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SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada's high subarctic.

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SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada's high subarctic.

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Abstract

Objectives: To determine the cardiorespiratory impacts of 2.5 months of severe, unabating wildfire smoke in Canada’s high subarctic.

Design: A retrospective cohort study using hospital, clinic, pharmacy, and environmental data analyzed using Poisson regression.

Setting: Secondary care center and clinics in Yellowknife.

Participants: People from Indigenous-majority communities and the territorial capital city who presented to a secondary care centre and community clinics between 2012-2015.

Main outcome measures: Emergency Room (ER) presentations, hospital admissions and clinic visits for cardiorespiratory events, and outpatient salbutamol prescriptions.

Results: The median 24-hour mean Particulate Matter (PM_{2.5}) was five-fold higher between June 15-August 31st in 2014 compared to 2012, 2013, and 2015 (median= 30.8 µg/m³), with the mean peaking at 320.3µg/m³. A 10 µg/m³ increase in PM_{2.5} was associated with an increase in ER visits of 11% for asthma (IRR(95% CI):1.11 (1.07, 1.14)) and 6% for pneumonia (IRR(95% CI):1.06 (1.02, 1.10)). Compared to 2012/13, in 2014 pharmacy dispensations for salbutamol increased 48%; clinic visits for asthma, pneumonia and cough increased; ER visits for asthma doubled; and ER visits for pneumonia increased 45%. There was no statistically significant change in cardiac ER visits or hospital admissions in 2014.

Conclusions: Severe wildfire smoke was associated with a doubling of ER visits for asthma over a 2.5 month study period. Public health advisories asking people to stay inside were inadequately protective and poorly tolerated, with compliance possibly adversely impacted by the isolation and decreased physical activity associated with being restricted indoors over a prolonged period. Future research should investigate the optimal use of at-home air filtration systems, clean air shelters, and public health messaging which addresses mental health impacts and the need to support physical activity.

Funding: Health Canada’s Climate Change and Health Adaptation Program for First Nations and Inuit Communities

Strengths and Limitations of the Study

Strengths:

-This study investigates the respiratory health impacts of one of the most severe and prolonged episodes of wildfire smoke that has been examined in the literature base, with impact on respiratory health measured through analysis of records in a remote, well-defined catchment area in terms of emergency department and clinic services.

-The area's usually pristine air quality means that background air pollution does not confound the results as it does in most other studies.

-The sister arm of this study represents an analysis of 30 interviews which explored the lived experience of community members during the summer of smoke, insights from which help to inform the analysis of this study, facilitating practical recommendations for improved public health and clinical management of future smoky summers.

Weaknesses:

-This study was unable to estimate the outflow of potential patients from the region as the smoky summer progressed, though qualitative information indicates that at least some severely impacted people left the area.

-Records were not available for inpatient salbutamol dispensation, so estimates of the salbutamol used in the region are limited to community dispensations.

Summary Box

Climate change is leading to increasingly severe wildfires in many parts of the world, necessitating more intensive management of the health threat of both fires and smoke by primary care and public health practitioners. Wildfire smoke is associated with increased use of asthma reliever medications, and exacerbations of asthma and chronic obstructive pulmonary disease, with increasing evidence for an association with all-cause mortality. Few studies examining severe exposures longer than a few weeks exist in the literature and almost no available research combines quantitative and qualitative methods to determine the overall tolerability of smoky periods.

This study indicates that two and a half months of unabating wildfire smoke exposure is poorly tolerated, with a 10 µg/m³ increase in two-day average 24-hour mean PM_{2.5} associated with an 11% increase in ER visits for asthma (IRR(95% CI):1·11 (1·07, 1·14)) and 6% for pneumonia (IRR(95% CI):1·06 (1·02, 1·10)). Compared to 2012/13, in 2014 pharmacy dispensations for salbutamol increased 48%; clinic visits for asthma, pneumonia and cough increased; ER visits for asthma doubled; and ER visits for pneumonia increased 45%. There was no statistically significant change in cardiac ER visits or hospital admissions in 2014. Public health advisories to stay inside for many days over such a long period were inadequately protective and poorly-tolerated.

Further study is needed to evaluate multipronged approaches to extreme wildfire seasons which include proactive primary care-based attention to the needs of vulnerable populations, involving prescription of asthma-reliever medications and consideration for at-home air filtration; public health-based coordination with municipal leaders to improve access to clean air shelters with recreation activities; and communications approaches which attend to the complex interaction between smoke, isolation, climate change and mental health.

Introduction

Extreme wildfires linked to altered temperature and precipitation patterns are increasing in many parts of the world as the climate changes, with major consequences for planetary health, including its biospheric and human subsystems.¹⁻³ Direct human health impacts of fire include death, trauma, major burns,⁴ and post-traumatic-stress-disorder.^{5,6} Wildfire smoke also travels vast distances,¹ exposing populations to a complex mixture of the products of combustion,⁷ most commonly measured as either particulate matter less than 2.5 microns in diameter (PM_{2.5}) or less than 10 microns in diameter (PM₁₀).¹ Exposure to wildfire smoke has been shown to increase asthma reliever medication use,^{8,9} and is consistently associated with exacerbations of asthma and chronic obstructive pulmonary disease (COPD), with growing support for an association with respiratory tract infections and all-cause mortality.¹ Evidence relating smoke exposure to cardiovascular impacts is inconsistent.^{1,10} Greenhouse gas emissions from wildfires are significant, meaning that the fires themselves have the potential to speed climate change, with further adverse impacts on planetary health.² Current wildfire-related public health approaches were conceived to protect populations during relatively shorter wildfire seasons: the effectiveness and tolerability of these recommendations have not been well-examined in seasons of longer duration. As climate change progresses in the Anthropocene, both biospheric ecosystems and human society must prepare for an increasingly disturbed future of forests in order to anticipate and minimize health impacts.^{3,11}

Yellowknife, the capital of Canada's high-subarctic Northwest Territories (NWT), has experienced a 2.5 °C increase in annual average temperature over the past 70 years.¹² In 2014 and 2015, moderate-to-severe drought conditions contributed to the worst and second-worst fire seasons on record in the NWT,^{13,14} leading in 2014 to 385 fires which impacted 3.4 million hectares of forest¹³ (Figure 1) and two and a half months of unabating wildfire smoke exposure for residents of Yellowknife and the adjacent Indigenous communities of N'Dilo and Dettah. Residents also endured months of closed highways, isolation indoors, reduced physical activity, stress and worry associated with a constant state of evacuation readiness, with people of the Dehcho Dene from the Ka'a'gee Tu First Nation near Kakisa Lake, south of Yellowknife, actually evacuated.^{2,15} Some NWT residents referred to this season as "the lost summer."¹⁵

The Summer of Smoke (SOS) project was designed to generate a holistic view of planetary health impacts of the 2014 NWT wildfires by pairing quantitative and qualitative perspectives in order to inform adaptation to future smoke-filled summers. Drawing on quantitative data, this article analyzes and describes the air quality exposure in Yellowknife, Dettah, and N'Dilo during the summers of 2014 and surrounding years; assesses the risk of cardiorespiratory health encounters associated with increasing particulate matter, and examines changes in salbutamol dispensation and health resource utilization compared to prior periods with little smoke. Few studies examining severe exposures of longer than a few weeks exist in the literature and almost no available research combines quantitative and qualitative analysis to determine the overall tolerability of a given smoke-exposure period for a community. This study's subarctic location puts it at the leading edge of climate-related impacts and the project's multifaceted approach paints a picture of interactions between smoke exposure, physical health, mental health and health systems that can inform primary care and public health adaptations to the increasingly severe wildfire seasons that can be expected as the Anthropocene advances.

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Methods

Project Structure and Context

SOS is a community-based, interdisciplinary project which investigated the impacts of the NWT’s 2014 extreme wildfire season on the health and wellbeing of people in four affected communities: Yellowknife (population=20,497, 24% Indigenous); and the near 100% Indigenous Yellowknives Dene communities of N’Dilo (adjacent to Yellowknife, population=345), and Dettah (across a bay from Yellowknife, population:=252); and the Ka’a’gee Tu First Nation in Kakisa (southwest around Great Slave Lake from Yellowknife, population: 36)¹⁶ (See map in Figure 1). Many Indigenous individuals in this area maintain a strong connection to the land, continuing traditional hunting, fishing and plant-gathering practices.¹⁷

Study Partners

This project was initiated by representatives of the Yellowknives Dene First Nation, Yellowknife physicians, and Ecology North (an environmental non-governmental organization in Yellowknife), and carried out in partnership with the Dene of the Dehcho from the Ka’a’gee Tu First Nation, with support from external academic collaborators.

Patient and Public Involvement

Representatives of the Yellowknives Dene and the Ka’a’gee Tu First Nation helped to define the overall project structure from the outset. They contributed to the decision to include both quantitative and qualitative elements¹⁵ in order to evaluate the impact of wildfires on traditional land-based activities and overall wellness, with the goal of optimally informing practical adaptation policies. They were partners on the grant application, co-defined the centrality of respiratory issues to the study and collaboratively generated the interview guide and community engagement strategy. Decision-makers, business leaders, and public health leaders in Yellowknife were also engaged and interviewed. Plain language summaries and videos were prepared to facilitate effective communication of initial findings, and were presented at community gatherings. (see supplementary materials). A final plain language policy paper and three short video vignettes on the community-level adaptive interventions identified as being most likely to improve health during future fire years (clean air shelters with recreation activities, active fire preparation, and attention to both respiratory health and ecoanxiety) have been prepared in association with the study’s coordinators and will be distributed to communities across the NWT (see supplementary materials).

This project was reviewed and approved by the Stanton Territorial Hospital Ethics Board and Wilfrid Laurier University Research Ethics Board (REB #4700), as well as by the Aurora Research Institute (license numbers 15733; 15801). Interview subjects consented to video recording, including public dissemination of the footage, and analysis of their remarks.

Statistical Analysis

Descriptive

Air quality

Data for particulate matter (PM_{2.5} and PM₁₀) and covariates (humidity and temperature) from June 15-Aug 31st 2012-2015 were obtained from the Yellowknife Air Quality Monitoring station, which provides information relevant to Yellowknife, N'Dilo and Dettah.¹⁸ 24-hour mean PM_{2.5} levels were examined for each study year, and the proportion of study days each year where the 24-hour mean PM_{2.5} exceeded the WHO recommended 24-hour mean air quality threshold of 25 µg/m³ was determined.¹⁹ PM₁₀ was described to facilitate comparison with other studies (Table 1).

