York Health Economics Consortium

CYSTIC FIBROSIS TRUST

Air Quality and Cystic Fibrosis: A Pragmatic Review

Final Report

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12/06/2025

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Abbreviations

CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
CI	Confidence interval
DEFRA	Department for Environment, Food & Rural Affairs
ECAT	Elemental carbon attributable to traffic sources
HR	Hazard ratio
MRSA	Methicillin-resistant *Staphylococcus aureus*
NA	Not applicable
NHS	National Health Service
NO_2	Nitrogen dioxide
NTM	Nontuberculous mycobacteria
O_3	Ozone
PAH	Polycyclic aromatic hydrocarbons
PM	Particulate matter
PPB	Parts per billion
SHS	Second-hand smoke
SSP	Shared Socio-economic Pathways
TOMPS	Toxic organic micro-pollutants
UFP	Ultrafine particles
UK	United Kingdom
US	United States
VOC	Volatile organic compounds
WHO	World Health Organization

1 Plain Language Summary

Key messages

- Exposure to some types of indoor air pollution, including second-hand smoke (SHS) and forced hot air (a type of central heating system where air from inside the house is drawn in, heated and redistributed through air ducts) has been associated with poorer clinical outcomes in people with cystic fibrosis (CF), compared to people with CF who were not exposed.
- Higher levels of some outdoor air pollutants have been associated with poorer clinical outcomes in people with CF, including a higher risk of lung disease exacerbations, a faster reduction in lung function and a higher likelihood of acquiring bacteria that can cause serious infections.
- Some environmental factors, including higher temperatures and higher saturated vapour pressure (a measure of how much moisture the air can hold at a given temperature), have been associated with poorer clinical outcomes in people with CF, including lower lung function, lower sodium levels and a higher likelihood of acquiring bacteria that can cause serious infections.
- Actions that policies could focus on to improve air quality include supporting renewable energy sources, electric cars and infrastructure supporting public and active travel.

What is cystic fibrosis?

CF is a life-limiting genetic condition. The genetic changes lead to a build-up of sticky mucus which affects the lungs and digestive system. Lung disease tends to gradually worsen over time, with intermittent worsening called “exacerbations.” Lung disease exacerbations can be triggered by different factors. Recently, research has begun to investigate whether poor air quality may be a trigger.

How might air quality and climate change be related to outcomes in cystic fibrosis?

The quality of the air we breathe is important for our health. Air is made up of gases, water vapour and solid particles called aerosols. Air pollutants include both gases and aerosols. The World Health Organization estimates that air pollution is responsible for around 7 million deaths each year, in addition to diseases affecting the heart, lungs and blood vessels. Lung disease in CF may mean that people with CF are more likely to experience the harmful effects of poor air quality.

Climate change refers to long-term shifts in temperature, water cycles and extreme weather events. Human activities such as deforestation and burning fossil fuels have contributed to climate change. Climate change and air quality are closely related. More extreme temperatures, wildfires and changing weather patterns influence the formation and distribution of air pollutants. Therefore, the effects of climate change may influence air quality, which may in turn affect outcomes for people with CF.

What did we want to find out?

Our research aimed to answer two questions.

1. We wanted to find out how air quality affects people with CF.
2. We wanted to find out what interventions can help to protect people with CF against poor air quality.

What did we do?

We searched for scientific journal articles and online resources that investigated the effects of any air quality measurements (for example, pollutants and micro-organism presence) on outcomes for people with CF (for example, admissions to hospital, rate of change of lung function or rate of lung disease exacerbations). We also searched for articles and online resources that investigated interventions to protect people with CF against poor air quality. We then compared and summarised the results of the studies.

What did we find?

We found 29 scientific journal articles that were relevant to our first research question. We included the 17 most relevant studies, which included people with CF from the United Kingdome, France, Belgium, Australia, New Zealand, Brazil, and United States.

We found 8 scientific journal articles that were partially relevant to our second research question. These included research from Germany, Austria, France and the United States. We included these articles along with the 5 most relevant online resources.

Main results

Exposure to some sources of indoor air pollution was associated with poorer clinical outcomes in people with CF.

- Indoor exposure to SHS or forced hot air was associated with a faster decline in lung function in children and adolescents with CF, compared to those who were not exposed.
- Indoor exposure to SHS was associated with more hospitalisations each year in adults with CF, compared to those who were not exposed.

- Exposure to indoor mould at home was associated with a greater likelihood of having fungi present in the airway. However, it is unclear how this relates to CF outcomes.

Exposure to higher levels of outdoor air pollution was associated with poorer clinical outcomes in people with CF.

- Some studies found that increasing levels of outdoor air pollutants were associated with a higher risk of lung disease exacerbations and faster reduction in lung function in people with CF.
- Motor vehicles are a substantial source of air pollution. One study found that the closer a person with CF lived to a major road, the higher their likelihood of having multiple lung disease exacerbations.
- Two studies found that higher levels of particulate matter less than 2.5 micrometers in diameter ($PM_{2.5}$) were associated with an increased risk of acquiring two different bacteria (Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* (*P. aeruginosa*)). These bacteria can cause serious infections in people with CF.

Six studies investigated the effect of environmental factors on outcomes for people with CF. Five of these focussed on temperature. These studies found that higher temperatures were associated with lower lung function, lower sodium levels and higher rates of having the *P. aeruginosa* bacteria. One study found that a higher saturated vapour pressure was associated with an increased likelihood of having a positive result for nontuberculous mycobacteria (NTM). NTM is a group of bacteria that can cause serious infections in people with CF.

