Air pollution in Reykjavík and use of drugs for obstructive airway diseases

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Thesis submitted for Master of Public Health (MPH) degree
University of Iceland
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Loftmengun í Reykjavík og notkun lyfja gegn teppusjúkdómum í öndunarvegi

Hanne Krage Carlsen

Ritgerð til meistaraprófs í lýðheilsuvísindum
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Abstract

Introduction: Iceland's capital region has overall good air quality, but sulphur gas (H_2S) emissions from geothermal power plants and particle pollution (PM) are of concern. Short-term effects of ambient H_2S at moderate levels are largely unknown. PM is known to aggravate symptoms of respiratory disease. This is the first study to examine the association between daily air pollution levels and respiratory health in Iceland's capital area.

Data: A timeline of the daily number of adults in the capital area who were dispensed one or more drugs for obstructive pulmonary diseases (WHO ATC category R03) were obtained from by the Directorate of Health drug registry. Data on PM_{10}, NO_2, O_3 and H_2S as well as weather factor measurements were provided by the City of Reykjavík Environmental Office. The study period was from February 22nd 2006 to September 30th 2008.

Methods: The daily number of individuals dispensed drugs for obstructive pulmonary disease was modeled as a function of three-day moving average- and the three-day moving average of the daily maximum 1-hour mean (peak pollution) of the pollutants with lag 0 to 14 days using Poisson regression. The model included covariates to adjust for climate, time trends, influenza season and day-of week. Insignificant covariates were excluded from the model.

Results: There was a positive association between air pollution levels and the daily number of individuals who were dispensed drugs with a lag of three days. The association was significant ($p < 0.05$) for lag 3 to 5 of the 24-hour mean of H_2S and PM_{10} in a three-day moving average model. The increase corresponds to an increase in the number of individuals who were dispensed drugs of 3% and 2% between the 10th and 90th percentile of PM_{10} and H_2S respectively. Risk estimates for the number of individuals dispensed drugs as a function of peak pollution were similar to estimates for three-day moving average for PM_{10} and H_2S, 6% and 5% for NO_2 and O_3, all significant.

Conclusion: There was a small but statistically significant association between ambient air pollution in Iceland's capital and dispensings of respiratory drugs, particularly for peak pollution. The results indicate that intermittent exposure to ambient H_2S may aggravate symptoms of respiratory disease.

Ágrip

Inngangur: Loftgæði á höfuðborgarsvæði Íslands eru yfirleitt góð en brennisteinsmengun (H_2S) frá jarðhitavirkjunum og svifryk (PM) eru áhyggjuefni. Skammtímaáhrif brennisteinsvetni á heilsu eru nær óþekkt en sýnt hefur verið fram á að svifryk veldur versnun á einkennum öndunarfærasjúkdóma. Þetta er fyrsta rannsóknin á sambandi loftmengunar og öndunarfæraheilsu á höfuðborgarsvæði Íslands.

Gögn: Fenginn var daglegur fjöldi einstaklinga 18 ára og eldri sem leysti út lyf gegn teppusjúkdómi í öndunarvegi (ATC-lyfjaflokkur R03A) úr lyfjagagnagrunni Landlæknisembættisins. Gögn um magn svifryks (PM_{10}), níturoxíðs (NO_2), ósons (O_3), brennisteinsvetnis (H_2S) og veðurskilyrði voru fengin frá Umhverfissviði Reykjavíkurborgar. Rannsóknartímabilið var frá 22. febrúar 2006 til 30. september 2008.

Aðferðir: Poisson aðhvarfsgreining var notuð til að greina samband daglegs mengunarmagns og fjölda einstaklinga sem leystu út lyf gegn teppusjúkdómi í öndunarvegi (R03) sem og fjölda þeirra sem leystu út adrenvirk innúðunarlyf gegn teppusjúkdómum í öndunarvegi (R03A). Meðaltal sólarhringsmælinga og meðaltal hæsta klukktímagildis var reiknað fyrir þriggja daga tímabil og notað sem tæri, með 0-14 daga seinkun (lag). Leiðrétt var fyrir áhrifum veðurs, tímaþætti, flensutímabilum og vikudögum. Eingöngu marktækar leiðréttingarbreytur voru hafðar með í reiknilíkani.

Niðurstöður: Jákvætt samband reyndist á milli loftmengunar og daglegs fjölda einstaklinga sem leysti út lyf með þriggja daga seinkun. Sambandið var tölfræðilega marktækt fyrir lag 3-5 fyrir þriggja daga meðaltal H_2S og PM_{10}. Áhrif mengunar á fjölda einstaklinga sem taka út lyf samsvarar 3% og 2% aukningu þegar mengun fór úr 10^{nda} upp í 90^{sta} hundraðshlutamark fyrir PM_{10} og H_2S. Áhrifin voru svipuð fyrir þriggja daga meðaltal hæsta klukkutímagildis en þá reyndust NO_2 and O_3 einnig hafa marktæk aukin áhrif á lyfjanotkun.

Ályktun: Aukin loftmengun á höfuðborgarsvæði Íslands virðist hafa væg en tölfræðilega marktæk áhrif á lyfjanotkun borgarbúa við teppusjúkdómi í öndunarvegi, ekki síst þegar litið er til hæstu mengunargilda. Niðurstöður rannsóknarinnar benda til að H_2S auki einkenni öndunarfærasjúkdóma jafnvel þegar aukin mengun varir aðeins í skamman tíma.

Preface

The following work is a Masters of Public Health (MPH) thesis written at the Centre of Public Health sciences at the University of Iceland. The student will graduate from the Faculty of Medicine. The thesis counts 60 ECTS of the studies.

The thesis is formatted according to the regulations of the Faculty of Medicine,[1] and is written in the format in which part of the thesis is an article manuscript to be submitted for publication. This paper therefore contains a thorough theoretical background with an introduction to the current work ending with the research questions, as well as an article, followed by a conclusion with certain respects to Reykjavík and the current work, references and appendices. References are formatted in Vancouver style with references in alphabetical order. The article is partially formatted according to the journal to which it will be submitted (Environmental Health Perspectives) and contains: title, authors, abstract, keywords, introduction, methods, results, discussion, conclusion, references, figures and tables. The references of the article are formatted in EHP style[2].

Acknowledgements

I would like to thank my instructor, Þórarinn Gíslason, for his comments, help and strategic academic advise as well as invaluable aid with navigating the minefield of financial support which ultimately made it possible for me to concentrate on this project.

I would like to thank my supervisors, Birgir Hrafnkelsson for his patience and thoroughness in figuring out how to best model these unruly data in a statistically sound manner. Helga Zoëga has been a superb help and her patience and cunningness is admirable and the advise is always useful.

Also a big thank you to Unnur Anna Valdimarsdóttir for much advise, help and her always good spirits that always installs me with renewed faith in what I'm doing.

Many thanks also to my co-student and partner in the study of health effects of air pollution in Iceland, Ragnhildur Guðrún Finnbjörnsdóttir, who was a great help with the initial data preparation. It has been very good to have another student with a different background when sorting out these overwhelming amounts of data.

I would like to thank the following individuals and institutions for help with providing the necessary data and for their willingness to answer my many questions and thus contributing

1 http://www.hi.is/is/heilbrigdisvisindasvid_deildir/laeknadeild/nam/fragangur_meistararitgerda
2 http://ehp03.niehs.nih.gov/static/instructions.action#ref

invaluable information to the project: Anna Rósa Böðvardsdóttir, City of Reykjavík Department of Environment (Public Health Authority), the staff of the Directorate of Health (Landlæknisembættið), Kristinn Jónsson, Ása Atladóttir, Júlíana Héðinsdóttir, and Margrét Hallsdóttir of the National Institute of Natural History (Náttúrufræðistofnun Íslands).

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I would also like to thank the other staff and students of the Center of Public Health Sciences, especially my office mates in 104. I also would like give a shout-out to my good friends here who have faith in me and thank Jessica Bowe, who proofread the thesis with short notice.

Last but not least I will thank my family and my husband Steinn Steingrímsson who has been a great support and encouragement. It has been great to have someone who is always willing to talk biostatistics and epidemiology over dinner.

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Abbreviations

ATC Anatomical Therapeutic Chemical system; used by WHO to classify drugs according to their usage.

AIC Akaike's Information Criterion

BC Black Carbon

BS Black Smoke

CI Confidence Interval

COPD Chronic Obstructive Pulmonary Disease

CVD Cardiovascular Disease

DDD Defined Daily Dose; the assumed mean maintenance dose per day, WHO.

H_2S Hydrogen Sulfide

IHD Ischemic Heart Disease

IQR Interquartile Range

NO_2 Nitrogen Dioxide

O_3 Ozone

OR Odds Ratio

PM Particle Matter

RH Relative Humidity

RR Relative Risk

SABA Short-Acting β-Agonists

SD Standard Deviation

SO_2 Sulphur Dioxide

TSP Total Suspended Particles

WHO World Health Organization

VOC Volatile Organic Compounds

1 INTRODUCTION

In this chapter, the history and background of the project is briefly described as well as the scope and goals of this project and the subsequent article. Theoretical background, previous studies in the field (particularly those using drug dispensings as health outcome) are outlined as well as a small overview of statistical methods used in previous studies. Information about air pollution and conditions in Reykjavík are provided as well as information regarding the study population and the drugs used as outcome in the study.

1.1 Background

The subject of this thesis is to assess whether day-to-day increases in the levels of four specific air pollutants; particle matter (PM_{10}), nitrogen dioxide (NO_2), hydrogen sulphide (H_2S) and ozone (O_3) in the capital area of Iceland may cause an increase in the dispensing of drugs for obstructive pulmonary diseases to the adult population.

Jóhannsson (2007) highlighted in his MSc thesis (20) that PM pollution in Reykjavík can be very severe for short periods of time and can thus be a health concern. His thesis and the following debate highlighted the need for further research on this subject in Iceland as no large study has been carried out on the local health effects of air pollution. Also, H_2S emissions from two new geothermal power plants east of Reykjavík cause capital area inhabitants to complain about a rotten-egg-odor. There is precious little existing research on the health effects of background exposure to H_2S and especially short-term effects. Currently, as of November 2009, a debate is playing out in the Icelandic media (16, 17) about which guideline health limits to use as reference when evaluating sulphur gas levels.

The current study on the health effects of air pollution levels in the Icelandic capital area is therefore an essential contribution to this debate as it seeks to quantify a problem that we currently do not know the extent of, respiratory health effects of air pollution in Iceland's capital area. The study's initial proposal, framework and brainstorming were developed by the University of Iceland Institute for Sustainability Studies (Stofnun Sæmundar fróða) and the University of Iceland Center of Public Health Science (Miðstöð í Lýðheilsuvísindum).

Traditional health measures used in studies of short-term respiratory health effects and air pollution, such as mortality rates and hospital admissions (see Systematic Literature Review, Appendix A), are likely to be too small or rare in a small population to yield meaningful results with sufficient statistical power. Use of drugs to relieve symptoms of respiratory disease could be a better marker of morbidity as it would track more subtle changes in disease severity. Research using actual drug usage calls for intensive patient monitoring, but drug dispensings, the filling of a prescription in a pharmacy, are routinely registered in some countries for insurance and monitoring reasons. A study by Naureckas et al (28), using register-based methods (Medicaid insurance data), established that the dispensing of short-acting-β-agonists (SABA) are highly associated with emergency room (ER) visits for asthma during the previous days and concluded that drug dispensings can fill as a marker of asthma morbidity. This study did not include information about air pollution, only ER visits and dispensings. As filling a prescription in a pharmacy is a more common event than for example ER visits, this may be a better marker of respiratory health (50). Hence, dispensing of drugs to relieve respiratory symptoms in a population that already has impaired lung function or is sensitized to bad air quality is a more sensitive indicator for respiratory health in a smaller population with good access to health care. All pharmacy dispensings of prescription drugs in Iceland are registered in the The Medicines Registry of the National Directorate of Health which presents a unique opportunity to conduct an ecological study on the health effects of ambient air pollution. In this study, we employ pharmacoepidemiological methods and use data on ambient air pollution levels to investigate the association between levels of air pollutants and the daily amount of dispensed drugs for obstructive pulmonary diseases in the capital area of Iceland.

Illustration 1*: Dusty road in central Reykjavík in spring.*

View from the Hringbraut - Snorrabraut bridge to the north, picture taken April 2008.

2 PREVIOUS STUDIES

The adverse health effects of air pollution has been systematically studied since the Meuse Valley episode in Belgium in 1930 (30) and the London fogs of 1948-1956 (24) which both cost human lives due to a massive short term exposure to anthropogenic air pollution. While many aspects are not yet fully understood about the biological mechanisms by which air pollution harms human health, the pulmonary effects are quite well known. PM pollution increases inflammation in the airways and thus causes exacerbation of respiratory disease and harms the gas exchange. Systemic and cardiac effects of PM pollution is believed to involve reactive oxygen species from the particles which cause oxidative stress to the cells in the lungs. The immune response to the oxidative stress then alters the clotting factors in the blood and increases the allergic response (29).

Long term health effects of urban air pollution have been studied since the 1970s, most often analyzing the association between the spatial distribution of background exposure and rates of various health outcomes in different areas. For example, many studies have sought to associate spatial differences in the prevalence of certain diseases with pollution levels. These studies require large study populations and are highly sensitive to confounding differences in the populations between areas.

However, studies have shown consistent associations between air pollution levels and respiratory-related mortality (57), myocardial infarction-related mortality (27), all-cause mortality rates (15, 33) and shortened life expectancy (34). While there are no studies from Iceland, an international study (42) of air pollution and the risk of chronic bronchitis included subjects from Iceland. The study showed that residence closer to traffic was associated with increased prevalence of respiratory symptoms.

In later years, as statistical methods have evolved, there have been more studies on the short-term respiratory effects of air pollution, which will be discussed in the following section.

2.1 Panel studies

Studies of intermittent symptom exacerbation that do not cause subjects to seek professional medical care (visiting an ER or calling an emergency number) are rare as they require questionnaire methods or spirometry (the measuring of lung output), which is inaccurate and time consuming. Panel studies, in which smaller groups of people with respiratory disease are followed for shorter periods of time, show the subjects to be immediately affected by increased air pollution exposures. In one such study, Lagorio et al (21) studied a panel of subjects with chronic obstructive pulmonary disease (COPD), asthma and ischemic heart disease (IHD). During the study period, subjects were monitored daily with spirometry. Decreases in lung function of COPD subjects were associated with increased levels of fine particle matter (particles with an aerodynamic diameter of < 2.5 µm, $PM_{2.5}$,) and nitrogen dioxide, NO_2. In asthmatic subjects, only NO_2 was associated with decreased lung function. The IHD sufferers who had no lung disease were not affected by pollution. In another study, von Klot et al (52) enrolled a panel of adult asthmatics who recorded symptoms and medication usage and found that 14-day cumulative exposure of fine and ultrafine particles ($PM_{2.5}$ and $PM_{0.1}$, particles with an aerodynamic diameter < 0.1 µm) and NO_2 was most strongly associated with use of corticosteroids while beta-agonist usage was associated with 5-day mean of NO_2 and the total number of ambient particles (the number concentration) of PM. Finally, Trenga et al (46) observed adults with or without COPD and used personal exposure monitors and spirometry to monitor respiratory health. The results showed decreased lung function (FEV1) associated with $PM_{2.5}$ with a 1-day delay, called a *lag* (see chapter 3.1 for a more detailed explanation of lags). In a WHO meta-analysis of European panel studies with bronchodilator use in adults with respiratory symptoms, Anderson et al (2) found the odds ratio (OR) associated with 10 µg/m^3 increase of PM_{10} and O_3 to be 1.01 (95% CI, 0.99-1.31) and 1.41 (95% CI,1.14-1.91) respectively.

