**ORIGINAL COMMUNICATION**

# Anger, hostility and risk of stroke: a meta-analysis of cohort studies

Hanze Chen[1] · Beidi Zhang[2] · Weishuang Xue[1] · Jinwei Li[1] · Yuru Li[1] · Kailei Fu[1] · Xinxin Chen[1] · Miao Sun[1] · Han Shi[3] · Li Tian[4] · Weiyu Teng[1]

## Abstract

**Objective** A growing number of studies have been conducted on the relationship between anger and hostility and the risk of stroke, and their conclusions are not consistent. Accordingly, we performed a meta-analysis to evaluate the relationship between anger and hostility and the risk of stroke.

**Methods** We searched the PubMed and Embase databases for cohort studies, focusing on the relationship between anger and hostility and risk of stroke. Then studies were selected according to the inclusion and exclusion criteria. Study results were pooled using a random effects model.

**Results** Ten studies from seven articles involving 52,277 participants were included in this meta-analysis. No significant association was found between anger and hostility level and risk of stroke (hazard ratio 1.08; 95% confidence interval 0.79–1.47). However, a positive association was seen when people with high socioeconomic status were excluded (hazard ratio 1.30; 95% confidence interval 1.06–1.59).

**Conclusion** A higher level of anger and hostility is not associated with elevated risk of stroke. However, the association is positive among people with lower socioeconomic status.

**Keywords** Stroke · Anger · Hostility · Cohort studies · Meta-analysis

## Introduction

Anger is an emotional state encompassing feelings of differing intensities, such as mild irritation, annoyance, intense fury and rage [1]. Hostility is a psychological notion including negative emotion, cognition and behaviour towards others [2]. Prior studies have found that high level of anger and hostility is associated with some risk factors of cardiovascular disease, including more alcohol and tobacco use, higher body mass index and hypertension [3–7]. Moreover, several prospective cohort studies [8–10] found that people with high levels of anger or hostility have a high risk of coronary heart disease. Later, a meta-analysis confirmed that anger and hostility are associated not only with risk but also with outcomes of coronary heart disease [1].

To date, a growing number of studies on the relationship between anger and hostility and stroke have emerged. A case-crossover study found that anger is an independent trigger for ischemic stroke [11]. There have been several cohort studies on the risk of stroke; however, the results of these studies are conflicting. A study in Finland with an average follow-up period of 8.3 years found that the risk of stroke in a population with a high level of expressed anger was twice as high as that of a population with a low level of expressed anger [12]. However, another study with a follow-up of 2 years studying a cohort of professionals reached the opposite conclusion. They concluded that moderate anger expression has a protective effect [13]. In addition, other studies have suggested that a high level of hostility has no impact on stroke risk [14]. The distinct results may be due to the differences in the study populations, the follow-up

✉ Li Tian
  tianlicmu2@126.com

✉ Weiyu Teng
  tengweiyucmu@sina.com

[1] Department of Neurology, The First Affiliated Hospital, China Medical University, Shenyang, China

[2] Department of Endodontics, School of Stomatology, China Medical University, Shenyang, China

[3] Clinical Department One, China Medical University, Shenyang, China

[4] Department of Geriatrics, Shengjing Hospital, China Medical University, Shenyang, China

periods, and the evaluation methods. Thus, performing a meta-analysis of these studies was necessary to explore the role of anger and hostility in the pathogenesis of stroke. The previous review only conducted a retrospective analysis of the literature and did not carry out a meta-analysis based on the different research results. To date, no meta-analysis has analysed the relationship between anger and hostility and the risk of stroke. Therefore, we conducted a meta-analysis on this issue. Although there are some differences in interpretation, anger and hostility are closely related and the boundary between them is vague; thus, we combined anger and hostility for our analysis [1, 15, 16]. We hope that we can better explore the relationship between anger, hostility and stroke risk and provide a scientific basis for the prevention of stroke vis-à-vis anger and hostility.

## Methods

### Search strategy

This meta-analysis was conducted according to the statement for meta-analysis of observational studies [17]. It was registered in the International Prospective Register of Systematic Reviews (CRD42018097436) [18].

We searched the literature published before May 2018 in PubMed, Embase and Web of Science for cohort studies on the association between anger and hostility and risk of stroke. The search terms for PubMed were (stroke OR cerebrovascular disorder OR cerebrovascular disease OR cerebrovascular attack OR cerebral infarction OR intracranial haemorrhage) AND (anger OR hostility OR aggression) AND (humans OR persons OR inpatients OR outpatients OR patients OR volunteers OR subjects OR participants). The search terms for Embase and Web of Science were similar. Moreover, we conducted a manual search by searching the reference lists of relevant articles.

### Study selection

We included studies meeting the following criteria: (1) English language publication; (2) cohort study; (3) the exposure of interest was anger or hostility; (4) the outcome was stroke; (5) a relative risk (RR) or hazard ratio (HR) was available; and (6) the association between anger and/or hostility and the risk of stroke was evaluated. Reviews, letters, commentaries, animal studies, case–control studies and cross-sectional studies were excluded. If the same populations were reported in different studies, we included the study with longest follow-up period. Two investigators on our team screened all studies independently. Any disagreement was resolved by conferring with a third investigator.

