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Widowhood and cognitive decline in adults aged 50 and over: a systematic review and meta-analysis

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Abstract

While widowhood is known to be associated with poorer physical and mental health outcomes, studies examining the association of widowhood with cognition have yielded mixed results. This review aimed to elucidate the link between widowhood and cognitive decline.

A systematic search of Medline, Embase, PsycInfo, CINAHL and Scopus (until December 2020) was conducted to identify studies on the association between widowhood (vs. being married) and cognition in cognitively healthy adults aged 50+.

A cross-sectional meta-analysis (of 10 studies; *n*=24,668) found a significant association of widowhood with cognition (*g*=-0.36, 95% CI [-0.47, -0.25], *p*=<.001). Meta-regressions suggested that study design, cognitive domain measured, sample age, difference in mean age between widowed and married groups, and study continent did not account for observed heterogeneity. A longitudinal meta-analysis (of 3 studies; *n*=10,378) found that the "continually widowed" group (from baseline to follow-up) showed significantly steeper declines in cognition compared to the "continually married" group (*g*=-0.15, 95%CI [-0.19, -0.10], *p*=<.001).

Findings indicate that widowhood may be a risk factor for cognitive decline. As there are no effective treatments for cognitive impairment, studying mechanisms by which widowhood might be associated with poorer cognition could inform prevention programs for those who have experienced spousal bereavement.

Keywords:

Widowhood, Cognitive decline, Meta-analysis, Systematic review, Meta-Regression

1. Introduction

Spousal loss or widowhood is considered one of the most stressful life experiences (Holmes and Rahe, 1967). A national survey in 2017 found that 1 in 4 over 65 year olds were widowed in the UK, and in over 85s, 35% of men and 76% of women were widowed (ONS, 2018). In the US, more than 900,000 older adults are widowed each year (Elliott and Simmons, 2011).

Widowhood is associated with poorer physical and mental health including increased risk of illness, disability and mortality (Rendall et al., 2011), weaker immune response (Phillips et al., 2006), weight loss (Stahl and Schulz, 2014), sleep difficulties (van de Straat and Bracke, 2015), depression (Kristiansen et al., 2019) and substance abuse (O'Farrell et al., 1998). Studies examining the relationship between widowhood and cognitive decline have yielded mixed results, with some finding significant associations between widowhood and cognitive decline (e.g., Aartsen et al., 2005; Karlamangla et al., 2009), and others not (e.g., Vidarsdottir et al., 2014). Indirect evidence indicates that numerous health (e.g. hypertension, alcohol intake and obesity (Livingston et al., 2020) and social factors (e.g. loneliness (Boss et al., 2015) and social isolation (Evans et al., 2019) that are known to be associated with cognitive decline are also associated with widowhood (Buckley et al., 2012; Pilling et al., 2012; Shahar et al., 2001). Indeed, a recent meta-analysis found that living alone was associated with a significantly elevated risk of incident dementia which conferred greater population risk of dementia than relatively more well-known risk factors such as hypertension and obesity (Desai et al., 2020). Given the lack of efficacious treatments to treat cognitive decline, identifying at-risk subgroups within the population becomes paramount so that targeted prevention programs can be implemented to delay or slow down the rate of cognitive decline.

To our knowledge, no meta-analysis has examined the link between widowhood and cognitive function. The most closely related meta-analysis (Sommerlad et al., 2018) which examined the relative risk of being widowed on dementia found that widowed people have a 20% higher risk of developing dementia compared to those who were married. Due to a lack of available data, they were unable to address the effect of widowhood duration on cognition. While some studies have pointed to a linear relationship between time since spousal loss and

cognitive decline (Shin et al., 2018), other studies have found no such associations (Lyu et al., 2019).

We aim to extend the findings of Sommerlad et al. (2018)'s meta-analysis in three ways. First, the present meta-analysis will focus on cognition as a continuous rather than a binary outcome (e.g., dementia vs. no dementia), which might enable the detection of subtler differences or changes in cognition, as well as non-dementia related cognitive decline. Second, we will assess whether widowhood is associated with cognitive function in both cross-sectional and longitudinal studies, to explore *changes* in cognition over time. Third, we will attempt to synthesise the available data to examine whether length since spousal loss moderates the relationship between widowhood and cognitive decline.

2. Method

This review was registered on PROSPERO prospectively https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020191976 and is reported according to PRISMA guidelines (Page et al., 2021).

2.1. Search Strategy and Selection Criteria

A comprehensive search strategy was implemented across the following databases: MEDLINE, Embase, PsycInfo, CINAHL and Scopus from inception until December 2020. The search strategy consisted of a combination of keyword and MESH subject heading search, with terms adapted from two recently published meta-analyses that explored (separately) widowhood (Kristiansen et al., 2019) and cognitive decline (John et al., 2019). The search terms consisted of two blocks. The first contained keywords related to widowhood, and the second contained keywords related to cognition (see supplementary materials A for full list of terms) . The inclusion criteria were as follows:

- Peer-reviewed journal articles published in English
- Cross-sectional or longitudinal study
- Cognitive function was assessed as a continuous variable
- The study stratified participants by marital status, and must have had a "widowed" group (comparison group) and "married" group (reference group) respectively

- Mean and standard deviation of cognitive function, as well as the sample size for both the “widowed” group and the “married” group, were available (either from the paper or from contacting authors) so that a measure of effect size (hedges’ g) could be calculated
- Participants included in the study sample were all over the age of 50, or a separate analysis was run only for participants above the age of 50
- Participants did not have a diagnosis of any form of cognitive impairment or dementia

2.2. Screening Procedure

A 3-step approach was used with articles screened by title, followed by abstract. Finally, the full-text of identified articles were read and included or excluded based on inclusion criteria. All stages were conducted by the primary reviewer (TS). At the title and abstract screening stages, 10% of all articles were randomly selected and screened by another independent rater (GB). At the full-text screening stage, 25% of the remaining articles were randomly selected and screened by the independent rater (GB). Disagreements were discussed and resolved by consensus. References lists of all included articles were manually searched to identify any other potentially relevant papers.

