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**Awareness of Memory Functioning and Quality of Life for
People with Dementia and Their Caregivers**

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Doctorate in Clinical Psychology

The University of Edinburgh

May 2016

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Dedication/acknowledgements

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Thesis Abstract

Background: Unawareness of memory functioning is a key symptom of Alzheimer's disease and dementia that has been demonstrated to be related to a number of important factors for the person with dementia (PwD) and their family caregivers including quality of life and depression. Understanding more about how awareness relates to these factors will help inform how PwD and their caregivers are best supported.

Objective: A meta-analysis was conducted in order to examine the relationship between Awareness and depression in dementia. An empirical study was conducted to examine the contribution awareness provides to explaining PwDs' Quality of Life (QoL). PwD have been found to be aware of factors that affect their caregiver and so caregiver wellbeing and quality of life and the quality of the caregiving relationship were also investigated as well as more established predictors of quality of life for PwD. Both PwD self-ratings and caregiver ratings of the PwD they care for of QoL were examined as they have been shown to be affected by different factors.

Method: *Meta-analysis:* A search of electronic databases Psycinfo, Embase and Medline was conducted. A meta-analysis of correlations was undertaken examining the relationship between awareness and depression in dementia. *Empirical study:* 27 PwD and their caregivers were recruited. In order to assess the research aims the PwD completed measures of: Quality of life (Quality Of Life-Alzheimer's Disease scale), awareness of memory functioning (Memory Awareness Rating Scale-Adjusted), cognitive functioning (Addenbrooke's Cognitive Exam-R), depression and anxiety (Hospital Anxiety and Depression Scale). The caregiver completed measures of: PwD Quality of life (Quality

Of Life-Alzheimer's Disease scale proxy), Memory Functioning Scale (from MARSA), self-ratings of depression and anxiety (Hospital Anxiety and Depression Scale), activities of daily living (Disability Assessment in Dementia), Neuropsychiatric symptoms (Neuropsychiatric symptoms inventory-Questionnaire), caregiver burden (Zarit Burden Inventory), and rating of relationship quality with PwD (Burns Relationship Satisfaction Scale).

Results: *Meta-analysis:* Thirty-one studies were identified. A small association was found between awareness and depression with substantial amount of heterogeneity (-0.23). Analysing the studies that excluded major depression demonstrated that mild depression had a moderate negative relationship with awareness (-0.42). Subgroup analysis showed that the different measures of awareness used seemed to suggest different effects with depression for different measures. *Empirical study:* Awareness was not found to predict PwD rated or caregiver rated QoL. No caregiver variables predicted PwD QoL. Depression and neuropsychiatric symptoms predicted PwD QoL. Caregiver rated QoL was predicted by activities of daily living and caregiver rated quality of caregiving relationship.

Conclusions: *Meta-analysis:* The effect between mild depression and lack of awareness but not major depression supports the assertion that unawareness is a psychological response to decline in memory functioning in dementia. Neither depression nor awareness appear to be unitary constructs in PwD. *Empirical study:* Awareness not related to PwD QoL. The quality of caregiving relationship is important to QoL in a dementia context. PwD and their caregivers rate the QoL of PwD differently.

Meta-Analysis

Title A Meta-Analysis of the Relationship Between Awareness and Depression in People with Dementia.

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Abstract

Background: Unawareness of cognitive impairment is considered to be a defining symptom of people with Alzheimer's disease (AD). Unawareness and depression have been demonstrated to be important factors in determining quality of life for people with AD and their caregivers. The evidence in the literature for the relationship between awareness and depression in people with AD has been inconsistent. Some studies found a negative association while others found no association. It has also been argued that mild depression has a different relationship with awareness to major depression. There is also great variance in how awareness is conceptualised and measured.

Objectives: The purpose of this study was to determine the whether there is an effect between awareness of cognitive functioning and depression in people with AD and to determine whether level of depression or measure of awareness used affects that relationship.

Method: A search of electronic databases Psycinfo, Embase and Medline was conducted. A meta-analysis of correlations was undertaken examining the relationship between awareness and depression in dementia.

Results: Thirty-one studies were identified. A small association was found between awareness of cognitive functioning and depression with substantial amount of heterogeneity (-0.23). Analysing the studies that excluded major depression demonstrated that mild depression had a moderate negative relationship with awareness (-0.42). Subgroup analysis of the different measures of awareness used in the sample seemed to suggest that different effects with depression were present for different measures.

Conclusions: The effect between mild depression and lack of awareness but not major depression supports the assertion that unawareness is a psychological response to decline in memory functioning in dementia. Neither depression nor awareness appear to be unitary constructs in PwD.

Keywords: Awareness, Depression Dementia, Meta-Analysis, Alzheimer's disease

Introduction

Alzheimer's Disease

Alzheimer's disease (AD) is a disorder that is estimated to affect 5-7% of the population over 60 years old in most regions of the world. The number of people with AD is predicted to double by 2030 (Prince et al., 2013). The most recent estimate of the AD population in the UK was that there are 670,000 people aged over 65 with AD (2011)(Matthews et al., 2013). The burden of AD on community and inpatient settings is substantial and there are many areas where our understanding is lacking. Awareness of memory functioning and depression have been shown to be key factors in determining Quality of life in AD (Conde-Sala et al., 2013; Trigg et al., 2011) and it is important to understand their relationship in order to provide the best support for people with AD and their caregivers.

Awareness

There are multiple terms to describe lack of awareness in AD including Anosognosia (meaning lack of knowledge of disease) (Babinsky., 1914), unawareness, self-awareness, insight, and denial (Aalten et al., 2005a). Clare et al. (2012b) defined awareness as “reasonable or realistic perception or appraisal of a given aspect of one’s situation, functioning or performance, or the resulting implications, which may be expressed implicitly or explicitly.” Currently there is no agreed upon definition of awareness and precise definitions of awareness vary which make comparing research studies problematic and these definitions can vary (Aalten et al., 2005a).

Awareness in AD is variable in its presentation and severity with some people completely unaware of their difficulties while others simply minimise their difficulties and dismiss them as normal aging (Mograbi and Morris, 2014). Picton & Stuss (1994) suggested that awareness ranges across different levels from basic physiological arousal through to elements of self-perception in complex social contexts. Clare et al. (2011) built on this describing a multifactorial model acknowledging the contribution and interaction of organic and psychosocial factors with four levels of awareness; sensory registration (basic awareness of environment), performance monitoring (ability to monitor performance on a certain task), evaluative judgment (evaluation of ability in a specific domain such as memory), and meta-representation (reflection on changes of a person’s situation and their impact). It seems apparent that there are different constructs that make up awareness; however, it can be difficult to differentiate the neurologically based impaired awareness that is part of the disease process and the psychological response to changes in functioning

that manifest as denial or avoidant coping. Awareness is also likely to be affected by other factors such as depression, personality changes and psychotic experiences, consequences and the wider socio-cultural context (Clare et al., 2005a). Unawareness can present a significant challenge to care givers affecting decisions of capacity, treatment, care management and risk (Starkstein et al., 2007). There is evidence to suggest that people with AD who are more aware report a decline in quality of life more than those who are more unaware (Conde-Sala et al., 2014; Hurt et al., 2010; Trigg et al., 2011).

Most often in the literature when awareness is described it is referring to evaluative judgements regarding awareness of cognitive and memory functioning. However, some studies also discuss “awareness” when examining awareness of functioning of activities of daily living or a combination of awareness of cognitive functioning and activity functioning. There are also studies that examine the performance monitoring (e.g. awareness of performance on a task they just completed) and meta-representation levels of awareness (e.g. awareness of progression of their diagnosis). As there is no consensus in the literature on the definition of awareness this study will use it as a universal term to encompass the concepts described above. Using a more focussed definition would mean that the review would only be able to relate to proportion of the literature.

Awareness in Dementia

Lack of awareness in AD is considered to be a defining symptom of the illness and has been shown to occur more frequently in AD than in other forms of dementia

(DeBettignies et al., 1990). It is thought that this higher prevalence is accounted for to an extent by the neurobiological changes that occur with the disorder. Psychological and social factors also provide further explanation (Mograbli and Morris, 2014). Lack of awareness in AD most commonly takes the form of a person overestimating their current abilities although people who underestimate their abilities would also be considered to lack awareness. The majority of studies examining awareness have examined exclusively late onset AD patients and so it can be difficult to make generalisations regarding other dementia aetiologies such as vascular dementia (Aalten et al., 2005b). There are a small number of studies that include vascular dementia participants along with AD and have reported similar levels of awareness (Verhey et al., 1993; Zanetti et al., 1999). Young onset dementia has been demonstrated to have a different relationship with awareness to late onset. In a study comparing awareness in young onset and late onset AD it was found that unawareness seems to be more of a characteristic of late onset AD as it has been found that people with late onset AD are more than double the odds of being unaware of their cognitive deficits compared to the people with young onset AD (van Vliet et al., 2012). It has also been demonstrated that unawareness is correlated with age of onset with increase in age of onset being associated with more severe unawareness. It was suggested that the differences found in unawareness may be associated to the neurological differences between young and late onset AD (Kashiwa et al., 2005).

Awareness has been shown to present differently in People with Parkinson's disease compared to people with AD as they have been demonstrated have relatively preserved awareness in regards to memory functioning However, it was found that when memory impairment was present the participants were more likely to overestimate their abilities.

(Lehrner et al., 2015; Seltzer et al., 2001; Sitek et al., 2011). It was also found that participants who reported more symptoms of depression were also more likely to overestimate their memory functioning.

Measurement of Awareness

There are three main categories of assessments that have been used to examine awareness in AD: Clinician rating, discrepancy ratings between patients and caregiver informants or clinician ratings, and discrepancy ratings between predicted performance and actual performance (Starkstein, 2014). The object of focus for assessing awareness is variable across the different measures and types of measures with some focussing on memory functioning and others on broader domains of cognitive functioning and activities of daily living. Some methods place more emphasis on perceived current functioning, while others on perception of impact of difficulties and progression (Clare et al., 2005a). Each method also has its own assumptions.

There are a range of Clinician rating methods for assessing patient's awareness. A semi-structured or standard interview with the patient and sometimes an informant is often used where they are rated into a category of awareness ranging from a dichotomous classification to a point on a Likert scale depending on the measures used (Clare et al., 2005a). The advantages of this method are that it is quick and there is potential for answers to be explored in more depth (Sevush and Leve, 1993). Clinician ratings methods make

the assumption that awareness is a symptom that can be reliably assessed in an interview which is made more difficult by the lack of standardised diagnostic criteria and the unknown validity and reliability of the measures used (Starkstein, 2014). Clare et al. (2005) state that, while global ratings from clinicians are practical, they can miss variations within participants in different domains and these ratings will be affected by the clinician; the factors they see as most relevant how they interpret the patient's account, and their expectations is considered normal awareness.

Awareness has most often been operationalised in terms of a discrepancy between the individual's explicit responses and some kind of standard. The most common type being comparing self-report of patient's awareness against that of an informant who knows them well and calculating the discrepancy between the two ratings as the level of awareness (Clare et al., 2005a). Therefore any deviation from the informant is seen to reflect a loss of awareness. A positive score reflects that the PwD is overestimating their ability and a negative score reflects that they are underestimating. This method assumes that the informant is able to provide an accurate, objective and valid rating and caregiver ratings are known to be affected by factors such as depression or burden which can influence ratings (Starkstein, 2014). There seems to be conflicting evidence to as to the extent that this is the case. There are some studies where caregiver ratings have been demonstrated to be accurate; Clare et al. (2002) found that caregiver ratings to be comparatively more accurate than patient ratings but their accuracy overall was somewhat low. Whereas Snow et al. (2004) found that they were significantly associated with clinician ratings and Starkstein et al. (2006) showed that caregiver assessments of deficits are associated with Mini mental state exam (MMSE), a measure of symptom severity. Another limitation of

P/I discrepancy ratings is that using a simple discrepancy score also weights the overall score more heavily towards the caregiver rating (Clare et al., 2010).

A less widely used method is the prediction of performance discrepancy which is based on patient's perception of their performance on a given neuropsychological task and is scored as the difference between patient's estimation of performance and score on the test. These methods use standardised assessments with strong psychometric properties and self-report measures that generally have established validity and reliability (Clare et al., 2005a). The ecological validity of this procedure is unknown as patients may minimise functional problems while acknowledging performing poorly on a cognitive test and vice versa. Duke et al. (2002) found that there were only modest correlations between performance based methods of measuring awareness and a questionnaire-based method which would seem to suggest that using different methods of measurement may examine different aspects of awareness. This would be consistent with Clare and colleagues (2011) four level model as one is a task of performance monitoring and the other an evaluative judgement. A limitation of this method is that awareness tends more to be about functional problems rather than neuropsychological test performance (Starkstein, 2014). An additional difficulty with comparing self-ratings of everyday functioning and performance on cognitive tests is that the self-rating and performance measures may not be closely related, thus giving disproportionately high discrepancy values (Clare et al., 2005a).

Other methods of assessing have been used to evaluate awareness including self-report questionnaires and vignettes (Clare et al. 2012a). There is no definitive method to assess awareness; there are strengths and shortcomings to each procedure. Starkstein (2014)

argues that the best assessment is by an experienced clinician with an informant providing extra information. Clare et al. (2005) states that, in order to overcome the limitations of the methods used, the first step is to acknowledge that different measures may be evaluating different constructs and to be precise in how the assessment of awareness is described (e.g. measure of awareness of memory functioning).

Depression in AD

The causes of depression in AD has been shown to be complex, with family and personal history of depression, genetic factors, genetics, a common neurobiological basis with AD pathology, and a psychological reaction to changes related to the illness, all considered to be factors in its development (Mograb and Morris, 2014). The frequency of depression in awareness is estimated to be present in the range of 20-40% of cross-sectional samples, this large range is thought to be dependent on a number of factors such as severity of dementia, sample bias, and the variety of differing assessments used to measure depression (Starkstein, 2014). Nakaaki et al. (2008) state that older adults with depression often report subjective memory complaints when there is no objective evidence of a memory problem so it seems consistent that older adults with mild AD may also be more aware of their memory disturbances than AD patients without depression. There is evidence to suggest that major and minor depression are distinct disorders in AD, with major depression being associated with more severe psychopathological and neurological symptoms (Starkstein et al., 2005).

Awareness and Depression

There have been three narrative reviews which have examined the relationship between awareness and depression (Aalten et al., 2005a; Mograbi and Morris, 2014; Starkstein, 2014). However, these reviews have investigated depression as one of multiple clinical correlates and only described the literature rather than systematically evaluate it or conduct a meta-analysis. All the reviews agreed that when an association was found that the literature suggested that higher awareness is associated with more depression. However, there are a number of studies that have failed to find an association between depression and awareness (Cummings et al., 1995; DeBettignies et al., 1990; Verhey et al., 1993; Vogel et al., 2010). There are also studies that found that the association was only between mild depression and awareness but not major depression (Migliorelli et al., 1995b; Starkstein et al., 1997; Troisi et al., 1996). It has been suggested that this association may be indicative of an emotional reaction to awareness of deficits rather than experiencing some of the somatic symptoms associated with depression such as fatigue and slowness (Troisi et al., 1996). Nakaaki et al. (2008) found that patients with AD and depression may estimate their memory ability either more accurately or more negatively (underestimate their functioning) than patients without depression. The reason for this inconsistency between studies may be because different conceptual models of awareness and different assessment methods are being used as well as there being heterogeneity in sample size and level of disease severity between the studies (Aalten et al., 2005a). Mograbi & Morris (2014) concur stating that different findings may in part be due to

awareness not being a unitary concept and the associations found with depression may be dependent upon the specific type of awareness measured; for example, the association with mood and awareness of cognitive deficits may well be different to the association found with functional awareness. Therefore the use of complementary measures of awareness would help discern which constructs and facets of these two phenomena are related.

The primary aim of this study is to provide a meta-analysis of the association between awareness of cognitive functioning in AD and depression. The secondary aims are to; 1) Examine whether the relationship between the two variables is different depending on the level of depression as there is some suggestion in the literature that mild depression is more strongly associated than moderate depression 2) Examine whether how awareness is measured affects its relationship to depression, as although it is often treated as a unitary construct there is great variability in the literature as to how it is operationalised and defined.

Hypothesis 1: There will be at least a small effect between depression and awareness of cognitive functioning in AD.

Hypothesis 2: Mild depressive symptoms will have a stronger negative relationship to unawareness than moderate depression.

Hypothesis 3: The variance in effects measured by the studies will be accounted for by the variance between the different measures rather than differences in populations examined.

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Method

Inclusion criteria

The inclusion criteria were that the studies had to be 1) published in a peer reviewed journal in English, 2) the primary group of participants being investigated are people with probable Alzheimer's disease, 3) include an assessment of depression either from a standardised and validated rating scale or established diagnostic criterion, 4) include an assessment of awareness that are not items or a subscale from another measure (e.g. a single question about insight or using the awareness related questions from the Geriatric Depression Scale) or that are unstructured clinical judgement, 5) provide appropriate statistics that can be converted into an effect size for the purposes of meta-analysis, and 6) the sample in the paper is independent from other papers included in the analysis.

Awareness was broadly defined "as appraisal of one's deficits, functioning, situation" in line with the definition by Clare et al. (2012a). The study included any paper that measured depression using a standardised measure or diagnostic criteria. This study is primarily concerned with examining papers with participants who have received a diagnosis of Alzheimer's disease, papers primarily examining other forms of cognitive impairment were not included as they have been shown to have a different relationship to awareness. Alzheimer's disease or dementia was defined as meeting criteria for ICD, DSM, or the National Institute of Neurological and Communicative Disorders and Stroke criteria and the Alzheimer's Disease and Related Disorders Association criteria for probable Alzheimer's disease (NINCSD-ADRDA) (McKhann et al., 1984).

Search strategy

The electronic databases EMBASE, Medline and Psycinfo were searched to the beginning of February 2016 with the search terms: Alzheimer* OR Dementia AND Depression OR “low mood” OR “affective disorder” AND Anosognosia OR Insight OR Awareness OR Self-Awareness. The search was conducted for papers published in peer reviewed journals in English only. After duplicates were removed using the inbuilt function in the search engine, keywords and titles were screened. Then abstracts were reviewed of the remaining texts. The full texts of the remaining articles were subsequently screened and additional articles were added for screening through investigating previous relevant reviews and the bibliographies of screened articles. Papers that did not meet the inclusion criteria or did not have any data that could be used in the meta-analysis were excluded (Appendix A.). Figure.1 presents a flow chart outlining the search process and reasons for exclusion.