### Data extraction and quality assessment

Two investigators reviewed the included studies carefully and extracted the following information independently using a standard extraction form including study name, author, publication year, location, sample size, age, sex, follow-up time, exposure, categories of exposure, methods of measuring exposure, adjusted covariates, endpoints, outcomes ascertainment, number of cases, and RR or HR value with its 95% confidence interval (CI). We attempted to contact the authors when the information provided was insufficient. When different adjusted models existed in one study, we extracted the RR or HR value with the greatest number of adjusted confounding variables. Any discrepancy was resolved by discussion with other investigators.

The quality of each study was assessed independently by the same two investigators using the Newcastle-Ottawa scale (NOS) [19], a nine-star scale for nonrandomized study quality assessment in meta-analyses. Briefly, this scale has three broad perspectives as follows: selection, comparability and outcome of studies. Studies awarded more than six stars were considered high-quality studies.

### Statistical analysis

In the studies included in this meta-analysis, HRs or RRs were considered the effect size, and the majority of studies used Cox proportional hazard models and HRs to evaluate the relationship between anger and hostility and risk of stroke. Thus, we chose HRs and 95%CI as the effect size and viewed RRs as HRs in the present meta-analysis. We used a random-effected model to pool the HRs in all the included studies and to calculate between-study heterogeneity. Because of different categories of exposure in these studies, we only used the HRs of the highest versus the lowest category. Heterogeneity among studies was assessed by the Cochran's Q test and was considered significant when $P < 0.10$. The $I^2$ statistic was used to evaluate the proportion of variance caused by heterogeneity in observed variance. Moreover, we used a prediction interval (PI) to quantify the heterogeneity.

We also made a sensitivity analysis by removing one study at a time and evaluating the remaining studies to examine the effect of each single study and to analyse the source of heterogeneity. Studies included in this meta-analysis took place in different countries and at different time, and the basic characteristics of the participants varied. Moreover, inconsistent exposures and outcomes were used in these studies, and study quality was variable. As a result, we conducted a subgroup analysis based on the features of each study to explore additional details.

All analyses were performed by Stata version 12.0 (Stata-Corp, College Station, Texas, USA). All tests were two-sided, and the significance level was set as 0.05, with the exception of the Cochran's $Q$ test for heterogeneity.

## Results

### Literature search

After searching PubMed, Embase and Web of Science, we identified 1515 articles (475 from PubMed, 482 from Embase and 558 from Web of Science). After removing duplicates and screening titles and abstracts, 42 articles remained. Then, we read the full texts carefully and further excluded 35 articles. Finally, seven articles [12–14, 20–23] were included in our meta-analysis. The details of the screening process are shown in Fig. 1.

### Study characteristics

All included articles were cohort studies published between 1999 and 2014 and involving 52,277 participants. Five articles were from the USA while two from Europe (Finland and Germany). The participants were all men in two articles and all women in one article. The mean or median follow-up

time was more than 5 years in five articles. It is worth noting that the participants in two articles [14, 22] had coronary heart disease at baseline. Moreover, subjects in one article [13] were all professionals in various fields. Every article corrected for age, and most articles adjusted for the well-known risk factors of stroke such as smoking, alcohol consumption, body mass index and exercise. Five articles [13, 14, 20–22] had only one measure in each of them. Except for three studies [13, 14, 22], the majority of the included studies are of high quality. The details of the study characteristics are shown in Table 1. The result of quality assessment is shown in Table 2.

### Meta-analysis

Seven studies were included in the meta-analysis. The pooled HR was 1.08 (95% CI 0.79–1.47), with significant heterogeneity ($I^2 = 53.1\%$; $p = 0.046$; PI 0.46–2.54) (Fig. 2). Then, we conducted a sensitivity analysis by omitting one study at a time and found that one study [13] accounted for the observed heterogeneity (Fig. 3). In this study, the HR was 0.42 (95% CI 0.20–0.88). The pooled HR was 1.30 (95% CI 1.06–1.59) with no significant heterogeneity ($I^2 = 0.0\%$; $p = 0.478$; PI 0.97–1.73) (Fig. 4) when this study was removed.

