## Research

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# Under-provision of medical care for vascular diseases for people with dementia in primary care:

a cross-sectional review

#### **Abstract**

#### Background

Vascular diseases contribute to the causation and progression of clinical dementia.

To evaluate the quality of medical care for vascular diseases provided to people with dementia, the patient and practice characteristics that influence quality, and to compare care with that provided to those without dementia.

#### **Design and setting**

Observational, cross-sectional review of primary care records of people with dementia from 52 general practices from five primary care trusts in the UK, and comparison with publicly available summary data on patients without dementia.

A total of 700 patients with ≥1 diagnosed vascular disease or risk factor were identified from dementia registers. Quality of care was measured on 30 indicators from the UK Quality and Outcomes Framework (QOF) for hypertension, coronary heart disease, stroke, diabetes mellitus, atrial fibrillation, heart failure, and smoking. Overall quality of vascular care was calculated for each patient with dementia.

### Results

Level of care received by people with dementia was significantly lower compared with those without dementia for 22 of 30 (73%) indicators; most notably for measurement processes such as peripheral pulses check and neuropathy testing for diabetes, and cholesterol measures for stroke. Among people with dementia, women, those in care homes, and those with fewer comorbid physical conditions and medications were associated with lower scores for overall quality of vascular care.

#### Conclusion

The quality of medical care provided to people with dementia with regard to vascular diseases is not concordant with quality, as defined by the QOF. Research is needed to improve access to high-quality care.

dementia; general practice; health care; quality indicators; vascular diseases.

#### INTRODUCTION

An estimated 821 884 people have dementia in the UK.1 Compared with older people without dementia, people with Alzheimer's disease and other dementia subtypes have significantly reduced survival;2-4 this may, in part, be explained by the presence of comorbid vascular diseases, including congestive heart failure, ischaemic heart disease, diabetes, and cerebrovascular disease.5,6 Incidence of recurrent stroke is doubled in people with dementia.7 Whether other comorbid conditions are more frequent and underdiagnosed in people with dementia is debated8-10 and not all studies have found comorbid vascular diseases to predict a more rapid progression of dementia,11 however, there is some evidence that controlling high blood pressure, atrial fibrillation, and angina may slow cognitive decline in dementia. 12

Patient characteristics that have been associated with better quality of care include older age, greater dementia severity, 13 and greater comorbidity, although the latter's relationship with quality of care is not entirely clear.14-16 Compared with people living in the community, those living in care homes receive poorer care for conditions like heart disease and diabetes, and potentially harmful medications (for example, antipsychotics) are overprescribed. 17-19 Practice characteristics such as small list size, low level of socioeconomic deprivation, 20 and a large number of GPs<sup>21</sup> have also been associated with better quality of care for people with dementia.

The gaps in the quality of care for people with dementia are documented in terms of:

- · the detection rates of dementia, and associated behavioural and psychological symptoms of dementia;22-24
- end-of-life care;25 and
- care provided to those in care homes.<sup>26</sup>

A few studies based in secondary and long-term care settings have also found suboptimal care for individual comorbid diseases such as acute myocardial infarction,<sup>27</sup> prevention of secondary or recurrent stroke, 28,29 and atrial fibrillation.29

Primary care services are the first point of contact and main healthcare service for people with dementia. 30-32 It has been shown that the quality of annual reviews done in primary care for dementia is suboptimal and, despite a high prevalence of vascular diseases, over one-quarter of individuals diagnosed with dementia are prescribed antipsychotic medications that are known to increase the risk of cerebrovascular accidents and mortality.33 In the current study, the quality of care for vascular conditions and risk factors received by

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#### How this fits in

Vascular diseases are important in predicting the progression of dementia, including Alzheimer's disease, and contribute to increased risk for mortality. Suboptimal quality of care in the treatment of individual vascular diseases, such as myocardial infarction or stroke in people with dementia has previously been studied; however, none of the studies has investigated or combined the quality of care received by people with dementia who have comorbid vascular disease or risk factors across multiple domains. Despite high levels of vascular-related comorbidity and equitable intermediate outcomes, this study found that a greater proportion of people with dementia, compared with those without dementia, do not receive provision for routine care measurements outlined in Quality and Outcomes Framework targets for vascular diseases and risk factors. These findings support further research on the unique clinical and organisational challenges to the commissioning and administration of routine medical care for vascular-related conditions for people who have dementia. especially those who are living in care homes.

people with dementia within primary care were evaluated, together with the patientand practice-level factors associated with it.