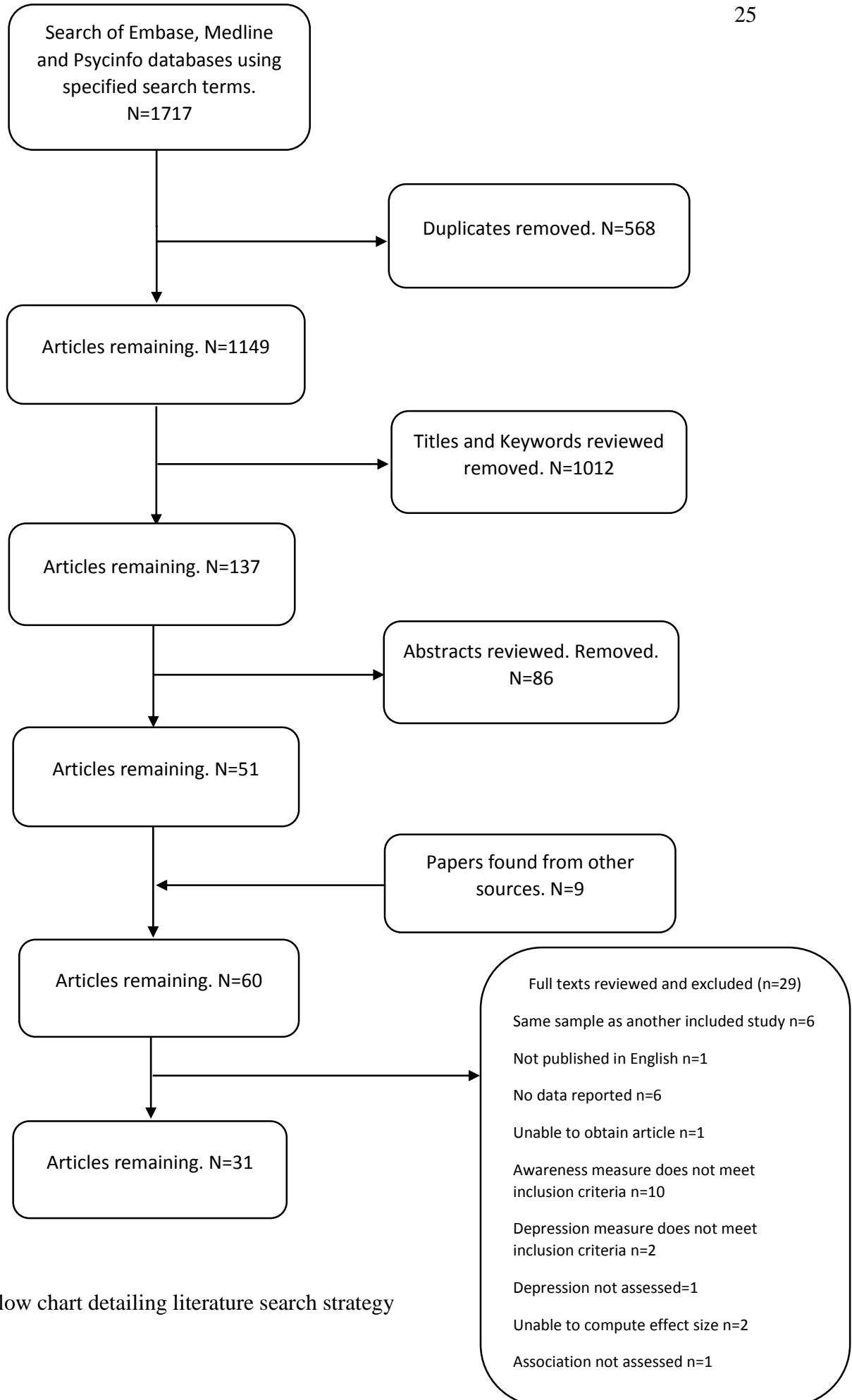


Figure 1 Flow chart detailing literature search strategy

Data extraction

The data extraction of study details was undertaken by the author and an independent co-rater using a pre-specified extraction form. Any disagreements were resolved through discussion.

As the majority of the data was correlational in nature, the different measures or coefficients were converted to Pearson's r . In the case of Spearman's rho calculations they were converted into approximate Pearson's r following Rupinski & Dunlap (1996). Standardised coefficients from multiple regression analyses have been demonstrated to be robust when considered equivalent to Pearson's r (Peterson and Brown, 2005) and so were entered into the analysis without conversion.

There are a myriad of awareness measures in the literature and of varying complexity and procedure. It is thought that discrepancy measures that compare the report of the person with dementia and an informant who knows them well is preferable to self-report or informant-only report or clinician interview. They are also the most widely used method (Clare et al., 2005a). Therefore discrepancy based measures were prioritised for data extraction. When there was no discrepancy measure other scores were extracted. Some of the measures rated higher awareness as a higher score and others rated higher unawareness as a higher score. The depression measures all rated higher scores as more depressed. The data extracted was transformed so that in all studies higher scores on the

assessment measures meant higher unawareness so that studies could be compared in the analysis.

When possible data relating only to participants with probable Alzheimer's disease was used, in some papers it was not possible to extract data only concerning this population. There are some papers included in the analysis containing a sub sample of mix or vascular dementia and some with healthy controls.

Depression is an often investigated correlate of awareness but there are few studies that examine their relationship as their primary outcome. Many of the papers examined include the associations are secondary data to main aims.

Awareness is a multi-domain concept covering many areas of a person with AD experience including cognitive functioning, daily functioning, and behavioural problems (Clare et al., 2005a). When studies reported data from measures examining different types of awareness the measure relating to memory functioning or cognitive functioning was extracted.

Data Analysis

The analysis was undertaken using the MetaXL software (http://www.epi-gear.com/index_files/metaxl.html). Meta-analysis of correlations were conducted. A random effects model was used due to the differences in measurement, sample type, analysis conducted, and the seemingly heterogeneous nature of awareness.

No quality criteria were assigned to the papers as it was not considered practical due to the number of papers included. The meta-analysis conducted weighs the papers in regards to their sample size and highlight areas of heterogeneity and potential bias and so additional quality criteria would provide little additional utility.

Results

Study Characteristics

The characteristics of the included studies are presented in Table.1. The majority of studies were cross-sectional with only two having longitudinal designs; in one of these studies the data was taken from baseline data (Aalten et al., 2006) and the other was taken from follow-up data (Starkstein et al., 1997). The majority of the studies took place in the USA, with five from South America, two from Japan, one from Taiwan and the remainder from Europe.

Table 1. *Characteristics of included studies*

Author, year, country	Sample	Design	Awareness Measure	Depression Measure	Data Extracted	Effect Size Entered
Aalten et al. (2006) The Netherlands	199 (146 AD 32 VD 2 LBD 19 mixed) 116 female age=76 (8) MMSE=18(4.7)	Longitudinal, Baseline data used	GRAD	CSDD	Odds ratios	-0.034
Bomfim et al. (2007), Brazil	21AD 9 female, age 72.4(8.5) MMSE 18.2(5) range 12-24	Cross-sectional	DIS	CSDD	Pearson's r^2	-0.219
Chen et al. (2014) Taiwan	55 Ad 32 female age=76.7(7.6) no MMSE	Cross-sectional	GRAD	CSDD	Means and standard deviations	-0.86
Cines et al. (2015) USA	104 ad age=77.55 (8.03) MMSE=24(2.64)	Cross-sectional	CRA	GDS (adapted)	Mediation model coefficient	-0.072
Clare et al. (2010) UK	80AD 43 female 76.5 (7.03) 56-89 NINCDS-ADRDA criteria 18>MMSE	Cross-sectional	MFD	HADS	Pearson's r	-0.072
Clare, et al. (2012a) UK	101 Early dementia, age=78.4 (7.71) range 51-91)	Cross-sectional	MFD	HADS	Pearson's r	-0.401
Conde-Sala et al. (2013) Spain	164AD 96 female age=77.6 (7.2) MMSE=10-28 mean 17.9 (5.8)	Cross-sectional	AQ-D	GDS	Spearman's Rho	-0.27

Table 1 continued

Author, year, country	Sample	Design	Awareness Measure	Depression Measure	Data Extracted	Effect Size Entered
Cummings et al. (1995) USA	33AD, age 71.7 (7.9) MMSE 17.5 11 female	Cross-sectional	Modified Memory Self-Rating Questionnaire	HDRS	Pearson's <i>r</i>	-0.06
Degirmenci et al. (2013) Turkey	30AD 15HC 36 female age P 71.1(8.9) 8severe on MMSE, 24 mod, 8 mild. HC 74 (6.8)	Cross-sectional	BCIS	HAMD	Pearson's <i>r</i>	-0.336
Dourado et al. (2014) Brazil	201AD age 75.6 (7.3) 58-93 130 female MMSE 20.3 (3.8)13-27	Cross-sectional	ASPIDD	CSDD	Pearson's <i>r</i>	-0.04
Feher et al. (1991) USA	38 ad age65.3 50-75MMSE 11-29	Cross-sectional	Memory Rating scale discrepancy	HDRS	Spearman's Rho	-0.3
Harwood, et al (2000) USA	91ad 7 female age 71-7(7.9) MMSE 11(8.6 range 0-28)	Cross-sectional	NRS	NRS	Pearson's <i>r</i>	-0.39
Horning et al. (2014) USA	107AD 19.91% female age 82.4 (6.6), MMSE=19.4(4.7)	Cross-sectional	NRS	NRS	Spearman's Rho	-0.22
Kashiwa et al. (2005), Japan	84AD 62 female, age=75.5(7.8) 53- 89, MMSE=19.5(5) 4-28	Cross-sectional	QAA	GDS	Pearson's <i>r</i>	-0.294
Koltai et al. (2001) USA	14AD age= 72.9(6.7) HC 8 age 73(7.2) MMSE=22.9(3.6)	Cross-sectional	EMQ.	GDS	Pearson's <i>r</i>	-0.591
Lehrner et al. (2015) Austria	967 total 43 AD 25 female age 74 (54-84), MMSE=25 (20-29)	Cross-sectional	FAI-VSRT delayed recall converted to z scores	BDI-II	Spearman's Rho	-0.140

Table.1 continued

Author, year, country	Sample	Design	Awareness Measure	Depression Measure	Data Extracted	Effect Size Entered
Mak et al. (2015) Singapore	36 AD age 72.6(8.1) 19 female, MMSE=18.2(4.3)	Cross-sectional	AQ-D	GDS	Standardised regression coefficient	-0.1
Migliorelli et al. (1995a) Italy	103AD <i>no other demographic data in available version of journal.</i>	Cross-sectional	AQ-D	HDRS	Means and standard deviations	-0.277
Nakaaki et al. (2008) Japan	42AD 23 females age 72.7(4.2) MMSE 19.7(1.4)	Cross-sectional	SMQ	PDCDAD	Correlation and ANOVA	-0.333
O'Connell et al. (2014) Canada	113 AD, age 75,81 (7.51) RBANS=66.16(10.09) (83 completed assessments)	Cross-sectional	Self-Rating of Memory Scale and RBANS	CESD	Pearson's <i>r</i>	-0.537
Ott et al (1996) USA	26AD 14 female age 72.5(7.5) MMSE 21(3.9), 16n 8 female age 70.2(5) MMSE 21 (3.9)	Cross-sectional	MOQ	CSDD	Pearson's <i>r</i>	-0.15
Seltzer (1995) USA	36AD 23 female age 74.6(6.1) MMSE=19.1(4.7) range 10-26	Cross-sectional	EMQ	CSDD	Pearson's <i>r</i>	-0.48
Sevush & Leve (1993) USA	128 AD 69 female age 69.23 (8.49) MMSE=17.07 (4.62)	Cross-sectional	Structured Clinician Interview	Structured Clinician Interview	Pearson's <i>r</i>	-0.338
Smith et al. (2000) USA	23AD 13 female age=75.3 MMSE=17.8 (4.4) range 10-26,	Cross-sectional	Assessment of Impaired Insight	GDS	Pearson's <i>r</i>	-0.26

Table.1 continued

Author, year, country	Sample	Design	Awareness Measure	Depression Measure	Data Extracted	Effect Size Entered
Snow et al. (2005) USA	66 AD 55 control 27% female age 74.36(8,21)	Cross-sectional	Clinician rated DDS	CSDD	Standardised regression coefficient	-0.17
Starkstein et al. (1996) Argentina	170ad 56 female 114 age 70.5(5.4) MMSE 18.8(6.6)	Cross-sectional	AQ-D	HDRS	Standardised regression coefficient	
Starkstein et al. (1997) Argentina	Dysphoria subgroup n=21 18 female MMSE=21 (6.4)	Longitudinal	AQ-D	HDRS, SCID	Pearson's <i>r</i>	-0.20
Starkstein et al. (2006) Argentina	750: Severe AD (n=49) 35 female age 75.3(8.3) MMSE=8.1(4.1), moderate AD(n=169) 107 female age 72.9(7.2) MMSE=16.7(4.6), mild AD (n=313) 198 female age 72.6(7) MMSE 22.3(4.1), very mild AD (219) 129 female age 68.4 (8.4) HC(n=32) 25 female age 68.2 (7.5) MMSE=29(1.1)	Cross-sectional	AQ-D	HDRS	Means and standard deviations	-0.224
Verhey et al. (1993) The Netherlands	103AD, 43 VaD, 24 other 94 females age 71.2(8.6) MMSE18.1(6.1) 2-29	Cross-sectional	GRAD	DSM-IIIR	Spearman's Rho	-0.03
(Verhülsonk et al., 2013) Germany	47AD age 76.55(7.06) 64-91 MMSE 19.66(5.88) 8-28	Cross-sectional	AQ-D	GDS, NPI, NOSGER	Standardised regression coefficient	-0.04

Table 1. *continued*

Author, year, country	Sample	Design	Awareness Measure	Depression Measure	Data Extracted	Effect Size Entered
(Vogel et al. (2010) Denmark	321 AD 176 female age 76.2(7.2) 54-92 MMSE=24.4(2.59)	Cross-sectional	ARS	CSDD	Spearman's Rho	-0.07
Zanetti et al. (1999) Italy	69 (37ad 32) VaD female 52 age 76.7(7.8) MMSE=17(6.4)	Cross-sectional	GRAD, CIR	GDS, NPI	Pearson's <i>r</i>	-0.15

Abbreviations: AD- Alzheimer's disease, HC- Healthy Controls, ad Vascular dementia

Depression scales: CSDD- Cornell Scale Depression in Dementia, GDS-Geriatric Depression Scale, HADS- Hosptial Anxiety and Depression Scale, HDRS- Hamilton Depression Rating Scale, BDI-II- Beck Depression Inventory 2, CESD- Centre for Epidemiologic Studies of Depression, DSM-IIIr Diagnostic and statistical Manual III-revised, NPI- Neuropsychiatric Inventory, NOSGER- Nurses Observation Scale for geriatric patients, SCID- Structural Clinical Interview DSM

Awareness scales: BCIS-Beck cognitive insight scale, GRAD- Guidelines for the Rating of Awareness Deficits: semi structured interview. NRS- Neurobehavioural rating scale score, ASPIDD- Assessment scale of psychosocial impact of diagnosis of dementia, ARS Anosognosia Rating scale, ASPIDD: Assessment scale of psychosocial impact of diagnosis of dementia. CIR: Clinician Insight Rating scale, MOQ-Memory observation questionnaire, RBANS repeatable battery of assessment neuropsychological status, SMQ- Short memory questionnaire discrepancy score, AQ-D Anosognosia Questionnaire Dementia, DDS- Dementia Deficits Scale. MFD Memory Functioning Discrepancy from MARS scale. FAI- Forgetfulness Assessment Inventory, VSRT- Verbal Selective Reminding Test, QAA- Quantitative assessment of Anosognosia, PDCDAD-The Provisional Diagnostic Criteria for Depression in Alzheimer's Disease.

^a Analysis conducted by Author from raw data presented in paper.

Association between Awareness and Depression

The correlation between awareness and depression is presented as a forest plot in Figure.2. The meta-analysis suggests that there was a small negative association between awareness and depression of -0.28 (CI=-0.36- -0.19, N=3468, Q=183.31, $p<0.001$, I²=84%). There was a great deal of heterogeneity in the model. The Cines et al.(2015) study stands out as an obvious outlier reporting a much larger effect size than the other studies. When the study was removed from the analysis the heterogeneity reduced considerably but was still significant suggesting multiple effects (Q=67.99, $p<0.001$, I²=57%) in the sample and the association reduced to -0.23 (CI -0.28- -0.17). In order to explain the heterogeneity found in the meta-analysis sensitivity analysis was conducted. Cines et al. (2015) was not included in any further analysis.

It was not possible to conduct systematic subgroup analysis due to inconsistent reporting across the studies included.

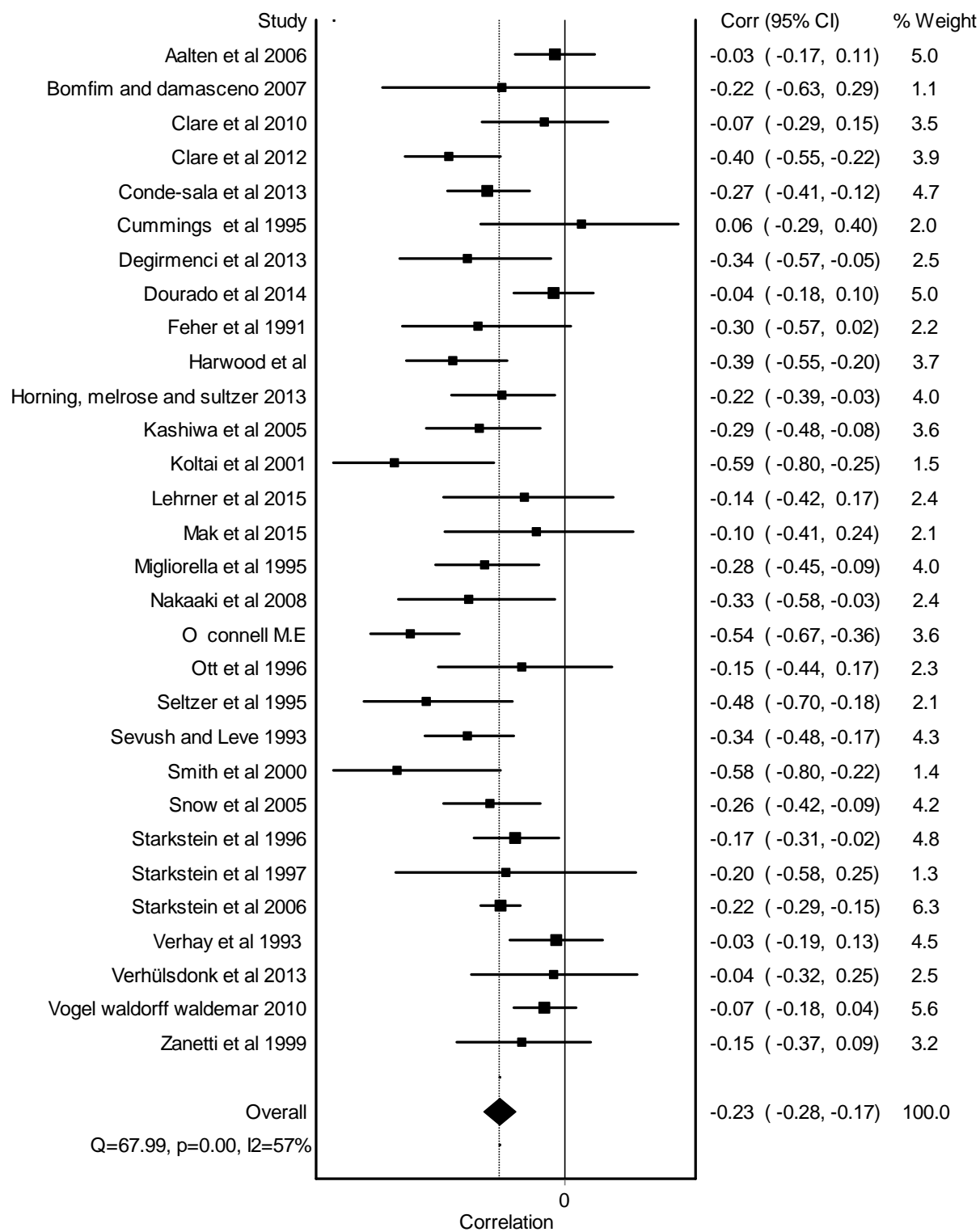


Figure 2. Forest plots for analyses of awareness and depression

Figure 3. Forest plots for analyses of awareness and depression

Subgroup analysis by participant subgroup included

In order to examine whether the impact of studies that included participants who did not have AD in their sample studies were split into sub groups based on their participants. The analysis is included in Figure 3. The mixed dementia participant subgroup (with some participants with Vascular dementia and Lewy Body dementia) estimated that the association between awareness and depression was -0.05 (CI-0.15- -0.05 , N= 414 (107 VD, 19 LBD) $Q=0.78$, $p=0.68$, $I^2=0\%$) with no heterogeneity. The subgroup with AD and Healthy controls presented with no heterogeneity suggested an association -0.26 (CI-0.38-0.12, N=207, $Q=4.83$, $p=0.67$, $I^2=0\%$). The subgroup with only AD presented with moderate heterogeneity and suggested an association -0.25 (CI-0.31-0.19, N=2847, $Q=54.83$, $p<0.001$, $I^2=58\%$). The AD only subgroup had the same level of association as when all the studies were included and the same amount of heterogeneity.