2.3. Data Extraction

Data extracted for evidence synthesis included author name(s), publication year, DOI, country, age of sample (and for “widowed” and “married” respectively), length of follow-up (if any), cognitive domains assessed, cognitive measure used, sample size (for “widowed” and “married” respectively), cognition score (mean and standard deviation) at each reported wave (for “widowed” and “married” respectively), length of time since spousal loss (if available) and methodological quality rating information (see below). If there was insufficient information to calculate an effect size (e.g., raw mean cognition scores not reported), authors were contacted for the required additional information. If there were multiple cognitive domains reported, a measure of global cognition (e.g., MMSE) was preferred. If this was not available, then a measure of memory was extracted. If studies reported stratified data (e.g., by gender), data were appropriately combined and pooled together.

2.4. Quality Rating

Methodological quality was assessed using the Newcastle-Ottowa Criteria (Wells et al., 2000) for studies with a longitudinal design, and the Joanna Briggs Institute checklist for studies with cross-sectional design (see Supplementary materials B and C for detailed items and ratings). The maximum score for cross sectional studies was 7. The longitudinal studies were rated out of a maximum score of 8. In the present study, for cross-sectional studies, scores of 6-7 were considered 'low risk of bias', 3-5 were considered 'medium risk of bias', and less than 3 were considered 'high risk of bias'. For longitudinal studies, scores of 7-8 were considered 'low risk of bias', scores of 4-6 were considered 'medium risk of bias', and scores less than 4 were considered 'high risk of bias'.

2.5. Data Analysis

2.5.1. Cross-sectional analysis

Both the cross-sectional and longitudinal studies identified were included in this analysis. For longitudinal studies reporting cognition scores at baseline and also at subsequent waves, only information at the final wave was used for the cross-sectional meta-analysis, as this allows for a longer time for declines in cognition to occur (John et al., 2019). For each study, a measure of effect size (hedges g) was calculated as the standardised mean difference (SMD) between the "widowed" group and the "married" group, using the R package – Metafor (Viechtbauer, 2010). The random-effects model (95% CIs) was used (Borenstein et al., 2011). Heterogeneity was assessed using I^2 with 25%, 50%, and >75% interpreted as representing low, moderate and high levels of heterogeneity, respectively (Higgins et al., 2003). In cases of substantial heterogeneity (pre-determined as $I^2 > 50\%$), meta-regressions were performed to assess whether, study design (cross-sectional vs. longitudinal), cognitive domain measured (global vs. memory-only), age of sample, difference in age (widowed vs. married), or continent (Europe/North America vs. Asia), might account for the observed heterogeneity. If there were sufficient data, a further meta-regression was planned a priori to assess for the potential moderating effect of length since spousal loss. Publication bias was assessed by inspecting funnel plots and Egger's test.

2.5.2. Longitudinal analysis

Included longitudinal studies needed to include a group who were already widowed at T1 and continued to be widowed until T2 (hereafter "continually widowed"). If studies only included a widowed group that was married at T1 and subsequently widowed at T2 (hereafter; "newly widowed"), they were excluded from this analysis. Furthermore, studies must have reported cognition data at T1 and subsequently at T2 for the same group of participants, allowing calculation of pre-post change. The mean and standard deviation of the pre-post change were calculated if this was not reported. Calculating the standard deviation of this pre-post change requires the correlation between the pre-post measures. Where this was not reported, an imputed value of r = 0.6 was used (c.f. Hallam et al., 2021) based on the median within-group correlation extracted from 811 measures of pre–post clinical trial arms (Balk et al., 2012). In cases where this imputed value is considerably different from the true pre-post correlation, the effect sizes tend to be inflated (Cuijpers et al., 2017), consequently, additional sensitivity analyses were conducted to evaluate the effect of different imputed r values.

3. Results

3.1. Selection processes

In total, 4836 references were retrieved. After duplicate removal, 3050 references remained. After the first step whereby all 3050 titles were screened (percentage agreement was 93%), abstracts of 217 references were screened of which 81 were assessed to be eligible (percentage agreement was 92.5%). After reading the full-text of the remaining 83 articles, 71 articles were excluded, consequently a total of 12 studies were included in the meta-analysis. More details can be found in the PRISMA diagram (Figure 1).

