

## Impact case study (REF3)

<b>Institution:</b> University of Edinburgh		
<b>Unit of Assessment:</b> 1		
<b>Title of case study:</b> A: Definitive demonstration of the adverse cardiovascular effects of air pollution leads to policy change at the local, national and international level		
<b>Period when the underpinning research was undertaken:</b> 2005 – 2020		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Mark Miller	Senior Research Fellow	2005 – present
Nick Mills	Personal Chair of Cardiology	2003 – present
Dave Newby	BHF Duke of Edinburgh Chair of Cardiology	2000 – present
Anoop Shah	Senior Clinical Lecturer	2011 – 2020
Ken Lee	Clinical Research Fellow	2017 – present
<b>Period when the claimed impact occurred:</b> August 2013 – December 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> N		
<b>1. Summary of the impact</b>		
<p><b>Underpinning Research:</b> University of Edinburgh (UoE) research showed that exposure to particulate matter in air pollution, particularly from vehicle emissions, has numerous harmful effects on cardiovascular health.</p> <p><b>Significance and Reach of Impact:</b> The direct causal link between air pollution and cardiovascular disease has contributed to the growing sense of urgency around improving air quality. In 2016, based on UoE research, the British Heart Foundation (BHF) named air pollution as their top priority for achieving societal change. Their 2020 campaign “Toxic Air: You’re Full Of It” has raised awareness of the issue, prompting 9,700 people to write to their Member of Parliament to demand change, and 44 parliamentarians to pledge their support for stricter guidelines.</p> <p>Through media presence, BHF campaigns, direct interaction with politicians and membership of the Committee for Medical Effects of Air Pollution (the main route by which the UK Government receives advice on air pollution and health), UoE research has substantially informed the Cleaner Air for Scotland strategy (2015), the UK Government’s Clean Air Strategy (2019) and the forthcoming Environment Bill. Worldwide, UoE research is cited in international expert opinions and is contributing to the forthcoming update to World Health Organization (WHO) Air Quality Guidelines and advice to health practitioners (2020).</p>		
<b>2. Underpinning Research</b>		
<p><b>The Challenge: Air pollution from vehicles is harmful to cardiovascular health</b></p> <p>Air pollution is a major threat to global health, with the WHO estimating that it is responsible for 7,000,000 premature deaths worldwide every year. Airborne particles, termed particulate matter (PM), are key components of outdoor pollution that drive the health effects of pollution and are monitored and regulated throughout the world as 2 size categories: PM<sub>10</sub> (less than 10µm in diameter) and PM<sub>2.5</sub> (less than 2.5µm). Ultrafine PM (less than 0.1µm), is a subset of PM<sub>2.5</sub> that chiefly originates from vehicle exhaust in urban environments.</p> <p>In the past, air quality legislation has focused on respiratory problems caused by large particles (PM<sub>10</sub> and PM<sub>2.5</sub>) and gaseous pollutants. In a pioneering 15-year programme (2005–2020) of British Heart Foundation (BHF)-funded research addressing possible mechanisms underpinning the observations that 50% of the mortality attributed to air pollution is from cardiovascular causes, UoE researchers have unequivocally shown that ultrafine PM from vehicle exhaust has a multitude of adverse effects on the cardiovascular system.</p> <p><b>Exposure to air pollution is associated with heart failure and stroke</b></p>		

In 2 landmark systematic reviews, UoE researchers revealed clear and robust temporal associations between short-term exposure to air pollution, particularly PM, and hospitalisation or death from heart failure and stroke [3.1; 3.2]. Modelling highlighted that even modest improvements in air quality standards would lead to major population health benefits; for example, in the United States, a mean reduction in PM<sub>2.5</sub> of 4µg/m<sup>3</sup> would prevent 7,978 heart failure hospitalisations per year (for context, PM<sub>2.5</sub> levels in a typical UK city centre range from 8 to 16µg/m<sup>3</sup>).