2.2 Time series studies

Time series analyses methods are useful when ecological data is available for a whole area but little or no individual information is at hand. Results show that ER visits and admissions frequency for respiratory causes are associated with increases in the concentration of PM_{10}, NO_2, and CO on the same day (13), or for 5- or 7-day moving averages of pollution exposure (51, 56). The effect is more pronounced for elderly patients or those with underlying respiratory disease (13 , 51, 56) and elderly patients who have previously been admitted to the hospital for a respiratory illness (5). Results from a review of time series and other studies concerning the short-term respiratory health effects are discussed in the systematic literature review in Appendix A. Overall, epidemiological studies show air pollution to affect respiratory health and increase cardiovascular disease (CVD) and respiratory mortality. Also, the symptoms of asthma and COPD sufferers, people already sensitized to bad air quality, are worsened by exposure to increased levels of air pollution.

2.3 Studies using drug dispensings as health outcome

While performing the current study, we have become aware of four studies from France and Italy that use dispensings of respiratory medication to estimate health effects of daily ambient air pollution (22, 32, 58), one study (50) used the weekly amount of dispensed individuals and number of defined daily doses (DDD). These studies found significant increments in the dispensing of various types of respiratory medication some days after, or during the same week, as increments in pollution levels. The delayed effect is expected as regular medication users will have a supply of medication in their home, but as they increase their dosage during days with increased pollution levels, they are forced to fill their prescriptions earlier than expected (see chapter 3.1 for more on lag effects). People who experience symptoms for the first time will also experience some delay since they need to see a doctor before being prescribed and subsequently dispensed drugs. Pollutants included in these studies are NO_2, sulphur dioxide (SO_2), black smoke (BS) and total suspended particles (TSP). The strongest effects are found during the same week (for the weekly data) or at lags 4-8 for NO_2 and lags 4-10 for PM_{10}. Not all studies find associations with SO_2. Laurent et al also included O_3, but did not find an association with dispensings of drugs (22).

3 METHODS FOR STUDYING HEALTH EFFECTS OF AIR POLLUTION

Traditional cohort studies enroll a number of people who are then monitored with respect to the exposure and outcome of interest, for example, risk factors for a certain disease , the classical example being smoking and lung cancer (6). This is very expensive and, depending on the incidence of the outcome, it can take many years to get results. Also, there are many possible confounders, which that the information about personal risk factors does not necessary adjust for such as regional differences in air pollution.

When individual-level data from registers are available for a population, it is useful to use case-crossover methods. In these studies, each person acts as their own control and bias due to personal risk factors are eliminated by design. Recently, pitfalls have been found in this design regarding control sampling that may cause increased bias. This issue of case-crossover designs is discussed in Whitaker et al (53). A study in the systematic literature review (Appendix A) comparing results from a case-crossover analysis with results from a time-series analysis shows the results not be significantly different from each other (10), but it is worth keeping in mind. Of the four studies that used drug dispensings as health outcome, the case-crossover study finds the highest risk estimates (22).

Over the past 15 years, due to improvements in computing and statistical techniques, time series studies with regression methods have developed considerably. In these, the short-term, or acute, effects of air pollution are studied by associating day-to-day pollution fluctuation within the same area with immediate health measures (e.g. emergency room visits for respiratory causes with air pollution levels of the previous days or weeks).

The article from Whitaker et al (53) suggests that a well-modeled Poisson regression with dummy variables is the best method available. In most studies of ecological count data (number of relevant health events in an defined area) a Poisson regression is used because its distribution is well suited for modeling counts and the results are given as a percent increase in morbidity. Adjustments for confounders such as pollen counts, weather factors and seasonality are usually applied through different methods such as dummy variables and sine/cosine variables or splines (6).

3.1 Adjustments

When adressing cause and effect in biology, the time that elapses from a change in a variable to the change in the proposed outcome variable is called a lag. In the study of air pollution effects, there is often a delay from the exposure (e.g. increased air pollution) to the presumed effect (e.g. a person visits the ER for asthma symptoms or is dispensed medication), and the analysis must account for this delay. Therefore, to estimate the effect of air pollution on the health outcome of a certain day, air pollution levels of a number of previous days are taken into account.

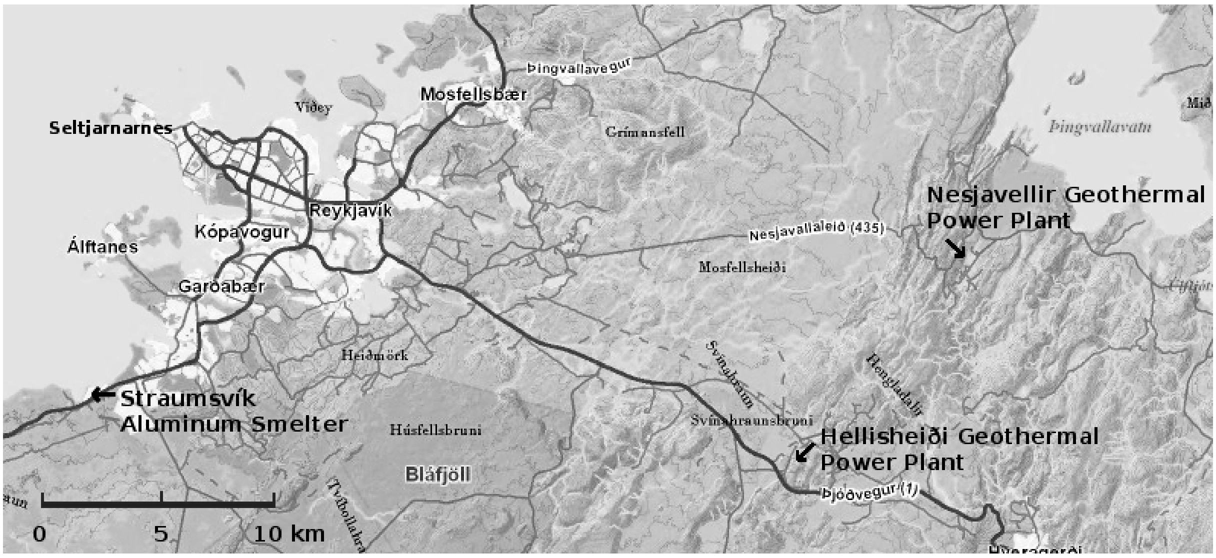
These days are denoted *lagged*, so the air pollution of the previous day is called lag 1, and five days before is lag 5. The same day is lag 0 (no delay). In the case of some health-related events, such as needing to fill a prescription for asthma medication, the event would be likely to happen within a certain time frame regardless, but because of a particular exposure, it happens at a particular time. This effect is called a *harvesting* effect (26). The day-of-week effects are strong in the case of pharmaceutical dispensing, as less people fill prescriptions during weekends, because most health care facilities and pharmacies are closed or have limited opening hours during weekends and holidays. Adjustments are made with binary dummy variables for each weekday.

A problem with studying the health effects of air pollution is that while many individual air pollutants are assumed to influence respiratory health, their individual effects can be hard to distinguish. For many pollutants, ambient concentration is dependent on the same set of underlying factors mainly emissions and weather so there is considerable intercorrelation. In regression analysis, variables are assumed to be independent, therefore correlations, interaction, and confounding must be addressed and only a limited number of pollution variables can meaningfully be included in a model (45).

4 AIR QUALITY IN REYKJAVÍK

The Icelandic capital area is located on a peninsula in the southwest corner of Iceland. The city spreads over low, rolling hills and some valleys. There are six municipalities in the capital area, with Reykjavík being the largest (see illustration 2).

Illustration 2: *Map: The capital area and surrounding landscapes*



Source: ja.is/kort. White areas are inhabited.

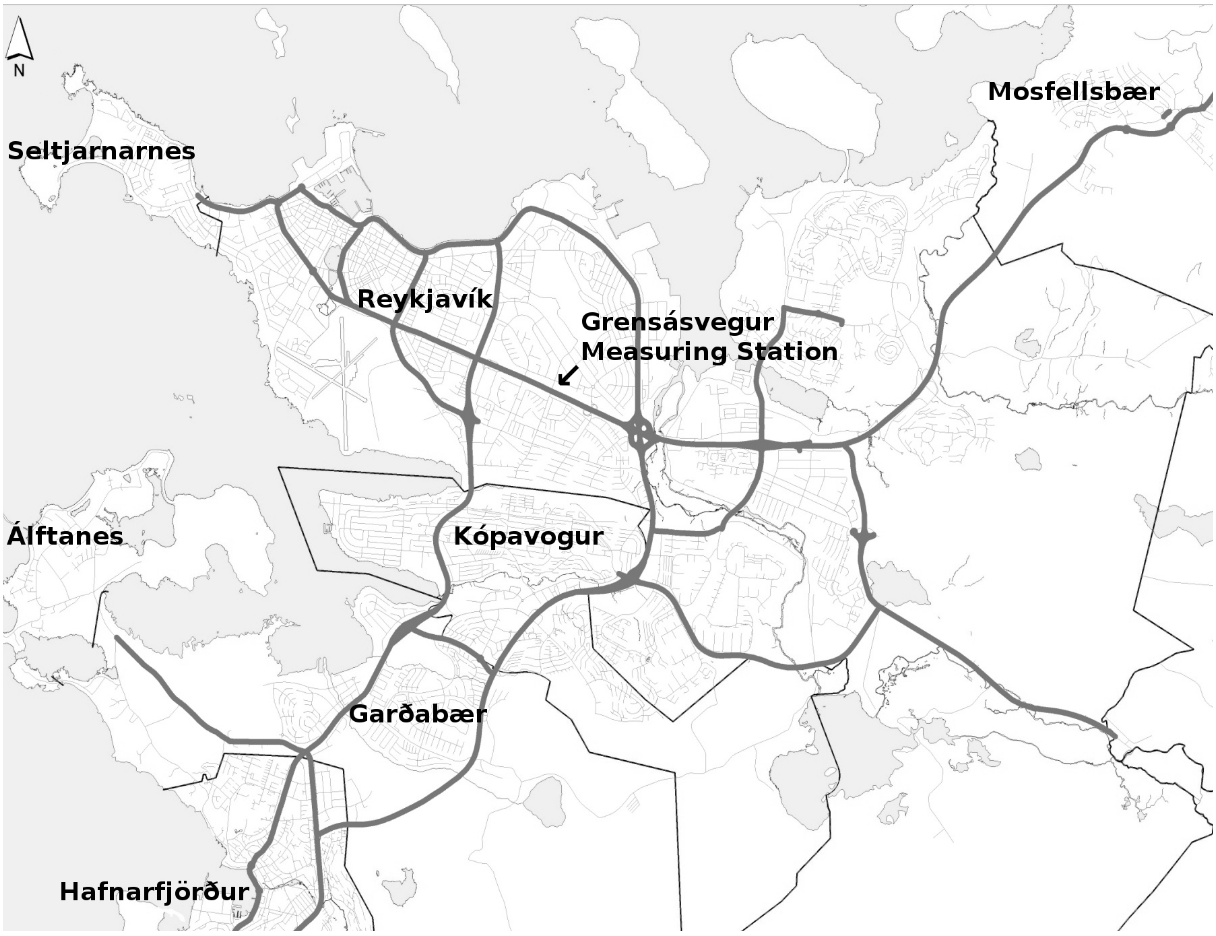
The surrounding villages and suburbs, the municipalities of Garðabær, Seltjarnarnes, Kópavogur, Hafnarfjörður, and Mosfelsbær have now expanded to such a degree that it is now difficult to differentiate municipal boundaries. Some 143,000 people lived in the capital area during the study period 2006-2008, which is twice as many as 50 years ago. The predominant urban landscape of the greater Reykjavík area is non-densely populated urban sprawl, much like in North America.

The number of automobiles per 1000 inhabitants is just over 600 in Iceland, one of the highest in the world (2007 numbers, 40, 43). Incidentally, car ownership is not significantly lower in the capital area, which is unusual for an urban area. Due to the weather, many cars are operated with studded tires for a large part of the year, though public awareness campaigns seem to have decreased the usage of studded tires in the city in recent years (48).

Other city efforts to minimize particle pollution include vigorous street cleaning and the introduction of particle-binding material to road surfaces. Much construction has been undertaken in recent years and is known to be a major source of particle pollution as construction vehicles carry soil and sand from construction sites onto the roads where they accumulate and are whirled back into the air by traffic in dry weather (20), see illustration 1.

See illustration 3 for a map of the large roads and location of the pollution measuring station. In Reykjavík, the most significant air pollution source is automobile traffic (48). No fossil-fuels are burned for house heating. Houses are heated with energy from geothermal sources harnessed from the volcanic regions east of the capital. Following the installment of the second and newest geothermal power plant (Hellisheiði, roughly 20 km southeast of the capital area) levels of volcanic gasses in Reykjavík have increased. The only industrial production to speak of is an aluminum smelter located south of the neighboring village Hafnarfjörður (Alcan Rio Tinto in Straumsvík).

Illustration 3: *Map: Main roads and municipality boundaries of the capital area.*



The thick lines represent main roads with more than 10.000 cars per day. Source: City of Reykjavík.

4.1 Weather conditions of Reykjavík

Weather has a profound effect on the severity of air pollution as weather factors such as rain and wind bind and disperse pollution respectively. Two sets of weather conditions are known to be associated with high pollution levels in Reykjavík: dry, sunny and still weather, in which accumulation of especially gaseous pollutants occur; and dry, cold and windy weather in which particles are whirled into the air in a sort of sandstorm, see illustration 4. Under these conditions, large amounts of particles can be measured in the air (48, 20, 39). The weather in Reykjavík is mild in winter and cool in summer owing to the seaside location, with a mean year temperature of ca. 4°C. The annual precipitation is approximately 1000 mm and the winds are predominantly easterly (9) with a mean wind speed of 5 m/s (18).

4.2 Air pollution

In the study of health effects of air pollution, a tradition has arisen for using certain pollutants as markers, or proxies, for pollution from certain sources as only experimental studies can assign particular health effects to single pollutants. Engine exhaust has many damaging components, but most often NO_2, is used as a marker pollutant, since it is very closely correlated with traffic levels when measured at roadsides. Also, because many pollutants are intercorrelated, a model using many pollutants may not be meaningful since the effects of individual pollutants cannot be distinguished. Overall pollution levels for an area are often deducted using modeling, but there is no exposure model for the capital area of Iceland. Some studies use the proximity of roads with heavy traffic to the subject's residence as a marker for pollution exposure.

While there are no studies that focus directly on O_3 and NO_2 in Reykjavík, research has described sources, concentrations and other properties of PM_{10} (20) and H_2S (31). In the following, individual pollutants used in the study are briefly described and what is known about them with respect to Reykjavík is outlined. It would have been useful to include $PM_{2.5}$ in this study, however, the measurements have been unreliable and not suitable for publication (Böðvarsdóttir, A.R. 2008, personal communication, September 24th. Permission to quote confirmed in mail, appendix D.).

4.2.1 Nitrogen dioxide (NO_2)

NO_2 is a yellow gas emitted from combustion engines which is used as an indicator for all combustion engine emitted pollutants in ambient air since levels of this pollutant are very well correlated with traffic volumes at nearby roads. Thus it is hard to distinguish the effects of NO_2 from other exhaust components such as carbon monoxide (CO), polyaromatic hydrocarbons (PaH's), volatile organic compounds (VOC's) and others. A WHO review (44) concludes that NO_2 is associated with short term effects on pulmonary function and increases airway allergic inflammatory reactions, but notes that NO_2 is an indicator of traffic related pollutants.

