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Is breathing our polluted air a risk factor for stroke?

Conrado J Estol

Abstract

The conference "Climate change, air pollution and health" was held at the Pontifical Academy of Sciences. The data presented highlighted that air pollution is a major, under-recognized and modifiable risk factor for stroke and heart disease. Air pollution causes 7.6% of all deaths making it the fifth cause of death globally, and this figure is expected to increase by 50% by 2050. Particulate matter causes endothelial dysfunction and induces thrombosis by altering reactive oxygen species, nitric oxide, insulin resistance, and lipid levels. Thirty-three articles published since 2002 were reviewed to assess the relation between air pollution and stroke with age, geographical location, particulate and gaseous matter type, duration of exposure, previous stroke, and comorbidities. It remains to be defined if air pollution has pathophysiological effects that preferentially predispose individuals to ischemic or hemorrhagic stroke. There is ample evidence showing an association between acute and chronic exposure to $PM_{2.5}$ or gaseous pollutants with stroke. This potentially avoidable scenario and its dramatic consequences are heavily under-recognized by health professionals and the wider public. Preventive measures in people at high vascular risk are warranted. Procrastination in implementing efforts to stop the current worldwide course of worsening air pollution is the seed of a potential global health catastrophe.

Keywords

Air pollution, stroke, cardiovascular disease, climate change

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> ***"Knowing is not enough; we must apply. Willing is not enough; we must do."***
> Johann Wolfgang von *Goethe*

The workshop "Climate Change, Air Pollution and Health" was held from 2–4 November 2017 at the Vatican Pontifical Academy of Sciences founded by Galileo Galilei in 1603. Presentations were made by a range of experts, including two Nobel Prize laureates, and spanned a diverse variety of fields including chemistry, physics, energy, epidemiology, anthropology, philosophy, economics, biodiversity, medicine, and biology. A statement has been released with the conclusions of the workshop, along with a message from Pope Francis, signed by all attendees.[1] The presentation on air pollution and cardiovascular disease at the aforementioned workshop prompted the following review on air pollution and stroke.

Cardiovascular disease

Cerebrovascular and coronary heart diseases are the leading causes of death worldwide accounting for a third of all deaths.[2] The burden is greatest in developing and emerging regions where 85% of all vascular events occur and the number of events has doubled over the last decade.[3,4] Critically, vascular events could be decreased by 80% simply by following available vascular disease guidelines and adopting healthy lifestyle habits (good nutrition, regular exercise and smoking avoidance).[5,6] However, in practice this is far from being the case, with epidemiological studies showing increases of 25% in stroke and 53% in ischemic heart disease between 2005 and 2016.[7] Surprisingly, one crucial controllable factor that is rarely taken into consideration is air pollution. Abundant robust data shows it is a significant factor associated with cardiovascular disease.

Stroke Unit, Sanatorio Guemes, Francisco Acuña de Figueroa 1240, C1180, CABA, Argentina

Corresponding author:
Conrado J Estol, Stroke Unit, Sanatorio Guemes, Francisco Acuña de Figueroa 1240, C1180 CABA, Argentina.
Email: conrado.estol@stat-research.com

Epidemiology of cardiovascular disease and air pollution

Vascular risk factors for stroke between 1990 and 2013 were analyzed in 188 high and low-income countries.[8] More than 70% of the population-attributable fraction of vascular disease was secondary to metabolic and behavioral factors. Air pollution accounted for close to a third of the population-attributable fraction (34% in low-income, 10% in high-income countries). During 2015, close to six million people died due to air pollution (one in eight deaths), 60% due to cardiovascular disease.[9] Ninety percent of those affected come from low and middle-income countries.[10]

Cohen et al.[10] studied deaths related to air pollution between 1990 and 2015 accounting for 79 risk factors in 195 countries. Because of non-linear exposure-response curves which show a greater response at lower particulate matter (PM) concentrations and lower response at higher PM concentrations, only a modest decrease in disease burden will occur in highly polluted areas. However, even this limited reduction will have significant health implications. Cognitive consequences of cerebrovascular disease should be included when measuring the burden of air pollution.[11,12] Air pollution has been recognized as a vascular disease risk factor by the American Heart Association (AHA), the European Cardiology Association, and the WHO.[13,14]

Mechanisms of cardiovascular damage due to air pollution toxins

Fossil fuel and biomass combustion generate 100% of gaseous toxins (CO, SO_2, NO_2, and O_3) and 85% of air particle toxins.[15] Particles up to 2.5 μm in diameter, termed $PM_{2.5}$, can cross the alveoli-endothelial barrier, reaching the circulation by direct translocation through the alveoli and vessel walls or by incorporation into macrophages that cross the lung-vessel barrier.[16,17] Alterations in sympathetic tone may induce vasoconstriction, increased vascular resistance, and reduced cerebral blood flow.[18] Increased blood viscosity and a hypercoagulable state have been also associated with air pollution.[14,19,20] A meta-analysis of studies with short and long-term exposure to air pollutants revealed an increased risk for hypertension, and another study showed that particulate pollution blunted the nocturnal blood pressure dip.[21,22]

Is there a safe $PM_{2.5}$ concentration?

