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**A systematic review of the relationship between
Behavioural and Psychological Symptoms (BPSD) and
caregiver wellbeing**

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Manuscripts

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3 **A systematic review of the relationship between Behavioural and Psychological Symptoms**
4 **(BPSD) and caregiver wellbeing**
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Individual BPSD and caregiver wellbeing

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Background: Behavioural and psychological symptoms in dementia (BPSD) are important predictors of institutionalisation as well as caregiver burden and depression. Previous reviews have tended to group BPSD as one category with little focus on the role of the individual symptoms. This review investigates the role of the individual symptoms of BPSD in relation to the impact on different measures of family caregiver wellbeing.

Methods: Systematic review and meta-analysis of articles published in English between 1980 and December 2015 reporting which BPSD affect caregiver wellbeing. Article quality was appraised using the Downs and Black Checklist (1998).

Results: 40 medium and high quality quantitative articles met the inclusion criteria, 16 were suitable to be included in a meta-analysis of mean distress scores. Depressive behaviours were the most distressing for caregivers followed by agitation/aggression and apathy. Euphoria was the least distressing. Correlation coefficients between mean total behaviour scores and mean distress scores were pooled for 4 studies. Irritability, aberrant motor behaviour and delusions were the most strongly correlated to distress, disinhibition was the least correlated.

Conclusion:

The evidence is not conclusive as to whether some BPSD impact caregiver wellbeing more than others. Studies which validly examined BPSD individually were limited, and the included studies used numerous measures of BPSD and numerous measures of caregiver wellbeing. Future research may benefit from a consistent measure of BPSD, examining BPSD individually, and by examining the causal mechanisms by which BPSD impact wellbeing by including caregiver variables so that interventions can be designed to target BPSD more effectively.

Key words: Behavioural and Psychological Symptoms of Dementia, Carer, Dementia, Neuropsychiatric Symptoms, Quality of life.

Introduction

BPSD can occur in up to 90% of people with dementia and have been associated with the breakdown of home care, increased psychiatric referral, misuse of medication, and increased health care costs (Cerejeira *et al.*, 2012). BPSD are described as a major source of distress for the caregiver (Tan *et al.*, 2005; Craig *et al.*, 2005; Bandeira *et al.*, 2007) and are composed of wide-ranging symptoms such as agitation, aggression, calling out repeatedly, sleep disturbance, wandering, and apathy. The majority of past research which has investigated the empirical relationship between BPSD and poor caregiver outcomes has used summative BPSD scores, therefore it remains unclear as to whether specific individual symptoms impact caregivers differentially (Rocca *et al.*, 2010; Mohamed *et al.*, 2010).

The limited research which has distinguished between symptoms is mainly exploratory and does not control for the effect of multiple BPSD (Ballard *et al.*, 1995; Gonzalez-Salvador *et al.*, 1999; Lim *et al.*, 2008; Neundorfer *et al.*, 2001). However, Ornstein *et al.* (2012) have advanced the field by examining how and why symptoms clusters impact caregiver depression. Nevertheless, the symptoms were clustered rather than individually represented and the systematic review did not employ a formal method of synthesis, but instead a descriptive analysis was given, along with tallying of symptoms.

It is often the case that BPSD are presented in a summative fashion due to the nature of the outcome measure and how the total score is calculated, and are consequently usually operationalized as a single construct of “behavior problem”; therefore the data cannot be extracted. Research by Fauth and Gibbons (2014) highlighted the extensive inconsistencies in identifying BPSD that are the most problematic. These inconsistencies are partly due to whether “problematic” is defined and measured in terms of symptom prevalence, intensity, distress rating, or association with caregiver outcomes, such as depressive symptoms (Ornstein *et al.*, 2012). A review by Black and Almeida (2004) has progressed our understanding of the association between BPSD as a whole, and the burden of care, and caregiver depression by performing a meta-analysis. However, multiple types of behavior measures, burden measures and measures of depression were pooled in the same meta-analysis. In future meta-analyses it is important to combine the same outcome measures of a particular construct such as “distress” in order to ensure the statistical analysis is valid rather than combining multiple types of measures. This is addressed in the current review.

As recommended by Ornstein *et al.* (2012) it is necessary to design future systematic reviews which capture the complexity of unique behaviours in order to further our understanding of their differential impact upon caregivers. The aim of this study was to respond to Ornstein’s recommendation and to systematically review the relationship between individual BPSD and caregiver wellbeing in order to identify which BPSD are the most problematic for caregivers. This was achieved by distinguishing between psychological constructs of caregiver outcome (distress, burden, strain, stress) within each meta-analysis, and by distinguishing between how BPSD are measured (prevalence, frequency and total score) within each meta-analysis.

Methods

Identification and selection of studies

A search strategy combining medical subject headings and text words relating to dementia, BPSD, mental disorders and behaviours, behaviours, elder care, significant others, carers, family, daughters, aged, carer burden, carer strain, carer distress and cost of illness was devised and adapted for five electronic databases. Searches of studies published between 1980 and December 2015 were carried out through PsycINFO, CINAHL EBSCO (Cumulative Index to Nursing and Allied Health), MEDLINE, EMBASE and Web of Science (including Science Citation Index-Expanded (SCI-EXPANDED), Conference Proceedings Citation Index-Science (CPCI-S), Social Science Citation Index (SSCI), Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH), and reference lists of included studies. Studies were restricted to peer-reviewed original articles published in English and included participants who were family caregivers of someone with dementia, used a measure of caregiver response to BPSD and a measure of BPSD, and reported data for both measures. Reviews, conference proceedings, conference abstracts, theses, supplements, reports, letters, and non-peer reviewed articles were excluded.

Quality appraisal

Two reviewers (AF and CS) assessed the included papers for methodological quality, and disagreements were resolved by discussion. The 27-item Downs and Black Checklist (1998) was used to assess quality. Quality thresholds were those used in a previous systematic review (Crellin *et al.*, 2014; $\geq 75\%$ for high quality, $\geq 50\%$ to 74% for medium quality). Agreement was measured using Cohen's Kappa (κ) weighted for closeness of scores.

