



Environmental Conditions, Air Pollutants, and Airways

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Giuseppe Morici, Fabio Cibella, Daniele Zangla, Pierpaolo Baiamonte, and Maria R. Bonsignore

Abstract

Air pollution is a major problem worldwide, which could be even more serious for athletes who train in urban environments. Exercise increases minute ventilation and exposure to pollutants, but the literature on the effects of air pollution in athletes is relatively scarce, with the exception of chlorine exposure in athletes of aquatic sports and air pollution secondary to ice resurfacing in athletes perform-

G. Morici

Dipartimento di Biomedicina Sperimentale e Neuroscienze Cliniche (BioNeC), Università di Palermo, Palermo, Italy

Istituto di Biomedicina e Immunologia Molecolare (IBIM), Consiglio Nazionale delle Ricerche (CNR), Palermo, Italy

e-mail: giuseppe.morici@unipa.it

F. Cibella

Istituto di Biomedicina e Immunologia Molecolare (IBIM), Consiglio Nazionale delle Ricerche (CNR), Palermo, Italy

e-mail: fabio.cibella@ibim.cnr.it

D. Zangla

Dipartimento di Scienze Psicologiche, Pedagogiche e della Formazione (SPPF), Università di Palermo, Palermo, Italy

e-mail: daniele.zangla@unipa.it

P. Baiamonte

Dipartimento di Biomedicina e Medicina Interna e Specialistica (diBiMIS), Università di Palermo, Palermo, Italy

e-mail: maiden59.mail@libero.it

M. R. Bonsignore (✉)

Istituto di Biomedicina e Immunologia Molecolare (IBIM), Consiglio Nazionale delle Ricerche (CNR), Palermo, Italy

Dipartimento di Biomedicina e Medicina Interna e Specialistica (diBiMIS), Università di Palermo, Palermo, Italy

e-mail: mariosaria.bonsignore@unipa.it

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ing in ice arenas. Although air pollution may exert detrimental effects on athletic performance, little has been published on this topic. The largest body of information regards the impact of air pollution during urban active transport, i.e., walking and cycling in cities, due to the potential risk of air pollution in citizens and the need to rethink urban transportation strategies accordingly. In healthy subjects, the benefits of physical activity largely outweigh the disadvantages of exposure to air pollutants. In susceptible individuals, however, such as patients with cardiac or respiratory disease and children, detrimental effects have been demonstrated. Improvement in air quality, individual protective behaviors, and prompt communication to the population of dangerous air quality may help to limit the negative effects of air pollution on respiratory health.

14.1 Introduction

Air pollution is increasingly considered as a major public health issue, especially since current estimates foresee that about 70% of the world population will live in very extended urban environments by 2050 [1]. Such scenario means that urban design, air pollution control, as well as detailed plans for public and private transportation [2–4] will be necessary to preserve population health from increasing levels of air pollutants.

Environmental evaluation, however, is a very complicated issue. First, exposure to multiple pollutants can derive from different sources (e.g., vehicle traffic, industries, but also fireworks, forest fires, or volcanic eruptions), making data obtained during exposure to single pollutants not necessarily generalizable to real-world situations and requiring complex statistical modeling [5]. Second, the pattern of climate and winds differs among locations, thus modifying exposure settings. Third, monitoring of air quality is evolving, from fixed monitoring stations to wearable devices [6, 7] allowing more precise definition of individual exposures. Finally, susceptibility to the noxious effects of pollutants varies according to age and pre-existing cardiovascular and respiratory diseases. There is evidence that air pollution is associated with cardiorespiratory diseases [8], and COPD patients are particularly vulnerable to air pollutants, both in terms of mortality or hospital admission risk and pollution-associated decline in respiratory function [9].

At the national level, the Environmental Protection Agency (EPA) in the United States focused on reducing air pollution and produced the National Ambient Air Quality Standards for pollutants in order to protect citizens' health. EPA created the air quality index (AQI), an index summarizing air quality day by day. Thus, American citizens can easily access AQI on the web to understand the possible threats for their own health and to access local pollution data [10].

The 2015 WHO Consultation [11] stated that air pollution has to be recognized as a threat to human health, being associated with increase in both mortality and morbidity worldwide. Moreover, the effects of environmental pollution increased steadily in the last decades. Almost all the more common ambient pollutants produce

Table 14.1 Type, source, and respiratory effects of the most common air pollutants^a [25]

Type	Source	Main respiratory effects
Ozone (O ₃)	Photochemical reactions from vehicular traffic (secondary pollutant)	Reduction of lung function Increase of bronchial hyperresponsiveness Reduced exercise tolerance
Nitrogen dioxide (NO ₂)	Each combustion process having atmospheric air as comburent	Increase of bronchial hyperresponsiveness Reduction of lung function Reduced exercise tolerance
Sulfur dioxide (SO ₂)	Fuel combustion (from industry and vehicular traffic)	Reduction of lung function
Respirable fractions of particulate matter	Fuel combustion (from industry and vehicular traffic), nonindustrial combustion processes	Reduction of lung function
United Nations. 2014. <i>World Urbanization Prospects: The 2014 Revision, Highlights</i> . New York: United Nations, Department of Economic and Social Affairs, Population Division. http://esa.un.org/unpd/wup/Highlights/WUP2014-Highlights.pdf	United Nations. 2014. <i>World Urbanization Prospects: The 2014 Revision, Highlights</i> . New York: United Nations, Department of Economic and Social Affairs, Population Division. http://esa.un.org/unpd/wup/Highlights/WUP2014-Highlights.pdf	United Nations. 2014. <i>World Urbanization Prospects: The 2014 Revision, Highlights</i> . New York: United Nations, Department of Economic and Social Affairs, Population Division. http://esa.un.org/unpd/wup/Highlights/WUP2014-Highlights.pdf

