Air quality and COVID-19
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Air pollution in COVID-19 epicentres in China and Italy

- NO₂ level falls in China and Italy during lockdown
Air pollution – Ogen, Sci Tot Env 2020 (reported 20 April)

78% of COVID-19 deaths across four countries were in the most polluted regions
Epidemiology of COVID-19 mortality

COVID death rates around 11% higher for each year older, double every 7 years. Men have double risk of women the same age.

COVID population death rates – log and linear scales

Based on 3,364 COVID–19 deaths in March, registered by Apr 6 (E+W)
18 deaths under 35 not modelled
Poisson regression with over-dispersion

RISK FACTORS other than age and sex

• Comorbidity
  • Hypertension
  • Diabetes
  • Heart disease
  • Kidney disease
  • Chronic respiratory disease
  • Dementia
• Obesity
• Non-white ethnicity – confounded by comorbidities, deprivation, occupation, geographic location (e.g. cities)

David Spiegelhalter, ONS England & Wales data
How might air quality impact on COVID-19?

**INDIRECT**

Increases risk of chronic disease. Chronic disease increases risk of severe COVID-19.

**DIRECT**

Increases infectivity

- Virus carriage
- General mechanisms e.g. lung inflammation
- Specific mechanisms e.g. virus receptors in the lungs, surfactant

Increases risk of severe disease once infected

- General mechanisms - inflammation in lung and body systems
- Specific mechanisms e.g. via infectivity and higher infecting dose

Expect risks to be similar to previous studies of air pollution & mortality

Interaction:
- Expect higher infection risk in polluted areas
- Expect higher case-fatality in polluted areas
Does air pollution enable carriage / persistence of SARS-CoV-2?

Role of aerosol transmission not established in community settings
- In rooms/inside spaces
- Outside
- From toilet flushing!

Setti et al. Preprint, reported UK Guardian 24 April 2020
https://www.medrxiv.org/content/10.1101/2020.04.15.20065995v2
Presence of SARS-CoV-2 viral RNA on 8 of 34 filters for PM10 in Bergamo
Could air pollution increase infectivity of SARS-CoV-2?

Figure from Alifano et al. Renin-angiotensin system at the heart of COVID-19 pandemic. *Biochimie*, 2020
Are there epidemiological studies on air quality and COVID-19?

• Where do I look?
  - PubMed
  - ?Medrxiv

• Outcome measures are not well understood and may be subject to bias [www.medrxiv.org/content/10.1101/2020.05.04.20090506v3](www.medrxiv.org/content/10.1101/2020.05.04.20090506v3)

• Methodological challenges relating to disease propagation especially for short-term (time-series) studies, where lockdown impacts on air pollution as well as transmission
Exposure to air pollution and COVID-19 mortality in the United States: A nationwide cross-sectional study

Xiao Wu, Rachel C. Nethery, Benjamin M. Sabath, Danielle Braun, Francesca Dominici
doi: https://doi.org/10.1101/2020.04.05.20054502

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

Abstract

Objectives: United States government scientists estimate that COVID-19 may kill tens of thousands of Americans. Many of the pre-existing conditions that increase the risk of death in those with COVID-19 are the same diseases that are affected by long-term exposure to air pollution. We investigated whether long-term average exposure to fine particulate matter (PM$_{2.5}$) is associated with an increased risk of COVID-19 death in the United States.