Analysis

Summary statistics for each comparable caregiver outcome associated with each behaviour (means, standard deviation and sample size) were extracted for each study and were used to calculate the pooled weighted mean and standard deviation for that outcome. The following formulae were used:

Mean for combined studies: $\frac{\sum_i n_i m_i}{\sum_i n_i}$ where n_i is the sample size for study 1 and m_i is the mean for study 1 (Price, 1970). The standard deviation of the combined studies: $\sqrt{[\sum_i (n_i - 1) (sd_i)^2 / ((\sum_i n_i) - T)]}$, where T is the number of studies (all summations from 1 to T) (Cohen, 1988). Standard deviations were converted to standard errors: $SE = SD / \sqrt{N}$.

MedCalc software (Version 15: Ostend, Belgium) was used to perform a meta-analysis of comparable studies where possible in order to produce a pooled effect. Studies with smaller standard errors and larger sample sizes were given more weight in the calculation. The I^2 statistic was calculated to denote the percentage of observed total variation across studies that is due to heterogeneity. A p value of >0.10 determines if heterogeneity is present, consequently the summary effect from the random-effects model rather than the fixed-effects model is utilised. In cases where data were not amenable to meta-analysis (either not comparable, or insufficient data) these studies were compared descriptively and tabulated.

Results

A total of 12,244 references were identified (Figure 1), of which 11,651 were excluded by screening the title, abstract, and the removal of duplicates. Of the remaining 593 references, full texts were sought, and 40 met the inclusion criteria regardless of quality. Reasons for exclusion can be seen in Figure 1.

Insert Figure 1

The 40 included studies were quantitative, mainly cross-sectional with two longitudinal studies (Berger *et al.*, 2005; Johnson *et al.*, 2013), 21 studies were graded as high quality, and 19 as medium quality. A brief summary of the demographic data of the studies is provided in table S1, along with a description of the measures used, quality score and the main findings. There was little consistency in the sample populations across studies. The included studies consisted of 10,978 caregivers in total, of these 67 % were female and had a mean age of 60 years. Only five studies reported ethnicity. Of those which reported dementia stage, 9 studies included participants with mild dementia, 20 with moderate and 1 with severe dementia.

Quality appraisal of included studies

Level of agreement between the 2 independent reviewers was $\kappa = 0.72$, $p = 0.002$, 95% CI (0.73, 0.78) indicating substantial agreement (Landis and Koch, 1977). The studies scoring the lowest on the checklist were Haley *et al.* (1987), Hishikawa *et al.* (2012), and Savorani *et al.* (1998). All studies lost points on questions covering external validity, validity and reliability of outcome measures and the reporting of statistics.

Meta-analysis of comparable studies

Sixteen of the 40 studies were suitable to be included in a meta-analysis of mean distress scores (see supplementary Table S2). All of these studies reported data on the mean and standard deviation of distress associated with the mean total score on the NPI for individual behaviors. Each adapted version of the NPI was reported as valid and reliable and all were administered by a researcher or clinician. Five studies utilised the 10-item version of the NPI, therefore data reporting distress associated with sleep and appetite/eating change were unavailable for these studies. Participants were recruited from clinic-based and population-based studies, had a mix of dementia participants and studies only including those with a diagnosis of Alzheimer's disease, Parkinson's disease dementia, and frontotemporal dementia (see Table S1). In Supplementary Table S3 the mean distress reported for the total NPI symptom can be seen for each of the 16 studies, along with the pooled standard deviations for each behavior across the studies. There is considerable variation between the studies for each of the symptoms, this can be seen in Figure 2, in particular there is substantial variation in the mean distress reported for the total score of irritable behavior: Baiyewu *et al.* (2003) reported 0.6 (between 'not at all distressing' and 'minimally distressing') and Balieiro *et al.* (2010) reported 3.6 (between 'moderately' and 'severely' distressing). However, it is possible to conclude that euphoria was the least distressing across the studies.

Insert Figure 2

Individual BPSD and caregiver wellbeing

As seen in Figure 3 the most distressing BPSD across the 16 studies was depression. Agitation/aggression was the second most distressing, followed by apathy. Euphoria was the least distressing and had the smallest standard error. Delusional and euphoric behaviors were the only two behaviors with a standard deviation exceeding the mean indicating high variance between studies for these behaviors.

Insert Figure 3

Four studies reported correlation data between mean NPI total scores and mean NPI distress (Balieiro et al., 2010; Davidsdottir et al., 2012; Huang et al., 2012; Matsumoto et al., 2007), all of these studies were involved in the previous meta-analysis other than Davidsdottir et al. (2012). Three of these studies reported data on all 12 behaviors. The sample size and the correlation coefficients were entered into MedCalc in order to produce a pooled effect size for each behavior. The pooled effect sizes within the fixed-effect model, random-effects model and heterogeneity statistics are reported in Table 1. Significant heterogeneity was identified between studies for all behaviors other than apathy and sleep. In contrast to the mean distress data, the meta-analysis of the correlation data identified that irritable behavior was the most strongly associated with caregiver distress followed by aberrant motor behavior and then delusions. Disinhibition had the weakest association with distress. Depression was seen to be one of the behaviors which was more strongly associated/correlated with distress across both meta-analyses. Appetite and eating-related behavior was one of the behaviors which had a weaker association/correlation with distress across both meta-analyses.

Insert Table 1

Non-comparable studies

Twenty of the 40 included studies were not suitable for meta-analysis. These studies were not comparable in terms of BPSD measure and the associated unit of measurement, caregiver wellbeing measure, and the associated unit of measurement. It was therefore only possible to compare these 20 studies descriptively due to their heterogeneity.

Prevalence of BPSD and the impact on caregiver wellbeing

Mean prevalence and mean distress were reported on the NPI by Haley *et al.* (2008) and de Vugt *et al.* (2006). Although these two studies both measure prevalence of BPSD, methods for measuring caregiver wellbeing differed (see Table S1).