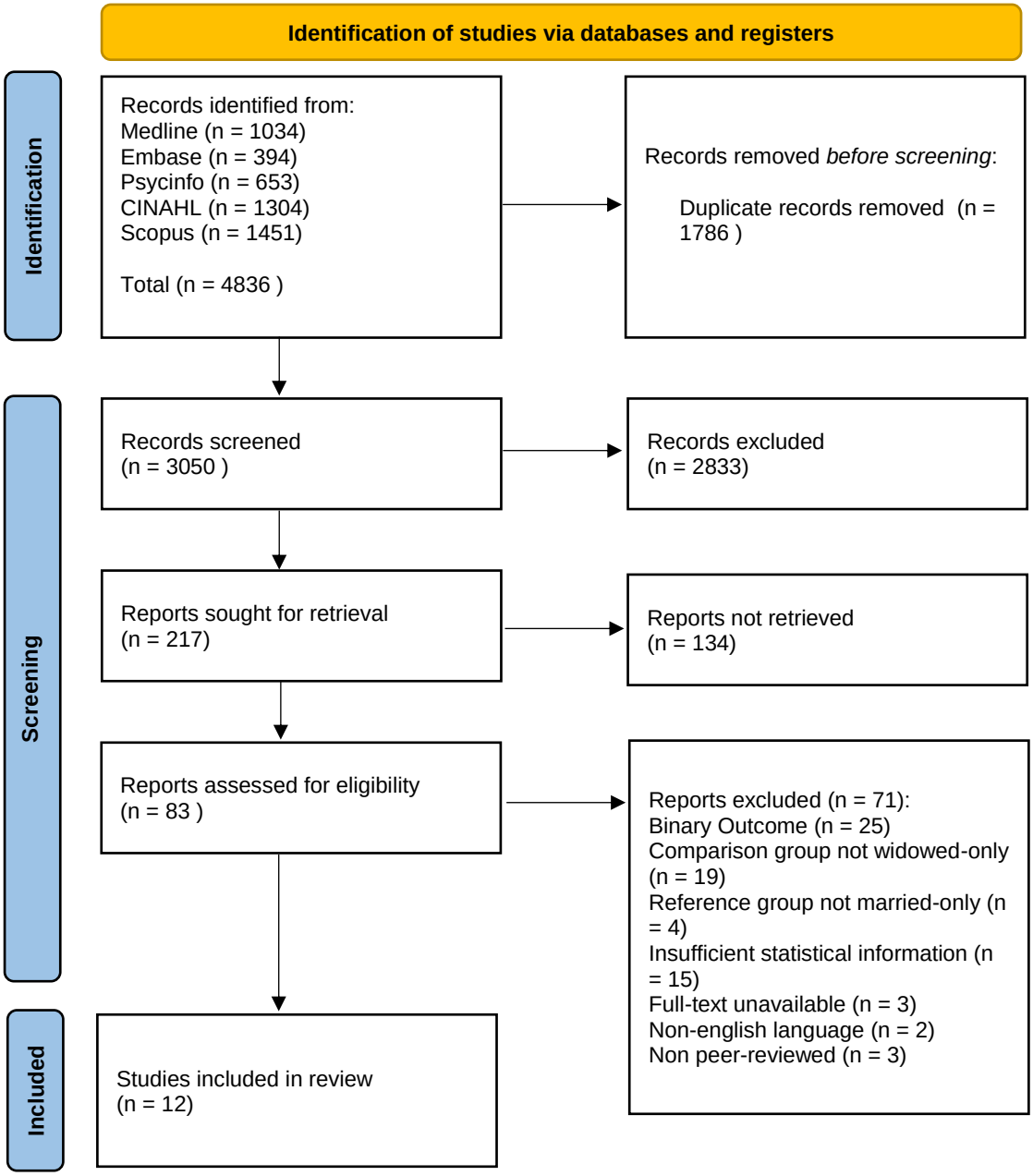

Figure 1: PRISMA flow diagram

3.2. Study characteristics and participants

There were a total of 25,531 participants across 12 studies, of whom *n* = 6,867 were "widowed" (comparison group) and *n* = 18664 were "married" (reference group). Study countries including India (K = 1), Singapore (K = 1), China (K = 2), Brazil (K = 1), Australia (K = 1), Netherlands (K = 1), Sweden (K = 1) and the US (K = 4). Five studies measured recall and/or recognition memory, and the other 7 studies included a global measure of cognition. Six studies were designed as cross-sectional studies and the other 6 studies were designed as

longitudinal studies. The assessed methodological quality of studies ranged from ‘low’ to ‘medium’ risk of bias. See Table 1.

Table 1: Characteristics of included studies

Sn	Author	Country	Cognitive Domain Assessed	Cognitive Measure	Study Design	Study Population Age Group	Age[a] ("Widowed" age/"Married" age)	Length since spousal loss (range) at latest time point	N Widowed (% female)	N Married (% female)	Risk of methodological bias ratings
1	Perkins 2016	India	Memory (immediate recall)	Recall of 10 commonly used words	cross-sectional	60+	Median range = 65-69 (Not reported)	0-4years (*n*=879) 5-9years(*n* =793) 10+years (*n* =1,913)	3585 (82.5)	5586 (33.8)	'low risk' of bias (cross)
2	O' Connor 2014	US	Global	MMSE	cross-sectional	62+	72.06 (72.0/72.1)	Not reported	45 (73.4)	32 (69.0)	'low risk' of bias (cross)
3	Feng 2014	Singapore	Global	MMSE	cross-sectional	55+	66.08 (71.5/64.9)	Not reported	414 (90.8)	1857 (56.6)	'low risk' of bias (cross)
4	Shahar 2001	US	Global	3MSE	cross-sectional	65+	77.6 (77.6/77.6)	6+ months (mean = 2.9 years)	58 (82.8)	58 (82.8)	'low risk' of bias (cross)
5	Rosset 2011	Brazil	Global	MMSE	cross-sectional	80+	84.6 (Not reported)	Not reported	163 (Not Reported)	92 (Not Reported)	'medium risk' of bias (cross)
6	Xu 2020	China	Global	MMSE	cross-sectional	60+	71 (Not reported)	Not reported	285 (70.5)	1018 (50.2)	'low risk' of bias (cross)
7	Byrne 1997	Australia	Global	MMSE	longitudinal	65+	74.93 (74.5/75.4)	Exactly 6 weeks	57 (0.0)	57 (0.0)	'low risk' of bias (cross)
8	[b]Biddle 2020	US	Global	MMSE	longitudinal	60+	74 (73.3/74.6)	5+ years (mean = 12.9, median = 17.4)	31 (45.0)	136 (88.0)	'low risk' of bias (cross) 'low risk' of bias (long)
9	Aartsen 2005	Netherlands	Memory (immediate and delayed recall)	15 words test	longitudinal	60+	75.30 (78.2/74.6)	0-6 years (mean = 37 months)	178 (70.0)	729 (38.0)	'low risk' of bias (cross)

10	Mousavi 2012	Sweden	Memory (recall and recognition)	Recall (Action/Noun) Recognition (Face/Name/Noun)	longitudinal	60+	76 (79.6/75.2)	5+ years	30 (87.7)	396 (41.2)	'low risk' of bias (cross)
11	[b]Zhang 2019	China	Memory (immediate and delayed recall)	10 Chinese nouns	longitudinal	55+	Median range = 62-66 (Not reported)	0-2years (N=209) 2+years(N=1084)	1293 (72.2)	6631 (46.5)	'low risk' of bias (cross) 'low risk' of bias (long)
12	[b]Lee 2019	US	Memory (immediate and delayed recall)	10 English nouns	longitudinal	50+	66.14 (72.9/64.6)	0-4 years (N=122) 4+years (N=424)	546 (85.5)	2072 (51.45)	'low risk' of bias (cross) 'medium risk' of bias (long)

[a] This refers to mean age for Married & Widowed sample only (where possible). If this was not possible, then the mean age of the entire sample was reported (this might include other marital status subgroups e.g., “divorced” and “single”). Age at final wave (where cognitive data were available) was reported as it was at this age that cognitive data were used for the cross-sectional meta-analysis.

[b] All studies were rated as cross-sectional studies since all studies were included in the cross-sectional meta-analysis. In addition, for studies that were included in the longitudinal meta-analysis, they were additionally rated as longitudinal studies. For such studies, two ratings were given – “(cross)” denoting it’s rating as a cross-sectional study, and “(long)” denoting its rating as a longitudinal study. It is important to note that not all longitudinal studies were included in the longitudinal meta-analysis because they did not measure ‘continually widowed status’.