The concentration of $PM_{2.5}$ considered safe by the WHO is 10 μg/m^3, the Global Burden of Disease study accepts 8.8 μg/m^3, and a more recent calculation estimates 4.2 μg/m^3 as safe.[9,23] If the latter is accurate, then the number of calculated deaths attributable to air pollution is even higher than published figures, which are based on the WHO and Global Burden of Disease levels.[24] Like smoking, it is difficult to define an innocuous particle concentration level since cardiovascular risk in general and stroke in particular occur below the threshold considered safe.[18] Most countries have average $PM_{2.5}$ values that range from two to three times to >100 times higher than the previously mentioned safe levels.[10] Close to 99% of all inhabitants in Asia are exposed to unsafe levels of $PM_{2.5}$ versus 20% of the population in North America.[25] It is not uncommon for values to reach 1000 μg/m^3 peaks in large cities in India and China. In 2017, in New Delhi, schools were closed, air, train and truck transportation halted, and construction cancelled, while hospital consultations for lung, vascular, and eye disease rose steeply.[26] Highly polluted cities pose a significant risk for acute events, although a decrease in the risk of stroke is possible by wearing N95 or other certified masks and using air filters. Three billion people cook and heat their homes by burning biomass, exposing themselves to severe health effects associated with air pollution.[27] Ironically, these same individuals who generate only 5% of the world's pollution, are those most affected by the pollution coming from the richest segment of the world's population. The significance of this is apparent in a US study of 61 million people showing a 7.3% increase in mortality per 10 μg/m^3 increase in $PM_{2.5}$, with a stronger correlation between $PM_{2.5}$ and death in Hispanic and non-Hispanic black Medicare members.[28] Conversely, improvement in air quality has also been shown to increase life expectancy.[29] Also, decreased pollution can result in significant economic benefits. In the US, GDP has increased more than two-fold since the 1970 Clean Air Act, while production decreases by 6% for every 10 μg/m^3 increase of PM.[30] Air pollution accounts for 7% of health expenses in emerging countries.[9]

Links between particulate matter, gaseous toxins, and atherosclerosis

A double-blind cross-over study was performed in Shanghai in 55 healthy students exposed for nine days to filtered indoor air or sham filters.[31] Subjects breathing filtered air had a 50% reduction in their average $PM_{2.5}$ concentrations. A significant improvement in all biomarkers and blood pressure was noted in subjects breathing purified air despite that pollutant levels (mean of 24 μg/m^3) were still well above those considered safe by WHO. Animal models have also shown the atherogenic effects of air pollution. In one study, mice were fed a high or normal-fat diet and exposed to $PM_{2.5}$

or filtered air.[32] Significantly, greater atherosclerosis and inflammation were found in the aortas of mice fed with the normal and high-fat diets and exposed to PM compared to the filtered air groups. Exposing healthy subjects to O_3 and PM resulted in a significant increase in diastolic blood pressure within minutes of exposure compared to controls.[33] In another double-blind randomized experiment, subjects exposed to diesel exhaust or filtered air for 2 h had a rapid and significant increase in systolic blood pressure.[34]

The multi-ethnic multicenter US study of atherosclerosis and air pollution (MESA) showed a significantly higher calcification load in the coronary arteries of individuals exposed to higher PM concentrations reflecting an accelerated atherosclerotic process. The response was more significant in older and hypertensive patients. In addition, there was an increase in carotid artery intima-media thickness confirming a double pathogenic effect of air pollution on both the endothelium and the vessel wall.[35,36] Earlier studies have also recognized the link between air pollution and atherosclerosis progression, arrhythmias, congestive heart failure, and sudden death.[13,14,37–41]

Air pollution as a risk factor for stroke

The first studies drawing attention to the association between air pollution and cardiovascular disease were published more than 25 years ago.[42] Since then, a wealth of well-designed studies have been published supporting this association.[43–46] Shah et al.[47] performed a meta-analysis of the association between air pollution, stroke admissions, and death from stroke. The authors reviewed studies including a total of 6.2 million stroke events across 28 countries that showed a strong correlation of stroke admissions and death with PM exposure and with CO, SO_2, and NO_2. Although a small proportion of studies originated in low- and middle-income countries, these countries showed the greatest proportion of stroke burden associated with pollution. Since both stable pollution levels and rapid changes (over a period of hours) in pollutant concentrations correlate with vascular events, it is important to consider the date of onset of symptoms (not the date of hospital admission or death) to correctly assess causal exposure to pollution.[48] In a study of 1000 stroke patients, the probability of finding a significant association increased by using the day of symptom onset which occurred a median of one day before admission. When the hospitalization date was used, there was a 60–66% bias towards the null hypothesis.[49] The significant methodological disparities between studies evaluating the interaction between air pollution and stroke limit the validity of inter-study comparisons (Tables 1 to 5).[47]

