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Air pollution exposure during pregnancy among rural Ugandan women

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Dissertation submitted in partial fulfilment of the requirements for the degree Master In Public Health (University of Cape Town)

in the

School of Public Health and Family Medicine

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FEBRUARY 2022

PREAMBLE

1. Declaration

I, Harmony Mahlaba (MHLHAR004), hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgments indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: Signed by candidate

Date: 31 January 2022

2. Acknowledgements

I would like to thank and appreciate my supervisor Associate Professor Maia Lesosky for her excellent guidance and motivation throughout the duration of my MPH degree. You are an inspirational leader, valuable academic guide and a great person in general.

To the University of Cape Town for awarding me with the Merit Award funding to pay my fees, thank you.

To the National Research Foundation for awarding me with a scholarship for my studies. I am very grateful for your assistance.

To my friends who have always been a source of encouragement and support; I appreciate you greatly.

To my family who have consistently supported my academic journey and life in general, thank you, I dedicate this feat to you!

To my God, who has been my ultimate source and strength, thank you for always keeping and guiding me. I will always love and honour You.

3. Dedication

I would like to make a special dedication to my mother (Matleke Mumsey Mahlaba), my father (Hlabane Frank Mahalaba), my grandmother (Lenah Meladi Seroka), my brother (Palabadi Mahlaba) and my sister (Maphuti Mahlaba) for being the best family I could have ever asked for. Your love and support have carried me to this point. Thank you, I love you deeply, you are my special blessing from God!

4. Thesis Abstract

Introduction: Air pollution monitoring of hazardous pollutants such as CO (Carbon Monoxide) and PM (Particulate Matter) are important for assessing whether air pollution thresholds are not exceeded in the environment. There is sparce data that has been collected in the African region for air pollution monitoring. In this study PM and CO are measured. Air pollution in pregnancy is associated with poor lung function in infants, in later life. The overall aim of this dissertation is to investigate air pollution exposure during pregnancy among rural Ugandan women.

Methods: This mini-dissertation covers two components; the research protocol (Part A) and a manuscript section (Part B). We measured the CO and PM 2.5 levels in the study location of the Kyamulibwa Health Demographic Surveillance Site (HDSS), with a total population size of 22,000. Our study population were pregnant women. Household energy use was measured using personal monitoring tools. The Dylos tool was used to measure PM 2.5 in the households, while the Lascar tool was used to measure CO once a week at two different points at the HDSS. Boxplots were used to compare the relationship between air pollution exposures (CO and PM 2.5) and respiratory symptoms. Boxplots were further used to compare the relationship between air pollution exposure and infant birth weight. Furthermore, logistic regression models were used to show associations between air pollution exposure levels and infant birth weight as well as respiratory symptoms respectively.

Results: The boxplots and regression models showing the relationship between air pollution exposure and respiratory symptoms suggest that mothers who presented no respiratory symptoms had lower levels of air pollution exposure compared to mothers who presented one or more symptoms. The boxplots and regression models also showed that air pollution exposure may not be a factor in low birthweight. Infants with low birth weight had lower air pollution exposure compared to infants with normal and high birth weight.

Conclusion: Although it is evident through the results that there is a relationship between air pollution exposure and respiratory symptoms, further research is necessary to understand context specific ways in which exposure to air pollution can be reduced in both households and the general outside environment.

5. List of Abbreviations

ANC	Antenatal Care
CO:	Carbon Monoxide
COPD:	Chronic Obstructive Lung Disease
HDSS:	Health Demographic Surveillance Site
HREC:	Human Research Ethics Committee
MRC:	Medical Research Council
NCD:	Non-Communicable Diseases
PM:	Particulate Matter
PNC:	Postnatal Care
WHO:	World Health Organization
BW:	Birth Weight
LPG	Liquefied petroleum gas

Table of Contents

6. List of tables

A. Protocol

B. Manuscript

7. List of tables

8. Table of figures

A. PROTOCOL

1. Introduction

Air pollution exposure is a known determinant of various adverse health issues that affect quality of life as well as life years in humans (Jiang, Mei, and Feng, 2016). Among other adverse effects, air pollution exposure affects respiratory health in humans, and exposure to air pollution *in-utero* has long term implications for respiratory health due to the sensitive period of lung development (Korten, Ramsey and Latzin, 2017). A significant number of morbidities and mortalities across the globe are attributable to air pollution exposure (Amegah and Agyei-Mensah, 2017), with a greater burden on low- and middle-income countries in comparison to high-income countries. Therefore, air pollution exposure during pregnancy is a public health concern.