3.3. Cross-sectional meta-analysis

A meta-analysis of all studies comparing widowed vs. married groups on a continuous measure of cognition found that being widowed was significantly associated with poorer cognitive functioning, as compared to being married (*g* = -0.80, 95% CI [-1.47, -0.13], *p* =.02, I^2 = 98%). Based on a visual inspection of the forest plot (see Supplementary material D), it was evident that 2 studies (Mousavi-Nasab et al., 2012; Rosset et al., 2011) were potential outliers. This was also confirmed via diagnostic plots (Viechtbauer and Cheung, 2010) using the 'dmetar' package in R (see Supplementary material E). Upon further examination of each of their study designs, it was observed that the Rosset et al. (2011) study had a significantly older population (80+ study population, mean age = 85) compared to the other studies, and the Mousavi-Nasab et al. (2012) study measured cognition in terms of z-scores which were calculated based on relative performance compared to a younger, all-male reference group. As such, this and all other meta-analyses were re-run (K = 10; *n* = 24,668) without these 2 studies.

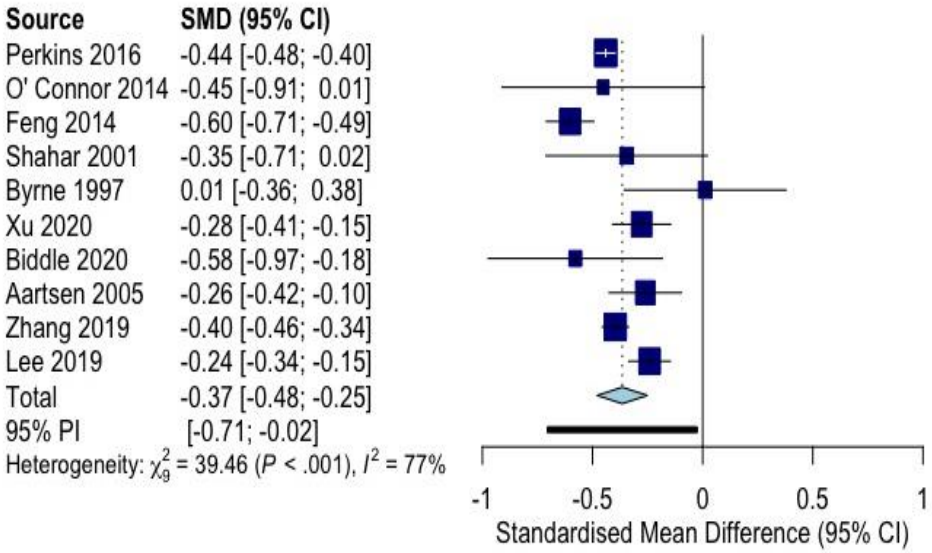

Figure 2: Forest plot for cross-sectional meta-analysis (K = 10)

A significant effect of widowhood (vs. married) on cognition remained, although pooled effect sizes were reduced, (*g* = -0.37, 95% CI [-0.48, -0.25], *p* = <.001). There was still significant heterogeneity in the full model (Q = 39.46, df = 9, *p* <.001, I^2 = 77%) (see Figure 2). Consequent

planned meta-regressions revealed that study design (p = .64), cognitive domain measured (p = .64), age of sample (p = .35), difference in age between "widowed" and "married" (p = .73), and continent (p = .19) did not significantly explain the observed heterogeneity (see Supplementary material F for detailed results of subgroup analyses).

3.3.1. Secondary analysis by length since spousal loss

Not every study reported data on length since spousal loss but for some it could be inferred. Specifically, for the "newly widowed" studies we could infer that they were widowed sometime *within* T1-T2 whereas for the "continually widowed", we could infer that they were widowed for *at least* the length of the follow-up period. If the length since spousal loss was not reported or could not be reasonably inferred, studies were left out of this analysis. This meant 3 studies (Feng et al., 2014; O'Connor and Arizmendi, 2014; Xu et al., 2020) were excluded. Based on available data, it was decided that the studies would be split into 2 subgroups ("less than 4 years" since widowhood vs. "more than 4 years" since widowhood). If a study reported a range that overlapped across the 4-year period, and if the mean/median length since widowhood was also reported, the mean/median length was used to decide which subgroup ("less than 4 years" vs. "more than 4 years") the study fell into. For example, Aartsen et al. (2005) included participants who were widowed for a period of 0-6 years, but because the mean length reported was 37 months, this study was put in the "less than 4 years" subgroup. Some studies could be represented in both subgroups because they presented results stratified by length since spousal loss. For example, Perkins et al. (2016) presented results separately for 0-4 years, 5-9 years and 10+ years. Therefore, the data reported for the "0-4 years" were included in the "less than 4 years since widowhood" subgroup, while the data reported for the 5-9 years and the 10+ years were pooled together and included in the "more than 4 years since widowhood" subgroup. In order to partially mitigate against the resulting 'unit of analysis error' whereby the same "married" group was used as the reference group and thus 'double counted' (Higgins and Green, 2020),the sample size for the "married" reference group was split equally across the different comparisons. This does not fully account for the unit of analysis issue but tentatively allows for comparisons between "less than 4 years since widowhood" and "more than 4 years since widowhood" (Higgins and Green, 2020).

In total, data from 6 studies were included in the "less than 4 years since widowhood" subgroup (Aartsen et al., 2005; Byrne and Raphael, 1997; Lee et al., 2019; Perkins et al., 2016; Shahar et al., 2001; Zhang et al., 2019), and data from 3 studies were included in the "more than 4 years since widowhood" subgroup (Biddle et al., 2020; Lee et al., 2019; Perkins et al., 2016). As shown below in Figure 3, the pooled effect size for the "less than 4 years since widowhood" subgroup was smaller than the pooled effect size for the "more than 4 years since widowhood" (g = -0.24 vs. g = -0.41), although this difference was not statistically significant ($B = 0.16$, p = .11, R^2 = 23.75%). Substantial heterogeneity was also present within both subgroups. As a sensitivity analysis, we excluded the two studies (Aartsen et al., 2005; Shahar 2001) which overlapped the 4-year period, and found similar results (see Supplementary material G).