Ischemic versus hemorrhagic stroke

Data relating to subtypes of ischemic stroke are rarely reported and there are few reports of a correlation between air pollution and hemorrhagic stroke.[51,53,54,56–58] This could be due to the smaller proportion of patients having hemorrhagic stroke and to the pathophysiological mechanisms underlying it. Vascular malformations are unlikely to be affected by air pollution. However, an acceleration of small vessel lipohyalinosis could lead to hypertensive vascular changes, namely Charcot–Bouchard aneurysms, and intracerebral hypertensive hemorrhage. A study in Taiwan found a strong correlation between $PM_{2.5}$, PM_{10}, and NO_2 with intracerebral hemorrhage in the middle-aged and elderly.[62] Some studies have suggested an increased risk of small vessel disease, others have noted a higher prevalence of large vessel disease, and a higher proportion of embolic strokes (likely mediated by a higher risk of atrial fibrillation) has also been reported.[52,55,56,59]

The influence of age on pollution-related stroke

The effect of air pollution on strokes according to age varies. A study in the Israeli desert found a correlation with ischemic strokes for adults younger than 55 years, as well as a same-day increase in the average concentration range for both PM_{10} and $PM_{2.5}$.[60] The authors propose that a healthy vasculature in younger people may be more susceptible to an acute reaction with increased vascular resistance leading to stroke compared to the vessels with atherosclerosis in older persons. Misclassification by age is likely since older people spend more time indoors, and in some cultures tend to use masks more frequently than younger individuals. There are conflicting reports in terms of susceptibility to air pollution, with some arguing for an association with advanced age while others argue that advanced atherosclerosis protects arteries rendering younger people more vulnerable.[14,63–65] One study showed a significant association with ischemic stroke for individuals between 65 and 79 years of age, and other studies have shown the elderly to be more vulnerable.[58,50]

Geographical location and stroke

Not surprisingly, studies of different geographical regions report an interaction between strokes and pollution in terms of the weather. Overall, stroke rates are higher in winter but mortality is more frequent in hot weather.[71–73] Air pollution adds a complex and as yet not completely understood interaction in terms of

Table 1. The relationship between air pollution and stroke subtypes

References	Pollutant types	No. of subjects	Outcome
Hong, et al.[50]	CO, NO_2, O_3, SO_2, TSP	IS: 7137	>IS with NO_2, SO_2, CO, O_3
		HS: 11,868	>HS with TSP
Wellenius, et al.[51]	CO, NO_2, PM10, SO_2	IS: 155,503	>IS
		HS: 19,314	HS no association
Henrotin, et al.[52]	CO, NO_2, O_3, PM10, SO_2	150,000	O3 > LV/TIA >in men
			HS no association
Andersen, et al.[53]	CO, NO, O_3, PM10, UFP	IS: 6798	>IS with UFP (most significant), and with NO_2, CO
		HS: 687	>thrombotic (SV?) without AF
			Most were mild strokes
Oudin, et al.[54]	NO_2, O_3, PM10	IS: 11,267	>IS with PM10
		HS: 1681	O_3, NO_2, no correlation with IS or HS
O'Donnell, et al.[55]	PM2.5	9202	LV and SV
			Inverse association with CE
Wellenius, et al.[56]	CO, NO_2, O_3, PM2.5, SO_2	IS: 1705	>IS LV and SV
			Not CE
Villeneuve, et al.[57]	CO, NO_2, O_3, PM2.5, SO_2	5927	HS and TIA no association
		(IS: 2804)	>IS (NO_2 and PM2.5)
Maheswaran, et al.[58]	NO_2, PM10	IS: 1832	>IS (only in age subgroup)
		HS: 348	HS no association
Corea, et al.[59]	CO, NO_2, O_3, PM10, SO2	781	PM10 > carotid circulation SV in men and women.
		(IS: 593, HS: 85, TIA: 94)	SV and LV carotid in men
Sade, et al.[60]	PM2.5, PM10	IS: 4353	>IS
		HS: 484	HS no association
Maheswaran, et al.[61]	CO, NO_2, O_3, PM10, SO_2	2590	NO_2 association with SV
Chien, et al.[62]	NO_2, O_3, PM2.5, PM10	HS: 39,053	All pollutants correlated with HS (PM2.5 and more with PM10)

IS: ischemic stroke; LV: large vessel; SV: small vessel; CE: cardioembolism; HS: hemorrhagic stroke; TIA: transient ischemic attack; AF: atrial fibrillation; TSP: total suspended particles.

temperature. Studies in several countries in almost 200,000 patients provide evidence of a link between stroke and air pollution in warmer weather, although not all studies confirm this.[57,63,65,67–69] One possible explanation is people spending more time outdoors during warm weather. One of the studies found a correlation for both ischemic and hemorrhagic strokes on cold days.[67]