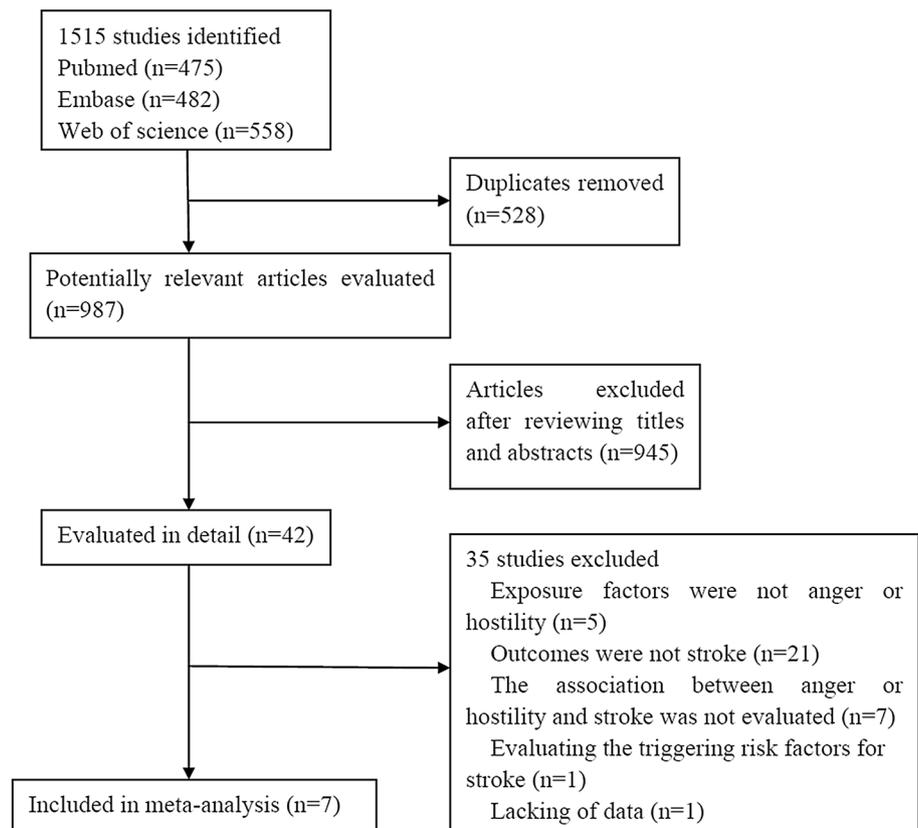**Fig. 1** Flow chart of study selection

**Table 1** Characteristics of studies included

| References | Country | Cohort | Cases | Age (years) | Follow-up (years) | Anger and hostility | Scales | Stroke (measurement) | Effect size, HR/RR (95% CI) | Covariates |
|---|---|---|---|---|---|---|---|---|---|---|
| Everson et al. [12] | Finland | 2074M | 64 | Mean 53.0 | Mean 8.3 | Anger in/out/control | AX | Incident stroke (medical record) | 2.03 (1.05–3.94) 0.98 (0.56–1.72) 0.96 (0.54–1.70) | Age, SBP, BMI, LDL, HDL, fibrinogen, smoking, alcohol consumption, SES, prevalent diabetes and use of antihypertensive medication |
| Chaput et al. [14] | U.S. | 792F | 54 | Mean 67.0 | Mean 4.1 | Hostility | CMHS | Incident stroke/TIA (medical record) | 0.83 (0.39–1.78) | Age, race, education, marital status, tobacco use, alcohol consumption, BMI, LDL-C, HDL-C, triglycerides, lipoprotein(a), diabetes, hypertension, prior MI ≥ 2, creatinine clearance < 40 ml/minute, self-rated general health, exercise ≥ 3 times/week, and use of β-blocker, aspirin, and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors |
| Williams et al. [20] | U.S. | 13851MF | 257 | 48–67 | Median 6.5 | Trait anger | TAS | Incident stroke (medical record) | 1.19 (0.75–1.89) | Age, race/ethnicity, sex, educational attainment, waist-to-hip ratio, cigarette-years of smoking, LDL-C, diabetes, hypertensive status, von Willebrand factor, prevalent coronary heart disease, and left ventricular hypertrophy |

**Table 1** (continued)

| References | Country | Cohort | Cases | Age (years) | Follow-up (years) | Anger and hostility | Scales | Stroke (measurement) | Effect size, HR/RR (95% CI) | Covariates |
|---|---|---|---|---|---|---|---|---|---|---|
| Eng et al. [13] | U.S. | 23522M | 57 | Mean 61.9 | 2 | Anger-out | AX | Incident stroke (medical record) | 0.42 (0.20–0.88) | Age in years; smoking history; alcohol intake; BMI; physical activity; hypertension; high serum cholesterol; diabetes; history of MI in parent aged less than 60; β-blocker use; antidepressant use; tranquiliser use; routine physical exam in last 2 years; energy-adjusted intakes of total fat, saturated fat, folate and fibre; multivitamin and vitamin E supplement use; employment status; and Berkman-Syme Social Network Index |
| Stürmer et al. [21] | Germany | 4267MF | 62 | Mean 53.4 | Median 8.5 | Anger control | - | Incident stroke (medical record) | 0.76 (0.31–1.87) | Age, sex, body mass index, smoking status, alcohol consumption, exercise, comorbidity (history of stroke, cancer, hypertension, hyperlipidaemia, and diabetes), family history of stroke, and education |
| Wong et al. [22] | U.S. | 1022MF | - | Mean 66.8 | Mean 7.4 | Hostility | CDS | Incident stroke/TIA (medical record) | 1.42 (0.73–2.74) | Age |

**Table 1** (continued)

| References | Country | Cohort | Cases | Age (years) | Follow-up (years) | Anger and hostility | Scales | Stroke (measurement) | Effect size, HR/RR (95% CI) | Covariates |
|---|---|---|---|---|---|---|---|---|---|---|
| Everson-Rose et al. [23] | U.S. | 6749MF | 195 | Mean 62.1 | Median 8.5 | Hostility/trait anger | TAS/CMHS | Incident stroke/TIA (medical record) | 2.00 (1.15–3.47) 1.41 (0.95–2.10) | Age, race, sex, education, study site, systolic blood pressure, alcohol use, smoking status, physical activity, BMI, height, use of anti-hypertensives, diabetes/fasting blood glucose status, HDL-C, and triglycerides |

