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Association of smoking with risk of stroke in middle-aged and older Chinese

Evidence from the China National Stroke Prevention Project

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Abstract

Although the impacts of smoking on health are well established, it is unclear on how they affect the Chinese population aged ≥40 years. This study aimed to investigate the association between smoking and risk of stroke in middle-aged and older Chinese adults, based on the data from the China National Stroke Prevention Project.

A community-based cross-sectional study with 12,704 (5681 men, 7023 women) Chinese adults aged ≥40 years was conducted to examine the association of smoking with stroke. Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

Among the study population, a total of 524 stroke survivors were identified. The age-adjusted prevalence of stroke was 4.06% for both sexes, 2.95% for women, and 5.38% for men. The multivariate-adjusted ORs (95% CI) of stroke associated with current cigarette smoking and former cigarette smoking were 1.67 (1.24–2.25) and 1.93 (1.29–2.87), respectively. Compared with those who were never-smokers, the multivariate-adjusted OR of stroke (95% CI) were 1.48 (0.96 to –2.29), 1.75 (1.20–2.56), and 2.37 (1.20 to –4.68) for those who smoked 1 to 10, 11 to 20, and ≥21 cigarettes per day; and 0.51 (0.19 to –1.42), 1.90 (1.36 to –2.67), and 2.01 (1.17 to –3.46) for those who smoked 1 to 19, 20 to 39, and ≥40 years, respectively (both $P < .001$ for linear trends). Among former smokers, the multivariable-adjusted ORs of stroke by duration of smoking cessation (compared with never smokers) for <5, 5 to 19, and ≥20 years were 3.47 (1.42–8.49), 3.37 (1.95–5.80), and 0.95 (0.49–1.84), respectively ($P = .009$ for linear trend). The increased odds of stroke with smoking were more evident among participants who were men, >60 years old, or without family history of stroke than their counterparts.

This study suggests the increased odds of stroke in current cigarette smokers with a graded increase in prevalent risk that depended on how many cigarettes and how many years were smoked. Moreover, quitting smoking appears to decrease this excess risk substantially.

Abbreviations: AF = atrial fibrillation, BMI = body mass index, BP = blood pressure, CI = confidence interval, CSPP = China National Stroke Prevention Project, CVD = cardiovascular disease, DBP = diastolic blood pressure, ECG = electrocardiogram, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, OR = odds ratio, SBP = systolic blood pressure, SD = standard deviation, WHO = World Health Organization.

Keywords: epidemiology, risk factors, smoking, stroke

Editor: Meixia Lu.

Sources of Funding: This study was supported by the Fundamental Research Funds for the Central Universities, Huazhong University of Science and Technology, China (2016YXMS215), the China Postdoctoral Science Foundation funded project (2018M630870), and the by National Natural Science Foundation of China (71804049). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

We declare that we have no conflict of interest.

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Medicine (2018) 97:47(e13260)

Received: 19 August 2018 / Accepted: 23 October 2018

http://dx.doi.org/10.1097/MD.0000000000013260

1. Introduction

Cardiovascular disease (CVD) has become the leading cause of death and exert extorts heavy social and economic costs globally.[1] Stroke can cause permanent disability, with major direct and indirect costs because of functional impairments.[2,3] In China, stroke accounts for the greatest proportion of CVD and is the most prominent factor for disability-adjusted life-years.[4] Thus, early prevention and control of stroke is an important public health priority.

The China National Stroke Prevention Project (CSPP) was launched by the Chinese government as the key national action on stroke screening and intervention since 2011. The CSPP aimed to decrease the incidence of stroke in the general population and establish the stroke prevention and control system. Some provincial or large city hospitals across the country were designated by the CSPP, and the hospitals were involved in the stroke prevention and control project. The stroke screening was organized and coordinated by the designated hospitals and performed by primary health institutions. Shenzhen Second People's Hospital, designated a large city hospital by the CSPP, was the organizer of the screening survey for Shenzhen.