^aG. Viegi, S. Baldacci. Epidemiological studies of chronic respiratory conditions in relation to urban air pollution in adults. *Eur Respir Mon* 2002, 21, 1–16

respiratory effects (Table 14.1, Ref. [12]) in individuals, in particular in vulnerable categories (children, subjects affected by chronic respiratory disease such as asthma or chronic obstructive pulmonary disease, subjects affected by cardiovascular diseases, older adults). In its 2015 revision of air quality guideline [11], WHO experts identified 32 air pollutants divided in 4 groups. For most of them, recent evidence justifies re-evaluation: in particular, particulate matter (PM), ozone, nitric dioxide (NO₂), sulfur dioxide (SO₂), and carbon monoxide (CO) need systematic re-evaluation due to increased knowledge about their detrimental effects on health. Along the same line, the American Thoracic Society (ATS) has recently published an estimate of excess mortality and morbidity in the United States, including lung cancer, according to the ATS-recommended thresholds for PM_{2.5} and ozone concentrations [13], which are lower than the currently recommended values (Table 14.2).

14.2 Air Pollution and Exercise

It is well established that physical exercise has important benefits on individual's health [14]. On the other hand, people living in urban or highly industrialized areas are exposed to high levels of environmental pollution. Recreational outdoor exercise

Table 14.2 Upper limit values for outdoor pollutants

Pollutant	Limit	Recent ATS recommendations [13]
PM _{2.5} ^a	10 µg/m ³ annual mean 25 µg/m ³ 24-h mean	≤11 µg/m ³ annual mean ≤25 µg/m ³ 24-h mean
PM ₁₀ ^a	20 µg/m ³ annual mean 50 µg/m ³ 24-h mean	
O ₃ ^a	100 µg/m ³ 8-h mean	≤0.060 ppm 8-h mean
NO ₂ ^a	40 µg/m ³ annual mean 200 µg/m ³ 1-h mean	
SO ₂ ^a	20 µg/m ³ 24-h mean 500 µg/m ³ 10-min mean	
CO ^b	10 mg/m ³ 8-h mean 40 mg/m ³ 1-h mean	

^aWHO Regional Office for Europe (2006). *Air quality guidelines global update 2005: particulate matter, ozone, nitrogen dioxide and sulfur dioxide*. Copenhagen, WHO Regional Office for Europe. Available at http://www.euro.who.int/__data/assets/pdf_file/0005/78638/E90038.pdf

^bEPA—United States Environmental Protection Agency. National Ambient Air Quality Standards (NAAQS). Available at <https://www.epa.gov/criteria-air-pollutants/naaqs-table>

in subjects living in urban areas is associated with increased exposure to pollutants, due to several reasons: (a) increased ventilation during exercise increases exposure to pollutants, partly as a result of the shift from nasal to oral ventilation, with loss of nasal filtering function, and (b) the deposition fraction of ultrafine particles increases during exercise [15], especially in children compared to adults and in asthmatic compared to non-asthmatic children [16]. Moreover, exposure during exercise is affected by factors such as time of the day, proximity to road, and traffic intensity. There is evidence of protective behaviors, i.e., decreased physical activity among adults during days or periods of high exposure to air pollutants [17]. The reader is referred to extensive reviews [18, 19] for detailed analysis of the effects of exposure to single pollutants during exercise and in athletes with exercise-induced bronchoconstriction [20]. The following paragraphs will briefly summarize the main effects of pollutants at rest and during exercise.

Ozone: Increased concentration of ozone in breathed air can induce decrements in lung function in healthy young human subjects along with causing airway inflammation [21]. The effect of ozone inhalation on lung function has been extensively evaluated [22–24]. A threshold concentration of 60–80 ppb has been identified for negative health effects of ozone [25]. It is worth noting that the effect of outdoor activities on lung function is controversial: at low levels of exposure, increasing O₃ levels were associated with airway obstruction [26], while lung function tests did not show any consistent pattern of decrease at similar ozone levels even though an increase in exhaled nitric oxide (eNO) concentration was found [27]. Exposure to ozone may produce airway inflammation as evaluated by means of eNO measures [28].

During exercise, effects of ozone exposure may vary in different population subgroups. Höppe and coworkers reported significant decrease in lung function in asthmatic patients and children, whereas elderly subjects or athletes were little affected

[29]. A high ozone concentration may impact on athletic performance, but heat and humidity usually associated with ozone pollution appear to play a major role in reducing the performance of endurance-trained runners [30].