*AX* Spielberger anger expression scales, *CMHS* Cook–Medley hostility scale, *CDS* cynical distrust scale, *TAS* Spielberger trait anger scale, *SBP* systolic blood pressure, *BMI* body mass index, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SES* socioeconomic status, *MI* myocardial infarction

Subgroup analyses were conducted based on all the studies except one [13] because of the heterogeneity it brought. The results of subgroup analyses are shown in Table 3. The positive association between anger and hostility and stroke risk was consistent in Americans (1.37 [1.08–1.73]; $I^2 = 0.0$; $p$ for heterogeneity $= 0.41$), older people ($\geq 60$ years) (1.40 [1.01–1.93]; $I^2 = 16.3\%$; $p$ for heterogeneity $= 0.30$) and people without coronary disease (1.33 [1.06–1.67]; $I^2 = 1.8\%$; P for heterogeneity $= 0.38$). Moreover, similar associations persisted after pooling studies with more participants (1.45 [1.11–1.89]; $I^2 = 1.6\%$; $p$ for heterogeneity $= 0.31$), higher quality (1.33 [1.06–1.67]; $I^2 = 1.8\%$; $p$ for heterogeneity $= 0.38$) and follow-up longer than 5 years (1.34[1.09–1.66]; $I^2 = 0.0\%$; $p$ for heterogeneity $= 0.54$). However, the association was of no statistical significance in Europeans, younger people, people with coronary disease, and after pooling studies with less participants, shorter follow-up, and lower quality. It is noteworthy that although the stroke risk increased significantly when we put anger and hostility together, neither anger (1.23 [0.97–1.57]) nor hostility (1.41 [0.86–2.29]) alone had a significant effect on the risk of stroke.

## Discussion

This meta-analysis of cohort studies showed no significant association between anger and hostility and risk of stroke. However, it showed that anger and hostility significantly contribute to a higher risk of stroke when one study focusing on male health professionals [13] was excluded, and this association was more obvious in Americans, people more than 60 years old and people without coronary disease than in Europeans, people less than 60 years old and people with coronary disease.

Most of the studies did not find a significant association between anger and hostility and risk of stroke. However, one study based in Finland [12] found that men with the highest level of expressed anger have double the risk of stroke compared to men with the lowest level of expressed anger. Similarly, 15 years later, another study [23] based in the U.S. found the same association between hostility and risk of stroke. However, the opposite result was shown in a study [13] enrolling healthy American male professionals. In this study, anger expression was inversely associated with the risk of stroke and the participants were of high socioeconomic status (SES), which may have led to a different conclusion. Additionally, the follow-up time in this study was only 2 years, which was far less than that of other studies. As a result, it is difficult to detect differences between control and exposed groups. Nonetheless, other factors could weigh heavily in studies with distinct results, such as different measures of exposure, locations and ages of participants.

**Table 2** Quality assessment

| References | Selection | | | | Comparability[a] | Outcome/exposure | | |
|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 1 | 1 | 2[b] | 3 |
| Everson et al. [12] | ☆ | ☆ | | ☆ | ☆ ☆ | ☆ | ☆ | ☆ |
| Chaput et al. [14] | | ☆ | | | ☆ ☆ | ☆ | | ☆ |
| Williams et al. [20] | ☆ | ☆ | | ☆ | ☆ ☆ | ☆ | ☆ | ☆ |
| Eng et al. [13] | | ☆ | | ☆ | ☆ ☆ | ☆ | | ☆ |
| Stürmer et al. [21] | ☆ | ☆ | | | ☆ ☆ | ☆ | ☆ | ☆ |
| Wong et al. [22] | | ☆ | | | ☆ | ☆ | ☆ | ☆ |
| Everson-Rose et al. [23] | ☆ | ☆ | | ☆ | ☆ ☆ | ☆ | ☆ | ☆ |