Frequency of BPSD and caregiver wellbeing

Memory-related behaviors were reported as most stressful and problematic across 3 studies (Muangpaisan *et al.*, 2010; Nygaard, 1988; Quayhagan and Quayhagen, 1988). However, Robinson *et al.* (2001) and Fauth and Gibbons (2014) both found the frequency of memory-related behaviors was associated with the least amount of reactivity. Disruptive behaviors were associated with the most reactivity, followed by depressive behaviors (Fauth and Gibbons, 2014; Robinson *et al.*, 2001). In all of the studies which measured hallucinations caregivers reported this behavior as less problematic, burdensome and distressing compared to many of the other behaviors. Verbal aggression across 3 of the 5 studies was reported as problematic and burdensome. Across 2 of the 5 studies which reported sexual disinhibition, this behavior was reported as the least problematic. Reports of wandering across 4 of the studies were not consistent, since some of the studies reported this behavior as much more problematic and burdensome than others.

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2 Across 4 of the 5 studies which reported incontinence, this was consistently reported as one of the
3 more burdensome, stressful and problematic behaviors. Physical aggression was only measured in 3
4 studies and only 1 study reported this behavior as a common problem. Both studies which reported
5 irritability identified this behavior to be one of the most problematic and burdensome.
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7 *Correlational data between BPSD and caregiver wellbeing*

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9 Sleeping and eating-related behaviors were found to be significantly correlated to burden and strain,
10 however, they had a stronger association with burden (Donaldson *et al.*, 1998). With regard to adult-
11 child caregivers, 4 (delusions, agitation, disinhibition, and appetite/eating change) of the 8 behaviors
12 reported by Conde-Sala *et al.* (2010) as being significantly associated with burden were also found to
13 be significantly associated with burden by Allegri *et al.* (2006). Apathy and irritability were reported
14 to be significantly associated with burden in the study conducted by Conde-Sala *et al.* (2010), but no
15 significant relationship was reported by Allegri *et al.* (2006). Spousal caregivers only found
16 appetite/eating change burdensome (Conde-Sala *et al.*, 2010). Apathy had a moderate significant
17 association with burden in spousal and adult-child caregivers (Conde-Sala *et al.*, 2010), but this
18 association was non-significant in the data reported by Allegri *et al.* (2006). Delusional and irritable
19 behaviors were also reported as non-significantly related to burden (Allegri *et al.*, 2006) but were
20 significantly related to burden by Conde-Sala *et al.* (2010). In contrast to the previous studies
21 reporting the weak association between euphoria and distress, Fuh *et al.* (2001) reported a significant
22 correlation between euphoria and burden. No other behaviors on the NPI had a significant correlation
23 with burden (Fuh *et al.*, 2001).
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28 In agreement with the data concerning at the association between the frequency of the behavior
29 within each subscale on the RMBPC and reactivity, disruptive behaviors had the largest correlation
30 of the three subscales with burden (Huang *et al.*, 2012). Using the BEHAVE-AD (Reisberg *et al.*,
31 1982) and the NOSGER (Speigel *et al.*, 1991) mood, social behaviors and disturbing behaviors were
32 found to have a significant moderate association with burden but no significant correlations with
33 depression in caregivers. Chiu *et al.* (2013) noted that all of the behaviors on the NPI significantly
34 predicted sleep disturbance in caregivers other than anxiety and aberrant motor behavior.
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39 *Predictive data between BPSD and wellbeing*

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41 Conde-Sala *et al.* (2010), Chappell and Penning (1996), Davis and Tremont (2007), and Slachevsky
42 *et al.* (2013) used the same burden measure, but used different measures of BPSD. Apathy
43 significantly predicted burden across 3 studies, although it was less burdensome for adult-child
44 caregivers and did not predict apathy in the study by Davis and Tremont (2007). Three studies (Khoo
45 *et al.*, 2013; Lee *et al.*, 2013; Mourik *et al.*, 2004) reported data identifying which behaviors
46 predicted distress as measured by the NPI. Apathy was a significant predictor across two of the three
47 studies. Delusions and anxiety were the only other comparable behaviors across two of the three
48 studies and were both significant predictors of distress. Covinsky *et al.* (2003) did not use a formal
49 behavior scale but identified that anger and aggressive behaviors were stronger predictors of
50 caregiver depression, followed by dangerous behaviors to self and others, and then behaviors which
51 wake the caregiver up at night.
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56 **Discussion**

Individual BPSD and caregiver wellbeing

To our knowledge this is the first review to control for the effect of multiple BPSD on caregiver wellbeing by discriminating between individual BPSD, and also discriminating between caregiver outcomes of wellbeing. Additional advantages of this review were the use of a formal method of synthesis and the decision to distinguish between how BPSD and caregiver wellbeing are measured, which ensured valid conclusions were drawn by only synthesising comparable data. Only two meta-analyses were possible, due to limited homogeneous studies. Categories in which the relationship between BPSD and wellbeing were qualitatively examined included minimal studies displaying considerable variation, therefore valid conclusions could not be drawn. The results are discussed in the context of previous research.

Meta-analysis of mean distress scores

As seen in Figures 2 and 3, even within one measure and one criterion (distress associated with total score on the NPI) variability in distress ratings for each symptom can be seen between the 16 studies. This was also evident in research conducted by Fauth and Gibbons (2014), in which a wide variation in the prevalence of NPI symptoms was seen between studies. However, data regarding distress associated with euphoria and delusions demonstrated high levels of variance in terms of the ratio between the mean and the standard deviation resulting in considerable variability between scores. Therefore, the ratio of the mean distress ratings compared with the standard deviation associated with the other 10 behaviors signifies that there is low variance between the 16 studies. It is unclear at present why there is increased variability for euphoric and delusional behaviors. In terms of total score, depression followed by agitation/aggression and apathy were found to be the most distressing for caregivers across 16 studies in the meta-analysis (Figure 3). This suggests that it is mood-related behaviors which are associated with increased distress. Fauth and Gibbons (2014) examined the relationship between total score of BPSD and distress and found similar results, however, even with identical analysis there were noteworthy discrepancies, such as delusions being the most distressing but only the fourth most distressing in the current review. Consistent with the current meta-analysis of mean data, apathy and depression related-behaviors have been reported as distressing in numerous studies (Aarsland *et al.*, 2007; Kosberg *et al.*, 2007; Teri, 1997; deVugt *et al.*, 2003). Similarly, depression in the person with dementia is associated with depression in the caregiver (Waite *et al.*, 2004).