Cigarette smoking, a major global public health challenge, is associated with several serious health consequences, including diabetes, CVD, and all-cause mortality.[5–7] China, the world's most populous nation, is the largest producer and consumer of cigarette. Some studies conducted in the Western populations have indicated an independent relationship between smoking and the risk of stroke.[8–10] However, this relationship has not been well established in the general Chinese populations. Therefore, investigating the association between smoking and the risk of stroke in the Chinese general populations will promote the development of effective prevention strategies aimed at reducing stroke-related mortality and disability burden in China.

The purpose of the present study is to examine the relationship of smoking, including smoking intensity and duration, and smoking cessation, with stroke risk among middle-aged and older Chinese adults who were involved in the stroke screening survey between 2013 and 2015 in Shenzhen, China.

2. Methods

2.1. Study population

A community-based cross-sectional study was conducted between January 2013 and June 2015 in Futian and Bao'an districts, Shenzhen, China. Residents were invited to participate if they met the following criteria: participants were adults aged 40 years or older; participants who agreed to complete the CSPP survey; and participants who had lived for at least 6 months in the area. The researchers selected the eligible participants into the screening process according to the above-mentioned inclusion criteria. Initially, 5325 and 8555 adults aged ≥40 years lived in the 2 communities of Meilin and Taoyuan Ju, respectively. All participants were registered at the local government office. Of these adults, 12,808 received the stroke screening with a response rate of 92.28%. Due to omitted cigarette smoking and stroke status information, 104 questionnaires were discarded. Finally, 12,704 participants were included in the analysis.

This study was approved by the Research Ethics Committee in Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. Written informed consent was provided for each respondent, and the identifying details of all study subjects were kept confidential.

2.2. Assessment of smoking status

Smoking was defined as smoking at least 1 cigarette per day continuously for at least 1 year. Participants were classified as never, former, or current smokers. Current smokers were people who had ever smoked and who were still smoking during the survey period. Former smokers were those who had stopped smoking for at least 1 year. Never smokers were those who had never smoked at least 1 cigarette a day continuously for at least 1 year. For participants who reported former or current cigarette smoking, information on the number of cigarettes smoked per day along with the duration of cigarette smoking was also collected.

2.3. Ascertainment of stroke

Stroke history was evaluated through the combination of self-reporting and the judgment of a neurologist or physician according to the World Health Organization (WHO) MONICA Project definition.[11]

2.4. Data collection and assessment of covariates

The data on demographic characteristics, status of risk factors, medical history, lifestyle risk factors, and family history of chronic diseases were obtained by trained medical staff using a standardized questionnaire administered upon exit from the community health centers. The questionnaire used in this study was derived from the CSPP.

Physical examinations included the assessment of height, weight, and blood pressure (BP) and an electrocardiogram (ECG). Laboratory examinations included the measurements of serum lipids (total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], triglycerides [TG]) and fasting plasma glucose (FPG).

The defining criterion of risk factors was guided by the Adult Treatment Panel III and the WHO.[12,13] Alcohol drinking was based on self-reports of drinking ≥100 mL spirit alcohol >3 times per week. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Categories of BMI (normal weight <25 kg/m^2, overweight 25–30 kg/m^2, or obesity ≥30 kg/m^2) were defined based on the BMI classification for adults defined by the WHO.[14] Hypertension was defined as resting systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg or defined by the use of antihypertensive drugs.[15,16] Hyperlipidemia was identified for individuals taking antilipemic drugs or having ≥1 of the following: TC ≥5.2 mmol/L, LDL-C ≥3.4 mmol/L, HDL-C ≤1.04 mmol/L, or TG ≥1.7 mmol/L.[17] In this study, diabetes mellitus was defined as FPG ≥7.0 mmol/L, or defined by the use of diabetes medication.[18] In this study, atrial fibrillation (AF) was identified for those with a history of persistent AF or defined based on past electrocardiogram (ECG) or ECG result. Physical activity was defined (based on self-reports) as ≥3 times per week for at least 30 minutes each time (including industrial and agricultural labor). Family history of stroke was defined based on self-report.