Particulate matter: The effects of particulate matter (PM) of different sizes have been extensively studied, with special regard to PM_{10} and $PM_{2.5}$, according to their diameter in μm , as well as ultrafine particles (diameter $< 0.1 \mu m$). Healthy subjects exposed to ultrafine carbon particles (without any other component adsorbed) at different concentrations showed a high deposition in the respiratory system, which increased during exercise [31]. During moderate exercise in adult men with prior myocardial infarction, brief exposure to dilute diesel exhaust promoted ST-segment depression, i.e., an important predictor of adverse cardiovascular events [32]. Even mild exercise in a polluted environment may cause increase in biomarkers of airway inflammation and decreased lung function. Adult subjects affected by mild to moderate bronchial asthma walked in Oxford Street, a busy street in London, or in Hyde Park, demonstrating that the degree of traffic exposure may interfere with daily activities in real life [33]. Similarly, in the same ambient conditions, short-term exposure to traffic prevented the beneficial cardiopulmonary effects of walking in subjects affected by chronic obstructive pulmonary disease or ischemic heart disease as well as in healthy individuals [34]. Exposure to diesel exhaust particles ($300 \mu g/m^3$ of $PM_{2.5}$) during moderate or intense exercise in fit young subjects did not acutely modify endothelial function or blood endothelin-1 levels but increased plasma nitrate and nitrite (NOx) concentrations, while exercise intensity did not affect the results [35]. At present, there is suggestive evidence of causal relationships between exposure to traffic-related air pollution and impaired lung function [36].

A current hot topic regards the possible detrimental role of air pollution in healthy people using active transport strategies, i.e., cycling and walking, to commute to study or work as opposed to the use of private cars. The advantages and disadvantages of active transport are being extensively studied, since active transport promotes healthy behavior in the population while decreasing overall traffic volume. Current evidence underlines the pros of active transport [37], although the health benefits of physical exercise appear modified in polluted compared to clean-air areas [38–40].

Figure 14.1 shows an interesting model, where all-cause mortality risk is calculated for air pollution exposure during active transport, with special attention to two points. The “tipping point” represents the amount of cycling per day associated with the highest benefit in terms of risk reduction; the “break-even point” represents the amount of cycling per day beyond which increasing the amount of cycling is associated with increased pollution-related risk [41]. Authors calculated that physical activity should be shortened in very heavily polluted cities, which however represent a low percentage of urban sites in the world [41]. In more complex models, the chronic exposure to pollutants was the main determinant of reduced heart rate variability and increased diastolic blood pressure, whereas the amount of exercise did not exert any significant effect [42]. Therefore, the evidence available to date indicates no additional harm associated with active transport, unless heavy pollution situations occur or cycling is prolonged for many hours per day [41].

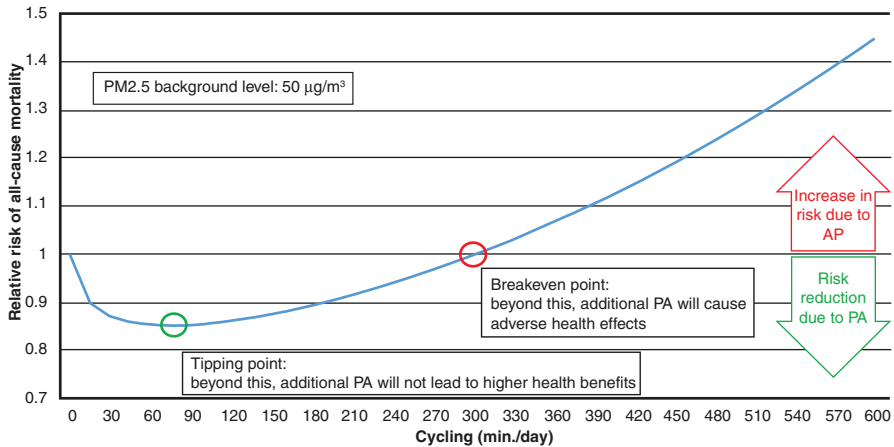


Fig. 14.1 All-cause mortality risk calculated for air pollution exposure during cycling (active transport). The “tipping point” represents the amount of cycling per day associated with the highest benefit in terms of risk reduction; the “break-even point” represents the amount of cycling per day beyond which increasing the amount of cycling is associated with increased pollution-related risk [41]

NO₂: Despite a striking discordance between positive epidemiological associations and results from controlled clinical *NO₂* exposure, subjects affected by asthma or allergic diseases are the subgroups most susceptible to *NO₂*-induced pulmonary effects. Pulmonary adverse effects are not frequent without a co-exposure to specific or nonspecific stimuli [43]. In this context, while studies continue to provide evidence of short-term associations between *NO₂* and respiratory outcomes, it has been demonstrated that these associations are not confounded by co-pollutants, including PM and other gaseous pollutants typically used in multipollutant analyses [21]. *NO₂* has been used as a marker of air pollution in the Danish study on elderly urban residents, showing positive effects of outdoor physical activity such as cycling and gardening that were especially evident in subjects exposed to low-to-moderate residential *NO₂* levels [44].

Sulfur dioxide (SO₂): Inhalation of sulfur dioxide during exercise may produce decrements in lung function [45] with a dose-response relationship in asthmatic volunteers [46].