#### **Unique experiments in humans show direct effect of vehicle exhaust on heart health**

In addition to demonstrating the link on a population level, the UoE team was the first to directly demonstrate the effects of diesel exhaust on the human cardiovascular system. Through collaboration with Umeå University (Sweden) and the National Institute for Public Health and the Environment (Netherlands), the team had access to unique facilities where inhalation of specific pollutants could be precisely controlled to mimic concentrations representative of urban city centres, without many of the confounding variables of epidemiological work. The team demonstrated that a 1-hour exposure to dilute diesel exhaust in healthy volunteers caused an impairment of vascular function that lasted more than 24 hours, and decreased levels of proteins, such as t-PA antigen, that prevent excessive blood clotting [3.3].

These studies were followed by a clinical trial demonstrating that exposure to dilute diesel exhaust reduced blood flow in the coronary vessels of patients with heart disease [3.4]. This trial therefore demonstrated, for the first time, that air pollution from vehicle exhaust can directly exacerbate existing heart disease in a clinically relevant manner.

#### **Particulate matter can cross from the lungs to the bloodstream**

The UoE team next explored the mechanisms by which PM promotes cardiovascular disease. In a seminal study combining complementary preclinical and clinical models, they used inert gold nanoparticles as a model for ultrafine PM to track the fate of inhaled particles. This revealed that the nanoparticles were able to cross from the lung into the blood and be carried to all organs of the body. Importantly, the nanoparticles preferentially accumulated in sites of cardiovascular disease, such as atherosclerotic plaques, both in a mouse model of vascular disease and in patients with a history of stroke [3.5]. These findings provided a direct mechanism by which particles from vehicle exhaust could exacerbate the risk of heart disease, heart attack and stroke. Furthermore, they highlighted that it is the ultrafine particles in vehicle exhaust, rather than the gaseous co-pollutants, that drive the cardiovascular harms of air pollution. This was a key observation, as ultrafine PM are currently inadequately measured by prevailing PM<sub>10</sub> and PM<sub>2.5</sub> metrics, and thus cannot be rigorously monitored [3.6].

UoE's mechanistic research has provided unique and robust evidence for the causal association between air pollution and cardiovascular morbidity and mortality, overcoming the uncertainty of epidemiological findings that had previously hindered the mandate for changes in air quality.

### **3. References to the research**

[3.1] [Shah AS](#), [Langrish JP](#), [Nair H](#), [McAllister DA](#), [Hunter AL](#), [Donaldson K](#), [Newby DE](#) & [Mills NL](#) (2013). Global association of air pollution and heart failure: a systemic review and meta-analysis. *Lancet* 382:1039-48. [doi:10.1016/S0140-6736\(13\)60898-3](https://doi.org/10.1016/S0140-6736(13)60898-3)

[3.2] [Shah AS](#), [Lee KK](#), [McAllister DA](#), [Hunter A](#), [Nair H](#), [Whiteley W](#), [Langrish JP](#), [Newby DE](#) & [Mills NL](#) (2015). Short term exposure to air pollution and stroke: systematic review and meta-analysis. *BMJ* 350:h1295. [doi: 10.1136/bmj.h1295](https://doi.org/10.1136/bmj.h1295)

[3.3] [Mills NL](#), [Tornqvist H](#), [Robinson SD](#), [Gonzalez M](#), [Darnley K](#), [MacNee W](#), [Boon NA](#), [Donaldson K](#), [Blomberg A](#), [Sandström T](#) & [Newby DE](#) (2005). Diesel exhaust inhalation causes vascular dysfunction and impaired endogenous fibrinolysis. *Circulation* 112:3930-6. [doi: 10.1161/CIRCULATIONAHA.105.588962](https://doi.org/10.1161/CIRCULATIONAHA.105.588962)

[3.4] [Mills NL](#), Tornqvist H, Gonzalez MC, [Vink E](#), [Robinson SD](#), Soderberg S, [Boon NA](#), [Donaldson K](#), Sandstrom T, Blomberg A & [Newby DE](#) (2007). Ischemic and thrombotic effects of dilute diesel-exhaust inhalation in men with coronary heart disease. *NEJM* 357:1075-82. doi: [10.1056/NEJMoa066314](https://doi.org/10.1056/NEJMoa066314)

