

## Vascular disease/risk and late-life depression in a Korean community population

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**Background** Associations between vascular risk factors and late-life depression are controversial.

**Aims** To investigate the association between measures of vascular disease/risk and depression and confounding and effect modification by APOE genotype and cognitive function.

**Method** In a Korean community population aged 65+ ( $n=732$ ), diagnosis of depression (Geriatric Mental State Schedule) and information on vascular status, disability, APOE genotype and cognitive function were obtained.

**Results** Previous stroke and lower high-density lipoprotein cholesterol level (but neither hypertension nor diabetes) were significantly associated with depression (independently of disability and cognitive function). These associations were stronger in participants with borderline cognitive impairment, although not to a significant extent.

**Conclusions** Except for previous stroke and an atherogenic lipid profile, associations between depression and other common risk factors for cerebrovascular disease were not evident.

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The role of cerebrovascular disease in depression arising in late life has attracted increasing research, with studies suggesting greater than expected comorbidity (Alexopoulos *et al*, 1997). Important but unresolved issues are whether people at risk of cerebrovascular disease are at increased risk of depression and, if so, the extent to which this is accounted for by levels of general disability (Stewart *et al*, 2001). We sought to address these questions in a community study of older people carried out in South Korea. Vascular disease is recognised to be an important risk factor for dementia that may be preceded by depression as a prodromal syndrome, accounting for associations with cerebrovascular disease. A further objective, therefore, was to investigate whether associations between vascular risk factors and depression were stronger in the presence of cognitive impairment.

### METHOD

A community survey of late-life psychiatric morbidity was carried out in Kwangju, South Korea in 2001, in collaboration with the 10/66 Dementia in Developing Countries Research Programme (10/66 Dementia Research Group, 2000). The study has been described in detail in previous publications (Kim *et al*, 2003a).

### Study population

Potential participants for this study were recruited from all inhabitants aged 65 years or over recorded in national residents registration lists within two areas (one urban, one rural) of Kwangju, South Korea, in 2001. The study was approved by Chonnam National University Hospital Review Board. After sending a letter explaining the purpose of the study to all eligible older people, written informed consent was obtained from all participants.

### Assessment procedures and measures

This study was conducted in two phases. Sixteen graduate-level research assistants, trained and supervised by the project psychiatrist, carried out home-based interviews with participants and their family members. This included a fully structured diagnostic interview for depression, information on vascular risk/disease and data on demographic characteristics, disability and cognitive function. At a second interview (attempted in all participants), further examination for vascular risk/disease and blood tests for APOE genotype were administered by two expert teams consisting of a psychiatrist, a senior nurse and a psychologist. At both stages, home visits were repeated on at least two occasions if no contact was made. The mean (s.d.) interval between the two interviews was 9 (5.4) days.

### Depression

A community version of the Geriatric Mental State Schedule was used (GMS B3; Copeland *et al*, 1986). This is a fully structured diagnostic interview designed for administration by lay personnel that has been widely used and validated in international settings (Copeland *et al*, 1991). Procedures for its Korean translation and validation have been described elsewhere (Kim *et al*, 2003b). Case-level depression was defined using the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) algorithm, using standard (3+) cut-points for diagnostic confidence. This computer algorithm has been designed to elicit the presence of depression of clinical significance, incorporating both moderate and severe syndromes. The AGECAT algorithm gives Stage 1 (non-hierarchical) and Stage 2 (hierarchical) diagnoses of mental disorder. For the purposes of this analysis, depression was classified using the Stage 1 output because we wished to include cognitive function in the explanatory model and investigate rather than exclude comorbidity.

### Information on vascular risk/disease

Self-reported diagnoses of and treatment histories for stroke, heart disease, hypertension and diabetes were recorded at the first phase of interviews. For stroke, it was coded only if there was clear history of sudden onset of unilateral paralysis and/or loss of

speech and/or blindness lasting for at least 2 days. Smoking history was ascertained.

#### Examinations for vascular risk/disease

Examinations were carried out at a second phase of interviews. Resting blood pressure was taken with an automatic sphygmomanometer on the left arm in the sitting position. The lower of two consecutive readings was used. Atherosclerotic vascular disease is associated with raised total cholesterol and, in particular, with a profile of raised low-density lipoprotein (LDL) cholesterol and low high-density lipoprotein (HDL) cholesterol. Blood tests therefore were assayed for total, LDL and HDL cholesterol as well as glucose, triglycerides and APOE genotype. Participants were instructed to be fasting, and blood sampling was performed during the mornings when possible. Height, weight, waist and hip were measured.