Table 1: 24-hour mean PM_{2.5} and PM₁₀ from June 15-Aug 31

	Median PM_{2.5} (Q1,Q3)* µg/m³	Maximum PM_{2.5} µg/m³	% of days with PM_{2.5} ≥ 25 µg/m³	Median PM₁₀ (Q1,Q3) µg/m³
2012	6.2 (5.6, 8.9)	65.7	4 (3 days)	13.3 (9.5, 17.9)
2013	6.7 (4.4, 14.5)	67.6	9 (7 days)	12.6 (8.4, 22.0)
2014	30.8 (16.2, 85.0)	320.3	55 (43 days)	43.8 (26.5, 100.7)
2015	6.4 (4.6, 11.5)	99.6	12 (9 days)	14.9 (10.3, 28.8)
*Q1- first quartile; Q3- third quartile				

Risk of Particulate Matter for Emergency Room Visits and Hospital Admissions

Routinely-collected administrative data from emergency room (ER) visits and hospital admissions for June 15-August 31, 2012-2015 was retrieved from Stanton Territorial Hospital (the NWT referral hospital). Cause-specific diagnoses using the most responsible diagnosis were coded using International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA) codes for cardiorespiratory diagnoses (footnote of Table 2). Administrative records included information on age, sex, and ethnicity (non-Indigenous and Indigenous groups: Inuit, Dene, Metis). Indigenous/Non-Indigenous status was determined from NWT personal health numbers. Patients from out of territory were considered to be Non-Indigenous. Population estimates by age, sex, and ethnicity were obtained from the Territorial Bureau of Statistics.¹⁶

Generalized linear Poisson regression models were used to estimate the effect of daily PM_{2.5} on population rates of cardiorespiratory ER visits and hospital admissions. Asthma and pneumonia were modeled separately because they were commonly highlighted in the literature. Subgroup analyses for asthma and pneumonia were done by age, sex, and ethnicity. We hypothesized that

the effect of PM_{2.5} on asthma might change during the summer of 2014 as population members fled the territory or filled asthma medications. To assess this we examined the relationship of PM_{2.5} with asthma in early summer (June 15-July 31 2014) and late summer (August 1-August 31, 2014). All models were adjusted for: age, sex, ethnicity, day of week, humidity, and temperature.

The primary particulate matter exposure was assessed using a 2-day average 24-hour mean PM_{2.5} (i.e. average of previous and current day 24-hour mean PM_{2.5} levels), as per previously published literature that found it to be more highly-associated with clinical outcomes than a 1-day 24-hour mean.^{8,10} Sensitivity analyses were conducted for primary outcomes using 1-day 24-hour mean PM_{2.5} and PM₁₀ exposures. All incidence rate ratios were calculated for a 10µg/m³ increase in measured PM_{2.5}.

Health resource utilization during the summer of 2014

To assess the burden of wildfire smoke on health resources in 2014 compared to non-extreme fire years (2012-2013), we examined salbutamol dispensations, clinic visits for respiratory symptoms and diagnoses, as well as cardiorespiratory ER visits and hospital admissions. 2015 was the NWT’s second-worst fire season on-record, and was thus not used as part of the baseline, but is included to examine whether health utilization decreased after 2014.

Monthly outpatient salbutamol dispensation information was gathered from Yellowknife’s five pharmacies. Salbutamol data from Stanton Hospital was unavailable. An equivalency between metered-dose inhaler (MDI) and nebulized salbutamol was generated using similar equivalencies to those used in a Cochrane review²⁰ (see Appendix) and calculations were done equating 1 outpatient dose to 2 puffs by MDI or 833 mcg of nebulized salbutamol. The correlation with the proportion of days where the 24-hour mean PM_{2.5} was greater than the WHO recommended air quality threshold was determined.

De-identified data on clinic visits for respiratory symptoms and diagnoses were retrieved using the practice search function of the Yellowknife Health and Social Services (YHSSA) Wolf electronic medical record by YHSSA employees on the research team. Visits for upper respiratory tract infections, conjunctivitis, bronchitis, cough, asthma, chronic obstructive pulmonary disease, pneumonia, and allergy were searched using standard case insensitive terms. Chi-squared tests were performed to assess differences in the number of symptoms and diagnoses by year.

To determine changes in ER visits for cardiorespiratory diagnoses in 2014 compared to 2012-13, we calculated standardized incidence ratios (SIRs). Territorial statistics demonstrated that there was no significant change in the study population (Yellowknife, Dettah, N’Dilo) between 2012-2015.¹⁶ Therefore, we calculated the expected number of ER visits by averaging the number of visits in 2012 and 2013. To calculate the SIRs we divided the observed number of ER visits in 2014 by the expected number of visits.

All analyses were performed using SAS 9.4 Cary, N.C., USA.

Results

Figure 2 and Table 1 show the distribution of 24-hour mean $PM_{2.5}$ by year. The median 24-hour mean $PM_{2.5}$ was five-fold higher in 2014 compared to 2012, 2013, and 2015, and reached a peak of $320.3 \mu\text{g}/\text{m}^3$ on August 5, 2014 (highest hourly recorded $PM_{2.5}$ that day was $873 \mu\text{g}/\text{m}^3$). The maximum 24-hour mean PM_{10} was $350 \mu\text{g}/\text{m}^3$ on August 3, 2014 (hourly maximum that day was $772 \mu\text{g}/\text{m}^3$). In 2014, $PM_{2.5}$ levels were above the recommended WHO threshold of $25 \mu\text{g}/\text{m}^3$ 43 (55%) days.

Spikes in $PM_{2.5}$ in 2012, 2013, and 2015 are related to intermittent forest fires. The 2015 maximum 24-hour mean $PM_{2.5}$ on June 30, 2015 was $99.6 \mu\text{g}/\text{m}^3$, lower than 2014 highs, but higher than 2012 and 2013. 12% of days in 2015 exceeded the WHO threshold.

Risk of Particulate Matter for Cardiorespiratory Emergency Department Visits

A $10 \mu\text{g}/\text{m}^3$ increase in two-day average 24-hour mean $PM_{2.5}$ was associated with a 3% increase in ER visits for respiratory diagnoses [Incidence Rate Ratio (IRR) 95% CI: 1.03 (1.01, 1.05)] (Table 2). Sensitivity analyses show consistency using 24-hour mean $PM_{2.5}$ exposure [IRR (95% CI): 1.03 (1.01, 1.05)], and 24-hour mean PM_{10} [IRR (95% CI): 1.03 (1.01, 1.04)]. This increase in ER visits was highest for asthma (11% increase per $10 \mu\text{g}/\text{m}^3$ in $PM_{2.5}$: IRR (95% CI): 1.11 (1.07, 1.14), an impact that was consistent across subgroups of age, sex and ethnicity.

$PM_{2.5}$ increases were also related to ER visits for pneumonia (6% increase per $10 \mu\text{g}/\text{m}^3$ in $PM_{2.5}$: IRR (95% CI): 1.06 (1.02, 1.10), but this effect was only evident in children aged ≤ 19 , the elderly (age ≥ 60 years), males, and the Inuit population (Table 2).

An increase in $PM_{2.5}$ of $10 \mu\text{g}/\text{m}^3$ in the extreme fire summer of 2014 was more highly associated with an increase in asthma visits early in the summer (June 15-July 31 [IRR (95% CI): 1.19 (1.07, 1.32)]), than later in the summer (Aug 1-Aug 31 [IRR (95% CI): 1.04 (0.99, 1.01)]).

Overall, the relationship between $PM_{2.5}$ and inpatient hospital admissions for asthma and pneumonia were similar to those with ER visits. (Table 2) However, the effect of increased $PM_{2.5}$ and asthma admissions was more prominent in males, and non-Indigenous persons compared to ER visit analyses.

No significant association was seen between $PM_{2.5}$ and cardiovascular ER visits [IRR (95% CI): 0.99 (0.84, 1.04)] or inpatient hospital admissions [IRR (95% CI): 1.04 (0.98, 1.10)]. (Table 2)

Table 2: Adjusted risk of cardiorespiratory emergency room visits and inpatient hospital admissions per $10 \mu\text{g}/\text{m}^3$ increase in 2-day averaged 24-hour mean $PM_{2.5}$. All models adjusted for age, sex, ethnicity, day of week, humidity and temperature.

Outcome	Emergency Room Visits Incidence Rate Ratio (95% confidence interval)	Inpatient Hospital Admissions
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		Incidence Rate Ratio (95% confidence interval)
Cardiovascular Basket ¹	0·99 (0·94, 1·04)	1·04 (0·98, 1·10)
Respiratory Basket ¹	1·03 (1·01, 1·05)	1·03 (0·98, 1·07)
Asthma ¹		
ALL	1·11 (1·07, 1·14)	1·11 (0·99, 1·25)
Male	1·12 (1·08, 1·17)	1·20 (1·01, 1·43)
Female	1·07 (1·03, 1·12)	1·05 (0·86, 1·27)
Inuit	1·11 (1·04, 1·19)	1·01 (0·78, 1·29)
Dene	1·09 (1·00, 1·19)	NE
Non-Indigenous	1·10 (1·06, 1·15)	1·27 (1·06, 1·51)
Age <5 years	0·99 (0·73, 1·35)	0·97 (0·36, 2·61)
Age 5-19 years	1·07 (1·01, 1·14)	1·12 (0·97, 1·29)
Age 20-39 years	1·09 (1·04, 1·14)	0·98 (0·71, 1·36)
Age 40-59 years	1·12 (1·07, 1·18)	NE
Age 60+ years	1·11 (0·96, 1·30)	NE
Pneumonia ¹		
ALL	1·06 (1·02, 1·10)	1·02 (0·94, 1·11)
Male	1·09 (1·04, 1·14)	1·04 (0·95, 1·15)
Female	1·00 (0·92, 1·08)	0·97 (0·82, 1·14)
Inuit	1·10 (1·06, 1·16)	1·09 (0·99, 1·19)
Dene	NE (not estimable)	0·84 (0·57 , 1·23)
Non-Indigenous	0·97 (0·87, 1·09)	0·60 (0·26, 1·37)
Age <5 years	1·13 (1·06, 1·20)	1·12 (1·01, 1·25)

Age 5-19 years	1.09 (0.99, 1.19)	0.98 (0.79, 1.22)
Age 20-39 years	0.95 (0.78, 1.14)	NE
Age 40-59 years	0.96 (0.84, 1.10)	1.10 (0.92, 1.32)
Age 60+ years	1.06 (0.99, 1.14)	0.80 (0.57, 1.13)
¹ International Statistical Classification of Diseases and Related Health Problems, 10 th Revision, Canada (ICD-10-CA) Codes All cardiac (I00-I52) All respiratory (J00-J99) Asthma (J45-J46) Pneumonia (J12-J18)		

Pharmaceutical dispensation and health services impacts of increased smoke exposure in 2014

There was a 48% increase in dispensed outpatient doses of salbutamol in 2014 compared to 2012-13, and this number fell in 2015 [2012: 105618 doses; 2013:130888 doses; 2014:175208 doses; 2015: 147738 doses]. The number of salbutamol doses was positively correlated with the proportion of days that PM_{2.5} exceeded the WHO 24-hour mean guideline value of 25µg/m³ (r=0.89, p=0.11).