Carbon monoxide (CO): Studies performed on healthy subjects and patients affected by ischemic heart disease demonstrated that exposure to low-level mixture of CO is able to reduce the exercise time in normal subjects [47] and in patients with coronary artery disease and stable exertional angina [48]. Exercise performance decreased also in COPD patients exposed to 100 ppm of CO for 1 h [49]. In normal young subjects, performing constant power exercise at 85% of maximal *O₂* consumption, exposure to 18.9 ppm of CO for 2 h did not affect cardiorespiratory variables but decreased muscle oxygenation assessed by near-infrared spectroscopy (NIRS) [50]. Such an effect was partly reversed by *O₂* administration for 1 h after CO exposure [50].

14.3 Athletes and Air Pollution

14.3.1 Data from the Olympic Games

The Olympic Games are major events with large participation of athletes and public. Attention to environmental issues has been far from ideal, with the potential of detrimental effects not only on health but also on athletic performance [51]. For example, during Olympic Games in Beijing 2008, one of the most polluted cities in the world, despite major efforts by authorities to reduce air pollution, i.e., traffic limitation and shutdown of industrial plants, air quality was suboptimal [52]. Similarly, traffic-related air pollution and poor water quality in Guanabara Bay were major problems in Rio de Janeiro 2016 [53]. Monitoring of air quality during Turin Winter Games 2006 showed increased benzene concentrations both in the city and at 1500 m altitude, associated with increased vehicle traffic during the Olympic period [54]. The next Summer Olympic Games in Japan 2020 promise a better air quality and will likely increase the well-being of participating athletes [55].

14.3.2 Which Sports Carry a High Air Pollution Risk?

Analysis of pro-inflammatory effects of air pollutants in athletes is complicated by the effects of exercise per se on airway inflammation, especially in athletes of endurance sports [20, 56]. We have studied the effects of environmental conditions and pollutant concentrations in amateur runners before and after running races at different times of the year. Although during the races pollutant concentrations were below the alert thresholds, ozone concentration was highest in summer. Results showed that apoptosis of airway neutrophils in runners was directly proportional to pollutant concentrations, whereas apoptosis of bronchial epithelial cells appeared mostly affected by intense exercise [57].

There are surprisingly few studies on markers of airway inflammation in athletes exposed to pollutants. In non-elite athletes running for 20 min along a roadway, increased blood levels of toluene, ethylbenzene, and xylenes were documented postexercise [58]. Cavalcante de Sá and coworkers reported that exhaled breath condensate (EBC) pH increased after 5 days in amateur runners training in a clean-air environment (forest), but not in those exposed to air pollution (street). Moreover, impaired nasal mucociliary clearance occurred more often after street than forest training [59]. No differences were found in serum interleukin (IL)-6 or interleukin-10 concentrations, highlighting the lack of sensitive and reliable markers of inflammatory damage in athletes. No changes in breath pH after exercise under clean-air and high ozone and high-PM conditions had been reported by a previous study in high school athletes, but pH in this group was lower than in adult sedentary controls [60].

Some athletes are constantly exposed to pollutants/irritants during training and may develop respiratory symptoms. The best examples are swimmers, who are exposed to chlorine derivatives in indoor swimming pools, and athletes active in ice

arenas (hockey players, skaters) who are exposed to CO or NO₂ secondary to malfunction in ice resurfacing process and ultrafine particles [61–63]. The reader is referred to comprehensive reviews dedicated to these topics [20, 64]. Some authors have suggested that high training volumes in elite athletes might justify classification of airway dysfunction as an occupational disease [65]. Technology is under development to decrease high chlorine exposures in swimming pools [66].

14.3.3 Prevention of Negative Effects of Air Pollution

Several simple, common-sense strategies can be adopted to limit the impact of air pollution on health, especially during exercise [67]. These include:

1. Avoiding exercising along high-traffic roads or taking alternative bicycle paths far from traffic [68].
2. Avoiding exercise during the middle of the day, when ozone concentration is highest, especially during summer.
3. Getting real-time information on pollutant levels, wherever available.
4. Training indoor under condition of severe air pollution.
5. Using of protective masks during exercise.

The problem of prevention is particularly relevant in China, where air quality is still far from ideal, children and elderly are used to exercise outdoor, there are no public plans for prevention to pollutant exposures, and the indoor facilities are insufficient to cover the needs of a huge population [69].

There is some evidence that a healthy diet and vitamin C and D supplementation can help to limit air pollution-related respiratory damage [70]. Interestingly, a recent experimental study in mice reported a role of gut microbiome in the pathogenesis of increased bronchial reactivity in response to ozone exposure [71]. This is a new and poorly explored field, which deserves further study.

14.4 Conclusions

Figure 14.2 tries to summarize the current knowledge on the effects of exercise under conditions of air pollution in athletes. While there is evidence that exercise does potentiate exposure to pollutants, the possibility that healthy well-trained athletes may develop protective defense mechanisms has been not explored to date. Exercise training is associated with pro- and anti-inflammatory changes, and a heightened response to oxidative stress as a result of training may well contribute to limit the damage linked to air pollution. Much work needs to be done in this respect, as well as studies on air pollutant thresholds which may affect performance.