No studies specifically measured the effectiveness of interventions to protect people with CF from the harmful effects of poor air quality. However, several general recommendations were identified. These include:

- Actions that individuals can take to improve indoor air quality, including appropriate monitoring, ventilation, appliance testing and cleaning.
- Actions that individuals can take to protect against poor outdoor air quality, including monitoring, masking, adjusting activities and using a reliever inhaler if prescribed.
- Actions that individuals can take to reduce their contribution to air pollution, including using public or active transport rather than driving a private vehicle, using an electric vehicle rather than a diesel or petrol-powered car, using energy from renewable sources and avoiding wood-burning.
- Actions that communities can take to improve air quality in their area, including raising local awareness and supporting existing efforts (for example, low emission zones).
- Actions that policies could focus on to improve air quality, including supporting renewable energy sources, electric cars and infrastructure supporting public and active travel.

What are the limitations of the evidence?

Researchers commented on the relatively small number of studies investigating these topics in people with CF, compared to the amount of research focusing on other populations (for example, people with asthma). Few articles focused on indoor air quality and there were no studies that measured the effectiveness of protective interventions for people with CF. The lack of research means that we cannot yet be certain of the amount of risk that air pollution holds for people with CF.

What are our recommendations?

This review has summarised several studies that have found an association between poorer air quality and poorer clinical outcomes for people with CF. Further research on this topic would help us to be more sure of the amount of risk that air pollution holds for people with CF. Research investigating the effects of indoor air quality and the effectiveness of protective interventions would inform the current gap in available research. The results of this research could be used to inform evidence-based strategies to minimise the risk of poor air quality to people with CF.

2 Introduction

2.1 Background

2.1.1 Cystic fibrosis

CF is a life-limiting genetic condition, most prevalent among individuals of European descent, with an incidence ranging from 1 in 3,000 to 1 in 6,000 live births [1]. CF is caused by mutations in the CF transmembrane conductance regulator (CFTR) gene [2]. These mutations lead to a build-up of sticky mucus which affects the lungs and digestive system [3]. This usually causes long-term, progressive lung disease with frequent exacerbations as well as pancreatic insufficiency and premature death [4, 5]. Both genetic and non-genetic factors contribute to the frequency of pulmonary exacerbations and progressive loss of lung function in CF [4, 6, 7]. Air quality is one such non-genetic factor that has been increasingly investigated over the last two decades. Air quality guidance tends to recognise that some groups of people, including people with CF, may be more vulnerable to the harmful effects of air pollution than the general population [8, 9].

2.1.2 Air quality

The quality of the air we breathe is important for our health. Air consists of a mixture of gases, water vapour and solid particles called aerosols [10]. The primary components of air include nitrogen (78%), oxygen (21%), and trace amounts of gases such as argon, carbon dioxide, and ozone. Water vapor varies depending on location and weather conditions, while aerosols originate from both natural processes (for example, volcanic eruptions and sea spray) and human activities (for example, industrial emissions and vehicle exhaust fumes) [10]. Air pollutants include both gases and aerosols [8].

Aerosols play a significant role in air pollution, acting as carriers for harmful pollutants including particulate matter (PM), which are classified based on their size—PM_{10} (particles with a diameter of 10 micrometers or less), $PM_{2.5}$ (2.5 micrometers or less) and UFP (10 nanometers or less) [11, 12]. Sources of PM_{10} consist mainly of pollen, sea spray and wind-blown dust from erosion and agricultural spaces. Finer particles ($PM_{2.5}$) can be derived from primary sources (for example, fuel combustion) and secondary sources (for example, chemical reactions between gases) [13, 14]. In the UK, the Department for Environment, Food and Rural Affairs (DEFRA) provides daily measurements and forecasts of air quality [15].

Poor air quality is linked to a range of adverse health outcomes, including respiratory diseases, cardiovascular conditions, and premature mortality [13, 16, 17]. The World Health Organization (WHO) estimates that air pollution is responsible for around 7 million deaths each year [13]. In the UK, mortality due to human-generated air pollution is estimated to fall between 28,000 and 36,000 deaths each year [8]. Between 2015 and 2017, air pollutants are estimated to cost the NHS and social care system £1.6 billion [8].

2.1.3 Climate change

Climate change refers to long-term shifts in temperature, precipitation patterns, and extreme weather events caused primarily by human activities, such as fossil fuel combustion and deforestation. Global temperatures have risen by approximately 1.1°C since the pre-industrial era, with projections indicating further warming unless greenhouse gas emissions are significantly reduced [18]. Without a substantial global reduction in greenhouse gas emissions, projections indicate that the rise in global temperature will exceed 2ºC before 2050 [19]. Shared Socio-economic Pathways (SSP) scenarios project that the temperature rise in Europe, comparing temperatures from 1981-2010 to 2071-2100, is projected to increase from between 1.2ºC to 3.4ºC (in scenario SSP1-2.6) or 4.1ºC to 8.5ºC (in scenario SSP5-8.5) [19].

Climate change and air quality are closely interconnected, with each influencing the other in multiple ways. Rising global temperatures accelerate the formation of ground-level ozone (O_3), a major air pollutant [20]. Climate change leads to more frequent and intense wildfires, which release large amounts of $PM_{2.5}$, carbon monoxide, and toxic chemicals into the air [21]. Climate change also alters wind patterns, and heatwaves and droughts can trap pollutants in urban areas, which affects pollutant dispersion and stagnation [22]. Given these links, climate change may have substantial implications for the adverse health effects associated with poor air quality.

2.2 Research aims

The aim of this pragmatic literature review was to investigate the impact of air quality on people living with CF, particularly regarding changes in air quality due to climate change and more extreme temperatures.

This review was guided by two research questions:

1. How do different air quality parameters (for example, pollutants and microbial content) contribute to key outcomes in individuals with CF?
2. What interventions (for example, air purifiers and ventilation systems) help to protect people with CF against the negative effects of poor air quality?

