

## **Online Supplemental Material**

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**eTable 1. Study quality of included citations**

Reference	1. Hypothesis/aims (specific for stroke)	2. Study design reported (cohort)	3. Sampling frame	4. Inclusion/exclusion criteria	5. Response higher than 75%	6. Information about non-responders versus responders	7. Participant characteristics	8. Follow-up at least 5 years?	9. Lost to follow-up <20%	10. Information about completers vs non-completers?	11. Depression measured by DSM/ICD	12. Depression measured by validated questionnaire	13. Stroke measured by medical record	14. Baseline stroke excluded	15. Repeated measurements	16. Statistical methods	17. Correction for potential confounders?	18. Estimates of random variability	19. Subgroups	20. Generalisability: other populations	Overall quality score
Vogt et al, <sup>19</sup> 1994	0	1	1	1	1	0	1	1	0	0	0	1	1	1	0	1	1	1	0	1	13
Wassertheil-Smoller et al, <sup>20</sup> 1996	1	1	1	1	0	0	1	0	1	1	0	1	1	0	0	1	0	0	0	0	10
Everson et al, <sup>21</sup> 1998	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	0	1	17
Simons et al, <sup>16</sup> 1998	1	1	1	0	0	0	1	1	1	0	0	1	1	0	0	1	1	1	1	1	13
Whooley and Browner, <sup>17</sup> 1998	0	1	0	0	0	0	1	1	1	1	0	1	1	0	0	1	1	1	0	1	11
Jonas and Mussolino, <sup>22</sup> 2000	1	1	1	1	0	0	1	1	1	0	0	1	1	1	0	1	1	1	1	1	15
Larson et al, <sup>23</sup> 2001	1	1	1	1	1	0	1	1	0	0	1	0	0	1	0	1	1	1	0	1	13
Ohira et al, <sup>24</sup> 2001	1	1	0	1	0	0	1	1	1	1	0	1	1	1	0	1	1	1	1	1	15
Ostir et al, <sup>25</sup> 2001	1	1	1	1	0	0	1	1	0	0	0	1	1	1	0	1	1	1	1	1	14
May et al, <sup>26</sup> 2002	1	1	1	1	1	0	1	1	1	0	0	1	1	1	0	1	1	1	1	1	16
Yasuda et al, <sup>27</sup> 2002	0	1	1	1	0	1	1	1	1	1	0	1	1	0	0	1	1	1	0	1	14

Wassertheil-Smoller et al, <sup>28</sup> 2004	0	1	0	1	0	0	1	1	0	0	0	1	1	0	0	1	1	1	1	0	10
Gump et al, <sup>29</sup> 2005	0	1	1	1	0	0	1	1	1	0	0	1	1	1	0	1	1	1	0	0	12
Avendano et al, <sup>30</sup> 2006	1	1	1	1	1	0	1	1	1	0	0	1	0	1	0	1	1	1	1	1	15
Stürmer et al, <sup>31</sup> 2006	0	1	0	0	0	0	1	1	1	1	0	0	1	1	0	1	1	1	0	1	11
Arbelaez et al, <sup>32</sup> 2007	1	1	1	1	0	0	1	1	1	0	0	1	1	1	0	1	1	1	1	1	15
Kawamura et al, <sup>33</sup> 2007	0	1	1	1	1	0	1	1	0	0	1	1	0	1	1	1	0	0	0	1	12
Salaycik et al, <sup>34</sup> 2007	1	1	1	1	0	0	1	1	0	0	0	1	1	1	0	1	1	1	1	1	14
Bos et al, <sup>35</sup> 2008	1	1	1	1	1	0	1	1	0	0	0	1	1	1	0	1	1	1	1	1	15
Lee et al, <sup>36</sup> 2008	1	1	1	1	0	1	1	1	1	0	1	0	1	1	0	1	1	1	0	0	14
Liebetrau et al, <sup>37</sup> 2008	1	1	1	1	0	1	1	0	1	0	1	1	1	1	0	1	0	1	1	0	14
Surtees et al, <sup>38</sup> 2008	1	1	1	1	0	0	1	1	1	0	1	0	1	1	0	1	1	1	1	1	15
Whooley et al, <sup>39</sup> 2008	0	1	1	1	0	0	1	0	1	1	0	1	1	0	0	1	1	1	0	0	11
Wouts et al, <sup>40</sup> 2008	1	1	1	1	0	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	17
Glymour et al, <sup>41</sup> 2010	1	1	1	1	1	0	1	1	1	1	0	1	0	1	0	1	1	1	1	1	16
Nabi et al, <sup>42</sup> 2010	1	1	1	1	0	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	17
Peters et al, <sup>43</sup> 2010	0	1	0	1	0	0	1	0	1	1	0	1	1	0	0	1	1	1	0	0	10
Pan et al, <sup>18</sup> 2011	1	1	1	1	0	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	17
% Studies scoring "Yes"	19	28	23	25	8	5	28	24	20	12	6	24	24	21	3	28	25	26	16	21	14