4.2.2 Ozone (O_3)

Atmospheric O_3, or ozone (ozone at ground level, as opposed to in the ozone layer, which is in the stratosphere, 7 to 17 km above the earth's surface), is formed in a reaction of nitrogen gasses (NOx), and atmospheric air. The reaction is facilitated by UV-radiation, sunlight, and heat. The reaction typically happens downwind from the nitrogen source so ozone levels can be higher when measured at a background site than at a roadside. Ozone usually peaks hours after the source NOx is emitted. O_3 is a highly reactive gas associated with adverse effects on long-term health, including pulmonary function, respiratory symptoms, and mortality (19) and increased respiratory medication usage (44).

4.2.3 Particle Matter (PM)

Another pollutant that has been the subject for much research is particle matter (PM). PM consists of small particles which are suspended in the air. Often, the particles have a solid core, as opposed to gaseous pollutants such as NO_2, NO, SO_2, CO_2, CO and O_3, volatile organic carbons (VOC's, benzene, toluene, xylene) and polyaromatic hydrocarbons (PaH's). Chemicals in gaseos form, pollen and organic matter can bind to PM. PM is usually divided into coarse, fine and ultrafine particles, where the particles have an aerodynamic diameter smaller than 10, 2.5 and < 0.1 µm respectively.

This classification of particles is based on their behavior in ambient air and deposition rates in the respiratory system. In particular, particle size (aerodynamic diameter) determine how far the particles are inhaled into the lungs, where some fraction of the particles are deposited, the rest is exhaled. Particles larger than 10 µm are not usually suspended in stale air for long, these particles are *inhalable,* meaning that they can be breathed into the body, but are most often deposited in the nose, throat and above the vocal chords (at *larynx*). Particles that are 10-2.5 µm in aerodynamic diameter are called *thoracic*, they pass below the larynx and can be deposited there. Particles with an aerodynamic diameter less than 2.5 µm are *respirable* which means that they enter the alveoli and some are deposited there (4).

Particle size is largely dependent on the source. Larger particles, (PM_{10}), tend to originate from mechanical processes such as grinding (for example that of studded tires against asphalt) while engine combustion tends to generate smaller particles ($PM_{2.5}$).

Illustration 4: *Visibility over the capital area.*

Images taken from the Esja mountain north of Mosfellsbœr. Top; main city features and mountains of the Reykjanes peninsula are visible. Below; visibility is decreased and the horizon obliterated (PM levels were > 120 µg/m^3). Both pictures are taken on cold, clear autumn days, on the picture below, it was also windy.

Once emitted, particles can accumulate into larger particle conglomerates. Most air pollution regulation and monitoring is based on the mass of the particles in the air (measured as microgram/m^3, µg/m^3). While this is practical, particle toxicity is highly dependent on a number of factors beyond mass. These include number concentration (the number of particles in a given air volume), density of the individual particles and the size of the surface area as well as chemical composition. PM with a high metal content seems to be more toxic (4).

Overall, PM has been found to alter lung inflammatory reactions and increase respiratory symptoms and medication use (29, 44).

Total suspended particles (TSP), black smoke (BS) and black carbon (BC) are older terminology used in some articles about air pollution. TSP is the mass of all particles suspended in the air but makes no further distinction that allows speculation about wheter the particles are respirable, their source, or other properties. Black smoke is a measure of the soot content of PM; it is measured by light absorbance of the filters used to gather particulate matter from the air. Black carbon is an index of ambient particles measured by reflectometry representing black particles smaller than 4 µm in diameter (4, 15).

An analysis of the ambient PM10 samples from the measuring stations in Reykjavík show them to contain 55% asphalt, 25% soil, 11% salt, 7% soot from exhaust and 2% brake lining (39). The large percentage of asphalt has been attributed to the use of studded tires during winter. Also, during the construction boom happening in Reykjavík in recent years, dust control has not been a priority. Thus, vehicles leaving construction sites carry mud stuck to the wheels onto the roads and streets where it is subsequently introduced into circulation by traffic in dry weather (20). Some events where air particle concentrations rise dramatically are due to soil erosion outside the city, but with the current data, there is no way in distinguishing the source of pollution. In the capital area, PM levels pass the health limits roughly 25 times every year, usually happening during winter and early spring in cold, dry weather (9).

4.2.4 Hydrogen sulphide (H_2S)

H_2S is a gas which is emitted from geothermal processes and certain industrial processes (e.g. paper mills, 54). During the fall of 2006, a new geothermal power plant, Hellisheiði (see illustration 5), was implemented some 25 kilometers from the eastern part of the capital area, in addition to an older plant, Nesjavellir (operating since 1990), located slightly to the north east (see map of the area page 15). The addition of the new power plant in September 2006 prompted the city of Reykjavík to commence continuous monitoring of ambient H_2S concentrations in Reykjavík half a year before the plant began operations. The measurements revealed that the mean level of H_2S increased drastically after the plant began operations (see Figure 1). Further analysis has shown that the levels measured in Reykjavík are very dependent on wind direction and wind speeds and therefore levels can become very high when the winds come from the east. The H_2S concentration can also be very different across the capital area because of subtle differences in landscape morphology and wind turbulence (31).

Sulphur gasses from geothermal sources near populated areas are only known in volcanic regions such as Hawaii, New Zealand and the Azores. Background exposure to these gasses are associated with increased prevalence of respiratory disease (1, 7, 25) and other diseases (23). We have not found any studies of short-term effects.

Another sulphur gas, SO_2, has traditionally been included in air pollution studies in industrialized countries as it is prevalent in relation to coal burning. SO_2 can be oxidized from H_2S (31) but the main source of this gas in Iceland is automobile exhaust (48). In addition, SO_2 is very well correlated with nitrogen gas levels, which is an indicator of traffic density. SO_2 levels are very low in Reykjavík; the mean for year 2006 is 1.7 µg/m^3 (48).

Illustration 5: *The Hellisheiði Geothermal Power Plant*

View to the south over Hellisheiði Geothermal Plant which opened September 2006 and is one of two plants located in the Hengill volcano area, some 20 kilometers east of the capital area. Winds are easterly, so this emission cloud will not disturb capital area residents.

4.3 Health limits for ambient air pollution

The official limits for ambient air pollution in Iceland are adapted from EU regulations. The limits discussed here health limits, which are; "based on scientific knowledge to prevent or reduce harmful effects to human health and/or the environment. The limit can be set to protect the environment as a whole eða specific parts of it (such as health protection limits...).” (author's translation, 37).

Health limits for three pollutants in this study are shown in table 1. PM_{10} has a 24-hour health limit, which is exceeded 17-29 times annually in Reykjavík during the study period; the one-hour health limit for NO_2 is exceeded a number of times every year.

Table 1: Health protection limits for NO_2, PM_{10} and O_3 in Icelandic regulation 2006-2008.

	Time frame	Health limit (µg/m^3)	Interval[a] (year)	Number of times the health limit is surpassed (year)
NO_2				
	1-hour mean	200	18	-
	1-hour mean	110	175	42 (2006)[b], 5 (2006)[c], 7 (2008)[c]
	24 -hour mean	75	7	-
	Winter mean	30	-	-
	Annual mean	30	-	-
PM_{10}				
	24 -hour mean	50	29 (2006), 23 (2007), 18 (2008)	29 (2006)[b], 17 (2007)[c], 28 (2008)[c]
	Annual mean	20	40% - 20% (CL)	-
O_3				
	8-hour mean	120	-	-

Reference: Icelandic regulation 251/2002(37) and 745/2003 (38).

[a]*The number of times the health limit may be surpassed every year or the confidence limit (CL) according to regulations. Year indicates the validity period.*

[b]*according to the newest report available (47).*

[c]*Böðvarsdóttir, A.R. (Public Health officer, City of Reykjavík Department of Environment) 2009.Personal communication (email), December 14th. From annual reports for 2007 and 2008 which are not yet published.*

O_3 only has an 8-hour health limit which is not exceeded during the years 2006-2008. Overall, health limits and the range of the confidence limits are becoming lower and stricter. Because research has failed to yield a safe level for most air pollutants, regulation seeks to lower pollution as much as possible.

4.3.1 Guidelines for H_2S

Based on knowledge of the toxicity of H_2S to humans as described in table 2, WHO determined a guideline value 24-hour mean of 150 µg/m^3 which is not to be exceeded if H_2S is not to pose a threat to human health. In the report from 2000; "Air quality guidelines for Europe" (54), WHO recommends that if the smell of H_2S is not to become a nuisance, the 30-minute mean concentration should not be allowed to exceed 7 µg/m^3. However, WHO notes that in some regions, H_2S is emitted from natural sources (54).

The odor nuisance value is exceeded often in Reykjavík, where the highest measured 24-hour mean is 62 µg/m^3 during the study period. In February 2009, the Environment Agency of Iceland commenced monitoring of H_2S levels in Hveragerði, a town very close to the power plant at Hellisheiði.

Table 2: Established dose-response effect relationships of H_2S.

Concentration (mg/m^3)	Health effect
15-30	Threshold for eye irritation
70-140	Serious eye damage
210-350	Loss of olfactory sense
450-750	Pulmonary edema with risk of death
750-1400	Strong central nervous system stimulation, hyperapnea followed by respiratory arrest
1400-2800	Immediate collapse with paralysis of respiratory system

Reference: WHO (54).

Monitoring at this site has shown that H_2S concentrations are quite high, the 24-hour mean is 30-40 µg/m^3 most days (49) far exceeding the odor protection guideline from WHO, but still far below the WHO health guideline limit of 150 µg/m^3 per 24-hour mean (54). The only valid health limit for H_2S which is ratified in Icelandic regulation (36) is the occupational safety limit of 15 mg/m^3 per 8-hour mean. In EU regulation, there are no official health limits for ambient H_2S as hydrogen-related exposures are rather rare; only a few places in the world experience naturally occurring H_2S emissions. Some American states have H_2S regulations, with the most strict regulation existing in Hawaii, which is comparable to Iceland in the sense that it has substantial naturally occurring H_2S emissions from volcanic sources. The 1-hour health limit for is H_2S is 35 µg/m^3 in Hawaii (14).

5 RESPIRATORY DISEASES AND DRUGS

The population of interest in this study is restricted to adults. Two medical conditions generally account for most non-infectious respiratory morbidity in the adult population, adult asthma and COPD. Collectively, asthma and COPD are known as obstructive pulmonary diseases. Due to the small population in the study area and good access to health care, most respiratory patients have adequate access to medicine and primary care thus ER visits and hospital admission for respiratory disease are relatively rare events (28). Adult asthma is a chronic disease of the lungs caused by both genetic and environmental factors but underlying mechanisms are not fully understood (29). Disease characteristics include airway inflammation, bronchial hyperresponsiveness and episodes of airway obstruction, where the patient experiences wheezing, tightness of the chest and other symptoms and needs medication to reopen the airways. Asthma can be allergic, where the attacks are associated with exposure to an allergen which triggers symptoms. Asthma severity is determined by frequency and acuteness of the episodes (8).

COPD is a term used for a number of chronic and usually progressive lung diseases characterized by narrowed airways and decreased lung function. Patients use medication to relieve symptoms. The prevalence of COPD in Iceland is 18% in subjects 40 years and older and is increasing with age and smoking habits (3). Other factors influence respiratory health such as smoking, housing characteristics and others (12).

5.1 Drug classification

The drugs used as health outcome in this study are categorized as R03 in the ATC (Anatomical-Therapeutical-Chemical Classification) system (55). The ATC system is developed by WHO and classifies drugs according to 1) which organ they affect affect (anatomical), 2) the pharmacological/therapeutical effects (therapeutical), and 3) the pharmaceutical/chemical formula of the active substance (chemical). *R* is respiratory system medication and *03* refers to drugs for obstructive pulmonary diseases, sometimes also called anti-asthma drugs. Within the R03 category, there are sub-categories A-D. R03A is composed of *adrenergenic inhalants*. In this category, there are short and long-acting β-agonists (SABA and LABA) which relieve constriction in the bronchi to ease breathing. R03B contains *other inhalants, which reduce inflammation, including corticosteroids*. R03C pertains to *adrenergenics for systemic use in tablet form*. R03D denotes *other systemic drugs for* *obstructive airway diseases*. Drugs for obstructive pulmonary diseases are sold by prescription only.

5.2 Drug usage

In a 1997 survey study by Gíslason et al (11) of those who were dispensed R03 drugs in March 1994 in Iceland, 67% of respondents claimed to have asthma. It was estimated from the data that the proportion of the total population that used drugs for obstructive pulmonary diseases was 2.3%, rising to 6% of the population over 65 years old (11). Usually, R03 drugs are taken regularly by patients with chronic illness, but they may be prescribed to persons for relief of intermittent symptoms. Drug dosage can be increased for regular users when disease is exacerbated (21, 46, 52). Some previous studies of air pollution effects focus on SABA (22) as they are a popular choice of drug to relieve immediate worsening of symptoms. Other studies also included cough and cold preparations (32, 58).

From the current data we can see that of the dispensed drug volume (DDD), some 95% of drugs for obstructive pulmonary diseases dispensed during the study period are inhalants, (R03A and R03B), with adrenergenics (R03A) make op 74% of those. The remainder of the drugs (R03C andR03D) is very specialized and rather rarely used.

6 STUDY POPULATION AND DATA SOURCES

The study population of the current study consists of all adults (≥ 18 years) livings in the capital area in Iceland during the period 2006 to 2008 as defined by the national registry (41). All out-patient dispensings of prescription medication in Iceland are registered in The Medicines Registry of the National Directorate of Health by date, sales outlet, the buyer's national identity number and other information since 2003. Adult residents of the capital area who have been dispensed drugs for obstructive pulmonary diseases (ATC code R03) are subjects of the study. On average, about 75 individuals fill a prescription in a pharmacy for medicines in this category every day. More individuals are dispensed drugs during winter (on average 78 individuals per day) than in summer (on average 71 individuals per day). A larger variation is that between weekends and weekdays, 101 individuals are dispensed drugs every day on weekdays, but the average is 21 individuals per day during weekends. The adult population of the denser part of the capital area during the study period was 142,500 individuals (41) and we can estimate the number of users by applying the calculation technique used by Gislason, T et al 1997 in a study of usage of the same drugs (11). Here, the monthly sum of users was assumed to be one third of all users, as most medications are sold as 3-month supplies. In his 1997 study, Gíslason et al found usage to be 2.3% of the population, 6% for those 65 years and older (11). In the current data, there are 27,500 cases of an individual being dispensed one or more anti-asthma drugs per year. Assuming each individual fills his or her prescription 4 times per year, the proportion of the adult population who take drugs for obstructive pulmonary diseases should thus be approximately (27.500 dispensed per year * 100 / 4) / 142,481 = 4.8%. According to our data, the most commonly dispensed drugs are adrenergenic inhalants (R03A), SABA and LABA, with 86% of individuals being dispensed these drugs. 17% of individuals are dispensed other inhalants (R03B). 0.3% of individuals are dispensed adrenergenics for systemic use (R03C) and 5% are dispensed other systemic drugs (R03D). As these numbers indicate, some individuals use more than one kind of medication while a small amount of dispensings are for more specialized drugs.

Levels of relevant air pollutants are measured continuously by the City of Reykjavík, Departmen of Environment (Public Health Authority) in cooperation with The Environment Agency of Iceland during the study period. The Agency has now (since 2008) taken over the daily operation and management of the measuring stations. There are two fixed-location measuring stations, one at a busy road intersection (Grensásvegur, 70,000 cars per day (48) since 1999 (see Appendix C for measuring device details), another measure urban background pollution in a nearby park (The Reykjavík Family Park and Zoo, since 2002). In total, 15 pollutants and 7 weather factors are measured continuously. The data from recent years is given as 30-minute means.