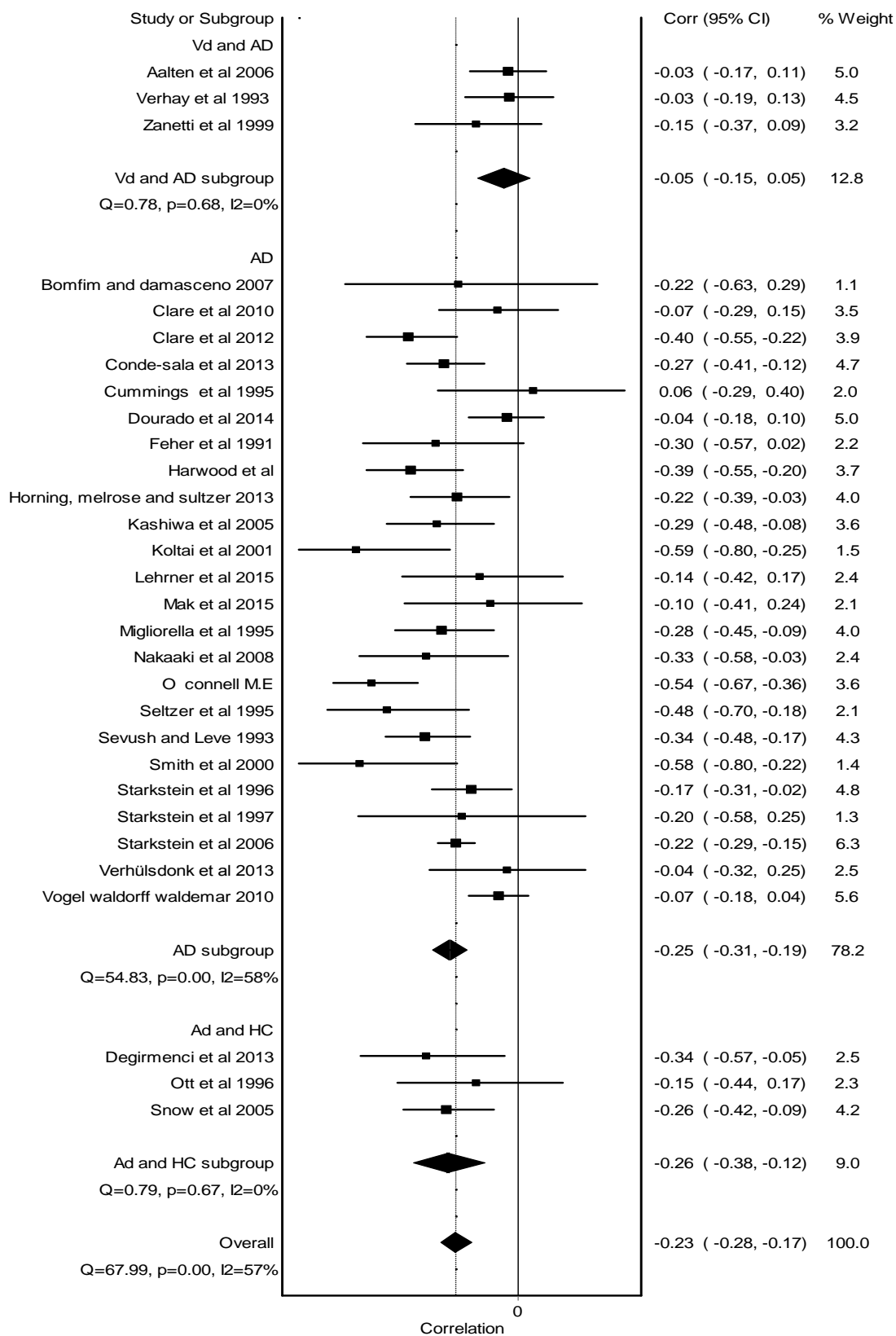


Figure 4 Forest plot for Participant population subgroup analyses of awareness and depression

Dysphoria subgroup analysis

It has been found in some studies that mild depression and dysphoria have a different relationship with awareness compared to major depression (Migliorelli, 1995a; Starkstein et al., 1997). A subgroup analysis of the meta-analysis was conducted to investigate this effect. The studies where it could be determined that their sample examined a dysphoria sample or studies where major depression was part of their exclusion criteria were analysed separately in a subgroup. Six studies contained data that met this criteria although for two of the studies the dysphoria data was not the data that was extracted (Migliorelli et al., 1995a; Starkstein et al., 1997) and so that data was extracted for a separate analysis. This analysis presented with moderate heterogeneity, suggesting a correlation of -0.35 (CI: -0.51 - -0.17 , $N=224$, $Q=8.48$, $P=0.13$, $I^2=53\%$). The heterogeneity was largely attributable to a single study (Cummings et al., 1995). Once the study was removed the meta-analysis indicated an association of -0.42 (CI -0.55 - -0.42 , $N=191$, $Q=1.90$, $p=0.75$, $I^2= 0\%$) (Figure.4) with non-significant heterogeneity and an increase in association. This result would seem consistent with the literature that there is an association between dysphoria and mild depression opposed to depression as a whole.

A mixed depression meta-analysis was conducted (Figure.5) with the dysphoria studies removed (including the whole sample data of (Migliorelli et al., 1995a; Starkstein et al., 1997) and the analysis demonstrated an association of -0.22 (CI -0.27 - -0.16 , $N=3332$, $Q=57.58$, $p<0.001$, $I^2=58\%$) with significant heterogeneity.

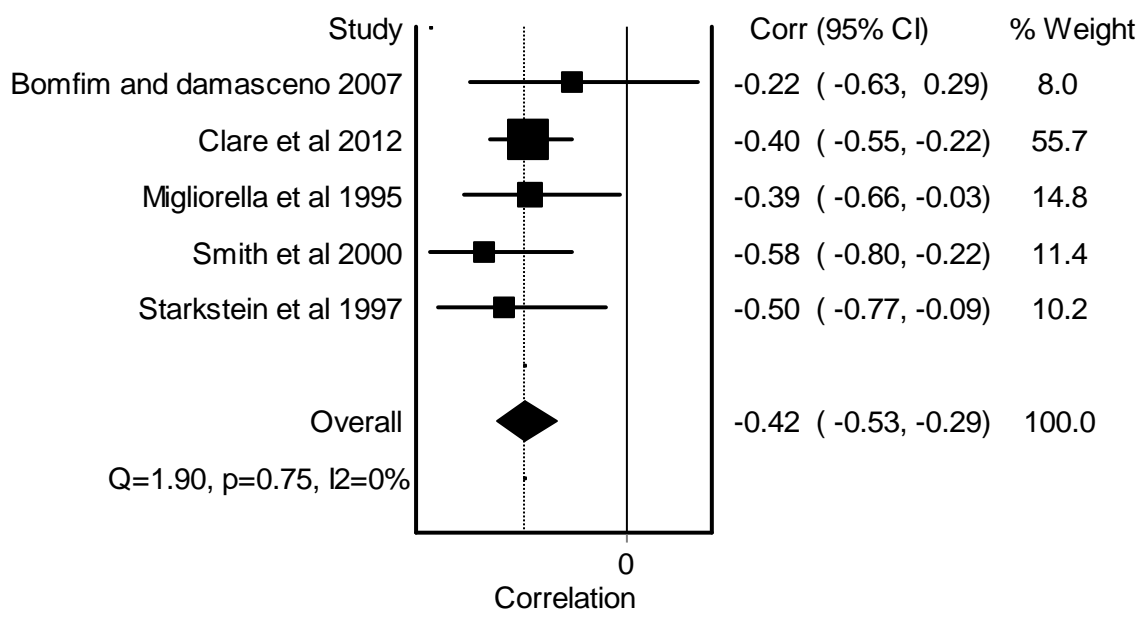


Figure 7 Forest plot for Dysphoria subgroup analyses of awareness and depression

Figure 8 Forest plot for Dysphoria subgroup analyses of awareness and depression

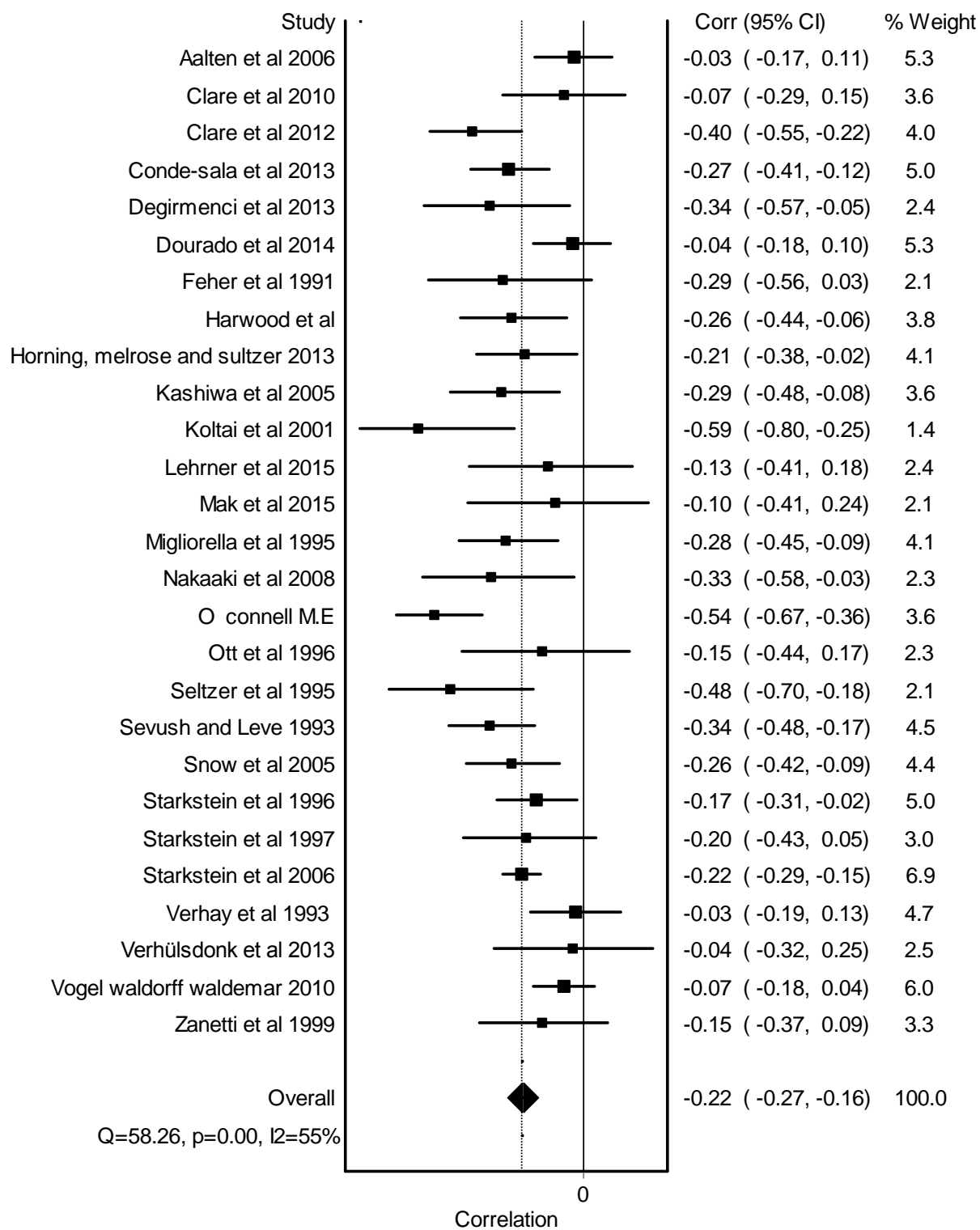


Figure 9 Forest plot for mixed depression subgroup analysis of awareness and depression

Subgroup analysis by Awareness measure

In order to explain the heterogeneity of the analysis further the studies were split into subgroups based on the awareness measure used. The analysis is presented in Figure.5. When three or more studies used the same measure then those studies were grouped together. When a measure was only used by one or two studies it was put into the subgroup for the type of awareness measure it belonged to; patient/informant (P/I) discrepancy, clinical interview, predicted performance discrepancy, or self-report. The studies which excluded major depression were not included in this analysis.

The clinician rating subgroup estimated that the association between awareness and depression was -0.32 (CI- 0.41 - -0.21 , N= 326 Q=1.11, $p=0.40$, I $^2=0\%$) with minimal heterogeneity. The GRAD (Verhay et al. 1993), a four question clinician interview scale, similarly presented with no heterogeneity but the three was a suggestion of no association -0.05 (CI- 0.15 - 0.05 , N=314, Q=0.68, $p=0.71$, I $^2=0\%$).

The P/I discrepancy subgroup estimated the association was -0.18 (CI- 0.28 - -0.07 , N=843, $p=0.06$, I $^2=51\%$) with substantial heterogeneity. The AQ-D (discrepancy) (Migliorelli et al., 1995a) presented with an association of -0.22 (CI -0.27 - -0.17 N=1391, Q=3.48, $p=0.75$, I $^2=0$) and no apparent heterogeneity.

The performance discrepancy measures suggested an association of -0.37 (CI- 0.68 - 0.06 , N=126, Q=5.62, $p=0.02$, I $^2=82\%$) with significant heterogeneity. The self-report

subgroup suggested an association of -0.44 with some non-significant heterogeneity (CI-0.066- 0.016, N=119, $Q=1.52$, $p=0.022$, $I^2=34\%$).

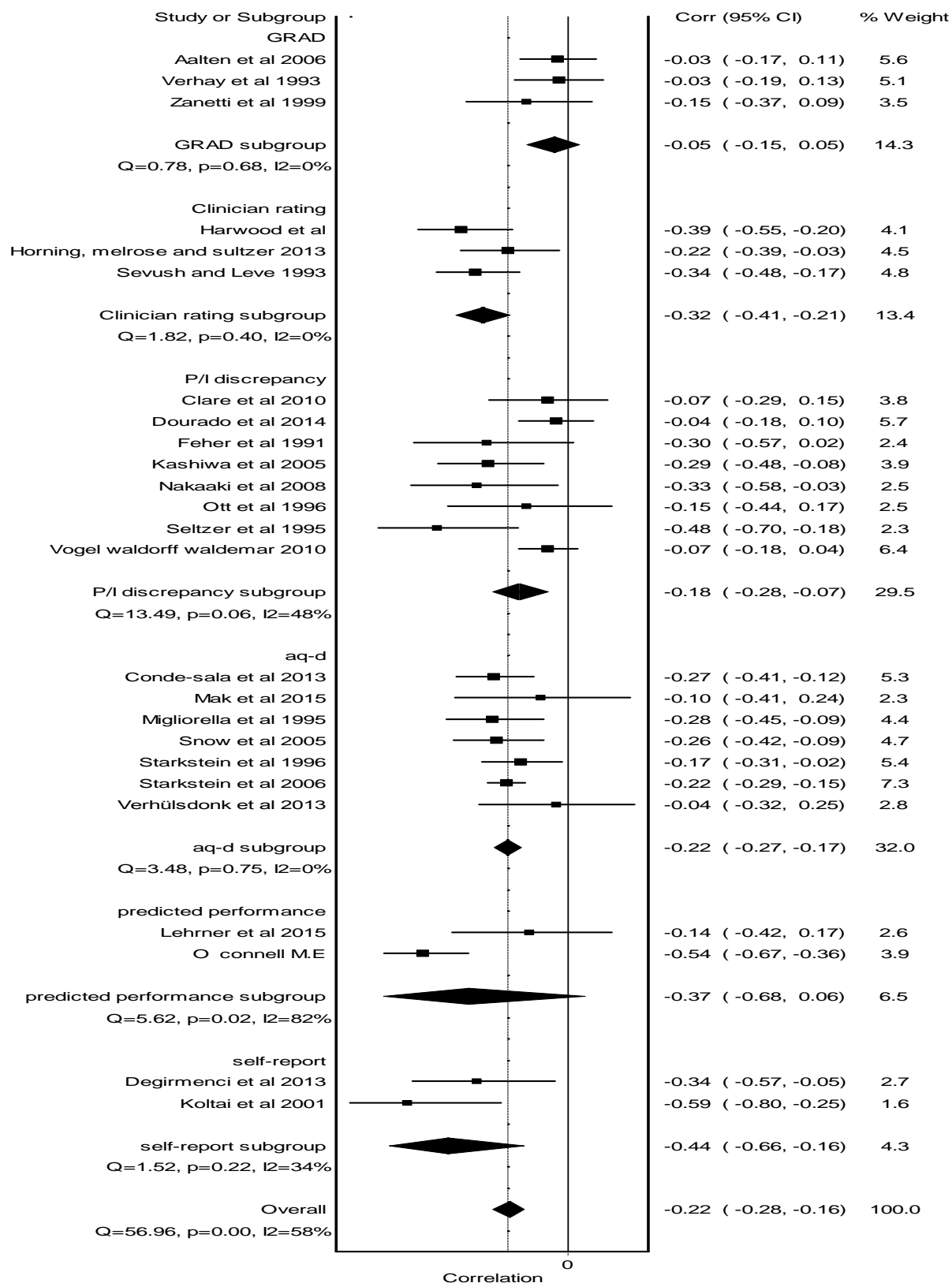


Figure 10 Forest plot for awareness measure subgroup analyses of awareness and depression

Figure 11 Forest plot for awareness measure subgroup analyses of awareness and depression

Discussion

The results of the meta-analysis suggested that there is small association between awareness and depression in the literature. With those who are more aware, they were more likely to report higher levels of depression. There was a large amount of heterogeneity suggesting that there were multiples effects being measured within the sample of studies. The heterogeneity was reduced when a clear outlier was removed (Cines et al., 2015) but was still significant which further suggested that multiple effects were present. The studies that had non-AD participants included did not affect the strength of the association or the level of heterogeneity present.

The Cines et al. (2015) study reported a much greater effect size than the other studies. It was distinct from the other studies in multiple ways; it used an unstandardised version of the GDS so the validity of measure is not known. The authors argue that this ensured the association was not driven by redundancy between the measures. The data extracted was a standardised coefficient from mediation analysis between awareness and quality of life with depression as a mediator which would mean that any shared variance would be controlled for. As this was the only study to examine this it is not possible to determine whether this study is different because it is an anomaly or that the nature of relationship between the two variables is different when quality of life and the awareness in the GDS are controlled for. Preacher & Kelley (2011) argue that using a standardised coefficient from a mediation analysis as an effect size measure is unsatisfactory as it does not convey

the full meaning of an indirect effect so it may be that the data extracted for the analysis may inaccurately represent the findings of the study further. These findings would indicate that this study was different to the other studies included, both methodologically and conceptually and therefore it was justifiable to remove it from the analysis.

Depression/ Dysphoria subgroup analysis

It has been argued that mild depression or dysphoria and major depression had different relationships with awareness, with increases in subclinical levels of depression being associated with increased awareness and major depression not being associated (Migliorelli et al., 1995b; Starkstein et al., 1997; Troisi et al., 1996). The subgroup analysis conducted in this meta-analysis supports the assertion that there are different relationships with awareness for mild and major depression. The dysphoria subgroup was found to demonstrate a much stronger association than the other studies and had zero heterogeneity suggesting the studies were examining the same effect. This subgroup did not account for all of the studies that reported a large association however, by examining the means and standard deviations of some of these studies it could be interpreted that they had a mild depression sample (Cines et al., 2015; Koltai et al., 2001; O'Connell et al., 2014). However, the studies in the mixed depression subgroup did not differentiate between levels of depression and so will likely have a range of mild, moderate and major depression within and between studies. This may account for some of the heterogeneity in effects as only studies included in the mild depression subgroup for the analysis were studies where it was clear from their methodology that they had excluded major

depression. Nakaaki et al. (2008) argued that moderate, clinical depression has a different relationship with awareness, with decreased mood leading to either more accurate or underestimation of memory functioning. This was the only study to put forward this perspective but it cannot be ruled that this effect is contributing to the heterogeneity in the analysis.