1 = "Yes", 0 = "No", "Unable to determine" or "Not applicable".

**eTable 2.** Confounding factors and methods for adjustment

Reference	Statistical Model <sup>a</sup>	Risk Expression	Adjusted covariates	Total stroke	Nonfatal stroke	Fatal Stroke	Ischemic Stroke	Hemorrhagic stroke
Vogt et al, <sup>19</sup> 1994	Cox	HR	Age, sex, smoking status, socioeconomic status, self-reported health status, and duration of health plan membership	1.19 (0.82-1.75)				
Wassertheil-Smoller et al, <sup>20</sup> 1996	Crude incidence rate comparison	RR	NA	0.86 (0.45-1.65)				
Everson et al, <sup>21</sup> 1998	Cox	HR	Age, sex, race, education, smoking status, alcohol, BMI, comorbidity (hypertension and diabetes)	Impute from fatal stroke results		1.55 (0.97-2.47)		
Simons et al, <sup>16</sup> 1998	Cox	RR	Age, sex, marital status, BMI, antihypertensive drugs, blood pressure, atrial fibrillation, HDL cholesterol, peak expiratory flow, physical disability	Impute from ischemic stroke results		2.30 (1.14–4.64)	1.41 (1.01–1.96)	
Whooley and Browner, <sup>17</sup> 1998	Cox	HR	Age, smoking status, perceived health, cognitive function, comorbidity (myocardial infarction, stroke, chronic obstructive pulmonary disease, hypertension, and diabetes)	Impute from fatal stroke results		1.70 (0.80-3.50)		
Jonas and Mussolino, <sup>22</sup> 2000	Cox	RR	Age, sex, race, education, smoking status, alcohol use, BMI, non-recreational physical activity, serum cholesterol, SBP, history of diabetes and heart disease	1.73 (1.30-2.31)				
Larson et al, <sup>23</sup> 2001	Logistic	OR	Age, sex, race, and educational attainment, smoking status, history of diabetes, heart problems, and high blood pressure	2.67 (1.08-6.63)				
Ohira et al, <sup>24</sup> 2001	Cox	RR	Age, sex, smoking status, alcohol use, BMI, SBP level, serum total cholesterol level, current treatment with antihypertensive medication, and a history of diabetes	1.9 (1.1–3.5)			2.7 (1.2–6.0)	0.9 (0.3–3.1)