#### **METHOD**

The study sample selection and dataextraction methods have previously been described in detail.33 In brief, primary care electronic and paper records of 1006 people with dementia from dementia registers of a stratified random sample of 52 general practices from five primary care trusts (PCTs) in Greater Manchester were examined by trained researchers, using a proforma tool designed and piloted for the study purpose. From these, 12 people who had revoked diagnoses or were deceased were excluded. People with dementia (n = 700) who were diagnosed to have at least one of the vascular diseases or risk factors were included in the current analyses (Figure 1). Data collected included patient demographics (age, sex, living situation), subtype of dementia, comorbid physical and mental health conditions, current medications, and all recorded consultations and tests.

#### Quality-of-care measures

To measure quality of care received for vascular diseases and risk factors, 30 quality indicators for hypertension, coronary heart disease, stroke/transient ischaemic attack (TIA), diabetes mellitus, atrial fibrillation, heart failure, and smoking were used. These were taken from the UK Quality and Outcomes Framework (QOF) guidelines for general-practice remuneration.34

A total quality-of-vascular-care score was calculated for each patient as follows:

> number of relevant indicators for which care was provided

number of indicators for which the patient was eligible

Not all indicators applied to all patients. Expressed as a percentage, the score represents the proportion of indicators adhered to for each patient, within a range of 0-100%. This approach has been used in studies of overall quality of care for major chronic diseases;35 it gives each patient equal weight, regardless of the number of indicators for which they are eligible. 35,36 All quality indicators were treated equally as all those that were appropriate should have been recorded.

#### Comparison data on patients without dementia

The study obtained information on the number of patients who were eligible for (that is, all patients on each disease register, including those with dementia), and who had met, each QOF indicator in each participating practice from online QOF 2008/2009 databases (NHS: Health and Social Care Information Centre [NHSIC], www.ic.nhs.uk).

Practices have the capacity to remove individual patients from the calculations of practice achievement for specific indicators; for example, if a patient is unsuitable for treatment or is newly registered with the practice. This is called 'exception reporting'. Achievement levels were adjusted to incorporate the number of patients with dementia who were exception reported in relevant indicator denominators (obtained from NHSIC online databases), as this information was not originally collected as part of the study.

For each indicator, the numbers of people with dementia with a record of an indicator being met and those eligible for it were subtracted from the numerator and denominator respectively, creating a 'without-dementia' comparison group. For example, if 35 000 out of 40 000 individuals with hypertension received a bloodpressure check, and 300 out of 400 people

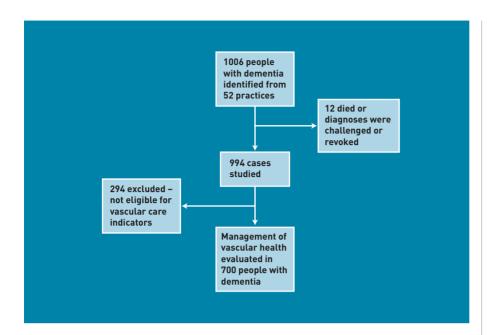


Figure 1. Selection of people with dementia eligible for vascular care.

with dementia and hypertension also did; then this would leave 34 700 (35 000 - 300) out of 39 600 (40 000 - 400) individuals without dementia.

#### Statistical analysis

Descriptive statistics were analysed using SPSS for windows (version 16.0). The proportion of people with dementia who had received care for each quality indicator from those who were eligible for it was calculated. Comparisons between the care received by people with dementia and that of all other patients with the disease (not known to have dementia) for all 30 QOF vascular indicators were made using Pearson  $\chi^2$  tests (or Fisher's exact test, where a cell size was <5), with a Bonferroni correction of the alpha level (0.05) for the multiple comparisons.

To investigate the factors influencing total quality of vascular care, multilevel linear regression analysis was used, as it deals with a lack of independence within clusters, such as patients grouped into practices and practices grouped into PCT.37,38 There were three levels in the multilevel analyses: patient, practice, and PCT.

Univariate associations were initially explored, with patient-level and practicelevel independent variables. Patient-level variables were:

- · age;
- sex;
- dementia duration;
- living situation (living in nursing/care home versus community);

- comorbid physical conditions;
- medications; and
- dementia subtype (Alzheimer's disease, including mixed dementia, vascular dementia, and other dementia).