The Cummings et al. (1995) study accounted for all the heterogeneity in the dysphoria subgroup. The exclusion criteria for the sample differed greatly from the rest of the sample studies in regards to depression, excluding anyone who was currently taking antidepressants or had experienced depression in the past. This would indicate, therefore, that the sample they investigated is likely to be different from the other studies in the subgroup.

Troisi et al. (1996) argued in their study that psychological but not somatic symptoms of depression are associated with awareness. Unfortunately, it is not possible to examine this notion within this review as the majority of the depression measures used in the included studies examine a range of depression symptom types.

Awareness measures analysis

The method used to assess awareness was found to have an impact on the association between awareness and depression with some measures finding a small association and others not. The findings that different measures found different sized effects reinforces the view of Clare et al. (2005) and Snow et al. (2004) that a multi-dimensional approach

to measuring awareness is needed in order to account for the differing effects found with different measure types. The effects found in each subgroup are discussed below.

Clinician rating subgroups

From the studies that used the GRAD (Verhey et al., 1993) there was no association while those using other mixed clinician rating methods found an effect more in line with the whole sample analysis. This would seem to suggest that the lack of the association found in the studies in the subgroup was to do with the nature of the measure. These three papers are also the three papers included in the analysis that included participants with vascular dementia which may also provide some explanation for the lack of association found. The GRAD is a four question structured interview examining memory functioning, full awareness scores are given when the individual with dementia reports complaints of their memory functioning to the question “tell me about the problems you are here for?” and their responses are consistent with caregiver reports. It seems likely that people with dementia could fail to respond as desired to that question for reasons other than awareness of memory function. Therefore, this measure would be assessing individuals on more than just that object of awareness. The fact that all three studies reported a similar level of association would seem to demonstrate that the measure is consistent from the data available but the aspect of awareness it is examining appears to be different from other measures included in the analysis.

The mixed clinician rating subgroup contained a variety of measures but there was a lack of heterogeneity in effects found and a slightly higher effect was reported for this group.

This would suggest that despite the different measures used, the same effect was being measured. This would support the notion that clinicians have an expectation of what “normal” awareness is and they consider similar factors important (Clare et al., 2005a) and those factors are associated with depression.

Patient/Informant discrepancy measures subgroups

The AQ-D demonstrated no heterogeneity and a small association. The Snow et al. (2005) data included in the AQ-D analysis was comparing the patient/clinician discrepancy as the data for the patient/caregiver model was regression model was not included. Despite this difference the analysis appeared to have little affected as the results extracted are in line with other studies in the group. This demonstrates that the AQ-D consistently examined the same effect. The AQ-D is a general measure of awareness and examines two different objects of awareness, cognitive functioning and behavioural changes.

The mixed patient/informant group demonstrated moderate heterogeneity and a small association. The moderate heterogeneity may be accounted for by the range of different measures used examining different aspects of awareness. Many of the measures report that the object of awareness examined is cognitive functioning/difficulties or memory functioning/difficulties. The heterogeneity found in this subgroup would seem to suggest that these measures are not examining the same effect even though their reported object of functioning appears to be similar. This assessment method assumes that informants are able to provide objective and reliable ratings of patient awareness, the evidence as to

whether this is the case is unclear (Clare et al., 2002; Snow et al., 2004; Starkstein et al., 2006). Therefore, the notion that heterogeneity in the findings of the mixed subgroup studies could also be explained by the potentially inconsistent and unreliable informant reports cannot be ruled out.

Performance discrepancy subgroup

There were only two studies using predicted performance measures in the analysis and so it is difficult to draw conclusions about the nature of this subgroup. The neuropsychological measures the studies used examined different constructs with (Lehrner et al., 2015) examining delayed recall and (O'Connell et al., 2014) examining a performance of a number of neuropsychological tasks including memory, language, attention and visuospatial abilities, so it is unsurprising that they found such different results. Theoretically it would be expected that the performance discrepancy group would differ from the other subgroups as they examine a different level of awareness i.e. performance monitoring rather than evaluative judgement of their memory functioning.

Self-report subgroup

The self-report group suggested a small association consistent with the larger analysis and demonstrated some significant heterogeneity. Similarly, to the performance discrepancy

group it only contained two studies subgroup using different measures and so little conclusion can be drawn about the nature of this subgroup.

Limitations of the review

There were some methodological limitations to the data extraction which may have had an impact upon the findings of this analysis. As most of the data extracted was secondary data, the data needed for this review was not always a priority for the researchers to report. Some of studies screened did not report non-significant findings so could not be used in the analysis. The effect size found in the meta-analysis was small so it is not clear the effect these studies would have had on the overall correlation coefficient. Some of the studies had small sample sizes and may have just been underpowered so they may have contributed to the overall effect or they might have reduced it. Some of the included studies also did not report non-significant findings which may have been more appropriate for data extraction. Rather than not include studies it was decided to convert other statistics that were reported even if they were not the preferable measure, for example a correlation with caregiver rated depression and awareness (Starkstein et al., 2006). This may have introduced bias into the analysis as these statistics tended to be reported because they were significant. It may have also introduced more heterogeneity.

It may be that there are relevant studies that have not been included in the analysis. There were some studies that were omitted that the author was unable to obtain that seemed to be appropriate from reviewing the abstract. No attempt was made to contact authors and

obtain unpublished studies or raw data to include in the analysis as these papers would not have been subjected to peer review. It may be then that the analysis is open to the publication bias of studies with significant findings being more likely to be published. As the data being extracted was predominantly secondary data the analysis may be less effected by publication bias.

Clinical implications

This meta-analysis would seem to suggest that there are distinct relationships between mild and major depression and awareness. This would support the notion that mild depression in awareness may be a psychological response to adapting to changes in AD (Migliorelli et al., 1995b). Therefore, it would be important for services to assess awareness using a patient/informant discrepancy measure when assessing depression. A patient/informant measure should be used as this is the type of awareness measure used in the studies which found the effect. It would also be important to choose the measure of awareness depending on what aspect of awareness it was considered important to investigate such as awareness of memory functioning. Being able to identify those with awareness more readily can also be helpful in identifying how best to support those dealing with dementia as those who have awareness, would be likely to benefit from extra support and counselling whilst, those with dementia who lack awareness, it would be more appropriate to provide support to the family caregivers (Clare and Wilson, 2006).

Future Research

This analysis illustrates that only mild depressive symptoms are associated with awareness. Further research is needed to determine whether the depressive symptoms associated with awareness are psychological responses and the factors that influence the responses people tend to make. It also means that it would be important to examine further relationship that other psychological responses such as anxiety and distress have with different types of awareness. There is already some evidence to suggest that these factors are associated (Clare et al., 2011). It is also important that future research is conducted with measures that have a clear object of awareness.

Conclusions

The meta-analysis conducted suggests that there is small effect between depression and awareness. There appear to be multiple effects present. Mild depression appears to have a separate moderate effect with awareness. It would seem that the different methods of assessing awareness are likely to be measuring different aspects of awareness and that these aspects have differing relationships with depression. These findings demonstrate that neither depression nor awareness are unitary concepts in AD and therefore highlights the importance when assessing them of utilising a multi-dimensional approach.

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Journal Article

Title: Awareness of Memory Functioning and Quality of Life for People with Dementia and Their Caregivers.

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Abstract

Background: Unawareness of memory functioning is a key symptom of Alzheimer's disease and dementia that has been demonstrated to be related to Quality of Life (QoL) and other important factors for the person with dementia (PwD) and their family caregivers. Understanding more about how awareness relates to these factors will help inform how PwD and their caregivers are best supported.

Objective: The present study examined the contribution awareness and caregiver related factors provide to explaining PwDs' QoL. Both PwD self-ratings and caregiver ratings of the PwD they care for of QoL were examined as they have been shown to be affected by different factors.

Method: 27 PwD and their caregivers were recruited. In order to assess the research aims the PwD completed measures of: Quality of life (Quality Of Life-Alzheimer's Disease scale), awareness of memory functioning, cognitive functioning, depression and anxiety. The caregiver completed measures of: PwD Quality of life, memory functioning proxy, self-ratings of depression and anxiety, activities of daily living, Neuropsychiatric symptoms, caregiver burden, and relationship quality with PwD.

Results: Awareness was not found to predict PwD or caregiver rated PwD QoL. No caregiver variables predicted PwD QoL. Depression and neuropsychiatric symptoms predicted PwD QoL. Caregiver rated QoL was predicted by activities of daily living and caregiver rated quality of caregiving relationship.

Conclusions: Awareness was not found to be related to PwD or caregiver PwD QoL. The quality of caregiving relationship is important to QoL in a dementia context. PwD and their caregivers rate the QoL of PwD differently.

Introduction

Quality of life in Alzheimer's disease and Dementia

Alzheimer's disease (AD) is a chronic, progressive illness which often leads to significant emotional and physical distress as well as an array of complex behaviours that challenge. Many people with dementia (PwD) (of which AD is one of the most common forms of) have to move into care homes when their needs become too great as the illness progresses. Those who remain at home are often primarily reliant upon informal caregivers most frequently spouses and adult children. Informal caregiving is the act and experience of providing help and assistance to relatives or friends who are unable to provide for themselves (Hunt, 2003). It is estimated that for every thousand people with dementia there are 850 people acting as primary caregivers (Knapp et al., 2007; NICE, 2006). These factors suggest that research and interventions should focus on further understanding and measuring Quality of Life (QoL) or Health related QoL (HRQL) in Alzheimer's disease and dementia as well as cognition and behaviour (Banerjee et al., 2009). There is no clear definition of QoL in dementia but there is agreement about what many of the key components are; ability to experience positive emotions, enjoyment and feelings of belonging, and absence of depressed mood and anxiety are generally agreed to be

important factors in QoL in dementia. There is disagreement, however, about the breadth of the definition as, if it is too broad, it starts to lose utility and become reflective of other symptoms of the disease such as functional impairment (Ready et al., 2004).

The most common ways of measuring QoL is to use self-report assessments (QoLp) or informant/ caregiver rated assessments (QoLc)(Selai et al., 2001). Measuring self-rated QoL can be difficult due to poor recall, time perception, insight and communication in many PwD. The literature seems to suggest that self-report QoL ratings of PwD can have good validity and reliability in the majority of cases in mild to moderate dementia (Banerjee et al., 2009). Karlawish et al. (2001) demonstrated caregivers of people with mild to moderate dementia could provide ratings of patient QoL with good test-retest reliability. caregiver proxy and PwD ratings of QoL have been found to be strongly associated (Thomas et al., 2006) although caregivers are have been found to rate QoL lower than PwD and that disagreement was shown to be associated with lack of awareness (Vogel et al., 2006).

Nature of Awareness in Dementia

One variable that has received much focus in recent studies in terms of what determines QoL is “awareness of symptoms” or “insight”. The terms Anosognosia, unawareness, and denial of illness have also been used to describe this phenomenon (Clare, 2004). There is no agreed upon definition of awareness (as it will be referred to in this study) but it can be defined as the “reasonable or realistic perception or appraisal of a given aspect of one’s

situation, functioning or performance, or the resulting implications, which may be expressed implicitly or explicitly.”(Clare et al., 2012b). In AD, when awareness is examined it is most frequently referring to the symptom of lack of awareness of memory/ cognitive functioning, for the purposes of this study when awareness is discussed it will be referring to awareness of memory functioning unless otherwise stated. A four factor biopsychosocial theoretical model of awareness has been proposed which identifies awareness phenomena operating at different levels: sensory registration (basic awareness of environment), performance monitoring (ability to monitor performance on a certain task), evaluative judgment (evaluation of ability in a specific domain such as memory), and meta-representation (reflection on changes of a person’s situation and their impact)(Clare et al., 2011b). This is a recent new model and much of the literature does not conceptualise awareness using this model or even differentiate between the levels of awareness. Most measures used in studies investigating awareness examine the evaluative judgement level of the model although there are some studies examining performance monitoring awareness (Lehrner et al., 2015; Woods et al., 2014). Awareness is a complex, multifactorial construct requiring precise in-depth analysis to understand each of the proposed levels and explain the contribution made by organic and psychosocial factors in influencing those levels. Due to its complex nature it is important to acknowledge that different measures examining awareness may be evaluating different constructs and so it is important to be precise in how assessments of awareness are described (Clare et al., 2005a). In order to be consistent with the majority of the literature this study is concerned with examining the evaluative judgement level of awareness.

Influence of Awareness on Quality of Life

Banerjee et al. (2009) reported in a systematic review of studies of determinants of QoL up to 2007 that awareness (defined simply and broadly as “insight”) was not found to be associated with QoL in early dementia and that there was a lack of data investigating moderate to severe dementia. Since the review was published there have been a number of studies suggesting that increased awareness is related to lower QoL. It has been argued that unawareness may be protective for PwD from comprehending the changes they are experiencing and is often reported by caregivers that they feel that this is the case (Hurt et al., 2010). Hurt et al. (2010) demonstrated that awareness to be predictive of QoL in PwD in regression analyses for both mild and moderate dementia with impaired awareness being associated with better QoL. However, awareness in this study was measured by a single dichotomous item rather than a validated measure of awareness. Trigg et al. (2011) found a similar association using the Memory Functioning Scale from the Memory Awareness Rating Scale (MARS), a validated and reliable measure of awareness and found that awareness was the strongest predictor of QoL ratings (as rated by Bath Assessment of Subjective Quality of Life in Dementia (BASQID)) with activity performance and enjoyment of activities also being significant predictors in a sample of people with mild Alzheimer's disease. Conde-Sala et al. (2014) also found awareness to be the strongest predictor of self-rated QoL in PwD (measured by QOL-AD), using the Anosognosia questionnaire- Dementia (Migliorelli et al., 1995a) which examines cognitive awareness and behavioural changes. Awareness was also found to be a significant predictor in caregiver rated QoL of PwD although functional abilities was the

strongest predictor. Awareness was also the strongest predictor of the discrepancies between the ratings of caregivers and PwD. Woods et al. (2014) demonstrated that awareness (memory functioning discrepancy scores and functional activities discrepancy scores) was associated with QoLp (QOL-AD) in bivariate correlations but when they were entered into their regression model with other variables they were no longer significant predictors and they concluded that awareness plays little, if any, role in predicting QoLp.

Depression and Awareness in relation to Quality of life

The literature on depression and awareness suggested that higher awareness is associated with more depression. However, there are a number of studies that have failed to find an association between depression and awareness (Aalten et al., 2005a; Mograbi and Morris, 2014; Starkstein, 2014). There are also studies that found that the association was only between mild depression and awareness but not major depression (Migliorelli et al., 1995b; Starkstein et al., 1997); in particular associated with psychological symptoms of depression (mood, ideation, anxiety) rather somatic symptoms (fatigue, slowness). It has been suggested that mild depression in awareness may indicate an emotional reaction to awareness of functional deficits and that it may be protective for them, a perspective often reported by caregivers (Hurt et al., 2010; Migliorelli et al., 1995b).

Depression has consistently been established as a strong predictor of low QoL when rated by PwD (Banerjee et al., 2009; Conde-Sala et al., 2014; Hurt et al., 2010; Naglie et al., 2011a). This makes intuitive sense as depression and mood is often considered a key

component of QoL. Woods et al. (2014) demonstrated through mediation analysis that the relationship between awareness and QoLp was mediated by depression and self-concept. Cines et al. (2015) also reported that awareness and QoL had medium to large indirect association via depressed mood. A modified geriatric depression scale was used in the study with awareness related items removed so there was no overlap between the measures. These studies argue that the association between awareness and QoLp is dependent on depression. This brings into question the findings of Trigg et al. (2011) in relation to awareness of memory functioning and QoLp as a measure of depression was not included in their model and so any variance that could potentially explained by depression was not accounted for.

Person with Dementia self-ratings of Quality of Life

As well as examining depression and awareness in relation to QoLp, there have been a number of studies examining factors that predict PwD ratings of their own QoL particularly in recent years. There is a large variation in the variables that have been included in each study's regression models which makes it difficult to compare the studies and draw conclusions about the respective contributions each variable provides to explaining QoLp.

The most comprehensive study examining predictors of QoLp in terms of number of variables examined was Woods et al. (2014) in their study of early stage dementia in Wales. They conducted six initial models examining different domains (person with dementia domains: background, psychosocial, and neuropsychological, Caregiver ratings

of PwD, caregiver self-ratings and background variables, and Awareness) and then derived their final model from the significant predictors in those domains. Their final model explained 57% of the variance in their sample, a larger proportion than other models have reported (Naglie et al., 2011a; Orgeta et al., 2015) and comparable with Conde-Sala et al. (2014). The model included depression, severity of irritability (an item from the Neuropsychiatric inventory), self-concept (a person's self-knowledge), PwD rated quality of relationship, and male gender as significant predictors. Other large studies have demonstrated that neuropsychiatric symptoms (behaviours that challenge) significantly negative predict QoLp (Conde-Sala et al., 2014), although Naglie et al. (2011a) found them to only explain a small amount of variance in their large Canadian multisite study. These studies examined total scores of the measure rather than examining the items individually. Positive ratings of the relationship to the caregiver has also been shown to be a predictor of QoLp in other studies, both in a cross-sectional study (Menne et al., 2009) and in a longitudinal study although caregiver rated quality of relationship was not found to predictive (Clare et al., 2014). PwD rated Quality of caregiving relationship has not investigated as frequently as other variables but its positive relationship with QoLp is a consistent finding. The caregiver participants in the studies were mostly spousal caregivers with adult children making up the majority of the remaining participants.

Banerjee et al. (2009) stated in their review that there was little evidence that activity limitation had an impact upon QoLp. Since that review was published a number of studies have supported that position (Gary Naglie et al., 2011; Woods et al., 2014) and some

studies that have found an increase in activities of daily living leads increased QoLp (Conde-Sala et al., 2014; Trigg et al., 2011).

The evidence in the literature would seem to suggest that caregiver burden/ caregiver stress does not predict QoLp. Some of the large studies of have found that it is not predictive of QoLp (Conde-Sala et al., 2014; Naglie et al., 2011a). Orgeta et al. (2015) found caregiver burden to be the only significant predictor of QoLp in their model of caregiver factors and explained a very small amount of variance (3%). It was only entered with caregiver wellbeing and self-rated health which were not significant predictors and it seems unlikely that if it were entered with stronger predictors of QoLp that it would remain a significant predictor. Taking these factors into account this makes this finding consistent with Woods et al. (2014) who showed that caregiver burden was associated with QoLp but was not a significant predictor in their caregiver self-rating model of QoLp.

Caregiver ratings of Quality of Life for person with dementia they care for

Caregiver ratings of PwD QoL have not received the same amount of attention as PwD ratings but it is important to examine factors determining their ratings as they are often considered the most accurate account of how the PwD they care for is feeling. It seems apparent in the literature that the way that caregivers appraise PwD QoL is different to the PwD themselves, variables that do not seem to be predictors of QoLp have been demonstrated to be predictors of QoLc. Unlike in PwD self-ratings of QoL Activity limitation/ activities of daily living has been consistently shown to be a strong predictor across studies of PwD in community settings with increases in ability to take part in daily activities leading to increases in QoL (Conde-Sala et al., 2014; G Naglie et al., 2011b;

Orgeta et al., 2015; Snow et al., 2005a). It has been shown to be an important predictor of QoLc in care home residents as well (Sloane et al.2005). There is somewhat strong evidence that Neuropsychiatric symptoms are negatively associated with QoL ratings by caregivers (Banerjee et al., 2006; Hoe et al., 2007; Karlawish et al., 2001) although some studies have not found the relationship (Naglie et al., 2011b). Similarly caregiver burden has been demonstrated to be predictive of PwD QoL by some large studies models (Josep L Conde-Sala et al., 2014; Orgeta et al., 2015) but not in others (G Naglie et al., 2011).