Meta-analysis of correlation data

As seen in Table 1 there were high levels of heterogeneity between the studies included in the second meta-analysis investigating which behaviors were associated with distress. Only apathy and sleep-related behaviors displayed homogeneity between studies. Furthermore, behaviors which had stronger correlations with distress (Table 1) did not have strong associations in the previous meta-analysis (Figure 3) regarding distress associated with behaviors. At present it is unclear why this discrepancy exists, and also why distress correlated with apathy and sleep-related behaviors is more homogenous between studies than the other behaviors. Since only a few studies contributed to this meta-analysis, more research is needed to investigate the pooled effects. Nevertheless, a meta-analysis of this nature has not been performed previously and the random-effects model was used to report a more conservative estimate for the heterogeneous pooled effects in order to reduce bias.

Apathy, and irritable behaviors were not consistently significantly correlated to burden across multiple studies, whereas delusions, agitation, disinhibition and appetite/eating change were; these associations were also reported in other studies (Rocca *et al.*, 2010; Rymer *et al.*, 2002). In contrast, a review by Ornstein and Gaugler (2012) reported that anger/aggression and depression were the most frequently cited BPSD associated with caregiver burden; depression was also linked to caregiver burden in a review by Black and Almeida (2004). In addition to burden, delusional

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2 behavior was consistently associated with distress across studies, with a significant correlation also
3 being seen with stress (Kosmala and Kloszewska 2004). Berger *et al.* (2005) noted that behaviors
4 which are significantly correlated with burden are not correlated with depression. This demonstrates
5 the importance of including multiple measures of wellbeing since the same behaviors affect
6 caregivers differently, which has implications for future interventions.
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10 *Studies unamenable to quantitative synthesis*

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12 Only 2 studies reported the prevalence of BPSD and the impact on caregiver wellbeing; due to
13 differences between studies, comparisons were not possible. Although 5 studies reported the
14 frequency of BPSD, each measure of caregiver wellbeing was different. Memory-related behaviors,
15 verbal aggression, incontinence, and irritability were reported to affect wellbeing across multiple
16 studies: these findings were also seen in previous research (Bruce & Paterson., 2000; Farran *et al.*,
17 2004). However, Fauth and Gibbons (2014) and Robinson *et al.* (2001) did not find that memory-
18 related behaviors were distressing despite being the most frequent type of behavior on the RMBPC.
19 Hallucinations, sexual disinhibition, and physical aggression were consistently reported to affect
20 wellbeing less than the other behaviors. Although this finding is reflected in the majority of studies,
21 Haley *et al.* (2008) and Arango-Lasprilla *et al.* (2009) reported contradictory results.
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25 It is noteworthy that aggression/agitation, when measured in terms of total score, was reported as the
26 second most distressing across 16 of the studies, but when measured in terms of frequency only 1 of
27 the 3 studies reported physical aggression as a common problem. However, the frequency of verbal
28 aggression consistently affected wellbeing. It is not possible to provide an explanation for this
29 discrepancy, but it may be because of the distinction between how aggression/agitation is measured
30 (i.e. total score or frequency), or that verbal and physical aggression have been differentiated and
31 therefore affect caregiver wellbeing differently.
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34 Predictive data were limited and heterogeneous in the present review, however, it was possible to
35 conclude that apathy predicted burden and distress across studies. Anger, restlessness,
36 combativeness, dangerous to others, and embarrassing behavior were found to be strong predictors of
37 burden in a study by Gaugler *et al.* (2011). Only one study reported the predictors of caregiver
38 depression.
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41 *Potential explanations for variability in caregiver wellbeing*

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43 Difference in study quality does not appear to be an explanation for the variation in distress rating
44 across studies, since even between two medium quality studies there was considerable variation
45 (Baliero *et al.*, 2010, displaying one of the highest mean distress scores and Baiyewu *et al.*, 2003,
46 displaying one of the lowest). Two studies consistently had the highest mean distress rating across
47 each of the behavior domains: Balieiro *et al.* (2010) and Tan *et al.* (2005). Both of these studies were
48 clinic-based, higher distress ratings would be expected as those experiencing more BPSD might be
49 more likely to attend a clinic, as, indeed, were the majority of studies included in the meta-analysis.
50 It may be possible that dementia severity is an explanation, since participants in the studies with the
51 highest distress scores (Balieiro *et al.*, 2010; Tan *et al.*, 2005) had moderate and severe dementia
52 respectively, whereas Baiyewu *et al.* (2003), who consistently reported the lowest distress scores
53 across each of the behavior domains, included participants with mild dementia. However, both
54 Aarsland *et al.* (2007) and de Vugt *et al.* (2006) reported lower mean distress scores in comparison
55 with the other included studies, and they both included participants with moderate dementia.
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2 Furthermore, Davidsdottir *et al.* (2012) found that there was no significant difference between
3 caregiver distress scores depending on dementia severity.
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5 Baiyewu *et al.* (2003) had a much smaller sample of spousal caregivers in comparison to Tan *et al.*
6 (2005), which might account for the lower distress scores. This is in agreement with Almgren *et al.*
7 (1997) who reported that spouses experience greater levels of burden. However, three studies which
8 had consistently higher mean distress scores across all behaviors (Balieiro *et al.*, 2010; Huang *et al.*,
9 2012; Tan *et al.*, 2005), were mainly comprised of adult-child caregivers. When comparing a study
10 solely comprised of spousal caregivers (deVugt *et al.*, 2006) with a study (Baiyewu *et al.*, 2003) with
11 minimal spousal caregivers (2.5%) it was possible to see that spousal caregivers were substantially
12 more distressed with depressive, apathetic and anxiety-related behaviors. Although distress ratings
13 can be differentiated between behavior types for spousal and non-spousal caregivers both Baiyewu *et*
14 *al.* (2003) and de Vugt *et al.* (2006) had two of the lowest distress scores across all behaviors in
15 comparison to the other studies in the meta-analysis.
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18 The explanation may also be cultural since Baiyewu *et al.* (2003) and Baiyewu *et al.* (2012) (with
19 similarly low distress scores across behaviors) were the only Africa based studies in the meta-
20 analysis. Baiyewu *et al.* (2003) and Baiyewu *et al.* (2012) were also both community-based studies
21 which may also be a reason for the reduced distress ratings. There is every reason to believe that
22 BPSD are present across cultures (Shaji *et al.*, 2009), however, the low levels of public awareness of
23 dementia have many implications (Prince, 2000). One of these implications may be the
24 misinterpretation of BPSD as deliberate, consequently affecting the wellbeing of the carer (Shaji *et*
25 *al.*, 2009). It is beyond the scope of this paper to determine why there is considerable variation
26 between studies reporting caregiver distress for identical behaviors using identical measures.
27 However, it is likely that it is the caregiver characteristics rather than the characteristics of the person
28 with dementia (such as dementia severity) which may underlie the explanation as to why variation
29 between studies exists.
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35 **Limitations**

