Multi-pollutant analyses in MAPLE, Medicare and ELAPSE cohorts

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Jie Chen on behalf of the ELAPSE, MAPLE and Harvard teams

ELAPSE

MAPLE

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Background

Most air pollution epidemiological studies have focused on single-pollutant research

Limitations of single pollutant models

- Not clear whether the observed association reflects the effect of the analyzed pollutant
- Not characterizing the complexity of the exposures and their health impacts

Multi-pollutant approaches estimate:

- the **independent effect of a single pollutant** in the presence of other pollutants

Challenges in interpretation:

- Highly correlated pollutants
- Differential measurement error – the lowest ME show the most consistent association
- Pollutants treated symmetrically despite the hierarchical natural
- Inclusion of multiple pollutants supported by biologic mechanism (e.g., toxicology)

This presentation:

- Share experience in interpreting results from multi-pollutant analyses

- Stacked CanCHEC (1991, 1996, 2001); N = 7.1 million
- The Canadian Community Health Survey (CCHS); N = 0.54 million
- Age ≥25 y at baseline, censored at 89 y
- Follow-up until end of 2016
- Non-accidental mortality

- **$PM_{2.5}$**, annual average, 1x1km resolution
- **O_3**, warm season
- **O_x**, combined oxidant capacity of O_3 and NO_2

$$O_x = \frac{((1.07 \times NO_2) + (2.075 \times O_3))}{3.145}$$

Associations between $PM_{2.5}$ and non-accidental mortality

	N deaths	Single-pollutant model	Two-pollutant model adjusting for O_3	Two-pollutant model adjusting for O_x
Stacked CanCHEC	1,253,300	1.084 (1.073, 1.096)	1.039 (1.027, 1.051)	1.022 (1.010, 1.035)
CCHS with behavior	50,100	1.086 (1.021, 1.155)	1.016 (0.948, 1.089)	0.995 (0.924, 1.071)

HR per 10 μg/m^3 $PM_{2.5}$

Stratified $PM_{2.5}$ by terciles of O_3 or O_x

Stacked CanCHEC

	HR for $PM_{2.5}$ in tertiles of O_3	HR for $PM_{2.5}$ in tertiles of O_x
Lowest	1.091 (1.065, 1.118)	0.895 (0.874, 0.917)
Middle	1.041 (1.020, 1.062)	1.006 (0.985, 1.027)
Highest	1.099 (1.078, 1.120)	1.086 (1.064, 1.108)

MAPLE

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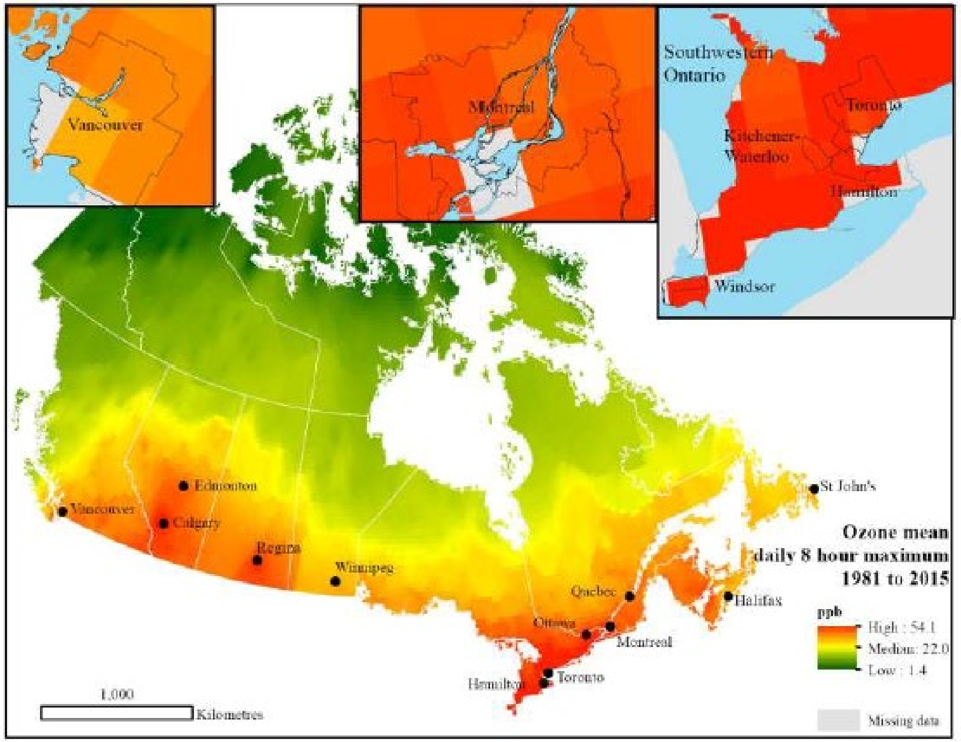