[a]Adjusted variables in different studies are listed in Table 1

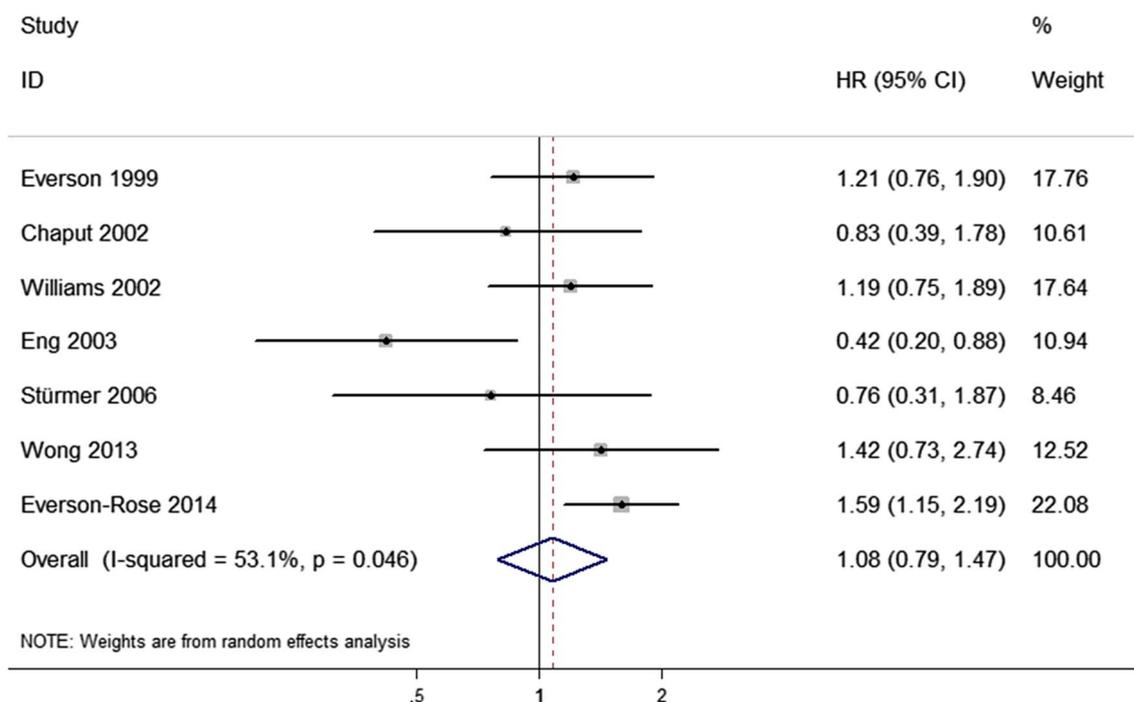[b]Studies with more than 5 years of follow-up are indicated by ☆



**Fig. 2** Forest plot of anger and hostility and risk of stroke

Studies have shown that people with higher levels of anger and hostility are more likely to have additional factors that are known to affect health, such as smoking, alcohol consumption, caffeine consumption, physical inactivity, elevated lipid ratios, elevated BMI and hypertension [6, 22, 24], and the effect of anger and hostility on increasing the risk of stroke is attenuated after adjusting for these factors [14, 20, 23]. Thus, these factors may be potential mediators that increase stroke risk. A previous meta-analysis showed that hostility, aggression, or type-A behaviour were associated with increased cardiovascular (heart rate or blood pressure) reactivity [25]. Moreover, high-hostile people had shorter telomeres and elevated telomerase activity, which can promote cellular ageing [26]. In addition, anger and

hostility are also associated with poor endothelial function [27], high platelet reactivity [28, 29], high levels of inflammatory biomarkers [30–33] and high cortisol concentrations [33, 34]. All these effects may lead to increased stroke risk. However, the situation may be different for people with high SES. First, people with different SES may have different understandings of anger and hostility. Second, high-SES participants may have more resources to treat the potentially adverse effects of anger expression [35, 36]. Third, anger expression may be a reliable index of social privilege for those who have high SES and express anger when feeling dominant and privileged, and anger expression may be stress release and thus leads to fewer negative social or physiological consequences [37]. Under these circumstances, anger