3 Methods

3.1 Eligibility criteria

A set of eligibility criteria was defined for each research question. These criteria were used to develop the search methods and ensure that studies that best answered each question were found.

The eligibility criteria are shown in Table 3.1 and

Table 3.2, respectively.

Table 3.1 Eligibility criteria for Question One

Criteria	Eligible studies	Ineligible studies
Population	People of any age with CF.	Studies where results pertaining to people with CF are not able to be distinguished from results for people with other respiratory diseases.
Exposure	1. Pollutants included in the WHO global air quality guidelines (for example, $PM_{2.5}$, PM_{10}, nitrogen dioxide, ozone, carbon monoxide, sulphur dioxide, lead, PAHs, formaldehyde and radon)[23]. 2. Other air quality parameters (for example, carbon dioxide, black carbon, UFP, mould, other nitrogen oxides, PM_1, VOCs, TOMPS, benzene, 1,3-butadiene, other heavy metals, methane). [23] [2, 24]. 3. Additional air quality parameters related to climate change (for example, temperature).	Studies assessing air quality parameters solely in the context of tobacco smoking or vaping.
Comparator	Various levels of exposure to pollutants.	NA.
Outcomes	Pulmonary CF exacerbations, lung function tests (for example, FEV_1 values), hospitalisations, respiratory symptoms, antibiotic prescriptions for respiratory infections.	NA.
Study designs	Any design except case reports.	Case reports.
Limits	English language.	Non-English language studies.

Abbreviations: CF – cystic fibrosis; FEV_1 – forced expiratory volume in one second; NA – not applicable; PAH – polycyclic aromatic hydrocarbons; PM – particulate matter; TOMPS – toxic organic micro-pollutants; VOC – volatile organic compounds; WHO – World Health Organization.

Table 3.2 Eligibility criteria for Question Two

Criteria	Eligible studies	Ineligible studies
Population	People of any age with CF.	Studies where results pertaining to people with CF are not able to be distinguished from results for people with other respiratory diseases.
Exposure	Any intervention that helps to protect against the negative effects of poor air quality.	Interventions for aspects of CF other than cardiorespiratory health.
Comparator	Alternative or no intervention.	NA.
Outcomes	Pulmonary CF exacerbations, lung function tests (for example, FEV_1 values), hospitalisations, respiratory symptoms, antibiotic prescriptions for respiratory infections.	NA.
Study designs	Any design except case reports.	Case reports.
Limits	English language.	Non-English language studies.

Abbreviations: CF – cystic fibrosis; FEV_1 – forced expiratory volume in one second; NA – not applicable.

3.2 Search methods

The search methods (including search strategy design and selection of search resources) reflected the pragmatic review context. The methods were highly focused to target records most likely to be relevant whilst enabling searches to be conducted and results assessed within project resources. The pragmatic approach was discussed and agreed at protocol stage.

3.2.1 Search strategy

A MEDLINE (OvidSP) search strategy was designed to identify studies that report on CF in the context of air quality. One search strategy was used to inform both questions. Full details of the final MEDLINE strategy are presented in Appendix A: Ovid MEDLINE search strategy

A MEDLINE (OvidSP) search strategy was designed to identify studies that report on CF in the context of air quality. One search strategy was used to inform both questions. Search strategy design reflected the pragmatic review context. The pragmatic approach was discussed and agreed at protocol stage.

Details of the final MEDLINE strategy are presented in Figure A.1 below. The strategy comprised two concepts:

- CF (search lines 1 to 3).
- Air quality (search lines 4 to 52).

The concepts were combined as follows: CF AND air quality.

The search terms for the air quality concept (search lines 4 to 52) included a pragmatic selection of terms relating to the following:

- Non-specific air quality (search lines 4 to 7).
- Climate change (search lines 8 to 18).
- Non-specific pollution (search lines 19 to 21).
- Examples of specific air quality parameters identified by the research team, including:
    - Particulate matter (PM1, PM2.5, and PM10) (search lines 22 to 26).
    - Microbial content (search lines 27 to 36).
    - Greenhouse gases (carbon dioxide, nitrous oxide, methane, ozone) (search lines 37 to 47).
    - Other air pollutants (benzene, black carbon, butadiene, formaldehyde, lead, nitrogen dioxide, other heavy metals, polycyclic aromatic hydrocarbons, radon, sulphur dioxide, toxic organic micro-pollutants, volatile organic compounds) (search lines 48 to 52).

The strategy was devised using a combination of subject indexing terms and free text search terms in the Title, Abstract and Keyword Heading Word fields. The search terms for the concepts were identified through discussion within the research team, scanning background literature, and browsing database thesauri.

The strategy excluded animal studies from MEDLINE using a standard algorithm (search line 54). The strategy also excluded some publication types which were unlikely to yield relevant study reports (editorials, news items and case reports) and records with the phrase 'case report' in the title (search line 55).

Reflecting the eligibility criteria, the strategy was restricted to studies published in English language (search line 57). No date restriction was applied.

The final Ovid MEDLINE strategy was peer-reviewed before execution by a second Information Specialist. Peer review considered the appropriateness of the strategy for the review scope and eligibility criteria, inclusion of key search terms, errors in spelling, syntax and line combinations, and application of exclusions.

Figure A.1: Search strategy for Ovid MEDLINE® ALL

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3.2.2 Resources searched

The literature search was conducted in MEDLINE(R) ALL using the OvidSP interface. The MEDLINE results were downloaded in a tagged format and loaded into bibliographic management software (EndNote).