#### Other potential risk factors for depression

Demographic data on age, gender and education were recorded. Participants were asked about any previous episodes of depression prior to age 60 years. Disability was assessed using the Korean version of the World Health Organization Disability Assessment Schedule II (WHODAS II), which has been validated for assessing disability in old people and recommended for international use (Epping-Jordan *et al*, 2002). Cognitive function was evaluated using the Korean version of the Mini-Mental State Examination (MMSE-K; Park & Kwon, 1990), which has been developed specifically for use in older Korean populations, with revised items taking into account low educational attainment and high rates of illiteracy. Standard cut-offs have been recommended for this measure (Park *et al*, 1991), with scores of 21–24 (out of 30) representing borderline cognitive function and 20 or below representing significant impairment. All these measures were taken at the first stage of interviews.

#### Statistical analysis

Vascular risk factors and the presence of clinical vascular disease were compared according to case-level depression in all participants at the first interview. All subsequent analyses were restricted to those who completed the two interviews and the blood tests. Potential associations between vascular risk/disease and depression

( $P < 0.1$  in univariate analysis) were analysed further using stepwise logistic or linear regression models to investigate confounding by demographic characteristics and mediation by disability (WHODAS II) and cognitive function (MMSE-K). Secondary analyses were carried out to investigate effect modification by cognitive function, using recommended cut-offs for the MMSE-K (Park *et al*, 1991) for stratified analyses, and likelihood ratio tests for interaction terms within regression models. As a final procedure, analyses were repeated by excluding participants who reported any episode of depression occurring before age 60 years.

## RESULTS

### Recruitment

Of 1566 inhabitants aged 65 years or over identified from the registration lists, 1204 (77%) completed the first interview with research assistants. Of the remainder, contact could not be established with 195 (12%), 71 (5%) refused to participate, 55 (4%) had no fixed abode, 28 (2%) had changed address and 9 (1%) had died before the visit. No significant differences were observed in age (mean ages of 72.2 and 72.4, respectively) and gender ratio (58% and 62% female, respectively) between participants and non-participants.

Of the participants in the first interview, 732 (61%) participated in the second, more-intensive examination. Of non-participants at this stage, contact could not be established with 321 (27%), 92 refused (8%), 4 had died in the interval (<1%) and data were missing for 55 (5%). The principal apparent reason for attrition was that contact could not be established because the person was repeatedly away from home at the time of research visits. Participants at both interviews were less educated than those present at the first interview only (mean (s.d.) years of education were 3.4 (4.2) and 4.0 (4.4), respectively;  $P=0.035$ ) and had lower cognitive function (mean (s.d.) scores on the MMSE-K were 23.3 (5.0) and 24.3 (5.1), respectively;  $P=0.002$ ). However, no significant differences were observed between the participants and non-participants in terms of age (mean ages of 72.8 and 72.2, respectively), gender (59% and 57% female), disability (mean WHODAS II scores of 7.1 and 5.9) and GMS depression (14% and 13%). There were also no

substantial differences in associations between vascular risk factors (ascertained at the first phase) and depression between all participants of the first phase and the subgroup who were present at the second phase. For example, the odds ratios (95% CI) for the associations between depression and stroke, hypertension and diabetes were 4.57 (2.74–7.62), 1.32 (0.93–1.88) and 1.35 (0.82–2.23), respectively, for all participants in the first phase ( $n=1204$ ) and 3.68 (1.99–6.79), 1.48 (0.97–2.27) and 1.67 (0.94–2.99) in those present at the second phase ( $n=732$ ). Further analyses therefore were restricted to the subgroup present at both interviews.

### Univariate associations with depression

Depression was present in 101 (14%) of the 732 participants at the second interview. Univariate associations between depression and vascular disease/risk are summarised in Table 1. Depression was associated significantly with reported stroke and heart disease in the sample at both interviews. Depression was associated positively with reported hypertension and diabetes, with associations bordering on statistical significance. Depression was associated significantly with a lower level of HDL cholesterol and a higher level of LDL cholesterol.