Table 2. The relationship between air pollution and age at stroke onset

References	Pollutant types	No. of subjects	Outcome
Wellenius, et al.[51]	CO, NO_2, PM10, SO_2	IS: 155,503	>65 (Medicare)
		HS: 19,314	
Kettunen, et al.[63]	CO, PM2.5, SO_2, UFP	3265	<65 No correlation
Maheswaran, et al.[58]	NO_2, PM10	IS: 1832	>IS 65–79 Not for 40–64
Ljungman, et al.[64]	Short-term exposure	Review	>Stroke elderly women
	Long-term exposure		>Stroke in >60 years
Stafoggia, et al.[46]	NO_2, PM2.5, PM10	99,446 in 11 cohorts:	PM2.5 stronger association with IS in >65 years
		(IS 3086)	
Sade, et al.[60]	PM2.5, PM10	IS: 4353	>IS in patients <55 years (living within 75 m from roads)
		HS: 484	
Chien, et al.[62]	All pollutants	39,053	<25 No correlation
	NO_2		25–44 >HS
	NO_2, PM2.5, PM10		>45–79 >HS
	NO_2		>80 >HS
Huang, et al.[65]	CO, O_3, NO_2, SO_2	147,624	>Stroke in >65 years
Tian, et al.[66]	PM2.5	IS: 63,956	No difference between < and > than 65 years

IS: ischemic stroke; LV: large vessel; SV: small vessel; CE: cardioembolism; HS: hemorrhagic stroke; TIA: transient ischemic attack; AF: atrial fibrillation; TSP: total suspended particles.

Table 3. The relationship between geographic location, air pollution, and stroke

References	Pollutant types	No. of subjects	Outcome
Tsai, et al.[67]	CO, NO_2, O_3, PM10, SO_2	23,179	>IS and HS in warm weather
	CO		>IS in cold weather
Kettunen, et al.[63]	CO, PM2.5, SO_2, UFP	1304 warm season stroke deaths	>Stroke with PM2.5, UFP, CO in warm season
		1961 cold season stroke deaths	No stroke death association in cold season
Oudin, et al.[54]	NO_2, O_3, PM10	IS: 11,267	Lower risk in warm days, but:
		HS: 1681	Cold/warm season no significant effect

(continued)

Table 3. Continued

References	Pollutant types	No. of subjects	Outcome
Henrotin, et al.[68]	O_3	1574	>Stroke in warm season, <in cold
	CO		<Stroke in warm season,
	O3		>in cold
			>Stroke with no season difference
O'Donnell, et al.[55]	PM2.5	9202	Winter: >IS with <temp
			Summer: <IS with >temp
Villeneuve, et al.[57]	CO, NO_2, O_3, PM2.5, SO_2	5927	>IS on warm season for NO_2 and PM2.5 (which was inversely correlated with temperature)
Xiang, et al.[69]	NO_2, PM10, SO_2	IS: 5422	>Stroke admissions in cold season with NO_2 and PM10
		HS: 2225	Warm season and SO_2: no correlation
Sade, et al.[60]	PM2.5, PM10	IS: 4353	Spring only (average temp. 20.2 ±3.6°C)
		HS: 484	
Huang , et al.[65]	NO2, SO2	147,624	>stroke in warm than cold season

IS: ischemic stroke; LV: large vessel; SV: small vessel; CE: cardioembolism; HS: hemorrhagic stroke; TIA: transient ischemic attack; AF: atrial fibrillation; TSP: total suspended particles.

Table 4. The relationship between air pollution and comorbidities

References	Pollutant types	No. of subjects	Outcome
Henrotin, et al.[68]	CO, NO_2, O_3, PM10, SO_2	2590	No association with pre-existing RF's
Oudin, et al.[70]	NO_2	7244	>IS in patients with DM but not with other RFs
O'Donnell MJ, et al.[55]	PM2.5	9202	>IS with DM
Villeneuve, et al.[57]	CO, NO_2, O_3, PM2.5, SO_2	5927	>IS with NO_2 and history of stroke, heart disease, hypertension and diabetes
Wellenius, et al.[56]	CO, NO_2, O_3, PM2.5, SO_2	IS: 1705	No increases risk with history of stroke, hypertension, DM or AF
Maheswaran, et al.[61]	O_3	1574	>IS with multiple RF's
			Highest with DM

IS: ischemic stroke; LV: large vessel; SV: small vessel; CE: cardioembolism; HS: hemorrhagic stroke; TIA: transient ischemic attack; AF: atrial fibrillation; TSP: total suspended particles.