Design: A nationwide, cross-sectional study using county-level data. Data sources: COVID-19 death counts were collected for more
<table>
<thead>
<tr>
<th>Wu</th>
<th>Liang</th>
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</thead>
<tbody>
<tr>
<td><strong>Death counts from Johns Hopkins database</strong></td>
<td><strong>Deaths and cases from New York Times, USAFACTS, and 1Point3Acres.com databases</strong></td>
</tr>
<tr>
<td>All up to April 22</td>
<td>Jan 22-April 29</td>
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<tr>
<td>3,087 counties (98% population)</td>
<td>3122 US counties</td>
</tr>
<tr>
<td><strong>45,817 deaths</strong></td>
<td>58,489 deaths and 1,027,799 cases</td>
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<tr>
<td><strong>PM$_{2.5}$ 2000-2016</strong></td>
<td><strong>NO$<em>2$, PM$</em>{2.5}$, Ozone 2010-2016</strong></td>
</tr>
<tr>
<td>Negative binomial mixed model, random intercept by state</td>
<td>Zero-inflated negative binomial mixed model, random intercept by state</td>
</tr>
<tr>
<td>Comprehensive confounder adjustment + quantified unmeasured confounder bias</td>
<td>Comprehensive confounder adjustment including ‘spatial autocorrelation’</td>
</tr>
<tr>
<td>6 secondary analyses, 68 sensitivity analyses</td>
<td>4 sets of sensitivity analyses</td>
</tr>
<tr>
<td><strong>PM$_{2.5}$ associated with +8% (95% CI: 2% to 15%) mortality rate per 1 $\mu$g/m$^3$ increase</strong></td>
<td><strong>PM$_{2.5}$ associated with +10.8% (95% CI: -1.1% to 24.1%) mortality rate per IQR increase (3.4 $\mu$g/m$^3$)</strong></td>
</tr>
<tr>
<td><strong>NO$_2$ associated with +11.2% (95% CI 3.4% to 19.5%) mortality rate per IQR increase (4.6 ppb)</strong></td>
<td><strong>Ozone – no association</strong></td>
</tr>
<tr>
<td><strong>Coefficient is 11x higher than for all-cause mortality in a previous analysis</strong></td>
<td><strong>One IQR reduction in NO$_2$ would have avoided 4,181 deaths</strong></td>
</tr>
</tbody>
</table>

Average PM2.5 levels were 8.4 mcg/m3 (SD 2.5)
Inference from epidemiological studies

- Epidemiological studies are observational not experimental
  
  *Experimental studies can stand alone if needed e.g. RCT of a specific drug*  
  *Results from observational studies usually viewed in the light of (all) other knowledge*

- Natural experiments can be very useful
- Ecological (area-level) studies (e.g. Wu, Liang) are often used in initial assessments
- Individual follow-up studies (cohort studies) provide the highest quality observational evidence but are time-consuming and can be expensive
It would be surprising NOT to see a link between air pollution and COVID-19

- Air pollution kills 4.2 million people per year (WHO)

- PM$_{2.5}$ caused an estimated 7.6% of total global mortality in 2015 (Global Burden of Disease, Cohen et al, Lancet 2017)

- 91% of the world’s population live in places where air quality exceeds WHO guideline limits
What can we learn from SARS?

- Standard public health infection control measures controlled the disease (before genotyping/vaccine)
- A high profile case-control Lancet study early on (Seto et al, 2003) established importance of PPE to prevent healthcare worker infection – but masks most important!
- Clusters but also some super-spreaders
- A vaccine for SARS was not developed
  - Some reports suggest vaccine candidates made the disease worse
- One study on SARS case-fatality and air pollution:
  - Cui et al, Env Health 2003.
  - Hospital in-patient data: 349 deaths, 5327 cases
  - No control for confounders so not very informative
  - SARS patients from regions with high APIs were twice as likely to die from SARS compared to those from regions with low APIs. (RR = 2.18, 95% CI: 1.31–3.65)

[For Influenza pandemics see CDC website https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html]
COVID-19 in LMICs – some good news, some bad news

Countries with an established strong public health workforce have been able to control outbreaks (e.g. Thailand with local community health workers in every village).

Public health measures are low tech: Restriction of contacts, limit/organise movements outside the house and WASH (water sanitation hygiene) or using alternative to water to clean hands.

Sharing guidance & hotlines e.g. WHO guidance on keeping mildly ill patients out of hospital.

Limited testing, PPE etc. – logistics (lockdown), test charges

Migrant workers - contact tracing, disease spread

Stigma for diagnosed cases - education

Fake news - risk communication & education
Conclusions

1. Air pollution is associated with all-cause mortality and many specific causes of death including pneumonia and cardiovascular disease – it is unlikely there is no association with COVID-19.

2. Two good quality area-level studies in the US suggest associations of COVID-19 with traffic related air pollution, but further studies are needed including mechanistic studies.

3. Evidence to date does not warrant specific public health measures against COVID-19 in high air pollution areas that are different from low pollution areas.

4. Epidemiological data to date have many gaps – understanding asymptomatic disease, risk factors for disease progression, data from developing countries, key components of PPE, aerosol disease transmission etc..

5. Well-functioning public health systems can achieve low disease transmission including in LMICs.

6. Lockdowns break transmission but may increase mortality from impacts on healthcare & economy and/or decrease it through improvements in air quality, road traffic accidents etc.
Thank you!