With respect to other independent variables, depression was associated significantly with female gender (odds ratio (OR)=2.02; 95% CI 1.28–3.30), a greater number of physical illnesses (OR per illness reported=1.39; 95% CI 1.22–1.58) and lower scores on the MMSE-K (OR per single point decrease=1.05; 95% CI 1.01–1.09). Associations with increased age (OR per year increase=1.03; 95% CI 0.99–1.07) and lower education (OR per year decrease=1.03; 95% CI 0.99–1.08) were of borderline significance.

### Univariate associations with APOE genotype

The APOE genotype frequencies were as follows: e2/2, 1.5%; e2/3, 9%; e2/4, 1%; e3/3, 71%; e3/4, 16%; e4/4, 1.5%. The APOE e4 allele was present in 132 participants (18%). Previous stroke was reported more frequently in participants with the e4 allele (11% *v.* 6%,  $P=0.067$ ) and mean body mass index levels were significantly lower in those with e4 than in those without (mean (s.d.) 22.1 (3.6) and 22.8 (3.5) kg/m<sup>2</sup>,

**Table 1** Unadjusted associations between depression and vascular risk/disease

	No depression (n=631)	Depression (n=101)	Odds ratio or mean difference (95% CI)	P <sup>1</sup>
Information on vascular risk/disease (n, %)				
Previous stroke	34 (5)	18 (17)	3.68 (1.99 to 6.79)	<0.001
Heart disease	117 (18)	36 (34)	2.32 (1.48 to 3.64)	<0.001
Hypertension	198 (31)	42 (40)	1.48 (0.97 to 2.27)	0.069
Diabetes	66 (10)	17 (16)	1.67 (0.94 to 2.99)	0.078
Current smoker	254 (41)	48 (46)	1.05 (0.60 to 1.45)	0.29
Examination for vascular risk/disease (mean, s.d.)				
Systolic blood pressure (mm Hg)	146.8 (26.0)	147.8 (30.1)	1.0 (−4.5 to 6.5)	0.73
Diastolic blood pressure (mm Hg)	87.7 (22.1)	88.4 (22.7)	0.7 (−3.9 to 5.3)	0.77
Blood glucose (mg/dl)	104.5 (50.2)	113.6 (66.3)	9.1 (−4.5 to 22.6)	0.19
Total cholesterol (mg/dl)	175.1 (34.1)	178.4 (39.7)	3.3 (−4.3 to 10.8)	0.45
High-density lipoprotein cholesterol (mg/dl)	48.7 (14.2)	43.9 (11.1)	−4.8 (−7.8 to −1.8)	0.002
Low-density lipoprotein cholesterol (mg/dl)	96.0 (31.1)	105.0 (36.3)	9.0 (2.2 to 15.9)	0.023
Triglyceride (mg/dl)	153.0 (88.2)	147.5 (64.0)	−5.5 (−24.0 to 12.9)	0.56
Body mass index (kg/m <sup>2</sup> )	22.5 (3.5)	22.8 (4.2)	0.23 (−0.51 to 0.98)	0.59
Waist/hip ratio	0.9 (0.1)	0.9 (0.1)	0.0 (−0.02 to 0.02)	0.24

1.  $\chi^2$  or *t*-tests.

respectively;  $P=0.041$ ). There were no significant associations between presence of the *e4* allele and any of the other factors measured (vascular risk/disease, depression, disability and cognitive function). The APOE *e4* allele was associated overall with a more atherogenic lipid profile, but differences were not significant ( $P>0.1$ ). Mean (s.d.) levels of cholesterol were 180 (39) mg/dl in those with the *e4* allele and 175 (34) mg/dl in those without this allele. Respective levels (mg/dl) were: HDL cholesterol, 47 (14) and 48 (14); LDL cholesterol, 100 (34) and 97; triglycerides, 162 (105) and 150 (81).

### Multivariate analysis of depression and vascular disease/risk factors

Results of regression analyses are summarised in Table 2. All associations between depression and vascular disease/risk were weakened by the inclusion of confounding variables, particularly level of disability. The positive associations with stroke and a lower level of HDL cholesterol remained significant, whereas those with other vascular factors were substantially diminished both in strength and significance. Further adjustment for the APOE *e4* allele made no substantial difference. The odds ratio (95% CI) for the association between depression and previous stroke was 2.73 (1.37–5.59) in Model 3 (see Table 2) after further adjustment for the *e4* allele. The *B* values for the association between depression and HDL/LDL cholesterol levels were

−4.17 (−7.34 to −1.01) and 5.10 (−1.93 to 12.14) in Model 3 after further adjustment for *e4*.