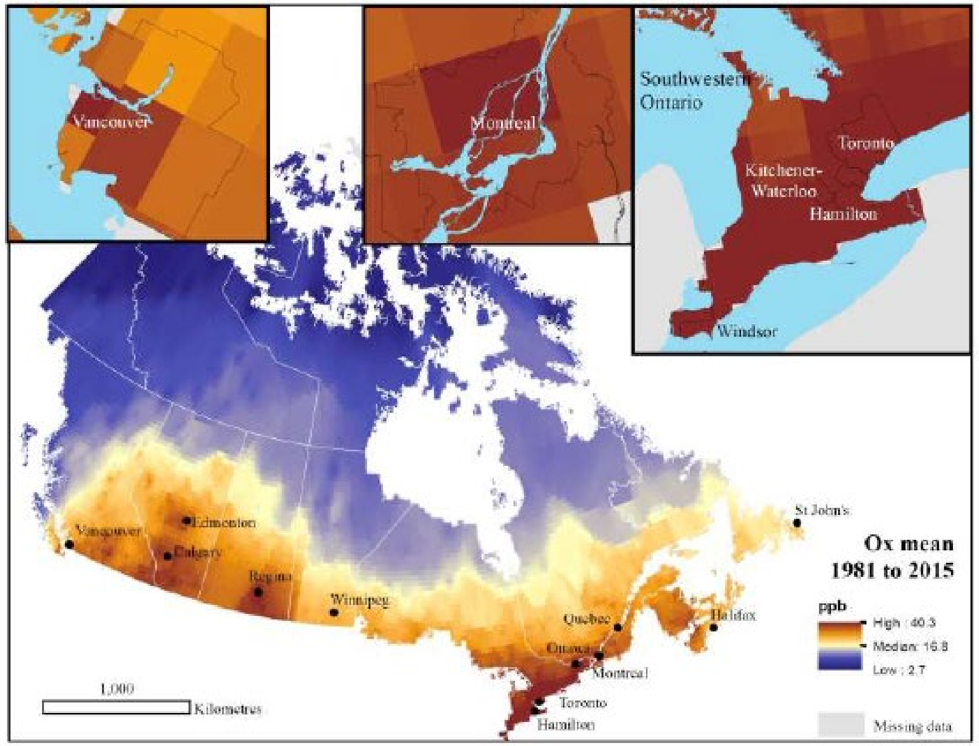

MAPLE

- The strongest association observed in areas with higher oxidant gases

- The observed impact of oxidant gases on associations for $PM_{2.5}$ concentrations likely reflects spatial variations in atmospheric processes/sources that can impact the toxicity of overall air pollution mixtures (e.g., particle aging/oxidation of organic components) and not a direct biological impact of the oxidant gases themselves

- Pooling eight ESCAPE cohorts and the Danish Nurse Cohort (N = 325,367)
- Large administrative cohorts from seven countries in Europe (N = 28 million)
- Age ≥30 y at baseline
- Non-accidental mortality

- Annual average of $PM_{2.5}$, NO_2, BC and warm season O_3 at 100x100 m resolution, year 2010
- Two-pollutant linear models for all combinations of $PM_{2.5}$, NO_2, BC and O_3