Air pollutant gases and duration of exposure

Various studies have assessed the relationship between different fractions of air pollutants and stroke,[62] although to date, the combined effects of $PM_{2.5}$ and PM_{10} have not been assessed. Moreover, until the 1990s, measuring $PM_{2.5}$ concentrations posed technical challenges, and studies mainly reported the effects of PM_{10}. A cross-over study in Sweden with low average levels of PM_{10} ambient pollution showed a 13%

Table 5. The relationship between air pollution gases and duration of exposure

References	Pollutant types	No. of subjects	Outcome
Hong, et al.[50]	CO, NO_2, O_3, SO_2, TSP	IS: 7137	>IS in same day exposure
		HS: 11,868	Significant association also in 0–4 days exposure
Wellenius, et al.[51]	CO, NO_2, PM10, SO_2	IS: 155,503	>IS admissions with same-day exposure
		HS: 19,314	No correlation with HS 0–2 days before admission
			>Stroke admissions with short-term PM10 exposure (day before)
Andersen, et al.[53]	CO, NO_2, PM10, UFP	IS: 6798	Seven-day exposure. IS correlated with high PM10 on day of admission
		HS: 687	
Henrotin, et al.[68]	O_3	1574	Five-day exposure studied: significant association with exposure four days before admission
Oudin, et al.[54]	NO_2, O_3, PM10	IS: 11,267	No stroke correlation in 0–47 h before onset (sensitivity analysis used six days lag)
		HS: 1681	
O'Donnell, et al.[58]	PM2.5	9202	IS correlated with a three-day lag
Corea,et al.[59]	CO, NO_2, O_3, PM10, SO_2	IS: 593	Maximal exposure: 4 days
		HS: 85	>IS SO_2 same day, NO_2, CO 1 day lag, O_3 3 day lag.
		TIA: 94	>HS with TSP same day
Xiang, et al.[69]	NO_2, PM10, SO_2	IS: 5422	Lag one to two days also evaluated. None of single pollutant models were associated with admissions
		HS: 2225	
Stafoggia, et al.[46]	PM2.5, PM10, NO_2	99,446 in 11 cohorts:	Significant association on day of event. One to four days legged exposure tested
		IS 3086	
Sade, et al.[60]	PM2.5, PM10	IS: 4353	>Stroke in same-day admissions
		HS: 484	
Maheswaran, et al.[61]	CO, NO_2, O_3, PM10, SO_2	2590	No correlation with 0–6-days exposure
Tian, et al.[66]	PM2.5	IS: 63,956	2.5 years exposure

IS: ischemic stroke; LV: large vessel; SV: small vessel; CE: cardioembolism; HS: hemorrhagic stroke; TIA: transient ischemic attack; AF: atrial fibrillation; TSP: total suspended particles.

increase of ischemic stroke admissions for same and previous-day exposure at $>30\,\mu g/m^3$ compared to $<15\,\mu g/m^3$.[54] After adjustment for $PM_{2.5}$, PM_{10} did not show a significant association with vascular hospitalizations, suggesting that $PM_{2.5}$ have more significant damaging effects on the vascular system (due to their chemical composition and longer air suspension time). A study of Medicare patients showed increased stroke admissions on the day of higher PM_{10} concentration.[51] One study carried out over 10-years in London evaluated PM_{10} and gaseous pollutants in 2500 stroke patients with first-time strokes. With a six-day lag, no correlation was found between exposure and stroke subtypes except for lacunar strokes and NO_2.

The study was probably underpowered and $PM_{2.5}$ effects were not analyzed.[58,61,74] Another study found an association between O_3 and recurrent stroke. Although particle matter pollution was not studied, the authors argued that gaseous toxins could be a proxy to particle pollutants.[68] In Italy, a study of 780 subjects evaluating the effects of PM_{10} and gaseous pollutants revealed an association between lacunar strokes in men and women and for all carotid artery territory strokes in men only.[59] A Danish study among 7500 stroke admissions found a correlation between exposure for three to four days to ultrafine particles (<0.1 μm) with thrombotic strokes (non-cardioembolic),[53] with a 21% increased risk for admission. A study in Shanghai including 2426 stroke deaths, found a significant increase in relative risk with PM_{10} and NO_2 pollution.[75] A Korean study between 1991 and 1998 evaluated stroke mortality and air pollution, confirming increased mortality for each interquartile same-day increase in PM_{10} and O_3.[50] Mortality also increased with each interquartile range increase in SO_2, NO_2, and CO. An interactive effect among pollutants was confirmed regarding death risk and the elderly and women were more susceptible.

Most studies have shown that both short- and long-term exposure to air pollution is associated with increased stroke risk,[64] and most short-term exposure shows a stronger association with small and large vessel atherosclerotic disease.[56,64] Tian et al.[66] evaluated the short-term effect of air pollution in 63,956 stroke admissions over 2.5 years in Beijing, although their "low concentration" of <100 μg/m^3 corresponds to 10 times the PM concentration accepted by current standards. Every 10 μg/m^3 increase in PM was associated with a 0.31% (95%CI, 0.17–0.45) same-day stroke risk increase. The association was observed up to four days after exposure and across all age groups. The exclusive evaluation of first-time strokes may explain the relatively lower stroke admission rate compared to other air pollution studies evaluating $PM_{2.5}$ and PM_{10}, since individuals with a history of cardiovascular disease, diabetes, or multiple vascular risk factors are at greater risk of recurrence.[14,55,64,76,77] Oudin et al.[54,70,78] highlighted an increased risk for PM_{10}-related stroke exclusively in individuals with a previous cerebrovascular event.