### Stratification by APOE and MMSE-K (Table 3)

Associations between depression, stroke and lower HDL cholesterol were stronger in the presence of the *e4* allele. However, interaction terms did not approach statistical significance (data not shown; *P* values for interaction terms  $>0.1$ ). Associations between depression and vascular risk factors also were generally stronger in groups with borderline cognitive impairment (MMSE-K, 21–24), although again no individual interaction terms approached significance (Table 3; *P* values for interaction terms  $>0.1$ ).

### Restriction by previous history of depression

Of the 732 participants at the second interview, a previous history of depression prior to age 60 years was reported by 16 (16%) of the 101 with current depression and by 17 (3%) of the 631 without current depression. No marked or consistent differences were found in the results when the above analyses were repeated in those without a past history of depression (data not shown).

## DISCUSSION

In a community sample of older Koreans we found that depression was associated

with reported previous stroke and with a reduced level of HDL cholesterol. For other vascular risk factors, such as hypertension and diabetes, associations with depression bordered on significance after adjustment for age, gender and education but were reduced substantially in strength after adjustment for general disability. Associations were not explained substantially or modified significantly by APOE genotype or cognitive function.

### Methodological issues

Previous community studies investigating these research questions have been limited by the use of brief screening instruments to define depression (Stewart *et al*, 2001) or have focused on specific sub-populations (Kim *et al*, 2002). A strength of this study was that depression was ascertained using a diagnostic instrument that has been validated widely in a variety of international settings. In terms of sample representativeness, government registration lists represent a highly inclusive sampling frame for epidemiological research in South Korea because an accurate entry is required for many daily needs, including pension provision. The two-phase recruitment procedure potentially reduced the representativeness of the participants compared with the source population because of attrition between interviews, giving an overall response rate of  $<50\%$ . In retrospect, a single-stage procedure would have been preferable. However, we feel that it is unlikely that the

**Table 2** Multivariate associations between depression and vascular disease/risk factors

Factor <sup>1</sup>	Unadjusted model	Adjusted		
		Model 1 <sup>2</sup>	Model 2 <sup>3</sup>	Model 3 <sup>4</sup>
Stroke	3.68*** (1.99 to 6.79)	4.38*** (2.30 to 8.34)	2.56* (1.26 to 5.22)	2.59** (1.27 to 5.29)
Heart disease	2.32*** (1.48 to 3.64)	2.22** (1.40 to 3.52)	1.43 (0.83 to 2.43)	1.47 (0.86 to 2.52)
Hypertension	1.48 (0.98 to 2.27)	1.45 (0.94 to 2.24)	1.25 (0.79 to 1.96)	1.24 (0.79 to 1.95)
Diabetes	1.67 (0.94 to 2.99)	1.72 (0.95 to 3.09)	1.41 (0.75 to 2.64)	1.41 (0.75 to 2.64)
High-density lipoprotein cholesterol	-4.83** (-7.82 to -1.84)	-4.82** (-7.85 to -1.78)	-4.30** (-7.45 to -1.14)	-4.23** (-7.38 to -1.07)
Low-density lipoprotein cholesterol	9.05* (2.1 to 15.9)	5.76 (-0.96 to 12.5)	4.68 (-2.31 to 11.7)	4.58 (-2.42 to 11.6)

1. Each vascular disease/risk factor is entered into a regression model separately. Values are odds ratios (for stroke, heart disease, hypertension, diabetes) or B values (high- and low-density lipoprotein cholesterol) with 95% confidence intervals.  
 2. Adjusted for age, gender and education.  
 3. Adjusted as for Model 1 plus disability (measured using the Korean version of the World Health Organization Disability Assessment Schedule, WHODAS II).  
 4. Adjusted as for Model 2 plus cognitive function (measured using the Korean version of the Mini-Mental State Examination, MMSE-K).  
 \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

observed associations are explained by selection bias because neither vascular risk factor nor depression was associated with attrition. As well as this, the strength of association between the first-phase measures of vascular risk and depression were similar between the total sample and the analysed subgroup. It is therefore likely (although cannot be concluded definitely) that associations with factors measured at the second phase can be generalised to the source population.