The study period is February 22nd 2006 - September 30th 2008 and determined by the availability of complete data on drug dispensings and air pollution levels in Reykjavík.

7 SPECIFIC AIMS

The overall aim of this study is to answer in a register-based study of ecological data whether there is an association between day-to-day increases of four specific air pollutants (NO_2, PM_{10}, H_2S, and O_3) in the capital area of Iceland, and the dispensing (outpatient sales) of drugs for obstructive pulmonary diseases (ATC group R03) to the adult population ($\geq$18 years).

We hypothesize that a positive association between the level of these ambient pollutants and the number of individuals who are dispensed drugs for obstructive pulmonary diseases in the capital area does indeed exist, in other words that increased levels of NO_2, PM_{10}, H_2S, and O_3 will lead to increases in dispensings of drugs for obstructive pulmonary diseases to the adult population of Reykjavik.

More specifically, when adjusting for day of tbe week, time trend, season, weather conditions, influenza and pollen counts, we seek to answer:

1. Whether increases in levels of specific airborne pollutants have differential (or interacting) effects on the daily dispensings of drugs for obstructive pulmonary diseases to the adult population in the Reykjavík area when analyzed in multi-pollutant and single-pollutant models.
2. Whether the association between day-to-day fluctuations in air pollution (PM_{10}, $N0_2$, H_2S and O_3) and day-to-day fluctuations in dispensing of drugs for obstructive pulmonary diseases to the adult population in the Reykjavík is dependents upon a delay in time of up to 14 days (lag 14) following an event of increased pollution levels.
3. Whether the duration of the pollution peak (e.g. if measured as the highest daily 1-hour mean, 24-hour mean, or three-day moving average) modifies the observed association.

This is the first study of short-term health effects of air pollution in Iceland. Furthermore, it is the first population-based study which encompasses the population of the entire capital area in Iceland and is also one of the largest studies of air pollution effects on drug dispensings to date.

8 ARTICLE MANUSCRIPT TO BE SUBMITTED TO EHP

TITLE: Hydrogen sulphide and urban air pollution levels are associated with increased dispensings of anti-asthma drugs in Iceland's capital

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KEYWORDS: Obstructive pulmonary diseases, pharmaceutical dispensing, hydrogen sulphide, PM_{10}, traffic pollution.

Abstract

BACKGROUND: Air pollutants in Iceland's capital area include hydrogen sulphide (H_2S) emissions from geothermal power plants, particle pollution (PM_{10}) and other traffic-related pollutants. Short-term health effects of air pollution have not been studied before in Iceland. This is one of first studies to investigate short-term health effects of ambient H_2S exposure.

OBJECTIVES: To investigate the associations between daily ambient levels of PM_{10}, H_2S, nitrogen dioxide (NO_2) and ozone (O_3), and the use of drugs for obstructive pulmonary diseases (anti-asthma drugs) to adults in Iceland's capital area.

METHODS: The study period was February 22nd 2006 to September 30th 2008. The daily number of adults in the capital area who were dispensed one or more anti-asthma drugs (ATC category R03), were fitted to air pollution and weather factor measurements using log-linear Poisson regression. A three-day moving average of the exposure variables was the best fit to the data. The final model included significant covariates adjusting for climate, time trends, and other factors.

RESULTS: Daily air pollution levels and the number of individuals dispensed drugs were positively associated ($p < 0.05$) at lag 3-5 for three-day moving averages of H_2S and PM_{10}. The effect corresponded to 3% and 2% increase in the number of dispensings between the 10th and 90th percentile of PM_{10} and H_2S levels.

CONCLUSION: We found significant but moderate associations between air pollution levels in Iceland's capital and dispensings of anti-asthma drugs. Our results indicate that intermittent exposure to ambient H_2S may aggravate symptoms of respiratory disease.

Introduction

The influence of urban air pollution on respiratory health is well known from epidemiological studies from USA and Europe dating back to the 1970s (Pope et al. 1995, Hoek et al 2002; Dominici et al. 2003; Sunyer et al. 2000). These studies have found an association between increased levels of ambient nitrogen dioxide (NO_2), particle matter with an aerodynamic diameter < 10 µm (PM_{10}) and ozone (O_3) and mortality, emergency room (ER) visits or admission frequency due to respiratory causes. However, in small populations, such as Iceland, hospital admission frequency and mortality rates are likely to be too low to provide sufficient statistical power to confirm such associations. Naureckas et al suggested in a 2005 paper that the dispensing of medication for chronic respiratory disease as a more sensitive measure of respiratory morbidity. In that study, a clear temporal association was demonstrated between an individual visiting an ER for asthma and subsequently filling a prescription for short-acting β-agonist (SABA) bronchodilator medication and researchers concluded that dispensing can fill as a marker for respiratory morbidity. The direct association between air pollution levels and medication usage has been studied in panels studies. In these studies, panels of adult patients with asthma (von Klot et al. 2002) and chronic obstructive pulmonary disease (COPD) (Trenga et al. 2006; Lagorio et al. 2006) were closely monitored. Air pollution levels were positively associated with symptom severity and medication usage the same day or the day after.

Four studies from France and Italy have investigated the association between ambient air pollution and respiratory medication dispensing to adults in a single area or medium-sized town (Laurent et al. 2009; Vegni et al. 2005; Pitard et al. 2003; Zeghnoun et al. 1998). All studies demonstrated significant associations between increased air pollution levels and the dispensing of various types of respiratory medication in the following days, or in the same week as the increased pollution levels.

Air pollution in Iceland's capital area, which includes Reykjavík and its surrounding municipalities, is moderate and health limit violations are few overall (city of reykjavik ref).

However, fluctuations in the levels of PM and H_2S, which is emitted from geothermal harnessing, are the main concerns. During dry, windy weather conditions during winter and spring, PM levels may increase sharply and surpass those of much larger European capitals (Jóhannsson 2007). While there are diverse sources for PM, the main source of is traffic (UHR 2007), many cars are driven with studded tires during winter and per capita car ownership in Iceland is among the highest in the world (Economist 2009).

Iceland's capital has a reputation for being one of the cleanest metropolitan areas in the world, since there is little industrial pollution and all geothermal energy for house heating has completely replaced the use of fossil fuels for house heating. H_2S emission from two plants east of Reykjavík is somewhat of a concern as the particular smell of rotten eggs is sometimes detectable in the city (East is the predomininant wind direction). Toxic effects of H_2S in occupational settings is well known (WHO 2000). Previous epidemiological studies of background exposure due to H_2S from geothermal sources in Hawaii, New Zealand and the Azores have indicated that H_2S has serious effects on respiratory health (Durand and Wilson 2006, Longo 2008; Amaral and Rodrigues 2007). These studies focused on long-term effects, yet we found no current studies of short-term effects of ambient H_2S.

The objective of this study was to evaluate the possible respiratory health effects of air pollution in the capital area of Iceland. As such, we examined whether increases in levels of air pollutants were associated with changes in the dispensing of drugs to relieve obstructive pulmonary diseases.

Material and methods

Study Design. The present study is an ecological time series study in which the daily number of individuals who were dispensed drugs for obstructive pulmonary diseases is modeled as a function of daily air pollution levels and covariates using Poisson regression methods. The study population included only adult individuals (≥ 18 years) living in the capital area of Iceland at the time of the study according to Statistics Iceland (2009). Permissions for studying and extracting data were obtained from the National Bioethics Committee (ref. no: VSNb2008050023/03-15) and the Data Protection Authority (ref. no: 2008080569). No person-identifiable information was present in the study data.

Drug data. The Directorate of Health registers all dispensings of outpatient prescription medicine in Iceland in the national Medicines Registry. Drug data are registered according to the Anatomical Therapeutical Chemical classification (ATC), (WHO 2009). In this study, we measured daily number of individuals who are dispensed one or more drugs for obstructive pulmonary diseases (ATC group R03) from February 22nd 2006 to September 30th 2008. The dispensings data were stratified into the followint sub-categories A-D; adrenergenic inhalants (R03A), other inhalants (R03B), adrenergenics for systemic use (R03C) and “other drugs” (R03D).

Environmental data. The City of Reykjavík Department of Environment and The Environment Agency of Iceland continuously measures air pollutants and a few weather factors at a measuring station located at a large intersection of main roads in the city of Reykjavík. Approximately 70,000 cars pass this intersection daily (UHR 2008). Based on existing knowledge of health effects, available data and intercorrelation, we chose four pollutants to incorporate into our model: PM_{10}, NO_2, O_3 and H_2S. PM_{10} is measured with Andersen EMS IR Thermo and NO_2 , O_3 and H_2S are measured with Horiba APNA, APOA and APSA 360 respectively. The data were provided to us as 30- or 60 minute means by the City of Reykjavík Department of Environment. Data were available for all four pollutants from February 22nd 2006 to September 30th 2008, but with gaps due to downtime of the measuring equipment. In the analysis, days with missing values were removed. Of the 937 days within the study period, 535 days had complete information and were used in the main analyses. We calculated the daily 1-hour peak pollution (the highest daily 1-hour mean) and the daily 24-hour mean concentrations from midnight to midnight of all four pollutants.

The following covariates were included in the analysis; relative humidity and temperature (measured at the same station as the pollutants); daily pollen counts during summer (provided by the Icelandic Institute of Natural History); and the monthly number of influenza cases reported from primary health care units and hospitals to the Directorate of Health.

The monthly number of influenza cases was recalculated into a binary variable (cut-off: 300 registered cases/month) to indicate whether there was an influenza epidemic. Binary variables were introduced to adjust for day-of-week effects and public holidays as these may modify the number of drug dispensings. A time trend term was also introduced into the model. Furthermore, sine and cosine terms drawing curves with the wavelengths 2, 2.4, 3, 4, 6 and 12 months were calculated to adjust for seasonal variations in the medication dispensings not due to air pollution.

Statistical Methods. We calculated descriptive statistics for pollution variables and the number of daily dispensings and calculated correlations (Pearson's correlation coefficient) between pollutants and weather variables. The associations between air pollution and the number of daily cases were modeled with a log-linear Poisson model with dummy time variables, a common modeling method for ecological count data (Dominici et al. 2003; Whitaker et al. 2007). Finally, the data was fitted to a Poisson model with a linear log-mean function of the form:

log(mean daily number of individuals who were dispensed drugs) = constant + Air pollution terms + Day-of-week terms + Climate terms + Pollen terms + Influenza term + Seasonal terms

where the air pollution terms included daily 24-hour mean or the daily 1-hour peak values with lags 0 to 14 days.

The daily number of individuals who were dispensed a drug was first modeled with single-pollutant models which included all covariates. Effect modification and intercorrelation effects were explored in pairwise two-pollutant models with covariates. Finally, all pollutants were introduced into multi-pollutant models. Insignificant covariates were removed (exclusion criteria: $p > 0.05$). Multi-pollutant models with individual day or three-day moving average exposure variables were fitted to the data. Overall, the three-day moving average models gave the best fit to the data (Likelihood ratio tests and Akaike's information criterion, AIC) and were used for the final analysis. Multi-pollutant models of the daily number of individuals dispensed drugs as a function of three-day moving average and three-day moving average of peak pollution were fitted. In addition, the daily number of individuals that were dispensed different categories of drugs were modeled to see if any drug sub-category was a better fit. Final models were inspected for autocorrelation and found acceptable.

From the model outputs, we estimated the relative risk (RR) associated with each model parameter. The exponential of each coefficient multiplied by 10 corresponds to the RR associated with a 10 $\mu g/m^3$ change in pollutant concentration and are reported as such in results. An RR equal to 1.01 is interpreted as a 1% increase in the number of cases per 10 µg/

m^3 pollutant increase.

The exponential of the model coefficients minus 1 and that difference multiplied by 100 was found. This number corresponds to the percent change in the number of individuals per unit change of the pollutant. We multiplied this number with the difference between the 10^{th} and the 90^{th} percentile of the three-day moving averages as it provided a realistic estimate of the increase in dispensed individuals associated with a change in pollution levels going from low to high.

All statistical analyses were performed using R- statistical software (R Core Development Team 2008), packages ”stats”, ”epitools”, ”lattice”, "survival", "gplots" and “lmtest”.

Results

The time series plot of daily means of pollutants and the daily number of individuals dispensed a drug during the period February 22^{nd} 2006 to September 30^{th} 2008 (figure 1) shows that all pollution variables had a seasonal pattern, the gaps represent missing data. A *t*-test of means showed that the mean of the daily number of individuals who were dispensed a drug from the excluded data (due to missing values) was not significantly different from that of the included data (p=0.932). The 24-hour health limits (Reglugerð 251/2002) are shown for PM_{10} and NO_2 (horizontal dotted line). The health limit for O_3 (120 µg/m^3 for an 8-hour mean (Reglugerð 745/2003)) was never surpassed. Iceland does not have health limits for ambient H_2S levels, but WHO (2000) suggests a 24-hour mean health guideline value of 150 µg/m^3, whereas the 30-minute mean should not exceed 7 µg/m^3 for the smell not to become a nuisance.

Descriptive statistics. Table 1 shows the descriptive statistics for the study data; air pollutants (24-hour mean and 1-hour peak) as well as weather factors and the daily number of individuals who were dispensed drugs for the whole study period and stratified by season, winter and summer. Winter pollution means, both the 24-hour average and daily 1-hour peak were higher for all pollutants. In particular, means and standard deviations of the average 24-hour mean and 1-hour peak for PM_{10} were much higher in winter than summer and the mean of 1-hour peaks were much higher than mean 24-hour averages - most distinct for PM_{10} and H_2S. Seasonal differences were moderate for NO_2 and O_3. The mean annual relative humidity was 77%, marginally higher in winter. The annual mean temperature was 5°C, 9°C in summer and 2°C in winter. On average, 75 (+/- 39.9) individuals were dispensed drugs every day, slightly more during winter. During weekdays, the annual mean was 101 individuals who were dispensed and 21 per day on weekends, and the number of days with an influenza epidemic in the data set was 134. Table 2 shows the correlation coefficients between exposure terms of which the highest correlation was found between the 1-hour peak and 24-hour mean of the same pollutants. Most correlations were small or negative, the strongest correlation was found between NO_2 and temperature (-0.414) and NO_2 and O_3 (- 0.622).

The initial analysis of the daily number of individuals who were dispensed drugs for obstructive pulmonary disease and pollution in single-pollutant models yielded very small estimates of the relative risk, which were not statistically significant (results not shown). The model that fitted the best included all four pollutants, adjustments for day-of-week, time trend, and season. The terms for relative humidity on the same day and two days before, temperature on the same day and the day before, and influenza season were significant in some models (RR, 95% CI, and p-values for the results shown in figure 2-4 can be found in appendix B).

Three-day moving average exposure and all individuals who were dispensed drugs (R03). In Figure 2, we see that for all pollutants, there is a negative association between 10 µg/m^3 increases in the three-day moving average of pollution levels and the number of individuals who were dispensed at lag 0-2. The association is significant for O_3 and NO_2; RR = 0.96 (95% CI, 0.94-0.98) and RR = 0.97 (95% CI, 0.95 - 0.99) respectively. At lag 3-5 and following days, positive associations were found between pollution levels and the number of individuals dispensed. For PM_{10}, the increase at lag 3-5 is associated with increased risk of being dispensed a drug, RR = 1.01% (95% confidence interval (CI), 1.00 - 1.02). In the following days, lag 6-8, the effect is still positive, but not significant, and RR moves towards 1 at lag 9-11. For NO_2, dispensings were increased for lags 3-14, but only significantly at lag 12-14, RR = 1.03 (95% CI 1.00 - 1.05). H_2S is not associated with a change in dispensings at lag 0-2 but at lag 3-5 there is a significant increase, RR = 1.03 (95% CI, 1.01 – 1.05). At lag 6-8, the RR is close to 1 and negative at lag 9-11, RR = 0.98 (95% CI, 0.95 – 1.00). The change in RR for dispensings from the 10^{th} to the 90^{th} percentile of PM_{10}, NO_2 and H_2S is 3%, 9% and 2% at lag 3-5, lag 12-14 for NO_2.