2.5. Statistical analysis

Continuous variables were presented as means and categorical data were presented as percentages. Student *t* test was used to compare variable means between participants with and without stroke. One-way analyses of variance (ANOVAs) were used to

compare variable means among smoking status groups, and chi-square test was used to compare variable percentages among smoking status groups or stroke status groups. Multivariable logistic regression model was used to examine the associations between smoking status and stroke risk. The age-adjusted and multivariable-adjusted prevalence of stroke by smoking status and sex were estimated respectively. Age and multivariate-adjusted logistic regressions were conducted to calculate odds ratios (ORs) and 95% confidence intervals (CIs) of stroke by smoking status (never smoker as the reference group). Tests for trend were conducted to assess the dose–response relation across smoking and smoking cessation categories. Test for trend was conducted using smoking dose, intensity and smoking cessation duration as a continuous variable. We tested for the smoking status × sex interaction by using an interaction term generated by multiplying smoking status with sex and found that there were no significant interactions. Thus, we present the combined data for men and women in the primary analysis.

We controlled for the following potential confounders: age (continuous), sex (female, male), marital status (single, widowed, divorced, married), education level (primary, junior, senior, college), BMI (<25, 25–29, 30+ kg/m^2), health insurance status (yes, no), family history of stroke (yes, no), history of diabetes (yes, no), history of hypertension (yes, no), history of hyperlipidemia (yes, no), history of heart disease (yes, no), history of AF (yes, no), smoking status (never, former, current smoker), alcohol drinking (never, 1–2 times, 3+ times per week), and physical activity (yes, no), screening site (2 communities).

We examined if the association between smoking and the risk of stroke differed by age groups (<60 years, ≥60 years), family history of stroke (yes, no), and BMI (<25 kg/m^2, ≥25 kg/m^2). We evaluated interaction by entering a product term of smoking status categories and the above variables, and the *P*-value for interaction was determined by a Wald test. All statistical procedures were 2-sided and performed via the Statistical Analysis System (SAS) 9.2 for Windows (SAS Institute Inc., Cary, NC) with a significance level of 0.05.

3. Results

The main characteristics of participants are reported in Table 1. A total of 12,704 participants (5681 men, 44.72%) were investigated in this study. The ages of the participants ranged from 40 to 107 years (mean age of 57.08 and standard deviation [SD] = 10.71). Overall, 85.08% of participants were never smokers, 2.83% were former smokers, and 12.10% were current smokers, with the prevalence of current cigarette smoking higher in men than in women (95.06% vs 4.94%).

Compared with never smokers, former and current smokers were more likely to be men, attained higher level of education, and consumed more alcohol. Former and current smokers were more likely to be covered with insurance, reported higher prevalence of diabetes and hypertension, and had less physical activity. Former smokers had the lowest prevalence of AF and heart disease, while they were more likely to be older and had the highest prevalence of hyperlipidemia (Table 1). Comparing with non-cases, stroke cases were more likely to be man, older, have more physical inactivity, and were more likely to have a family history of stroke. Stroke cases also had a higher prevalence of hypertension, heart disease, AF, and hyperlipidemia (Table 1).

The age-adjusted and multivariable-adjusted prevalence of stroke by smoking status and sex are shown in Table 2, respectively. The age and multivariable-adjusted stroke prevalence in former and current smokers was higher than that of never smokers. The multivariable-adjusted prevalent rate of stroke was 484 per 100,000 population in men and 299 per 100,000 population in women.

Table 3 presents the association between smoking and stroke risk for all subjects. The ORs of stroke were 1.67 (95% CI: 1.24–2.25) and 1.93 (95% CI: 1.29–2.87) for current smokers and former smokers, respectively, in the multivariable model.

We further investigated the relationship between smoking intensity and duration and stroke risk. There was a significant and linear association between both the number of cigarettes smoked per day and pack-years smoked and stroke prevalence in the

Table 1

Description of selected characteristics by smoking status and stroke (number [%] or mean [SD]).