The MEDLINE search was supplemented by the following search activities:

- Contact with CF Trust. CF Trust was asked to supply citation details for any additional studies they knew to be relevant.
- Targeted web-searching. This was conducted to identify further supporting evidence for Question Two in response to an identified literature gap.
- Reference list searching. When a paper eligible for full-text review referenced another potentially eligible publication, this reference was identified and screened in the same way as the MEDLINE search results.

3.3 Data synthesis

Potentially eligible studies were identified by checking the title and abstract of each study against the eligibility criteria of the review. This list of potentially eligible studies was further narrowed down by checking the full text of studies. In collaboration with CF Trust a list of the most relevant and recent studies was decided upon and included in this report.

4 Results

4.1 Results of the literature search

The MEDLINE search was conducted on February 4th, 2025. In total 602 results were retrieved from the MEDLINE search and supplementary search approaches (Table 4.1). These results were then assessed for relevance.

Table 4.1: Literature search results

Resource	**Number of records identified**
Databases	
MEDLINE ALL	577
Total records identified through database searching	577
Other sources	
Targeted web-searching	7
Reference list searching	18
Total additional records identified through other sources	25
Total number of records retrieved and assessed	**602**

494 records were excluded following title and abstract review. Therefore, 96 records were reviewed at full text. A total of 12 full text records were not freely available for 12 records. However, based on title and abstract screening, these records were less relevant to the research questions than other available texts and therefore full text review was not pursued.

29 full texts were eligible and relevant to Question One. In collaboration with CF Trust, these were narrowed to the 17 documents that were most relevant for inclusion in this review. This selection was based on consideration of the research question, number of participants and measured exposures and outcomes criteria.

There were no records from the MEDLINE search that met all eligibility criteria for Question Two. However, 8 full texts were considered partially eligible and were included in this review. These were supplemented with the 5 most relevant results of the targeted web-searching, leading to a total of 13 resources included for Question Two.

In total, 30 resources were included in this review.

4.2 Results: Question One

4.2.1 Effect of indoor air quality on people with cystic fibrosis

Carson et al.'s US-based study was the largest study included in this review that investigated the effects of indoor air quality on people with CF [4]. The study compared outcomes between people with CF who were exposed to different types of indoor air pollution to people with CF who were not exposed. The study found that exposure to second-hand smoke (SHS) or forced hot air (a type of central heating system where air from inside the house is drawn in, heated and redistributed through air ducts) was associated with a faster rate of lung function decline in children and adolescents (an increase of 0.60% and 0.46% FEV_1 predicted per year, respectively). In comparison, exposure to a wood stove or a fireplace did not have a significant effect on the rate of lung function change in this age group.

In the adult age group, the study found that exposure to SHS was associated with a 42% higher annual hospitalisation rate in adults. Exposure to forced hot air, a wood stove or a fireplace did not significantly affect CF outcomes (including rate of lung function change, rate of pulmonary exacerbations and rate of hospitalisations) in this age group. Overall, this study demonstrates that exposure to some sources of indoor air pollution, including SHS and forced hot air, is associated with poorer clinical outcomes in people with CF, compared to people with CF who were not exposed.

Two studies explored the relationship between indoor mould exposure, fungal colonisation of the airway in people with CF and CF outcomes [25, 26]. Mould is a type of fungus, and indoor mould exposure is of interest because fungal spores can be breathed in, which may result in infection [25, 26]. One study used electrostatic dust fall collectors to measure the amount and types of fungi in the homes of 16 people with CF [26]. This study found that a particular type of mould called *Aspergillus fumigatus* (*A. fumigatus*) was present in 15 out of the 16 homes. Additionally, the concentration of *A. fumigatus* was higher in the homes of people with allergic bronchopulmonary aspergillosis (ABPA), a complication of infection with this type of fungus [26].

The remaining study included 61 people with CF, 49% of whom had a positive fungal airway culture [25]. The study found that exposure to indoor mould at home was associated with a five times greater likelihood of having a positive fungal airway culture. They also found that those younger than 30 with a positive fungal culture had lower lung function measurements than those with a negative fungal culture. The authors note that the clinical significance of fungal airway colonisation in people with CF is uncertain [25]. Researchers have recommended further study in this area, to better understand the potential risks and inform risk-minimisation strategies (for example, home cleaning or refurbishing) [25, 26].

4.2.2 Effect of outdoor air quality and environmental factors on people with cystic fibrosis

4.2.2.1 Outdoor air quality

Eight studies investigated the effect of outdoor air quality parameters on outcomes for people with CF. The outcomes measured included pulmonary exacerbations (these are intermittent episodes of worse lung symptoms [27] and were assessed in 4 studies [28-31]), lung function (assessed in 3 studies [28, 32, 33]) and pathogen acquisition (assessed in 2 studies [34, 35]).

Pulmonary exacerbations

Goss et al. were the first to report the association between increasing annual average exposure to air pollutants and adverse CF outcomes [28]. Their US-based study found that as average annual exposure increased, there was an associated increased risk of pulmonary exacerbations. For each increase of 10micrograms/m^3 in PM_{10} or $PM_{2.5}$ the odds of a person experiencing two or more pulmonary exacerbations increased by 8% (95% CI 2 to 15%) and 21% (95% CI 7 to 33%). For each increase of 10 parts per billion (ppb) in ozone the odds increased by 10% (95% CI 3 to 17%). The association between increasing ozone concentration and increased risk of pulmonary exacerbations has also been seen in research from Brazil and Belgium [29, 30]. Research from Belgium also found that increased levels of PM_{10} and nitrogen dioxide (NO_2) were associated with a significantly higher risk of having a pulmonary exacerbation [30].