The study was cross-sectional in design, which limits the extent to which cause and effect relationships can be clarified. It also raises the issue of information bias, although we feel that this is unlikely because the risk factors at the first phase were ascertained before the diagnostic interview for depression was administered and, furthermore, the data at the second phase were collected by a professional who did not have knowledge of the GMS findings. Information on vascular risk factors such as hypertension and diabetes relied on

self-reported diagnoses and so corroboration by medical records was not feasible. There are certain other limitations in inference that should be considered: most 'case' participants will have had moderate levels of depression rather than the more severe forms that have been the focus for research in clinical samples; previous episodes of depression were ascertained by self-report, which is likely to have limited validity and the final restricted sample may not have had a truly 'late-onset' disorder; and differential rates of institutionalisation and mortality might conceivably have obscured the association between vascular risk and depression in this cross-sectional community study. Institutions were not sampled in this survey because there were none within the sampling areas. However, in Korea, provision of institutional care is limited and care at home is preferred by residents and their families, even in severe dementia. Mortality is therefore more likely to be a source of prevalence bias than institutionalisation.

**Stroke and depression**

Depression occurs frequently following stroke, and the association between previous stroke and depression observed in this sample has been reported in a similar Korean sample with cognitive impairment (Kim *et al*, 2002) and in other community studies (Fuh *et al*, 1997; Stewart *et al*, 2001). The association was reduced following adjustment for level of disability, but only partially so. This is consistent with findings in other populations (Stewart *et al*, 2001) and suggests that other mediating pathways may be present, which may include the direct effect of an infarct on brain structure or chemistry but might also include functional impairment specific to stroke, or its psychological impact, which did not contribute to the disability scale.

**Cholesterol subfractions and depression**

We found no association between total cholesterol levels and depression, which was

**Table 3** Associations between depression and vascular risk/disease stratified by cognitive function (Korean version of the Mini-Mental State Examination, MMSE-K)

Factor <sup>1</sup>	Total sample (n=732)	MMSE-K score		
		25-30 (n=333)	21-24 (n=222)	0-20 (n=177)
Stroke	4.38*** (2.30 to 8.34)	3.55* (1.23 to 10.2)	6.07** (1.67 to 22.0)	3.93* (1.30 to 11.9)
Heart disease	2.22** (1.40 to 3.52)	2.29* (1.10 to 4.78)	3.14** (1.38 to 7.17)	1.59 (0.66 to 3.86)
Hypertension	1.45 (0.94 to 2.24)	1.11 (0.55 to 2.25)	1.32 (0.59 to 2.99)	2.20* (1.01 to 4.76)
Diabetes	1.72 (0.95 to 3.09)	1.12 (0.40 to 3.12)	2.27 (0.79 to 6.50)	1.85 (0.64 to 5.34)
High-density lipoprotein cholesterol	-4.82** (-7.85 to -1.78)	-5.07* (-9.76 to -0.37)	-7.07* (-12.85 to -1.28)	-2.02 (-7.69 to 3.66)
Low-density lipoprotein cholesterol	5.76 (-0.96 to 12.5)	1.36 (-9.04 to 11.8)	5.06 (-7.85 to 18.0)	12.4 (-0.30 to 25.1)

1. Values are odds ratios (stroke, heart disease, hypertension, diabetes) or B values (high- and low-density lipoprotein cholesterol) with 95% confidence intervals. All values adjusted for age, gender, and education. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

consistent with findings from some studies (Brown *et al*, 1994; McCallum *et al*, 1994; Blazer *et al*, 2002), although depression has been found to be associated with lower cholesterol levels in others (Morgan *et al*, 1993; Partonen *et al*, 1999), including a prospective study (Cervilla *et al*, 2000). One study of an elderly sample found depression to be associated with lower levels of LDL cholesterol (Äijänseppä *et al*, 2002). Another study of a younger sample (aged 31–65 years) found an association with higher levels of HDL cholesterol (Horsten *et al*, 1997). Our finding in the opposite direction might reflect racial or age-related differences in the aetiology and/or salience of vascular risk factors, but further research is required to clarify inconsistencies.