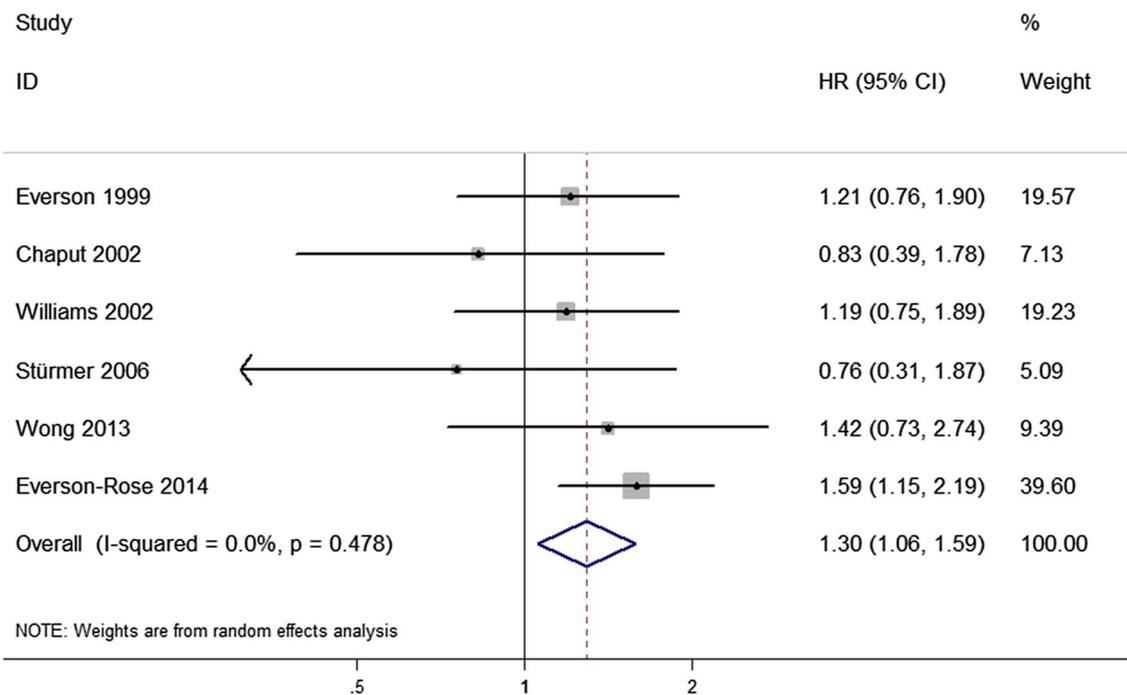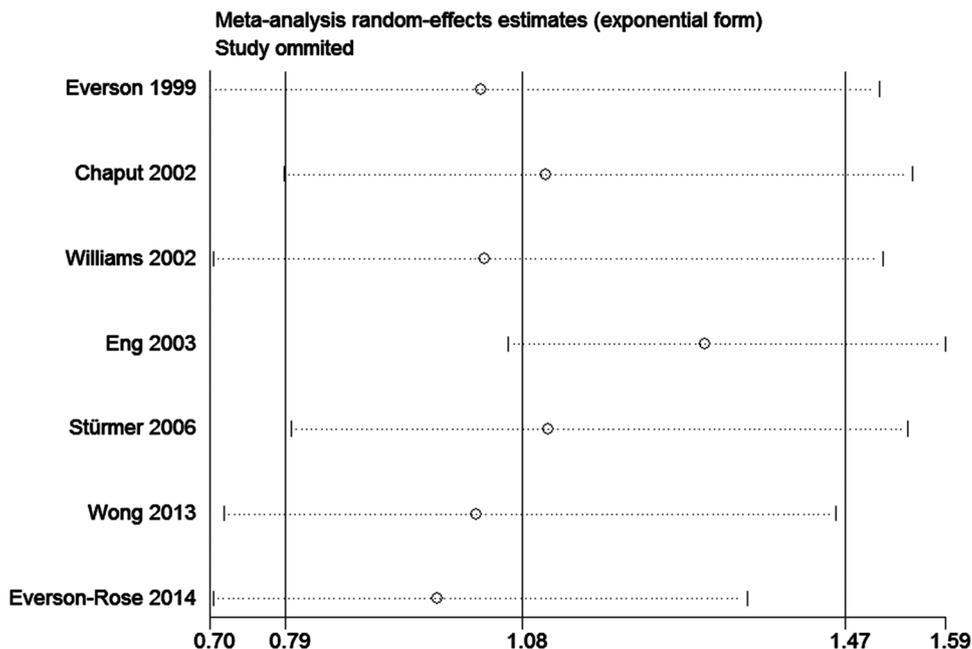**Fig. 3** Sensitivity analysis



**Fig. 4** Forest plot when omitting the study enrolling people with high SES

and hostility expression may be health protective, which is consistent with a study by Eng et al. [13].

Our study has several strengths. First, this study is the first quantitative analysis concerning anger and hostility and the risk of stroke, garnering a clearer comprehension on the effect of psychosocial factors. Furthermore, all the studies included in our analysis are cohort studies, and

most of them are of high quality. As a result, selection bias, recall bias and reverse causality were largely reduced. Finally, PI was used to evaluate the heterogeneity in our analysis because the $I^2$ statistic is not an absolute measure of heterogeneity according to recent findings [38]. The PI in this meta-analysis indicates that it is possible for future studies to show both increased and decreased stroke risks

**Table 3** Subgroup analysis of the risk of stroke

|  | No. of studies | HR (95%CI) | p for hetero-geneity | I² (%) | p for test |
|---|---|---|---|---|---|
| Sex |  |  |  |  |  |
| Male | 1 | 1.21 (0.76–1.90) | – | – | – |
| Female | 1 | 0.83 (0.39–1.78) | – | – | – |
| Location |  |  |  |  |  |
| U.S. | 4 | 1.37 (1.08–1.73) | 0.41 | 0.0 | 0.01 |
| Europe | 2 | 1.10 (0.73–1.65) | 0.37 | 0.0 | 0.65 |
| No of participants |  |  |  |  |  |
| ≥ 5000 | 2 | 1.45 (1.11–1.89) | 0.31 | 1.6 | 0.01 |
| < 5000 | 4 | 1.11 (0.81–1.52) | 0.59 | 0.0 | 0.52 |
| Follow-up |  |  |  |  |  |
| ≥ 5 years | 5 | 1.34 (1.09–1.66) | 0.54 | 0.0 | 0.01 |
| < 5 years | 1 | 0.83 (0.39–1.78) | – | – | – |
| Quality |  |  |  |  |  |
| ≥ 7 | 5 | 1.33 (1.06–1.67) | 0.38 | 1.8 | 0.01 |
| < 7 | 2 | 1.12 (0.67–1.89) | 0.30 | 8.5 | 0.66 |
| Mean age |  |  |  |  |  |
| ≥ 60 years | 3 | 1.40 (1.01–1.93) | 0.30 | 16.3 | 0.04 |
| < 60 years | 3 | 1.14 (0.84–1.55) | 0.64 | 0.0 | 0.41 |
| Exposure |  |  |  |  |  |
| Anger | 4 | 1.23 (0.97–1.57) | 0.66 | 0.0 | 0.09 |
| Hostility | 3 | 1.41 (0.86–2.29) | 0.18 | 40.8 | 0.17 |
| Participants |  |  |  |  |  |
| With coronary disease | 2 | 1.12 (0.67–1.89) | 0.30 | 8.5 | 0.66 |
| Without coronary disease | 4 | 1.33 (1.06–1.67) | 0.38 | 1.8 | 0.01 |

in people with higher anger and hostility levels compared to those with lower anger and hostility levels.

