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Ambulatory blood pressure monitoring in older people with dementia: a systematic review of tolerability.

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Ambulatory blood pressure monitoring in older people with dementia: a systematic review of tolerability

Abstract n = 255

Background: Ambulatory Blood Pressure Monitoring (ABPM) may be helpful for the management of hypertension, but little is known about its tolerability in people with dementia.

Objective: to review the published evidence to determine the tolerability of ABPM in people with dementia.

Methods: English language search conducted in MEDLINE and EMBASE, using 'Ambulatory blood pressure' AND 'Dementia' (and associated synonyms) from 1996-March 2015. Inclusion criteria: people diagnosed with dementia AND in whom blood pressure was measured using ABPM. The initial search was undertaken using title and abstract reviews, with selected papers being agreed for inclusion by two reviewers. Potentially eligible papers were assessed, and high quality papers retained. Two reviewers agreed the abstracted data for analysis. Meta-analysis was used to combine results across studies.

Results: Of the 221 screened abstracts, 13 studies (6%) met inclusion criteria, five had sufficient data and were of sufficient quality, involving 461 participants, most of whom had mild-moderate dementia.

77.7% (95% CI 62.2-93.2%)were able to tolerate ABPM; agreement with office BP was moderate to weak (two studies only - coefficients 0.3-0.38 for systolic blood pressure

and 0.11-0.32 for diastolic blood pressure). One study compared home BP monitoring by a relative or ambulatory BP monitoring with office BP measures, and found high agreement (κ 0.81). The little available evidence suggested increased levels of dementia being associated with reduced tolerability.

Conclusions: ABPM is well-tolerated in people with mild-moderate dementia, and provides some additional information over and above office BP alone. However, few studies have addressed ABPM in people with more severe dementia.

Key words

- Hypertension
- Dementia
- Ambulatory blood pressure monitoring

Key points

- Essential hypertension and dementia commonly co-exist
- People with dementia are particularly susceptible to the potential harms associated with over-treatment of hypertension
- Ambulatory Blood Pressure Monitoring is a useful adjunct to office blood pressure monitoring, and is tolerated in people with dementia able to attend clinics
- There is a paucity of data on the tolerability of blood pressure monitoring in people with more advanced dementia

Background

Hypertension is a global health challenge, with a prevalence of 50% in community dwelling people aged 65 years or older [1]. Out-of-office Blood Pressure (BP) is an important adjunct to conventional office or clinic measurement, which presently remains an important method for screening, diagnosing and managing hypertension [2]. Out-of-

office BP monitoring includes 24-hour Ambulatory Blood Pressure Monitoring (ABPM), as well as home blood pressure monitoring (HBPM); both have the advantage of capturing a number of BP measurements in a more natural environment [2]. ABPM is therefore particularly useful in patients with anxiety, or potential haemodynamic side effects such as symptomatic hypotension, or where BP variability is expected or observed. The 2011 National Institute for Health and Clinical Excellence (NICE) guidelines suggested that the diagnosis and treatment decisions in hypertension should no longer be based on office measurements alone, and that confirmatory out-of-office measurements should be mandatory [1].

Dementia represents another global health challenge, affecting 35.6 million people worldwide in 2010 [3]. The prevalence of hypertension in people with dementia ranges between 35%-84% [4]. ABPM is likely to be particularly useful in the management of hypertension in people with dementia, who commonly experience issues such as anxiety, haemodynamic side-effects and BP variability. However, for ABPM to be useful in widespread practice in people with dementia, it needs be tolerable and acceptable, and produce results that are complementary to office measures.

The most recent European guidelines do not advise on the management of hypertension in older people with dementia [2]. It appears that little is known about the tolerability of ABPM in people with dementia, so we undertook a review of the existing literature.

The aim of this systematic review was to determine the tolerability of home BP monitoring in older people with hypertension and dementia, defined as follows:

- Tolerability of using 24 hour ambulatory BP measurement in people with dementia
- The correlation between ABPM and office blood pressure measurements

Methods

An English language search of Medline and EMBASE databases (1996+) was conducted in December 2013 and updated in March 2015; the search terms were:

- dementia.mp. OR exp Dementia, Vascular/ OR exp Dementia, Multi-Infarct/ OR exp Dementia/

AND

- ambulatory blood pressure.mp. OR exp Blood Pressure Monitoring, Ambulatory/ OR 24 hour blood pressure.mp.

