Methodological considerations for studying an association between air pollution and COVID-19

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COVID First Outbreaks in Canada

Edmonton

Doctors who contracted COVID-19 at a bonspiel dug into how they got it. Here's what they found

Edmonton tournament was a superspreader event linked to at least 54 cases

Newfoundland and Labrador reports Atlantic region’s first COVID-19 death

As of Sunday, Newfoundland and Labrador was reporting 135 confirmed cases. It has attributed the growth of infections to a clustering of cases linked to two services held earlier this month at Caul’s Funeral Home in St. John’s.
Risk factors for COVID-19 incidence and mortality

- Person to person contact
- Public health measures
- Travel
- Occupation
- Indoor transmission
- Outdoor Air pollution?
  - Direct effect vs mediating role
  - Chronic and acute exposure
Air Pollution and Covid - Background

- Ecological study of ~3000 US counties
- Average county level exposure 2000-2016
- Magnitude of association (mortality):
  - April 2020: 1 µg/m$^3$ increase PM2.5 $\triangleleft$ 15% COVID
  - Nov 2020: 1 µg/m$^3$ increase PM2.5 $\triangleleft$ 11% COVID
  
  Wu et al, Science Advances, 2020

- Similar design for Canada for COVID-19 incidence found a 7% increase per 1 µg/m$^3$

Stieb et al, Environmental Research, 2020
Methodological challenges

Villeneuve and Goldberg, Env Health Perspect 2020

• Incomplete ascertainment of COVID-19 (incidence and mortality)
• Ecological study design
• Differential detection by time and space
  • Asymptomatic cases
• Differences in transmissibility across variants of concern
• Spatiotemporal differences in public health measures
• Correlated data
Ecological studies

- Covid-19 cases influenced by a large number of factors
- Substantial variability in these factors within areas and over time
- Ecological studies unable to account for heterogeneity in risk factors
- Outcome ascertainment susceptible to bias
Timing on a pandemic curve

- Larger cities tended to be first areas impacted
- Likely introduces bias on studies of COVID-19 and air pollution
- Temporal trends can be influenced by many other factors
  - Public health measures
  - More transmissible variants
  - Season (indoor vs outdoor spread)
  - Pandemic fatigue
  - Super-spreader events
- **Implication: ecological studies yield risks that vary over time

CDC. MMWR Weekly / November 20, 2020 / 69(46);1753
Impact of longer study period – US county data

• Updated US county COVID-19 mortality analyses
• Same data sources as the Wu et al paper
• COVID mortality through March 1, 2021
• Updated findings:
  • Non-linear associations between PM2.5 and COVID-19 mortality
  • Positive association in small number of counties with higher PM2.5
• Interpretation:
  • County-level risk estimates changes over time
  • Questionable validity given ecological data

COVID-19 mortality rates by county level PM2.5, through March 2021
Ecological Data for Prevalent HIV and Ambient PM2.5 in the United States (2018)

- Modelled PM2.5 (2000 through 2016)
- Prevalent HIV in 2018 for US counties
- Findings suggest that increased PM2.5 associated with lower prevalence of HIV
- Can ecological data truly provide a valid answer?
Moving to a more highly resolved spatial scale

- Intra-urban studies offer some advantages to between cities comparisons
  - Screening/testing methods
  - Public health control measures
  - Higher spatial resolution of air pollution
  - Possible access to individual level data

- Recent example by Stieb et al for Toronto, Canada
  - increase of 7% increase in COVID-19 incidence for a IQR increase in ROS PM2.5

- Variables:
  - Time since first case, peak of epidemic
  - Neighbourhood measures of SES

AJRCC: https://doi.org/10.1164/rccm.202011-4142OC

Can within city studies inform on causality?

**Source of transmission matters**

- Example: Barrie, Ontario
- Outbreak in long term care facility
  - January/February 2021
  - 70 deaths
  - 200+ infected
- Accounted for most COVID-19 cases in Barrie at that time
- Outbreak was due to person to person contact in LTC home in middle of winter
Air Pollution and COVID-19
Barrie, Ontario

At Long Term Care Home
NO2 exposure (2016)= 13.3 ppb

At other postal codes in Barrie
NO2 exposure (2016)= 8.8 ppb
Other outbreaks

Cargill Meat Packers
>1500 COVID cases
~20% of Alberta’s total

Quebec gym
>450 COVID cases

Nunnery, Quebec City >100 cases
Outbreaks can be drivers of COVID-19 in cities

• Toronto outbreaks
  • 640 cases in Amazon factory
  • Multiple outbreaks in meat packing plants
  • 280 Canada Post workers
  • 45% of outbreaks tied to restaurants and bars (Sept 2020)
  • 20 homeless shelters (April 27)

• Workplace spread in essential workers and related risk factors:
  • Minority populations
  • Live intergenerational homes
  • Experience more barriers to testing, treatment, vaccination
  • Live in areas of higher air pollution
COVID-19 inequities in Ontario