Our study has some limitations. First, all participants in our analysis were Americans and Europeans; therefore, the effect of anger and hostility on stroke risk may not be generalizable to people from other areas. Second, the level of anger and hostility was assessed by self-report questionnaires in all studies. Thus, measurement error may exist and the association between anger and hostility and risk of stroke may be understated. Moreover, the evaluation criteria for anger and hostility were not consistent between studies. However, the criteria used are all reliable and well accepted. Third, confounding factors listed in each study varied, and there may be other risk factors that should be adjusted. We chose RRs with the greatest number of adjusted confounding factors in our meta-analysis. Fourth, our meta-analysis did not focus on stroke subtypes, such as cerebral infarction and cerebral haemorrhage, because no relevant literature was found on such subtypes. Future studies should include specific stroke subtypes. Finally, considering the observational design of the included studies, the possibility of residual confounding could not be excluded.

## Conclusions

In summary, the results from this meta-analysis do not support the hypothesis that a higher anger and hostility level is associated with elevated risk of stroke. However, a positive association is shown when people with high SES are excluded. Studies with lager sample sizes and longer follow-up periods are required to confirm these conclusions.

## Compliance with ethical standards

**Conflicts of interest** The authors declare that they have no conflicts of interest.

**Ethical standards** This manuscript does not contain clinical studies or patient data.

# References

1. Chida Y, Steptoe A (2009) The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. J Am Coll Cardiol 53(11):936–946. https://doi.org/10.1016/j.jacc.2008.11.044

2. Barefoot JC, Dodge KA, Peterson BL, Dahlstrom WG, Williams RB Jr (1989) The Cook–Medley hostility scale: item content and ability to predict survival. Psychosom Med 51(1):46–57

3. Airagnes G, Lemogne C, Gueguen A, Hoertel N, Goldberg M, Limosin F, Zins M (2017) Hostility predicts alcohol consumption over a 21-year follow-up in the Gazel cohort. Drug Alcohol Depend 177:112–123. https://doi.org/10.1016/j.drugalcdep.2017.03.034

4. Progovac AM, Chang YF, Chang CH, Matthews KA, Donohue JM, Scheier MF, Habermann EB, Kuller LH, Goveas JS, Chapman BP, Duberstein PR, Messina CR, Weaver KE, Saquib N, Wallace RB, Kaplan RC, Calhoun D, Smith JC, Tindle HA (2017) Are optimism and cynical hostility associated with smoking cessation in older women? Ann Behav Med Publ Soc Behav Med 51(4):500–510. https://doi.org/10.1007/s12160-016-9873-x

5. Scherwitz LW, Perkins LL, Chesney MA, Hughes GH, Sidney S, Manolio TA (1992) Hostility and health behaviors in young adults: the CARDIA study. Coronary artery risk development in young adults study. Am J Epidemiol 136(2):136–145

6. Siegler IC, Peterson BL, Barefoot JC, Williams RB (1992) Hostility during late adolescence predicts coronary risk factors at mid-life. Am J Epid 136(2):146–154

7. Everson SA, Goldberg DE, Kaplan GA, Julkunen J, Salonen JT (1998) Anger expression and incident hypertension. Psychosom Med 60(6):730–735

8. Boyle SH, Michalek JE, Suarez EC (2006) Covariation of psychological attributes and incident coronary heart disease in U.S. Air Force veterans of the Vietnam war. Psychosom Med 68(6):844–850. https://doi.org/10.1097/01.psy.0000240779.55022.ff

9. Gallacher JE, Yarnell JW, Sweetnam PM, Elwood PC, Stansfeld SA (1999) Anger and incident heart disease in the caerphilly study. Psychosom Med 61(4):446–453

10. Koskenvuo M, Kaprio J, Rose RJ, Kesaniemi A, Sarna S, Heikkila K, Langinvainio H (1988) Hostility as a risk factor for mortality and ischemic heart disease in men. Psychosom Med 50(4):330–340

11. Koton S, Tanne D, Bornstein NM, Green MS (2004) Triggering risk factors for ischemic stroke: a case-crossover study. Neurology 63(11):2006–2010

12. Everson SA, Kaplan GA, Goldberg DE, Lakka TA, Sivenius J, Salonen JT (1999) Anger expression and incident stroke: prospective evidence from the Kuopio ischemic heart disease study. Stroke 30(3):523–528

13. Eng PM, Fitzmaurice G, Kubzansky LD, Rimm EB, Kawachi I (2003) Anger expression and risk of stroke and coronary heart disease among male health professionals. Psychosom Med 65(1):100–110

14. Chaput LA, Adams SH, Simon JA, Blumenthal RS, Vittinghoff E, Lin F, Loh E, Matthews KA (2002) Hostility predicts recurrent events among postmenopausal women with coronary heart disease. Am J Epidemiol 156(12):1092–1099

15. Martin R, Watson D, Wan CK (2000) A three-factor model of trait anger: dimensions of affect, behavior, and cognition. J Pers 68(5):869–897