Air quality in some sub-Saharan regions has significantly deteriorated due to population growth and the rapid expansion of the industrial sector (Amegah and Agyei-Mensah, 2017); combined with high levels of household air pollution due to biomass fuel usage, high levels of air pollution exposure is a lived reality for most people living in low- and middle-income countries (Duflo, Greenstone and Hanna, 2016). A cohort study of pregnant women in rural Uganda, with air pollution exposure measurements, pre- and post-natal, provides the opportunity to investigate air pollution exposure in a rural low-income context.

2. Background

Air pollution exposure is a major environmental health issue that affects both rural and urban areas. In 2016, the global annual rate of premature deaths that were attributable to outdoor air pollution exposure was estimated to be 4.2 million, and the vast majority of those deaths (91%) occur in low- and middle- income countries (World Health Organisation, 2018). Air pollution exposure is a risk factor for morbidity attributable to various non-communicable diseases, such as asthma and chronic obstructive lung disease (COPD) as well as cardiovascular disease (World Health Organisation, 2018). The “vast majority of outdoor air pollution deaths are due to strokes and cardiovascular diseases” (World Health Organisation, 2018). WHO has further estimated that 58% of premature outdoor air pollution-related deaths in 2016 were due to ischaemic heart disease and strokes, while 18% were due to respiratory diseases, and 6% was attributed to lung cancer (World Health Organisation, 2018). Although there are numerous sources of outdoor air pollution, the greatest contributors include

automobile emissions, stationary power generating plants and emissions from industrial and agricultural activity (Guarnieri and Balmes, 2014).

Indoor air pollution exposure contributes to an estimated 3.8 million mortalities every year (World Health Organisation, 2018). This estimate of annual deaths is mainly linked to the "inefficient use of solid fuels and kerosene for cooking within households" (World Health Organisation, 2018). Globally, an estimated 3 billion people still use solid fuels and kerosene as a means for cooking. These cooking practices are common among people living in poverty; consequently, high levels of these health-damaging pollutants are emitted into their homes and inhaled daily. The health of mothers and children is the most compromised as they spend more time being exposed to these pollutants indoors.

In 2016, 18% of premature indoor air pollution-related deaths were due to strokes, while 27% were attributable to ischaemic heart disease and pneumonia; furthermore, 20% were due to respiratory diseases, and 8% was attributable to lung cancer (World Health Organisation, 2018).

3. Aim and Objectives

Study aim

The overall aim of this dissertation is to investigate air pollution exposure during pregnancy among rural Ugandan women.

Objectives

- To describe the air pollution exposure as measured by questionnaire in all the women.
- To describe the air pollution exposures of the women as measured by personal air pollution monitoring.
- To describe the relationship between respiratory symptoms experienced by the women and air pollution exposure.
- To describe the relationship between infant birth weight and air pollution exposure.

4. Methods

This project is a secondary data analysis, no participants will be recruited or followed with any study procedures. For completeness, an outline of the parent study follows. The parent study has completed recruitment and study measures for the data used in this analysis.

4.1. Study location and characteristics

The parent study is a birth cohort study that aims to investigate maternal and household factors associated with lung function in infants. The study is located at the Kyamulibwa Health Demographic Surveillance Site (HDSS), which has a population of 22,000 in total. The HDSS is situated in the Kyamulibwa sub-county, Kalungu district, South Western Uganda. Within the HDSS are 25 rural villages as well as a small township falling within the Kyamulibwa Town Council.

The main source of economic productivity in the area is agriculture. Most of the agricultural activity includes small farms that grow a variety of food products such as coffee beans, bananas, legumes, as well as various vegetables that include potato and cassava root crops. The agricultural activity also includes small-scale farming of animals such as pigs, goats, and cattle.

The most common type of farming is subsistence farming, though cash crops are often raised for sale. These savings are used to meet other household needs such as healthcare, salt, educational material and toiletries such as soap. The level of education among the rural population is generally low, with only a third of the adolescent/adult population able to pursue secondary education.

The study region includes five health care facilities that provide basic medical care. Three of these health care facilities provide maternity services, in the form of antenatal care (ANC), deliveries and postnatal care (PNC). The Medical Research Council (MRC) has an established clinic within the HDSS area, providing free HIV and general outpatient health care services. Patients residing within the HDSS who are in need of being hospitalised are referred to the Masaka regional referral hospital, which is 32km away from Kyamulibwa town.

4.2. Study population and sampling

The study population will include pregnant women, their households and new-born infants that enrolled and consented to take part in the parent study. Pregnant women were recruited consecutively by trained study staff at routine ANC visits, no population sampling or randomisation was undertaken. The study progressed over a four-year period.

4.3. Recruitment and enrolment

Pregnant women, their new-born infants as well as their households were recruited into the study. Children in the recruited households that are younger than five will also be recruited, with the purpose of understanding their nutritional health-status as well as their access to food within the household, and how these factors relate to the lung function of infants that reside in those households. The parent study has robust infrastructure that is utilized for data management and to process and store sample information. Furthermore, the parent study has employed diverse expertise in epidemiology, social and basic sciences.