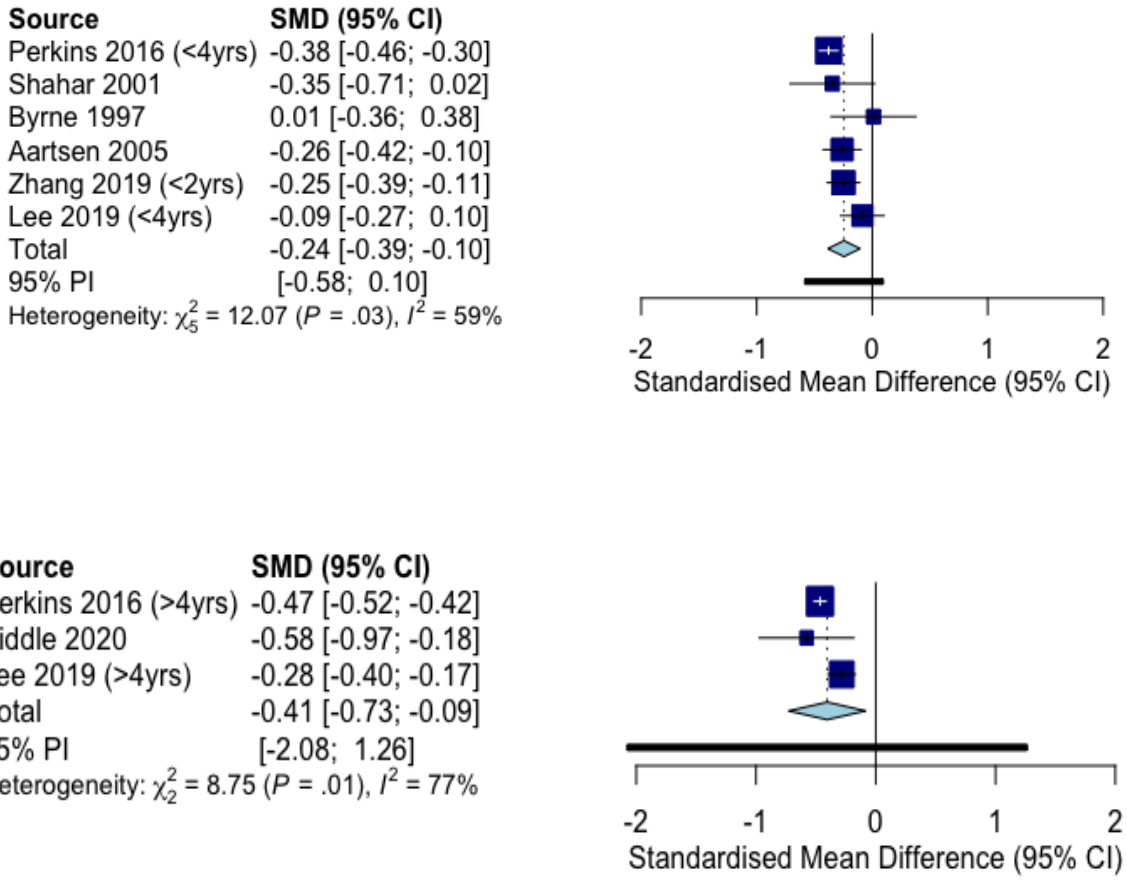

Figure 3: Forest plot for length since spousal loss subgroups: less than 4 years (above) vs. more than 4 years (below).

3.4. Risk of publication bias

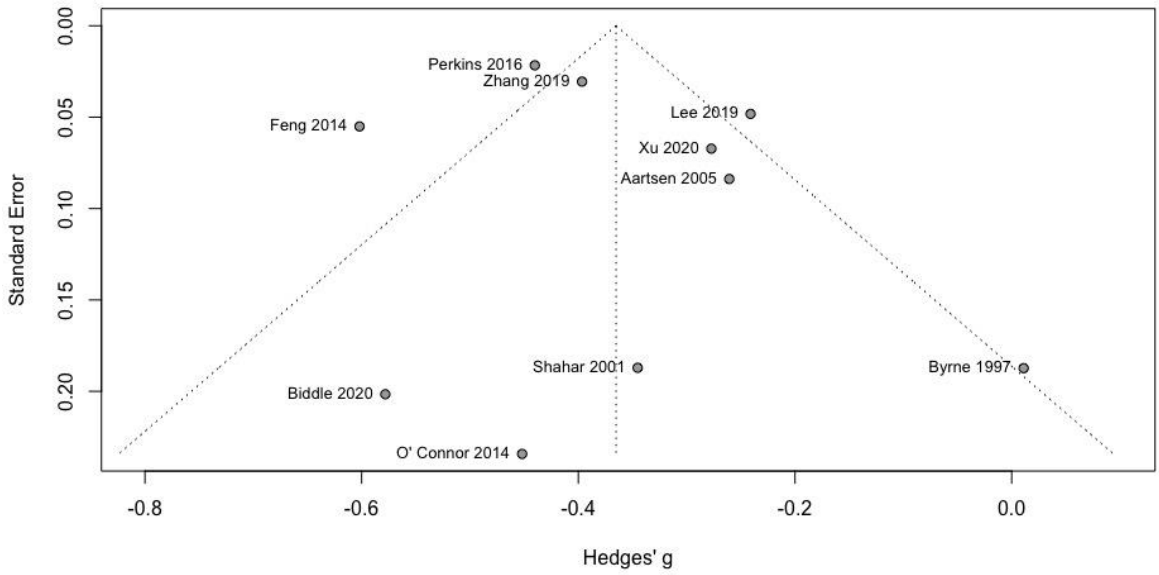

Figure 4: Funnel Plot for cross-sectional analysis (K = 10)

A visual inspection of the funnel plot in Figure 4 was used to assess publication bias. Furthermore, egger's test was used to assess for funnel plot asymmetry. Egger's test was found to be non-significant (t = 0.855, p = .40), which indicated that there was a low likelihood of publication bias.

3.5. Longitudinal meta-analysis

The aim of the longitudinal meta-analysis was to assess whether those who were "continually widowed" from T1 to T2 experienced a greater decline in memory, compared to those who were "continually married" over the same time period. Out of the 6 longitudinal studies, 3 studies (*n = 10,378)* used such a design and were included in this analysis (Biddle et al., 2020; Lee et al., 2019; Zhang et al., 2019).

