

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. $2.5\text{mg}/3= 833 \text{ mcg of nebulized ventolin}= 1 \text{ standard outpatient dose nebulized ventolin}$.

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>