PwD/Caregiver ratings discrepancies

It is clear that from previous research PwD appraise ratings of their own QoL differently from their caregivers. Fernanda et al. (2013) showed that awareness of disease and depressive symptoms, played an important role in the differences between the self-reported QoL ratings and the caregivers' QoL ratings. Conde-Sala et al. (2014) furthered this finding also showing that awareness and depression were predicative of the discrepancies in ratings but also showing that severity of dementia and caregiver gender were predictive. Gitlin et al. (2014) suggested that the disparity in ratings of PwD and caregivers may be due to caregivers viewing PwD as suffering while higher ratings may be due to caregivers viewing PwD as having greater capacity than they actually have. In a study examining caregiver burden and patient QoL rated by patients and caregivers, half of the caregivers of PwD thought their ratings of patient QoL would be different to how the patient would rate them. It was suggested that this could be attributed to the caregiver's experience of depression and burden leading them to view the situation more negatively

(Karlavish et al., 2001). Both PwD and caregiver perspectives need to be considered and it may be that caregivers would benefit from interventions that improve their understanding of PwD needs, perspectives, and capabilities to improve quality of life for both groups (Gitlin et al., 2014).

Caregiver mental health and wellbeing and quality of life

One area that has received limited investigation is the relationship that caregiver's own wellbeing and QoL has with ratings of PwD QoL. It has been demonstrated that a significant proportion of PwD are aware of their caregiver's anxiety and psychological health and while that may mean they are more able to in turn support their caregiver it may also mean that they become distressed themselves. Awareness of caregiver's psychological health awareness was found to be independent awareness of memory functioning therefore suggesting that those with poor memory functioning awareness may have an awareness of their caregiver's emotional state (Ablitt et al., 2010). This awareness combined with the finding that caregivers are more likely to report poor QoL compared to aged matched peers in the general population (Argimon et al., 2004) would seem to suggest that caregiver wellbeing is likely to have an effect upon PwD QoL. There is some evidence to suggest this is the case. Increases in caregiver mental health has been shown to be associated with increases in QoLp (Argimon et al., 2004). Caregiver QoL has been found to significantly predict caregiver rated QoL in a model along with NPI and activity limitation. It was also found that caregiver depression related to patient depression and partially condition PwD QoL (Thomas et al., 2006), This was with a moderate to severe

dementia sample whereas much of the research literature has examined mild dementia. Caregiver depression has been demonstrated to significantly predict caregiver rated QoL in a model along with patient depression and activity limitation (Snow et al., 2005a). However, caregiver mental health measured by GHQ was found to not be a significant predictor of QoLp, with NPI and age being the only significant predictors of QoLp in that model (Banerjee et al., 2006).

Research questions and Hypotheses

The present study aims to investigate the factors influencing PwD QoL as measured by the QOL-AD with particular focus on awareness of memory functioning (MF) and variables relating to the caregiver and caregiving relationship. By understanding more about the nature of awareness and factors impacting on QoL means that interventions can be tailored more to people's needs. It has been demonstrated that caregivers appraise PwD QoL differently to self-report and so it is important to understand both perspectives. Particularly as caregiver perceptions of PwD and their QoL are frequently how clinicians are informed of PwD wellbeing. It has also been shown that there are multiple levels to awareness and so it is important to examine how differing levels relate to PwD QoL, namely evaluative judgements of memory functioning and performance monitoring of memory functioning. There is some evidence to suggest that awareness of memory functioning is related to PwD QoL but at this time its relationship is unclear. It is important to examine variable's relating to caregivers wellbeing and Quality of Life as it has been

shown that caregivers' distress and their responses to it can have an impact upon the PwD (Ablitt et al., 2010). Low caregiver QoL has also been demonstrated to be a predictor for admission of PwD to a nursing home (Argimon et al., 2005). PwD rated relationship quality has been found to be predictive of QoLp and therefore it would seem that caregivers' perception of relationship quality influence QoLc. Much of the research examining awareness has focussed on early stage dementia and it was planned to include more moderately cognitively impaired participants and the adjusted version of the Memory Awareness Rating Scale (MARSA).

Research question 1: Does awareness of memory functioning and factors affecting caregivers (caregiver-rated relationship quality, caregiver burden caregiver wellbeing and quality of life) significantly predict PwD ratings of their own Quality of life?

Hypothesis 1: Increases in awareness of memory functioning will significantly predict decreases in PwD ratings of their quality of life. Increases in caregiver rated relationship quality, caregiver wellbeing and quality of life will significantly predict increases in PwD ratings of their quality of life.

Research question 2: Do awareness of memory functioning and factors affecting caregivers significantly predict how caregivers rate quality of life for the PwD they care for?

Hypothesis 2: Increases in awareness of memory functioning will significantly predict decreases in caregiver ratings of quality of life for the PwD they care for. Increases in caregiver rated relationship quality, caregiver wellbeing and quality of life will

significantly predict increases in caregiver ratings of quality of life for the PwD they care for.

Secondary research question: Does awareness predict caregiver quality of life?

Hypothesis: Decreases in the level of PwD awareness will predict significant decreases in caregiver quality of life.

Method

Design

The study used a cross-sectional design, using hierarchical multiple regression analyses to investigate the relationships between the criterion variable, patient rated quality of life and patient and caregiver predictor variables of; patient and caregiver mood, caregiver burden, behaviour that challenge, caregiver quality of life, relationship quality and awareness (patient/ informant discrepancy ratings and predicted performance).

This study presents cross-sectional data from initial assessments of a longitudinal study examining awareness and quality of life in people with mild to moderate dementia. Ethical approval for the study was granted by University of Edinburgh and NHS Lothian Ethics Committees (Appendix B.)

Participants

The sample comprises 27 people with mild to moderate dementia and their caregivers who were selected from patients diagnosed with Alzheimer's disease who are supported by caregivers and were involved with the Community Mental Health Team-Older Adults. The Dementia Link and Community Psychiatric Nurses' caseloads were screened to identify eligible participants. People with dementia who were identified as potentially eligible were invited to consider participating in the study when they are attended clinics or appointments with nurses and then were approached by researchers if agreeable. Participants were seen at home and people with dementia were seen separately to their caregivers. All gave informed consent. In order to minimise participant burden patients were typically seen in two one hour appointments and were supported to complete measures. If participants did not feel they were able to complete that length of appointment shorter appointments were offered. Researchers regularly checked with participants to determine how they were coping with the measures and if there were any indications that they were struggling it was suggested that an additional appointment was made.

Inclusion criteria

- Patient participant must have a diagnosis of Alzheimer's disease or mixed dementia (Alzheimer's/ Vascular dementia) from their consultant psychiatrist
- Patient participant must have a Mini Mental State examination (MMSE) (Folstein et al., 1975) score above 12 at their last appointment with the Dementia Link Nurse. The MMSE is a dementia screening tool routinely used and scores under 12 are considered to suggest severe dementia.
- The caregiver participant must spend at least 4 hours per day at least 4 days per week with the patient and have some knowledge about the patient's daytime and night time behaviours (as recommended by the Neuropsychiatric Inventory which has the most conservative definition of all the measures being proposed).
- Patient participant aged over 65.
- Patient participant must be receiving cognitive enhancer medication or eligible to receive cognitive enhancer medication.
- Participants must have sufficient visual and auditory sensory performance to complete measures.
- Participants must be able to speak sufficient English to complete assessments.

Exclusion criteria

- The presence of dementia of non-Alzheimer's dementia pathology in the patient participant, including Parkinson's disease, Frontotemporal dementia.

- The presence of clinically significant acquired brain injury, substance misuse or other factor contributing to abnormal brain functioning in the patient participant.
- Clinically significant functional psychiatric symptomology for patient participant.
- A diagnosis of moderate, severe or profound learning disability for either participant.
- Delirium in patient participant.
- Caregiver participants must be free of dementia or other significant mental health problem.

Demographic Questionnaire

A questionnaire collecting demographic information (Appendix I.) was administered examining; the characteristics of the patient and caregiver: Age, gender, patient dementia diagnosis, socioeconomic status (profession/previous profession), and other health conditions/support needs. The characteristics of relationship: relationship of caregiver to patient, living arrangements, and any additional support provided from other sources.

Quality of life- Alzheimer's disease

Quality of life-AD (QOL-AD) (Logsdon et al., 1999) is a 13-item measure developed to rate the quality of life of people with dementia with reports from both the patient and caregiver. Higher scores suggest better quality of life. The caregiver scale is administered in self-report format while the patient scale is administered in an interview format. The

QOL-AD has been found to have good reliability and validity for those scoring over 10 on the MMSE, demonstrating good concurrent validity with measures of depression and everyday functioning (Logsdon et al., 2002). It was the preferred measures in an evaluation of outcomes measures in psychosocial interventions in dementia (Moniz-Cook et al., 2008). The patient rated and caregiver rated QOLAD were found to be highly reliable in this sample ($\alpha=0.862$ and $\alpha=0.871$ respectively).

Memory Awareness Rating Scale Adjusted

Memory Awareness Rating Scale Adjusted (MARSA) (Hardy et al., 2006) is an updated version of the Memory Awareness Rating Scale (MARS) (Clare et al., 2002) developed to be more suitable for use with a broader range of participants such as those with moderate Alzheimer's disease. The MARSA has two scales and generates two discrepancy scores. The first is the patient/informant discrepancy score derived from the participants and informants' responses to the Memory Functioning scale (MFS). The MFS items ask participants about their own perceived memory ability in a range of typical everyday scenarios and the same items are given to their caregiver. A positive discrepancy suggests a participants' overestimation in their abilities and a negative discrepancy suggests an underestimation. The discrepancy is calculated using a corrected discrepancy $((MFS-P - MFS-C)/((MFS-P + MFS-C)/2))$ so that equal weight is given to both ratings that subtracting the caregiver score from the PwD score does not achieve (Clare et al., 2010). This scale examines the evaluative judgement level of awareness. In the second scale the participant is asked to complete some memory tasks and they are asked how they thought they performed. Their objective performance is then compared to their perceived

performance and an objective/perceived performance discrepancy score is calculated. In the MARSA the tasks from the MARS based on the Rivermead Behavioural Memory Test (Wilson., et al, 1985) and Severe Impairment Battery (Panisset et al., 1994). This scale examines the performance monitoring level of awareness. The MARSA was found to have good internal consistency and good test-retest reliability (Hardy et al., 2006). The scales of the MARSA were all found to be reliable in this sample (MFS-C $\alpha=0.868$, MFS-P $\alpha=0.897$ MARSA task $\alpha=0.795$ MARSA task self-rating $\alpha=0.714$)

Adenbrooke's Cognitive Examination Revised

The Adenbrooke's Cognitive Examination Revised (ACE-R) is a well validated and reliable screening measure of cognitive impairment and has been found to be useful in detecting and differentiating between different forms of dementia (Hsieh et al., 2013). In a systematic review of the ACE-R's validity and clinical utility it was found to differentiate well between those with and those without cognitive impairment (Crawford et al., 2012). The internal consistency of this scale was high in this sample ($\alpha=0.830$)

WHOQOL- BREF

The World Health Organisation Quality of life Brief (WHOQOL-BREF) is a 26 item question that examines four domains relating to quality of life: physical health, social relationships, psychological and environment and an item on overall quality of life and general health (WHOQOL group, 1998a). It has been demonstrated to have good discriminant and content validity, internal consistency and test-retest reliability

(WHOQOL group, 1998a). The social relationship subscale was not found to be reliable in this sample ($\alpha=0.047$) and so was not included in any of the analysis. The other subscales were found to be reliable (physical health $\alpha=0.795$, psychological $\alpha=0.707$, environment $\alpha=0.721$).

Zarit Burden Interview

Zarit Burden Interview (ZBI) (Zarit et al., 1980) is a 22 item self-report measure administered to the caregiver. It assesses the burden the caregiver feels related to functional/behavioural impairments and day to day living with the patient. The ZBI has been found to be reliable and have good construct validity, particularly in relationship to depressive mood and challenging behaviour (Hebert., et al 2000). The ZBI was found to be highly reliable in this sample ($\alpha=0.906$).

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) is a 14 item self-report measure with two sub-scales, one measuring depression and one measuring anxiety. It has been shown to have good reliability and validity and to be applicable in community settings as a screening tool (Snaith, 2003). Dennis et al., (2007) found that the anxiety sub-scale of the HADS while not completely adequate, along with BAI, was the most suitable measure to use with older adults. It also has been demonstrated to have a clear two factor structure, good homogeneity and internal consistency (Mykletun et al., 2001). The HADS has been demonstrated to adequately screen depression in those

with dementia (Wands et al., 1990). It was also chosen for use in the study as not all caregiver participants in the study would be older adults. The patient rated and caregiver rated HADS were found to be highly reliable in this sample (patient: Anxiety $\alpha=0.785$, Depression $\alpha=0.829$ caregiver: Anxiety $\alpha=0.820$ Depression $\alpha=0.774$).

Burns Relationship Satisfaction Scale

The Burns Relationship Satisfaction Scale (BRSS) (Burns & Sayers, 1988) is a 7 item self-report measure that assesses different areas of relationship satisfaction including communication and openness, conflict, affection and intimacy and overall satisfaction with the relationship. It has been demonstrated to have internal consistency and to correlate strongly with other relationship satisfaction measures, Dyadic Adjustment scale and Norton's Quality of Marriage Index (Heyman et al., 1994). The BRSS was found to be highly reliable in this sample ($\alpha=0.964$).

Neuropsychiatric Inventory Questionnaire

The Neuropsychiatric Inventory Questionnaire (NPI-Q) (Kaufers et al., 2000) is based on the Neuropsychiatric Inventory (Cummings, 1997). The NPI is a short structured interview conducted with a caregiver of a person with dementia. It assesses the severity, frequency and distress of 12 types of disturbances common in dementia. The NPI-Q was designed as a brief 12 item self-report measure; caregivers are asked if a symptom is present, to rate the severity of the symptom and the level of distress it causes them. A total score can be derived by multiplying the distress scale by severity of symptoms. The NPI-

Q has demonstrated good test-retest reliability and convergent validity with the NPI (Kaufer et al., 2000) which has established content validity, concurrent validity, inter-rater reliability, and test-retest reliability (Cummings, 1997). The NPI-Q subscales were found to be highly reliable in this sample (Severity $\alpha=0.835$ distress $\alpha=0.856$).

Disability Assessment for Dementia

The Disability assessment for Dementia (DAD) (Gélinas et al., 1996) is a 40 item measure administered to caregivers examining functional disability in people with dementia. The items focus on basic self-care and instrumental activities of daily living. It has been demonstrated to have strong internal consistency and good interrater and test-retest reliability (Gélinas et al., 1996). In a systematic review of activities of daily living scales (ADL), the DAD was thought to be of moderate quality and thought to have good reliability and content validity. The DAD was found to be highly reliable in this sample ($\alpha=0.846$).

Sample Size

When the study was designed and planned there was one study examining the relationship between awareness using the MARS on patient Quality of life and used the BASQUID measure (Trigg et al., 2011). It reported a large effect size ($f^2=0.66$). Using Gpower 3 (Faul et al., 2007), it was calculated that for a multiple regression model with seven

predictor variables with an α -level set at 0.05 and power set at 0.80; that 30 participant dyads would need to be recruited in order to detect a large effect size.

Subsequently there have been more studies published examining the relationship and have found a range of effect sizes smaller than the one reported in the Trigg et al (2011) paper (Cines et al., 2015; Conde-Sala et al., 2014; Woods et al., 2014).

Statistical Analysis

Pearson r correlations were conducted on demographic and predictor variables to test for multicollinearity and explore potential associations of variables with QoLp and QoLc. No evidence of potential multicollinearity was found (Correlations >0.8) between any of the variables and therefore it was considered appropriate for all variables to be used independently.

In order to test the hypothesis that awareness of MF and caregiver ratings predict QoLp, an initial stepwise hierarchical multiple regression model with patient rated QOL as the criterion variable and PwD related variables as predictor variables (self-rated depression (HADSDp), neuropsychiatric symptoms (NPIQ-total), Memory functioning discrepancy (MFD), and anxiety (HADSAp)) was conducted. A second stepwise hierarchical regression model was conducted with the caregiver related variables as predictors (Relationship quality (BRSS), caregiver burden (ZBI), caregiver depression and anxiety (HADSDc and HADSAc) and caregiver psychological wellbeing (WHQOLpsyc)). The significant predictors from each models were then combined into a final QoLp model.

In order to test the hypothesis that awareness of MF and caregiver ratings predict QoLc, the same methodology was employed with QoLc as criterion variable and PwD related variables (activities of daily living (DAD), Neuropsychiatric symptoms (NPIQtotal), was conducted. Followed by a second stepwise hierarchical regression model with caregiver related variables as predictors (Relationship quality (BRSS), caregiver burden (ZBI), caregiver depression and anxiety (HADSDc and HADSAc) and caregiver psychological wellbeing (WHQOLpsyc)). The significant predictors from each models were then combined into a final QoLc model.

A backwards regression model will also be conducted examining whether awareness of memory function and factors found to associate with caregiver QoL predicts caregiver QoL.

All statistical analysis was conducted on SPSS v.21.

Missing data

The data was examined for missing items and Little's missing completely at random (MCAR) test was conducted for each of the measures with missing data, all the missing items were found to be MCAR. One ZBI case had over 30% of the data missing and so omitted from the analysis. One participant refused to answer some of the MARSAs tasks and one refused to answer some of the ACE-R items and so those individual cases were also excluded from the analyses. The missing data was addressed using individual mean

imputation which has been demonstrated to be robust when dealing with limited amounts of data are missing (Shrive et al., 2006).

Results

Sample

The study sample consisted of 27 people with dementia and their caregivers. The mean age of PWD were 78.9 (SD 6.54) and caregivers mean age was 74.8 (7.94). Nine patients were women and 20 caregivers were women. Twenty-five were Spouses and two were children of PWD. A total of 26 caregivers lived with the PWD. The scores on the ACE-R ranged from 44 to 89 and the mean was 70.11 (SD 12.35). All the participants were White British.

Table 1. *Participant characteristics*

PwD		<i>N=27</i>
	Age	78.93
	Gender	9 female, 18 male
	Education level	15 I, 3 II, 2 III, 5 IV, 2 V
	Diagnosis	20 AD, 7 mixed AD/VaD
	ACE-R (N=26) (MMSE)	70.11(23.26)
Caregivers		
	Age	74.86
	Gender	20 female, 7 male
	Education level	13 I, 2 II, 6 III, 5 IV, 1 V
	Relationship to PwD	25 Spouse, 2 adult child
	Living with PwD	26 Yes, 1 no

PwD, People with dementia, AD Alzheimer's disease VaD Vascular dementia; MMSE, Mini-Mental State Examination; VaD vascular dementia; Alzheimer's disease; Education levels; I, high school; II Trade certificate; III College Diploma; IV University degree; V Postgraduate degree

Descriptive statistics

The mean PwD's ratings of QOL (39.93 SD 5.48) were higher than mean caregiver's ratings (33.04 SD 5.87). This difference in means was found to be statistically significant (df=52 $t=4.46$ $p<0.0001$). Similarly, PwD rated their memory functioning (44.41 SD 8.72) higher than their caregiver's (33.78 SD 10.18) did and this difference in means was also found to be significant (df=52 $t=4.121$ $p<0.0001$). There was no significant difference in the awareness (MFD) between those diagnosed with AD and those diagnosed with mixed dementia (df=25 $t=0.481$ $p=0.635$).