Primary care clinic visits for cough and pneumonia doubled in 2014 and clinic visits for asthma increased more than 50% compared to earlier years (p<0.0001 for each). Clinic visits with these presentations decreased in 2015 but remained higher than 2012/13 levels (Figure 3).

ER visits for asthma demonstrated a more than two-fold increase in 2014, an effect that was exaggerated in females and adults aged ≥40 years. There was no increase in ER visits for combined respiratory diagnoses in 2014 compared to 2012-13 [SIR(95% CI):1.08 (0.95, 1.22)] (Table 3). Visits for pneumonia showed a 57% increase, and were more common in males, in people aged < 40 years, and the Inuit. ER visits for asthma and pneumonia dropped in 2015 compared to the 2014 peak (Table 3).

Table 3- Standardized Incidence Ratios for Cardiorespiratory Emergency Room (ER) visits in extreme fire year 2014 compared to 2012-2013.

	A Mean Observed ER visits	B Number ER visits 2014	C Standardized Incidence Ratio=A/B	D Number ER visits 2015

	2012+ 2013 =2014 Expected	(Observed)		
CARDIOVASCULAR BASKET	(51+48)/2=49.5	62	1.25 (0.97, 1.60)	63
RESPIRATORY BASKET	(251 +239)/2=245	265	1.08 (0.95, 1.22)	223
ASTHMA				
ALL	(26+32)/2=29	59	2.03 (1.56, 2.61)	21
Male	(13+16)/2=14.5	22	1.52 (0.98, 2.26)	6
Female	(13+16)/2=14.4	37	2.55 (1.82, 3.48)	15
Age <5	(1+3)/2=2	4	2.00 (0.64, 4.82)	2
Age 5-19	(9+11)/2=10	13	1.30 (0.72, 2.17)	7
Age 20-39	(11+12)/2=11.5	20	1.74 (1.09, 2.64)	8
Age 40-59	(5+5)/2=5	19	3.80 (2.36, 5.82)	4
Age 60+	(0+1)/2=0.5	3	6.00 (1.53, 16.33)	0
Inuit	(8+8)/2=8	16	2.00 (1.18, 3.18)	5
Non-Indigenous	(13+16)/2=14.5	27	1.86 (1.25, 2.67)	7
Dene	(2+1)/2=1.5	5	3.33 (1.22, 7.39)	2
PNEUMONIA				
ALL	39+40/2=39.5	62	1.57 (1.21, 2.00)	43
Male	(19+19)/2=19	38	2.00 (1.44, 2.72)	25
Female	(20+21)/2=20.5	24	1.17 (0.77, 1.72)	18
Age <5	(6+4)/2=4.5	16	3.56 (2.11, 5.65)	13
Age 5-19	(2+6)/2=4	13	3.25 (1.81, 5.42)	4
Age 20-39	(2+4)/2=3	9	3.00 (1.46, 5.51)	11
Age 40-59	(15+10)/2=12.5	9	0.72 (0.35, 1.32)	4
Age 60+	(14+17)/2=15.5	15	0.97 (0.56, 1.56)	11
Inuit	(14+12)/2=13	29	2.23 (1.52, 3.16)	15
Non-Indigenous	(12+12)/2=12	15	1.25 (0.73, 2.02)	9
Dene	(3+8)/2=5.5	3	0.55 (0.14, 1.48)	8

There was no statistically significant change in cardiac ER visits or cardiorespiratory hospital admissions in 2014.

Discussion

Statement of Principal Findings

Air quality in Yellowknife was poor in 2014: the 24-hour mean $PM_{2.5}$ was five-fold higher compared to other years, and reached a peak of $320.3 \mu\text{g}/\text{m}^3$ on August 5th 2014. A $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ was associated with an 11% increase in asthma-related ER visits, an effect which was strongest early in the summer. Outpatient salbutamol dispensations increased by 45%; primary care visits for cough, asthma and pneumonia increased; and ER visits for asthma doubled. There was no increase in cardiac ER visits nor cardiorespiratory hospital admissions.

Explanation of the Findings in Relation to Other Studies

The 11% increase in ER visits for asthma per $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ seen here was high compared to similar studies: in 2013, Yao et al found a 3% increase in asthma visits per $10 \mu\text{g}/\text{m}^3$ of $PM_{2.5}$ (1.10 (95% CI: 1.00, 1.21) for $30 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$),²¹ while in 2016 the same group found a 6% increase in asthma visits per $10 \mu\text{g}/\text{m}^3$ over a fire season where the mean daily $PM_{2.5}$ was $10.2 \mu\text{g}/\text{m}^3$ on extreme fire days, which is lower than our median daily mean $PM_{2.5}$ of $30.8 \mu\text{g}/\text{m}^3$.⁹ Henderson et al found a 5% increase in the odds of an asthma-specific physician visit with a $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} .²² The strong relationship between $PM_{2.5}$ and asthma visits in our study may be associated with the fact that people with airways sensitive to air pollution may not have had medications on-hand given Yellowknife's excellent baseline air quality ($PM_{2.5} = 6 \mu\text{g}/\text{m}^3$). The length and severity of the smoke exposure would also have worsened indoor air quality despite closed windows.^{10,23, 24} Incomplete compliance with public health advice to stay inside could have exacerbated health impacts: a telephone survey of 441 Yellowknife residents in July 2014 reported that 76% of respondents had seen or heard air quality related announcements asking them to stay inside,²⁵ but only 48% had spent less time outdoors.²⁵ Of those who did change their activities, almost one-fifth of respondents reported reduced strenuous aerobic activity or exercise,²⁵ an undesirable adaptation given the health benefits of exercise.²⁶ Analysis of 30 interviews conducted as part of the project and published elsewhere confirmed reduced physical activity, decreased feelings of wellness, and a sense of isolation that one subject compared to being in jail.¹⁵ Many participants worried that the smoke and uncomfortable coping strategies could be a "new normal" as a result of the changing climate.¹⁵

A stronger association between $PM_{2.5}$ levels and ER visits for asthma was seen earlier in 2014 than later, a previously-noted phenomenon which has been attributed to prescriptions for asthma-relieving medications being filled during the first part of fire seasons.³⁰ Also, later in the summer some residents spontaneously evacuated¹⁵ and leaders coordinated to offer free recreation opportunities in clean air shelters, which may have decreased symptoms from outdoor exercise.⁴

The effect of $PM_{2.5}$ on pneumonia was pronounced in the young and the elderly, in males, and in the Inuit. Studies are inconsistent regarding differential effects of smoke by age, and smoke has been linked to poorer outcomes for people of lower socioeconomic status.¹ Poor housing and increased exposure to environmental tobacco smoke may contribute to respiratory symptoms in the Inuit population in Canada.²⁷ Studies from Australia found a stronger relationship between PM_{10} levels and respiratory hospital admissions for Indigenous populations than non-Indigenous populations,^{28,29} with one study controlling for socioeconomic factors.¹⁶

Strengths and Weaknesses of the Study

The NWT’s excellent baseline air quality enables the influence of PM_{2.5} on respiratory outcomes to be more directly attributed to wildfires than in most studies.¹⁰ Also, the smoke exposure was particularly long and severe, making results useful for forward-looking adaptation planning in the Anthropocene.¹⁰ In addition, interview data from the project’s qualitative arm facilitated practical policy-relevant interpretations of our results. Limitations of our study were the inability to estimate outmigration of symptomatic people who self-evacuated to other provinces or regions, lack of ethnicity information for out-of-territory residents, and an inability to report on inpatient salbutamol use due to lack of data availability.

Meaning of the Study

This severe, prolonged wildfire smoke exposure was associated with important respiratory impacts which may have been compounded by low compliance with public health messaging to stay inside due to the isolation, anxiety, and decreased physical activity associated with being restricted indoors for a prolonged period. Healthy adaptation to extreme wildfires requires a planetary health-based holistic approach and improved coordination between public health, primary care, municipal and recreation leaders.

Future studies

There is a need to investigate the long-term impacts of acute, prolonged smoke exposure as well as differential impacts on people of low socioeconomic status. Further study is needed to evaluate multipronged health-systems approaches which include primary care-based attention to the needs of vulnerable populations involving proactive prescription of asthma-reliever medications and consideration for at-home air filtration^{28, 30}; public health-generated coordination to improve access to clean air shelters with recreation activities, and public health strategies that encourage populations to go outside during clean air windows and which attend to the complex interaction between smoke, isolation, climate change-related eco-anxiety and other mental health impacts.³¹

Policy implications and future directions

Severe wildfires have recently impacted communities from Canada to California to Australia and beyond, with increasing frequency and intensity forecast as global surface temperatures rise.¹ This study demonstrates a need to be better prepared, a hope which was expressed by community members who found that uncertainty was associated with anxiety, whereas active preparation not only decreased risk but also worry.¹⁵ Primary care practitioners can identify and prepare smoke-susceptible individuals prior to wildfire season. Public health practitioners can utilize satellite-based smoke forecasting to ready appropriate adaptation interventions that include maximizing opportunistic outdoor and accessible, well-ventilated indoor recreation and socializing opportunities. Climate-related health impacts are here, but healthier adaptation is possible.

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Author Contributions

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Contributions: Study conception and design, building of team, grant application, review of qualitative interview content, collection of quantitative data, study write-up and editing.

2-Caren Rose, PhD

Contributions: Study design, quantitative data analysis, study write-up and editing.

3-Warren Dodd, PhD

Contributions: Qualitative data collection, qualitative data analysis, consultation on statistical analyses of quantitative data, review and editing of study write-up.

4-Katherine Kohle, MD

Contributions: Study conception and design, grant application, collection of quantitative data, study editing.

5- Craig Scott, BES

Contributions: Study conception and design, grant application, project management and community outreach, study editing.

6- Patrick Scott, PhD

Contributions: Study conception and design, grant application, interview design and qualitative information, study editing

7-Ashlee Cunsolo, PhD

Contributions: Study design, qualitative interview design, study editing.