ELAPSE

ELAPSE

Air pollution and non-accidental mortality in the **pooled cohort**

Pollutant	Single pollutant HR	HR adjusted for $PM_{2.5}$	HR adjusted for NO_2	HR adjusted for BC	HR adjusted for O_3
$PM_{2.5}$	1.130 (1.106, 1.155)	NA	1.083 (1.054, 1.113)	1.092 (1.062, 1.123)	1.089 (1.061, 1.117)
NO_2	1.086 (1.070, 1.102)	1.050 (1.031, 1.070)	NA	1.074* (1.038, 1.112)	1.053 (1.032, 1.074)
BC	1.081 (1.065, 1.098)	1.039 (1.019, 1.060)	1.012* (0.977, 1.048)	NA	1.044 (1.024, 1.065)
O_3	0.896 (0.878, 0.914)	0.935 (0.913, 0.957)	0.940 (0.914, 0.966)	0.930 (0.906, 0.955)	NA

N=325,367;

HR for increase in $PM_{2.5}$ – 5 $\mu g/m^3$, NO_2 – 10 $\mu g/m^3$, BC – $0.5\times10^{-5}/m$, O_3 – 10 $\mu g/m^3$

Air pollution and non-accidental mortality: meta-analysis of 7 **administrative cohorts**

Pollutant	Single pollutant HR	HR adjusted for $PM_{2.5}$	HR adjusted for NO_2	HR adjusted for BC	HR adjusted for O_3
$PM_{2.5}$	1.053 (1.021, 1.085)	NA	1.003 (0.982, 1.025)	1.021 (0.997, 1.046)	1.031 (0.999, 1.064)
NO_2	1.044 (1.019, 1.069)	1.042 (1.020, 1.065)	NA	1.041* (1.009, 1.073)	1.040 (1.012, 1.069)
BC	1.039 (1.018, 1.059)	1.030 (1.012, 1.049)	1.004* (0.985, 1.022)	NA	1.028 (1.005, 1.051)
O_3	0.953 (0.929, 0.979)	0.972 (0.947, 0.996)	0.987 (0.961. 1.014)	0.976 (0.948, 1.005)	NA

N= 28,153,138;

HR for increase in $PM_{2.5}$ – 5 μg/m^3, NO_2 – 10 μg/m^3, BC – 0.5×10^{-5}/m, O_3 – 10 μg/m^3

- Associations observed not only for $PM_{2.5}$, but also NO_2
- $PM_{2.5}$ HR reduced with NO_2, cannot be interpreted as an artefact related to multi-collinearity (moderate correlation and the width of CI only modestly increased)

- The NO_2 association may reflect direct effects of NO_2 or correlated combustion-related particles such as ultrafine particles.
- The reduction of the $PM_{2.5}$ HR did not imply that particles had no effect, as adjustment for NO_2 also adjusted for particles from the sources shared with NO_2, including motorized traffic and other fossil fuel combustion sources.

Medicare

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- Open cohort of Medicare enrollees (N = 68.5 million)
- Period 2000 – 2016
- Age ≥ 65 y
- All-cause mortality