Table. 2 *Descriptive Statistics*

	Mean	Std. Deviation	Range
QOLADp	39.93	5.48	31-50
QOLADc	33.06	5.86	23-44
MF PwD	44.41	8.72	15-55
MF Caregiver	34.30	10.59	17-54
MFD	0.27	0.39	-0.87-0.95
MPD	3.02	7.35	-10.67-19
HADSDp	4.41	3.61	0-14
HADSAp	5.00	3.16	0-12
HADSDc	4.22	3.14	0-13
HADSAc	7.00	4.14	0-16
NPIQtotal	15.67	20.63	0-104
DAD	0.75	0.15	0.48-1
BRSS	31.52	11.01	2-42
ZBI (N=26)	30.95	13.65	6-67
WHOQOL-PH	64.57	16.90	30.4-88
WHOQOL-PSY	68.30	13.59	31-88
WHOQOL-ENV	75.56	13.47	31-100
WHOQOL-QOL item	3.89	0.70	2-5
WHOQOL- Health item	3.70	0.82	2-5

Abbreviations: QOLAD, Quality of life Alzheimer's Disease; p, person with dementia; c, caregiver; MFD, Memory functioning Discrepancy; MPD, Memory Performance Discrepancy; HADS, Hospital Anxiety and Depression Scale, A, Anxiety, D, Depression; NPIQ,

Neuropsychiatric symptoms Inventory Questionnaire; Disability Assessment for Dementia; BRSS, Burns Relationship Satisfaction Scale; WHOQOL, World Health Organisation Quality of Life, PH, Physical Health, PSY, Psychological, SR, Environment, Overall quality of life item, overall health item.

Correlations

The bivariate correlations (Pearson's r) of variables are presented in Table 3. Neither measure of awareness was found to correlate with patient rated QOL-AD (QOL-ADp) (MFD $r=0.107$ $p=0.594$, MPD $r=0.140$ $p=0.505$) nor caregiver rated Qol-AD (QOL-ADc) (MFD $r=-0.156$ $p=0.472$, MPD $r=0.0.025$ $p=0.439$). Although patients' assessment of their memory functioning was found to be significant associated with QOL-ADp ($r=-0.552$ $p=0.003$). Patient rated and caregiver rated QOL were not found to be significantly correlated ($r=0.351$ $p=0.085$).

Patient depression and anxiety (HADSp) were found to significantly negatively correlate with QOL-ADp ($r=-0.689$ $p<0.0001$, $r=-0.605$, $p<.0001$ respectively). QOLP was found to significantly negatively correlate with NPI-Q total score ($r=-0.489$ $p=0.01$) and ZBI caregiver burden ($r=-0.547$ $p=0.006$) and positively correlate with relationship quality ($r=0.492$ $p=0.009$). None of the WHOQOL subscales were found to correlate with QOLD-ADp. WHOQOL psychological wellbeing was found to negatively correlate with ZBI ($r=-0.547$ $p=0.006$) and HADSp depression ($r=-0.547$ $p=0.006$) and positively correlate with BRSS caregiver rated quality of relationship ($r=-0.547$ $p=0.006$) which all were found to significantly correlated with QOL-ADp. It was therefore decided to enter

it into the caregiver variable QoLp regression model. There does not seem to be any indication of multicollinearity between the variables as all correlations are below 0.8.

QOL-ADc was found to significantly positively correlate with DAD activity limitation ($r=0.691$ $p<0.0001$), and BRSS relationship quality ($r=0.516$ $p=0.006$) It was found to negatively correlate with ZBI caregiver burden ($r=-0.539$ $p=0.004$) and NPI-Q total score ($r=-0.499$ $p=0.008$).

The two measures of awareness (MFD and MPD) were found to correlate with each other ($r=0.550$ $p=0.004$). MFD was found to negatively correlate with depression ($r=-0.497$ $p=0.008$). Caregiver ratings of PwD MF were found to positively correlate with PwD performance on memory functioning tasks ($r=-0.574$ $p=0.002$).

BRSS and the WHOQOL overall QoL item were found to significantly correlate ($r=-0.644$ $p<0.0001$)

No demographic variables were found to significantly correlate with QoLp or QoLc

Partial correlations were conducted with ACE-R as a control variable to examine whether severity of cognitive impairment had an impact upon associations between variables. There was no change in significance between any of the partial and bivariate correlations relating to QoLp and QoLc.

Table 3. Bivariate correlations

Participant age	Gender	Academic performance	Carer age	Carer academic	Carer gender	Diagnosis	MFSpatient	MFScarer	MFDcorrected	MFtasks	MPD	HADSap	HADSdp	HADSac	HADSdc	QOLADp	QOLADc	QOLAD										WHOQOL				
																		discrepancy	MMSE	ACER	DAD	ZBI	BRSS	NPIQseverity	NPIQdistress	NPIQtotal	physhealth	psyc	environment	QOL	PHitem	
Participant age	1	-0.106	-0.023	0.26	0.138	-0.091	0.099	0.3	-0.06	0.215	-0.129	0.316	-0.27	-0.101	0.106	-0.125	0.322	-0.221	520**	-0.169	-0.056	-0.047	0.046	-0.062	-0.167	-0.036	-0.083	0.127	-0.178	-0.103	0.2	0.01
Gender	1	0.11	0.097	-0.418*	-0.756**	-0.12	-0.122	-0.501**	0.372	-0.295	0.354	0.051	0.126	0.329	0.102	-0.273	-0.114	-0.128	-0.06	-0.067	-0.184	0.234	-0.417*	0.01	0.133	0.128	-0.123	-0.279	-0.125	-0.115	0.13	
Academic performance		1	0.232	0.343	0.083	-0.106	0.355	0.231	0.028	0.184	0.213	-0.109	-0.09	-0.11	-0.234	0.151	0.028	0.075	437*	509**	0.262	-0.033	-0.153	0.102	0.149	0.138	0.124	0.022	0.229	-0.063	0.125	
Carer age			1	-0.044	0.307	0.109	0.173	0.2	-0.062	-0.104	0.117	-0.118	-0.143	0.048	0.011	0.358	-0.084	384*	-0.216	-0.283	0.11	-0.456*	-0.059	-0.121	-0.132	-0.194	-0.096	-0.022	-0.233	-0.079	-0.201	
Carer Academic				1	0.316	0.029	0.19	0.31	-0.19	0.19	0.019	-0.018	-0.051	-0.124	-0.168	0.065	-0.062	0.102	401*	521**	0.174	0.252	0.083	0.205	0.274	0.231	-0.192	0.235	0.46*	0.233	0.167	
Carer gender					1	0.09	0.162	0.490**	-0.355	0.303	-0.29	-0.144	-0.212	-0.439*	-0.241	0.389*	0.103	0.222	-0.066	-0.164	0.239	-0.436*	0.395*	-0.048	-0.119	-0.141	0.035	0.436*	0.112	-0.043	-0.135	
Diagnosis						1	0.051	0.17	-0.096	0.191	-0.078	0.136	0.194	-0.063	-0.125	-0.165	-0.228	0.127	-0.166	0.094	-0.276	0.029	0.026	0.213	0.055	0.102	0.051	0.177	-0.185	0.096	0.008	
MFSpatient							1	0.095	0.549**	-0.123	0.564**	-0.665**	-0.684**	-0.271	-0.335	0.552**	0.088	0.383*	0.17	0.262	0.032	-0.222	0.063	-0.175	-0.13	-0.093	0.211	0.284	0.13	0.204	0.328	
MFScarer								1	-0.761**	0.574**	-0.272	0.005	0.032	0.007	0.23	0.268	0.349	-0.081	0.382*	0.386	0.536**	-0.228	0.242	-0.195	-0.225	-0.186	0.231	-0.052	0.062	0.051	-0.122	
MFDcorrected									1	-0.531**	0.550**	-0.413*	-0.497**	-0.134	-0.355	0.144	-0.156	0.251	-0.195	-0.107	-0.357	0.002	-0.163	0.006	0.043	0.052	-0.011	0.212	0.006	0.117	0.347	
MFtasks										1	-0.567**	0.191	0.104	-0.049	0.188	0.084	0.133	-0.049	0.544**	0.484*	0.504**	-0.097	0.128	0.013	-0.055	-0.021	-0.003	-0.042	-0.132	-0.189	-0.244	
MPD											1	-0.357	-0.251	0.061	-0.272	0.223	0.025	0.171	-0.231	-0.045	-0.174	0.098	-0.188	-0.237	-0.062	-0.078	-0.029	-0.088	0.06	0.181	0.311	
HADSap												1	0.802**	0.134	0.24	-0.640**	-0.039	-0.477*	-0.151	-0.047	-0.027	0.203	-0.039	0.363	0.27	0.219	-0.317	-0.292	0.016	-0.209	-0.354	
HADSdp													1	0.201	0.219	-0.719**	-0.252	-0.331	-0.186	-0.055	-0.283	0.426*	-0.122	0.326	0.295	0.212	-0.126	-0.422*	-0.044	-0.165	-0.385*	
HADSac														1	0.736**	-0.263	-0.035	-0.203	0.078	0.079	0.07	0.298	-0.540**	-0.176	-0.058	-0.109	0.011	-0.759**	-0.254	-0.371	-0.011	
HADSdc															1	-0.198	-0.074	-0.095	0.157	0.023	0.044	0.282	-0.543**	0.076	0.035	0.049	-0.153	-0.725**	-0.478*	-0.514**	-0.479*	
QOLADp																1	0.396*	0.467*	0.047	-0.014	0.430*	-0.585**	0.389*	-0.545**	-0.510**	-0.489**	0.046	0.227	-0.04	0.31	0.021	
QOLADc																	1	-0.619**	0.099	0.211	0.691**	-0.539**	0.516**	-0.613**	-0.544**	-0.499**	0.178	0.155	0.375	0.480*	0.333	
QOLADdiscrepancy																		1	-0.233	-0.313	0.021	-0.144	0.121	0.074	0.052	-0.117	0.042	-0.117	0.042	-0.376	-0.155	-0.313
MMSE																			1	0.832**	0.412*	0.06	-0.06	0.079	0.105	0.153	0.042	-0.037	0.04	-0.066	0.146	
ACER																				1	0.349	0.12	0.02	0.034	0.015	0.056	0.138	0.016	0.238	0.266	0.325	
DAD																					1	-0.548**	0.286	-0.509**	-0.383*	-0.361	0.144	0.046	0.193	0.128	0.17	
ZBI																						1	-0.551**	0.621**	0.665**	0.651**	-0.124	-0.419*	-0.01	-0.252	-0.058	
BRSS																							1	-0.426*	-0.526**	-0.549**	0.069	0.526**	0.425*	0.644**	0.2	
NPIQseverity																								1	0.860**	0.874**	-0.223	-0.012	-0.064	-0.328	-0.265	
NPIQdistress																									1	0.970**	-0.065	-0.107	0.028	-0.357	-0.081	
NPIQtotal																										1	-0.038	-0.042	-0.014	-0.337	-0.06	
WHOQOLphyshealth																											1	-0.004	0.154	0.203	0.445*	
WHOQOLpsyc																												1	0.466*	0.450*	0.414*	
WHOQOLsocialrel																													0.22	0.275	0.06	
WHOQOLEnvironment																													1	0.489**	0.622**	
WHOQOLQOL																														1	0.476*	
WHOQOLPHitem																																1

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

* $p < 0.05$, ** $p < 0.01$

Abbreviations QOLAD, Quality of life Alzheimer's Disease; p, person with dementia; c, caregiver; MFD, Memory functioning Discrepancy; MPD, Memory Performance Discrepancy; HADS, Hospital Anxiety and Depression Scale, A, Anxiety, D, Depression; NPIQ, Neuropsychiatric symptoms Inventory Questionnaire; Disability Assessment for Dementia; BRSS, Burns Relationship Satisfaction Scale; WHOQOL, World Health Organisation Quality of Life, PH, Physical Health, PSY, Psychological, SR, Social Relationships, Environment

Significance are included to present the data fully and indicative only as they have not been corrected for multiple comparisons.

Person with Dementia rated Quality of Life regression model

Person with Dementia variables

The data met the assumption of independent errors (Durbin Watson= 1.8) and there did not seem to be a suggestion of multicollinearity as tolerance scores were above 0.2 and Variance inflation factor scores (VIF) were below 10. No outliers were found. The data for the model is presented in Table 3.

QOLADp was significantly predicted by a model containing PwD rated HADSp depression and NPIQ total score ($F_{2,24}=20.894$, $p<0.0001$, adjusted $R^2=0.605$), with both variables individually significant. MFD and HADSp Anxiety were added in subsequently into the model but did not contribute significantly to the variance and were not individually significant. Increases in QOLADp were associated with decreases in depressed mood and Neuropsychiatric symptoms. The observed statistical power of the model was 0.999.

In order to further investigate the relationship of awareness of memory functioning to QOLADp an additional model was conducted with PwD ratings of MF being added to the model instead of MFD. No additional variance was explained and PwD ratings of MF were found to be a significant predictor.

As mood is a component of QoL and the QOLAD and therefore is redundancy between the measures, inter-item correlations were conducted on the HADSDp and QOLADp. Significant negative correlations were found between a number of items and not just the

QOLAD Mood item which would suggest that the relationship demonstrated is not just an artifact of measuring the same construct.

Caregiver variables

A second hierarchical stepwise regression model was conducted exploring the variance explained by the caregiver variables (Table. 3). The data met the assumption of independent errors (Durbin Watson= 2.4) and there did not seem to be a suggestion of multicollinearity as tolerance scores were above 0.2 and VIF were below 10.

QoLADp was significantly predicted by a caregiver variable model containing ZBI caregiver burden and BRSS caregiver rated relationship quality ($F_{2,23}=6.141$, $p=0.007$, adjusted $R^2=0.291$), When entered individually BRSS was a significant predictor but once ZBI was entered into the model it no longer became significant while ZBI was a significant predictor. Caregiver HADS anxiety, HADS depression, and WHOQoL-Bref psychological subscale was added subsequently but did not contribute significantly to the variance explained. Increases in QoLADp were associated with decreases in ZBI caregiver burden. The observed statistical power of the model was 0.898.

Combined model

The two QoLADp models were then combined and ZBI caregiver burden was then added to the previous research model (Table 3). QoLp was significantly predicted by HADSp depression and NPIQ total score ($F_{2, 24}=19.593$, $p<0.0001$, adjusted $R^2=0.598$). Both with

individually significant predictors. Adding ZBI caregiver burden to the model did not explain a significant amount of additional variance.

Table 4. Regression analyses Beta and p-values for predictors of QOLADp and adjusted R² values for each model.

Models	Previous research		Caregiver variables		Final Model	
	beta	p	beta	p	beta	p
Adjusted R ²	0.601		0.291		0.598	
HADSDp	-0.644	<0.0001			-0.624	<0.0001
NPIQtotal	-0.353	0.01			-0.368	0.01
ZBI			-0.532	0.015	-	-

Caregiver rated PwD Quality of Life regression model

Person with Dementia variables

The data met the assumption of independent errors (Durbin Watson= 1.4) and there did not seem to be a suggestion of multicollinearity as tolerance scores were above 0.2 and VIF were below 10. The data for the model is presented in Table. 5

QOLADc was significantly predicted by a model containing DAD activities of daily living ($F_{1,24}=20.724, p<0.0001, \text{adjusted } R^2=0.441$), NPIQ total score, and MFD were added in subsequently into the model but did not contribute significantly to the variance and were not individually significant. The observed power of the model was 0.995

Caregiver variables

The data met the assumption of independent errors (Durbin Watson= 2.19) and there did not seem to be a suggestion of multicollinearity as tolerance scores were above 0.2 and VIF were below 10. QOLADc was significantly predicted by model (Table. 4) containing ZBI caregiver burden and BRSS relationship quality ($F_{2,23}=8.262$, $p=0.002$, adjusted $R^2=0.367$). HADSc anxiety and depression, and WHOQOL psychological were subsequently added to the model but did not significantly contribute to the variance of the model and were not individually significant. The observed statistical power of the model was 0.926.

Combined model

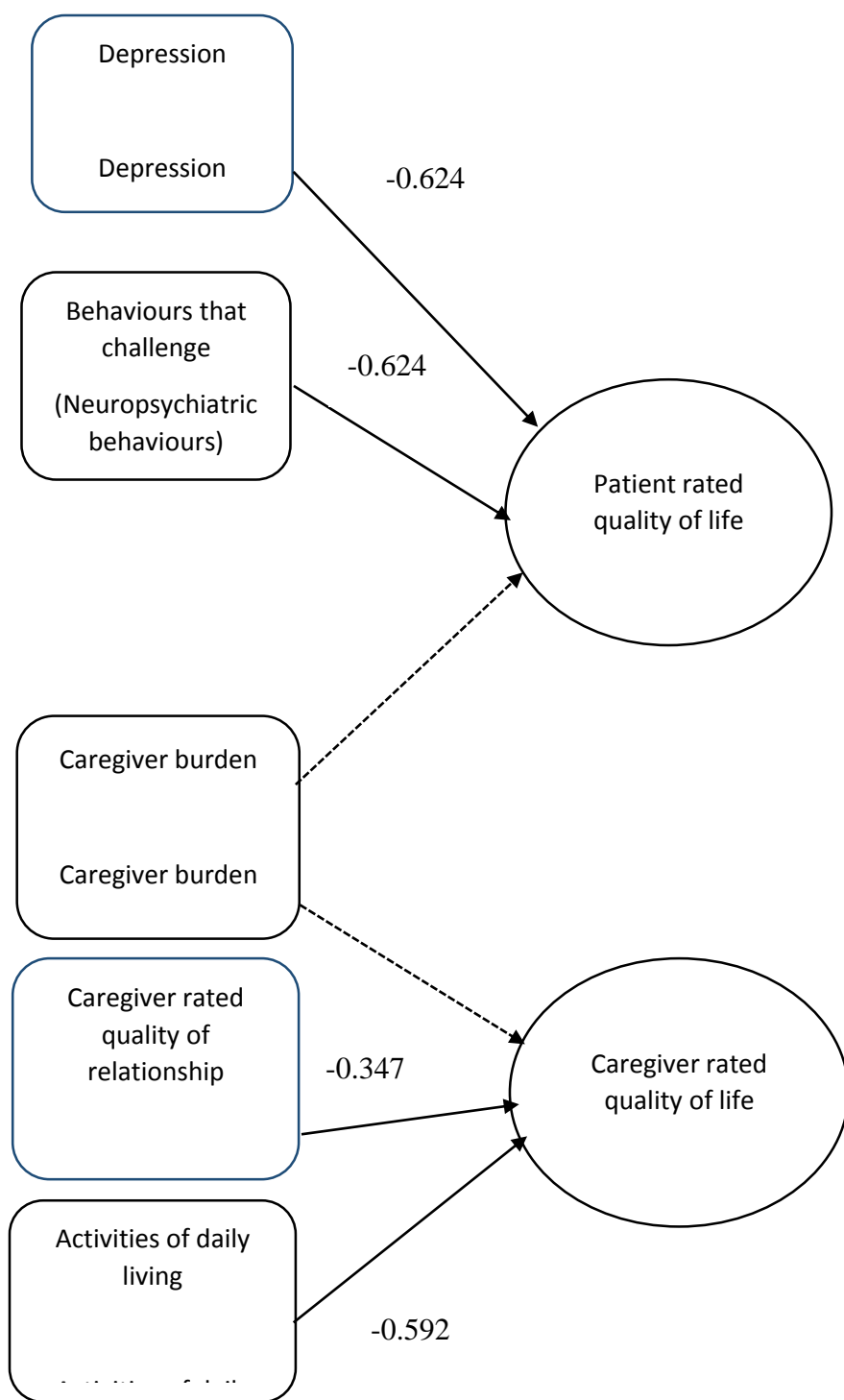
QOLADc was significantly predicted by a model containing DAD activities of daily living and BRSS caregiver rated relationship quality ($F_{2,23}=16.452$, $p<0.0001$, adjusted $R^2=0.553$). Increases in QOLADc was associated with increases in DAD activities of daily living and BRSS relationship quality. The observed power of the final model was 0.999.

Table. 5 Regression analyses, Beta and *p*-values for predictors of QOLADc and adjusted R^2 values for each model.

Models	PwD variables		Caregiver Variables		Final model	
Adjusted R^2	0.441		0.367		0.553	
	beta	<i>p</i> -value	beta	<i>p</i> -value	beta	<i>p</i> -value
DAD	0.691	<0.0001			0.592	<0.0001
ZBI			-0.303	0.126	-	-
BRSS			0.516	0.006	0.347	0.021

A conceptual model of the predictors of QOLp and QOLc are presented in Figure

.1



Numbers are path coefficients. All path coefficients shown are statistically significant. Dotted lines represent non-significant paths.