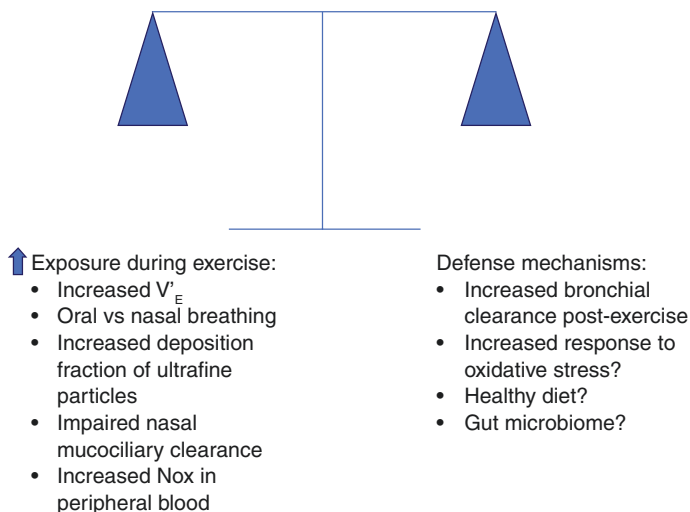


Fig. 14.2 Summary of mechanisms of increased exposure to pollutant during exercise in athletes. The impact of potential defense mechanisms has not been studied in detail

Air quality has improved in the last decades worldwide due to increased knowledge about health risks and implementation of preventive measures. Current evidence shows that the benefits of exercise in healthy subjects outweigh the effects of concurrent air pollution, suggesting that preventive strategies against exposure to pollutants should not become a recommendation for a sedentary lifestyle. Vulnerable populations, such as children, elderly, and patients with cardiorespiratory diseases, should refrain from exercising under air pollution conditions, as indicated by studies showing increasing mortality and morbidity risk.

Key Points

- Air pollution is a threat for human health, and exercise increases exposure to pollutants
- The benefits of physical exercise can be decreased by air pollution, but exercise-associated risk reduction in healthy subjects remains significant unless severe air pollution occurs
- Vulnerable groups such as children and patients with cardiorespiratory disease should avoid exercise in polluted areas
- Little is known on the effects of air pollution in athletes and on possible protective mechanisms evoked by habitual exercise which may help to limit the detrimental effects of air pollution on cardiorespiratory health

References

1. United Nations. World urbanization prospects: the 2014 revision, highlights. New York: United Nations, Department of Economic and Social Affairs, Population Division; 2014.. <https://esa.un.org/unpd/wup/Publications/Files/WUP2014-Report.pdf>. Accessed 13 May 2018
2. Mueller N, Rojas-Rueda D, Basagaña X, Cirach M, Cole-Hunter T, Dadvand P, Donaire-Gonzalez D, Foraster M, Gascon M, Martinez D, Tonne C, Triguero-Mas M, Valentín A, Nieuwenhuijsen M. Urban and transport planning related exposures and mortality: a health impact assessment for cities. *Environ Health Perspect*. 2017;125:89–96.
3. Brook JR, Setton EN, Seed E, Shooshtari M, Doiron D, The Canadian Urban Environmental Health Research Consortium (CANUE). The Canadian urban environmental health research consortium- a protocol for building a national environmental exposure data platform for integrated analysis of urban form and health. *BMC Public Health*. 2018;18:114. <https://doi.org/10.1186/s12889-017-5001-5>.
4. Götschi T, de Nazelle A, Brand C, Gerike R, Physical activity through sustainable transport approaches (PASTA) consortium. Towards a comprehensive conceptual framework of active travel behavior: a review and synthesis of published frameworks. *Curr Environ Health Rep*. 2017;4:286–95.
5. Vedal S, Kaufman JD. What does multi-pollutant air pollution research mean? *Am J Respir Crit Care Med*. 2011;183:4–6.
6. Jerrett M, Donaire-Gonzalez D, Popoola O, Jones R, Cohen RC, Almanza E, de Nazelle A, Mead I, Carrasco-Turigas G, Cole-Hunter T, Triguero-Mas M, Seto E, Nieuwenhuijsen M. Validating novel air pollution sensors to improve exposure estimates for epidemiological analyses and citizen science. *Environ Res*. 2017;158:286–94.
7. Dons E, Laeremans M, Orjuela JP, Avila-Palencia I, Carrasco-Turigas G, Cole-Hunter T, Anaya-Boig E, Standaert A, De Boever P, Nawrot T, Götschi T, de Nazelle A, Nieuwenhuijsen M, Int Panis L. Wearable sensors for personal monitoring and estimation of inhaled traffic-related air pollution: evaluation of methods. *Environ Sci Technol*. 2017;51:1859–67.
8. Requia WJ, Adams MD, Arain A, Papatheodorou S, Koutrakis P, Mahmoud M. Global association of air pollution and cardiorespiratory diseases: a systematic review, meta-analysis, and investigation of modifier variables. *Am J Public Health*. 2018;108(S2):S123–30.
9. Heinrich J, Schikowski T. COPD patients as vulnerable subpopulation for exposure to ambient air pollution. *Curr Environ Health Rep*. 2018;5:70–6.
10. Airnow. Air quality index- a guide to air quality and your health. https://airnow.gov/index.cfm?action=aqi_brochure.index. Accessed 13 May 2018.
11. WHO Expert Consultation: Available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs). http://www.euro.who.int/__data/assets/pdf_file/0013/301720/Evidence-future-update-AQGs-mtg-report-Bonn-sept-oct-15.pdf. Accessed 13 May 2018.
12. McDonnell WF, Stewart PW, Smith MV. Prediction of ozone-induced lung function responses in humans. *Inhal Toxicol*. 2010;22:160–8.
13. Viegi G, Baldacci S. Epidemiological studies of chronic respiratory conditions in relation to urban air pollution in adults. *Eur Respir Mon*. 2002;21:1–16.
14. Cromar KR, Gladson LA, Ghazipura M, Ewart G. Estimated excess morbidity and mortality associated with air pollution above American Thoracic Society-recommended Standards, 2013–2015. American Thoracic Society and Marron Institute Report. *Ann Am Thorac Soc*. 2018;15:542–51.
15. Blair SN. Physical inactivity: the biggest public health problem of the 21st century. *Br J Sports Med*. 2009;43:1–2.
16. Daigle CC, Chalupa DC, Gibb FR, Morrow PE, Oberdörster G, Utell MJ, Frampton MW. Ultrafine particle deposition in humans during rest and exercise. *Inhal Toxicol*. 2003;15:539–52.
17. Olvera HA, Perez D, Clague JW, Cheng Y-S, Li W-W, Amaya MA, Burchiel SW, Berwick M, Pingitore NE. The effect of ventilation, age and asthmatic condition on ultrafine particle deposition in children. *Pulm Med*. 2012;2012:736290. <https://doi.org/10.1155/2012/736290>.