Three-day moving average peak pollution exposure and all individuals who were dispensed drugs (R03). Model diagnostics show the three-day moving average of peak pollution is a better fit than the 24-hour mean (log likelihood test, $p < 0.001$, AIC was 4076, 4107 for the 24-hour mean model). Results from this model shown in Figure 3. In this model, relative humidity and temperature were not significant and were thus excluded. Influenza was insignificant and excluded from the model. Relative humidity at lag 2 is negatively significant. In general, this model generates more significant risk estimates, while the absolute RR values were lower for most pollutants and very small for PM_{10}. The pattern is somewhat similar to that of the three-day moving average exposure model; all risk estimates for drug dispensing at lag 0-2 were close to 1 or negative, but are positive at lag 3-5. For NO_2 the risk estimates do not go towards 1 at higher lags, but remain elevated, peaking at lag 12-14. O_3 was significantly associated with increase in the number of individuals who were dispensed drugs at lag 3-5, RR = 1.02 (95% CI, 1.00 – 1.03) and at lag 9-11, RR = 1.02 (95%, CI 1.01 - 1.03). The assocation between number of individuals dispensed and H_2S was positive and significant at lag 3-5, RR = 1.01 (95% CI, 1.00 - 1.01). The change in RR for dispensings from the 10^{th} to the 90^{th} percentile of the three-day moving average of peak PM_{10}, NO_2, O_3 and H_2S was 3%, 6%, 5% and 2% at lag 3-5, lag 12-14 for NO_2.

Three-day moving average peak pollution and individuals who were dispensed adrenergenic inhalants (R03 A). Finally, the data was fitted to the daily number of individuals who were dispensed different types of R03 drugs. Adrenergenic inhalant medication (R03 A) was fitted to the three-day moving average of 24-hr mean and 1-hour peak. The estimates from the 24-hour mean model were statistically significant for PM_{10} and NO_2, but not for other pollutants (data not shown). In a model of peak pollution and adrenergenic inhalant dispensing (Figure 4), all pollutants had positive, statistically significant associations with the number of individuals dispensed. In this model, relative humidity with 2-day lag, time trend and influenza season was significant. The diagnostics of this model suggests it to be a better fit than those previously explored (AIC = 3934). Most significantly improved were increases in peak NO_2 and the risk of being dispensed a drug; the risk was significantly increased from lag 6 and onwards and peaked at lag 12-14, RR = 1.01 (95% CI, 1.01 – 1.02). Peak O_3 was associated with increased number of individuals dispensed at lag 3-5 RR = 1.02 (95% CI, 1.00 – 1.04).

The change in RR for dispensings of adrenergenic inhalants from the 10^{th} to the 90^{th} percentile of the three-day moving average of peak PM_{10}, NO_2, O_3 and H_2S was 3%, 7%, 5% and 2% at lag 3-5, lag 12-14 for NO_2.

There was no association between the number of individuals who were dispensed other inhalants (R03B) in pollution in a three-day moving average mode, but there were significant positive associations when exposure was expressed as the moving average of peak pollution. These were found at lag 12-14 of PM_{10} and lag 9-11 of NO_2, but no other pollutants were significant (data not shown). There were not enough dispensings of drugs from the C and D category to yield useful results.

Discussion

Main findings. In the capital area of Iceland, increases in the average of PM_{10} and H_2S over a three-day period were associated with significant but small increases in number of individuals who were dispensed drugs for obstructive pulmonary diseases three to five days later.

The increased risks associated with a pollutant levels going from the 10^{th} to the 90^{th} percentile were 3% for PM_{10}, 6-7% for NO_2, 5% for O_3 and 2% for H_2S. For most pollutants, the association was strongest with a 3-5 day delay, but 12-14 days for NO_2. The estimates were surprisingly similar regardless of whether exposure was expressed as the three-day moving average of 24-hour means or daily peak levels, but more pollutants exhibited statistically significant associations in the peak pollution models.

When cases were stratified by the different drug categories, only inhalant adrenergenics yield statistically significant results, especially in association with moving averages of peak pollution rather than 24-hour mean levels.

The results suggest that increased air pollution in the capital area may induce symptoms of respiratory disease, or a worsening thereof, so that the need for drugs rises temporarily. Also, our findings suggest that a three-day average of daily peak pollution is a better approximation to the highly fluctuant pattern of some air pollutants in Reykjavík than the three-day moving average. Hourly means may therefore be a better predictor for respiratory health effects than the 24-hour mean, on which the current health limits that determine authority steps to limit salutation and raise public awareness are based.

Descriptives and time lines. During the study period, February 22nd 2006 – September 30th 2008, the highest peaks of PM_{10} far surpassed the 24-hour health limit of 50 µg/m^3. NO_2 only surpassed the 1-hour health limits (Reglugerð 251/2002) on a single occasion during the study period, but the 8-hour health limit of O_3, 120 µg/m^3 per 8-hour mean ((Reglugerð 745/2003)) is never surpassed. There are no health limits set for ambient H_2S, only an occupational health limit is legally ratified in Iceland. H_2S levels in Reykjavík were generally much under the recommended 24-hour guideline of 150 µg/m^3, the highest value during the study period was 62,7 µg/m^3, but levels were frequently above the annoyance guideline limit of 7 µg/m^3 per 30 minute mean (WHO 2000). As there were more data for the winter period, the yearly mean and standard deviations did not truly reflect the yearly mean. O_3 levels were higher in winter, which is unusual as O_3 is formed in a reaction of nitrogen oxide (NO), other engine exhaust components and atmospheric air, which is catalyzed by heat and sun radiation (UHR 2007). Heat and sun radiation are not abundant in Iceland during any season owing to the northerly location of Reykjavík (64° latitude), but we have found no further explanations for this anomaly. Perhaps, as O_3 tends to peak in spring, our division of summer and winter into categories may have has displaced some high spring levels into the winter season. Nevertheless, the levels for O_3 look genuinely higher in winter judging from the time line (Figure1). This unusual result may warrant further research on O_3 in Iceland.

Study strengths and limitations. Intercorrelation of pollutants is of interest as high correlations mask the effects of individual pollutants in the regression analysis and may thus violate the assumption of independence. Highest correlations were found between the 1-hour peak and 24-hour mean of the same pollutants. This does, however, not affect study results as 1-hour peaks and 24-hour means were used in separate models. The strong negative correlation between O_3 and NO_2, was expected as O_3 is a product of a reaction between nitrogen gasses and atmospheric air. As the two pollutants are negatively correlated they will effect modify each other and the effect of high NO_2 values will coincide with low O_3 values. A multi-pollutant model adjusts for this.

Bias. The amount of missing data is unfortunate, with 56% of the data from the study period acceptable for use. However, the insignificant *t*-test allows us to assume that there is no significant difference between the number of dispensings during the days included in the study period and those with missing data, so the results are unlikely to be different from those obtained from complete data.

The best models included all four pollutants. While researchers warn of intercorrelation (Tolbert et al. 2007) when including many pollution variables in models, the risk is minimal in our study as the intercorrelation between the different pollutants is minimal or negative. The similar overall pattern and outcome of the two exposure measures, three-day moving average of 24-hour mean and peak pollution, support the plausibility of the association between dispensings of drugs and air pollution.

In the model of three-day moving average, the significant results for PM_{10} and H_2S and non-significant for NO_2 and O_3 may reflect that the distributions of the two first are skewed and have a wide range so the very high peaks may explain most of the association, while NO_2 and O_3 levels (both 24-hour mean and 1-hour peak) are fairly normally distributed. The fact that the three-day moving average proved a better fit than the initial model with 24-hour mean or 1-hour peak pollution of each lag, supports this assumption as the three-day moving average normalizes the data by eliminating the most extreme values.

This study estimated exposure based on measurements from only one site in Reykjavík, although we assume that the whole population was equally exposed, at least that if the level of a given pollutant is elevated at the roadside measuring station, it will also be elevated in residential areas, but the absolute concentration will be lower. While essential factors that govern levels of the traffic-related pollutants, most importantly weather and traffic intensity, are similar across the capital area at any given time, there are many uncertainties associated with this assumption knowing that people live and work in various distances from pollution sources. For H_2S, the concentration measured as far from the source as the capital area are highly dependent on wind and landscape topography and can vary greatly (Ólafsdóttir 2007). The eastern edge of the city is much closer to the source and is likely to be far more exposed to H_2S than the western parts. More pollution monitoring stations are now in place in the area than were present during the study period, so a future study including information about subject residence may allow a to better estimation of the exposure.

As the study data did not include information in the characteristics of the individual subjects in the study population other than drug use, we cannot isolate any individual risk factors which are known to increase susceptibility to different air pollutants. Exposure, age, gene-environment, and diagnosis are all speculated or known to modify the effects of air pollution; for example, Lagorio et al. (2006) found that only NO_2 affected asthmatic subjects, but COPD sufferers were susceptible to both $PM_{2.5}$ and NO_2 levels. In our study, the identified association may be due to a small group of individuals with particular risk factors, that are particularly susceptible to air pollution exposure.

Effect size. The risk estimates for being dispensed medication and the association with PM_{10} and NO_2 found in our study are smaller than those found by Laurent et al. (2009) for SABA dispensings to subjects 0-40 years old in Strasbourg using case-crossover methods. Laurent et al. found that the risk of dispensing increased by 8.4% for PM_{10} and by 7.5% at lag 4-10 for NO_2 per 10 $\mu g/m^3$ pollutant increase. NO_2 levels were somewhat higher in Strasbourg. Case-crossover methods adjust for individual risk factors by design and that may be why the increased risk found by Laurent et al. is somewhat higher than those found by other research groups as well as in our study. A study by Vegni et al. (2005) studied weekly variations of total suspended particles (TSP), total number of cases that were dispensed drugs, and the dispensed drug volume (DDD's) of drugs for obstructive pulmonary diseases. They found that the number of cases increased by 8% and amount of DDD's increased by 14% when pollution increased from the 10^{th} to the 90^{th} percentile of TSP. Other studies using time series methods (Pitard et al 2004, Zeghnoun et al 1999), found the risk estimates associated with increased black smoke (BS), which is a PM fraction and NO_2 to be comparable to those found in our study. The improved fit of the data to the three-day mean of peak pollution is in line with results from a panel study of asthmatic children where lung function was associated with hourly rather than 24-hour means of fine PM (Delfino et al 2008).

Lags and patterns. In most of our analyses, we found consistent negative associations between drug use and most pollutants for lag 0-2. This initial negative trend in the association between dispensings and increased pollution has previously been demonstrated for the association between NO_2 and the sales of obstructive pulmonary disease drugs and cold medication(Pitard et al. 2004) and between NO_2, O_3 and PM_{10} and the odds ratio (OR) of individual dispensing of SABA medication to subjects 0-40 years old (Laurent et al. (2009). This was attributed to medication management techniques of individuals who take drugs regularly in these studies. As most drugs are prescribed for approximately three months at a time, it is unlikely that the supply will run out immediately when pollution is increased, but the increased pollution will deplete the supply sufficiently to urge the individual to refill a prescription soon after. Another possibility if that it reflects the background level of dispensing.

Laurent et al. (2009) found the outcome response for PM_{10} (lag 4-7) to be a bit later than what we found in our study (lag 3-5), while Zeghnoun et al. (1999) found the increased risk to be highest with a 4.6% increase (per two standard deviations) at lag 8 for NO_2. Zeghnoun et al. attributes this late response to dispensing to individuals who do not have previous respiratory disease and refill their prescription after a control consultation after one week, repeating the initial response. Pitard et al. (2004) found the most increase associated with NO_2 at lag 6-7, RR = 1.002 and RR= 1.007. In our analysis, the relative risk associated with NO_2 was positive from lag 3-5 and peaking at lag 12-14 for all analysis models. Laurent et al. (2009) also found the risk increase associated with NO_2 to not diminish in late lags. In Pitard et al (2004), the increased dispensing associated with NO_2 diminished after a high at lag 5 to lag 7.

Laurent et al. (2009) found no significant association with O_3 levels, but in our study the three-day moving average of peak pollution is significantly associated with increased dispensings.

We found that a model with exposure as peak pollution was a better fit to the data. While there are no studies of peak pollution and drug dispensing, this supports results found by Delfino et al. (2008), where asthma symptoms in children were associated with peak rather than 24-hour means. This could be an indication, that the 24-hour health limits for PM_{10} are inadequate as indicators for when the public should be alerted.

The daily number of individuals dispensed inhalant adrenergenic drugs were a better fit to the data and had significant positive associations with all modeled pollutants. Even though this category contains both long- and short-acting drugs, it may still be a more sensitive marker than the group of drugs for obstructive pulmonary disease as a whole.

While the acute toxic effects of occupational exposure to H_2S are well known (WHO 2000), we found no studies of immediate health effects of exposure to ambient H_2S pollution. Our results suggest that exposure to increased ambient levels of H_2S may have a significant effect on drug dispensing. Whereas the current study shows air pollution levels to be associated with increased dispensings of drugs for obstructive pulmonary disease, a future study should aim to better adjust for exposure, age and other individual risk factors that may influence sensitivity to air pollution

Conclusion

The current study is the first study of short-term respiratory health effects in Iceland. The results indicate that even for an area with moderate air collation, the exposure has adverse effects on respiratory health in the population of users of drugs for obstructive pulmonary diseases. The need for respiratory drugs was especially elevated in association with high levels of ambient PM_{10} and H_2S, warranting special interest to these pollutants. The results are likely to be effect modified due to age, residence and personal risk factors such as disease types and medications that we could not adjust for.

While the study's ecological design and somewhat indirect measure of health outcome limits the generalizability and interpretation of the results, they are an indication that air pollution exposures in Reykjavík and health effects to susceptible populations must be studied further.

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Figures and tables in article

Figure 1: Time series plot

Daily mean pollutant levels (24-hour health limits indicated with dotted line when applicable) and daily number of individuals who were dispensed drugs for obstructive pulmonary diseases during the study period. Notice very low H2S levels before fall 2006. The gaps in the lines are due to missing data. Y-axis scales are not uniform.