Figure 1. Conceptual model illustrating the predictors of Patient and caregiver rated quality of life

Caregiver Quality of Life regression model

The data met the assumption of independent errors (Durbin Watson= 1.1) and there did not seem to be a suggestion of multicollinearity as tolerance scores were above 0.2 and VIF were below 10. The data for the model is presented in Table. 6.

WHOQOL-Bref psychological was predicted by a model containing HADSc Anxiety, HADSc Depression and HADSp Depression ($F_{1,21}=17.094$, $p<0.0001$, adjusted $R^2=0.0.659$). HADSp depression was not an individually significant predictor. BRSS, ZBI, and MFD were removed from the final model. Increases with WHOQOL psychological wellbeing were associated in decreases with HADS Caregiver anxiety and HADS caregiver depression. The observed statistical power of the model was 0.999.

Table. 6 Regression analyses, Beta and p-values for predictors of WHOQOL-Bref psychological subscale.

	beta	p-value
HADSAc	-0.470	0.012
HADSDc	-0.323	0.043
HADSDp	-0.283	0.076

Discussion

Awareness of Memory functioning and PwD rated Quality of life

The results of the study do not support the hypothesis that awareness of memory functioning and caregiver related factors are predictive of QoLp. Depression and of neuropsychiatric symptoms total score were the only variables found to be predictive of QoLp, with decreases in both leading to increases in QoLp. The finding that awareness, at both the evaluative judgement level and performance monitoring level was not predictive of QoLp in a model including depression was consistent with the most comprehensive examination of awareness and factors that predict QoLp (Woods et al., 2014). A similar level of variance was also explained as their model and although non-significant the bivariate correlation between MFD and QoLp in the study (-0.144) was not much lower than the significant one reported by Woods et al. (2014) (-0.21). The lack of relationship with evaluative judgement awareness of memory function and QoLp appears to not be consistent with Trigg et al. (2011) and Conde-Sala et al. (2014) findings. These studies did not use the corrected discrepancy score described in (Clare et al. (2010) but rather used simple discrepancies which weight the scores more in favour of the caregiver ratings. The Trigg et al. finding was with a different measure of quality of life which may account for the differences found. Conde-Sala et al used a more general measure of awareness (Migliorelli et al., 1995b) which includes items on functional and behavioural changes as well as memory functioning which may have a different relationship to QoLp.

The lack of relationship between memory performance awareness and QoLp is consistent with previous findings (Woods et al., 2014). This may be because task-specific errors on memory performance tasks can be dismissed or rationalised as a normal part of aging and so do not affect PwDs appraisals of their memory or impact upon their QoL (Clare et al., 2011a).

A negative association between the evaluative judgement measure of awareness of MF (MFD) and depression was found consistent with the literature (Clare et al., 2012a), as was the negative association found between depression and QoLp. However, no direct association was found between awareness of MF and QoLp. Recent studies that have demonstrated that depression mediates the relationship between awareness of memory functioning and depression (Cines et al., 2015; Woods et al., 2014). These findings suggested that people with high awareness are only more likely to report low QoL if their mood is low. These findings would mean that an association between awareness of MF and QoLp would still be expected to be found in this study which it was not. The significant association found in those studies was a small effect so it may be that the sample size used here was not large enough to detect it. If the PwD ratings of their memory functioning are used rather than a discrepancy score of PwD and Caregiver ratings, then a direct association is found between those ratings and QoLp as well as a negative association with depression. This would suggest that the important factor is whether the PwD has a positive or negative appraisal of their MF as this does affect their ratings of their QoL while the accuracy of the PwD's appraisal of their MF does not affect ratings of their QoL. This would seem to fit with recent findings suggesting awareness of MF

relationship to QoLP is driven by level of depression. If PwD's mood is low then they are more likely to appraise their memory as worse and report lower QoL.

It may be that the association between unawareness of MF and depression is actually two different effects. It has been argued that unawareness is a psychological reaction to impairment in memory functioning (Migliorelli et al., 1995b) in sub-clinical depression and PwD overestimate their ability to as a form of coping/avoidance with their low mood and distress. It has also been suggested that those who met criteria for depression rate their MF more negatively or conservatively than those with better mood (Nakaaki et al., 2008) (underestimate their functioning). This is in line with the negative attribution bias commonly found in depression. Both of these positions highlight how appraisals of MF and thus evaluative judgement awareness are affected by depression although it seems that there are potentially two different awareness processes associated in a similar direction with depression. The mean awareness of MF combined with the low level of depression in this study would suggest that the sample as a whole overestimated their abilities supporting the notion of unawareness of MF being a psychological reaction to protect them from distress around their difficulties. However, there were a few participants in the sample that scored in the clinical range for depression that underestimated their abilities to a large degree. No firm conclusions can be drawn from this but it warrants further investigation as it potentially could be a separate effect. From clinical experience those with high levels of depression in this population report the most severe impairment in terms of memory functioning. Most studies in the literature have examined samples that predominantly overestimate their MF and have subclinical levels

of depression. Further research is needed to examine overestimation and underestimation separately and investigate whether they have differing relationships to clinical and subclinical depression.

Caregiver variables and PwD Quality of Life

The caregiver related variables were not found to explain any further variance in PwD QoL model. Caregiver psychological wellbeing was not found to be a predictor nor correlated with QoLp. Caregiver rated relationship quality initially predicted QoLp when entered into the model alone with better relationship quality leading to increases in QoLp but the variance it explained was accounted for better by caregiver burden. Caregiver rated relationship quality not being a significant predictor of QoLp is consistent (Clare et al., 2014) findings. When caregiver burden was entered into the final model with self-rated depression and impact of NP symptoms it was no longer a significant predictor. This would suggest that the variance explained by caregiver burden in relation to QoLp was better accounted for by the PwD's mood and impact of NP on PwD and caregiver. Caregiver burden was significantly correlated with severity of NP and distress experienced sub-scales of the NPI-Q. It makes sense that there is a great deal of shared variance among the measures as they both focus on the response to difficult experiences in the caregiving context and the caregiver's response to that. The fact that these caregiver focussed variables can be found to explain variance relating to QoLp supports the notion that PwD have an awareness of their caregivers' emotional state and attitude and that this has an impact upon them as has been suggested previously (Ablitt et al., 2010; Woods et

al., 2014). However, the model suggests that the impact of their caregiver's emotional state on PwD QoL is best accounted for by the way it affects the PwD level of depression rather than being a separate factor.

Predictors of PwD rated Quality of life

Whilst the hypotheses in relation to QoLp was not confirmed, the QoLp was able to provide further evidence for the role of depression and impact of neuropsychiatric symptoms in predicting QoLp with increased depression and neuropsychiatric symptoms being associated with worse QoLp. Consistent with the literature depression emerged as the strongest predictor of self-reported QoL. There is a low level of depression reported in the sample but it is consistent with the level found in other samples in the literature (Cines et al., 2015; Clare et al., 2010; Woods et al., 2014). While mood is conceptualised as part of QoL the item by item correlations conducted between the depression and QoLp measures demonstrated that it is not simply an artefact of measuring the same construct. The consistent finding of depression predicting QoL highlights the importance of professionals screening for low mood in PwD.

It has been suggested that multivariate analyses studies tended to confirm behavioural disturbance and affective symptoms as predictors of QoL (Banerjee et al., 2009) and this finding was furthered in this study. This study has a small sample size but the large amount of variance accounted for by the model, the strong observed power of the model, and consistency of the findings with the research literature means it can be stated with confidence that depression and neuropsychiatric symptoms predict QoLp. However, it

should be noted that some variables that have recently been demonstrated to predict QoLp were not included in the study (self-concept and PwD rated relationship quality) and it may be that those variables would explain additional variance or better explain some of the variance accounted for in this model.

Caregiver rated Quality of life for the PwD they care for

The second research hypothesis regarding caregiver rated QoL was also mostly disconfirmed. It would seem that Caregiver's perceptions of PwD QoL are driven by how functionally able they are how they are able to maintain their relationship with the caregiver. Activity limitation was found to be the strongest predictor of QoLp entirely consistent with previous research (Conde-Sala et al., 2014; Naglie et al., 2011b; Orgeta et al., 2015). Caregiver rated quality of relationship was also found to be a significant predictor with increases in caregiver perceived relationship quality leading to increases in QoLc. Awareness of MF, caregiver QoL and wellbeing, were not found to be predictors of QoLc. This is the first time that caregiver rated relationship quality has been investigated in predicting QoLc and represents a new and important finding. This finding provides further evidence to the importance of the caregiver relationship in the caregiver context. High relationship quality has already been found to be associated with low caregiver burden, better care provided by caregiver, and better caregiver wellbeing (Quinn et al., 2009; Steadman et al., 2007). This would seem to suggest that the caregiver related variables hypothesised to be predictive of QoLc are best understood in the QoL context in terms of caregiver relationship quality. This finding is borne out by clinical experience

as those with the most supportive caregiver relationships seemed to be report the highest functioning and QoL. There is still much to be understood around this finding. As current relationship quality was measured it is not clear to what extent it is a factor of premorbid relationship quality. The sample was also majority spousal caregivers, further investigation is need to examine whether this effect would be found in adult children caregivers. The significant predictors found for QoLc in this study reinforces further the notion that PwD and their caregivers rate PwD's QoL differently and it is therefore important to explore both perspectives when planning a clinical intervention to improve PwD QoL

Predictors of Caregiver Quality of life

The hypothesis to the secondary research question that awareness of memory functioning would predict affected caregiver QoL was not confirmed by this sample. The psychological wellbeing subscale of the WHOQOL was found to be predicted by caregiver anxiety and depression which would be expected as that is broadly what the measure examines and so provides little additional insight into the construct. PwD depression emerged as a non-significant predictor. It was found to correlate with caregiver burden and relationship quality but they were not significant predictors suggesting that the association is better accounted for by the significant predictor variables. As this investigation was only a subscale it does not present a holistic picture of caregiver QoL. There were no significant associations between study variables and the other subscales to

guide further analysis. The overall QoL item was associated with relationship quality further asserting the importance of the caregiving relationship.

Measuring and Sampling issues

The partial correlations conducted with level of cognitive impairment controlled for and the lack of associations between the measures of cognitive impairment and study measures would suggest that the level of cognitive impairment was not related to the results found. This is consistent with previous findings (Banerjee et al., 2009; Trigg et al., 2011; Woods et al., 2014). While the measures used would have accommodated a more moderate dementia sample, the majority of the PwD examined in the sample would be considered to have a mild level of cognitive impairment consistent with early-stage dementia. This was due to the convenience sampling nature of recruitment. The sample is comparable with other samples in the literature as they tend to be early/ mild dementia and recruited from memory clinics using a convenience sample methodology.

There are currently no studies to directly compare the use of the MARSA but the data produced with adjusted Memory functioning scale are comparable to studies that have used the Memory functioning scale (Clare et al., 2012a, 2010). The memory functioning discrepancy and memory performance discrepancy were significantly correlated which would seem to suggest that the caregivers were accurately rating their PwD memory functioning and that the two scales are measuring the same construct. This strength of correlation was not found in development of the measure (Hardy et al., 2006). This

difference may be due to using the corrected discrepancy score described in (Clare et al., 2010).

This study examines awareness in domain of memory functioning and performance. As stated previously, awareness is a complex multi-factorial concept and so it is important to define the nature of awareness studies and acknowledge the results found here in regards to awareness cannot be generalised outside the specific domains of awareness of memory functioning and memory performance awareness in line with recommendations in Clare et al. (2005).

The study sample was very small for a regression analysis, the observed power for the produced models and large effect size found would suggest that those models are adequately powered and those positive findings can be considered robust. However, the non-significant findings of the variables that did not fit into the final models should be treated with caution and it cannot be ruled out that the sample size was not big enough to detect those effects and there is possibility of Type II errors.

The study was cross-sectional in design so direct causation about any of the relationships presented cannot be determined. Mood and Neuropsychiatric symptoms are variables that can fluctuate within individuals and may fluctuate frequently and may fluctuate over time so it would important to examine these findings in a longitudinal study. Further research is needed to examine how these factors change over time. One recent study has found that QoLp at twenty is significantly predicted by baseline QoLp and quality of caregiving relationship (Clare et al., 2014).

This study's sample was a homogenous, mostly white male sample of PwD and their female spousal caregivers living in Scotland. The majority of the sample would be considered to be in early stage dementia. These factors should be acknowledged when considering the generalisability of the findings of this study. The findings reported here should also be considered to be only generalizable to family caregivers who are living with PwD. They are also only generalizable to spouse caregivers as the sample here was almost exclusively spouses. Spouse caregivers have been demonstrated to have different perceptions to other family caregivers. Spouse caregivers are more likely to have more positive perceptions of PwD QoL while adult children had more negative perceptions of PwD QoL which were associated with greater caregiver burden and higher levels of depression in the patient. Daughter caregivers' negative perception of QoL showed the strongest association with PwD mental health and caregiver burden (Conde-Sala et al., 2010).

Conclusions

This study did not find that awareness of memory functioning predicted either PwD or Caregiver QoL. Although PwD ratings of their memory functioning were found to be associated with QoL most likely as a function of PwD level of sub-clinical depression. None of the caregiver related variables examined were found to be predictive of PwD rated QoL. QoL was found to be negatively influenced by the level of PwD depression and the impact of neuropsychiatric symptoms. Caregiver burden was found to be associated with QoL but its relationship was better accounted for by PwD depression

and neuropsychiatric symptoms. Caregiver ratings of PwD QoL were demonstrated to be influenced by the ability of the PwD to complete daily activities of living and the caregiver's perceptions of the quality of the relationship with PwD. This supports the view that PwD and caregivers appraise different factors when rating PwD QoL and multiple perspectives should be considered when assessing PwD QoL. It also furthers the importance of examining the caregiving relationship when investigating QoL in dementia.

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Appendices

Appendix A: Reason for exclusion from Meta-analysis.

Study	Reason for Exclusion
Arkin et al 2001	Awareness measure did not meet inclusion criteria
Boyars et al 2014	Awareness measure did not meet inclusion criteria
Burke et al 1998	Awareness measure did not meet inclusion criteria
Chen et al 2012	Awareness measure did not meet inclusion criteria
Conde sala et al 2014	same sample as study already included in analysis
Debettingnes et al 1990	Awareness measure did not meet inclusion criteria
Derouesne et al 1999	Awareness measure did not meet inclusion criteria
Lin et al 2010	Awareness measure did not meet inclusion criteria
Maki et al 2012	Association not assessed
Michon et al 1994	No data reported
Mograbi et al 2012	Awareness measure did not meet inclusion criteria
Padoani et al 2001	No data reported
Reed et al 1993	No data reported
Rocca et al 2010	Unable to compute effect size
Satler 2013	No data reported
Seiffer et al 2005	No data reported
Seltzer et al 1995	Unable to obtain article
Sevush and Leve 1993	No data reported
Sousa et al 2015	Same sample as study already included in analysis
Spaletta et al 2012	Depression measure did not meet inclusion criteria
Triosi et al 1996	Awareness measure did not meet inclusion criteria
Van Viliet et al 2012	Unable to compute effect size
Vasterling et al 1997	Depression measure did not meet inclusion criteria
Vogel et al 2005	Depression not assessed
Vogel et al 2014	same sample as study already included in analysis
Waldorff et al 2010	same sample as study already included in analysis
Waldorff et al 2014	same sample as study already included in analysis
Woods et al 2014	same sample as study already included in analysis
Yoon et al 2013	In Korean

Appendix B: Research Ethics Committee approval letter

Scotland A Research Ethics Committee	Research Ethics Service 2 nd Floor Waverley Gate 2-4 Waterloo Place Edinburgh EH1 3EG Telephone: 0131 465 5680 www.nres.nhs.uk	
Dr Vivek Pattan Consultant Old Age Psychiatrist NHS Forth Valley CMHT-Older Adults Stirling Community Hospital Livilands Gate FK8 2AU	Date: 27 August 2014 Your Ref.: Our Ref.: 14/SS/1006 Enquiries to: Walter Hunter Extension: 35680 Direct Line: 0131 465 5680 Email: walter.hunter@nhslothian.scot.nhs.uk	

Dear Dr Pattan

Study title: Insight in Dementia: How does awareness of memory symptoms affect the Quality of Life and well-being for the patient and caregiver?
REC reference: 14/SS/1006
IRAS project ID: 117849

Thank you for responding to the Committee's request for further information on the above research.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mr Walter Hunter, Walter.Hunter@nhslothian.scot.nhs.uk.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation [as revised], subject to the conditions specified below.

Adults with Incapacity (Scotland) Act 2000

The Committee did not approve this research project for the purposes of the Adults with Incapacity (Scotland) Act 2000. The research may not be carried out on, or in relation to, a person who lacks capacity to consent at the time they were invited to take part in the project.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Chairman Dr Ian Zealley
 Vice-Chairman Dr Colin Selby

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management

permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
REC Application Form: REC_Form_13062014		13 June 2014
Research protocol	1	14 March 2014
Summary CV for Chief Investigator (CI)		
Summary CV for student	1	24 March 2014
Summary CV for supervisor (student research)		
Participant information sheet	1	24 February 2014
Participant consent form	1	24 February 2014
Participant consent form		
GP/consultant information sheets or letters	1	24 February 2014
Non-validated questionnaire: Demographics		
Validated questionnaire: NPI-Q		
Validated questionnaire: HADScale		04 April 2014
Validated questionnaire: MARSA response sheet	1	
Validated questionnaire: BRSS		
Validated questionnaire: DAD		
Validated questionnaire: Whoqol		
Validated questionnaire: QOL-AD		
Validated questionnaire: ACE R		04 April 2014
Validated questionnaire: Zarit burden interview		
Response to request for further information		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

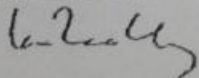
HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

REC reference number: 14/SS/1006-Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely

A handwritten signature in black ink, appearing to read 'I. Zealley'.

Dr Ian Zealley
Committee Chairman

cc: Mrs Rosemary Wilson, NHS Forth Valley
Tom Weavers

Appendix

C:

R&D

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Date: 11 December 2014
 Your Ref:
 Our Ref:
 Direct Line: 01324 677564
 Email: rosemarywilson@nhs.net
 R&D ref: FV 339

Dr Vivek Pattan
 Consultant Old Age Psychiatrist
 NHS Forth Valley
 CMHT – Older Adults
 Stirling Community Hospital
 Livilands Gate
 Stirling FK8 2AU

Dear Dr Pattan

Study title: Insight in Dementia: How does awareness of memory symptoms affect the Quality of Life and well-being for the patient and caregiver?
NRES number: 14/SS/1006

Following the favourable opinion from the Scotland A Research Ethics Committee on 27 August 2014, I am pleased to confirm continuation of Management Approval for the study above on 11 December 2014. This approval is subject to the following conditions:

- A letter of access for Dr Debbie Brown and Dr Kimberley Boyle

This approval is granted subject to your compliance with the following:

1. Any amendments to the protocol or research team must have Ethics Committee and R&D approval (as well as approval from any other relevant regulatory organisation) before they can be implemented. Please ensure that the R&D Office and (where appropriate) NRS are informed of any amendments as soon as you become aware of them.
2. You and any local Principal Investigator are responsible for ensuring that all members of the research team have the appropriate experience and training, including GCP training if required.
3. All those involved in the project will be required to work within accepted guidelines of health and safety and data protection principles, any other relevant statutory legislation, the Research Governance Framework for Health and Community Care and IHC-GCP guidelines. A copy of the Framework can be accessed via the Chief Scientist Office website at: <http://www.cso.scot.nhs.uk/Publications/ResGov/Framework/RGFEdTwo.pdf> and ICH-GCP guidelines may be found at <http://www.ich.org/LOB/media/MEDIA482.pdf>
4. As custodian of the information collected during this project you are responsible for ensuring the security of all personal information collected in line with NHS Scotland IT security policies, until the destruction of this data.
5. You or the local Principal Investigator will be required to provide the following reports and information during the course of your study:

V:\Research And Development\ALL PROJECT FOLDERS\Active NHS FV projects\FV339 Insight in Alzheimers\FV339 continuing approval letter 11 Dec 2014.doc

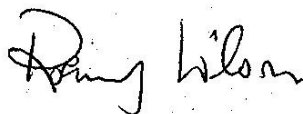
pproval

letter

- A progress report **annually**
- Recruitment numbers on a **monthly** basis (if your study should be added to the NIHR research Portfolio you will receive a separate letter from the R&D Office detailing the steps to be taken)
- Report on SAEs and SUSARs if your study is a Clinical Trial of an Investigational Medicinal Product
- Any information required for the purpose of internal or external audit and monitoring
- Copies of any external monitoring reports
- Notification of the end of recruitment and the end of the study
- A copy of the final report, when available.
- Copies of or full citations for any publications or abstracts

The appropriate forms will be provided to you by the Research and Development office when they are needed. Other information may be required from time to time.