Practice-level variables were:

- whether the practice was run by one GP (single-handed) versus several (multihanded).
- socioeconomic deprivation of practice location, as measured by the Index of Multiple Deprivation 2007;39 and
- the size of the registered population aged >65 years.

Multivariate models adjusting for all variables were then analysed. A normalising transformation could not be applied to the non-normally distributed dependent variable used in these analyses. Although regression analysis has been found to be reasonably robust to some nonnormality, 40 sensitivity of the main analyses were assessed by using a multilevel logistic model with a median-split outcome variable. No differences in significance were identified, hence, the main analysis is reported. All multilevel modelling analyses were performed using Stata (version 11.0).

#### **RESULTS**

#### Demographics

The study sample included 700 people with dementia (female 66%, mean [standard deviation, SD] age 82.1 [8.0] years) from 52 general practices (mean [SD] list size 7418 [3405]). Each patient had ≥1 comorbid conditions covered by at least one of the 30 indicators for vascular care (Table 1). The median duration of dementia since diagnosis was 2.8 years (interquartile range [IQR] 1.4-4.9 years), 52% lived in their own homes, and 531 (76%) showed evidence of multimorbidity (≥2 comorbidities, vascular or non-vascular, in addition to dementia). Among vascular-related conditions, hypertension (63%) was most frequent, followed by coronary heart disease (28%), stroke/TIA (24%), and diabetes (20%).

#### Quality of care for vascular diseases and risk factors

Table 2 shows quality of recorded care for each of the 30 indicators for vascular care in those with and without dementia. For 26 of 30 (87%) indicators, a lower proportion of people with dementia received the required quality of care,

Characteristic	Value
Age, years, mean (SD), range 43–102	82.1 (8.0)
Male, %	239 (34)
Dementia duration in years, median (IQR), range 0–31	2.8 (1.4-4.9)
Dementia subtype (%)	
Alzheimer's disease	255 (36)
Vascular	233 (33)
Mixed	61 (9)
Lewy bodies	21 (3)
Other	18 (3)
Unspecified	112 (16)
Living situation (%)	
Nursing/care home	262 (37)
Nursing home	114 (16)
Community	361 (52)
At home with carer	153 (22)
Home alone	60 (9)
Unknown	148 (21)
Unknown	77 (11)
Number of medications prescribed, mean (SD), range 0–25	7.6 (3.9)
Comorbid conditions	
Number of physical conditions, median (IQR)	2.0 (2.0–3.0
Patients with multimorbidity, ≥2 conditions (%)	531 (76)
Cardiovascular related (%)	
Hypertension	440 (63)
Coronary heart disease	195 (28)
Stroke or TIA	169 (24)
Diabetes	137 (20)
Atrial fibrillation	99 (14)
Heart failure	46 (7)
Other physical (%)	
Arthritis	237 (34)
Cancer, current or past	76 (11)
Respiratory disease	129 (18)
Kidney disease	125 (18)
Practice characteristics, n = 52 (SD)	
Number of GPs, mean	5.2 (3.2)
Practice deprivation, mean	28.5 (18.2)
List size, mean	7418 (3405)
Population aged >65 years, mean	1224 (1014)

compared to those without dementia, with the difference being statistically significant (*P*<0.001) for 22 (73%) indicators. Indicators with the lowest provision of recorded care received by people with dementia included those related to measuring processes, for example: record of cholesterol for patients with stroke: peripheral pulses check. neuropathy testing, retinal screening, and body mass index monitoring for diabetes; and smoking-cessation advice.

However, care was equitable or better for people with dementia compared with those without dementia for intermediate outcomes measures including: blood pressure  $\leq 145/85$  mmHg, HbA1c  $\leq 7.5$ , and

total cholesterol ≤5 mmol/l for diabetes; and blood pressure ≤150/90 mmHg for coronary heart disease. This was also the case for treatment indicators relating to the prescribing of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers for heart failure, and receiving flu vaccine in the preceding winter for diabetes, stroke, and coronary heart disease respectively.

#### Predictors of quality of vascular care

The median quality-of-vascular-care score for people with dementia was 67% (IQR 45-89). In univariate analyses (Table 3), better total vascular care was significantly associated with male sex, greater number of comorbid physical conditions, living in the community compared with living in a care home, vascular dementia subtype, and greater number of medications. There were no significant practice-level predictors.