- Neighbourhoods with the highest proportion of essential workers in non-healthcare settings experience a 3-fold higher incidence of SARS-CoV-2.
- Half of all COVID-19 cases in Ontario are within 20 per cent of neighbourhoods.
- Residents of neighbourhoods with the lowest risk of COVID-19 are 1.5 times more likely to have received at least one dose of a vaccine.
- Absence of policies to protect workers.
Air Pollution and COVID-19: Short-term ‘day to day’ studies

Challenges

• Ability to detect COVID-19 has changed over time
• Use of different screening tests
• Incomplete identification of cases
• Long latency intervals
• Changing guidelines around who gets tested
• Capacity in a given region to do tests
  • Changes over time
  • Set up of temporary testing centers based on need
  • Reluctance of some to seek treatment during surges
  • Return visits for hospitalization
• Many of these factors operate within and between regions
Guidelines for COVID-19 testing in Ottawa, Canada

<table>
<thead>
<tr>
<th>Date</th>
<th>Guidance for COVID-19 testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 5, 2021</td>
<td>Individuals (including young children) who are showing any sign(s) of COVID-19</td>
</tr>
<tr>
<td>October 1, 2020</td>
<td>Children who only have a runny nose, headache or sore throat can now return to school or daycare after 24 hours without a negative COVID-19 test result (as long as the symptoms are improving).</td>
</tr>
<tr>
<td>September 24, 2020</td>
<td>Testing for those &lt;br&gt;• With symptoms of COVID-19 &lt;br&gt;• Work or live in a setting that has a COVID-19 outbreak or have been exposed to a confirmed case of the virus. &lt;br&gt;• People with no symptoms of COVID-19 are not offered testing</td>
</tr>
<tr>
<td>March 14, 2020</td>
<td>Testing intended for those with &lt;br&gt;• Mild symptoms within 14 days of returning from international travel &lt;br&gt;• Have been in close contact with a confirmed case.</td>
</tr>
</tbody>
</table>
Ottawa Public Health – Who should be tested? (April 22, 2021)

• Showing symptoms
• You have been exposed to a person who tested positive for COVID-19:
• Long-term care, retirement homes, and other congregate settings
• You are a person who identifies as First Nations, Inuit or Métis; or
• You received a preliminary positive result through rapid testing;
• You require testing 72 hours before a scheduled (non-urgent or emergent) surgery (as recommended by your health care provider);
• You are a patient and/or their 1 accompanying escort travelling out of country for medical treatment;
• You are an international student that has passed their 14-day quarantine period;
• You are a farm worker;
• You are an educator who cannot access pharmacy-testing; or
• Targeted testing group (as per the Chief Medical Officer of Health)
Number of COVID tests done daily in Ottawa
Impacts of Vaccines

• Important consideration when trying to assess role of air pollution
• Differentially impact population subgroups
• Some vaccines may work better against some variants than other
• Policies for vaccinations ‘roll out’ vary regionally and temporally
• Decision making processes are continually evolving

• Is it possible to accurately identify a likely small ambient air pollution signal?
COVID-19 variants: changes over time

Figure 5. Number of confirmed COVID-19 cases and percent positive for mutations or VOCs: Ontario, February 7, 2021 to April 24, 2021
How relevant is outdoor air pollution for transmission of COVID-19?

• Odds of indoor transmission is 19 times higher than outdoors
• Less than 10% of cases worldwide are from outdoor transmission
• For these outdoor transmissions: lack of personal protective equipment, and occasional indoor gathering during a largely outdoor

  Bulfone et al. The Journal of Infectious Diseases, February 2021

• Contact tracing in Ireland
  • 232,164 cases of Covid-19
  • 262 were as a result of outdoor transmission (~0.1%)

  Health Protection Surveillance Centre (HPSC)

• A study of 1,245 cases in China
  • Of 318 identified outbreaks (3+ cases) all occurred in indoor environments

  Qian et al, 2020
Fauci tells CNN updated outdoor mask guidance likely very soon: “The risk when you’re outdoors – which we have been saying all along – is extremely low. And if you are vaccinated, it’s even lower. So you’re going to be hearing about those kinds of recommendations soon.”
Wish List for Studies of Air Pollution and COVID-19

1. Individual-level data
2. Ascertainment of COVID-19 that is not differential to exposure
3. Information on variant type
4. Data on vaccines (type, dose interval)
5. Data on source and timing of exposure
6. Risk factors for person to person spread
7. Statistical methods for correlated data
8. Thinking outside the box
9. Put findings into context

Case Control Study Design?
Policy implications

If there is a causal role of air pollution on COVID then what are possible actions?

- Adapt the AQI / AQHI
- Revisit Air Quality Standards (EPA/CAAQS)

If there is not a causal role, then what are the dangers?

- Misleading messages that outdoor environments facilitate spread
- Increase skepticism for other air pollution research
Concluding thoughts ...

The data may not contain the answer. The combination of some data and an aching desire for an answer does not ensure that a reasonable answer can be extracted from a given body of data.

John Tukey, 1986
Thank-you!

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