Ostir et al, <sup>25</sup> 2001	Cox	RR	Age, sex, marital status, household income, education, smoking status, BMI, heart attack, diabetes, hypertension	1.30 (0.85-1.99)			
May et al, <sup>26</sup> 2002	Cox	HR	Age, social class, marital status, smoking status, alcohol use, BMI, SBP, comorbidity (ischemic heart disease, diabetes, respiratory disease, or retirement due to ill health)	Impute from ischemic stroke results	1.10 (0.71–1.69)	2.56 (0.97–6.75)	1.26 (0.85–1.85)
Yasuda et al, <sup>27</sup> 2002	Cox	HR	Age, sex, regular physical activity, availability of close or casual neighbors, and chronic conditions under treatment, anxiety and apathy subscale	Impute from fatal stroke results		3.62 (1.12-11.7)	
Wassertheil-Smoller et al, <sup>28</sup> 2004	Cox	RR	Age, race, education, income, smoking status, BMI, physical activity, hormone use, high cholesterol level requiring medications, diabetes, and hypertension	No baseline CVD: 1.01 (0.78-1.30); within baseline CVD: 1.45 (1.11-1.90)			
Gump et al, <sup>29</sup> 2005	Cox	HR	Age, intervention group, race, educational attainment, smoking status, trial averaged SBP, alcohol consumption, and fasting cholesterol, and the occurrence of nonfatal cardiovascular events during the trial	Impute from fatal stroke results		1.48 (0.93-2.36)	
Avendano et al, <sup>30</sup> 2006	Cox	HR	Age, sex, race, education and income	Age 65-74: 3.05 (1.63–5.70); age ≥75: 0.95 (0.46–1.98)			
Stürmer et al, <sup>31</sup> 2006	Cox	RR	Age, sex, education, smoking status, alcohol consumption, BMI, exercise, family histories of myocardial infarction, stroke, and cancer, comorbidity (myocardial infarction, cancer, hypertension, hyperlipidaemia, and diabetes)	Impute from nonfatal stroke results	1.53 (0.83-2.80)		
Arbelaez et al, <sup>32</sup>	Cox	HR	Age, sex, race, occupation, income,	Impute			1.25 (1.02– Not

2007				education level, marital status, smoking status, BMI, blood cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides levels, comorbidity (hypertension, diabetes, CHD), C-reactive protein	from ischemic stroke results	1.53)	significant, data not shown
Kawamura et al, <sup>33</sup> 2007	Kaplan-Meier survival analysis	RR	NA		Impute from fatal stroke results	1.25 (0.82–1.90)	
Salaycik et al, <sup>34</sup> 2007	Cox	HR	Age, sex, smoking status, blood pressure, diabetes, atrial fibrillation, CVD, left ventricular hypertrophy on the ECG	Age <65: 3.59 (1.76–7.33); Age ≥65: 0.93 (0.59–1.47)			
Bos et al, <sup>35</sup> 2008	Cox	HR	Age, sex, smoking status, SBP, intima-media thickness, medication use (antithrombotic drug, antihypertensive drug, cholesterol lowering drug, psycholeptic drug and psychoanaleptic drug), comorbidity (diabetes, myocardial infarction, PTCA or CABG, TIA)	1.21 (0.80–1.83); men: 2.17 (1.11–4.23); women: 0.91 (0.55–1.53)		1.43 (0.87–2.35); men: 3.21 (1.62–6.38); women: 0.78 (0.39–1.59)	
Lee et al, <sup>36</sup> 2008	Cox	HR	Age, sex, geographic location, income, urbanization, substance abuse, comorbidity (diabetes, hypertension, hyperlipidemia, renal disease)	5.43 (3.47–8.51)			
Liebetrau et al, <sup>37</sup> 2008	Cox	HR	NA	2.6 (1.5–4.6); men: 1.4 (0.3–6.8); women: 2.9 (1.6–5.3)			
Surtees et al, <sup>38</sup> 2008	Cox	HR	Age, sex, social class, education, smoking status, obesity, SBP, total cholesterol, diabetes, hypertension treatment, myocardial infarction, family history of stroke, and antidepressant medication use	1.08 (0.67–1.75)	1.18 (0.70–1.97)	0.45 (0.11–1.84)	