Characteristic	Smoking status			Prevalent stroke status	
	Never	Former	Current	Stroke cases	Non-cases
No. of subjects	10,808 (85.08)	359 (2.83)	1537 (12.10)	516 (4.06)	12,188 (95.94)
Age, mean (SD), y	57.19 (10.71)	60.80 (10.95)	55.39 (10.37)	63.92 (10.96)	56.79 (10.60)
BMI, mean (SD), kg/m^2	24.26 (3.13)	24.23 (2.46)	24.33 (2.80)	24.16 (3.13)	24.27 (3.07)
Male, %	3887 (35.96)	333 (92.76)	1461 (95.06)	313 (60.66)	5368 (44.04)
College degree or above, %	2242 (20.74)	86 (23.96)	419 (27.26)	89 (17.25)	2658 (21.81)
Married, %	10395 (96.18)	343 (95.54)	1480 (96.75)	475 (92.05)	11750 (96.41)
Health insurance status, %	8347 (80.33)	295 (82.87)	1262 (83.97)	367 (72.67)	9537 (81.20)
Family history of stroke, %	735 (6.97)	25 (7.04)	129 (8.50)	88 (17.50)	801 (6.72)
Diabetes, %	1952 (18.20)	126 (36.00)	376 (24.74)	122 (22.00)	2342 (19.38)
Hypertension, %	4097 (38.41)	166 (47.03)	599 (39.25)	289 (56.56)	4573 (38.00)
Hyperlipidemia, %	3565 (33.00)	110 (30.99)	592 (38.62)	195 (38.09)	4072 (33.44)
Heart disease, %	697 (6.45)	43 (12.01)	72 (4.68)	65 (12.62)	747 (6.13)
AF, %	365 (3.42)	28 (7.80)	47 (3.28)	32 (6.58)	408 (3.41)
Alcohol drinking, %					
Never	9926 (91.84)	221 (61.56)	761 (49.51)	440 (85.27)	10468 (85.89)
1–2 times/wk	698 (6.46)	124 (34.54)	537 (34.94)	52 (10.08)	1307 (10.72)
3+ times/wk	184 (1.70)	14 (3.90)	239 (15.55)	24 (4.65)	413 (3.39)
Physical inactivity,%	1765 (16.68)	82 (22.84)	321 (22.06)	131 (26.63)	2037 (17.12)

Note: All differences among never, former, and current smokers were statistically significant ($P < .001$) except for BMI ($P = .67$), marital status ($P = .43$), and family history of stroke ($P = .10$).
All differences between stroke cases and non-cases were statistically significant ($P < .001$) except for BMI ($P = .39$), history of diabetes ($P = .14$), and alcohol drinking ($P = .29$).
AF = atrial fibrillation, BMI = body mass index.

Table 2

Age-adjusted and multivariable-adjusted prevalence (95% CI) of stroke according to smoking status and sex.

	Age-adjusted	Multivariable-adjusted
Smoking status		
Never smokers	3.46 (3.12–3.80)	3.49 (3.13–3.86)
Former smokers	10.65 (7.76–13.55)	5.98 (4.05–7.90)
Current smokers	6.74 (5.45–8.04)	5.50 (4.25–6.75)
Sex		
Male	5.38 (4.80–5.95)	4.84 (4.24–5.43)
Female	2.95 (2.56–3.35)	2.99 (2.54–3.43)

Note: The multivariable model was adjusted for age, sex, marital status, education, health insurance status, alcohol drinking, physical inactivity, BMI, family history of stroke, history of diabetes, heart disease, hypertension and atrial fibrillation, and screening site.

multivariable-adjusted model (*P* values for linear trends <.001) (see Table 3). Among former smokers (non-smoker as the reference group), the ORs (95% CIs) of stroke by duration of smoking cessation (1–4, 5–19, 20+ years) were 3.47 (1.42–8.49), 3.37 (1.95–5.80), and 0.95 (0.49–1.84), respectively (*P* for trend = .009).

ORs and 95% CIs for sex, age, family history of stroke, and BMI stratified analyses for smoking status are reported in Table 4. The odds of increased risk were greater in men than in women. The positive association between smoking and the risk of stroke was slightly stronger for adults aged 60 years and above compared with adults younger than 60 years. Intriguingly, we found that middle-aged and older Chinese adults without a family history of stroke were more likely than their counterparts to have had stroke. In addition, among current smokers, normal individuals were more likely than overweight and obese individuals to have higher odds of stroke.