In the multivariate model, being male, having greater physical comorbidity, living in the community (compared with in a nursing/care home), and having a greater number of medications remained significantly associated with better quality of vascular care.

#### **DISCUSSION**

### Summary

The study findings show a greater proportion of people with dementia, compared with those without dementia, do not receive routine care measurements outlined in QOF targets for vascular diseases and risk factors. This was particularly so for process, rather than intermediate or treatment outcomes, and despite high levels of vascular comorbidity. Among people with dementia, women, individuals living in care homes, and those with less comorbid physical conditions and medications appear to be the most disadvantaged.

#### Strengths and limitations

The practices were selected through a random stratified sampling process. All patients on dementia registers were included; however, dementia may remain undiagnosed in up to 50% of patients, which could have led to underestimation of true effect.<sup>41</sup> Measures of care that rely on the evaluation of medical records, such as history taking, have been associated with poorer overall quality of care<sup>42</sup> and medical records may not give an accurate reflection of the actual care provided. However, documented care is, in itself, a measure of quality.43

GPs perceive people with dementia as

Table 2. Patients with and without dementia who received the
appropriate care specified by each indicator

Quality of ca	are indicator	With dementia, n (%)	Without dementia, n(%)	Difference,	$\chi^2$
Hypertensio		,	77,07		
HT 4	BP <sup>a</sup>	324 (74)	37 742 (91)	-17	<i>P</i> <0.001
HT 5	BP is ≤150/90 mmHg <sup>a</sup>	294 (67)	32 238 (77)	-10	<i>P</i> <0.001
	<u>~</u>	274(07)	02 200 (77)		7 401001
Coronary he CHD 5	BP <sup>a</sup>	167 (86)	11 978 (97)	-11	<i>P</i> <0.001
CHD 5	BP is ≤150/90 mmHg <sup>b</sup>	161 (83)	11 004 (89)	-11 -6	P = 0.005
CHD 7	Total cholesterol <sup>b</sup>			-o -24	
CHD 7	Total cholesterol ≤5mmol/lb	113 (68) 110 (56)	11 339 (92)	-24 -21	<i>P</i> <0.001 <i>P</i> <0.001
CHD 11	Patients with a history of myocardial infarction (diagnosed after 1 April 2003) currently treated with an ACE inhibitor	11 (52)	9459 (77) 1523 (84)	-32	P<0.001 P<0.001
CHD 12	or angiotensin II antagonist <sup>c</sup> Record of influenza immunisation in the preceding 1 September–31 March	152 (78)	9890 (80)	-2	P=0.493
Stroke/TIA					
STROKE 5	BP <sup>b</sup>	139 (82)	5084 (96)	-14	<i>P</i> <0.001
STROKE 6	BP is ≤150/90 mmHg <sup>b</sup>	130 (77)	4621 (87)	-10	<i>P</i> <0.001
STROKE 7	Total cholesterol <sup>b</sup>	92 (54)	4708 (89)	-35	<i>P</i> <0.001
STROKE 8	Last total cholesterol ≤5mmol/lb	73 (43)	3746 (70)	-27	<i>P</i> <0.001
STROKE 10	Record of influenza immunisation in the preceding 1 September–31 March	131 (78)	3977 (75)	3	P=0.494
Diabetes					
DM 2	BMI <sup>b</sup>	81 (61)	11 835 (92)	-31	<i>P</i> <0.001
DM 5	HbA1c <sup>b</sup>	101 (74)	12 085 (94)	-20	<i>P</i> <0.001
DM 7	Last HbA1c is ≤10 <sup>b</sup>	98 (72)	11 371 (88)	-16	<i>P</i> <0.001
DM 9	Presence or absence of peripheral pulses		10 665 (83)	-46	<i>P</i> <0.001
DM 10	Neuropathy testing <sup>b</sup>	51 (37)	10 523 (82)	-45	<i>P</i> <0.001
DM 11	BP <sup>b,c</sup>	115 (84)	12 445 (97)	-13	<i>P</i> <0.001
DM 12	Last BP is ≤145/85 mmHg	116 (85)	10 085 (79)	4	P = 0.083
DM 16	Total cholesterol <sup>b</sup>	113 (83)	12 062 (94)	-11	<i>P</i> <0.001
DM 17	Last total cholesterol ≤5mmol/lb	96 (70)	9967 (78)	-8	P = 0.038
DM 18	Record of influenza immunisation in the preceding 1 September–31 March	113 (83)	9855(77)	6	P= 0.116
DM 20	Last HbA1c is ≤7.5 <sup>b</sup>	74 (54)	8323 (65)	-11	P = 0.010
DM 21	Retinal screening <sup>b</sup>	53 (39)	10 891 (85)	-46	<i>P</i> <0.001
DM 22	eGFR or serum creatinine testing <sup>b</sup>	112 (82)	12 141 (95)	-13	<i>P</i> <0.001
Atrial fibrilla	ation				
AF3	Patients with AF currently treated with anticoagulation/anti-platelet therapy	75 (76)	3693 (91)	-15	<i>P</i> <0.001
Heart failur	e				
HF3	Patients with a current diagnosis of HF due to LVD currently treated with ACE inhibitor or angiotensin receptor blocker	2 (100)	1200 (83)	17	P=0.527
Smoking					
SMOKE 3	CHD, stroke/TIA, HT, DM, COPD or asthma patients, whose notes record smoking status <sup>b</sup>	172 (82)	64 256 (95)	-13	<i>P</i> <0.001
SMOKE 4	CHD, stroke/TIA, HT, DM, COPD or asthma patients, who smoke whose notes have record of smoking cessation advice/referral to specialist offered <sup>b,c</sup>	23 (48)	11 247 (92)	-44	<i>P</i> <0.001