8-James Orbinski, MD

Contributions: Study design, grant application, consultation on quantitative analysis, review and editing of study write-up, oversight of project.

Declaration of Interests

Competing interests: all authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.No conflicts of interest exist.

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Transparency statement

All authors had full access to the data and take responsibility for data integrity and the accuracy of the analysis. The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data Sharing

The authors are happy to share anonymized patient level data should requests be made.

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Figure and Table Legend:

- Figure 1: 2014 Northwest Territories Fire Locations Map.
- Figure 2: 24-hour mean PM_{2.5} from Yellowknife Air Quality Station June 15-August 31, 2012-2015.
- Figure 3: Yellowknife Health and Social Services primary care clinic visits for respiratory symptoms and diagnoses June 15-August 31, 2012-2015.
- Table 1. 24-hour mean PM_{2.5} and PM₁₀ from June 15-Aug 31, 2012-2015.
- Table 2. Adjusted risk of cardiorespiratory emergency room visits and inpatient hospital admissions per 10µg/m³ increase in 2-day averaged 24-hour mean PM_{2.5}.
- Table 3. Standardized Incidence Ratios for cardiorespiratory Emergency Room visits in extreme fire year 2014 compared to 2012-2013.



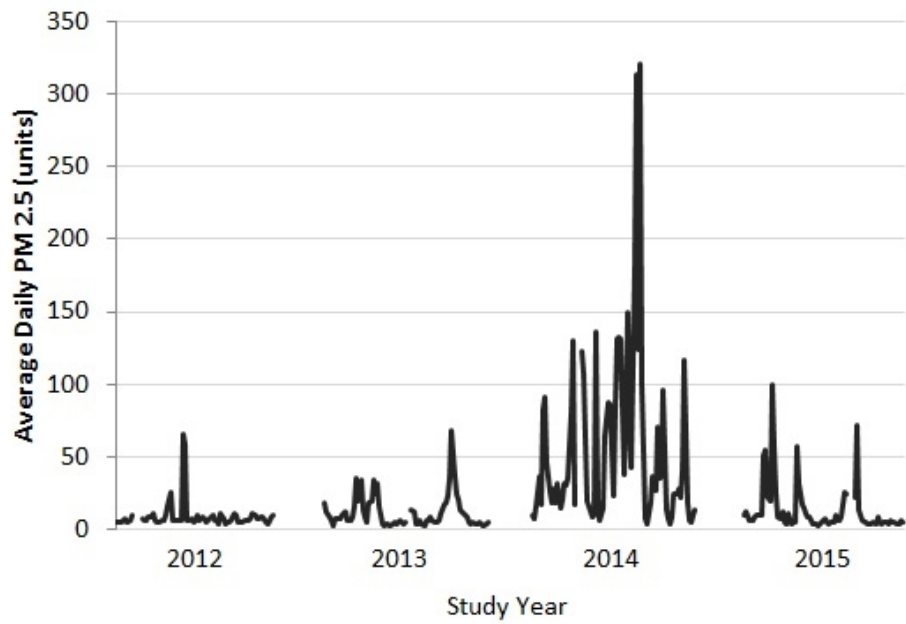


Figure 2: 24-hour mean PM2.5 from Yellowknife Air Quality Station June 15-August 31, 2012-2015.

48x30mm (300 x 300 DPI)

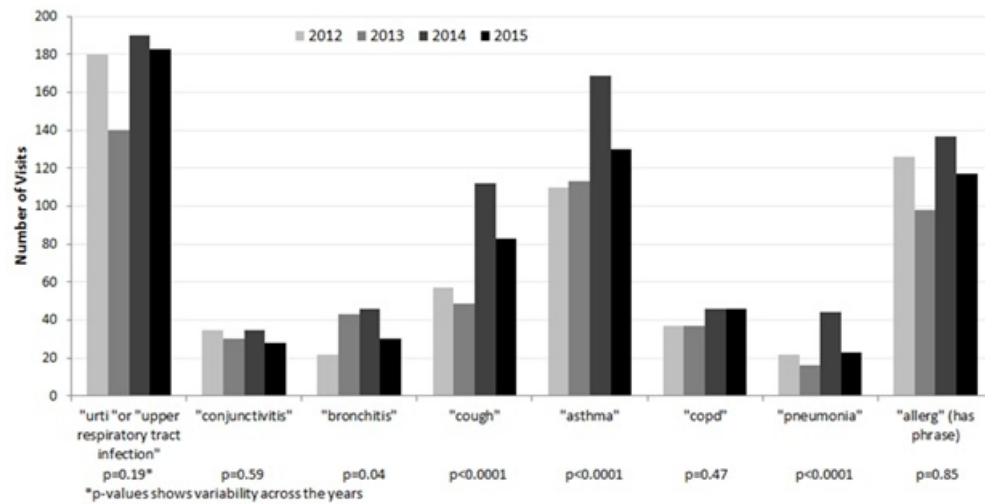


Figure 3: Yellowknife Health and Social Services primary care clinic visits for respiratory symptoms and diagnoses June 15-August 31, 2012-2015.

52x26mm (300 x 300 DPI)

Supplementary Materials for:

SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada’s high subarctic.

A-Appendix 1: Conversion Factor for Nebulized Salbutamol to Salbutamol Administered via Metered Dose Inhaler

The Summer of Smoke study tracks the dispensation of outpatient doses of salbutamol, a beta-agonist, between years. Most salbutamol in Yellowknife is dispensed from pharmacies in the form of metered-dose inhalers (MDIs), meant to be used with a spacer, or in diskus form, but a small amount is dispensed in nebulers. We wanted to analyze them together, and decided that the most clinically-relevant endpoint, a “dose,” would be the most useful.

Our efforts to find a standard conversion factor were not successful, so one was derived using a Cochrane review comparing nebulized salbutamol to salbutamol administered via MDI.

1-The standard outpatient salbutamol dose prescribed by Canadian doctors is 2 puffs by MDI or by diskus. We therefore decided: 1 salbutamol dose=2 puffs.

2-The Cochrane review, “*Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma*,”(1) which found no significant advantage to nebulers over treatment with MDI and spacer, reported that, “The dosage ratio between delivery methods varied from 1:1 to 1: 13, with the larger doses administered via nebuliser. The median dose administered via nebuliser was four times that administered via spacer, a dosage ratio of 1:4 (interquartile range (IQR) 1:2 to 1:8).” There is substantial variability in doses: they state, “In clinical practice the dose of beta -agonist delivered to the airways varies depending on the type of nebuliser or spacer used and the characteristics of the individual’s airways at that time.”

3-To obtain a value for the purposes of our calculation, we divided the standard Canadian emergency room (ER) nebulized dose of salbutamol (2.5 mg) and divided it by the median dosage ratio of 1:4 from the Cochrane review (2.5mg/4=625mcg), reasoning that the average study would therefore have been comparing a 2.5mg nebule to 625 mcg of MDI + spacer administered treatment.

4-We then used that ratio between nebulers and MDI doses to determine a nebule equivalent to the standard outpatient dose, which we’d defined as 2 puffs by MDI: 625mcg (ER dose MDI)/200mcg (outpt dose MDI)=about 3 fold difference between ER usual MDI dose and outpatient standard MDI dose.

5-To calculate a standardized outpatient dose of nebulized ventolin, we maintained equivalency to the MDI dose by also dividing by 3. 2.5mg/3= **833 mcg of nebulized ventolin= 1 standard outpatient dose nebulized ventolin.**

Over the time interval that we are interested in, pharmacies dispensed nebules in 1mg, 2mg, 2.5mg and 5mg doses. The above ratio would make nebules equivalent to: 1mg nebule/833mcg=1.2 standard outpatient nebulized doses 2mg=2.4 standard outpatient doses

2.5mg=3 doses standard outpatient doses 5mg=6 doses standard outpatient doses

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SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada's high subarctic.

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SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada's high subarctic.

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Abstract

Objectives: To determine healthcare service utilization for cardiorespiratory presentations and outpatient salbutamol dispensation associated with 2.5 months of severe, unabating wildfire smoke in Canada’s high subarctic.

Design: A retrospective cohort study using hospital, clinic, pharmacy, and environmental data analyzed using Poisson regression.

Setting: Secondary care center and clinics in Yellowknife, Northwest Territories, Canada.

Participants: Individuals from Yellowknife and adjacent Indigenous communities presenting for care between 2012-2015.

Main outcome measures: Emergency Room (ER) presentations, hospital admissions and clinic visits for cardiorespiratory events, and outpatient salbutamol prescriptions.

Results: The median 24-hour mean Particulate Matter (PM_{2.5}) was five-fold higher in the summer of 2014 compared to 2012, 2013, and 2015 (median= 30.8 µg/m³), with the mean peaking at 320.3µg/m³. A 10 µg/m³ increase in PM_{2.5} was associated with an increase in asthma-related (IRR(95% CI):1.11 (1.07, 1.14)) and pneumonia-related ER visits (IRR(95% CI):1.06 (1.02, 1.10)), as well as an increase in COPD hospitalizations (IRR(95% CI):1.11 (1.02, 1.20)). Compared to 2012 and 2013 salbutamol dispensations in 2014 increased 48%; clinic visits for asthma, pneumonia and cough increased; ER visits for asthma doubled, with highest rates in females, those ≥40 years, and Dene people, while pneumonia increased 57%, with higher rates in males, those <40 years, and Inuit people. Cardiac variables were unchanged.

Conclusions: Severe wildfires in 2014 resulted in extended poor air quality associated with increases in health resource utilization; some impacts were seen disproportionately among vulnerable populations, such as young children and Indigenous individuals. Public health advisories asking people to stay inside were inadequately protective, with compliance possibly impacted by the prolonged exposure. Future research should investigate use of at-home air filtration systems, clean-air shelters, and public health messaging which addresses mental health and supports physical activity.

Funding: Health Canada’s Climate Change and Health Adaptation Program for First Nations and Inuit Communities (Grant Number N/A)

Strengths and Limitations of the Study

Strengths:

-This study investigates the respiratory health impacts of one of the most severe and prolonged episodes of wildfire smoke that has been examined in the literature base, with impact on respiratory health measured through analysis of records in a remote, well-defined catchment area in terms of emergency department and clinic services.

-The usually pristine air quality of Yellowknife, Northwest Territories and the surrounding communities means that background air pollution does not confound the results as it does in most other studies.

-The sister arm of this study represents an analysis of 30 interviews which explored the lived experience of community members during the summer of smoke, insights from which help to inform the analysis of this study, facilitating practical recommendations for improved public health and clinical management of future smoky summers.