[3.5] [Miller MR](#), [Raftis J](#), [Langrish JP](#), [McLean SG](#), Samutrtai P, [Connell S](#), [Wilson S](#), [Vesey AT](#), Fokkens PHB, Boere AJF, Krystek P, Campbell CJ, [Hadoke PWE](#), [Donaldson K](#), Cassee FR, [Newby DE](#), [Duffin R](#) & [Mills NL](#) (2017). Inhaled nanoparticles accumulate in atherosclerotic lesions. *ACS Nano* 11:4542-4552. doi: [10.1021/acsnano.6b08551](https://doi.org/10.1021/acsnano.6b08551)  
This paper has generated an Altmetric score of 590.

[3.6] [Newby DE](#) & European Society of Cardiology Working Group on Thrombosis, Cardiovascular Prevention and Rehabilitation, and ESC Heart Failure Association (2015). Expert position paper on air pollution and cardiovascular disease. *Eur Heart J* 36:84-93b. doi: [10.1093/eurheartj/ehu458](https://doi.org/10.1093/eurheartj/ehu458)

#### 4. Details of the impact

##### Pathways to impact: Extensive mainstream media coverage

UoE publications on air pollution and cardiovascular health have received widespread media attention. For example, paper [3.5] was covered by 25 major news outlets including the BBC, the *Independent*, the *Times*, Reuters and *Financial Times* [5.1a]. Miller was interviewed on BBC 5 live [5.1b] and Channel 4 Evening News [5.1c] about his findings. Furthermore, since this paper was published, mainstream media regularly references the fact that PM can cross into the blood as the key reason why air pollution can have adverse effects throughout the body (e.g. *The Guardian*; [5.1d]). UoE research has also featured on several television documentaries, including Channel 4 Dispatches (*“Dirty Secrets: What’s Really in Our Air”*, Dec 2016), BBC2 *Fighting for Air* (Jan 2018) and BBC *Inside out* (Jan 2020) [5.1e].

##### Impact on British Heart Foundation priorities

UoE research identifying the causal link between air pollution and cardiovascular morbidity brought air pollution, for the first time, onto the agenda of the UK’s largest heart disease charity, the BHF. Its Senior Public Affairs Officer writes: *“It was research by University of Edinburgh staff [...] that first brought the deleterious effects of air pollution to BHF’s agenda. [...] The transformative effect of the University of Edinburgh research findings on the BHF’s overall strategy is reflected in our influencing prioritisation exercise in 2016 that listed air pollution as our top influencing priority in prevention and public health – above tobacco, diet and physical activity.”* [5.2].

##### Impact on public awareness and behaviour

To raise awareness of the cardiovascular harms of air pollution among both the general public and national policymakers, in January 2020 the BHF launched a GBP900,000 national campaign called *“Toxic Air: You’re Full Of It”*. This campaign highlighted that air pollution, particularly from vehicle emissions, is a public health emergency and called for the UK to adopt the more stringent WHO guideline on PM emissions (PM<sub>2.5</sub> concentration of 10µg/m<sup>3</sup> versus the current 25µg/m<sup>3</sup>). The campaign website, featuring highlights of UoE research findings, enables visitors to email their Member of Parliament to ask them to support the commitment to WHO guidelines [5.3a]. By August 2020, 9,700 people (at least 1 from each of the UK’s 650 constituencies) had done this [5.3b].

##### Impact on policymaker awareness and attitudes

As part of the *“Full Of It”* campaign, the BHF held an event at Westminster in February 2020, giving UoE researchers the opportunity to directly address politicians. Some 59 parliamentarians attended the event, including the Minister for Science, Research and Innovation and the Shadow Environment Secretary, and 44 parliamentarians formally marked their support for the proposal to adopt WHO guidelines [5.3b]. The BHF also submitted formal evidence to the Environment, Food and Rural Affairs (EFRA) Select Committee inquiry on Air Quality ([launched in June 2020](#)) on the UK Government’s progress on its clean air pledges. This evidence cites UoE papers [3.5] and [3.6] to highlight that air pollution is a public health

emergency requiring urgent adoption of the WHO guidelines [5.3c]. The findings of this inquiry will inform the upcoming 2022 Environment Bill.