Whooley et al, <sup>39</sup> 2008	Cox	HR	Age, smoking, medication adherence, physical activity, CRP, Left ventricular ejection fraction, history of myocardial infarction, stroke, heart failure, diabetes	1.47 (0.70-3.11)		
Wouts et al, <sup>40</sup> 2008	Cox	HR	Age, sex, Mini-Mental State Examination score, smoking status, functional limitations, obesity, hypertension, and diabetes	1.15 (0.76-1.73) <sup>b</sup>		
Glymour et al, <sup>41</sup> 2010	Cox	HR	Age, BMI category, ethnicity, birth place, parental educations, self education, income, wealth and marital status, year of enrollment, alcohol and smoking status, and self-reported diagnoses of hypertension, diabetes, or heart disease	1.25 (1.12-1.39); men: 1.34 (1.10-1.62); women: 1.44 (1.26-1.64)		
Nabi et al, <sup>42</sup> 2010	Cox	HR	Age, sex, education, smoking status, alcohol use, sedentary lifestyle, obesity, comorbidity (hypertension, diabetes, incident CHD)	0.87 (0.57–1.32)		
Peters et al, <sup>43</sup> 2010	Cox	HR	Age, sex, treatment group, treatment allocation, country area, educational level, living status, number of comorbidities, previous CVD, previous treatment for hypertension and hypertension	1.82 (1.19–2.78)		
Pan et al, <sup>18</sup> 2011	Cox	RR	Age, marital status, ethnicity, smoking status, alcohol consumption, BMI, physical activity level, menopausal status, postmenopausal hormone therapy, current aspirin or multivitamin use, Dietary Approaches to Stop Hypertension dietary score, parental history of myocardial infarction, comorbidity (diabetes, hypertension, hypercholesterolemia, heart disease and cancer)	1.29 (1.13-1.48)	1.11 (0.91-1.35)	1.20 (0.80-1.79)

Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; CVD, cardiovascular disease; CHD, coronary heart disease; CBVD, cerebrovascular disease; CRP, C-reactive protein; ECG, Electrocardiography; HR, hazard ratio; NA, not available; OR, odds ratio; PCTA, percutaneous transluminal coronary angioplasty; RR, relative risk; SBP, systolic blood pressure; TIA, transient ischemic attack.

<sup>a</sup>Cox refers to Cox proportional hazards regression analysis, logistic refers to logistic regression analysis.

<sup>b</sup>The data were unpublished data from the authors.