Conversely, Jassal et al. did not find that ozone and $PM_{2.5}$ exposure differed between groups that had two or more, or one or fewer, pulmonary exacerbations [31]. However, this was the first published study to report on how the distance between address and traffic exposure influences CF outcomes. Motor vehicles are a substantial source of air pollution and areas closer to highways and major roads are more affected by traffic emissions [36]. This study found that there was a significant relationship between residential proximity to a major road and the odds of having two or more exacerbations: for each 1000m that a residence was closer to a major road, the odds of having two or more exacerbations were 6.7 times greater. Notably, the study did not find a significant relationship between exacerbation frequency and residential proximity to a motorway.

Lung function

Goss et al. found that greater average annual exposure to $PM_{2.5}$ was associated with a fall in lung function. After adjusting for confounders, this study found that every 10microgram/m^3 increase in $PM_{2.5}$ was associated with a 24mL reduction in FEV_1 (95% confidence interval 7 to 40mL) [28]. In 2023, another US-based study found that higher three-month exposure to elemental carbon attributable to traffic sources (ECAT) was associated with a faster decline in lung function [32]. Increasing ECAT by 0.1ug/m3 was associated with a more rapid decline in FEV_1 of 0.104% predicted per year, when other environmental exposures, clinical and demographic characteristics were accounted for. This aligns with a study of social-environmental adversity in people with CF, which found that traffic-related air pollution was a driver of social-environmental adversity [33].

Pathogen acquisition

US-based studies by Psoter et al. have found that higher levels of $PM_{2.5}$ are associated with acquisition of Methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* (*P. aeruginosa*) acquisition in young children with CF [34, 35]. Each 10 microgram/m^3 increase in $PM_{2.5}$ exposure was associated with a 56% increase in the risk of acquiring MRSA (HR = 1.56; 95% CI: 1:13, 2.14)) and a 24% increase in the risk of acquiring *P. aeruginosa* (95% CI 1% to 51%).

4.2.2.2 Environmental factors

Six studies investigated the effect of environmental factors on outcomes for people with CF. Five of these focussed on temperature and one focussed on saturated vapour pressure.

Studies including US and Australasian populations with CF have found that living in warmer areas was associated with higher rates of *P. aeruginosa* colonisation [6, 37], acquisition of *P. aeruginosa* at a younger age [6] and lower lung function compared to people with CF living in colder areas [6]. An increase in temperature of 1ºC was associated with a 13% increase in the risk of acquiring *P. aeruginosa* (HR 1.13, 95% CI 1.08 to 1.17) [37]. One Australian study found an association between higher average maximum annual temperatures and incidence of both first and recurrent *P. aeruginosa* acquisition, but this was not statistically significant [38]. The relationship between temperature and lung function has been found to be partially explained by the presence of *P. aeruginosa,* mucoid *P. aeruginosa* and MRSA [6, 39].

Additionally, research in Brazil found that for infants with CF, warmer temperatures were associated with a fall in sodium levels (for every 1ºC increase in temperature, sodium concentration fell by 0.53mmol/L)[5].

A US-based study reported that higher annual average saturated vapour pressure (a measure of how much moisture the air can hold at a given temperature) was associated with an increased likelihood of nontuberculous mycobacteria colonisation (NTM) [40]. Further, saturated vapour pressure is highly correlated with temperature. The authors suggest that the higher NTM risk could be due to greater numbers of mycobacteria in the outside air, or due to more moist indoor conditions that support bacterial growth [40]. NTM is an important group of bacteria for people with CF because it can cause lung infections that can be difficult to treat; treatment usually lasts for at least one year and requires at least three antibiotics [41].

4.3 Results: Question Two

There are several general recommendations to protect against poor air quality that could be employed by people with CF.

4.3.1 Individual-level interventions

4.3.1.1 Indoor air quality

Interventions relating to indoor air quality are summarised in Table 4.2.

Table 4.2: Interventions to improve indoor air quality

Monitoring	▪ Monitor indoor levels of carbon monoxide and radon [42, 43]. High radon levels can be addressed by building works, such as additional ventilation or a radon sump [44]. ▪ Microbiological monitoring has benefitted outcomes in people with asthma [45]. However, it has not yet been evaluated in people with CF [46].
Ventilation	▪ Ventilate homes by opening appropriate windows and using extractor fans [42, 47]. However, it is recommended to keep windows and outside doors facing busy roads shut, especially during periods of heavy traffic [8, 48]. ▪ Adequate ventilation may be particularly useful after activities such as physiotherapy, which have been associated with high levels of airborne bacteria after the activity [49].
Appliances and heating	▪ Ensure that fuel-burning appliances are fitted properly, adequately ventilated and serviced regularly [42]. ▪ Avoid using open fires for heating if possible [42]. ▪ Follow manufacturer instructions for the cleaning, servicing and filter changing of forced hot air central heating systems [4].
Products, cleaning and indoor mould	▪ Avoid smoking [42]. ▪ Use cleaning and personal care products with mild chemicals and smells, or unscented varieties [42]. ▪ Promptly address any causes of damp or mould to minimise exposure [50]. Currently, there is insufficient evidence to support the use of dehumidifiers and air filters to reduce indoor mould growth [50]. ▪ Indoor reservoirs of fungi include pets, pot plants, dishwashers and humid indoor environments [46]. Minimising exposure to these factors may reduce exposure to, and therefore acquisition of, fungal pathogens [51].

4.3.1.2 Outdoor air quality

Interventions relating to outdoor air quality are summarised in Table 4.3. Importantly, while an association between air quality and CF outcomes has been demonstrated (Section 4.2.2), the expert opinion from a review by Szczesniak et al. was that current evidence at the time of publication (2020) did not necessarily support moving to a different area to avoid potentially detrimental environmental exposures [52].