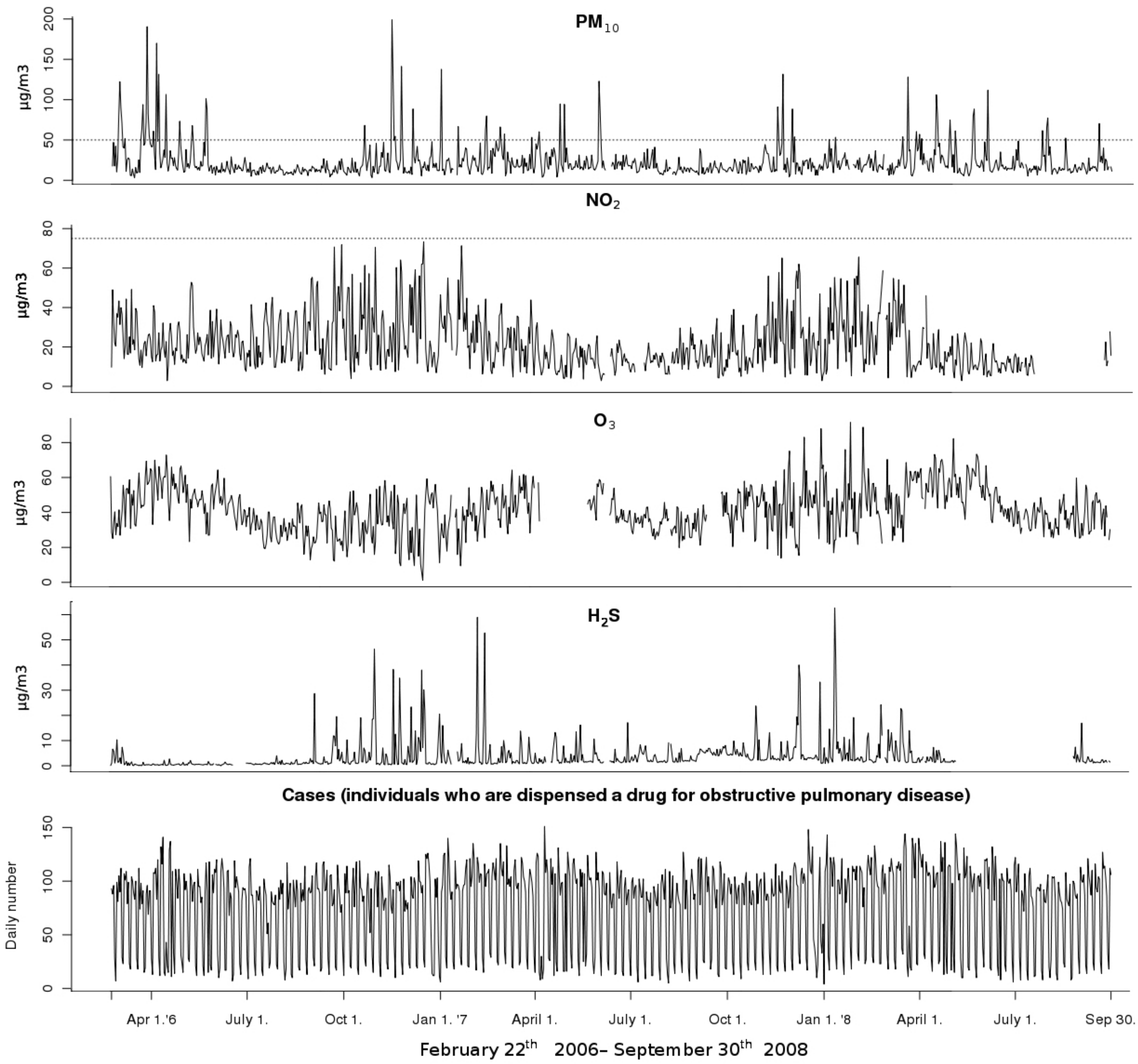


Table 1: Descriptive statistics of daily pollution levels, weather and dispensings
Pollution, (24-hour means and maximum daily 1-hour means) weather factors and daily number of individuals who were dispensed drugs for obstructive pulmonary diseases during the study period.

	All year (n=535)		**Summer** (n = 214)[a]		**Winter** (n = 321)[b]	
	Mean (+/- SD)	Range	Mean (+/- SD)	Range	Mean (+/- SD)	Range
Pollution (24-hour mean)						
PM_{10} (µg/m^3)	24.2 (+/-23.1)	3.2 – 198.9	16.9 (+/-12.5)	3.4 – 101.4	29.1 (+/-27.0)	3.2 – 198.9
NO_2 (µg/m^3)	24.3 (+/-14.2)	2.9 – 73.3	23.0 (+/-14.2)	4.1 – 71.9	25.1 (+/-14.2)	2.9 – 73.3
O_3 (µg/m^3)	41.2 (+/-13.9)	1.2 – 87.9	36.2 (+/-11.5)	12.2 – 82.3	44.5 (+/-14.5)	1.2 – 87.9
H_2S (µg/m^3)	4.1 (+/-7.4)	0.1 – 62.7	3.1 (+/-5.1)	0.3 – 46.3	4.8 (+/-8.6)	0.1 – 62.7
Peak pollution (max daily 1-hour mean)						
PM_{10} (µg/m^3)	88.1 (+/-154.6)	11.6 – 1779.0	56.1 (+/-72.4)	11.9 – 652.3	109.2 (+/-187.7)	11.6 – 1779.0
NO_2 (µg/m^3)	56.6 (+/-30.4)	6.3 – 209.6	53.2 (+/-35.6)	10.2 – 209.6	58.8 (+/-26.1)	6.3 – 126.7
O_3 (µg/m^3)	59.8 (+/-14.8)	7.1 – 136.2	52.0 (+/-11.8)	26.0 – 111.5	65.0 (+/-14.3)	7.1 – 136.2
H_2S (µg/m^3)	16.3 (+/-29.4)	0.3 – 176.6	12.6 (+/-25.3)	0.5 – 169.7	18.7 (+/-31.6)	0.3 – 176.6
Weather conditions						
Relative humidity(%)	77.3 (+/-11.6)	43.2 – 101.2[f]	77.4 (+/-10.5)	48.3 – 96.8	77.2 (+/-12.3)	43.2 – 101.2[f]
Temperature (°C)	5.0 (+/-5.1)	-7.8 – 15.6	9.4 (+/-3.7)	-1.6 – 15.6	2.3 (+/-3.5)	-7.8 – 9.7
Dispensing of drugs						
No. of cases[c]	75.3 (+/-37.9)	4 – 148	71.2 (+/-37.7)	5 – 144	78.0 (+/-41.3)	4 – 148
No. of cases weekdays[d]	101.0 (+/-16.5)	51 – 148	95.2 (+/-14.3)	51 – 144	105.0 (+/-16.8)	60 – 148
No. of cases weekends[e]	21.5 (+/- 9.0)	4 – 58	18.7 (+/-6.9)	5 – 36	23.3 (+/-9.8)	4 – 58

Abbreviations: No, number; SD, standard deviation.
[a]May 1st - October 30th.
[b]November 1st - April 31th.
[c]The daily number of individuals living in the capital area who are dispensed a drug for obstructive pulmonary disease.
[d]Monday-Friday.
[e]Saturday, Sunday and other holidays.
[f]The maximum value of relative humidity is 100%, there is a 1% error margin in the measuring equipment.

Table 2: Pollution and weather variable correlation matrix[a]

	PM_{10}		NO_2		O_3		H_2S		Temp	RH
	24-hr	1-hr max	24-hr	1-hr max	24-hr	1-hr max	24-hr	1-hr max	24-hr	24-hr
PM_{10}										
24-hr	1.00									
1-hr max	0.82#	1.00								
NO_2										
24-hr	0.16#	0.04	1.00							
1-hr max	0.15#	0.05*	0.88#	1.00						
O_3										
24-hr	0.08**	0.10#	-0.62#	-0.46#	1.00					
1-hr max	0.17#	0.14#	-0.20#	-0.05	0.78#	1.00				
H_2S										
24-hr	0.05	0.03	0.30#	0.24#	-0.29#	-0.09*	1.00			
1-hr max	0.05	0.06	0.31#	0.29#	-0.29#	-0.08*	0.85#	1.00		
Temp										
24-hr	-0.29#	-0.23#	-0.41#	-0.44#	0.00	-0.29#	-0.23#	-0.26#	1.00	
RH										
24-hr	-0.32#	-0.22#	0.06**	0.06**	-0.10#	-0.04	0.02	-0.03	0.12#	1.00

Abbreviations: max, maximum; RH, relative humidity; Temp, temperature; 24-hr, 24-hour mean; 1-hr max, maximum daily 1-hour mean.
[a]Pearsons correlation coefficients (p-value); *n*=535 for all measurements.
* $p < 0.05$; ** $p < 0.01$; # $p < 0.001$.

Figure 2: All dispensings (R03) and mean pollution

Multivariate Poisson regression models (relative risk, RR and 95% CIs). RR for individuals being dispensed drugs for obstructive pulmonary diseases (R03) associated with 10 µg/m^3 increase in three-day moving average of each pollutant. Adjusted for influenza, temperature, relative humidity, season, day-of-week and time. Results for individual pollutants are adjusted for other pollutants.

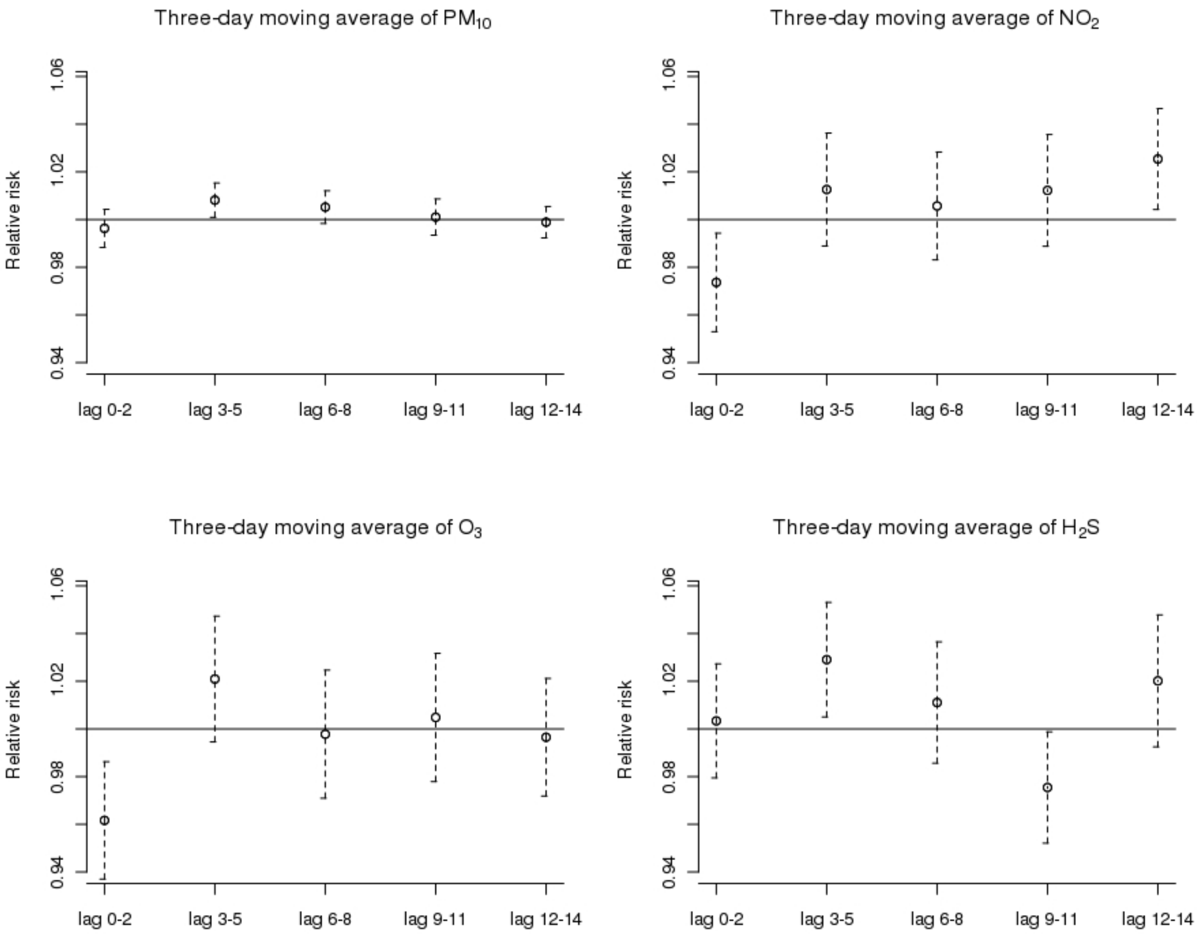


Figure 3: All dispensings (R03) and peak pollution

Multivariate Poisson regression models (relative risk, RR and 95% CIs). RR for individuals being dispensed drugs for obstructive pulmonary diseases (R03) associated with 10 µg/m^3 increase in the three-day moving average of the highest daily 1-hr mean of each pollutant. Adjusted for influenza, temperature, relative humidity, season, day-of-week and time trend. Results for individual pollutants are adjusted for other pollutants.

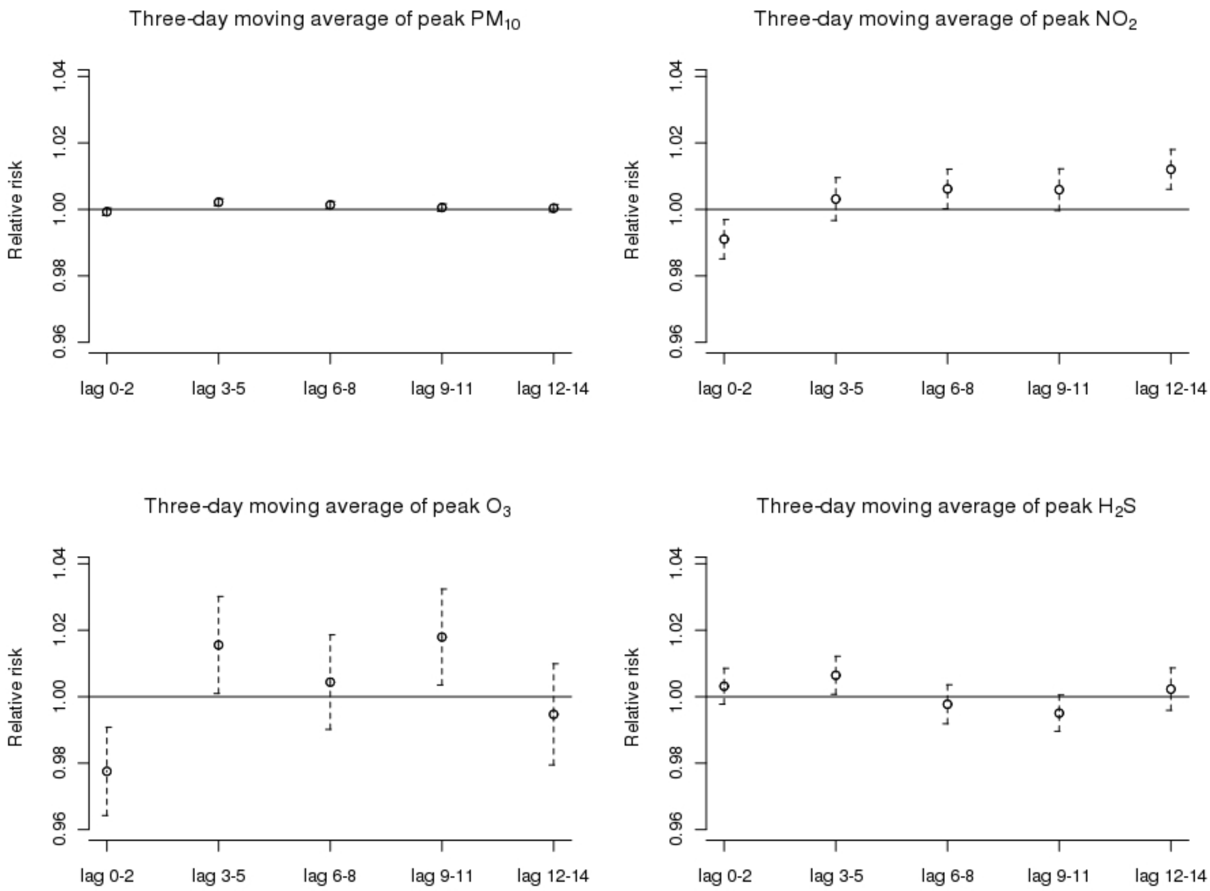
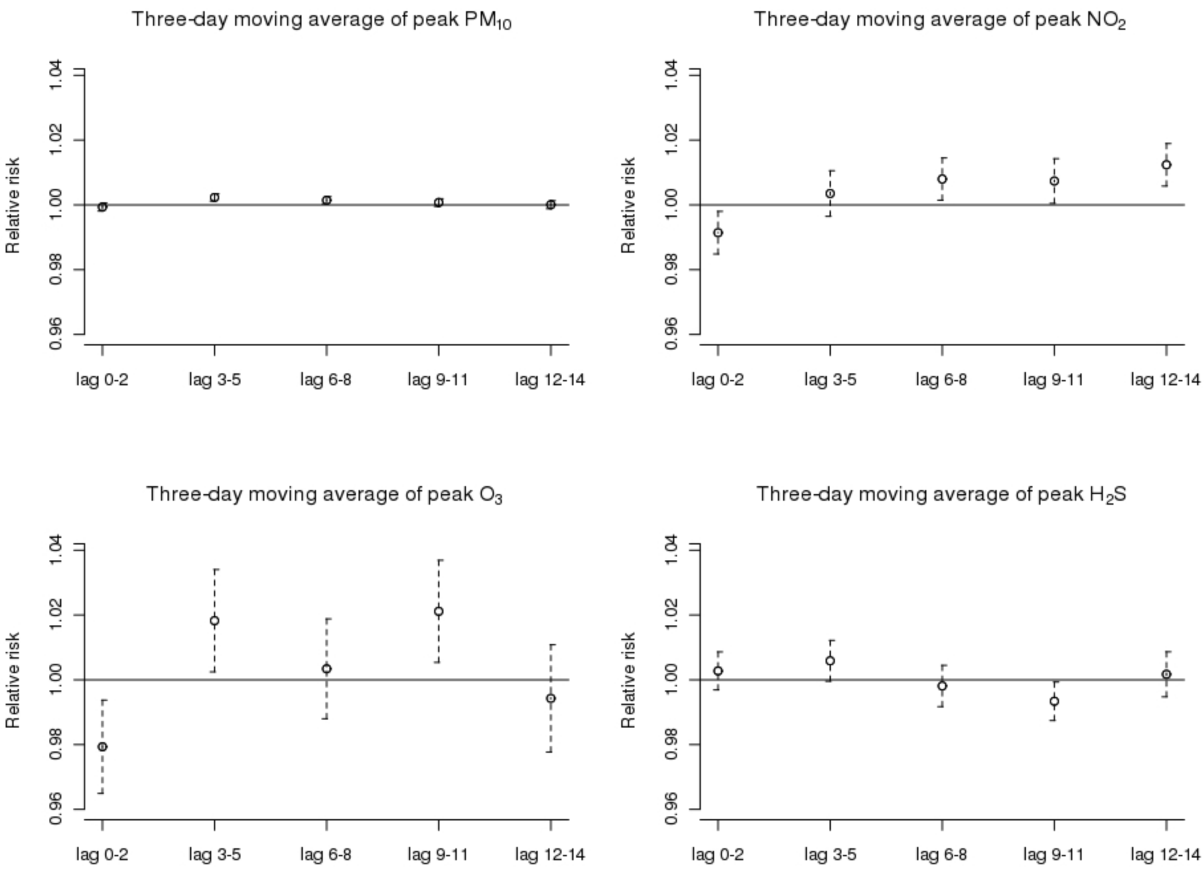