Limitations:

-This study was unable to estimate the outflow of potential patients from the region as the smoky summer progressed, though qualitative information indicates that at least some severely impacted people left the area.

-Records were not available for daily outpatient salbutamol dispensations or inpatient salbutamol dispensation, so estimates of the salbutamol used in the region are limited to monthly community dispensations.

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Introduction

Extreme wildfires linked to altered temperature and precipitation patterns are increasing in many parts of the world as the climate changes, with major consequences for planetary health, including its biospheric and human subsystems.¹⁻³ Human health impacts of fire include death, trauma, major burns,⁴ anxiety and post-traumatic-stress-disorder.^{5, 6} Wildfire smoke also travels vast distances,¹ exposing populations to a complex mixture of the products of combustion,⁷ most commonly measured as either particulate matter less than 2.5 microns in diameter (PM_{2.5}) or less than 10 microns in diameter (PM₁₀).¹ Exposure to wildfire smoke has been shown to increase asthma reliever medication use,^{8, 9} and is consistently associated with exacerbations of asthma and chronic obstructive pulmonary disease (COPD), with indications of an association with low birth weight and growing support for an association with respiratory tract infections and all-cause mortality.¹ Evidence relating smoke exposure to cardiovascular impacts is inconsistent.^{1, 10} Studies on the long term impacts of severe acute exposure are minimal, but indicate concern; for example, a group of Rhesus monkeys exposed to wildfire smoke as infants had reduced lung function during adolescence,¹¹ and recent evidence shows that mean prenatal exposure to air pollution related to the 1997 Indonesian forest fires was associated with a half standard deviation decrease in height-for-age metrics at age 17.¹²

Greenhouse gas emissions from wildfires are also significant, meaning that the fires themselves have the potential to speed climate change, with further adverse impacts on planetary health.² Current wildfire-related public health approaches were conceived to protect populations during relatively shorter and less-severe wildfire seasons: it is necessary to reevaluate the effectiveness and tolerability of health interventions as wildfires intensify. As climate change progresses in the Anthropocene, both biospheric ecosystems and human society must prepare for an increasingly disturbed future of forests in order to anticipate and minimize health impacts.^{3, 13}

Yellowknife, the capital of Canada’s high-subarctic Northwest Territories (NWT), has experienced a 2.5 °C increase in annual average temperature over the past 70 years.¹⁴ In 2014 and 2015, moderate-to-severe drought conditions contributed to the worst and second-worst fire seasons on record in the NWT,^{15, 16} leading in 2014 to 385 fires which impacted 3.4 million hectares of forest¹⁵ and two and a half months of unabating wildfire smoke exposure for residents of Yellowknife and the adjacent Indigenous communities of N’Dilo and Dettah. Residents also endured months of closed highways, isolation indoors, and reduced physical activity, as well as stress and worry associated with a constant state of evacuation readiness, with people of the Dehcho Dene from the Ka’a’gee Tu First Nation near Kakisa Lake, south of Yellowknife, actually evacuated.^{2, 17} Some NWT residents referred to this season as “the lost summer.”¹⁷

The Summer of Smoke (SOS) project was designed to generate a holistic view of planetary health impacts of the 2014 NWT wildfires by pairing quantitative and qualitative perspectives in order to inform adaptation to future smoke-filled summers. Drawing on the quantitative data from the overarching project, this article analyzes and describes the air quality exposure in Yellowknife, Dettah, and N’Dilo during the summers of 2014 and surrounding years; assesses the risk of cardiorespiratory health encounters associated with increasing particulate matter; and examines changes in salbutamol dispensation and health resource utilization compared to other years. Few studies examining severe exposures of longer than a few weeks exist in the literature

and almost no available research combines quantitative and qualitative analysis to determine the overall tolerability of a given smoke exposure for a community. This study's subarctic setting puts it at the leading edge of climate-related impacts and the project's approach provides insights on interactions between and among smoke exposure, physical health, mental health and health systems that can inform primary care and public health adaptations to the increasingly severe wildfire seasons that can be expected as the Anthropocene advances.

Methods

Project Structure and Context

SOS is a community-based, interdisciplinary project which investigated the impacts of the NWT's 2014 extreme wildfire season on the health and wellbeing of people in four affected communities: Yellowknife (population=20,497, 24% Indigenous); and the near 100% Indigenous Yellowknives Dene communities of N'Dilo (adjacent to Yellowknife, population=345) and Dettah (across a bay from Yellowknife, population=252); and the Ka'a'gee Tu First Nation in Kakisa (southwest around Great Slave Lake from Yellowknife, population: 36).¹⁸ Many Indigenous individuals in this area maintain a strong connection to the land, continuing traditional hunting, fishing and plant-gathering practices.¹⁹

Study Partners

This project was initiated by representatives of the Yellowknives Dene First Nation, Yellowknife physicians, and Ecology North (an environmental non-governmental organization in Yellowknife), and carried out in partnership with the Dene of the Dehcho from the Ka'a'gee Tu First Nation, with support from external academic collaborators.

Patient and Public Involvement

Representatives of the Yellowknives Dene and the Ka'a'gee Tu First Nation helped to define the overall project structure from the outset. They contributed to the decision to include both quantitative and qualitative elements in the larger project¹⁷ in order to evaluate the impact of wildfires on traditional land-based activities and overall wellness, with the goal of optimally informing practical adaptation policies. They were partners on the grant application, co-defined the centrality of respiratory issues to the study and collaboratively generated the interview guide and community engagement strategy. Decision-makers, business leaders, and public health leaders in Yellowknife were also engaged and interviewed. Plain language summaries and videos were prepared to facilitate effective communication of initial findings, and were presented at community gatherings. A final plain language policy paper and three short video vignettes on the community-level adaptive interventions identified as being most likely to improve health during future fire years (clean air shelters with recreation activities, active fire preparation, and attention to both respiratory health and ecoanxiety) were prepared in association with the study's coordinators and distributed to communities across the NWT.

This project was reviewed and approved by the Stanton Territorial Hospital Ethics Board and Wilfrid Laurier University Research Ethics Board (REB #4700), as well as by the Aurora Research Institute (license numbers 15733; 15801).

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Statistical Analysis

Descriptive

Air Quality

Data for particulate matter (PM_{2.5} and PM₁₀) and covariates (humidity and temperature) from June 15-Aug 31st 2012-2015 were obtained from the Yellowknife Air Quality Monitoring station, which provides information relevant to Yellowknife²⁰ as well as N'Dilo and Dettah, both of which are approximately 3km from the outskirts of Yellowknife. 24-hour mean PM_{2.5} levels were examined for each study year, and the proportion of study days each year where the 24-hour mean PM_{2.5} exceeded the WHO recommended 24-hour mean air quality threshold of 25µg/m³ was determined.²¹ PM₁₀ was described to facilitate comparison with other studies (Table 1).

Risk of Particulate Matter for Emergency Room Visits and Hospital Admissions

Routinely-collected administrative data from emergency room (ER) visits and hospital admissions for June 15-August 31, 2012-2015 was retrieved from Stanton Territorial Hospital (the NWT referral hospital). Cause-specific diagnoses using the most responsible diagnosis were coded using International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada (ICD-10-CA) codes for cardiorespiratory diagnoses (footnote of Table 2). Administrative records included information on age, sex, and ethnicity (non-Indigenous and Indigenous groups: Inuit, Dene, Métis). Indigenous/non-Indigenous status was determined from NWT personal health numbers. Patients from out of territory were considered to be non-Indigenous. Population estimates by age, sex, and ethnicity were obtained from the Territorial Bureau of Statistics.¹⁸

Generalized linear Poisson regression models were used to estimate the effect of daily PM_{2.5} on population rates of cardiorespiratory ER visits and hospital admissions. Subgroup analyses for asthma, pneumonia and chronic obstructive pulmonary disease (COPD) were conducted by age, sex, and ethnicity. We hypothesized that the effect of PM_{2.5} on asthma might change during the summer of 2014 as population members fled the territory or filled asthma medications. To assess this, we examined the relationship of PM_{2.5} with asthma in early summer (June 15-July 31 2014) and late summer (August 1-August 31, 2014). All models were adjusted for: age, sex, ethnicity, day of week, humidity, and temperature. Goodness of fit and Poisson regression assumptions were checked for all models.

The primary particulate matter exposure was assessed using a 2-day average 24-hour mean PM_{2.5} (i.e. average of previous and current day 24-hour mean PM_{2.5} levels), as per previously published literature that found it to be more highly-associated with clinical outcomes than a 1-day 24-hour mean.^{8, 10} Sensitivity analyses were conducted for primary outcomes using 1-day 24-hour mean PM_{2.5} and PM₁₀ exposures. All incidence rate ratios were calculated for a 10µg/m³ increase in measured PM_{2.5}.

Health Resource Utilization During the Summer of 2014

To assess the burden of wildfire smoke on health resources in 2014 compared to non-extreme fire years (2012-2013), we examined salbutamol dispensations, clinic visits for respiratory symptoms and diagnoses, as well as cardiorespiratory ER visits and hospital admissions. 2015 was the NWT's second-worst fire season on-record, and was thus not used as part of the baseline, but is included to examine whether health utilization decreased after 2014.

Aggregate monthly salbutamol dispensation information was gathered from Yellowknife's five out-patient pharmacies (daily data and inpatient dispensations were unavailable). An equivalency between metered-dose inhaler (MDI) and nebulized salbutamol was generated using similar equivalencies to those used in a Cochrane review²² (see Appendix) and calculations were done equating one outpatient dose to two puffs by MDI or 833 mcg of nebulized salbutamol. The correlation with the proportion of days where the 24-hour mean PM_{2.5} was greater than the WHO recommended air quality threshold was determined.

De-identified data on clinic visits for respiratory symptoms and diagnoses were retrieved using the practice search function of the Yellowknife Health and Social Services (YHSSA) Wolf electronic medical record by YHSSA employees on the research team. Visits for upper respiratory tract infections, conjunctivitis, bronchitis, cough, asthma, COPD, pneumonia, and allergy were searched using standard case insensitive terms. Chi-squared tests were performed to assess differences in the number of symptoms and diagnoses by year.

To determine changes in ER visits for cardiorespiratory diagnoses in 2014 compared to 2012-13, we calculated standardized incidence ratios (SIRs). Territorial statistics demonstrated that there was no significant change in the study population (Yellowknife, Dettah, N'Dilo) between 2012-2015.¹⁸ Therefore, we calculated the expected number of ER visits by averaging the number of visits in 2012 and 2013. To calculate the SIRs, we divided the observed number of ER visits in 2014 by the expected number of visits.