A hand search of the references of extracted articles was also conducted to identify potential studies not captured in the electronic database searches.

Inclusion criteria

- Studies including people diagnosed with dementia
- BP was measured using HBPM or ABPM

One team member (MK) screened abstracts identified from the initial search. If a study met the initial selection criteria or its eligibility could not be determined from the title or abstract, the full text was retrieved. Two reviewers (MK and SC) then independently assessed the full text papers for inclusion eligibility; any discrepancies were resolved through discussion.

Included studies were graded using the Critical Appraisal Skills Programme (CASP) tool for observational studies by both reviewers [5]. A cut-off score of more than 50% for scored items was used for retaining papers, with disagreements again resolved through discussion.

Outcomes

The primary outcome of interest was the proportion of individuals with dementia who were able to tolerate ABPM (as defined according to the individual study criteria, or if not stated, then using the definition of tolerability from O'Brien *et al* [2003][6] which requires a minimum of 14 readings during the day and seven readings at night). Secondary outcomes included:

- Agreement between ABPM readings versus clinic BP in people with dementia
- Any reasons why ABPM was not tolerated in people with dementia

Data were extracted from the selected papers using a spreadsheet by both reviewers independently, and where this was not available, the original authors were contacted for further information. Considerable efforts were made to track down primary data including web searches to identify authors that had changed institution and personal contacts with co-authors or collaborators; if the authors were not contactable or the data not available, the study was excluded.

The PRISMA statement [7] was used to guide design and reporting.

Analysis

Data were abstracted from the original papers by two reviewers (MK, SC), and cross-checked for accuracy.

The proportion of people able to tolerate 24-hour ABPM was combined in a meta-analysis. Heterogeneity was quantified with the I^2 statistic, which measures the percentage of variation among studies due to heterogeneity rather than to chance. We considered heterogeneity to be important when I^2 was more than 30%. As it was deemed appropriate to combine studies, if there was high heterogeneity, a random effects model was used. The meta-analysis was undertaken using MedCalc Statistical Software version 15.2.2 (MedCalc Software, Ostend, Belgium; http://www.medcalc.org; 2015).

A similar approach was used for the correlation coefficients (and accompanying standard deviations); Cohen's interpretation was used (0.10-0.29 - weak relationship, 0.30-0.49 - medium relationship, ≥0.50 - strong relationship [8]).

Any descriptive data on the tolerability of ABPM was to be synthesised using a thematic analysis.

This work was undertaken during MK's academic clinical fellowship, there was no specific funding.

Results

221 abstracts were identified from the initial search of which 10 (5%) met the inclusion criteria (see Figures 1 and 2) [Nesti 2014 [9], Plichart 2013 [10], Chen 2013 [11], Kim 2012 [12], Mossello 2012 [13], Kennelly 2011 [14], Zulli 2008 [15], Yamamoto 2002 [16], Yamamoto 2005 [17] and Puisieux 2001 [18]]. Two of the papers referred to the same cohort of patients assessed at different time points, so both were considered potentially eligible [Yamamoto 2002 & 2005].

At least some outcome data were available for five papers [Nesti 2014 [9], Plichart 2013 [10], Kennelly 2011 [14], Mossello 2012 [13] and Zulli 2008 [15]]; for remaining five papers, the data were missing or unobtainable. The five papers with missing data for our primary outcome were broadly similar to the included studies, and in total looked at 268 older people with vascular or Alzheimer's dementia in a clinic setting.

Of the studies for which there was data, four were cohort studies [Nesti 2014, Plichart 2013, Mossello 2012, Kennelly 2011] and one was a case-control study [Zulli 2008]; all scored more than 50% on the CASP scores. The studies reported upon 461 participants, with mean ages ranging from 69 to 81 years, and most patients included in the studies had mild to moderate dementia, with a Mini-Mental State Examination (MMSE) score ranging from 9 to 23. All reported upon ABPM, with no studies reporting upon home BP monitoring. The overall quality of studies was good (mean CASP score 79%). The study selection process in shown in figure 1 and the summary data are shown in table 1.