4. Discussion

In this large, community-based study, we found that there was an independent and dose–response relationship between smoking and stroke risk among middle-aged and older Chinese adults. The risk increased with the amount of cigarettes smoked per day and the duration of cigarettes smoked (≥20 years). The increased excess risk among former smokers declined with time after smoking cessation in a dose–response manner. However, stopping smoking for ≥20 years virtually eliminated the excess stroke risk associated with smoking. In addition, the results showed that current smoking was significantly associated with risk of stroke in men but not in women.

Our results on the benefits of smoking cessation are particularly noteworthy because to date the effect of cessation on stroke risk has rarely been studied in middle-aged or older adults. The duration of time since smoking cessation was linearly associated with decreased risk of stroke in this study. Similar results were found in a review by Mons et al[19] in the CHANCES consortium of CVD; quitting for ≥20 years was associated with a mortality risk of 1.15 (1.02–1.30). This slight increase in risk could be related to the long-term effects of smoking on other cancers. The findings might support a net cardiovascular benefit of smoking cessation in the middle-aged and older Chinese adults. Several studies have reported the attenuated risks with longer duration of smoking cessation in the general populations.[20,21] Additional prospective studies investigating the effect of prolonged smoking cessation on stroke are needed.

Previous studies have showed a stronger association between cigarette smoking and the risk of stroke in women compared with men.[22–25] By contrast, our findings showed that current smoking was significantly associated with risk of stroke in men but not in women. It suggests that there was clear evidence of a significant sex difference between men and women. One possible interpretation was that the number of cigarettes smoked per day was generally higher in men compared with women. Importantly, in the present study, women smoked fewer cigarettes than their male equivalents: 10 cigarettes per day versus 15 cigarettes per day. Similarly, it was also reported in other areas of Asia.[26] In addition, in our study, the current

Table 3

ORs and 95% CIs for smoking and risk of stroke by smoking status, intensity, duration, and smoking cessation duration.

	No. of participants (n = 12,704)	No. of case (n = 516)	Model 1	Model 2
Smoking status				
Never smokers	10,808	376	1.00	1.00
Former smokers	359	46	3.45 (2.47–4.82)	1.93 (1.29–2.87)
Current smokers	1537	94	2.05 (1.62–2.60)	1.67 (1.24–2.25)
Years of smoking among current smokers				
Never smokers	10,808	376	1.00	1.00
1–19 years	363	6	0.70 (0.31–1.59)	0.51 (0.19–1.42)
20–39 years	969	63	2.26 (1.71–2.99)	1.90 (1.36–2.67)
40+ years	205	25	2.69 (1.73–4.16)	2.01 (1.17–3.46)
P for trend			<0.0001	<0.0001
Number of cigarettes per day among current smokers				
Never smokers	10,808	376	1.00	1.00
1–10 cig/d	680	32	1.61 (1.10–2.34)	1.48 (0.96–2.29)
11–20 cig/d	689	51	2.42 (1.78–3.30)	1.75 (1.20–2.56)
21+ cig/d	168	11	2.30 (1.23–4.31)	2.37 (1.20–4.68)
P for trend			<0.0001	0.0002
Number of years of smoking cessation among former smokers				
Never smokers	10,808	376	1.00	1.00
1–4 years	38	10	6.52 (3.08–13.81)	3.47 (1.42–8.49)
5–19 years	137	22	5.84 (3.62–9.43)	3.37 (1.95–5.80)
20+ years	184	14	1.71 (0.97–3.00)	0.95 (0.49–1.84)
P for trend			<0.0001	0.009

BMI = body mass index, CI = confidence interval, Cig = cigarette, OR = odds ratio. Model 1: adjusted for age, Mode 2: model 1 plus sex, marital status, education, health insurance status, alcohol drinking, physical inactivity, BMI, family history of stroke, history of diabetes, heart disease, hypertension and atrial fibrillation, and screening site.

Table 4

ORs and 95% CIs for smoking and risk of strokes stratified by sex, age, family history, and BMI*.