All analyses were performed using SAS 9.4 Cary, N.C., USA.

Results

Figure 1 and Table 1 show the distribution of 24-hour mean PM_{2.5} by year. The median 24-hour mean PM_{2.5} was five-fold higher in 2014 compared to 2012, 2013, and 2015, and reached a peak of 320.3 µg/m³ on August 5, 2014 (highest hourly recorded PM_{2.5} that day was 873 µg/m³). The maximum 24-hour mean PM₁₀ was 350 µg/m³ on August 3, 2014 (hourly maximum that day was 772 µg/m³). In 2014, PM_{2.5} levels were above the recommended WHO threshold of 25 µg/m³ 43 days (55%).

Table 1: 24-hour mean PM_{2.5} and PM₁₀ from June 15-Aug 31

	Median PM _{2.5} (Q1,Q3)* µg/m ³	Maximum PM _{2.5} µg/m ³	% of days with PM _{2.5} ≥ 25 µg/m ³	Median PM ₁₀ (Q1,Q3) µg/m ³
2012	6.2 (5.6, 8.9)	65.7	4 (3 days)	13.3 (9.5, 17.9)
2013	6.7 (4.4, 14.5)	67.6	9 (7 days)	12.6 (8.4, 22.0)
2014	30.8 (16.2, 85.0)	320.3	55 (43 days)	43.8 (26.5, 100.7)
2015	6.4 (4.6, 11.5)	99.6	12 (9 days)	14.9 (10.3, 28.8)
*Q1- first quartile; Q3- third quartile				

Spikes in PM_{2.5} in 2012, 2013, and 2015 were related to intermittent wildfires. The 2015 maximum 24-hour mean PM_{2.5} on June 30, 2015 was 99.6 µg/m, lower than 2014 highs, but higher than 2012 and 2013. 12% of days in 2015 exceeded the WHO threshold.

Risk of Particulate Matter for Cardiorespiratory Emergency Department Visits and Hospital Admissions

A 10 µg/m³ increase in two-day average 24-hour mean PM_{2.5} was associated with a 3% increase in ER visits for respiratory diagnoses [Incidence Rate Ratio (IRR) 95% CI:1.03 (1.01, 1.05)](Table 2). Sensitivity analyses show consistency using 24-hour mean PM_{2.5} exposure [IRR (95% CI):1.03 (1.01,1.05)], and 24-hour mean PM₁₀ [IRR(95% CI):1.03 (1.01, 1.04)]. This increase in ER visits was highest for asthma (11% increase per 10µg/m³ in PM_{2.5}: IRR(95% CI):1.11 (1.07, 1.14), an impact that was consistent across subgroups of age (except among children aged <5 years)), sex and ethnicity. Increasing PM_{2.5} was suggestive of increased inpatient asthma admissions overall, with strong effects seen among males, and non-Indigenous persons (Table 2).

PM_{2.5} increases were also related to ER visits for pneumonia (6% increase per 10µg/m³ in PM_{2.5}:IRR(95% CI):1.06 (1.02, 1.10), an effect that was evident in children aged <5 years, males and the Inuit population, with a suggestive effect among children aged 5 to 19 and adults aged ≥60 years (Table 2). Pneumonia hospitalizations did not increase overall with higher PM_{2.5} but children aged <5 years did have a 12% increase in admissions per 10µg/m³ in PM_{2.5} IRR(95% CI):1.12 (1.01, 1.25).

PM_{2.5} was not related to ER visits for COPD, but inpatient admissions were increased 11% per 10µg/m³ in PM_{2.5} IRR(95% CI):1.11 (1.02, 1.20). The effect was most noticeable among males, in the Inuit and Dene populations, and among individuals ≥60 years of age.

In sensitivity analyses, an increase in PM_{2.5} of 10 µg/m³ in the extreme fire summer of 2014 was more highly associated with an increase in asthma ER visits early in the summer (June 15-July 31 [IRR (95%CI: 1.19 (1.07, 1.32))], than later in the summer (Aug 1-Aug 31 [IRR (95% CI): 1.04 (0.99, 1.01)]).

No significant association was seen between PM_{2.5} and cardiovascular ER visits [IRR (95% CI): 0.99 (0.84, 1.04)] or inpatient hospital admissions [IRR (95% CI): 1.04 (0.98, 1.10)]. (Table 2)

Table 2: Adjusted risk of cardiorespiratory emergency room visits and inpatient hospital admissions per 10µg/m³ increase in 2-day averaged 24-hour mean PM_{2.5}. All models adjusted for age, sex, ethnicity, day of week, humidity and temperature.		
Outcome	Emergency Room Visits Incidence Rate Ratio (95% confidence interval)	Inpatient Hospital Admissions Incidence Rate Ratio (95% confidence interval)
Cardiovascular Basket	0.99 (0.94, 1.04)	1.04 (0.98, 1.10)
Respiratory Basket	1.03 (1.01, 1.05)	1.03 (0.98, 1.07)
Asthma		
ALL	1.11 (1.07, 1.14)	1.11 (0.99, 1.25)
Male	1.12 (1.08, 1.17)	1.20 (1.01, 1.43)
Female	1.07 (1.03, 1.12)	1.05 (0.86, 1.27)
Inuit	1.11 (1.04, 1.19)	1.01 (0.78, 1.29)
Dene	1.09 (1.00, 1.19)	NE
Non-Indigenous	1.10 (1.06, 1.15)	1.27 (1.06, 1.51)
Age <5 years	0.99 (0.73, 1.35)	0.97 (0.36, 2.61)
Age 5-19 years	1.07 (1.01, 1.14)	1.12 (0.97, 1.29)
Age 20-39 years	1.09 (1.04, 1.14)	0.98 (0.71, 1.36)
Age 40-59 years	1.12 (1.07, 1.18)	NE

Age ≥60 years	1.11 (0.96, 1.30)	NE
Pneumonia¹		
ALL	1.06 (1.02, 1.10)	1.02 (0.94, 1.11)
Male	1.09 (1.04, 1.14)	1.04 (0.95, 1.15)
Female	1.00 (0.92, 1.08)	0.97 (0.82, 1.14)
Inuit	1.10 (1.06, 1.16)	1.09 (0.99, 1.19)
Dene	NE (not estimable)	0.84 (0.57 , 1.23)
Non-Indigenous	0.97 (0.87, 1.09)	0.60 (0.26, 1.37)
Age <5 years	1.13 (1.06, 1.20)	1.12 (1.01, 1.25)
Age 5-19 years	1.09 (0.99, 1.19)	0.98 (0.79, 1.22)
Age 20-39 years	0.95 (0.78, 1.14)	NE
Age 40-59 years	0.96 (0.84, 1.10)	1.10 (0.92, 1.32)
Age ≥60 years	1.06 (0.99, 1.14)	0.80 (0.57, 1.13)
Chronic Obstructive Pulmonary Disease^{1,2}		
ALL	0.97 (0.89, 1.06)	1.11 (1.02, 1.20)
Male	0.99 (0.90, 1.09)	1.12 (1.02, 1.23)
Female	0.89 (0.70, 1.14)	1.09 (0.91, 1.31)
Inuit	0.51 (0.18, 1.44)	1.15 (1.01, 1.31)
Dene	0.16 (0.004, 6.33)	1.17 (1.04, 1.33)
Non-Indigenous	1.00 (0.91, 1.09)	0.66 (0.34, 1.27)
Age 40-59 years	0.81 (0.56, 1.19)	0.95 (0.64, 1.42)
Age ≥60 years	0.99 (0.90, 1.08)	1.12 (1.03, 1.22)
International Statistical Classification of Diseases and Related Health Problems, 10 th Revision, Canada (ICD-10-CA) Codes All cardiac (I00-I52) All respiratory (J00-J99)		

Asthma (J45-J46)
 Pneumonia (J12-J18)
 Chronic Obstructive Pulmonary Disease (J44)
 Chronic Obstructive Pulmonary Disease only in age ≥ 40 years

Pharmaceutical Dispensation and Health Services Impacts of Increased Smoke Exposure in 2014

There was a 48% increase in dispensed outpatient doses of salbutamol in 2014 compared to 2012-13, and this number fell in 2015 [2012: 105618 doses; 2013:130888 doses; 2014:175208 doses; 2015: 147738 doses]. The number of salbutamol doses dispensed each summer was positively correlated with the proportion of days that PM_{2.5} exceeded the WHO 24-hour mean guideline value of 25 $\mu\text{g}/\text{m}^3$ ($r=0.89$, $p=0.11$).

Primary care clinic visits for cough and pneumonia doubled in 2014 and clinic visits for asthma increased more than 50% compared to earlier years ($p<0.0001$ for each). Clinic visits with these presentations decreased in 2015 but remained higher than 2012/13 levels (Figure 2). There was no change seen in clinic visits for upper respiratory tract infection, conjunctivitis, bronchitis, COPD, or allergies.

ER visits for asthma demonstrated a more than two-fold increase in 2014, an effect that was exaggerated in females, adults aged ≥ 40 years, and Dene people. There was no increase in ER visits for combined respiratory diagnoses in 2014 compared to 2012-13 [SIR(95% CI):1.08 (0.95, 1.22)] (Table 3). Visits for pneumonia increased 57% [SIR(95% CI):1.57 (1.21, 2.00)], and were more common in males, in people aged < 40 years, and in Inuit people. Both ER visits and inpatient admissions for pneumonia were significantly increased in children under five. ER visits for asthma and pneumonia dropped in 2015 compared to the 2014 peak (Table 3). There was no change in cardiac ER visits in 2014.

Table 3- Standardized Incidence Ratios for Cardiorespiratory Emergency Room (ER) visits in extreme fire year 2014 compared to 2012-2013.