18. An R, Zhang S, Ji M, Guan C. Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis. *Persp Public Health*. 2018;138:111–21.
19. Carlisle AJ, Sharp NCC. Exercise and outdoor ambient air pollution. *Br J Sports Med*. 2001;35:214–22.
20. Giles LV, Koehle MS. The health effects of exercising in air pollution. *Sports Med*. 2014;44:223–49.
21. Rundell KW, Anderson SD, Sue-Chu M, Bougault V, Boulet LP. Air quality and temperature effects on exercise-induced bronchoconstriction. *Compr Physiol*. 2015;5:579–610.
22. WHO Regional Office for Europe. Review of evidence on health aspects of air pollution—REVIHAAP project: technical report. Copenhagen, WHO Regional Office for Europe. 2013. http://www.euro.who.int/__data/assets/pdf_file/0004/193108/REVIHAAP-Final-technical-report.pdf. Accessed 13 May 2018.
23. McDonnell WF, Stewart PW, Smith MV. The temporal dynamics of ozone-induced FEV1 changes in humans: an exposure-response model. *Inhal Toxicol*. 2007;19:483–94.
24. McDonnell WF, Stewart PW, Smith MV, Kim CS, Schelegle ES. Prediction of lung function response for populations exposed to a wide range of ozone conditions. *Inhal Toxicol*. 2012;24:619–33.
25. Schelegle ES, Morales CA, Walby WF, Marion S, Allen RP. 6.6-hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans. *Am J Respir Crit Care Med*. 2009;180:265–72.
26. Thaller EI, Petronella SA, Hochman D, Howard S, Chhikara RS, Brooks EG. Moderate increases in ambient PM2.5 and ozone are associated with lung function decreases in beach lifeguards. *J Occup Environ Med*. 2008;50:202–11.
27. Nickmilder M, de Burbure C, Carbone S, Dumont X, Bernard A, Derouane A. Increase of exhaled nitric oxide in children exposed to low levels of ambient ozone. *J Toxicol Environ Health A*. 2007;70:270–4.
28. Berhane K, Zhang Y, Linn WS, Rappaport EB, Bastain TM, Salam MT, Islam T, Lurmann F, Gilliland FD. The effect of ambient air pollution on exhaled nitric oxide in the Children’s Health Study. *Eur Respir J*. 2011;37:1029–36.
29. Höpfe P, Peters A, Rabe G, Praml G, Lindner J, Jakobi G, Fruhmans G, Nowak D. Environmental ozone effects in different population subgroups. *Int J Hyg Environ Health*. 2003;206:505–16.
30. Gomes EC, Stone V, Florida-James G. Investigating performance and lung function in a hot, humid, and ozone-polluted environment. *Eur J Appl Physiol*. 2010;110:199–205.
31. Frampton MW. Systemic and cardiovascular effects of airway injury and inflammation: ultra-fine particle exposure in humans. *Environ Health Perspect*. 2001;109(Suppl. 4):529–32.
32. Mills NL, Törnqvist H, Gonzalez MC, Vink E, Robinson SD, Söderberg S, Boon NA, Donaldson K, Sandström T, Blomberg A, Newby DE. Ischemic and thrombotic effects of dilute diesel-exhaust inhalation in men with coronary heart disease. *N Engl J Med*. 2007;357:1075–82.
33. McCreanor J, Cullinan P, Nieuwenhuijsen MJ, Stewart-Evans J, Malliarou E, Jarup L, Harrington R, Svartengren M, Han IK, Ohman-Strickland P, Chung KF, Zhang J. Respiratory effects of exposure to diesel traffic in persons with asthma. *N Engl J Med*. 2007;357:2348–58.
34. Sinharay R, Gong J, Barratt B, Ohman-Strickland P, Ernst S, Kelly FJ, Zhang JJ, Collins P, Cullinan P, Chung KF. Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *Lancet*. 2018;391:339–49.
35. Giles LV, Tebbutt SJ, Carlsten C, Koehle MS. The effect of low and high-intensity cycling in diesel exhaust on flow-mediated dilation, circulating NOx, endothelin-1 and blood pressure. *PLoS One*. 2018;13(2):e0192419.
36. Health Effects Institute. Panel on the Health Effects of Traffic-Related Air Pollution. Traffic-related air pollution: a critical review of the literature on emissions, exposure, and health effects. 2010. <https://www.healtheffects.org/publication/traffic-related-air-pollution-critical-review-literature-emissions-exposure-and-health>. Accessed 13 May 2018.

