusted models as well as all proxies of social engagement.

social engagement and cognitive function. We pre-specified a statistical analysis plan that maximised the utility of the available data, for example in view of the variability in data completeness, we focussed on individual questionnaire items related to social engagement, as well as separate cognitive task, rather than composite scores. This also allowed us to investigate the specificity of associations across the various measures of social engagement and types of cognitive tasks.

Our results are hypothesis generating rather than definitive. Future studies with longitudinal follow-up are now needed. If the association between social engagement and cognition is proven, it would be informative to see if inclusion of measures of social engagement could improve the prediction of post-stroke cognitive problems, beyond the value of recognised, traditionally included risk factors. Finally, if the importance of social engagement to cognitive function is confirmed, the next step would be to explore the potential for developing interventions targeting social isolation among stroke survivors. Studies conducted in the general (older) population suggest that such interventions may indeed be successful in alleviating loneliness and isolation, yet it still seems uncertain whether they may in turn improve cognitive function[84,85].

## Conclusions

In summary, our results seem to confirm a task-specific association between certain markers of social engagement, particularly loneliness, and measures of post-stroke cognitive function. These associations are independent of demographic characteristics, health status, lifestyle factors and depression. In view of the inherent limitations of our retrospective, cross-sectional study design we must interpret our results with caution. Further studies are necessary to establish the nature of associations between social engagement and cognition following stroke, particularly within a longitudinal framework. Better understanding of these associations may help guide the development of successful interventions to improve post-stroke cognitive outcomes.

## Data availability

Data used in this study is held by the UK Biobank resource. We accessed this data under application no. 17689. Information regarding UK Biobank access procedures can be found here: http://www.ukbiobank.ac.uk/wp-content/uploads/2012/09/Access-Procedures-2011.pdf.

For the purpose of this study, we used variables with the following UK Biobank data field identifiers: 1031 (frequency of friend/family visits); 4559 (family relationship satisfaction); 4570 (friendships satisfaction); 2020 (loneliness, isolation); 2110 (able to confide); 6160 (leisure/social activities); 20023 (mean time to correctly identify matches); 20016 (fluid intelligence score); 399 (number of incorrect matches in round); 20018 (prospective memory result); 21022 (age at recruitment); 31 (sex); 6138 (qualifications); 189 (Townsend deprivation index at recruitment); 924 (usual walking pace); 6142 (disability); 2178 (overall health rating); 21001 (body mass index); 20002 (non-cancer illness code self-reported); 20009 (interpolated age of participant when non-cancer illness first diagnosed); 4598 (ever depressed for a whole week); 4631 (ever unenthusiastic/disinterested for a whole week); 4609 (longest period of depression); 5375 (longest period of unenthusiasm / disinterest); 4620 (number of depression episodes); 5386 (number of unenthusiastic/disinterested episodes); 2090 (seen doctor (GP) for nerves, anxiety, tension or depression); 2100 (seen a psychiatrist for nerves, anxiety, tension or depression); 1558 (alcohol intake frequency); 20116 (smoking status).

## Reporting guidelines

Figshare: STROBE checklist for cross-sectional studies for 'Social engagement after stroke – is it relevant to cognitive function? A cross-sectional analysis of UK Biobank data'; https://dx.doi.org/10.6084/m9.figshare.7613261.v1[86]



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# Open Peer Review

## Current Peer Review Status:

**Version 2**

Reviewer Report 15 August 2019

https://doi.org/10.21956/amrcopenres.13951.r26465



**Katharina S. Sunnerhagen**
Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

***Competing Interests:*** No competing interests were disclosed.

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 14 August 2019

https://doi.org/10.21956/amrcopenres.13951.r26464



**Christian Hakulinen**
Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Helsinki, Finland

Authors have responded to all my suggestions and the manuscript has been revised. I have no further suggestions.

***Competing Interests:*** No competing interests were disclosed.

***Reviewer Expertise:*** psychology, social epidemiology, psychiatry

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

**Version 1**

Reviewer Report 24 June 2019

https://doi.org/10.21956/amrcopenres.13928.r26423



?

**Christian Hakulinen**
Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Helsinki, Finland

Present study examines the associations between measures of social engagement with cognitive performance (reaction time, verbal-numerical reasoning, visual memory, and prospective memory) among stroke survivors. Authors show convincingly that there are few, if any, strong associations.

Study is well and clearly written, adequate statistical tests have been used, and study findings have been discussed in a balanced way. Thus, I have only few recommendations how the study could be potentially improved.