Conclusions

There is ample evidence showing an association between acute and chronic exposure to $PM_{2.5,}$ and gaseous pollutants with stroke. This potentially avoidable scenario and its dramatic consequences are underrecognized by health professionals and the wider public. Stroke neurologists must accept air pollution as a major contributor to cryptogenic strokes and most other manifestations of cerebrovascular disease. Death from air pollution is mostly preventable and depends on education generated by health professionals and Government initiatives. The immense cost of air pollution is hidden in most hospital admissions for stroke and preventive measures in people at high vascular risk are warranted. Pope Francis provided a powerful elaboration on the issue of climate change in the Encyclical letter Laudato Si.[79] This document provides valid and concrete data on the devastating consequences of climate change on "our common home." Climate change and air pollution cannot be issues for our future generations – they are about every one of us, right here and right now.

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ORCID iD

Conrado J Estol http://orcid.org/0000-0001-6481-7835

References

1. Ramanathan V, Sanchez Sorondo M, Dasgupta P, et al. *Final declaration*: *our planet, our health, our responsibility*. Vatican City: Pontificiae Academiae Scientiarum Scripta Varia, 2017, pp.1–15.
2. Writing Group Members, Mozaffarian D, Benjamin EJ, et al. Heart disease and stroke statistics – 2016 update: a report from the American Heart Association. *Circulation* 2016; 133: e38–360.
3. Feigin VL, Norrving B and Mensah GA. Global Burden of stroke. *Circ Res* 2017; 120: 439–448.
4. Feigin VL. Stroke epidemiology in the developing world. *Lancet* 2005; 365: 2160–2161.
5. Hackam DG and Spence JD. Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study. *Stroke* 2007; 38: 1881–1885.
6. Chiuve SE, McCullough ML, Sacks FM, et al. Healthy lifestyle factors in the primary prevention of coronary heart disease among men: benefits among users and nonusers of lipid-lowering and antihypertensive medications. *Circulation* 2006; 114: 160–167.
7. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79

behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016; 388: 1659–1724.
8. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016; 15: 913–924.
9. Lelieveld J, Evans JS, Fnais M, et al. The contribution of outdoor air pollution sources to premature mortality on a global scale. *Nature* 2015; 525: 367–371.
10. Cohen AJ, Brauer M, Burnett R, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017; 389: 1907–1918.
11. Ashby-Mitchell K, Burns R, Shaw J, et al. Proportion of dementia in Australia explained by common modifiable risk factors. *Alzheimers Res Ther* 2017; 9: 11.
12. Béjot Y, Reis J, Giroud M, et al. A review of epidemiological research on stroke and dementia and exposure to air pollution. *Int J Stroke* 2018; 13: 687–695.
13. Newby DE, Mannucci PM, Tell GS, et al. Expert position paper on air pollution and cardiovascular disease. *Eur Heart J* 2015; 36: 83–93 b.
14. Brook RD, Rajagopalan S, Pope CA, et al. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation* 2010; 121: 2331–2378.
15. Landrigan PJ, Fuller R, Acosta NJR, et al. The lancet commission on pollution and health. *Lancet* 2018; 391: 462–512.
16. Nemmar A, Vanbilloen H, Hoylaerts MF, et al. Passage of intratracheally instilled ultrafine particles from the lung into the systemic circulation in hamster. *Am J Respir Crit Care Med* 2001; 164: 1665–1668.
17. Oberdörster G, Sharp Z, Atudorei V, et al. Extrapulmonary translocation of ultrafine carbon particles following whole-body inhalation exposure of rats. *J Toxicol Environ Health Part A* 2002; 65: 1531–1543.
18. Wellenius GA, Boyle LD, Wilker EH, et al. Ambient fine particulate matter alters cerebral hemodynamics in the elderly. *Stroke* 2013; 44: 1532–1536.
19. Peters A, Döring A, Wichmann HE, et al. Increased plasma viscosity during an air pollution episode: a link to mortality? *Lancet* 1997; 349: 1582–1587.
20. Baccarelli A, Zanobetti A, Martinelli I, et al. Effects of exposure to air pollution on blood coagulation. *J Thromb Haemost* 2007; 5: 252–260.
21. Tsai D-H, Riediker M, Wuerzner G, et al. Short-term increase in particulate matter blunts nocturnal blood pressure dipping and daytime urinary sodium excretion. *Hypertension* 2012; 60: 1061–1069.
22. Cai Y, Zhang B, Ke W, et al. Associations of short-term and long-term exposure to ambient air pollutants with hypertension: a systematic review and meta-analysis. *Hypertension* 2016; 68: 62–70.
23. Lelieveld J, Klingmuller K, Pozzer A, et al. Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions. *European Heart Journal* 2019: 1–7. doi:10.1093/eurheartj/ehz135.
24. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2224–2260.
25. van Donkelaar A, Martin RV, Brauer M, et al. Use of satellite observations for long-term exposure assessment of global concentrations of fine particulate matter. *Environ Health Perspect* 2015; 123: 135–143.
26. Wu H. Breathing in Delhi air equivalent to smoking 44 cigarettes a day. CNN, www.cnn.com/2017/11/10/health/delhi-pollution-equivalent-cigarettes-a-day/index.html (accessed 10 May 2018).
27. Bailis R, Ezzati M and Kammen DM. Mortality and greenhouse gas impacts of biomass and petroleum energy futures in Africa. *Science* 2005; 308: 98–103.
28. Di Q, Wang Y, Zanobetti A, et al. Air pollution and mortality in the medicare population. *N Engl J Med* 2017; 376: 2513–2522.
29. Pope CA, Ezzati M and Dockery DW. Fine-particulate air pollution and life expectancy in the United States. *N Engl J Med* 2009; 360: 376–386.
30. US Environmental Protection Agency. National air quality: status and trends of key air pollutants, www.epa.gov/air-trends (accessed 9 May 2018).
31. Li H, Cai J, Chen R, et al. Particulate Matter exposure and stress hormone levels: a randomized, double-blind, crossover trial of air purification. *Circulation* 2017; 136: 618–627.
32. Sun Q, Wang A, Jin X, et al. Long-term air pollution exposure and acceleration of atherosclerosis and vascular inflammation in an animal model. *JAMA* 2005; 294: 3003–3010.
33. Brook RD, Urch B, Dvonch JT, et al. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. *Hypertension* 2009; 54: 659–667.
34. Cosselman KE, Krishnan RM, Oron AP, et al. Blood pressure response to controlled diesel exhaust exposure in human subjects. *Hypertension* 2012; 59: 943–948.
35. Adar SD, Sheppard L, Vedal S, et al. Fine particulate air pollution and the progression of carotid intima-medial thickness: a prospective cohort study from the multi-ethnic study of atherosclerosis and air pollution. *PLoS Med* 2013; 10: e1001430.
36. Kaufman JD, Adar SD, Barr RG, et al. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): a longitudinal cohort study. *Lancet* 2016; 388: 696–704.
37. Hoffmann B, Moebus S, Möhlenkamp S, et al. Residential exposure to traffic is associated with coronary atherosclerosis. *Circulation* 2007; 116: 489–496.
38. Künzli N, Jerrett M, Garcia-Esteban R, et al. Ambient air pollution and the progression of atherosclerosis in adults. *PLoS One* 2010; 5: e9096.