Table 4.3: Interventions to protect against poor outdoor air quality

Monitoring	▪ Stay up-to-date with local air pollution levels and adjust outdoor activities in accordance with the level – for example, avoiding travel or strenuous outdoor activity during times with high levels of air pollution [8, 53].
	▪ In the UK, air pollution information can be accessed via:
	  ▪ The DEFRA UK Air Information Resource, which provides an air pollution forecast and related health advice [15].
	  ▪ Social media updates from DefraUKAir on Twitter [54].
	  ▪ A freephone air pollution helpline (0800 55 66 77).
	  ▪ Text messaging alert services such as AirText for London and the South East [55], airAlert for the South East of England [56] and Know and Respond for Scotland [57].

Masking	▪ Wear a face mask when outside – a simple mask is estimated to halve exposure to air pollution, and a well-fitted mask (for example, an N95 mask) will further reduce exposure [48].
Adjust activities	▪ Choose walking routes that are further away from busy roads, even if only by a few metres [47, 48, 53]. ▪ Time your outside activities to periods when there are fewer vehicles on the roads, to avoid the peaks in air pollution associated with traffic [9, 48, 53]. ▪ Consider changing from outdoor physical activity to indoor physical activity when levels of air pollution are higher [53].
Medication	▪ If prescribed and applicable, keep a reliever inhaler with you and use as instructed [8, 53][1].

Abbreviations: DEFRA – Department for Environment, Food and Rural Affairs; UK – United Kingdom.

[1] Many people with CF use a bronchodilator inhaler to improve lung symptoms [58, 59]

Many resources highlighted actions that can be taken to reduce an individual's contribution to air pollution. These actions include:

- Using public or active transport where possible, in preference to driving a private vehicle, to reduce the amount of air pollution created [8, 47, 53, 60].
- Driving an electric car rather than a diesel or petrol-powered car [60]. However, using public or active transport remains preferable because electric vehicles still produce polluting particulate matter from road-surface wear to tyres and brakes [53].
- Using an electricity provider that uses renewable energy sources [60].
- Where applicable, supporting environmentally-sustainable farming methods to reduce farming emissions affecting air quality [53].
- Avoiding burning wood at home, due to the associated, substantial, emission of particulate matter [53].

4.3.2 Community- and policy-level interventions

Resources acknowledged the importance of upstream actions in improving and protecting air quality. Community-level actions included engagement in policy submissions, raising local awareness and supporting existing efforts to protect air quality (for example, low emission zones) [8, 47, 60].

Policy-level work is of particular importance [9]. Two potential areas that policies could focus on are:

- The decarbonisation of energy and transport sectors – for example, by supporting renewable energy sources and electric cars, and phasing out fuels like coal and cars requiring petrol and diesel [8, 47, 60].
- Supporting the accessibility of public transport and active travel, to reduce the requirement for people to drive [8, 47, 60].

5 Discussion

5.1 There is limited evidence on the effects of indoor air quality on people with CF

Most included studies focussed on exposure to outdoor air pollution and climate factors (n=14, 93.3%). Three studies investigated the effects of indoor air quality [4, 25, 26].

The literature search identified two additional studies which included some measures of indoor air quality. These were not prioritised for inclusion due to their limited investigation of factors relevant to this review. One was a study evaluating risk factors for lung function decline in young children with CF that included ‘wood-burning stove’ as an exposure [61]. This study did not find a significant difference in lung function between children who had a wood-burning stove in their home compared to those who did not. The other study explored environmental risks for NTM, but the only factors relevant to this review were the type of air conditioner and the use of a humidifier or vaporiser, neither of which was associated with a significant change in the odds of an NTM infection [62].

This literature gap pertaining to the effects of indoor air quality has been highlighted previously [48]. This gap may reflect differences in data acquisition processes for indoor and outdoor air quality measures. Many of the included studies sourced air quality data from national monitoring systems and linked these measurements to participants’ residential addresses. Conversely, measuring exposure to indoor air quality would require either self-report (as in Carson et al, 2022) or objective measurement within homes, which is a recommended area for future research [4].

While both indoor and outdoor air quality are undoubtedly important, the amount of time that people tend to spend indoors and the lack of research highlight a need for future studies to investigate the effects of indoor air quality on clinical outcomes for people with CF [8, 46]. Further research in this area is essential to better understand the risks of poor indoor air quality and, subsequently, inform risk minimisation strategies. The scope of potential indoor air quality research is broad. It includes both private homes and public spaces (for example, healthcare centres, schools, shopping centres and some workplaces). Both private and public spaces will need to be considered in future research efforts, to facilitate effective interventions.

5.2 Higher levels of outdoor air pollution are associated with acquisition of some pathogens

Two US-based studies found that higher levels of $PM_{2.5}$ were associated with a higher risk of young children with CF acquiring MRSA and *P. aeruginosa* [34, 35]. MRSA infection is likely to negatively impact lung function in people with CF and reduces the range of antibiotic treatment options, due to its innate antibiotic resistance [63]. *P. aeruginosa* can similarly cause lung infections in people with CF and is associated with increased morbidity and mortality [64]. It also has the potential to become antimicrobial-resistant and difficult to treat [65]. Limited strategies to prevent these infections are available [34, 35]. Therefore, identifying the link between higher levels of outdoor air pollution and acquisition of these two important pathogens is important because it may inform prevention strategies. The authors highlight the need for future research to identify other risk factors for these infections [34, 35].