UoE researchers have also presented their data to key policymakers in person, including the Leader of the Opposition of the UK Government [5.4a], Scottish Cabinet Secretary for Environment [5.4b], the Glasgow City Convener for Sustainability and Carbon Reduction [5.4c], and the Shadow Secretary of State for Scotland [5.4d] to convey the importance of tackling air pollution. The latter commented: *“I often refer to your research when speaking with colleagues and making the point about the importance of clean air. [...] I now have a new perspective on my commuting and taxi journeys, and this has hardened my resolve to promote greener forms of travel as part of my political campaigning.”* [5.4d].

### Impact on policy, guidelines and practice

#### Scotland

Through the BHF’s advocacy work, UoE research played a key role in shaping the Clean Air for Scotland (CAFS) strategy (2015) [5.5a], including pledging commitment to the WHO guidelines on PM emissions [5.5b]. Driven by UoE findings that much of the most harmful PM comes from the ultrafine PM within vehicle emissions, the BHF strongly supported proposals to achieve this commitment through Low Emission Zones (LEZs) [5.5a]. This support, together with evidence from other sources, contributed to the launch of Scotland’s first LEZ in Glasgow in December 2018, and to ongoing plans for other LEZs across Scotland [5.5c.d].

In 2017, an independent review of the progress of the CAFS specifically consulted and acknowledged both the BHF and the UoE researchers. The published report concluded that the *“health evidence reviewed justifies adopting a precautionary public health approach to air pollution reduction.”* [p. 7; 5.5c]. This review secured GBP10,800,000 additional funding from the Scottish Government for CAFS implementation work, such as retrofitting buses with particle traps and other preparations for LEZs in Glasgow and beyond [5.5a].

#### United Kingdom

The UK Government’s Clean Air Strategy 2019, published by the Department of Environment, Food, and Rural Affairs (DEFRA), specifically highlights UoE paper [3.5] as a case study and hails the results as *“hugely important”*, stating that they *“will help [DEFRA] to shape policies aimed at reducing the risk to people’s cardiovascular health.”* [5.6].

UoE research also informs UK Government policy through Expert Membership (Newby 2009–2012, Miller 2016–present) of the Committee on the Medical Effects of Air Pollutants (COMEAP) [5.7a], the body funded by the UK Department of Health to provide independent advice to government departments on the health risks of air pollution. COMEAP is currently directly advising DEFRA on plans for new UK air quality limits for PM, which will be introduced into legislation via the 2022 Environment Bill [5.7b].

UoE research has also contributed to practical initiatives aimed at improving air quality, through shaping COMEAP reports that are cited as evidence for the need for action. A notable example is the London Ultra Low Emission Zone (ULEZ, launched in April 2019): the Mayor of London group lists as supporting evidence [5.7c] a 2016 report by the Royal College of Physicians (*“Every Breath We Take”*), which cites 9 COMEAP reports as well as UoE papers [3.2] and [3.6] [5.7d]. Such interventions can make a difference: an analysis of the first 6 months of the London ULEZ indicated that PM<sub>2.5</sub> emissions had been reduced from 17 to 11 µg/m<sup>3</sup> in central London [5.7e]. To put it in context, Public Health England estimates that for each 1 µg/m<sup>3</sup> drop in PM<sub>2.5</sub> levels across the UK, 50,000 cases of coronary heart disease could be avoided by 2035 [5.7f].

#### International

UoE research has informed expert opinion worldwide, with key consensus statements referring to UoE research as evidence that air pollution presents a significant risk to health and

must be tackled urgently. These include the European Society of Cardiology expert position paper [3.6], the American Heart Association scientific statement on personal-level protective actions against PM exposure (2020; cites 4 UoE papers out of 138 [5.8a]), and the Review of Evidence on Health Aspects of Air Pollution (2013; cites 7 UoE papers) report by the WHO European Regional Office [5.8b].