Figure 1 Flow diagram of selection of studies focusing on ambulatory blood pressure measurement in people with dementia

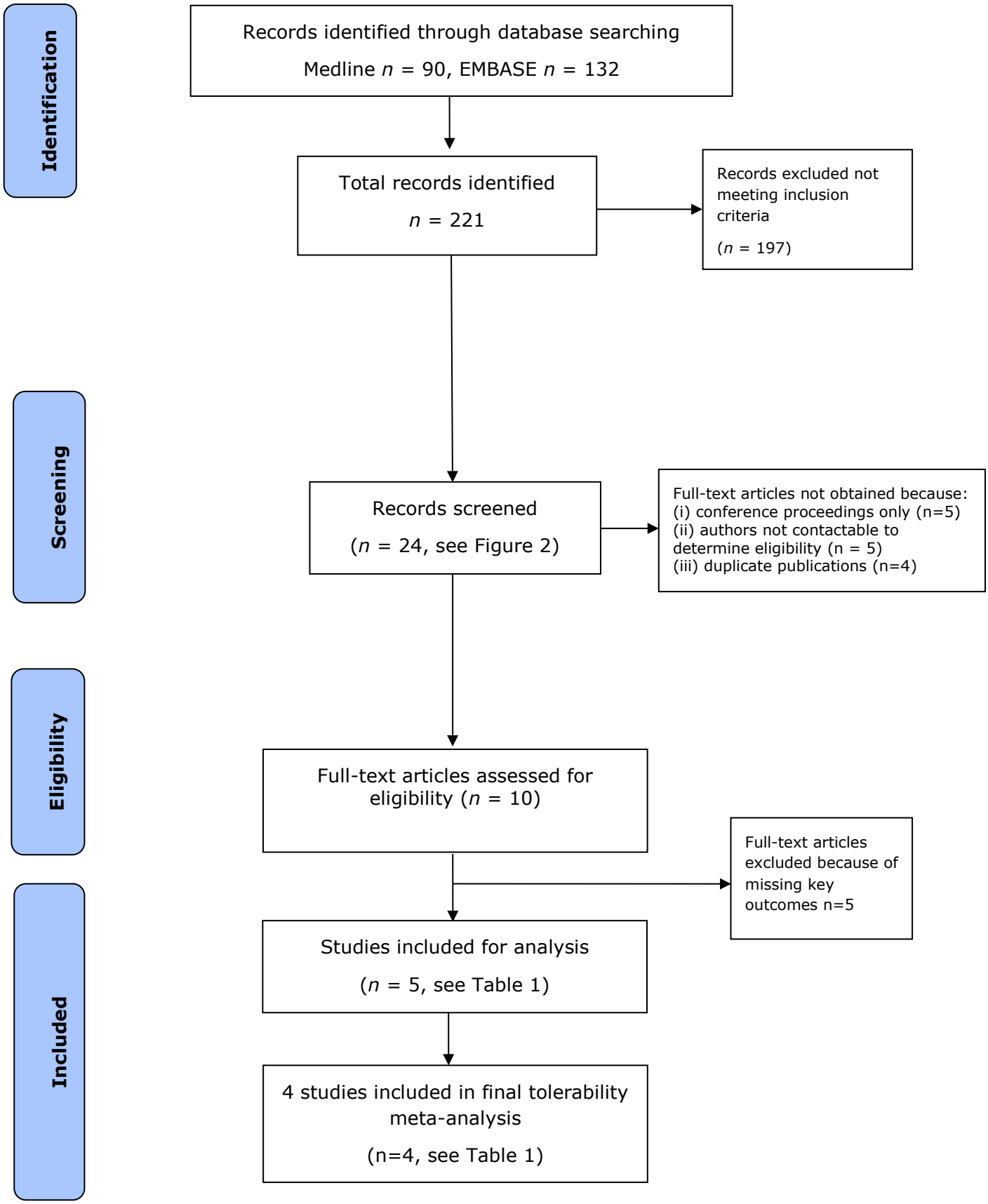


Table 1 Summary of the main study characteristics

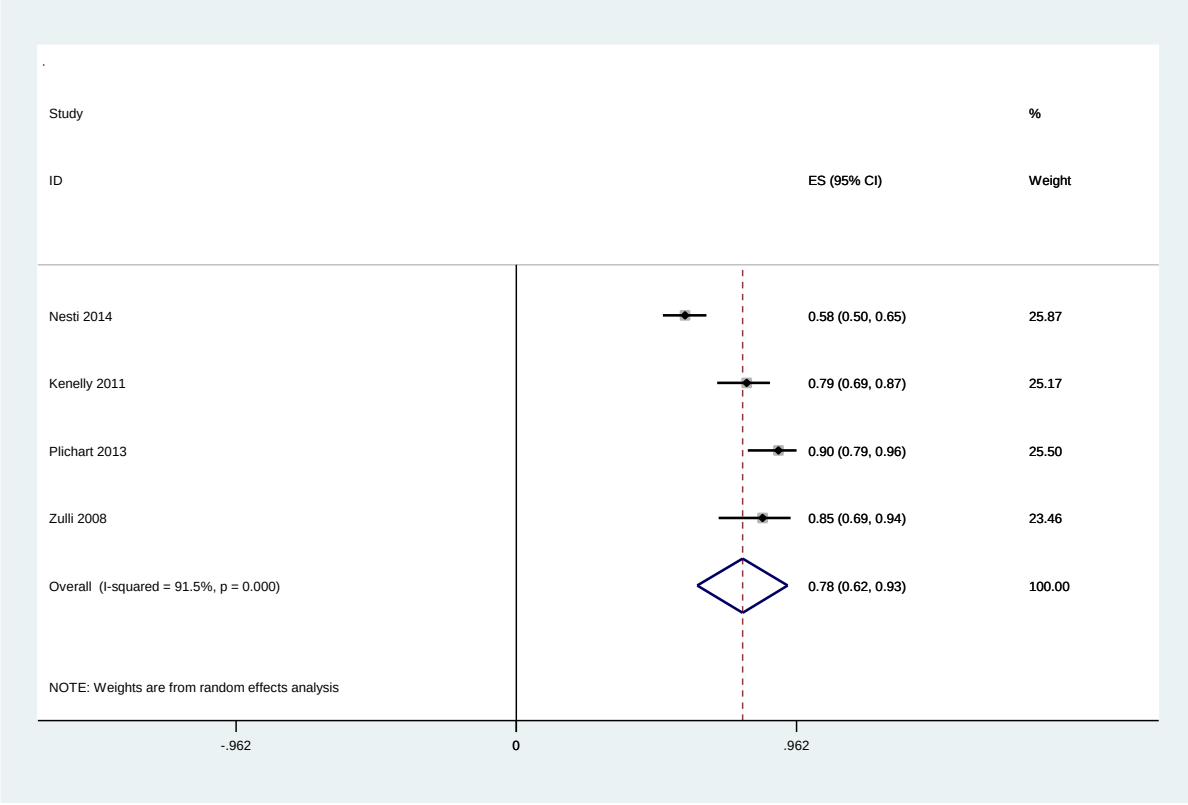
References	Population	Study design & CASP score	Measurement	Primary outcome Proportion able to tolerate 24-hour monitoring	Secondary outcomes Correlation between ABPM and office (cuff)	 Assessment of tolerability of ABPM
Nesti 2014	176 people with dementia (DSM-IV criteria) or MCI attending memory clinics Mean MMSE 21.7, range 10-27 Mean age 79 Italy	Cohort CASP score 91%	24-hour ABPM monitoring using SpaceLabs Medical 90207 device Tolerability defined as at least 54 readings over 24-hours	147/176 (84%) tolerated for 24 hours 45 of the 147 did not achieve the defined minimum for this study (mean for those not tolerating 49 (SD 5) readings) Overall tolerability rate using the criteria for this study = 102/176 (58%)	Not stated	Failure rates higher in those with MMSE score in the lower tertile (29%) vs upper tertile (7%) Failure rates higher in those with higher Neuropsychiatric Inventory Indexes (e.g. 30% vs 8%)
Plichart 2013	60 patients with dementia (criteria not stated) Mean MMSE 20.1 (SD 6.9) Mean age 80.8 France	Cohort, randomly allocated to sequential home BP monitoring by a relative OR 24-hour ABPM CASP score 82%	24-hour ABPM monitoring using Novacor DIASYS 200 device 12/18 readings for relative home BP monitoring	54/60 (90%)	Reported as agreement for diagnosis of hypertension with office BP – κ 0.81, 95% CI, 0.61–0.93, "strong".	No assessment of tolerability/acceptability
Mossello 2012	100 patients in a nursing home No. of patients with AD not defined, but mean MMSE in survivors 16.5, and 8.6 in those that died during follow-up	Cohort CASP score 68%	24-hour ABPM monitoring using Space Labs Medical 90207 device Number of readings for inclusion of	Not given	Systolic = 0.30, p=0.025 "weak" Diastolic = 0.11, p>0.05 "weak"	No assessment of tolerability/acceptability