36 The data available for this review allowed for only two meta-analyses to be conducted. There were
37 relatively few studies which assessed the relationship between individual BPSD and caregiver
38 wellbeing and which met the inclusion/exclusion criteria for the review. In an attempt to be
39 systematic based on prior recommendation, an effort was made to distinguish between how
40 “problematic” symptoms are measured. Consequently, studies were categorised into whether BPSD
41 were measured in terms of frequency or prevalence, and also categorised in terms of the statistical
42 analysis employed. Other than data regarding mean distress associated with NPI total score, only a
43 small amount of studies were included in each category and unfortunately it was often the case that
44 measures of caregiver wellbeing were dissimilar. From the 40 included studies there were 12
45 different measures of behavior and 17 different measures of wellbeing, making comparisons difficult
46 which may have contributed to the inconsistent findings.
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50 The majority of included studies recruited participants from clinics, therefore caregivers included in
51 the review were not representative of the population. In addition, the samples across the included
52 studies were heterogeneous in a number of factors, therefore caution should be taken when
53 interpreting the results. Although beyond the scope of this review, study characteristics such as
54 culture, gender, and relationship direction were not examined through subgroup analyses. Due to the
55 limited number of studies it was not possible to impose a quality criteria, however, all included
56 studies were either of high or medium quality as assessed by the Downs and Black Checklist (1998).
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2 Furthermore, all of the included studies relied on caregiver reports of BPSD, which may themselves
3 be affected by caregiver wellbeing; unfortunately it is not possible to determine if this was the case.
4 Nonetheless, two valid meta-analyses were completed and a number of comments can be made about
5 the relationship between BPSD and caregiver wellbeing.
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10 11 **Implications and recommendations**

12 The vast majority of studies addressing the relationship between BPSD and caregiver wellbeing did
13 not examine individual BPSD. Consequently, this comparatively limited the amount of studies
14 included in the present review. Therefore, if we are to understand this relationship more studies need
15 to examine individual BPSD in their research. In addition, it is more clinically relevant to examine
16 which BPSD affect wellbeing rather than BPSD as a whole, as this is essential in determining where
17 clinical staff should allocate resources most effectively. Nevertheless, there is preliminary data
18 suggesting it is mood-related behaviors which are associated with increased levels of distress,
19 therefore interventions for the management of BPSD should target these behaviors.
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23 The lack of consistency in the measurement of BPSD (neuropsychiatric or memory problems,
24 frequency or prevalence), and the measurement of caregiver wellbeing (the use of interchangeable
25 terminology such as stress, strain and burden meaning the same construct) limits our ability to reach
26 a consensus as to which BPSD result in the most negative outcomes for caregivers. For example,
27 Donaldson *et al.* (1998) used Gilleard's Strain Scale (1984) to measure burden and the General
28 Health Questionnaire (Goldberg *et al.*, 1979) to measure distress. Furthermore, four studies (see
29 Table S1) did not have formal scales to measure the impact of BPSD on wellbeing, and used terms
30 such as 'burdensome', 'serious', and 'disturbing'. This problem impacts upon the validity and
31 reliability of the original studies and consequently the review. However, this mainly occurred in the
32 earlier studies. Future research should also include more than one measure of wellbeing in order to
33 identify if individual BPSD differentially affect caregiver burden compared to caregiver distress as
34 identified in the current review. Furthermore, future research should identify why there is reduced
35 variability in distress ratings for certain behaviors compared to others, and why certain behaviors are
36 more distressing depending on which type of statistical analysis is used.
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40 Although there are potential methodological reasons (limited studies, inconsistent measures) for why
41 there is substantial variability when identifying which BPSD affect certain types of caregiver
42 wellbeing the most, there is growing evidence that factors associated with the person with dementia
43 (e.g. BPSD frequency, cognition) are only part of the story when explaining a caregiver's response to
44 BPSD. Caregiver characteristics have been shown to account for twice the variance of person with
45 dementia characteristics when reporting neuropsychiatric symptoms (Sink *et al.*, 2006), and the
46 presence of BPSD was not found to be a significant predictor of burden, whereas caregiver
47 characteristics such as confidence, neuroticism, and relationship quality were significant predictors
48 (Campbell *et al.*, 2008). Therefore, as recommended by Ornstein and Gaugler (2012), future studies
49 should focus on identifying pathways for the association between individual BPSD, caregiver
50 variables and caregiver outcomes. More research is needed to understand if and why certain BPSD
51 affect certain caregiver outcomes, and also how much of this is attributable to caregiver variability in
52 response to BPSD rather than the presence of BPSD itself. More longitudinal studies would be useful
53 to examine how changes in individual BPSD are associated with caregiver wellbeing over time. A
54 review by Black and Almeida (2004) examined the limited longitudinal studies available and
55 reported mixed findings between burden and BPSD, and found no association between BPSD and
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Individual BPSD and caregiver wellbeing

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distress. Although BPSD increased significantly over a 2-year period, caregiver burden remained stable, and depression was found to decrease (Berger *et al.*, 2005). Future research needs to examine caregiver factors over time (wellbeing, role captivity etc.) along with changes in individual BPSD in order to have a more valid understanding of this relationship.