In addition, UoE research is contributing to the ongoing update to the WHO Air Quality Guidelines, the most highly regarded global authority on air quality standards. On the basis of his authorship of the systematic review [3.1], Shah was approached in 2017 by the WHO European Regional Office to lead a new systematic review on global health effects of specific pollutants [5.8c]. Published in July 2020 [5.8d], this now forms part of the evidence base that will underpin the updated Air Quality Guidelines.

The World Heart Federation (WHF) also recognises air pollution as one of the most significant risk factors for cardiovascular health. To coordinate activities to improve air quality worldwide, the WHF established a new Air Pollution Expert Group (APEG) in 2019 [5.8e]. Together with WHO, the APEG has developed a toolkit aimed at clinicians in both primary and secondary care designed to strengthen their capacity to deal with air pollution and health worldwide. This toolkit cites 4 UoE publications in its evidence base [5.8f], and Miller as a member of the APEG had extensive input into its content [5.8g]. As a result, the toolkit covers pollutants from vehicles as an important health concern, identifies people with underlying cardiovascular conditions as being particularly vulnerable to the effects of air pollution, and provides individual risk assessment forms for clinicians to identify where a patient may be exposed to air pollution and how this may be mitigated (such as by wearing face masks when commuting) [5.8f]. The toolkit was launched in October 2020.

## 5. Sources to corroborate the impact

[5.1] Media coverage of UoE research papers. **a.** 25 articles covering [3.5] **b.** BBC 5 Live radio interview **c.** TV interview on Channel 4 Evening News **d.** [Guardian article on health risks of air pollution](#) **e.** Television documentaries: [Dirty Secrets: What's Really in Our Air? Channel 4 Dispatch](#); BBC2 "Fighting For Air", BBC1 "Inside Out".

[5.2] Testimonial from Senior Policy and Public Affairs Manager, British Heart Foundation

[5.3] BHF campaigning activities based on UoE research **a.** You're Full Of It campaign website **b.** Email from BHF Senior Public Affairs Officer Aug 2020 re responses to Full Of It campaign and attendance at event. **c.** [BHF submission to EFRA Committee Inquiry on Air Quality 2020 on Government website](#)

[5.4] **a.** Letter of support from UK Government Leader of the Opposition (Sir Keir Starmer) **b.** Visit by Scottish Secretary for Environment **c.** Visit by Glasgow City Convener for Sustainability **d.** Testimonial from Shadow Scottish Secretary of State

[5.5] Cleaner Air for Scotland Strategy, 2015 **a.** Scottish Government website story showing BHF on the CAFS drafting committee + financial support for LEZs **b.** Cleaner Air for Scotland strategy, 2015 **c.** Independent CAFS progress report, p. 4, 7

[5.6] DEFRA Clean Air Strategy 2019 (p. 26 for UoE case study)

[5.7] Membership on COMEAP and its impacts **a.** [COMEAP current membership](#) **b.** [COMEAP advising on Environment Bill](#) **c.** [Transport for London website citing RCP report](#) **d.** RCP "Every Breath We Take" report citing 9 COMEAP reports and 2 UoE papers **e.** London ULEZ 6-month report **f.** PHE report "Estimation of costs to the NHS and social care due to the health impacts of air pollution" (2018); p33.

[5.8] International impact **a.** [AHA Scientific Statement on protective actions against particulate matter air pollution exposure \(2020\)](#) **b.** REVIHAAP report **c.** WHO request for a systematic review **d.** Lee et al. 2020 Short-term exposure to carbon monoxide and myocardial infarction: A systematic review and meta-analysis. 2020 Environ Int 143:2015901 [doi: 10.1016/j.envint.2020.105901](#) **e.** [Establishment of WHF APEG](#) **f.** WHF Toolkit **g.** Letter of support from WHO Air Quality and Health Unit **h.** Minutes from WHF APEG meeting 20/10/20