4.4. Study design

The parent study is a cohort study design and will employ quantitative research methods for the collection of data.

Research procedures and data collection methods

The parent study conducted the data collection. Data was collected by questionnaire and clinical investigations at four time points: 1) during one antenatal care visit at the clinic; 2) one home visit pre-delivery at the home of the expectant woman; 3) during one postnatal visit at the health clinic (at week 6 since birth), and 4) one home-visit during postnatal period (week 5-6 post-delivery). Community and individual air-quality monitoring also took place, usually scheduled to coincide with the study team home visits.

4.5. Study Measures

Air pollution exposure will be measured by questionnaire and by personal air exposure monitoring. Personal monitoring tools were used to measure and monitor CO and PM 2.5 exposure levels. Details of device measurement and data preprocessing can be found in the Supplement. Exposures will be measured through a number of questionnaire instruments that were given to participants. Household air pollution data that have been measured by the parent study will also be used. Air pollution exposure is monitored and the PM2.5 concentrations are measured, as they are an indicator of ambient air pollution. Dylos instruments will be used to monitor PM2.5 concentrations. Once a week, every quarter, fixed monitors are installed at two different points at the HDSS to capture data during the different seasons of the year. Infant outcomes will be measured by questionnaire and medical record extraction. The main outcome of this study is infant and maternal characteristics in response to maternal air pollution exposure. Birthweight measures will be extracted from hospital record files.

PM monitoring devices were set to provide one measurement every 60 seconds, and PM2.5 values were calculated taking the difference between the censor reported values (“large” particles, and “small” particles). The censor provides PM measurements in particles per cubic foot, and these were converted to particles per cubic metres by dividing by 35.315. Total available measurement time per file was split into 24-hour periods and summary measures (mean, median, quantiles, standard deviation, geometric mean) calculated per 24-hour period.

CO monitors were set to take measurements every 60 seconds. Total available measurement time per file was split into 24-hour periods and summary measures (mean, median, quantiles, standard deviation, geometric mean) calculated per 24-hour period. In addition, the number of minutes per period, the duration above and below the limit of detection were summarised.

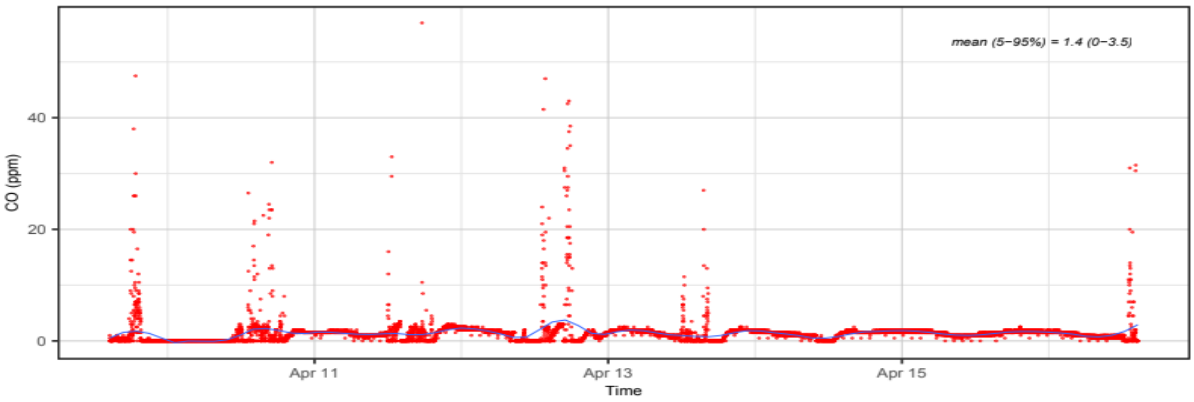

Figure 1. Sample of personal air pollution monitoring, in this case carbon monoxide (CO) emissions over a time period of 8 days.

Table 1. Study variables, including potential confounders and demographic measures to be used in analysis

Variables	**Measured by**
Carbon dioxide (CO2)	Personal air pollution monitoring
Particulate Matter (PM 2.5)	Personal air pollution monitoring
Maternal Age (years)	Questionnaire
Infant birthweight	Questionnaire
Infant General Health	Questionnaire
Maternal Health	Questionnaire
Household Energy Use	Questionnaire
respiratory symptoms	Questionnaire

4.6. Methodological approach

Descriptive statistics: All descriptive analysis of air pollution exposures and outcomes (maternal and infant) will be described by median (interquartile range), mean (standard deviation) or frequency (percent) as appropriate. Data analysis for each study objective will be done as follows:

a. Descriptive analysis of air pollution exposures (frequencies and percentages)

b. Plots of air pollution exposure

c. Boxplots were used to explore relationships between a set of risk factors, symptoms experienced by women, and infant characteristics. This applies for the following relationships:

- Relationship between respiratory symptoms experienced by the women and air pollution exposure.