Figure 4: Dispensings of adrenergenic inhalants (R03 A) and peak pollution

Multivariate Poisson regression models (relative risk, RR and 95% CIs). RR for individuals being dispensed adrenergenic inhalant drugs for obstructive pulmonary diseases (R03A) associated with 10 µg/m^3 increase in the three-day moving average of the highest daily 1-hr mean of each pollutant. Adjusted for influenza, temperature, relative humidity, season, day-of-week and time trend. Results for individual pollutants are adjusted for other pollutants.



9 CONCLUSION TO THE THESIS

The results of our study suggest that even in a relatively low-level pollution area such as Reykjavík, urban air pollution and emissions from geothermal power plants affect the dispensing of drugs for respiratory disease. The association is moderate, in the order of 2-3% increase in the number of individuals who are dispensed drugs for a change from the 10^{th} to the 90^{th} percentile of the three-day moving average of PM_{10} and H_2S and about 5-6% for NO_2 and O_3 pollution levels in a peak pollution model, but statistically significant and fairly robust. The associations were stronger for the peak pollution exposure models, though risk estimates for the number of dispensed individuals were not higher in absolute terms. It is remarkable that we found positive associations for NO_2 and O_3 which rarely or never exceed health limits.

More significant estimates of relative risks were found for the association between pollutants and dispensings of adrenergenic inhalants (R03 A), which includes the SABA drugs. SABA dispensing was used as the respiratory health indicator in the studies of Naureckas et al (28) and Laurent et al (22). In the latter, researchers found higher estimates of relative risk than we found in our study, indicating that perhaps dispensings of this drug type may be a more specific marker, and could be a focus for future study. It should be noted though, that the studied population of our and Laurent et al's study were not similar.

We found a small, significant association between pollution levels and an outcome measure which may indicate respiratory health effects for the whole population, but in this study, there are a number of sources of effect modification due to the ecological nature of the data used. The most important effect modifiers are probably individual risk factors that may cause increased risk to an individual such as the amount of exposure, age and the gene-environment of the person. This would mean that a subgroup of the individuals dispensed drugs experience a severe worsening in symptoms due to increased pollution levels in Iceland's capital area, while others are fairly unaffected. Future studies with individual data will hopefully shed some light on this aspect.

Currently, there are no models to estimate exposure to air pollutants in individual neighborhoods, and as this study treats the whole area as a single unit, we cannot make any assumptions about which areas are most affected. But it is certain, that residents of the capital area experience very inhomogenic exposures. While the distance from the residence of an individual to the nearest large road almost certainly is a factor that will influence the daily exposure of the individual and subsequently the risk of experiencing respiratory symptoms, there are more uncertainties when assessing H_2S exposure, as the source is located some distance away and dispersion is dependent on many factors (31).

Particle pollution

The municipalities in the capital area have taken several steps to limit PM pollution and while they are necessary, they may not be sufficient. It is known that the toxicity of PM to respiratory health is highly dependent on the source and composition. Unfortunately, we do not have good data on fine particle pollution ($PM_{2.5}$) from Reykjavík and we have not otherwise attempted to determine the source of PM pollution in the data. The sources of PM pollution in Reykjavík are as diverse as Saharan and Icelandic sand storms, asphalt grinded from the roads by studded tires, sand from construction sites, road sanding and salting (20, 39). It is very likely, that some of these sources have more detrimental health effects than others, but based on this study, we are unable to point to a single PM source that should be targeted to limit health effects of PM pollution.

Hydrogen sulphide

Geothermal energy has replaced fossil fuels as the energy source used for space heating in the capital area, greatly reducing carbon emissions and visible air pollution in central Reykjavík. However, the positive associations found between H_2S levels in the capital area, more than 20 km from the source, and drug dispensings indicate that the exposure may affect respiratory health of a susceptible population. Exposure to H_2S in the town of Hveragerði – located much closer to the power plants on a geothermally active area – is much higher and would also make an interesting study area.

The two geothermal power plants mentioned in this paper are owned and operated by Orkuveita Reykjavíkur (e. Reykjavík Energy) and provide electricity and hot water to all the capital region. Geothermal energy is rightfully considered to be more environmentally friendly and sustainable than the alternatives, but while this is true, our results indicate that emissions from geothermal power plants are not unproblematic and health effects should be studied further. There is no regulation of H_2S in Iceland outside of occupational settings, but the Icelandic government is currently considering regulation of ambient H_2S levels (35), which would be an important first step towards limiting emissions and setting guidelines when to alert the public of high levels.

Health limits

In our study, we found some association with our outcome, a health indicator, for all studies pollutants, including some that never exceed health limits. Health limits are based on the effects of pollutants on a healthy population, but the outcome in our study is prescription drugs for obstructive pulmonary diseases such as asthma and COPD. The users of these medications may be more sensitive to increased pollution levels, so the results cannot be extrapolated to the general population. It is however noteworthy that the peak pollution seemed to be a better predictor, as decisions about when to warn the public about PM_{10} levels, which are most often the problem in the capital area, are based on the expected 24-hour mean (the health limit). The high correlation coefficient between the 24-hour mean and 1-hour max (0.82) indicate high levels of the two will coincide on most occasions, but it should be a hint to authorities to warn the public when levels are high regardless of the expectations for the levels of the next 24-hours.

Further research

While particle pollution was a main concern and motivator when commencing this study, the results for other pollutants are a strong indicator that there is no such thing as a safe pollution levels for a whole population, for we found significant increases in a health indicator, drug dispensings, associated with pollution levels below the health limits. The short-term effects of background exposure to H_2S must be studied further as our study lack detail about subjects at risk and exposure. Also, our study did not include children, as their drug use pattern is somewhat different, but a future study should study this population as well.

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APPENDIX A : SYSTEMATIC LITERATURE REVIEW

February 2009

The systematic studying of air pollution and adverse human health effects was spurred by the Meuse Valley and London fog events. The Meuse Valley episode occurred in Belgium in 1930 when an atmospheric inversion occurred in a valley as winds were blowing from a nearby industrial area. During a three-day period, some 60 people died of causes that could be directly linked to the air pollution [5]. The London fog refers to three episodes of severely increased pollution over few days in winter during the period 1948 – 56. These episodes caused mortality to increase dramatically during the following days and weeks. Death rates in newborn and elderly were above normal and an excess of some 1000 deaths could not be attributed to the lower temperature or infectious disease epidemics in the same period[3]. The conditions during the London fog was caused by unfortunate weather circumstances in a city with much industrial activity inside city limits, an increasing number of cars, and coal burned for house heating [2]. Today, the industrial world has reduced coal burning for house heating, and a large effort has been put into reducing emissions or reducing the harmfulness of emissions from industry through filtering and other cleaning methods. Also, industrial production has been limited in inhabited areas. Cars emit a smaller volume of pollutants today than a few decades ago due to improvements in motor technology, such as the introduction of unleaded fuel and catalytic converters. On the other hand, urbanization as well as urban traffic has been increasing so more people are exposed. So while extreme air pollution episodes are rare in the westernized world today, research into the significance of even moderate urban air pollution to adverse human health continues with evolving statistical methods. A starting point was the famous “Six cities study” by Dockery and Pope [1] from the 1990s which found mortality in a cohort with 14 years of follow-up in 6 US cities and correlated it with each city's yearly mean of particle concentrations. The findings were disputed, but were later confirmed in a larger cohort study [4]. Since, other studies have confirmed these findings as well as establishing several associations between short-term changes in air pollution concentrations and intermittent health effects such as ER visits and hospital admissions for respiratory and cardiovascular causes, as well as mortality. This is a review of studies of short-term health effects in adult populations with respiratory ailments.

Methods

This critical literature review included literature relevant to the current study. That is, epidemiological studies of the short term health effects of air pollution on susceptible adult populations (i.e. people with respiratory disease and the elderly). A search on PubMed February 20th 2009 was made with combinations of the following search words:

- respiratory OR pulmonary OR asthma OR COPD
- traffic OR ambient air pollution
- NOT cancer, mortality, infant, reproduction, review, toxicology

The following limits were applied:

- include only articles with abstract
- include only articles in English
- humans
- adults (19+)
- published after February 21st 1999

Results

202 articles were found and all abstracts were read. The review sought to cover epidemiological studies of outdoor air pollution and health effects in adult asthmatics, COPD sufferers, elderly, heart patients or subjects ill enough to seek treatment, that is, studies of emergency room visits, hospital admissions and medical emergency phone calls for respiratory causes. 191 articles were excluded because of:

Unrelated content such as:

- irrelevant health outcome (47)
- prevalence studies of healthy populations (29)
- study of respiratory disease biomarkers (20)

Non-relevant pollutant measure (19)

- indoor air pollution (7)
- occupational exposure (12)

The study did not involve health outcome (16)

- study of community, attitudes and policy (4)

Other:

- experimental nature(16)
- included only smokers (5)
- children (6)
- small panels studies (n<200) (7)

Eleven articles remained. The studies were all from North America and Europe. Due to the cross disciplinary nature of the study subject, relevant articles were found in journals of general medicine, pulmonary medicine, environmental health and environmental science. Most studies were ecological time series studies of all admissions to one hospital or all hospital or ER visits in one area over a time, but a few case-crossover and cohort studies were reviewed. All studies adjusted for climate information as weather can be a confounder to the effect of the pollution. Some studies also adjusted for infectious diseases and pollen. The study populations all included or were exclusively adults. The health outcomes were hospital admissions (cardiopulmonary, respiratory, repeated respiratory, emergency pneumonia, asthma and COPD), ER visits and medical emergency calls. Time series analysis using Poisson regression with spline smoothing and case-crossover using conditional logistic regression are the most commonly used statistical methods. A study by Fung et al. used three types of analyses on the data to compare the results and investigate possible bias of either method [5]. Only selected, significant result regarding respiratory outcomes in adults are reported here. Results are reported schematically in Table 3 and 4.

Conclusion

All studies found an increase in the number of people seeking health care for respiratory causes on the same day or the days after increases in air pollution, especially in elderly subjects and those with respiratory disease. The only negative association was found by Zanobetti and Schwartz [11] who found O_3 to be negatively associated with emergency admissions for pneumonia. Some studies stratified results by season as pollution dispersion and reaction pattern can differ, mainly due to weather fluctuations but also because traffic patterns are different during holidays. Increases in admission and ER visits rates were in the order of a few percent increase per 10 µg/m^3 increase in levels of PM_{10} and NO_2. Some studies reported the changes in health outcome per interquartile (IQR) change or from the 10th to the 90th percentile. This unit-neutral form of reporting can be both practical and reasonable. It makes comparisons between high levels of pollutants easier, as ranges in absolute units differ between pollutants. A drawback is that this can make comparisons between areas difficult.

The highest increases in admissions rates were found in the Italian study [8], where 1 mg/m^3 increase of CO was associated with 26% increase in ER visits in elderly subjects. Other high estimates were found with ER visits for asthma in Canada [9], where the 5-day moving averages were associated with 10-15% increase in ER visits for all ages per IQR change. The increase in risk estimates for patients over 75 years old were consistently higher, 40-50%, for the 5-day averages of NO_2 and CO and about 15% for the three-day moving averages for $PM_{10-2.5}$ and PM_{10}. Again, estimates for O_3 were negative in summer. One study [5] compared Poisson time series and case-crossover methods to the Dewanji-Moolgawkar method that was developed to deal with repeated events, such as numerous admissions of the same patient during the study period. The results from the different models were not significantly different from each other.

In other studies of patients with repeated admissions, the risk associated with pollution levels seemed to higher for those who are repeatedly admitted than for those who are only admitted once during the study period [3, 10] . In Yang et al. [10], results were shown for individual lags and lags of an average of 2-7 days. Also single and two-p model estimates were shown together. The change in risk estimates associated with different pollutants and number of days included in the model were very variable. The risk associated with NO_2 increased as the exposure period in the model was prolonged. It reached a maximum of RR = 1.11 for a 6-day mean of NO_2. PM_{10} exhibited a similar pattern whereas other pollutants seem to not increase the effect with longer exposure [10]. Moving averages of between 3 to 7 days were most often used as exposure period in the studies. The largest study, the Dominici study [4] of respiratory admissions in a 11.5 mio strong Medicare cohort, had overall low risk estimates, but there were large regional variations.

Table 3: Appendix A - Systematic literature review.