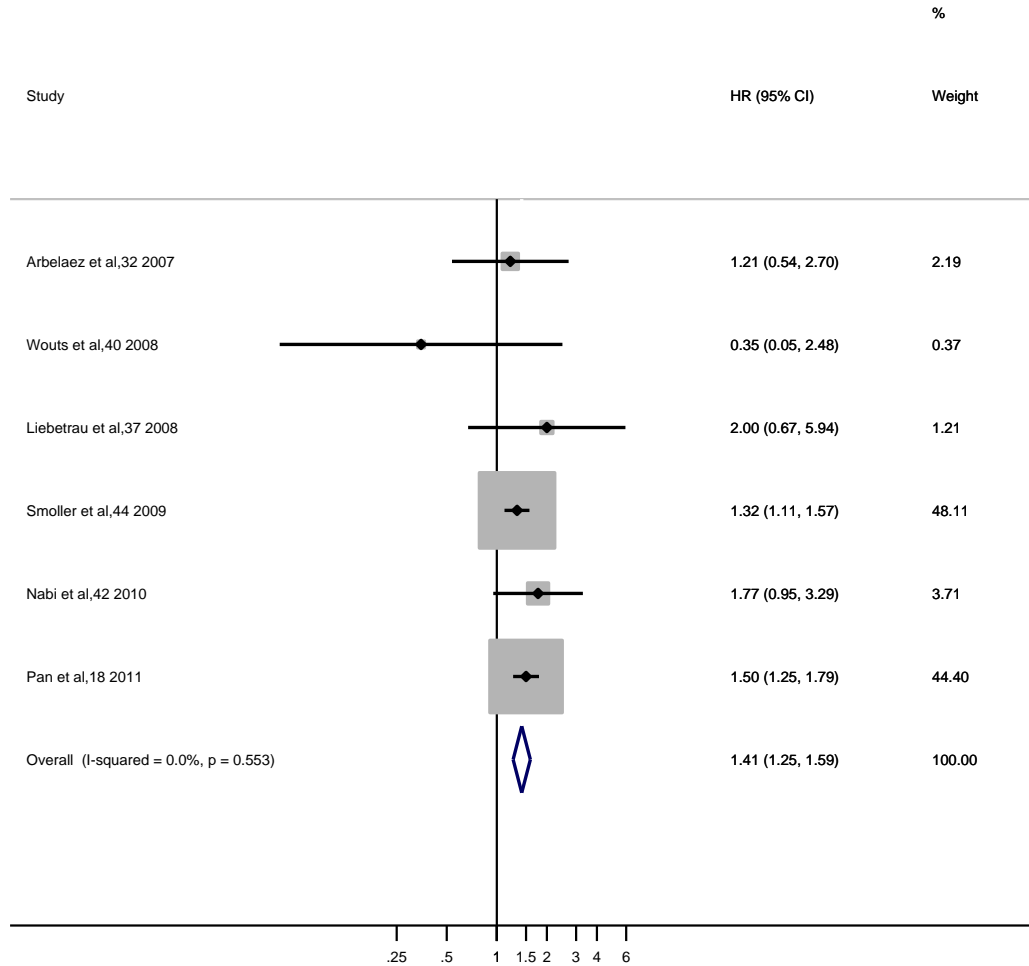
**eTable 3.** Stratified Analyses of Pooled Hazard Ratio (HR) of total Stroke according to Depression Status