Caution should be exercised when creating a measure of BPSD, since Jackson *et al.* (2014) found that the Revised Memory and Behaviour Problem Checklist (Teri *et al.*, 1992) might be more suitable in explaining caregiver depression than the NPI. It is important that the measure of BPSD is not biased towards explaining a more unique association between BPSD and a measure of caregiver wellbeing such as depression. As stated by Gitlin *et al.* (2014), item selection for measures of BPSD is often based upon specific disciplines (e.g. neurology, psychiatry, social sciences) and thus implicitly represents different conceptualisations of behavior. A shared framework for defining behaviors and their underlying causes must be created in order to move on from the implicit assumption of most measures that behaviors are a direct cause of neuropathology, and to develop measures which also address the contextual and caregiver characteristics associated with the behavior.

Conclusions

This study has improved our understanding of the impact of individual BPSD on caregiver wellbeing, in particular caregiver distress. The relationship between individual BPSD and caregiver wellbeing was inconsistent and varied according to behavioral symptom. Due to limited studies and heterogeneous data the results should be interpreted with caution, but advances have been made with respect to which behaviors are associated with distress. The inconsistencies may be partly explained by caregiver variables which were not taken into account in the review. Based on this review and previous research it is not possible to fully understand the relationship between BPSD and caregiver wellbeing without examining the influence of caregiver variables such as caregiver strategies, acceptance, gender, relationship with person with dementia, and confidence. We recommend that future studies are designed to examine individual BPSD rather than BPSD as a whole, use consistent measures for BPSD and wellbeing, use consistent terminology for psychological constructs (e.g. burden), and examine the causal mechanisms by which individual BPSD impact caregiver wellbeing by collecting data on a range of caregiver factors. These approaches will clarify whether it is important for clinicians to focus on the frequency or prevalence of certain BPSD, in addition to targeting the presence of certain caregiver characteristics and addressing unmet need.

Conflict of Interest

None

Description of authors' roles

A. Feast was responsible for developing the review objectives, writing the search strategies, conducting the searches, designing and completing study eligibility and data extraction forms, undertaking the quality appraisals, conducting the meta-analysis, and writing the article.

M. Orrell was responsible for developing the review objectives, advising on the review methodology, meta-analysis, and assisting in writing the article.

C. Stoner was responsible for undertaking the quality appraisals and assisting in writing the article.

G. Charlesworth was responsible for developing the review objectives, advising on the review methodology, meta-analysis, and assisting in writing the article.

E. Moniz-Cook was responsible for developing the review objectives, advising on the review methodology, meta-analysis, and assisting in writing the article.

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Individual BPSD and caregiver wellbeing

Zarit, S. H., Reever, K. E. and Bach-Peterson, J. (1980). Relatives of the impaired elderly: correlates of feelings of burden. *The Gerontologist*, 20, 649-655. doi:10.1093/geront/20.6.649

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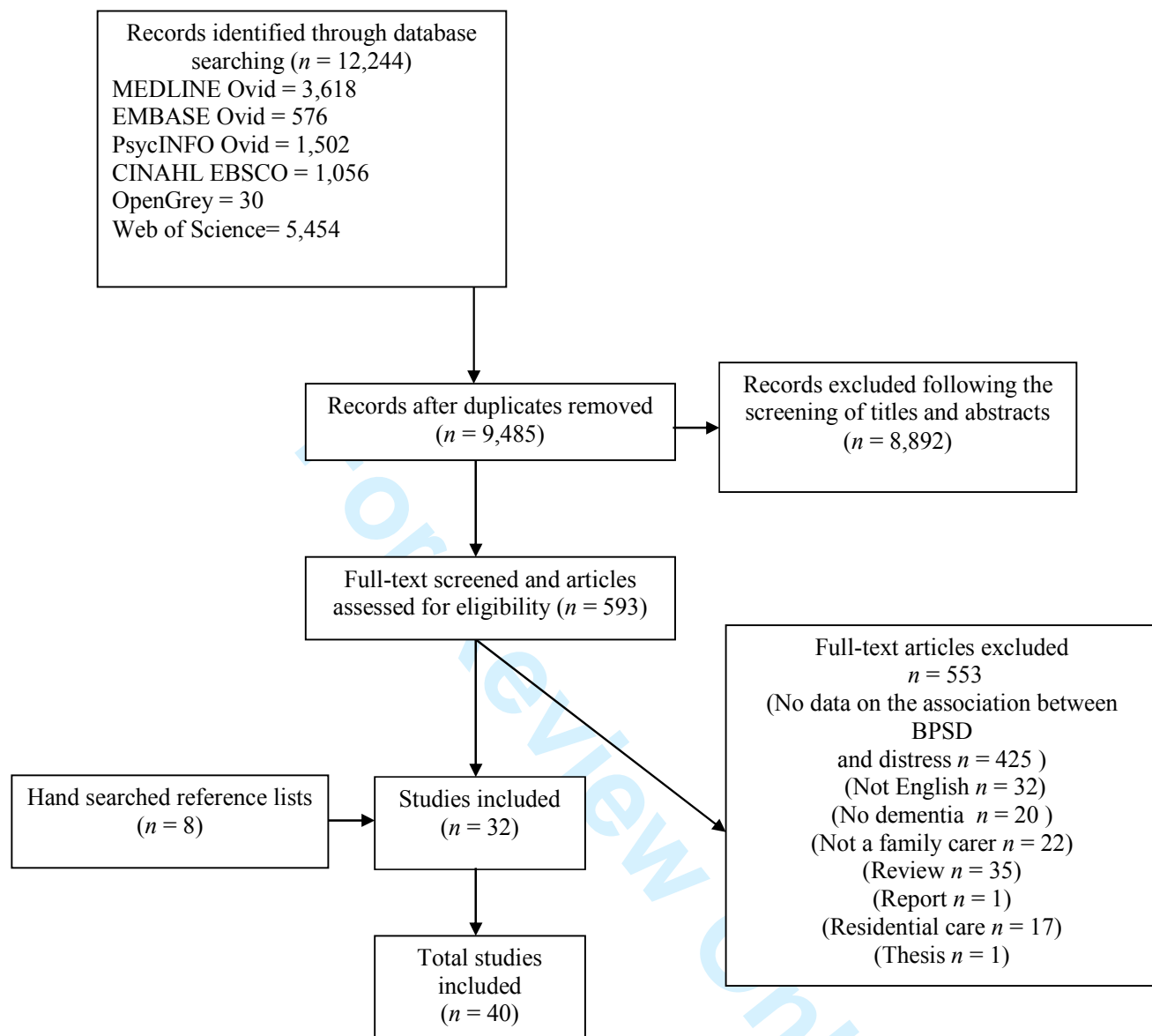