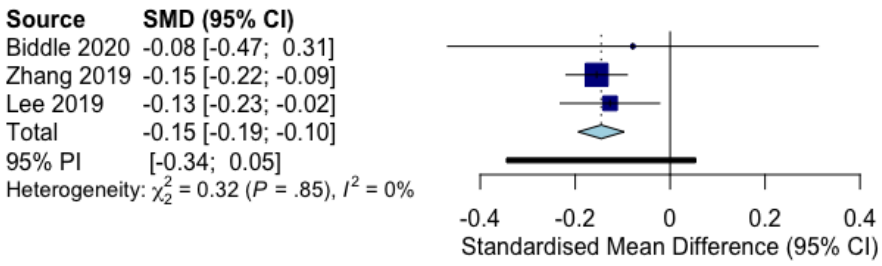

Figure 5: Forest plot for longitudinal meta-analysis ("continually widowed")

With reference to Figure 5, the pooled effect size indicated a small and statistically significant effect (*g* = -0.15, 95%CI [-0.19, -0.10], *p* = <.001), suggesting that those who were continually "widowed" showed a steeper decline in cognition over time, as compared to those who were continually "married". This effect remained significant even for differing imputed r-values (ranging from r = .20 to .80; see Supplementary material H). There was no observed heterogeneity in this model.

4. Discussion

We aimed to assess whether widowhood is a potential risk factor for cognitive decline. Overall, there was consistent evidence to suggest that being widowed, compared to being married, was associated with poorer cognition and steeper declines in cognition over time.

The cross-sectional meta-analysis found that those who were widowed had poorer cognitive functioning as compared to those who were married. This was irrespective of study design, cognitive domain measured, age, and continent of study. These findings must however be interpreted with caution due to the presence of substantial heterogeneity in all the models, and due to the width of the confidence interval for this meta-analysis being quite wide. Study design, cognitive domain measured, age and continent of study all did not account for much of the heterogeneity. We also extended the findings of a previous related meta-analysis (Sommerlad et al., 2018) by assessing whether length since widowhood (less than vs more than 4 years) moderated the relationship between widowhood and cognition. Although comparisons between these 2 subgroups should be made tentatively, there was some evidence that, when compared to those who were married, the effect size for those who were widowed for less than 4 years was smaller than those who were widowed for greater than 4

years, although this difference did not reach statistical significance. These findings trend in the direction of providing evidence for a 'dose-response' effect of widowhood on cognition, consistent with previous findings (e.g., Shin et al., 2018), providing additional evidence in support of widowhood being a risk factor for cognitive decline. However, more studies with more detailed information on precise lengths since widowhood are needed in order to explore this 'dose-response' effect more fully. Furthermore, such associations may not infer causality, and replication with a greater number of studies is essential.

Results from the longitudinal studies meta-analysis found that those who were "continually widowed" had significantly *steeper* declines in cognition as compared to those who were "continually married" over the same time period. Similar results were found even after sensitivity analyses were conducted for different imputed values of standard deviation of pre-post change. Once again, these results provide further evidence for widowhood being a risk factor for declines in cognition over time, although it should be noted that only a small number of studies met the criteria for inclusion in this analysis, and further research with stringent designs are necessary in order to infer causality.

Several plausible mechanisms for the link between widowhood and cognitive decline have been suggested. The marital resources theory (Waite and Gallagher, 2001) proposes that marriage affords the couple greater social, psychological and economic resources which have long-term positive consequences for health and well-being. For instance, married couples might benefit from economies of scale, and tend to be more actively engaged with social groups (e.g., in-laws or friends of one's spouse), which, in line with the cognitive reserve hypothesis (Stern, 2002), might be protective against brain degeneration (Evans et al., 2018). Another plausible mechanism is the stress model which posits that the stress experienced as a result of such a significant loss leads to negative cognitive outcomes. For example, Geoffroy et al. (2012) found that the experience of widowhood was associated with higher cortisol which in turn led to declines in memory. Overall, the current findings might lend support to both of the abovementioned theories. These results are also consistent with previous related meta-analyses which have found loneliness, living alone, and social isolation to be associated with poorer cognitive outcomes (Boss et al., 2015; Desai et al., 2020; Evans et al., 2019) and

complements (Sommerlad et al., 2018) meta-analysis findings that widowhood increases risk of dementia.

The present study has several limitations. Although we tried to account for heterogeneity noted in our analyses, no explored factor accounted for a significant amount of observed heterogeneity, suggesting there may be further differences between samples on unobserved factors. The lack of studies, especially for longitudinal analyses, reduced statistical power, and also limited the extent to which potential moderators such as length since spousal loss, could be further explored. Residual confounding (for example by age) rather than widowhood itself may have underpinned the general trend found in this study that those who were "widowed" had poorer cognition compared to those who were "married". Selective attrition could underestimate the association between being widowed and cognitive decline on the assumption that those who experience greater declines in cognition as a result of widowhood might be more likely to drop-out. Both the cross-sectional and longitudinal meta-analyses resulted in wide confidence intervals, suggesting that the results should be interpreted with caution. Finally, in the interest of pooling data from as many studies as possible to increase statistical power, we have aggregated potentially differing measures of cognition (e.g., immediate recall, recognition, delayed recall and MMSE). Sensitivity analysis including only studies that used the MMSE (global measure of cognition), supported the main findings, but further studies are needed to ascertain if these results are consistent across sub-domains of cognition.

Future studies with longer follow-ups are required to examine if declines in cognition are sustained linearly over time, or whether there may be a curvilinear relationship, whereby the effects of widowhood on cognition are attenuated over time (e.g., Vidarsdottir et al., 2014), as is consistent with the theory of cognitive plasticity (Lövdén et al., 2010). Declines in cognition that are found to be time-limited may be as a result of acute adjustment to widowhood such as poor sleep or lack of concentration, whereas declines over a sustained period of time may be more indicative of neurodegenerative disease such as dementia. Future meta-analyses could explore whether the effect of widowhood on cognition is moderated by gender as has been suggested previously (Leopold and Skopek, 2016; Wörn et al., 2020). This could not be explored in the present study due to a lack of available data.

Future research should also examine how the effect of widowhood on cognition varies across socio-cultural contexts. For example, there has been some evidence suggesting that this link is stronger in wester cultures that tend to emphasise individualism, as compared to asian cultures where co-residence with extended families may be the norm, which might buffer some of the effects of widowhood (Carr & Bodnar-Deren, 2009; Manzoli et al., 2007). Finally, more research is needed to ascertain the precise mechanisms by which widowhood is associated with cognitive decline. If, for example a key mechanism is found to be via a lack of social or cognitive engagement, bereavement programmes could consider including such components in their intervention. Alternatively, if the key mechanism is found to be via stress and anxiety as a result of spousal loss, then programmes for at-risk groups, such as those who have experienced spousal bereavement, could consider including a component on stress and anxiety management techniques. In the absence of effective treatments for cognitive impairment, identifying at-risk groups and providing targeted interventions based on mechanisms is paramount to delay or prevent older adults from experiencing the most debilitating effects of cognitive ageing.