5.3 Climate change may have unique impacts for people with CF, given the associations between increasing temperatures and adverse CF outcomes

Studies included in this review have highlighted associations between warmer temperatures and increased risk of colonisation with certain pathogens, lower lung function and low sodium levels in infancy [5, 6, 37, 38]. Low sodium levels can lead to vomiting, dehydration, anorexia, poor weight gain, confusion, reduced level of consciousness and seizures [66], which is particularly concerning for infants with CF living in warm climates without access to household temperature control [5]. Global warming associated with climate change is therefore of particular concern to people with CF, as the rise in temperatures may heighten the risks identified by these studies. In conjunction with research to establish effective interventions to protect people with CF against the adverse outcomes associated with warmer temperatures, population-wide actions to mitigate both global warming and climate change are essential.

5.4 There is limited evidence regarding CF-specific interventions to reduce exposure to air pollution

In the 577 results of this literature search, there were no records that quantified the effect of interventions to protect people with CF against the negative effects of poor air quality. This emphasises the previously identified literature gap [47]. While some studies referred to intervention studies among other population groups (for example, people with asthma [45, 67]), CF is a distinct clinical condition with distinct pathogenesis. Therefore, the generalisability of findings from populations with other medical conditions may be limited.

It is plausible that some of the interventions discussed in Section 4.3 apply to people with CF as well as the general population. However, research to investigate intervention efficacy for people with CF would facilitate the development of more personalised advice and mitigation strategies. Further research in this area is required. Specific research recommendations include:

- The use of large pollution-exposure datasets generated by citizen data collection to identify evidence-based strategies for avoiding polluted air [47, 68].
- The use of more precise measures of environmental exposures to explore the influence on CF-related outcomes [52].

6 Conclusion

This review has identified a range of air quality and environmental parameters, including temperature, residential proximity to major roads and levels of specific pollutants, that are associated with adverse outcomes and increased morbidity among people with CF. These outcomes include faster rates of lung function decline [4, 28, 32, 33], higher annual hospitalisation rates [4], increased likelihood of pulmonary exacerbations [28-31] and a greater risk of acquiring or colonisation by MRSA, *P. aeruginosa* and NTM [6, 34, 35, 37, 40].

While a range of resources discussed potential interventions to mitigate the effects of poor air quality, no resources were found that quantified the efficacy of interventions for people with CF. Interventions covered both indoor and outdoor air quality and ranged from individual-level actions to community- and policy-level recommendations.

Researchers acknowledge that evidence linking air pollution to CF outcomes is limited, particularly in comparison to the volume of research examining the effects of air pollution on patients with asthma [52, 69]. In addition, this review highlighted literature gaps regarding the effects of indoor air quality parameters and the efficacy of interventions to protect people with CF against the negative effects of poor air quality. Further research into these areas would help to inform personalised management and recommendations for people with CF.

Overall, despite the need for further research, evidence to date suggests that there is an association between poorer air quality and increasing morbidity in people with CF.

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Appendix A: Ovid MEDLINE search strategy

A MEDLINE (OvidSP) search strategy was designed to identify studies that report on CF in the context of air quality. One search strategy was used to inform both questions. Search strategy design reflected the pragmatic review context. The pragmatic approach was discussed and agreed at protocol stage.

Details of the final MEDLINE strategy are presented in Figure A.1 below. The strategy comprised two concepts:

- CF (search lines 1 to 3).
- Air quality (search lines 4 to 52).

The concepts were combined as follows: CF AND air quality.

The search terms for the air quality concept (search lines 4 to 52) included a pragmatic selection of terms relating to the following:

- Non-specific air quality (search lines 4 to 7).
- Climate change (search lines 8 to 18).
- Non-specific pollution (search lines 19 to 21).
- Examples of specific air quality parameters identified by the research team, including:
    - Particulate matter (PM1, PM2.5, and PM10) (search lines 22 to 26).
    - Microbial content (search lines 27 to 36).
    - Greenhouse gases (carbon dioxide, nitrous oxide, methane, ozone) (search lines 37 to 47).
    - Other air pollutants (benzene, black carbon, butadiene, formaldehyde, lead, nitrogen dioxide, other heavy metals, polycyclic aromatic hydrocarbons, radon, sulphur dioxide, toxic organic micro-pollutants, volatile organic compounds) (search lines 48 to 52).

The strategy was devised using a combination of subject indexing terms and free text search terms in the Title, Abstract and Keyword Heading Word fields. The search terms for the concepts were identified through discussion within the research team, scanning background literature, and browsing database thesauri.

The strategy excluded animal studies from MEDLINE using a standard algorithm (search line 54). The strategy also excluded some publication types which were unlikely to yield relevant study reports (editorials, news items and case reports) and records with the phrase 'case report' in the title (search line 55).

Reflecting the eligibility criteria, the strategy was restricted to studies published in English language (search line 57). No date restriction was applied.

The final Ovid MEDLINE strategy was peer-reviewed before execution by a second Information Specialist. Peer review considered the appropriateness of the strategy for the review scope and eligibility criteria, inclusion of key search terms, errors in spelling, syntax and line combinations, and application of exclusions.