	A Mean Observed ER visits 2012+ 2013 =2014 Expected	B Number ER visits 2014 (Observed)	C Standardized Incidence Ratio=A/B	D Number ER visits 2015
CARDIOVASCULAR BASKET	(51+48)/2=49.5	62	1.25 (0.97, 1.60)	63

RESPIRATORY BASKET	(251 +239)/2=245	265	1.08 (0.95, 1.22)	223
ASTHMA				
ALL	(26+32)/2=29	59	2.03 (1.56,2.61)	21
Male	(13+16)/2=14.5	22	1.52 (0.98, 2.26)	6
Female	(13+16)/2=14.5	37	2.55 (1.82, 3.48)	15
Age <5	(1+3)/2=2	4	2.00 (0.64, 4.82)	2
Age 5-19	(9+11)/2=10	13	1.30 (0.72, 2.17)	7
Age 20-39	(11+12)/2=11.5	20	1.74 (1.09, 2.64)	8
Age 40-59	(5+5)/2=5	19	3.80 (2.36, 5.82)	4
Age ≥60	(0+1)/2=0.5	3	6.00 (1.53, 16.33)	0
Inuit	(8+8)/2=8	16	2.00 (1.18, 3.18)	5
Non-Indigenous	(13+16)/2=14.5	27	1.86 (1.25, 2.67)	7
Dene	(2+1)/2=1.5	5	3.33 (1.22, 7.39)	2
PNEUMONIA				
ALL	(39+40)/2=39.5	62	1.57 (1.21,2.00)	43
Male	(19+19)/2=19	38	2.00 (1.44,2.72)	25
Female	(20+21)/2=20.5	24	1.17 (0.77,1.72)	18
Age <5	(6+4)/2=4.5	16	3.56 (2.11,5.65)	13
Age 5-19	(2+6)/2=4	13	3.25 (1.81,5.42)	4
Age 20-39	(2+4)/2=3	9	3.00 (1.46,5.51)	11
Age 40-59	(15+10)/2=12.5	9	0.72 (0.35,1.32)	4
Age ≥60	(14+17)/2=15.5	15	0.97 (0.56, 1.56)	11
Inuit	(14+12)/2=13	29	2.23 (1.52,3.16)	15
Non-Indigenous	(12+12)/2=12	15	1.25 (0.73,2.02)	9
Dene	(3+8)/2=5.5	3	0.55 (0.14,1.48)	8
CHRONIC OBSTRUCTIVE PULMONARY DISEASE¹				
ALL	(20+18)/2=19	11	0.58 (0.29,1.04)	16
¹ Subgroup analyses were not performed for Chronic Obstructive Pulmonary Disease because case numbers were too small.				

Discussion

Statement of Principal Findings

Air quality in Yellowknife was poor in the summer of 2014: the 24-hour mean $PM_{2.5}$ was five-fold higher compared to previous years, it was above the WHO recommended threshold for more than 50% of days and it reached a peak of $320.3 \mu\text{g}/\text{m}^3$ in early August. A $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ was associated with an 11% increase in asthma-related ER visits, a 6% increase in pneumonia-related ER visits and an 11% increase in COPD-related hospital admissions. An examination of outcomes in the presence of a severe wildfire season (2014) compared to previous seasons showed an increase in health service use (i.e. outpatient salbutamol dispensations increased by 45%; primary care visits for cough, asthma and pneumonia increased; and ER visits for asthma doubled). Some impacts were enhanced in subgroups such as young children and Indigenous populations. There was no increase in cardiac ER visits nor cardiac hospital admissions.

Explanation of the Findings in Relation to Other Studies

The 11% increase in ER visits for asthma per $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ seen here was high compared to similar studies: in 2013, Yao et al found a 3% increase in asthma visits per $10 \mu\text{g}/\text{m}^3$ of $PM_{2.5}$ (1.10 (95% CI: 1.00, 1.21) for $30 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$),²³ while in 2016 the same group found a 6% increase in asthma visits per $10 \mu\text{g}/\text{m}^3$ over a fire season where the mean daily $PM_{2.5}$ was $10.2 \mu\text{g}/\text{m}^3$ on extreme fire days, which is lower than our median daily mean $PM_{2.5}$ of $30.8 \mu\text{g}/\text{m}^3$.⁹ Henderson et al found a 5% increase in the odds of an asthma-specific physician visit with a $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} .²⁴ The strong relationship between $PM_{2.5}$ and asthma visits in our study may be associated with the fact that people with airways sensitive to air pollution may not initially have had medications on-hand given Yellowknife's excellent baseline air quality ($PM_{2.5}=6 \mu\text{g}/\text{m}^3$). The length and severity of the smoke exposure would also have worsened indoor air quality despite closed windows.^{10, 25, 26} Incomplete compliance with public health advice to stay inside could have exacerbated health impacts, as a telephone survey of 441 Yellowknife residents in July 2014 reported that 76% of respondents had seen or heard air quality related announcements asking them to stay inside,²⁷ but only 48% had spent less time outdoors.²⁷ Of those who did change their activities, almost one-fifth of respondents reported reduced strenuous aerobic activity or exercise,²⁷ an undesirable adaptation given the health benefits of exercise.²⁸ Analysis of 30 interviews conducted as part of the project and published elsewhere confirmed reduced physical activity, decreased feelings of wellness, and a sense of isolation that one subject compared to being in jail.¹⁷ Many participants worried that the smoke and uncomfortable coping strategies could be a "new normal" as a result of the changing climate.¹⁷

A stronger association between $PM_{2.5}$ levels and ER visits for asthma was seen earlier in 2014 than later, which may be due to patients managing their symptoms at home in the latter part of the summer after having filled their prescriptions. Also, later in the summer some residents spontaneously evacuated¹⁷ and leaders coordinated to offer free recreation opportunities in clean air shelters, which may have decreased symptoms related to outdoor exercise.⁴

The risk of asthma-related emergency room visits and inpatient hospital admissions per $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ was higher in men, but the relative change in asthma-related ER visits in the extreme fire year of 2014 compared to other years was enhanced amongst women. There was a stronger increase in the association between $PM_{2.5}$ levels and ER visits for asthma, as well as a

greater increase in ER visits, in people over forty years of age. Previous studies have more often shown increased risk of wildfire-related asthma symptoms in women and in middle-aged and older adults.¹⁰

The effect of PM_{2.5} on pneumonia was pronounced among the very young, the elderly, males, and Inuit people. Studies are inconsistent regarding differential effects of smoke by age, and smoke has been linked to poorer outcomes for people of lower socioeconomic status.¹

PM_{2.5} was not related to ER visits for COPD and neither were there increased overall ER visits or hospital admissions for COPD. However, hospital admissions for COPD did increase by 11% per 10µg/m³ PM_{2.5}, IRR(95% CI) 1.11 (1.02, 1.20), an effect that was strongest in males, in Inuit and Dene people, and in individuals over 60. This is slightly higher than the 6.9% increase in COPD admissions per 10µg/m³ of PM_{2.5} seen in a previous study,²⁹ and is generally in line with increasing evidence of an association between wildfire smoke and COPD exacerbations.

Indigenous Peoples in Canada experience pervasive health disparities due to “the socioeconomic, environmental, and political contexts of their lives, a context inextricable from past and contemporary colonialism.”³⁰ Poor housing and increased exposure to environmental tobacco smoke may contribute to respiratory symptoms among Inuit populations in Canada,³¹ for example, and rates of lower respiratory tract infections have been shown to be elevated in children.³² Studies from Australia found a stronger relationship between PM₁₀ levels and respiratory hospital admissions for Indigenous populations than non-Indigenous populations,^{33, 34} with one study controlling for socioeconomic factors.¹⁶ Targeted interventions for high-risk populations could reduce impacts: a US study found a significant increase in clinic visits for respiratory symptoms on the Hoopa Valley National Indian reservation during a smoke episode, and noted that longer use of high-efficiency particulate air cleaners lessened symptoms, while the use of masks and evacuation did not.³⁵

Strengths and Limitations of the Study

The NWT’s excellent baseline air quality enables the influence of PM_{2.5} on respiratory outcomes to be more directly attributed to wildfires than in most studies.¹⁰ Also, the smoke exposure was particularly long and severe, making results useful for forward-looking adaptation planning in the Anthropocene.¹⁰ In addition, interview data from the larger project facilitated practical policy-relevant interpretations of our results. Limitations of the study were the inability to estimate outmigration of symptomatic people who self-evacuated to other provinces or regions. Significant outflow would result in the study underestimating impacts. Given that impacts found were already substantial, this may not have resulted in material change to conclusions or recommendations. Additionally, ethnicity information was not available for the small number of out-of-territory residents, meaning that rates for Indigenous and non-Indigenous subgroups may have been slightly higher or lower than shown here. Finally, there was a lack of data availability with regards to daily salbutamol dispensations, inpatient salbutamol use, and daily clinic visits which limits detail in those areas, however the trends are clear and in line with previous studies, and the multiple areas of the health system investigated in this study combined with the qualitative information gathered in the sister study provide an overall multifaceted evaluation of the health impacts of the summer of smoke on this subarctic population.

Meaning of the Study

This severe, prolonged wildfire smoke exposure was associated with important respiratory impacts which may have been compounded by the difficulty of following public health messaging to stay inside due to the isolation, anxiety, and decreased physical activity associated with being restricted indoors for a prolonged period. Healthy adaptation to extreme wildfires requires a planetary health-based holistic approach and improved coordination between public health, primary care, municipal and recreation leaders.

Future studies

There is a need to investigate the long-term impacts of acute, prolonged smoke exposure as well as differential impacts on people of low socioeconomic status. Further study is needed to evaluate multipronged health-systems approaches which include primary care-based attention to the needs of vulnerable populations involving proactive prescription of asthma-reliever medications and consideration for at-home air filtration^{28, 36}; public health-generated coordination to improve access to clean air shelters with recreation activities, and public health strategies that encourage populations to go outside during clean air windows and which attend to the complex interaction between smoke, isolation, climate change-related eco-anxiety and other mental health impacts.³⁷

Policy implications and future directions

Severe wildfires have recently impacted communities from Canada to California to Australia and beyond, with increasing frequency and intensity predicted as global surface temperatures continue to rise.³ Climate-related health effects impact all populations, but are likely to disproportionately affect communities living at the frontlines of rapid climate change, as well as those experiencing systemic racism, socioeconomic and health disparities, and/or the enduring effects of colonization. This study demonstrates a need for active adaptation efforts to include attention to systemic factors and the social determinants of health, and to be more proactive. This aligns with comments by interviewees in the study's sister arm, who described how uncertainty was associated with anxiety, whereas active preparation not only decreased risk but also worry.¹⁷ Primary care practitioners can identify smoke-susceptible individuals prior to wildfire season and ensure salbutamol prescriptions and air filters are available as appropriate. Public health practitioners can utilize satellite-based smoke forecasting to enhance adaptation interventions that include maximizing opportunistic outdoor and accessible, well-ventilated indoor recreation and socializing opportunities. Climate-related health impacts are here, but healthier adaptation is possible.

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Author Contributions

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2
3 1-Courtney Howard, MD (Corresponding author)

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5 Contributions: Study conception and design, building of team, grant application, review of
6 qualitative interview content, collection of quantitative data, study write-up and editing.

7
8
9 2-Caren Rose, PhD

10
11 Contributions: Study design, quantitative data analysis, study write-up and editing.

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13 3-Warren Dodd, PhD

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15 Contributions: Qualitative data collection, qualitative data analysis, consultation on statistical
16 analyses of quantitative data, review and editing of study write-up.