39. Forastiere F and Agabiti N. Assessing the link between air pollution and heart failure. *Lancet* 2013; 382: 1008–1010.
40. Link MS, Luttmann-Gibson H, Schwartz J, et al. Acute exposure to air pollution triggers atrial fibrillation. *J Am Coll Cardiol* 2013; 62: 816–825.
41. Ensor KB, Raun LH and Persse D. A case-crossover analysis of out-of-hospital cardiac arrest and air pollution. *Circulation* 2013; 127: 1192–1199.
42. Dockery DW, Pope CA, Xu X, et al. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993; 329: 1753–1759.
43. Benziger CP, Roth GA and Moran AE. The global burden of disease study and the preventable burden of NCD. *Glob Heart* 2016; 11: 393–397.
44. Gold DR and Samet JM. Air pollution, climate, and heart disease. *Circulation* 2013; 128: e411–414.
45. Wang Y, Eliot MN and Wellenius GA. Short-term changes in ambient particulate matter and risk of stroke: a systematic review and meta-analysis. *J Am Heart Assoc* 2014; 3: pii: e000983.
46. Stafoggia M, Cesaroni G, Peters A, et al. Long-term exposure to ambient air pollution and incidence of cerebrovascular events: results from 11 European cohorts within the ESCAPE project. *Environ Health Perspect* 2014; 122: 919–925.
47. Shah ASV, Lee KK, McAllister DA, et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis. *BMJ* 2015; 350: h1295.
48. Rasche M, Walther M, Schiffner R, et al. Rapid increases in nitrogen oxides are associated with acute myocardial infarction: a case-crossover study. *Eur J Prev Cardiol* 2018; 25: 1707–1716.
49. Lokken RP, Wellenius GA, Coull BA, et al. Air pollution and risk of stroke: underestimation of effect due to misclassification of time of event onset. *Epidemiology* 2009; 20: 137–142.
50. Hong Y-C, Lee J-T, Kim H, et al. Air pollution: a new risk factor in ischemic stroke mortality. *Stroke* 2002; 33: 2165–2169.
51. Wellenius GA, Schwartz J and Mittleman MA. Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries. *Stroke* 2005; 36: 2549–2553.
52. Henrotin JB, Besancenot JP, Bejot Y, et al. Short-term effects of ozone air pollution on ischaemic stroke occurrence: a case-crossover analysis from a 10-year population-based study in Dijon, France. *Occup Environ Med* 2007; 64: 439–445.
53. Andersen ZJ, Olsen TS, Andersen KK, et al. Association between short-term exposure to ultrafine particles and hospital admissions for stroke in Copenhagen, Denmark. *Eur Heart J* 2010; 31: 2034–2040.
54. Oudin A, Strömberg U, Jakobsson K, et al. Estimation of short-term effects of air pollution on stroke hospital admissions in southern Sweden. *Neuroepidemiology* 2010; 34: 131–142.
55. O'Donnell MJ, Fang J, Mittleman MA, et al. Fine particulate air pollution (PM2.5) and the risk of acute ischemic stroke. *Epidemiology* 2011; 22: 422–431.
56. Wellenius GA, Burger MR, Coull BA, et al. Ambient air pollution and the risk of acute ischemic stroke. *Arch Intern Med* 2012; 172: 229–234.
57. Villeneuve PJ, Johnson JYM, Pasichnyk D, et al. Short-term effects of ambient air pollution on stroke: who is most vulnerable? *Sci Total Environ* 2012; 430: 193–201.
58. Maheswaran R, Pearson T, Smeeton NC, et al. Outdoor air pollution and incidence of ischemic and hemorrhagic stroke: a small-area level ecological study. *Stroke* 2012; 43: 22–27.
59. Corea F, Silvestrelli G, Baccarelli A, et al. Airborne pollutants and lacunar stroke: a case cross-over analysis on stroke unit admissions. *Neurol Int* 2012; 4: e11.