5. Conclusions

The present study adds to the current literature by demonstrating that widowhood is associated with poorer cognition in cognitively healthy adults over the age of 50, irrespective of study design, cognitive domain measured and continent of study. This study further demonstrated that widowhood (vs being married) is associated, not just cross-sectionally, but also longitudinally with steeper declines in cognition over time. Examining cognition as a continuous measure, rather than a binary outcome enabled the detection of subtler changes in cognition and might have been able pick up on non-dementia specific cognitive changes that are worth further exploration. In addition, the present study found tentative evidence for moderation of cognition by length of widowhood whereby the longer the exposure to widowhood, the poorer one's cognitive functioning. Put together, these findings provide good evidence in support of widowhood being a potential risk factor for cognitive decline.

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Supplementary Material

A) Full list of search terms

Search Terms:

1. widow*.mp.
2. bereave*.mp.
3. (spous* adj2 death).mp.
4. (spous* adj2 loss).mp.
5. (conjugal adj2 loss).mp.
6. (conjugal adj2 death).mp.
7. (partner adj2 loss).mp.
7. (partner adj2 death).mp.
9. exp *Widowhood/
10. exp *bereavement/
11. conigiti*.mp.
12. memory
13. “reaction time”.mp.
14. (speed adj2 processing).mp.
15. “processing speed”.mp.
16. intelligence.mp.
17. “Mental Ability”.mp.
18. “Executive Function”.mp.
19. “Neuropsychological Testing”.mp.
20. “Mini Mental State”.mp.
21. “Mental Status”.mp.
22. *Cognition/
23. exp *Neuropsychological Tests/
24. exp *Cognitive Dysfunction/
25. exp Executive Function/
26. exp Memory/
27. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
28. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
29. 27 and 28

B) <u>Complete methodological quality ratings for each study (cross-sectional) based on Joanna Briggs Institute Checklist</u>

Studies included in cross-sectional analysis	Perkins 2016	O'Connor 2014	Feng 2014	Shahar 2001	Rosset 2011	Byrne 1997	Xu 2020	Biddle 2020	Aartsen 2005	Mousavi 2012	Zhang 2019	Lee 2019
Were the criteria for inclusion in the sample clearly defined?	1	1	1	1	1	1	1	1	1	1	1	1
Were the study subjects and the setting described in detail?	1	1	1	1	1	1	1	1	1	1	1	1
Was the exposure measured in a valid and reliable way?	0	0	0	0	0	1	0	0	0	0	0	0
[a]Were objective, standard criteria used for measurement of the condition?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Were confounding factors identified?	1	1	1	1	0	1	1	1	1	1	1	1
Were strategies to deal with confounding factors stated?	1	1	1	1	0	1	1	1	1	1	1	1
Were the outcomes measured in a valid and reliable way?	1	1	1	1	1	1	1	1	1	1	1	1
Was appropriate statistical analysis used?	1	1	1	1	1	1	1	1	1	1	1	1
Total	6	6	6	6	4	7	6	6	6	6	6	6

Note:

[a]This item was seen as being not applicable ("NA") because there was no "condition" involved in the study due to the fact that the main outcome was a continuous (not binary) measure of cognition in a cognitively healthy sample.

C) Complete methodological quality ratings for each study (longitudinal) based on Newcastle-Ottowa Criteria (Wells et al., 2000)

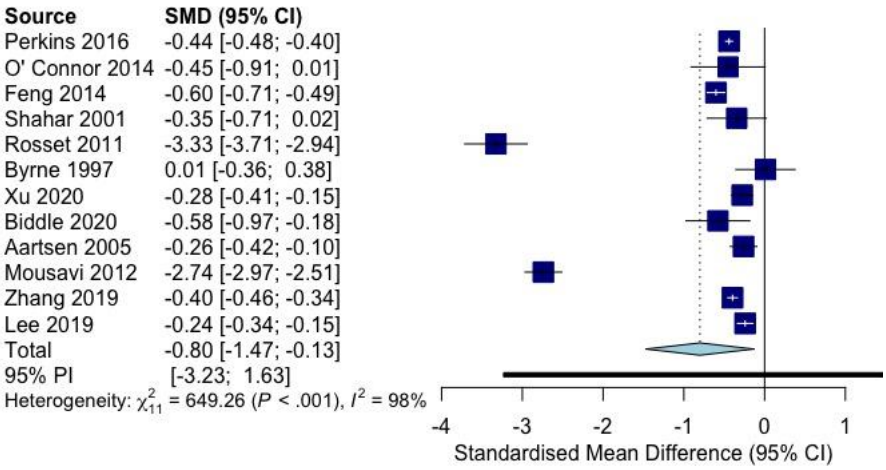
Studies included in longitudinal analysis		Biddle 2020	Zhang 2019	Lee 2019
Selection				
Representativeness of the exposed cohort				
Representative of the average in the community	*	1	1	1
Selected group of users e.g., nurses, volunteers etc.				
No description of the derivation of the cohort				
Selection of the non-exposed cohort				
Drawn from the same community as the exposed cohort	*	1	1	1
Drawn from a different source				
No description of the derivation of the non exposed cohort				
Ascertainment of exposure				
Secure record (e.g., surgical records)	*			
structured interview	*			
written self report		0	0	0
no description				
[a]*Demonstration that outcome of interest was not present at start*				
yes	*	NA	NA	NA
no				
Comparability				
Comparability of cohorts on the basis of the design or analysis				
study controls for (AGE & GENDER)	*	1	1	1
study controls for any additional factor (EDUCATION or SES)	*	1	1	1
Outcome				
Assessment of outcome				
Independent blind assessment / record linkage	*	1	1	1
self report				
no description				
Was follow-up long enough for outcomes to occur?				
yes	*	1	1	1
no				

Adequacy of follow up of cohorts				
Complete follow up or subjects lost to follow up & decription provided of those lost	*	1	1	
No description of those lost				0
no statement				
Total		**7**	**7**	**6**