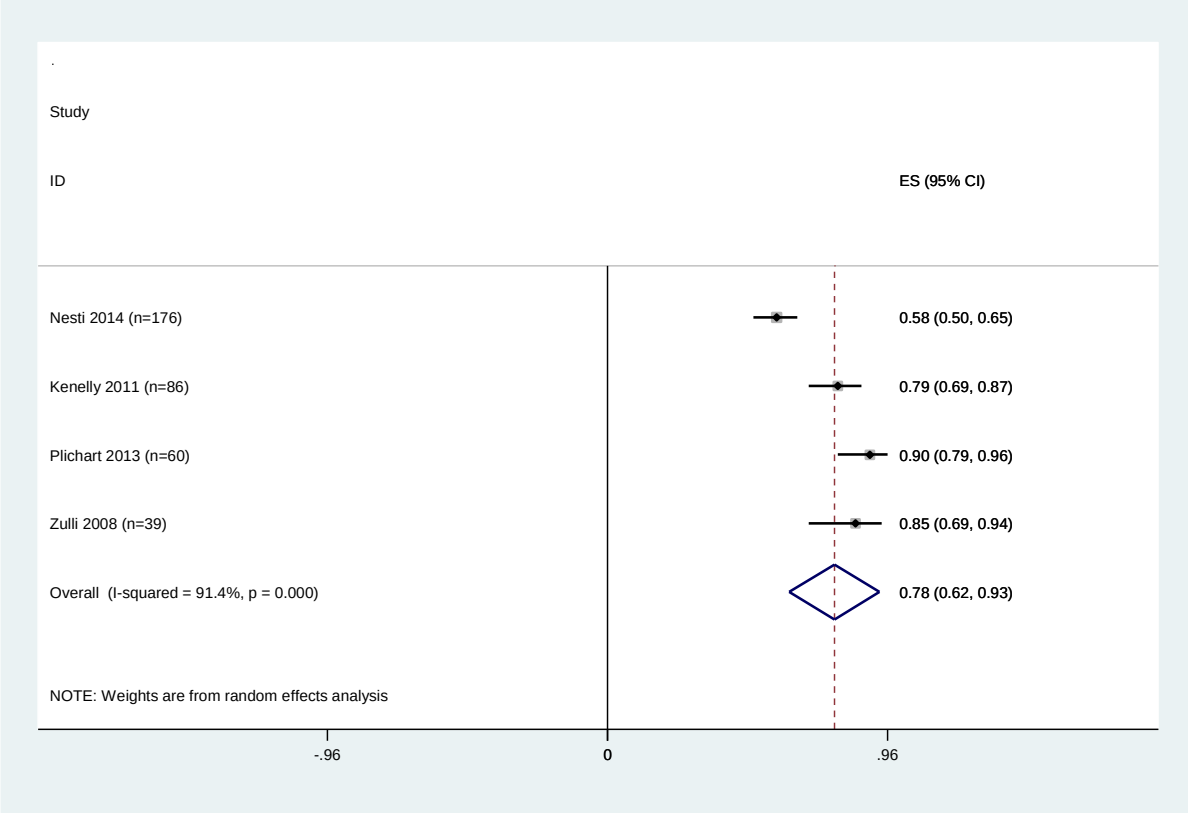
	Mean age survivors: 82, died during follow-up 85 Italy		ABPM results in the analysis not defined.			
Kennelly 2011	Diagnoses of probable AD according to NINCDS-ADRDA Alzheimer's criteria *Group A (no treatment) n=30* Mean age: 71.2 MMSE: 22.6 *Group B (treatment) n=56* Mean age: 69.3 MMSE: 21.5 Ireland	Cohort CASP score 80%	24-hour ABPM monitoring using A&D TM-2430 device Number of readings for inclusion of ABPM results in the analysis not defined.	68/86 (79%)	Systolic = 0.38 "moderate" Diastolic = 0.32 "moderate"	No assessment of tolerability/acceptability
Zulli 2008	39 patients with Alzheimer's dementia (DSM IV and NINCDS-ADRDA criteria) Male/Female, *n*: 13/20 Age, mean (SD): 72.1 (SD 8.2) Mean MMSE 19.0 (SD 4.3) Italy	Case control (data for 39 with dementia reported only) CASP score 73%	24-hour ABPM monitoring using SpaceLabs Medical 90207 device Number of readings for inclusion of ABPM results in the analysis not defined.	33/39 (85%)	Not stated	No assessment of tolerability/acceptability