Systematic review: *Selected significant results from reviewed articles. The sizes of the studies are given as either 1) the size of the population in population-based studies, 2) number of subjects, n, in cohorts or 3) number of health outcome events for case-crossover and time series studies. Climate variables were usually temperature and humidity but also precipitation.*

Reference Year	Duration Country	Type Population	Health outcome	Pollutant	Direction and size of Association[a]	Comments	Adjustments	Statistical methods
Arena et al 2006 [1]	1995-2000 USA	Ecological time series ≥ 65 yrs	Cardiopulmonary admissions (250.151)	PM_{10}	+ 1,22%	Per change in IQR.	Climate. Not other pollutants.	GAM with distributed lag, loess smoothing
Carracedo-Martinez et al 2008 [2]	1996-1999 Vigo, Spain, population 300.000	Case crossover	Medical emergency calls for respiratory causes	BS particles	+ 2% at lag 2	Several pollen types were significant in the analysis.	Climate, influenza	Symmetrical bidirectional conditional logistic regression
Chen et al 2005 [3]	1994-1998 Canada	Ecological time series ≥ 65 yrs *n*=8989	Repeated respiratory admissions	$PM_{10-2,5}$	+ RR 1,17	Risk of readmission per change in 7-day mean IQR.	Climate, season, gaseous pollutants	Poisson natural splines
Dominici et al 2006 [4]	1999-2000 200 US counties	Ecological time series > 65 yrs *n*=11,5 mio	Respiratory admissions	$PM_{2,5}$	+ 1-2% at lag 0 for COPD lag 2 for respiratory tract infections	Effect modification by region.	Region, climate, epidemics	Poisson natural cubic splines
Fung et al 2006 [5]	1995-1999 Canada	Compare DM[b] method to other ≥ 65 yrs *n*=18.866	Repeated respiratory admissions	SO_2 NO_2 $PM_{10-2,5}$	+ RR 1,04 at lag0-7 + RR 1,04 at lag0-5 + RR 1,02 at lag0-5	Per change in IQR of 7 and 5-day moving average.	Climate	Case-crossover, time series, DM method

Table 4: Appendix A - Systematic literature review contd.

Reference Year	Duration Country	Type Population	Health outcome	Pollutant	Direction and size of Association[a]	Comments	Adjustments	Statistical methods
Halonen et al 2009 [6]	1998-2004 Finland	Ecological time series $\geq$ 65 yrs *n*=7239	ER visits for asthma and COPD	NO_2 CO $PM_{10-2,5}$ $PM_{2,5}$	+ 4,8% + 3,7% + 2,5% + 3,1%	For change in IQR at lag 0 for patients >65 yrs. n.s. for younger subjects.	Time, trend, pollen, climate, respiratory infections	Poisson, GAM penalized thin plate splines
Linn et al 2000 [7]	1992-1995 USA	Ecological time series >30 yrs	Admissions for asthma and COPD (daily mean = 207 ∓ 54 events)	NO_2 CO	+ 0,008 (COPD) + 0,014 (Asthma) + 0,019 (COPD) + 0,028 (Asthma)	Regression coefficient per pphm/ppm change. Same day effect.	Climate, region, ethnicity	Poisson cubic splines
Vigotti et al 2007 [8]	2000 Italy	Ecological time series $\geq$ 65 yrs	ER visits for respiratory complaints (433 events)	PM_{10} CO	+ 8,5% at lag 2 + 26% at lag 4	Effect per mg/m^3 change in CO.	Climate, respiratory infections	Robust poisson GAM loess smoothe
Villeneuve et al 2007 [9]	1996-2000 Canada	Case crossover all ages	ER visits for asthma (57.912 events)	CO NO_2 O_3 PM_{10} $PM_{2,5}$	+ OR 1,18 + OR 1,14 + OR 1,11 + OR 1,08 + OR 1,08	Per change in IQR for 5-day mean. Results for all ages, summer.	Climate, epidemics, pollen	Time stratified Conditional logistic regression
Yang et al 2005 [10]	1995-1999 Canada	Cohort > 65 yrs *n*=6027	Hospital admissions for COPD	PM_{10} CO NO_2	+ RR 1,13 + RR 1,08 + RR 1,11	Per IQR increase of 7-day moving average.	Season, climate, time trend.	Poisson natural splines
Zanobetti and Schwartz 2006 [11]	1995-2000 USA	Case crossover >65 yrs *n*=24.857	Pneumonia emergency admissions	CO BC $PM_{2,5}$	+ 5% at lag 0 + 11,7 % at lag 0 & 1 + 6,5% at lag 0	Effect per change from 10[th] to 90[th] percentile. O_3 negative association in cold weather.	Climate	Regression spline, temperature matched control

[a] *Results were reported per 10 $\mu g/m^3$ unless other is stated. Results for CO were usually reported as effect per mg/m^3. +/- indicates if the association was positive or negative.*

[b] *Dewanji – Moolgawkar suggested a method to deal with recurring events with environmental covariates, see Dewanji, A and Moolgawkar, S.H. 2000. Environmetrics 11.*

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APPENDIX B : NUMERICAL RESULTS

Table 5: Results fom a model with individual lags of the 24-hour mean. Bold letters indicate significant parameters (p < 0.05).

	PM10				NO2				O3				H2S			
		95% CI				95% CI				95% CI				95% CI		
lag	beta	lower	upper	p	beta	lower	upper	p	beta	lower	upper	p	beta	lower	upper	p
lag0	0,997	0,992	1,003	0,323	1,006	0,991	1,022	0,435	0,991	0,971	1,010	0,345	1,013	0,996	1,030	0,123
lag1	0,996	0,991	1,002	0,220	0,972	0,956	0,988	**0,001**	**0,976**	**0,956**	**0,996**	**0,020**	1,013	0,995	1,030	0,159
lag2	1,004	0,998	1,009	0,214	0,988	0,971	1,005	0,154	0,992	0,972	1,012	0,447	0,989	0,973	1,005	0,183
lag3	**1,008**	**1,002**	**1,013**	**0,011**	1,016	0,999	1,033	0,060	**1,024**	**1,004**	**1,044**	**0,018**	1,014	0,998	1,030	0,088
lag4	1,000	0,994	1,006	0,968	1,014	0,996	1,032	0,130	0,999	0,979	1,020	0,944	1,001	0,983	1,020	0,880
lag5	1,003	0,998	1,009	0,204	**0,979**	**0,962**	**0,997**	**0,023**	0,993	0,972	1,013	0,478	1,017	0,997	1,036	0,087
lag6	**0,994**	**0,988**	**0,999**	**0,026**	**1,018**	**1,001**	**1,035**	**0,039**	**1,020**	**1,000**	**1,041**	**0,049**	**1,021**	**1,004**	**1,037**	**0,012**
lag7	**1,006**	**1,001**	**1,011**	**0,014**	1,002	0,986	1,019	0,775	0,992	0,972	1,012	0,409	**0,978**	**0,961**	**0,996**	**0,017**
lag8	1,005	0,999	1,010	0,103	0,994	0,977	1,011	0,489	0,994	0,974	1,015	0,593	1,011	0,992	1,029	0,248
lag9	0,998	0,992	1,004	0,437	1,010	0,992	1,028	0,280	1,000	0,980	1,022	0,968	0,997	0,980	1,013	0,696
lag10	1,001	0,995	1,007	0,795	0,996	0,979	1,013	0,648	1,007	0,986	1,027	0,526	0,992	0,976	1,009	0,365
lag11	1,002	0,996	1,007	0,583	1,012	0,995	1,030	0,176	1,001	0,980	1,022	0,931	0,985	0,966	1,004	0,114
lag12	0,996	0,990	1,002	0,185	1,009	0,992	1,026	0,305	0,998	0,978	1,018	0,832	**1,024**	**1,004**	**1,044**	**0,017**
lag13	1,001	0,996	1,007	0,680	0,995	0,978	1,011	0,523	0,992	0,973	1,012	0,429	0,995	0,978	1,013	0,598
lag14	1,001	0,996	1,006	0,637	1,017	1,001	1,032	0,032	1,006	0,986	1,025	0,568	1,014	0,996	1,032	0,117

RR, CI and p-value for results shown in figure 2-4.

Figure 2: Three day lag and all R03 dispensings

	RR	lower 95% CI	Upper 95% CI	p-value
PM 10 lag02	0.996	0.989	1.004	0.353
PM10 lag35	1.008	1.001	1.015	0.024
PM10 lag68	1.005	0.998	1.012	0.129
PM10 lag91	1.001	0.994	1.008	0.785
PM10 lag12	0.999	0.992	1.005	0.736
NO2 lag02	0.974	0.954	0.993	0.009
NO2 lag35	1.013	0.989	1.036	0.287
NO2 lag68	1.006	0.984	1.028	0.615
NO2 lag91	1.012	0.989	1.036	0.297
NO2 lag12	1.025	1.004	1.047	0.017
O3 lag02	0.962	0.939	0.985	0.001
O3 lag35	1.021	0.995	1.047	0.114
O3 lag68	0.998	0.972	1.024	0.868
O3 lag91	1.005	0.979	1.031	0.720
O3 lag12	0.996	0.973	1.021	0.774
H2S lag02	1.003	0.980	1.027	0.778
H2S lag35	1.029	1.005	1.053	0.016
H2S lag68	1.011	0.986	1.036	0.384
H2S lag91	0.975	0.953	0.998	0.032
H2S lag12	1.020	0.993	1.048	0.147

AIC 4107

Figure 3: Three-day moving average of peak pollution and all R03 dispensings

	RR	lower 95% CI	Upper 95% CI	p-value
Max PM10 lag02	0.999	0.998	1.000	0.062
Max PM10 lag35	1.002	1.001	1.003	0.000
Max PM10 lag68	1.001	1.000	1.002	0.015
Max PM10 lag91	1.000	0.999	1.001	0.508
Max PM10 lag12	1.000	0.999	1.001	0.949
Max NO2 lag02	0.990	0.984	0.996	0.001
Max NO2 lag35	1.002	0.996	1.009	0.468
Max NO2 lag68	1.006	1.001	1.012	0.032
Max NO2 lag91	1.006	1.000	1.012	0.064
Max NO2 lag12	1.012	1.006	1.017	0.000
Max O3 lag02	0.979	0.966	0.991	0.001
Max O3 lag35	1.015	1.000	1.029	0.044
Max O3 lag68	1.005	0.991	1.019	0.511
Max O3 lag91	1.019	1.005	1.034	0.008
Max O3 lag12	0.995	0.981	1.010	0.544
Max H2S lag02	1.003	0.997	1.008	0.316
Max H2S lag35	1.007	1.002	1.013	0.010
Max H2S lag68	0.999	0.993	1.005	0.715
Max H2S lag91	0.996	0.990	1.001	0.100
Max H2S lag12	1.003	0.997	1.009	0.321

AIC 4079

Figure 4: Three-day moving average of peak pollution and all R03A dispensings

	RR	lower 95% CI	Upper 95% CI	p-value
Max PM10 lag02	0.999	0.998	1.001	0.295
Max PM10 lag35	1.002	1.001	1.003	0.000
Max PM10 lag68	1.001	1.000	1.003	0.009
Max PM10 lag91	1.001	1.000	1.002	0.213
Max PM10 lag12	1.000	0.999	1.001	0.921
Max NO2 lag02	0.991	0.985	0.998	0.009
Max NO2 lag35	1.004	0.997	1.010	0.318
Max NO2 lag68	1.008	1.002	1.014	0.015
Max NO2 lag91	1.007	1.001	1.014	0.033
Max NO2 lag12	1.012	1.006	1.019	0.000
Max O3 lag02	0.979	0.966	0.993	0.004
Max O3 lag35	1.018	1.003	1.034	0.022
Max O3 lag68	1.003	0.988	1.019	0.659
Max O3 lag91	1.021	1.006	1.037	0.008
Max O3 lag12	0.994	0.978	1.010	0.486
Max H2S lag02	1.003	0.997	1.009	0.350
Max H2S lag35	1.006	1.000	1.012	0.063
Max H2S lag68	0.998	0.992	1.004	0.550
Max H2S lag91	0.993	0.988	0.999	0.025
Max H2S lag12	1.002	0.995	1.009	0.625

AIC: 3934

APPENDIX C : AIR POLLUTION MEASUREMENT DEVICES

PM_{10}:

Thermo EMS Andersen. Model FH 62 I – R

Nr. 42545/10 FNR 0650. Production year 2002

O_3:

Horiba. Model APOA, 360E

MFG NO 105001. Production year 2001.

No_x:

Horiba. Model APNA 360E

MFG NO 202008. Production year 2002.

H_2S/SO_2:

Horiba. Model APSA 360ACE

MFG NO 511004. PRODUCTION YEAR 2005.

Reference: Anna Rósa Böðvardsdóttir, Public Health officer of the Reykjavík City Department of Environment, email communication, November 30th 2009.

APPENDIX D : PERMISSION FOR USE OF PERSONAL COMMUNICATION

Aktuel mappe: **Indbakke** **Log ud**

Skriv ny Adresser Mapper Indstillinger Søg Hjælp Filters Hent Kalender RHI

Oversigt | Slet Forrige | Næste Videresend | Videresend som vedhæftet fil | Svar | S

Emne:	Re: pm2,5 og nafn USR á ensku aukaspurning
Fra:	Anna R. Böðvarsdóttir <anna.r.bodvarsdottir@reykjavik.is>
Dato:	Onsdag, 9/12 2009, 07:22
Til:	"Hanne Krage Carlsen" <hkc1@hi.is>
Prioritet:	Normal
Create Filter:	Automatically | From | To | Subject
Indstillinger:	Vis hele headeren | Vis printervenlig version | Download som en fil | Vis meddelelse

Sæl
1. Ef þetta er bara eitt gildi - eða mjög fá - að þá held ég að það sé best að henda gildinu svo þau eru ekkert að þvælast fyrir. En eins og ég segi að þá þekki ég ekki rakagögnin mjög mikið. Þau eiga að vera rétt, en ekki búið að yfirfara þessi gögn eins og fyrir loftmengandi efnin - en alltaf geta leynst skekkjur - hefur þú prófað að bera þessi gögn saman við niðurstöður mælinga á raka í FHG?
Þegar loftmengandi efni fara í mínus tölur þá er ekki venjan að taka tölur út nema vitað sé að eitthvað óeðlilegt sé í gangi - en slíkt þarf að meta í hverju tilfelli fyrir sig.
2. Velkomið að vitna munnlega í mig - en ástæðurnar að PM2,5 gögn eru ekki notuð frá Grensásveginum eru m.a. þær að gildin eru hærri en fyrir PM10 sem er ekki eðlilegt. Ekki hefur tekist að laga þetta vandamál, en ástæðan er talin vera hristingur á gámi þar sem undirstöður eru óstöðugar og verður vonandi lagað á næstunni. En niðurstöður mælinga fyrir PM10 eru örugglega, en farstöðin sem mælir einnig PM10 hefur verið notuð til samanburðar og hún hefur stutt
3. Enska heitið getur t.d. verið
Sviðið heitir í dag Umhverfis- og samgöngusvið. Heilbrigðiseftirlitið er síðan deild innan sviðsins.
City of Reykjavik - Department of Environment - (Public Health Authority).
Svo er ágætt að muna að Umhverfisstofnun hefur tekið þátt í rekstri föstu mælistöðvanna á tímabilinu 2004 - 2008. Nýverið tók Umhverfisstofnun yfir rekstur föstu mælistöðvanna við Grensásveg og í FHG og ber núna ábyrgð á rekstur mælistöðvanna og leiðréttingu gagna. En rekur stöðvarnar engu að síður í samstarfi við Umhverfis- og samgöngusvið næstu árin.
Bestu kveðjur,Anna Rósa

-----"Hanne Krage Carlsen" wrote: -----

To: "Anna R. Böðvarsdóttir"
From: "Hanne Krage Carlsen"
Date: 12/09/2009 01:49PM
Subject: Re: pm2,5 og nafn USR á ensku aukaspurning