16. Schulman JK, Stromberg S (2007) On the value of doing nothing: anger and cardiovascular disease in clinical practice. Cardiol Rev 15(3):123–132. https://doi.org/10.1097/01.crd.0000246318.59658.25

17. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (MOOSE) group. Jama 283(15):2008–2012

18. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 151(4):264–269, w264

19. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P (2011) The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 10 Oct 2018

20. Williams JE, Nieto FJ, Sanford CP, Couper DJ, Tyroler HA (2002) The association between trait anger and incident stroke risk: the atherosclerosis risk in communities (ARIC) study. Stroke 33(1):13–19

21. Stürmer T, Hasselbach P, Amelang M (2006) Personality, lifestyle, and risk of cardiovascular disease and cancer: follow-up of population based cohort. BMJ 332(7554):1359–1362. https://doi.org/10.1136/bmj.38833.479560.80

22. Wong JM, Na B, Regan MC, Whooley MA (2013) Hostility, health behaviors, and risk of recurrent events in patients with stable coronary heart disease: findings from the heart and soul study. J Am Heart Assoc 2(5):e000052. https://doi.org/10.1161/jaha.113.000052

23. Everson-Rose SA, Roetker NS, Lutsey PL, Kershaw KN, Longstreth WT Jr, Sacco RL, Diez Roux AV, Alonso A (2014) Chronic stress, depressive symptoms, anger, hostility, and risk of stroke and transient ischemic attack in the multi-ethnic study of atherosclerosis. Stroke 45(8):2318–2323. https://doi.org/10.1161/strokeaha.114.004815

24. Nabi H, Kivimaki M, Sabia S, Dugravot A, Lajnef M, Marmot MG, Singh-Manoux A (2009) Hostility and trajectories of body mass index over 19 years: the Whitehall II study. Am J Epidemiol 169(3):347–354. https://doi.org/10.1093/aje/kwn333

25. Chida Y, Hamer M (2008) Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: a quantitative review of 30 years of investigations. Psychol Bull 134(6):829–885. https://doi.org/10.1037/a0013342

26. Brydon L, Lin J, Butcher L, Hamer M, Erusalimsky JD, Blackburn EH, Steptoe A (2012) Hostility and cellular aging in men from the Whitehall II cohort. Biol Psychiatry 71(9):767–773. https://doi.org/10.1016/j.biopsych.2011.08.020

27. Gottdiener JS, Kop WJ, Hausner E, McCeney MK, Herrington D, Krantz DS (2003) Effects of mental stress on flow-mediated brachial arterial dilation and influence of behavioral factors and hypercholesterolemia in subjects without cardiovascular disease. Am J Cardiol 92(6):687–691

28. Shimbo D, Chaplin W, Kuruvilla S, Wasson LT, Abraham D, Burg MM (2009) Hostility and platelet reactivity in individuals without a history of cardiovascular disease events. Psychosom Med 71(7):741–747. https://doi.org/10.1097/PSY.0b013e3181ad18b6

29. Markovitz JH (1998) Hostility is associated with increased platelet activation in coronary heart disease. Psychosom Med 60(5):586–591

30. Brummett BH, Boyle SH, Ortel TL, Becker RC, Siegler IC, Williams RB (2010) Associations of depressive symptoms, trait hostility, and gender with C-reactive protein and interleukin-6 response after emotion recall. Psychosom Med 72(4):333–339. https://doi.org/10.1097/PSY.0b013e3181d2f104

31. Puterman E, Epel ES, O'Donovan A, Prather AA, Aschbacher K, Dhabhar FS (2014) Anger is associated with increased IL-6 stress reactivity in women, but only among those low in social support. Int J Behav Med 21(6):936–945. https://doi.org/10.1007/s12529-013-9368-0

32. Girard D, Tardif JC, Boisclair Demarble J, D'Antono B (2016) Trait hostility and acute inflammatory responses to stress in the laboratory. PLoS One 11(6):e0156329. https://doi.org/10.1371/journal.pone.0156329

33. Moons WG, Eisenberger NI, Taylor SE (2010) Anger and fear responses to stress have different biological profiles. Brain Behav Immunity 24(2):215–219. https://doi.org/10.1016/j.bbi.2009.08.009

34. Steptoe A, Cropley M, Griffith J, Kirschbaum C (2000) Job strain and anger expression predict early morning elevations in salivary cortisol. Psychosom Med 62(2):286–292

35. Gallo LC, Matthews KA (2003) Understanding the association between socioeconomic status and physical health: do negative emotions play a role? Psychological bulletin 129(1):10–51

36. Schieman S (2000) Education and the activation, course, and management of anger. J Health Soc Behav 41(1):20–39

37. Kitayama S, Park J, Boylan JM, Miyamoto Y, Levine CS, Markus HR, Karasawa M, Coe CL, Kawakami N, Love GD, Ryff CD (2015) Expression of anger and ill health in two cultures: an examination of inflammation and cardiovascular risk. Psychol Sci 26(2):211–220. https://doi.org/10.1177/0956797614561268

38. Borenstein M, Higgins JP, Hedges LV, Rothstein HR (2017) Basics of meta-analysis: $I^2$ is not an absolute measure of heterogeneity. Res Synth Methods 8(1):5–18. https://doi.org/10.1002/jrsm.1230