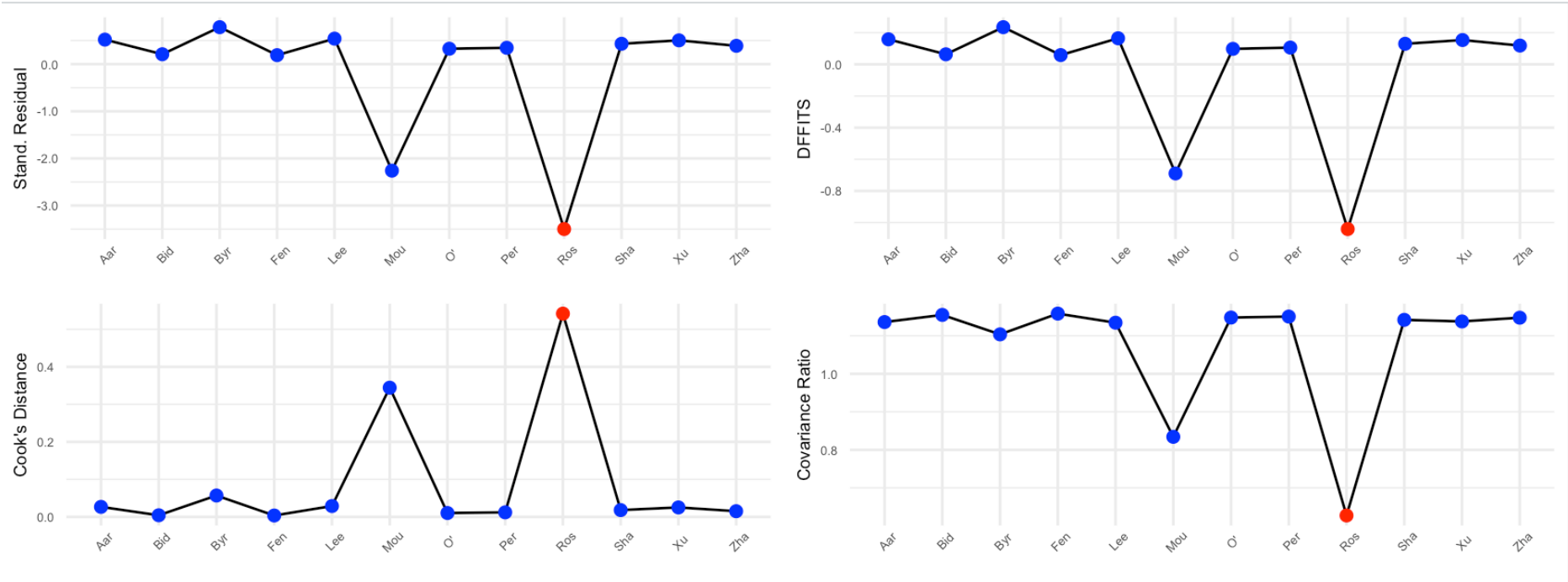
Note:

[a]This item was seen as being not applicable ("NA") because the 'outcome of interest' in this study was not binary, but rather a continuous measure of cognition in a cognitively healthy sample.

D) <u>Forest plot for cross-sectional meta-analysis including outliers (K = 12)</u>



E) Diagnostic plots (Viechtbauer & Cheung, 2010) to detect potential outliers using 'Dmetar' package in R



F) <u>Summary of all analyses conducted (cross-sectional meta-analysis), including results within and between subgroups</u>

Variable	Subgroup	K	Hedges' g (95% CI)	p-value	Heterogeneity	Between subgroup differences	Egger's test
All studies		12	-0.80 (-1.47, -0.13)	.02	I^2 = 98.0%		*p* = .20
All studies excluding outliers		10	-0.36 (-0.47, -0.25)	<.001	I^2 = 77.2%		*p* = .40
Study Design							
	Cross-sectional	6	-0.38 (-0.58, -0.17)	.005	I^2 = 75.7%		*p* = .53
	Longitudinal	4	-0.32 (-0.51, -0.14)	.01	I^2 = 69.5%	*B* = 0.05, *p* = .64, R^2 = 0%	*p* = .84
Cognitive Domain Measured							
	Memory (e.g., Recall)	4	-0.34 (-0.50, -0.19)	.005	I^2= 82.4%		*p* = .12
	Global (e.g., MMSE)	6	-0.38 (-0.62, -0.15)	.008	I^2 = 76.2%	*B* = 0.05, *p* = .64, R^2 = 0%	*p* = .49
Continent							
	Asia	4	-0.43 (-0.63, -0.22)	.006	I^2 = 81.6%		*p* = .98
	Europe/North America	5	-0.30 (-0.44, -0.15)	.004	I^2 = 0.00%	*B* = 0.12, *p* = .19, R^2 = 7.66%	*p* = .04
Length since spousal loss							
	Less than 4 years	6	-0.24 (-0.38, -0.10)	.006	I^2 = 58.6%		*p* = .09
	More than 4 years	3	-0.41 (-0.73, -0.09)	.03	I^2 = 77.1%	*B* = 0.16, *p* = .11, R^2 = 23.75%	*p* = .80
[#]Age of sample		9				*B* = 0.01, *p* = .35, R^2 = 0.00%	
Difference in age between "widowed" and "married"		7				*B = -0.01, p = .73, R^2 = 0.00%*	

Note:

[#]Age was entered as a continuous predictor. Where mean age was not reported, the mean age was estimated to be the middle value of the median age range. For example, if the median age range was reported to be 60-64 years, the mean age was estimated to be 62 years of age

G) <u>Sensitivity Analysis excluding the two studies that overlapped the 4-year period and hence needed to be 're-grouped' (length since spousal loss analysis)</u>

Variable	Subgroup	K	Hedges' g (95% CI)	p-value	Heterogeneity	Between subgroup differences
Length since spousal loss						
	Less than 4 years	4	-0.22 (-0.47, -0.04)	.075	I^2 = 74.5%	
	More than 4 years	3	-0.41 (-0.73, -0.09)	.032	I^2 = 77.1%	*B* = 0.19, *p* = .16, R^2 = 26.92%

H) Sensitivity Analysis for various imputed r-values (longitudinal meta-analysis)

	K	Hedges' g (95% CI)			
Imputed r value		**r = .60 (used in analysis)**	r = .20	r = .40	r = .80
Pre-post Change in cognition (ref group: married)	3	-0.15 (-0.19, -0.10)	-0.10 (-0.13, -0.07)	-0.11 (-0.15, -0.08)	-0.19 (-0.28, -0.10)