37. Mueller N, Rojas-Rueda D, Cole-Hunter T, de Nazelle A, Dons E, Gerike R, Götschi T, Int Panis L, Kahlmeier S, Nieuwenhuijsen MJ. Health impact assessment of active transportation: a systematic review. *Prev Med.* 2015;76:103–14.
38. Matt F, Cole-Hunter T, Donaire-Gonzales D, Kubesch N, Martinez D, Carrasco-Turigas G, Nieuwenhuijsen M. Acute respiratory response to traffic-related air pollution during physical activity performance. *Environ Int.* 2016;97:45–55.
39. Laeremans M, Dons E, Avila-Palencia I, Carrasco-Turigas G, Orjuela JP, Anaya E, Cole-Hunter T, de Nazelle A, Nieuwenhuijsen M, Standaert A, Van Poppel M, De Boever P, Int Panis L. Short-term effects of physical activity, air pollution and their interaction on the cardiovascular and respiratory system. *Environ Int.* 2018;117:82–90.
40. Laeremans M, Dons E, Avila-Palencia I, Carrasco-Turigas G, Orjuela-Mendoza JP, Anaya-Boig E, Cole-Hunter T, de Nazelle A, Nieuwenhuijsen M, Standaert A, Van Poppel M, De Boever P, Int Panis L. Black carbon reduces the beneficial effect of physical activity on lung function. *Med Sci Sports Exerc.* 2018;50(9):1875–81. <https://doi.org/10.1249/MSS.0000000000001632>.
41. Tainio M, de Nazelle AJ, Götschi T, Kahlmeier S, Rojas-Rueda D, Nieuwenhuijsen MJ, Héríck de Sa T, Kelly P, Woodcock J. Can air pollution negate the health benefits of cycling and walking? *Prev Med.* 2016;87:233–6.
42. Cole-Hunter T, de Nazelle A, Donaire-Gonzales D, Kubesch N, Carrasco-Turigas G, Matt F, Foraster M, Martinez D, Ambros A, Cirach M, Martinez D, Belmonte J, Nieuwenhuijsen M. Estimated effects of air pollution and space-time-activity on cardiopulmonary outcomes in healthy adults: a repeated measures study. *Environ Int.* 2018;111:247–59.
43. Hesterberg TW, Bunn WB, McClellan RO, Hamade AK, Long CM, Valberg PA. Critical review of the human data on short-term nitrogen dioxide (NO₂) exposures: evidence for NO₂ no-effect levels. *Crit Rev Toxicol.* 2009;39:743–81.
44. Andersen ZJ, de Nazelle A, Mendez MA, Garcia-Aymerich J, Hertel O, Tjønneland A, Overvad K, Raaschou-Nielsen O, Nieuwenhuijsen MJ. A study of the combined effects of physical activity and air pollution on mortality in elderly urban residents: the Danish Diet, Cancer, and Health Cohort. *Environ Health Perspect.* 2015;123:557–63.
45. EPA integrated science assessment for oxides of nitrogen – health criteria. https://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=526855. Accessed 13 May 2018.
46. Johns DO, Svendsgaard D, Linn WS. Analysis of the concentration-respiratory response among asthmatics following controlled short-term exposures to sulfur dioxide. *Inhal Toxicol.* 2010;22:1184–93.
47. Koike A, Wasserman K. Effect of acute reduction in oxygen transport on parameters of aerobic function during exercise. *Ann Acad Med Singap.* 1992;21:14–22.
48. Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Effects of carbon monoxide on myocardial ischemia. *Environ Health Perspect.* 1991;91:89–132.
49. Aronow WS, Ferlinz J, Glauser F. Effect of carbon monoxide on exercise performance in chronic obstructive pulmonary disease. *Am J Med.* 1977;63:904–8.
50. Keramidis ME, Kounalakis SN, Eiken O, Mekjavic IB. Carbon monoxide exposure during exercise performance: muscle and cerebral oxygenation. *Acta Physiol.* 2012;204:544–54.
51. Fitch K. Air pollution, athletic health and performance at the Olympic Games. *J Sports Med Phys Fitness.* 2016;56:922–32.
52. Schleicher N, Norra S, Chen Y, Chai F, Wang S. Efficiency of mitigation measures to reduce particulate air pollution-A case study during the Olympic Summer Games 2008 in Beijing, China. *Sci Total Environ.* 2012;42:146–58.
53. Gioda A, Ventura LMB, Ramos MB, Silva MPR. Half century monitoring air pollution in a megacity: a case study of Rio de Janeiro. *Water Air Soil Pollut.* 2016;227:1–17.
54. Bono R, Degan R, Pazzi M, Romanazzi V, Rovere R. Benzene and formaldehyde in air of two Winter Olympic venues of “Torino 2006”. *Environ Int.* 2010;36:269–75.
55. Donnelly AA, MacIntyre TE, O’Sullivan N, Warrington G, Harrison AJ, Igou ER, Jones M, Gidlow C, Brick N, Lahart I, Cloak R, Lane AM. Environmental influences on elite sport