1. Did the authors consider combining all four cognitive measures for a broad general cognitive performance, i.e., intelligence, scale?
2. Four figures and seven tables make the study a bit heavy to read at some points. It seems that Tables 1 to 3 contain descriptive statistics that could be presented in a single table. Similarly, Figures 1 to 3 would work very well in a single figure where it would also be possible to compare the associations between measures of social engagement with reaction time, verbal-numerical reasoning and visual memory.
3. In tables 4 to 7, is it necessary to report both unstand. and stand. beta with confidence intervals and also the p-values? To me, one statistical coefficient with confidence intervals would be enough – and I don't see strong rationale why exact p-values should be reported.
4. I think that it is a right decision to account for multiple testing using p-value 0.003 as the limit. However, if I understood correctly, in figures and tables 95% Confidence Intervals have been used? To me, it would make more sense to use 99.7% Confidence Intervals as it would be in line with the p-value threshold.
5. In tables 4 to 7, please state also what factors where included in the partially adjusted, fully adjusted, and complete models.
6. In figures, please state somewhere that also confidence intervals have been plotted.
7. Introduction is well written and is easy to follow. A recent paper where the associations between social isolation and loneliness with stroke in the UK Biobank data where examined could be mentioned, Hakulinen et al.[1].

**References**

1. Hakulinen C, Pulkki-Råback L, Virtanen M, Jokela M, et al.: Social isolation and loneliness as risk factors for myocardial infarction, stroke and mortality: UK Biobank cohort study of 479 054 men and women.*Heart*. **104** (18): 1536-1542 PubMed Abstract | Publisher Full Text

**Is the work clearly and accurately presented and does it cite the current literature?**
Yes

**Is the study design appropriate and is the work technically sound?**
Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**
Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Yes

***Competing Interests:*** No competing interests were disclosed.

***Reviewer Expertise:*** psychology, social epidemiology, psychiatry

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Author Response 01 Aug 2019

**Bogna Drozdowska**, University of Glasgow, Glasgow, UK

Dear Dr Hakulinen,

We kindly thank you for agreeing to review our paper and your helpful suggestions. We believe that through implementing your recommendations we are now able to offer a more reader-friendly, clear and consistent presentation of our results. This relates to the following points:

1. We have combined Tables 1 to 3;
2. We have combined Figures 1 to 3;
3. We have simplified our Results Tables by removing columns with unstandardised coefficients and exact p-values;
4. We have changed the confidence intervals throughout the manuscript from 95% to 99.7% to match the set p-value threshold of 0.003;
5. For each of the Results Tables we specified which variables were included in partially adjusted, fully adjusted and complete models;
6. In Figures, we have indicated that confidence intervals have been plotted.

In addition, following your suggestion, in the introduction we now mention the relevant UK Biobank publication on the relationship between social isolation and loneliness and myocardial infarction, stroke and mortality.

Regarding the question of combining the four cognitive measures to create a composite score: we favoured this approach due to both practical and theoretical concerns. Firstly, we considered that the high number of missing scores for the verbal-numerical reasoning task (nearly 70%) could have led to biased estimates. Moreover, responses on the prospective memory task constitute a binary outcome, with limited variance. Conceptually, on the other hand, it seemed arguable whether a composite score based on the included bespoke tasks would reflect a measure of general intelligence as is traditionally described and understood (i.e. eliminating task-specific noise), entailing challenges around interpretation of any observed effects. Finally, as mentioned in the introduction, based on previous findings we assumed that associations with proxies of social engagement may be task-specific.

***Competing Interests:*** We have no competing interests to disclose.

Reviewer Report 26 March 2019

https://doi.org/10.21956/amrcopenres.13928.r26311



?

**Katharina S. Sunnerhagen**

Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

The article is well written and the subject is interesting. The background is fine as well as the description of the material and the statistical reasoning.

I have one problem with the cognitive tests that are used. For the non-UK reader, it is of importance to know if these tasks have been validated against traditional cognitive tests for the same function. Disability is also defined a bit different from in other materials. Please elaborate on this.

Is there a problem with combining data on patients with stroke with those who had a TIA? Do you have any information on how the stroke diagnosis was set?

The results are interesting and indicate that in persons with stroke (as in other persons) social contacts are important to keep cognitive fit. I am a bit surprised of the finding that religious activities have a negative impact on cognition. Religious engagement in other studies have shown to have a mainly positive effect on health. Why do you think this comes up here? Is it those that only marked religious activities as their only activity?

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Yes

***Competing Interests:*** No competing interests were disclosed.

***Reviewer Expertise:*** rehabilitation

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Author Response 01 Aug 2019

**Bogna Drozdowska**, University of Glasgow, Glasgow, UK

Dear Professor Sunnerhagen,
We are very grateful for your careful review and thoughtful comments about our work. Following your suggestions, we have introduced several changes to this manuscript. We hope that through these revisions we now offer a publication that complies with the standards of AMRC Open Research and will be of interest and value to the readership. Below we respond to each of the comments.

1. Comparison of used cognitive tasks with standard measures.

Thank you for bringing our attention to this important issue. The cognitive assessment conducted as part of the UK Biobank data collection involved bespoke tasks. They were specifically designed to allow brief testing of cognitive performance on a large scale, without the need for examiner supervision. Alongside the advantages of this approach from a practical point of view, there are unfortunately also significant drawbacks. The assessment was not as comprehensive as routinely performed in clinical practice and research studies with a focus on cognitive outcomes, and the used tasks are not directly comparable to standard cognitive measures.