Figure A.1: Search strategy for Ovid MEDLINE® ALL

1 *Cystic Fibrosis/ (35524)
2 cystic fibros*.ti,ab,kf. (54109)
3 or/1-2 (57107)
4 air/ and environmental exposure/ (418)
5 (air adj6 (quality or qualities)).ti,ab,kf. (23132)
6 (air and (environment* adj3 expos*)).ti,ab,kf. (4870)
7 or/4-6 (27848)
8 climatic processes/ or climate change/ or climate/ (57170)
9 (climate* or climatic*).ti,ab,kf. (178796)
10 global warming/ (5059)
11 global warming.ti,ab,kf. (16038)
12 weather/ or exp extreme weather/ (13395)
13 weather*.ti,ab,kf. (39419)
14 air/ and exp temperature/ (2355)
15 (air adj6 temperature*).ti,ab,kf. (18495)
16 (temperature* adj3 (chang* or extrem* or increas* or rise or rises or rising or rose or drop* or reduc*)).ti,ab,kf. (127028)
17 (heatwave* or heat wave*).ti,ab,kf. (4710)
18 or/8-17 (354848)
19 environmental pollution/ or air pollution/ or air pollution, indoor/ or environmental pollutants/ or air pollutants/ (166277)
20 (pollut* or micropollut*).ti,ab,kf. (247716)
21 or/19-20 (339382)
22 particulate matter/ (32704)
23 particulate*.ti,ab,kf. (71170)
24 ((fine or ultrafine) adj2 (fiber* or fibre* or particle*)).ti,ab,kf. (11292)
25 (pm1 or pm-1 or pm10 or pm-10 or pm25 or pm-25 or pm2-5 or pm-2-5).ti,ab,kf. (32381)
26 or/22-25 (97108)
27 air microbiology/ (8618)
28 (environmental monitoring/ or environmental exposure/ or inhalation exposure/) and exp fungi/ (3232)
29 (environmental monitoring/ or environmental exposure/ or inhalation exposure/) and (bacteria* or fungal* or fungi or fungus* or microb* or mold or molds or mould* or spore or spores or viral or virus*).ti,ab,kf. (17048)
30 ((air or airborne) and (fungal* or fungi or fungus* or mold or mold or mould* or spore or spores)).ti,ab,kf. (8701)
31 ((domestic* or dwelling* or home or homes or house* or indoor*) and (fungal* or fungi or fungus* or mold or mold or mould* or spore or spores)).ti,ab,kf. (9274)
32 (expos* adj6 (fungal* or fungi or fungus* or mold or molds or mould* or spore or spores)).ti,ab,kf. (4664)
33 ((air or airborne) adj6 (bacteria* or microb* or viral* or virus*)).ti,ab,kf. (7436)
34 ((domestic* or dwelling* or home or homes or house* or indoor*) adj6 (bacteria* or microb* or viral* or virus*)).ti,ab,kf. (9812)
35 (expos* adj2 (bacteria* or microb* or viral* or virus*)).ti,ab,kf. (11186)
36 or/27-35 (63838)
37 greenhouse gases/ or greenhouse effect/ (9021)
38 (greenhouse or green house).ti,ab,kf. (39966)
39 (environmental monitoring/ or environmental exposure/ or inhalation exposure/ or gas poisoning/) and carbon dioxide/ (2372)
40 (environmental monitoring/ or environmental exposure/ or inhalation exposure/ or gas poisoning/) and (nitrogen oxides/ or nitrous oxide/) (1887)
41 methane/ (24207)
42 exp ozone/ (18974)
43 ((air or airborne or emission* or emitt* or expos* or gas or gases) adj6 (carbon dioxide* or carbonic anhydride*)).ti,ab,kf. (9349)

44 ((air or airborne or emission* or emitt* or expos* or gas or gases) adj6 (nitric oxide* or nitrogen oxide* or nitrous oxide* or nitrogen protoxide*)).ti,ab,kf. (9426)
45 methane.ti,ab,kf. (39396)
46 ozone*.ti,ab,kf. (29297)
47 or/37-46 (133581)
48 (environmental monitoring/ or environmental exposure/ or inhalation exposure/ or gas poisoning/) and (benzene/ or butadienes/ or carbon monoxide/ or carbon monoxide poisoning/ or formaldehyde/ or exp lead poisoning/ or lead/ or nitrogen dioxide/ or exp radon/ or soot/ or sulfur dioxide/) (19650)
49 ((air or airborne or emission* or emitt* or expos* or gas or gases) adj6 (actinon* or benzene* or benzol* or butadiene* or black carbon* or carbon black* or carbon monoxide* or cyclohexatriene* or formaldehyde* or formalin* or formol* or lampblack* or lamp black* or lead or methanal* or nitrogen dioxide* or nitrogen peroxide* or oxomethane* or radon* or soot or sulfur dioxide* or sulphur dioxide* or sulfurous anhydride* or sulphurous anhydride* or thoron*)).ti,ab,kf. (44915)
50 (environmental monitoring/ or environmental exposure/ or inhalation exposure/) and (exp polycyclic aromatic hydrocarbons/ or volatile organic compounds/ or exp metals, heavy/ or exp heavy metal poisoning/) (51831)
51 ((air or airborne or emission* or emitt* or expos* or gas or gases) adj6 (aromatic polycyclic hydrocarbon* or aromatic polynuclear hydrocarbon* or pah or pahs or polycyclic aromatic hydrocarbon* or polynuclear aromatic hydrocarbon* or tomp or tomps or volatile organic compound* or voc or vocs or heavy metal*)).ti,ab,kf. (21478)
52 or/48-51 (112508)
53 3 and (7 or 18 or 21 or 26 or 36 or 47 or 52) (657)
54 exp animals/ not humans/ (5304461)
55 (news or editorial or case reports).pt. or case report.ti. (3458276)
56 53 not (54 or 55) (596)
57 limit 56 to english language (577)

Key to Ovid symbols and commands:

*	Unlimited right-hand truncation symbol
ti,ab,kf.	Searches are restricted to the Title (ti), Abstract (ab) and Keyword Heading Word (kf) fields
adj	Retrieves records that contain terms next to each other (in the shown order)
adjN	Retrieves records that contain terms (in any order) within a specified number (N) of words of each other
/	Searches are restricted to the Subject Heading field
exp	The subject heading is exploded
*	The subject heading is searched as a major descriptor only
pt.	Search is restricted to the publication type field
or/1-2	Combines sets 1 to 2 using OR