Note: subject characteristics are for people with dementia within a given cohort conducted in the respective studies unless indicated otherwise, SBP: systolic blood pressure, DBP: diastolic blood pressure, NINCDS-ADRDA: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association, DSM: Diagnostic and Statistical Manual of Mental Disorders.

For the primary outcome (the proportion of individuals with dementia who were able to tolerate ABPM), I^2 was 91% indicating significant heterogeneity, therefore the random effects estimate was used for the summary estimate. In a population with predominantly mild-moderate and some with severe dementia, ABPM tolerability was 77.7% (95% CI 62.2-93.2%) (Figure 2).

Figure 2 Reported 24-hour ABPM tolerability for people with dementia





Only two studies reported agreement between office BP and home BP measurements (Kennelly, Mosselo); Pearson's correlation coefficients were moderate-weak for both

systolic and diastolic blood pressure (0.30-0.38 and 0.11-0.32 respectively). Plichart reported a kappa coefficient comparing home BP monitoring by a relative to ambulatory BP monitoring, which was strong (0.81). Given the paucity of data on correlation or agreement, a meta-analysis was not undertaken.

Only one study (Nesti 2014) examined further the issues underpinning tolerability, noting that people with more severe dementia or higher levels of agitation measured using the Neuropsychiatric Index were less tolerant of ambulatory BP monitoring.

Discussion

The overall tolerability of ABPM monitoring in people with dementia was 77.7% (95% CI 62.2-93.2%) based on our meta-analysis of four studies, which is similar to other patient cohorts [19, 20]. The correlation between ABPM and office BP measurements was moderate to weak, but based on only two studies. Little was reported on the reasons why ABPM was not tolerated, but more advanced dementia appears to be associated with less tolerability. People with more severe cognitive impairment were significantly under-represented in these studies; most of the studies only included populations that were well enough to attend clinic settings, including the five excluded studies for who our primary outcome was not available.

The studies included were heterogeneous in terms of design (cohort studies and case control studies), but similar in that they reported on blood pressure measurement in people with dementia; the overall quality was high (minimum CASP score 68%). Despite efforts to contact authors of original studies to identify all possible data, we were unable to obtain data from studies involving older people with moderate to severe dementia. The studies that were identified but not included in this review appeared similar in terms of the population studied, but it is possible that ABPM might be in use in those with moderate to severe dementia and only a limited amount of this experience has been studied and reported. This limits the generalisability of the findings to populations with more severe cognitive impairment.

The correlation between ABPM and office BP measurements was moderate to weak, in contrast to studies involving people without dementia, which find strong correlations of around 0.61 for systolic BP and 0.55 for diastolic BP [21]. Although this could be interpreted as demonstrating that ABPM is potentially inaccurate, a more likely interpretation is that there are important differences in ambulatory and clinic BP measures in people with dementia and hence that ABPM offers complementary information. However there were only two studies reporting on this and further studies would be required before making any clinical recommendations based on these data.

These findings provide some reassurance that, in a predominantly clinic-based population with dementia, ABPM will be feasible in the majority. This is helpful as older patients with cognitive dysfunction are at increased risk of white coat hypertension [22], and so might be used to avoid unnecessary treatment in those people who do not have sustained hypertension. Additional advantages of ABPM include identification of periods of hypotension, which is associated with a range of adverse outcomes in people with dementia, including accelerated cognitive decline [23-26] and falls [27]. ABPM can also identify orthostatic hypotension, which accompanies hypertension in around 30% of older people in general [28], which is associated with vascular mortality [29] and all-cause mortality [30].

This review has not fully addressed the issue of assessing blood pressure in people with more advance dementia, who were under-represented in the studies to date, and arguably who are at greater risk of harm.

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