	Never smoker (n = 10808) OR (95%CI)	Former smoker (n = 359) OR (95%CI)	Current smoker (n = 1537) OR (95%CI)	*P* value for interaction
Sex				
Male	1.00 (3887)	2.10 (1.39–3.18) (333)	1.76 (1.29–2.39) (1461)	.72
Female	1.00 (6921)	0.79 (0.10–6.53) (26)	1.57 (0.44–5.61) (76)	
Age, years				
<60	1.00 (6470)	2.26 (1.13–4.51) (164)	1.19 (0.71–1.97) (990)	.03
60+	1.00 (4338)	1.79 (1.10–2.91) (195)	1.95 (1.35–2.82) (547)	
Family history of stroke				
No	1.00 (9815)	1.63 (1.05–2.55) (330)	1.71 (1.24–2.35) (1389)	.13
Yes	1.00 (735)	8.44 (2.70–26.36) (25)	1.19 (0.50–2.84) (129)	
BMI, kg/m^2				
<25	1.00 (7012)	1.86 (1.15–3.02) (255)	1.74 (1.22–2.50) (1002)	.64
25+	1.00 (3796)	2.16 (1.05–4.46) (104)	1.61 (0.93–2.78) (535)	

* The models were adjusted for age, sex, marital status, education, health insurance status, alcohol drinking, physical inactivity, BMI, family history of stroke, history of diabetes, heart disease, hypertension and atrial fibrillation, and screening site; variables being stratified were not included in the corresponding multivariable models.

smoking prevalence was 25.72% in men and 1.08% in women. Hence, if smoking confers the same hazard in women as it does in men, one would expect male smokers to have a greater risk ratio of stroke compared with female smokers because of their greater cumulative exposure to smoking. This hypothesis is supported by the findings of this study. Another possible interpretation was that of the protective effects of estrogen on the cerebral circulation.[27] Previous studies showed that lifetime exposure to ovarian estrogens might protect against ischemic stroke.[28] Notably, the non-significant association between smoking and stroke in women may be due to chance because of limited cases. Additional studies are warranted to investigate the potential differences between both sexes.

4.1. Strengths and limitations

This study has several strengths. The strengths of this study include its large sample size and detailed information on intensity and duration of smoking and other confounders. To our knowledge, this is the first study of middle-aged and older adults to investigate the association of smoking with stroke in China, based on the data from the CSPP. In addition, we conducted a dose–response analysis to quantitatively elucidate the relationships between smoking and stroke and found a significant linear association of smoking intensity and duration with stroke.

There were several limitations in the present study. Firstly, this survey was a cross-sectional study, which restricted the interpretation of the observed associations in terms of causality. It is, however, considered unlikely that participants with stroke tend to have more prevalent smoking. Secondly, information on smoking and some covariates was collected by self-administered questionnaire, raising the potential issue of inaccurate reporting. In several validation studies, however, self-report of smoking[29] and other cardiovascular risk factors were reliable.[30] Thirdly, the study was carried out in middle-aged and older Chinese adults; therefore, our results may not be generalized to the populations of all ages, other poor regions, or other ethnicities. Finally, although many potential confounding factors were adjusted in our analysis, we were unable to rule out the possibility of residual and unmeasured confounders.

5. Conclusion

In conclusion, this study suggested that smoking is associated with an increased risk of stroke in a dose–response manner among middle-aged and older Chinese adults. Furthermore, quitting smoking for ≥20 years virtually eliminated the excess stroke risk associated with smoking. Smoking cessation intervention programs should be an urgent public health priority towards the middle-aged and older adults in China. More evidences from prospective and interventional studies are warranted to confirm the relationship of smoking and the risk of stroke in this population and other aged group Chinese populations.

Acknowledgments

The authors would like to thank all staff members involved in this study for their painstaking efforts in conducting the data collection. They also would like to thank Dr. Heng Jiang and Dr. Opoku Sampson for helpful comments and edits.

Author contributions

YG and ZXL conceived and designed the study. JW, SCZ, TTY and ZHW acquired the data. YG drafted the manuscript. YG carried out the statistical analysis. All authors contributed to revising the manuscript for important intellectual content. ZHW and ZXL were responsible for administrative, technical, or material support. ZXL was responsible for study supervision. ZXL had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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