60. Sade MY, Novack V, Ifergane G, et al. Air pollution and ischemic stroke among young adults. *Stroke* 2015; 46: 3348–3353.
61. Maheswaran R, Pearson T, Beevers SD, et al. Air pollution and subtypes, severity and vulnerability to ischemic stroke – a population based case-crossover study. *PLoS One* 2016; 11: e0158556.
62. Chien T-Y, Ting H-W, Chan C-L, et al. Does the short-term effect of air pollution influence the incidence of spontaneous intracerebral hemorrhage in different patient groups? Big Data analysis in Taiwan. *Int J Environ Res Public Health* 2017; 14: pii: E1547.
63. Kettunen J, Lanki T, Tiittanen P, et al. Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. *Stroke* 2007; 38: 918–922.
64. Ljungman PL and Mittleman MA. Ambient air pollution and stroke. *Stroke* 2014; 45: 3734–3741.
65. Huang F, Luo Y, Tan P, et al. Gaseous air pollution and the risk for stroke admissions: a case-crossover study in Beijing, China. *Int J Environ Res Public Health* 2017; 14: 189.
66. Tian Y, Xiang X, Wu Y, et al. Fine particulate air pollution and first hospital admissions for ischemic stroke in Beijing, China. *Sci Rep* 2017; 7: 3897.
67. Tsai S-S, Goggins WB, Chiu H-F, et al. Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. *Stroke* 2003; 34: 2612–2616.
68. Henrotin J-B, Zeller M, Lorgis L, et al. Evidence of the role of short-term exposure to ozone on ischaemic cerebral and cardiac events: the Dijon Vascular Project (DIVA). *Heart* 2010; 96: 1990–1996.
69. Xiang H, Mertz KJ, Arena VC, et al. Estimation of short-term effects of air pollution on stroke hospital admissions in Wuhan, China. *PLoS One* 2013; 8: e61168.
70. Oudin A, Strömberg U, Jakobsson K, et al. Hospital admissions for ischemic stroke: does long-term exposure to air pollution interact with major risk factors? *Cerebrovasc Dis* 2011; 31: 284–293.
71. Michelozzi P, Accetta G, De Sario M, et al. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *Am J Respir Crit Care Med* 2009; 179: 383–389.
72. Lanska DJ and Hoffmann RG. Seasonal variation in stroke mortality rates. *Neurology* 1999; 52: 984–990.
73. Myint PK, Vowler SL, Woodhouse PR, et al. Winter excess in hospital admissions, in-patient mortality and

length of acute hospital stay in stroke: a hospital database study over six seasonal years in Norfolk, UK. *Neuroepidemiology* 2007; 28: 79–85.
74. Maheswaran R, Pearson T, Campbell MJ, et al. A protocol for investigation of the effects of outdoor air pollution on stroke incidence, phenotypes and survival using the South London Stroke Register. *Int J Health Geogr* 2006; 5: 10.
75. Kan H, Jia J and Chen B. Acute stroke mortality and air pollution: new evidence from Shanghai, China. *J Occup Health* 2003; 45: 321–323.
76. Bateson TF and Schwartz J. Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. *Epidemiology* 2004; 15: 143–149.
77. Kwon HJ, Cho SH, Nyberg F, et al. Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. *Epidemiology* 2001; 12: 413–419.
78. Oudin A, Forsberg B and Jakobsson K. Air pollution and stroke. *Epidemiology* 2012; 23: 505–506.
79. Pope Francis. Laudato si'. On care for our common home. [Encyclical], http://w2.vatican.va/content/francesco/en/encyclicals/documents/papa-francesco_20150524_enciclica-laudato-si.html. (accessed 10 May 2018).