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18 4-Katherine Kohle, MD

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20 Contributions: Study conception and design, grant application, collection of quantitative data,
21 study editing.

22
23 5- Craig Scott, BES

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25 Contributions: Study conception and design, grant application, project management and
26 community outreach, study editing.

27
28 6- Patrick Scott, PhD

29
30 Contributions: Study conception and design, grant application, interview design and qualitative
31 information, study editing

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33 7-Ashlee Cunsolo, PhD

34
35 Contributions: Study design, qualitative interview design, study editing.

36
37 8-James Orbinski, MD

38
39 Contributions: Study design, grant application, consultation on quantitative analysis, review and
40 editing of study write-up, oversight of project.

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44 **Declaration of Interests**

45
46 Competing interests: all authors have completed the ICMJE uniform disclosure form at
47 www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the
48 submitted work; no financial relationships with any organisations that might have an interest in
49 the submitted work in the previous three years; no other relationships or activities that could
50 appear to have influenced the submitted work. No conflicts of interest exist.

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52
53
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Transparency statement

All authors had full access to the data and take responsibility for data integrity and the accuracy of the analysis. The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data Sharing

The data used in this study includes publicly available air monitoring data, and hospital, and clinic records that were requested from the relevant authorities. Pharmaceutical data was collected from local pharmacies. The data is held by the epidemiologist on our team and is available upon reasonable request.

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Figure and Table Legend:

Figure 1: 24-hour mean PM_{2.5} from Yellowknife Air Quality Station June 15-August 31, 2012-2015.

Figure 2: Yellowknife Health and Social Services primary care clinic visits for respiratory symptoms and diagnoses June 15-August 31, 2012-2015.

Table 1. 24-hour mean PM_{2.5} and PM₁₀ from June 15-Aug 31, 2012-2015.

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Table 2. Adjusted risk of cardiorespiratory emergency room visits and inpatient hospital admissions per 10µg/m3 increase in 2-day averaged 24-hour mean PM2·5.

Table 3. Standardized Incidence Ratios for cardiorespiratory Emergency Room visits in extreme fire year 2014 compared to 2012-2013.

For peer review only

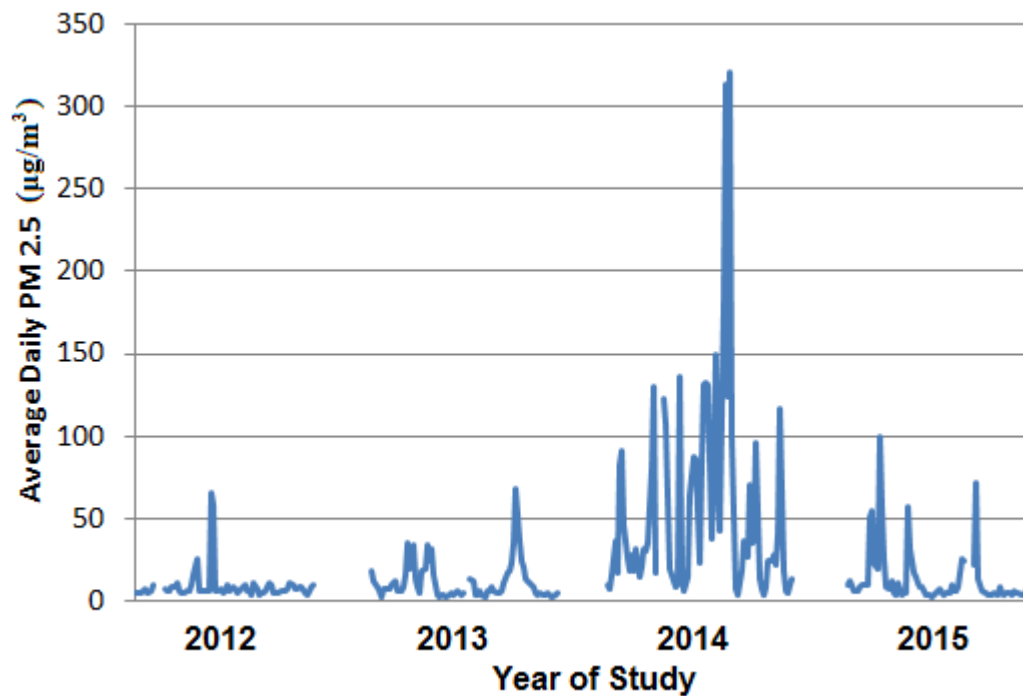


Figure 1: 24-hour mean PM_{2.5} from Yellowknife Air Quality Station June 15-August 31, 2012-2015.

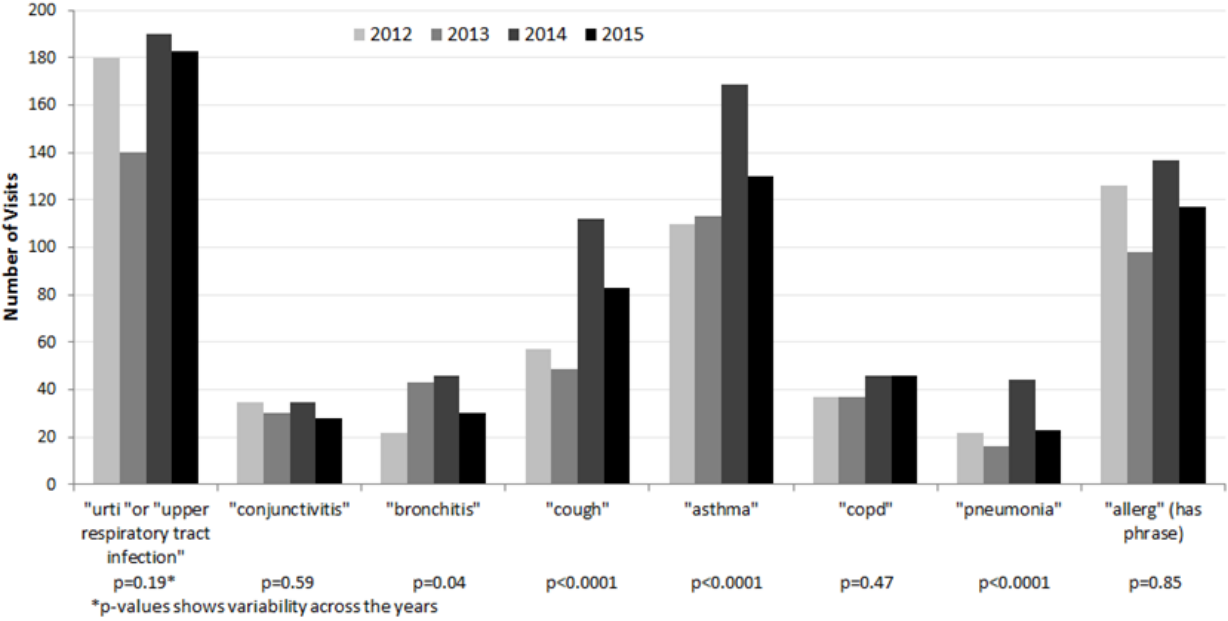


Figure 2: Yellowknife Health and Social Services primary care clinic visits for respiratory symptoms and diagnoses June 15-August 31, 2012-2015.

Supplementary Materials for:

SOS! Summer of Smoke: a retrospective cohort study examining the cardiorespiratory impacts of a severe and prolonged wildfire season in Canada's high subarctic.

A-Appendix 1: Conversion Factor for Nebulized Salbutamol to Salbutamol Administered via Metered Dose Inhaler

The Summer of Smoke study tracks the dispensation of outpatient doses of salbutamol, a beta-agonist, between years. Most salbutamol in Yellowknife is dispensed from pharmacies in the form of metered-dose inhalers (MDIs), meant to be used with a spacer, or in diskus form, but a small amount is dispensed in nebulers. We wanted to analyze them together, and decided that the most clinically-relevant endpoint, a "dose," would be the most useful.

Our efforts to find a standard conversion factor were not successful, so one was derived using a Cochrane review comparing nebulized salbutamol to salbutamol administered via MDI.

1-The standard outpatient salbutamol dose prescribed by Canadian doctors is 2 puffs by MDI or by diskus. We therefore decided: 1 salbutamol dose=2 puffs.

2-The Cochrane review, "*Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma*,"(1) which found no significant advantage to nebulers over treatment with MDI and spacer, reported that, "The dosage ratio between delivery methods varied from 1:1 to 1: 13, with the larger doses administered via nebuliser. The median dose administered via nebuliser was four times that administered via spacer, a dosage ratio of 1:4 (interquartile range (IQR) 1:2 to 1:8)." There is substantial variability in doses: they state, "In clinical practice the dose of beta -agonist delivered to the airways varies depending on the type of nebuliser or spacer used and the characteristics of the individual's airways at that time."

3-To obtain a value for the purposes of our calculation, we divided the standard Canadian emergency room (ER) nebulized dose of salbutamol (2.5 mg) and divided it by the median dosage ratio of 1:4 from the Cochrane review ($2.5\text{mg}/4=625\text{mcg}$), reasoning that the average study would therefore have been comparing a 2.5mg nebule to 625 mcg of MDI + spacer administered treatment.

4-We then used that ratio between nebulers and MDI doses to determine a nebule equivalent to the standard outpatient dose, which we'd defined as 2 puffs by MDI: 625mcg (ER dose MDI)/200mcg (outpt dose MDI)=about 3 fold difference between ER usual MDI dose and outpatient standard MDI dose.

5-To calculate a standardized outpatient dose of nebulized ventolin, we maintained equivalency to the MDI dose by also dividing by 3. $2.5\text{mg}/3= 833 \text{ mcg of nebulized ventolin}= 1 \text{ standard outpatient dose nebulized ventolin}$.

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Over the time interval that we are interested in, pharmacies dispensed nebules in 1mg, 2mg, 2.5mg and 5mg doses. The above ratio would make nebules equivalent to: 1mg nebule/833mcg=1.2 standard outpatient nebulized doses 2mg=2.4 standard outpatient doses 2.5mg=3 doses standard outpatient doses 5mg=6 doses standard outpatient doses

References:

1.Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Cochrane Database Syst Rev. 2013(9):CD000052.<https://www.ncbi.nlm.nih.gov/pubmed/24037768>

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6, 7
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6, 7
		(b) Describe any methods used to examine subgroups and interactions	6, 7
		(c) Explain how missing data were addressed	6, 7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	6, 7

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	N/A
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	N/A
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-12
		(b) Report category boundaries when continuous variables were categorized	7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14, 15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14, 15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.