 $Bold = significant\ at\ Bonferroni-corrected\ alpha\ level\ (alpha = 0.05/30 = 0.0017).\ ^oRecord\ in\ previous\ 9\ months.$ <sup>b</sup>Record in the previous 15 months. <sup>c</sup>Fisher's exact test (as one cell expected count <5). ACE = angiotensin $converting-enzyme. \ AF = a trial\ fibrillation. \ BMI = body\ mass\ index.\ BP = blood\ pressure.\ CHD = coronary\ heart$  ${\it disease. COPD = chronic obstructive pulmonary disease. DM = diabetes \ mellitus. \ eGFR = estimated \ glomerular}$  $filtration\ rate.\ HbA1c = glycosylated\ haemoglobin\ type\ A1c.\ HF = heart\ failure.\ HT = hypertension.\ LVD = left$ ventricular dysfunction. TIA = transient ischaemic attack.

Table 3. Multilevel linear regression results of the univariate and multivariate predictors of total quality of vascular care

	Qu	iality of vas	cular care ( <i>n</i> = 700)	
	Univariate		Multivariate	
	Coefficient % <sup>a</sup> (95%CI)	<i>P</i> -value	Coefficient % <sup>a</sup> (95%CI)	<i>P</i> -value
Patient level factors				
Age (per 10 years)	-1.5 (-4.4 to 1.4)	0.304		
Sex				
Female	cf		cf	
Male	11.6 (6.8 to 16.4)	<0.001	12.1 (6.7 to 17.5)	< 0.001
Living situation				
Community	cf			
Nursing/care home	-9.7 (-14.8 to -4.6	]<0.001	−7.0 (−12.8 to −1.3	0.016
Duration of dementia, years	-0.9 (-2.0 to 0.13)	0.084		
Dementia subtype				
Alzheimer's disease	cf			
Vascular dementia	6.2 (1.0 to 11.5)	0.020		
All other subtypes	0.6 (-5.5 to 6.7)	0.837		
Number of comorbid physical conditions	5.3 (3.4 to 7.2)	<0.001	3.4 (1.2 to 5.6)	0.003
Number of medications	2.0 (1.4 to 2.6)	<0.001	1.9 (1.1 to 2.6)	<0.001
Practice level factors				
Number of GPs				
Single-handed	cf			
Multi-handed practice	3.2 (-6.6 to 13.0)	0.525		
List size aged >65 years (per 1000 patients)	4.0 (-2.0, 9.0)	0.208		
Socioeconomic deprivation (IMD 2007) <sup>37</sup>	-0.1 (-0.3 to 0.1)	0.197		

represents the percentage points on the quality of vascular care measure. cf = comparison group. IMD = Index of Multiple Deprivation.