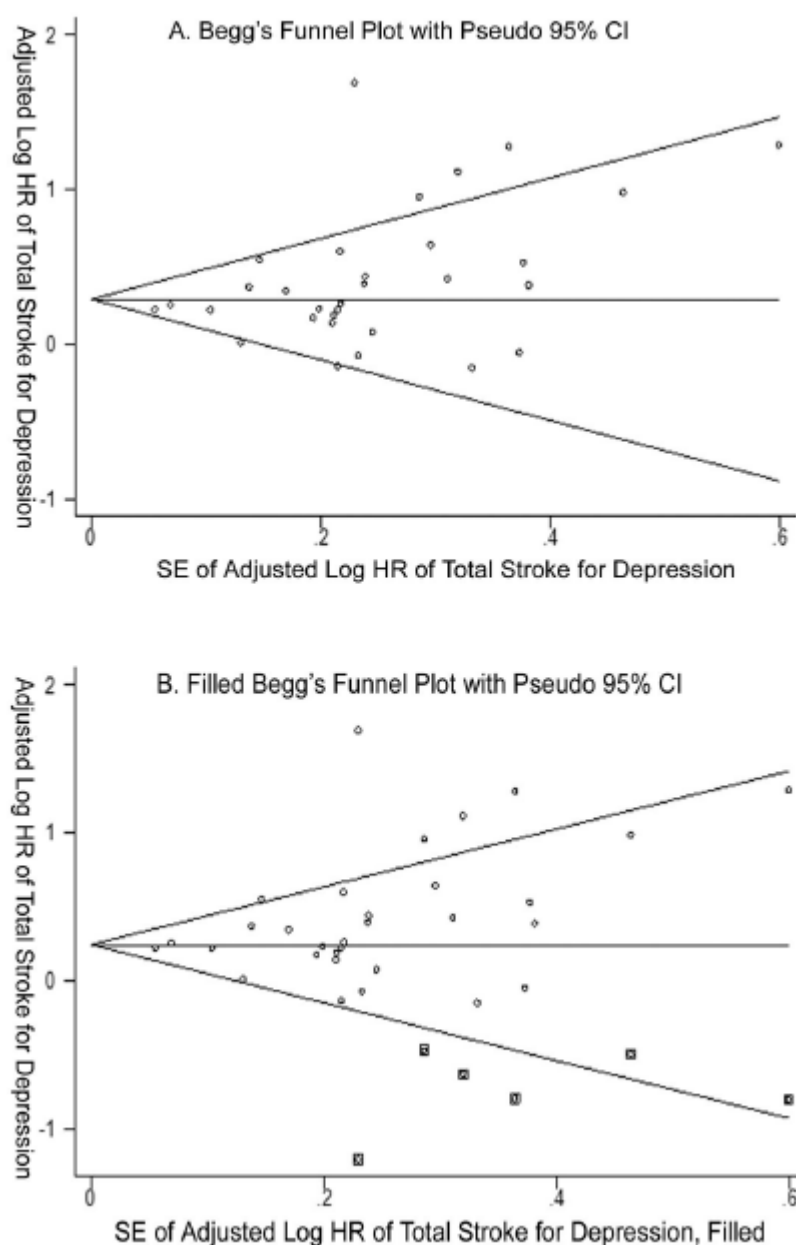
	No. of reports <sup>a</sup>	HR (95% CI)	Q-Statistic	P value for heterogeneity	I <sup>2</sup> value	P value between groups
Mean follow-up, y						
≤10	20	1.44 (1.23-1.68)	72.1	<.001	73.6	
>10	11	1.42 (1.26-1.60)	14.8	.14	32.3	.27
Publication years						
Before 2006	14	1.37 (1.23-1.53)	17.6	.17	26.1	
2006-2011	17	1.49 (1.25-1.78)	70.3	<.001	77.2	.61
Controlling physical activity in models						
Yes	8	1.32 (1.10-1.57)	15.0	.04	53.4	
No	23	1.51 (1.30-1.76)	72.5	<.001	69.6	.42
Controlling alcohol intake in models						
Yes	9	1.30 (1.21-1.40)	10.6	.22	24.5	
No	22	1.53 (1.27-1.83)	76.1	<.001	72.4	.24
Simultaneously controlling for BMI, smoking and alcohol use						
Yes	6	1.33 (1.19-1.48)	8.0	.16	37.7	
No	25	1.50 (1.29-1.74)	80.0	<.001	70.0	.84
Controlling diabetes status in models						
Yes	21	1.45 (1.26-1.67)	70.4	<.001	71.6	
No	10	1.46 (1.19-1.78)	16.5	.06	45.5	.28
Controlling hypertension status in models						
Yes	24	1.45 (1.27-1.64)	72.9	<.001	68.4	
No	7	1.46 (1.05-2.04)	14.9	.02	59.6	.55
Controlling comorbidity status in models						
Yes	25	1.45 (1.28-1.64)	73.0	<.001	67.1	
No	6	1.46 (1.00-2.13)	14.9	.01	66.3	.58

<sup>a</sup>Three studies reported their results by age groups or baseline cardiovascular disease status, therefore, there are 31 reports from 28 papers for total stroke.



**eFigure 1. Unadjusted Hazard Ratios of Total Stroke for Antidepressant Medication use**



**eFigure 2. Funnel Plots for Detection of Publication Bias for Total Stroke**

The pseudo 95% confidence interval (CI) is computed as part of the analysis that produces the funnel plot, and corresponds to the expected 95% CI for a given standard error (SE). HR indicates hazard ratio. The circular represents each identified study ( $n=31$  in A), and the square represents hypothesized missing studies ( $n=6$  in B) after adjustment for publication bias. The Duval and Tweedie nonparametric trim-and-fill procedure was used in Figure B. This method considers the possibility of hypothetical “missing” studies that might exist, imputes their HRs, and recalculates a pooled HR that incorporates the hypothetical missing studies as though they actually existed.

**eFigure 3. Summary Forest Plot for the Stratified Analyses of Total Stroke**