Figure 1. Study selection process.

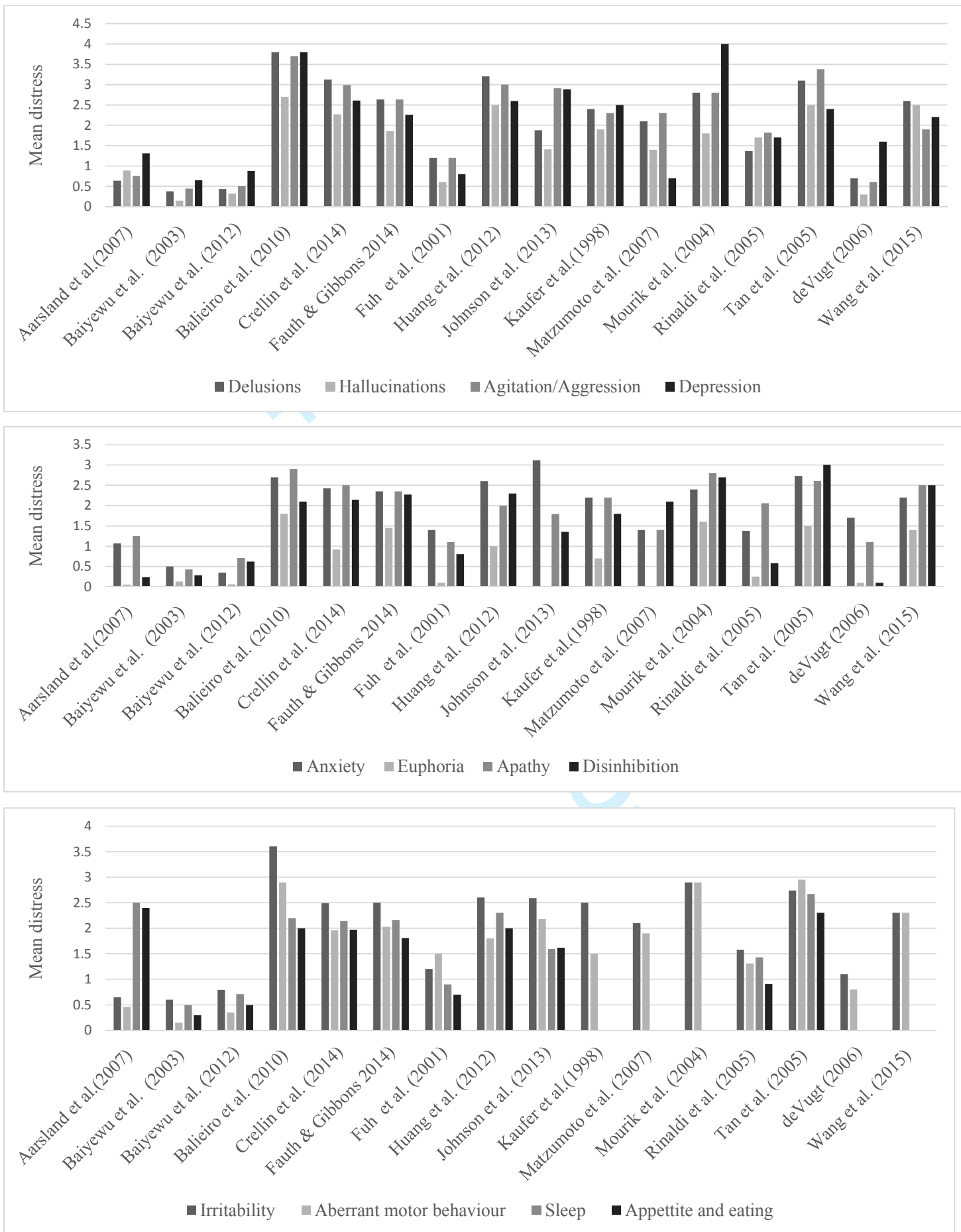


Figure 2. Mean distress scores across 16 studies for behaviours on the NPI (total score)

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Figure 3. Meta-analysis of mean distress for each BPSD associated with NPI total score