> being more difficult to manage and less amenable to improvements in quality of life, compared with patients who have heart disease and diabetes;44 this may result in the undertreatment and less aggressive management of medical conditions.<sup>45</sup> How far this reflects GPs' judgements that aggressive treatment is inappropriate, given the prognosis of a patient with dementia, or caution about exposing patients to sideeffects of preventative drugs, is unclear. This could lead to higher numbers of those with dementia being exception reported. No statistics regarding people with dementia who were exception reported from vascular-related disease indicators were found. However, it is worth noting that the 2008/2009 exception reporting rate for the QOF indicator for dementia (an annual review for patients on dementia registers only) was 7.64%; this is higher than the average for all clinical domains (4.87%).46

> Demographic confounders, such as age and sex, could not be controlled for in the comparisons between patients with and without dementia. There is evidence

that older age groups are less likely to receive guideline-recommended therapies for treatment of conditions such as acute myocardial infarction.<sup>47</sup> However, age discrimination in healthcare services should not take place, and will be banned by future laws as part of the Equality Act. 48 Previous research comparing people from older age groups, with and without dementia, has shown dementia to be independently associated with poor quality of care. 24-27 The findings of association between the quality of care and greater number of comorbid medical conditions and medications may be due to increased likelihood of attendance to consultations 15,24

#### Comparison with existing literature

The deficiencies in the quality of care received by people with dementia are consistent with previous studies demonstrating suboptimal care received by these patients in secondary and private care settings. 24-27

Although improved performance in care for individual conditions like diabetes has been apparent in recent years — and since the introduction of the QOF in UK general practice<sup>49,50</sup> — this is not necessarily true for all subgroups of patients. For example, women and ethnic minority groups are less likely to have targets for diabetes met compared with their counterparts.51 The findings suggest that people with dementia are also disadvantaged.

The results showed that patient, but not practice, characteristics were associated with poorer quality of care among those with dementia. The poorer quality of vascular care for those living in care homes is consistent with research on the monitoring of chronic diseases and appropriate drug treatment.17

Previous research has identified a reduced ability to recall and communicate symptoms or adverse effects,45 decreased decisionmaking capacity, and treatment adherence<sup>52</sup> as potential challenges in addressing health needs in those with dementia. QOF targets may be more difficult to complete in those with dementia, which may explain poor performance on indicators that require greater compliance from patients (for example, retinal screening); however, this is not the case for all indicators (for example, physical examination for peripheral pulses), suggesting that poor quality cannot be explained by patient-level factors alone.

The management of vascular disease and diabetes for people with dementia was equitable or better on targets for intermediate outcomes and treatment in some areas, suggesting effective clinical intervention, for

example heart-failure therapy and diabetes control. However, observations of better control of blood pressure, cholesterol, and HbA1c levels are in keeping with natural physiological changes that occur in people with dementia, such as declining blood pressure, and cholesterol levels. 53-55 Poorer process but better intermediateoutcomes indicators suggest that the latter should not be used on their own to assess quality of care in people with dementia. The more favourable performance of patients with dementia who have had an influenza vaccination compared to those patients without dementia may be due to Department of Health recommendations offering the vaccination to all persons aged ≥65 years.<sup>56</sup>

#### Implications for practice

It remains a concern that a significant proportion of people with dementia fail to receive appropriate vascular care, such as cholesterol checks in stroke, especially considering the increased likelihood of recurrent stroke7 and that control of vascular diseases may slow cognitive decline. 10,57 Improving equity of access to good quality medical care is underpinned by, for example, the Care Quality Commission,51

Healthcare Improvement Scotland, 59 and the National Dementia Strategies for England<sup>60</sup> and Scotland.61 Educational interventions developed for general practices may be one potential strategy, as they have already been shown to improve detection of dementia,62 and trials are underway to improve overall clinical management and adherence to management guidelines.63 The findings suggest that further research should focus on the unique clinical and organisational challenges to the commissioning and administration of routine medical care for comorbid vascular diseases in people with dementia, especially those who are living in care homes.

This study has quantified the quality of care received by people with dementia for vascular-related diseases and risk factors. The findings add to the growing literature, which highlights disparities in care for people with dementia, suggesting deficiencies in a number of areas in care for vascular-related health and sub-groups of people with dementia, who may be receiving the poorest care. Such information is important if the many challenges faced by primary healthcare services in the care for people with dementia are taken into consideration.

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#### **Ethical approval**

The project was approved by the Caldicott Guardians of each participating primary care trust. Ethical approval was not required as the data were collected to measure clinical practice.

#### **Provenance**

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#### **Competing interests**

The authors have declared no competing interests

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