Yours sincerely



PP

MISS TRACEY GILLIES
Medical Director

CC:

Dr Vivek Pattan
Consultant Old Age Psychiatrist
Stirling Community Hospital

Appendix D. Distribution Data of study and demographics variables

	Skewness		Kurtosis	
	Statistic	Std. Error	Statistic	Std. Error
MFSpatient	-1.465	.448	3.579	.872
MFSCaregiver	.099	.448	-.712	.872
MFDcorrected	-.636	.448	1.617	.872
MFTasks	-.105	.448	-.798	.872
MPD	.118	.456	-.181	.887
HADSAp	.985	.448	.218	.872
HADSDp	1.181	.448	1.344	.872
HADSAc	.394	.448	-.530	.872
HADSDc	1.233	.448	1.943	.872
QOLADp	-.046	.448	-.654	.872
QOLADc	.054	.448	-.903	.872
QOLADdiscrepancy	.334	.448	1.028	.872
MMSE	-.384	.448	-.307	.872
ACER	-.368	.456	-.704	.887
DAD	.021	.448	-.891	.872
ZBI	.532	.456	.860	.887
BRSS	-1.533	.448	1.765	.872
NPIQseverity	1.154	.448	1.789	.872
NPIQdistress	2.604	.448	9.433	.872
NPIQtotal	3.199	.448	13.098	.872
WHOQOLphyshealth	-.552	.448	-.231	.872
WHOQOLpsyc	-.722	.448	.545	.872
WHOQOLEnvironment	-1.124	.448	3.667	.872
WHOQOLQOL	-.579	.448	1.102	.872
WHOQOLPHitem	-.716	.448	.319	.872

QOLAD, Quality of life Alzheimer's Disease; p, person with dementia; c, caregiver; MFD, Memory functioning Discrepancy; MPD, Memory Performance Discrepancy; HADS, Hospital Anxiety and Depression Scale, A, Anxiety, D, Depression; NPIQ, Neuropsychiatric symptoms Inventory Questionnaire; Disability Assessment for Dementia; BRSS, Burns Relationship Satisfaction Scale; WHOQOL, World Health Organisation Quality of Life, PH, Physical Health, PSY, Psychological, SR, Environment, Overall quality of life item, overall health item.

Appendix E: Participant Information Sheet – Patient version



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PARTICIPANT INFORMATION SHEET

Awareness in Dementia: How does Insight affect the quality of life for patients and caregivers?

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Why is the study being done?

Alzheimer's disease can have a large impact on people's lives and on those around them. Our study is looking at a part of Alzheimer's disease called **insight**. If you have insight into your illness that means that you are aware that you have it and you know how it affects you, some people with Alzheimer's disease have more insight into their disease than others. This study aims to find out if there is any link between the amount of insight patients with Alzheimer's disease have, how well they feel and amount of things they need help with. We will also look at how patients and carers feel about their situation and other related factors.

Why have I been invited?

We are inviting you to participate because you are receiving care from the Community Mental Health Team for Older Adults. Everyone we ask is over 65 years old, has Alzheimer's disease and has someone close who knows them well and is happy to be interviewed. We asked your doctor to put forward people they thought would be suitable and they asked you if you would be agree to us speaking to you about it. We are inviting you to take part in an interview with one of the research workers to find out if you are eligible for the study. A total of 60 people will participate in the study.

Do I have to take part?

It is up to you to decide whether or not to take part in the study. We will describe the study and go through this information sheet, which we will then give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. If you decide not to take part, this will not affect the care you receive now or in the future.

What will happen to me if I take part?

If you agree you will first take part in an interview with a research worker to find out if you are eligible for the study. The interview will take part at a local clinic or in your own home

You will be involved in the research for 12 months (the study overall will last for 2 years).

You will be asked to complete some questionnaires and take part in assessments with the research worker at the start of the study, and then complete the same questionnaires 12 months later. The research worker will ask about how you have been feeling, how you have been coping and any problems you have experienced. Your caregiver will also be asked to complete some similar questionnaires as well. These assessments will take approximately an hour each to complete and can be spread over more than one visit depending on your preference

What do I have to do?

To enter the study all you need do is to agree to attend the appointments. These will be made to suit your convenience.

What are the disadvantages or risks of taking part?

The assessments involve talking about how you are feeling and seeing how well you can do certain tasks. It may be that this causes some clients discomfort or distress. you will have to give up some of your time to attend the appointments.

What are the possible benefits of taking part?

We hope that the assessments will be interesting and informative for you. However, we cannot promise this. As we will not be changing your treatment in any way, any benefit you might find will be purely coincidental. The information we get from this study may help us to improve the treatment of people with Alzheimer's Disease in future.

What happens when the research study stops?

Once the study is finished we will make the results available to other health care staff by publishing it in a journal and talking about it at conferences. The study should not alter your usual treatment. If you are agreeable, the researcher will pass on information about things you have helpful or unhelpful during session to health care worker.

Will my taking part be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential and will conform to the Data Protection Act of 1998 with respect to data collection, storage and destruction. It will be stored securely on NHS premises. When information is used it will be anonymised.

With your permission, your GP will be notified of your participation in the study as will your Community psychiatric nurse and psychiatrist. However, unless there is information which puts you or others at serious risk of harm, information collected in the study will not be fed back or exchanged without your consent.

We need to assess how your main care giver is coping and so will ask them to complete some questionnaires as well. You may decline permission for us to speak to your care giver. However, this will mean that you cannot take part in the study.

What will happen if I don't want to carry on with the study?

You can withdraw from the study completely at any time and this will not affect your usual treatment.

Will I get any expenses if I take part?

Yes. if you travel to and from the clinic we will refund your travelling expenses.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact number below). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the local hospital.

This study does not involve experimental medications or alter your routine treatment as such we do not expect serious adverse events. There are no special arrangements for compensation within the study.

What will happen to the results of the research study?

We aim to publish the results of the study in a scientific journal but will also make them available to all participants in a non scientific format. We do not expect the results to be available until after the end of the study (2016). Some of the results will also be written up as part of a doctoral thesis.

Who is organising and funding the research?

It is organised by Forth Valley Health Board in partnership with The University of Edinburgh.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by a Research Ethics Committee.

Contact for further information

If you require further information about the study you may contact one of the following people:

Dr Vivek Pattan
Consultant Psychiatrist
worker
CMHT- Older Adults
Stirling Community Hospital
Livilands Gate
Stirling
FK8 2AU

Phone :01786 454 667

Tom Weavers
Trainee Clinical Psychologist/ Research
CMHT- Older Adults
Stirling Community Hospital
Livilands Gate
Stirling
FK8 2AU

Phone: 01786 454 665

Thank you for taking time to read this information.

Version 1.1 date 02/12/14

Appendix F: Participant Information Sheet – Caregiver Version



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PARTICIPANT INFORMATION SHEET Carer Version

Awareness in Dementia: How does awareness of memory symptoms affect the quality of life for patient and caregiver

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Why is the study being done?

Alzheimer's disease can have a large impact on people's lives and on those around them. Our study is looking at a part of Alzheimer's disease called **insight**. If you have insight into your illness that means that you are aware that you have it and you know how it affects you, some people with Alzheimer's disease have more insight into their disease than others. This study aims to find out if there is any link between the amount of insight patients with Alzheimer's disease have, how well they feel and amount of things they need help with. We will also look at how patients and carers feel about their situation and other related factors.

Why have I been invited?

We are inviting you to participate because you are the main care giver for someone receiving care from the Community Mental Health Team for Older Adults who has a diagnosis of Alzheimer's Disease. We are inviting you to take part in an interview with one of the research workers to find out if you are eligible for the study. A total of 60 people will participate in the study.

Do I have to take part?

It is up to you and the person you care for to decide whether or not to take part in the study. You will receive this form in the post and then a researcher will come out to meet you and talk you through this information sheet about the study and answer any

questions you have. We will then ask you and your relative/ friend to sign a consent form to show you have agreed to take part. You are free to withdraw at any time,

without giving a reason. If you decide not to take part, this will not affect the standard of care received. If you or the person you care for does not wish to take then the other party will be able to take part.

What will happen to me if I take part?

You will be asked to complete some questionnaires and take part in assessments with the research worker at the start of the study, and then asked to complete some of the same assessments again after 12 months. The research worker will complete questionnaires about how you have been feeling, how you have been coping, the behaviour of the person you care for and problems you have experienced. These assessments will take approximately one hour to complete and can be spread over more than one visit depending on your preference.

What do I have to do?

To enter the study all you need do is to agree to attend the appointments. These will be made to suit your convenience.

What are the disadvantages and risks of taking part?

The assessments involve talking about how you are feeling and coping and the behaviour of you the person you care for. It may be that this causes some clients discomfort or distress.

What are the possible benefits of taking part?

We hope that the assessments will be interesting and informative for you. However, we cannot promise this. The information we get from this study may help us to improve the treatment of people with Alzheimer's disease.

What happens when the research study stops?

Once the study is finished we will make the results available to other health care staff by publishing it in a journal and talking about it at conferences. The study should not alter your usual treatment. If you are agreeable, the researcher will pass on information about things you have helpful or unhelpful during session to the health care worker of the person you care for.

Will my taking part be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential and will conform to the Data Protection Act of 1998 with respect to data collection, storage and destruction. It will be stored securely on NHS premises. When information is used it will be anonymised.

With your permission, your GP will be notified of your participation in the study as will your Community psychiatric nurse and psychiatrist. However, unless there is information which puts you or others at serious risk of harm, information collected in the study will not be fed back or exchanged without your consent. You may decline permission for us to speak to the person you care for. However, this will mean that you cannot take part in the study.

What will happen if I don't want to carry on with the study?

You can withdraw from the study completely at any time and this will not affect your usual treatment.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact number below). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the local hospital.

This study does not involve experimental medications or alter your routine treatment as such we do not expect serious adverse events. There are no special arrangements for compensation within the study.

What will happen to the results of the research study?

We aim to publish the results of the study in a scientific journal but will also make them available to all participants in a non scientific format. We do not expect the results to be available until after the end of the trial (2016). *Some of the results will also be written up as part of a doctoral thesis.*

Who is organising and funding the research?

This study is funded by the National Institute of Health Research. It is organised by Forth Valley Health Board in partnership with The University of Edinburgh.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by a Research Ethics Committee.

Contact for further information

If you require further information about the study you may contact one of the following people:

Dr Vivek Pattan
Consultant Psychiatrist
worker

CMHT- Older Adults
Stirling Community Hospital
Livilands Gate
Stirling
FK8 2AU

Phone :01786 454 667

Tom Weavers
Trainee Clinical Psychologist/ Research

CMHT- Older Adults
Stirling Community Hospital
Livilands Gate
Stirling
FK8 2AU

Phone: 01786 454 665

Thank you for taking time to read this information.

Version 1.1 date 02/12/14

Appendix G: Consent form – Patient

PATIENT CONSENT FORM

Awareness in Dementia: How does awareness of symptoms affect the quality of life for patient and caregiver

Please tick yes/no &
initial box

CONSENT FOR PARTICIPATION IN TRIAL

- | | | |
|---|---|-----------------|
| 1 | I confirm that I have read and understand the information sheet dated (version.....) for the above study and have had the opportunity to ask questions. | YES.....NO..... |
| 2 | I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. | YES.....NO..... |
| 3 | I understand that data collected during study may be looked at by individuals from regulatory authorities or from NHS. I give permission for these individuals to access to my records. | YES.....NO..... |
| 4 | I understand that my GP and my medical consultant will be informed of my participation in the trial. | YES.....NO..... |
| 5 | I agree to take part in the above study. | YES.....NO..... |

ADDITIONAL CONSENTS

- | | | |
|---|---|-----------------|
| 6 | I agree to be contacted again in a years time to see if I am willing to take part in the follow up part of the study. | YES.....NO..... |
|---|---|-----------------|

SIGNATURES

Name of Participant

Signature

Date

Researcher

Signature

Date

*Name of Person taking consent
(if different from researcher)*

Signature

Date

Appendix H: Consent form – Caregiver

CONSENT FORM for relatives & caregivers

Awareness in Dementia: How does awareness of symptoms affect the quality of life for patient and caregiver

CONSENT FOR PARTICIPATION IN TRIAL

Please initial box

- 1 I confirm that I have read and understand the information sheet dated (version) for the above study and have had the opportunity to ask questions. YES....NO....
- 2 I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights or those of my friend/relative being affected. YES....NO....
- 3 I agree to take part in the above study. YES....NO....

ADDITIONAL CONSENTS

- 4 I agree to be contacted again in a years time to see if I willing to take part in the follow up part of the study. YES....NO....

Name of Relative/Friend

Signature

Date

Researcher

Signature

Date

Appendix I: Demographic questionnaire

Demographics Data Sheet

Gender

Patient

- Male
- Female

Carer

- Male
- Female

Patient Age..... Carer age.....

Patient Probable diagnosis

- Alzhiemer's Disease
- Mixed AD/ Vascular
- Mixed AD/Other.....

Patient Marital Status

- Single (never Married)
- Married
- Partnered (other than married)
- Separated/ Divorced
- Widowed

Patient Relationship to Carer

- Spouse/ partner
- Sibling
- Son/ daughter
- friend
- other.....

Patient Highest Academic Achievement

- Primary school
- High School
- Trade or Technical Certificate
- College Diploma
- University degree
- Post Graduate degree
- other.....

Carer Highest Academic Achievement

- Primary school
- High School
- Trade or Technical Certificate
- College Diploma
- University degree
- Post Graduate degree
- other.....

Patient Living arrangements

- living at home (supported by family/ carer or partner)
- living with family/carers but not own home
- living alone
- living in sheltered accommodation
- Other.....

Carer living arrangements if not evident from patient living arrangements.....

Other patient health needs.....

Other Carer health needs.....

Ethnicity (Write P for Patient, C for Carer)

White

1. British
 2. Any other white background (please specify)
-

Black

1. British
 2. Caribbean
 3. African
 4. Any other black background (please specify)
-

Asian

1. British
 2. Indian
 3. Pakistani
 4. Bangladeshi
 5. Any other Asian background (please specify)
-

Chinese

1. British
 2. Chinese
 3. Any other Chinese background (please specify)
-

Mixed

1. White & Black Caribbean
2. White & Black African

3. White & Asian
 4. White & Chinese
 5. Any other mixed background (please specify)
-

Other ethnic group

1. Other ethnic group not above (please specify)
-

Appendix J: Guidelines for journal submission:

Author Guidelines

1. AIMS & SCOPE

The rapidly increasing world population of aged people has led to a growing need to focus attention on the problems of mental disorder in late life. The aim of the *International Journal of Geriatric Psychiatry* is to communicate the results of original research in the causes, treatment and care of all forms of mental disorder which affect the elderly. The Journal is of interest to psychiatrists, psychologists, social scientists, nurses and others engaged in therapeutic professions, together with general neurobiological researchers.

The Journal provides an international perspective on the important issue of geriatric psychiatry, and contributions are published from countries throughout the world. Topics covered include epidemiology of mental disorders in old age, clinical aetiological research, post-mortem pathological and neurochemical studies, treatment trials and evaluation of geriatric psychiatry services.

Further information about the Journal, including links to the online sample copy and contents pages, can be found on the [Journal homepage](#).

2. MANUSCRIPT CATEGORIES

The *International Journal of Geriatric Psychiatry* invites the following types of submission:

Research Articles

Research Articles are the Journal's primary mode of scientific communication. Peer-review of Research Articles will be handled by the most appropriate [Editor](#). Research Articles must not exceed **3500** words of body text, and are limited to 6 figures/tables.

Review Articles

Review Articles will typically be solicited by the Editors. Authors who wish to submit an unsolicited review should first contact one of the Editors to determine its suitability for publication in the Journal. All reviews will be peer-reviewed. Reviews must not exceed **4500** words of body text, and are limited to 6 figures/tables and 150 references.

Letters to the Editor

Letters to the Editor, or Correspondence, may be in response to issues arising from recently published articles, or short, free-standing pieces expressing an opinion, but should not exceed **700** words of body text, and are limited to 1 figure/table and 5 references. Letters are not subject to external peer-review.

3. MANUSCRIPT SUBMISSION

All submissions should be made online at the *International Journal of Geriatric Psychiatry* **ScholarOne Manuscripts** site— <http://mc.manuscriptcentral.com/gps>. New users should first create an account. Once a user is logged onto the site, submissions should be made via the Author Centre.

4. MANUSCRIPT PREPARATION

Manuscripts must be written in English.

Text should be supplied in a format compatible with Microsoft Word for Windows (PC). Charts and tables are considered textual and should also be supplied in a format compatible with Word. All figures (illustrations, diagrams, photographs) should be supplied in jpg, tiff or eps format.

All manuscripts must be typed in 12pt font and in double space with margins of at least 2.5 cm.

Manuscripts must comply with the word limits defined in section 2, and include:

Title Page

The first page of the manuscript should contain the following information:

- the title of the paper
- a running head not exceeding 50 characters
- 2–6 article keywords **and** up to 4 key points
- names of authors
- names of the institutions at which the research was conducted
- name, address, telephone and fax number, and email address of corresponding author
- the name(s) of any sponsor(s) of the research contained in the paper, along with grant number(s)
- the word count of the body text

Structured Abstracts

Authors submitting Research and Review Articles should note that structured abstracts (maximum 250 words) are required. The structured abstract should adopt the format: Objective, Methods, Results, Conclusions. (Authors of Reviews may use Design instead of Method.) Abstracts should contain no citation to other published work.

Letters to the Editor do not require abstracts.

Text

This should in general, but not necessarily, be divided into sections with the headings: Introduction, Methods, Results, Discussion, Conclusion.

Research Letters and Correspondence should be formatted in one continuous section.

Tables and Figures

Tables and figures should not be inserted in the appropriate place in the text but should be included at the end of the paper, each on a separate page.

Tables and figures should be referred to in text as follows: Figure 1, Figure 2; Table 1, Table 2. The place at which a table or figure is to be inserted in the printed text should be indicated clearly on a manuscript. Each table and/or figure must have a legend that explains its purpose without reference to the text.

Any figure submitted as a colour original will appear in colour in the Journal's online edition free of charge. Colour figures will be printed in the Journal on the condition that authors contribute to the associated costs: **£350** for the first page; **£150** for each subsequent page thereafter. Corresponding authors will be invoiced post-publication.

References

References should be in 'Harvard' format, i.e. names and dates in brackets in the text (Jones, 2000; Smith and Jones, 2001; Jones *et al.*, 2002), and the full reference listed at the end of the paper, in alphabetical order by first author, as follows:

Porteus SD. 1959. *The Maze Tests and Clinical Psychology*. Pacific Books: Palo Alto.

Rabbitt PMA. 1982. How do old people know what to do next? In *Aging and Cognitive Processes*, Craik FIM, Trehub S (eds). Plenum Press: New York; 79–98.

Chou K-L, Chi I. 2004. Combined effect of vision and hearing impairment on depression in elderly Chinese. *Int J Geriatr Psychiatry* **19** : 825–832. DOI: 10.1002/gps.1174

(Titles of periodicals should be abbreviated according to the style used in Index Medicus.)

We recommend the use of a tool such as EndNote for reference management and formatting.