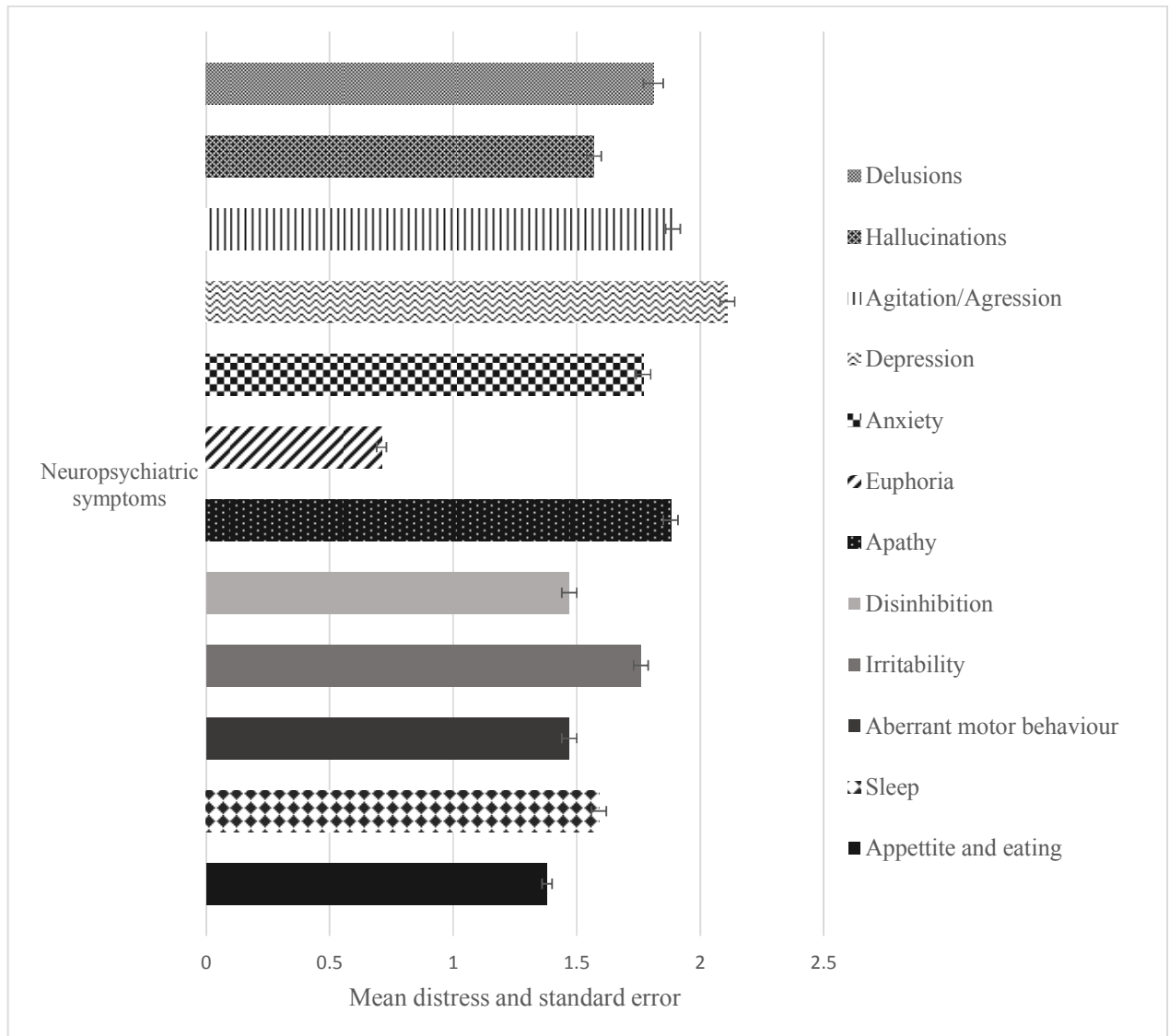


Table 1. Meta-analysis of mean distress scores correlated with behaviours using NPI total scores

| Behaviour | N | Pooled correlation coefficient | | <i>I</i> ² % | Test for heterogeneity | |
|--------------------------|-----|--------------------------------|--------------------------------|-------------------------|------------------------|------------------|
| | | Fixed- effects model (95% CI) | Random- effects model (95% CI) | | 95% CI | <i>p</i> |
| Delusions | 243 | 0.557 (0.462 to 0.640) | 0.567 (0.412 to 0.690) | 58.64 | 0.00 to 86.23 | <i>p</i> =0.0643 |
| Hallucinations | 243 | 0.502 (0.399 to 0.532) | 0.520 (0.198 to 0.791) | 87.71 | 70.81 to 94.82 | <i>p</i> <0.0001 |
| Agitation/ Aggression | 243 | 0.540 (0.443 to 0.625) | 0.537 (0.299 to 0.712) | 79.41 | 45.17 to 94.82 | <i>p</i> =0.0022 |
| Depression | 243 | 0.528 (0.429 to 0.615) | 0.564 (0.360-0.717) | 74.65 | 29.49 to 90.89 | <i>p</i> =0.0080 |
| Anxiety | 243 | 0.482 (0.377 to 0.575) | 0.481 (0.236 to 0.669) | 78.45 | 42.03 to 91.99 | <i>p</i> =0.0030 |
| Euphoria | 243 | 0.540 (0.443 to 0.625) | 0.480 (0.147 to 0.715) | 87.64 | 70.61 to 94.80 | <i>p</i> <0.0001 |
| Apathy | 243 | 0.456 (0.351 to 0.554) | 0.459 (0.351 to 0.540) | 0.00 | 0.00 to 84.23 | <i>p</i> =0.4834 |
| Disinhibition | 243 | 0.357 (0.240 to 0.464) | 0.371 (0.162 to 0.548) | 65.74 | 0.00 to 88.33 | <i>p</i> =0.0327 |
| Irritability | 243 | 0.668 (0.590 to 0.733) | 0.691 (0.486 to 0.823) | 82.81 | 56.01 to 93.29 | <i>p</i> =0.0006 |
| Aberrant motor behaviour | 243 | 0.606 (0.518 to 0.681) | 0.603 (0.437 to 0.730) | 67.64 | 3.71 to 88.71 | <i>p</i> =0.0280 |
| Sleep | 176 | 0.438 (0.307 to 0.552) | 0.436 (0.301 to 0.554) | 5.32 | 0.00 to 96.82 | <i>p</i> =0.3478 |
| Appetite and eating | 176 | 0.405 (0.271 to 0.523) | 0.442 (0.200 to 0.633) | 66.17 | 0.00 to 90.26 | <i>p</i> =0.0520 |