There is one recent study, where performance on the verbal-numerical reasoning task was found to correlate with three other, more common cognitive measures (Symbol-Digit Substitution, Matrix Reasoning and Trail-Making) with medium effect sizes (“Brain imaging correlates of general intelligence in UK Biobank”; Cox, et al.; 2019). The four cognitive tests were used to estimate a latent factor of general intelligence, with verbal-numerical reasoning presenting a comparable factor loading to the other tasks. Yet, overall, we recognise that evidence around validity of UK Biobank cognitive measures against more traditional tests is lacking, and we acknowledge the use of bespoke tasks as an important limitation of our study in the discussion.

2. Operationalisation of disability.

We derived information regarding disability from responses to a question on employment status, which allowed participants to select multiple options (data field 6142). We considered a participant to have a disability if they selected that they are “unable to work because of sickness or disability” only, as well as in cases where this response appeared in conjunction with other options, e.g.“retired” or “looking after home/family”. We chose this approach as the target response indicated a level of disability that limits one’s activity. Alternative options included a binary variable indicating having a “long-standing illness, disability or infirmity” (data field 2188) and a variable related to obtaining an attendance/disability/mobility allowance (data field 6146). We believed that the former might be to highly correlated with other included covariates, particularly as we focused on reports of specific chronic illnesses. Regarding being in receipt of an allowance, we were concerned that some participants may have not been successful in applying for such support or are in a position where they do not require it, despite having a disability. We hoped that through these considerations we chose the most adequate variable to represent an activity-limiting disability, however we agree that our approach is nonstandard. Therefore, we have now included some additional information on deriving this variable In the Methods section.

3. Combing data from stroke patients and TIA patients; identifying study participants.

This is an important issue to which we had given much consideration when designing this study. Instead of excluding TIA patients, we opted to combine their data with that of stroke patients, including a differentiation between the two conditions as one of the model covariates. As briefly outlined in the Methods section, our primary rationale for this was that stroke and TIA patients are recognised to share similar risk factors for cognitive impairment and decline (e.g. cardiovascular disease, diabetes), and the recently increasing reports of TIAs resulting in longer-term adverse sequelae. Another argument related to maintaining a large sample size. Although the UK Biobank is an impressive repository with data from over half a million participants, these numbers significantly diminish when focusing only on individuals with a specific condition, and decrease even further with adding multiple variables of interest to a regression model. Finally, we also found it relevant that in the UK Biobank medical conditions, including stroke and TIA, were identified through self-report. Some participants may have misclassified their condition, particularly with the existence of potentially confusing terms, such as *mini-stroke* and *minor stroke*.

We have included more details on the process of identifying participants with a specific medical condition in the Methods section. It consisted of two stages, with participants firstly indicating having one or more illnesses (including stroke) during a touchscreen questionnaire, and responses being subsequently confirmed in a verbal interview by a trained nurse. This second stage was designed to improve the accuracy of self-reported information, yet nonetheless there are reasonable concerns when comparing the applied method to identifying cases of stroke and TIA on the basis of clinical diagnoses from medical notes. We emphasise this limitation of our study in the Discussion.

4. Association between religious activity and cognitive performance.

Thank you for highlighting this interesting and somewhat surprising finding. To clarify, named categories of social activity applied to participants that reported being involved in only one specific type of activity, with a separate category for those involved in multiple activities. Although we considered investigating associations with cognition for particular combinations of activities, we decided this would introduce too much complexity to our analysis, which already included several proxies of social engagement.

Indeed, a number of studies have indicated a positive relationship between religious involvement and cognitive function, as concluded by Hosseini, Chaurasia, & Oremus in a 2017 publication: “The Effect of Religion and Spirituality on Cognitive Function: A Systematic Review”. This paper however also highlights several relevant factors that may contribute to obtained results, including: study design (cross-sectional vs longitudinal), definition of religious involvement (e.g. reading religious books, praying, attending a place of worship), considered covariates, cognitive measures used, and study population. Interestingly, in the one UK-based study included in the review (“Religiosity is negatively associated with later life intelligence, but not with age-related cognitive decline”; Ritchie, Gow, & Deary; 2014), religious involvement was not found to have a positive association with cognitive function. The complexity of a related association is further highlighted in a publication by Vaos & McAndrew; 2012; “Three puzzles of non-religion in Britain”, indicating that the relationship between religious engagement and education changes with decade of birth and differs depending on whether religious beliefs or practice are measured. The article also presents considerable local variation in religious identity across the UK (from 6% to 74% indicating no religious affiliation).

Taken together, we believe that our findings related to religious activity may be due to our specific design, methods, uncontrolled factors and even residual confounding from included covariates (e.g. demographics and health status). We now include this point in the Discussion. Yet it also seems noteworthy that the only observed significant association related to slower reaction times. As referenced in our paper, a similar finding was reported in another study (Parisi et al; 2009). We acknowledge the possibility of these results indicating a genuine direct association, for example based on differences in cognitive style between those involved and not involved in religious activity, however drawing any assumptions exceeds the scope of our analysis.

***Competing Interests:*** We have no competing interests to disclose.