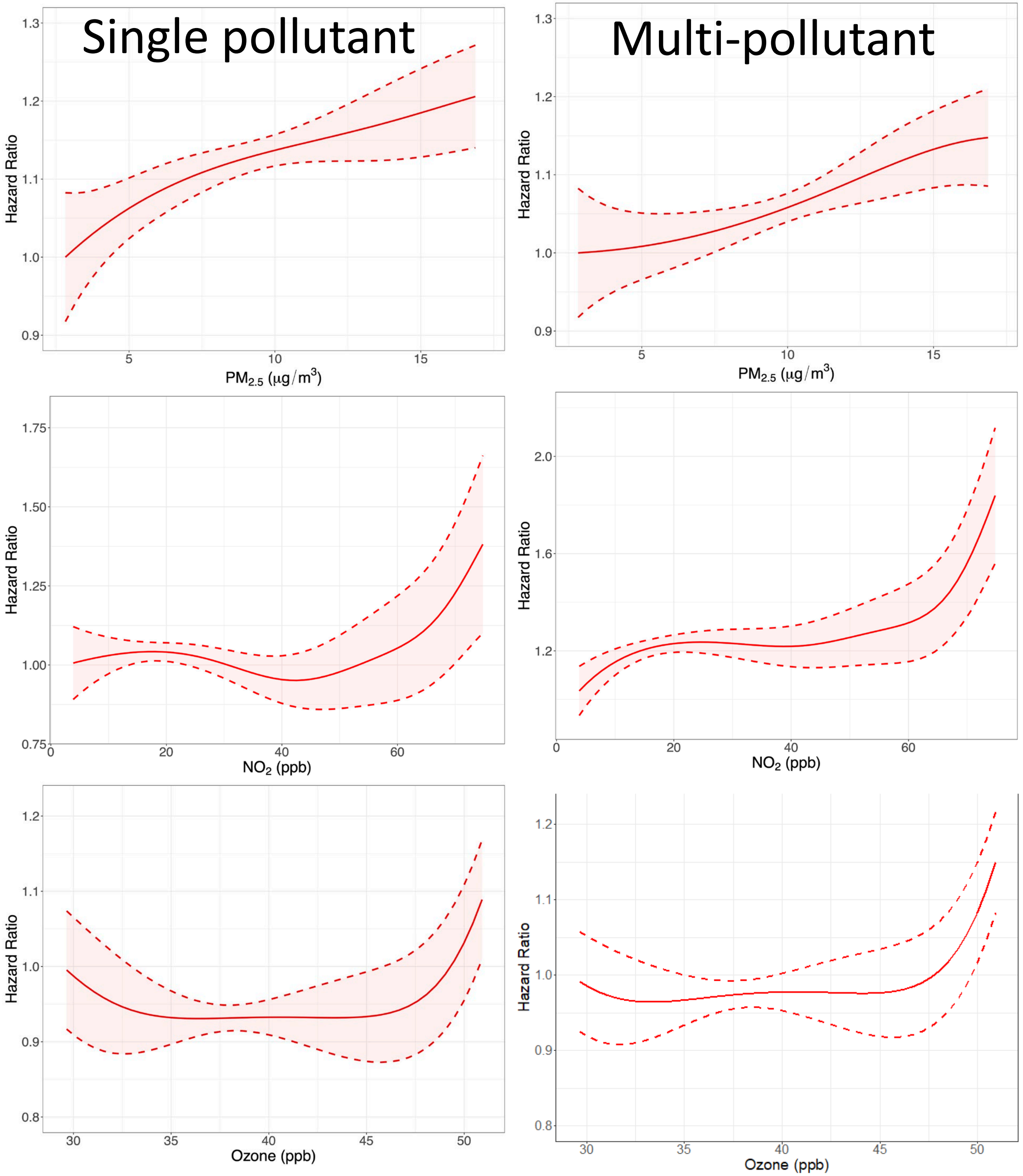
- Annual $PM_{2.5}$, NO_2 and warm season O_3, 1 × 1 km grid, 2000 to 2016

Two-pollutant linear model (Di et al., NEJM, 2017)

	Single-pollutant model	Two-pollutant model
$PM_{2.5}$	1.084 (1.081, 1.086)	1.073 (1.071, 1.075)
O_3	1.023 (1.022, 1.024)	1.011 (1.010, 1.012)

HR per 10 μg/m^3 $PM_{2.5}$ or per 10 ppb ozone

Causal exposure-response curve: air pollution and all-cause mortality (GPS matching)



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(Dominici et al.,
HEI final report, under review)

Summary

		MAPLE	ELAPSE	Medicare
Statistical methods				
	Linear two-pollutant	√	√	√
	Tercile analyses	√		
	GPS matching			√
Pollutants				
	$PM_{2.5}$	√	√	√
	NO_2		√	√
	O_3	√	√	√
	O_x	√		

- Attenuated associations between $PM_{2.5}$ and mortality after adjusting for other pollutants
- Results should be interpreted with caution (e.g., spatial variation, emission sources, correlations)

Ongoing work related to multi-pollutant analyses

- Each team will apply multi-pollutant approaches applied by the other two teams
- The Harvard and ELAPSE teams will additionally assess O_x
- The Harvard and MAPLE teams will use the same $PM_{2.5}$ and NO_2 exposure surfaces; the ELAPSE team is not able to assign new exposures

Thanks for listening!