- athletes well being: from gold, silver, and bronze to blue green and gold. *Front Psychol.* 2016;7:1167. <https://doi.org/10.3389/fpsyg.2016.01167>.
56. Bonsignore MR, Morici G, Vignola AM, Riccobono L, Bonanno A, Profita M, Abate P, Scichilone N, Amato G, Bellia V, Bonsignore G. Increased airway inflammatory cells in endurance athletes: what do they mean? *Clin Exp Allergy.* 2003;33:14–21.
 57. Chimenti L, Morici G, Paterno A, Bonanno A, Vultaggio M, Bellia V, Bonsignore MR. Environmental conditions, air pollutants, and airway cells in runners: a longitudinal field study. *J Sports Sci.* 2009;27:925–35.
 58. Blair C, Walls J, Davies NW, Jacobson GA. Volatile organic compounds in runners near a roadway: increased blood levels after short-duration exercise. *Br J Sports Med.* 2010;44:731–5.
 59. Cavalcante de Sá M, Nakagawa NK, Saldiva de André CD, Carvalho-Oliveira R, de Santana Carvalho T, Nicola ML, de André PA, Nascimento Saldiva PH, Vaisberg M. Aerobic exercise in polluted urban environments: effects on airway defense mechanisms in young healthy amateur runners. *J Breath Res.* 2016;10:046018.
 60. Ferdinands JM, Crawford CA, Greenwald R, Van Sickle D, Hunter E, Teague WG. Breath acidification in adolescent runners exposed to atmospheric pollution: a prospective, repeated measures observational study. *Environ Health.* 2008;7:10. <https://doi.org/10.1186/1476-069X-7-10>.
 61. Creswell PD, Meiman JG, Nehls-Lowe H, Vogt C, Wozniak RJ, Werner MA, Anderson H. Exposure to elevated carbon monoxide levels at an indoor ice arena--Wisconsin, 2014. *MMWR Morb Mortal Wkly Rep.* 2015;64:1267–70.
 62. Brat K, Merta Z, Plutinsky M, Skrickova J, Stanek M. Ice hockey lung – a case of mass nitrogen dioxide poisoning in the Czech Republic. *Can Respir J.* 2013;20(6):e100–3.
 63. Rundell KW. Pulmonary function decay in women ice hockey players: is there a relationship to ice rink air quality? *Inhal Toxicol.* 2004;16:117–23.
 64. Mountjoy M, Fitch K, Boulet LP, Bougault V, van Mechelen W, Verhagen E. Prevalence and characteristics of asthma in the aquatic disciplines. *J Allergy Clin Immunol.* 2015;136:588–94.
 65. Price OJ, Ansley L, Menzies-Gow A, Cullinan P, Hull JH. Airway dysfunction in elite athletes – an occupational lung disease? *Allergy.* 2013;68:1343–52.
 66. Gomà A, de Lluís R, Roca-Ferrer J, Lafuente J, Picado C. Respiratory, ocular and skin health in recreational and competitive swimmers: beneficial effect of a new method to reduce chlorine oxidant derivatives. *Environ Res.* 2017;152:315–21.
 67. Laumbach R, Meng Q, Kipen H. What can individuals do to reduce personal health risks from air pollution? *J Thorac Dis.* 2015;7:96–107.
 68. Cole-Hunter T, Jayaratne R, Stewart I, Hadaway M, Morawska L, Solomon C. Utility of an alternative bicycle commute route of lower proximity to motorized traffic in decreasing exposure to ultra-fine particles, respiratory symptoms and airway inflammation--a structured exposure experiment. *Environ Health.* 2013;12(1):29.
 69. Li F, Liu Y, Lü J, Linag L, Harmer P. Ambient air pollution in China poses a multifaceted health threat to outdoor physical activity. *J Epidemiol Commun Health.* 2015;69:201–4.
 70. Whyand T, Hurst JR, Beckles M, Caplin ME. Pollution and respiratory disease: can diet or supplements help? A review. *Respir Res.* 2018;19(1):79.
 71. Cho Y, Abu-Ali G, Tashiro H, Kasahara DI, Brown TA, Brand JD, Mathews JA, Huttenhower C, Shore SA. The microbiome regulates pulmonary responses to ozone in mice. *Am J Respir Cell Mol Biol.* 2018;59(3):346–54. <https://doi.org/10.1165/rmb.2017-0404OC>.