### Vascular risk factors and depression

Depression in later life has been found to be associated with changes suggestive of cerebrovascular disease, such as white matter hyperintensities on neuroimaging (Steffens *et al*, 1999; de Groot *et al*, 2000). The vascular depression hypothesis also proposes a syndrome where severe depression and vascular disease co-exist. In this analysis, we did not set out to test the existence of such a syndrome, but to investigate well-recognised risk factors for cerebrovascular disease as potential risk factors for depression. If there is a vascular aetiology for depression in late life, risk factors for cerebrovascular disease such as hypertension and diabetes also may be important population-level risk factors for depression because of high prevalence rates in many populations. However, there is currently little evidence from community samples to suggest strong causal relationships (Jones-Webb *et al*, 1996; Rajala *et al*, 1997; Stewart *et al*, 2001) and, where associations have been found, it is unclear whether these are specific to disorders affecting the vasculature or whether they are accounted for by well-recognised associations between depression and general poor health and disability (Prince *et al*, 1998). Hypertension and diabetes were associated with increased likelihood of depression in our study at borderline levels of statistical significance. However, these associations were substantially reduced in strength after adjustment for the WHODAS II score. This suggests that the impact of these disorders on depression may be mediated through

associated general disability rather than specific vascular effects. However, it should be borne in mind that ‘adjustment’ by disability in a cross-sectional study such as this one may obscure associations with any potential risk factor for depression because depression and reported disability are strongly interrelated.

The association with decreased HDL cholesterol therefore does suggest a more atherogenic lipid profile in people with late-life depression, but other conventional risk factors for stroke were not associated with depression. Interestingly, a pathological study found late-life depression to be associated with arterial atheroma rather than microvascular disease (Thomas *et al*, 2001). It is therefore possible that specific vascular pathways may underlie the disorder and there may be other vascular risk factors for depression (such as cerebral haemodynamics, blood pressure regulation and inflammatory processes) that were not investigated in this study. However, the direction of causality underlying cross-sectional associations is unclear because there is strong evidence from prospective research that depressive symptoms earlier in life are associated with increased risk of stroke (Jonas & Mussolino, 2000). Associations in later life may be the consequence of complex interrelationships between vascular risk and affective state over a long period (Stewart, 2002).

### Interactions with cognitive impairment and APOE genotype

The association between vascular risk factors and depression might conceivably be explained by well-recognised associations between vascular risk factors and dementia, and between depression and later dementia (Stewart, 2002). This would predict stronger associations between depression and vascular risk factors in people at risk of cognitive decline (e.g. those with the APOE e4 allele or those with cognitive function that is already impaired). Recently, a study found no interactions between APOE e4 allele and cholesterol level in associations with depression in cross-sectional and longitudinal analyses in a biracial elderly community sample (Blazer *et al*, 2002). To our knowledge, there has been no study to investigate effect modification by APOE genotype for other vascular risk factors and late-life depression. However, we found no evidence of substantial confounding or effect modification by APOE e4 allele for

the association of interest. All vascular risk factors were associated more strongly with depression in the presence of borderline (compared with normal) cognitive function (MMSE-K, 21–24). These findings provide partial support for our hypothesis and suggest that there might be an interface between vascular disease, depression and early dementia. However, individual interactions were not demonstrable at conventional levels of statistical significance and further research is required to address this question.

### Public health implications

Our findings support others in showing associations between late-life depression and clinical stroke, that were only partially explained by level of disablement. However, we found little evidence for associations with other vascular risk factors such as hypertension or diabetes. From a public health perspective regarding the prevention of depression, these support a focus on post-stroke populations and on reducing levels of general disability rather than on specifically targeting groups with vascular risk factors. The direction of causation for the association between depression and an atherogenic lipid profile cannot be concluded. However, at the very least it suggests that attention should be paid to cardiovascular risk profiles and the prevention of adverse vascular outcomes in older adults with depression.

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## CLINICAL IMPLICATIONS

- Previous stroke and lower levels of high-density lipoprotein cholesterol were associated significantly with late-life depression.
- Associations between other established risk factors for cerebrovascular disease, such as hypertension or diabetes, and late-life depression were not evident.
- Associations, where present, were stronger in the presence of borderline cognitive impairment, although not to a statistically significant extent.

## LIMITATIONS

- The focus was on moderate levels of depression rather than the more severe forms that have been the focus of research in clinical samples.
- There was an important level of attrition between interviews, although this was not associated with exposure or outcome measures of interest.
- The study was cross-sectional in design, limiting inferences regarding the direction of causation.

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