- Relationship between infant birth weight and air pollution exposure.

5. Ethical considerations

The parent study has been approved by local (Uganda) and host (Liverpool School of Tropical Medicine) ethical review boards, as well as data analysis and database hosting this study by the Faculty of Health Sciences Human Research Ethics Committee (HREC) (HREC:2018/806; 2018/R042).

Risks and benefits

This is a secondary study comprised of data analysis of already de-identified data, therefore, there are no direct risks to individuals. There is a potential indirect risk in the form of loss of confidentiality, which will be reduced by the use of de-identified data, restricted access to data sets, and keeping data sets on a password-controlled computer. Similarly, there are no direct benefits, however there might be indirect benefits in learning about the impact of air pollution in pregnancy.

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7. Appendices

CRF1. Shows the Respiratory Questionnaire

Confidential

Respiratory Questionnaire

Please complete the survey below.

Thank you!

Maternal ID	id
Date	date_survey_completed
Date of birth	date_birth
Age (in years)	age

Obubonero
COPD Symptoms

Q1. Okolola? (Bwekiba Nedda, genda ku kibuuzo nnamba 3.0) Q1. Do you have a cough? (If NO, proceed to 3.0)	resp_q1
Q2. Omaze bbanga lya myezi/myaka emeka ng'okolola? Q2. For how many months/years have you had this cough?	resp_q2

Obubonero

COPD symptoms

		Yee / Yes	Nedda / No	Simanyi / Don't know
Q3. Mu biseera ebyemabega, wali olwaddeko okukolo/ekifuba ekitawoona/ekyolutentezi? Q3. Have you ever suffered from chronic/recurrent cough?	resp_q3	○	○	○
Q4. Otera okukolola wadde nga tolina ssenyigga? Do you usually cough when you don't have a cold?	resp_q4	○	○	○
Q5. Waliwo ko emyezi gy'otera okukolola ennyo, kumpi buli lunaku? Are there months in which you cough on most days?	resp_q5	○	○	○

		Yee/Yes	Nedda/No	Simanyi/Don't know
Q6. Waliwo ekiseera lw'okolola kumpi buli lunaku okumala nga emyezi esatu mu mwaka? Do you cough on most days for as much as three months each year?	resp_q6	○	○	○
Q7. Otera okuleeta ekikolondolwa? Do you usually bring up phlegm from your chest?	resp_q7	○	○	○

Q8. Omaze emyaka emeka ngo'lina ekikolondolwa?
Q8. For how many years have you had this phleghm? resp_q8 _____

		Yee/Yes	Nedda/No	Simanyi/Don't know
Q9. Waliwo ekiseera lwokalubirirwa okuwandula ekikolondolwa, naddala nga tolina ssenyiga? Do you usually have phlegm in your chest that is difficult to bring up when you don't have a cold?	resp_q9	○	○	○
Q10. Waliwo ko emyezi nga otera okufuna ekikolondolwa kino kumpi buli lunaku? Are there months in which you have this phlegm most days?	resp_q10	○	○	○
Q11. Ebikolondolwa bitera okubeera ebingi ng'era bikwaafu?Is this phlegm frequently wet?	resp_q11	○	○	○
Q12. Wali ogendereddeko nolaba nga ebikolondolwa byeyongera bu bungi okusinziira ku ludda lwewebakiddeko? Is the phlegm worse when you lie in certain positions (on one side or the other)?	resp_q12	○	○	○
Q13. Oteera okufuna ekikolondolwa enaku ezisinga nga kyenkana nga myezi esatu mumwaka? Do you bring up this phlegm on most days for as much as three months each year?	resp_q13	○	○	○

Q14. Wali ofunyeeko okuziyira mu kifuba mu myezi 12 egyiyise?
Q14. Have you had wheezing or whistling in the chest in the past 12 months? resp_q14

○ Yee / Yes
○ Nedda / No
○ Simanyi / Don't know

Q15. Mu myezi 12 egyiyise, wafunako okuziyira emirundi emeka? Wandika namba

Q15. How many attacks of wheezing have you had in the past 12 months? (Write number)

resp_q15 _____

Q16. Mu myezi 12 egyiyise, wafunako okutawanyizibwa mu kussa ng'obadde webase emirundi emeka? In the past 12 months, how many times has your sleep been disturbed due to wheezing?

resp_q16 _____

	Yee/ Yes	Nedda/ No	Simanyi/ Don't know
Q17. Mu myezi 12 egyiyise, wali ofunyeko okuziyira nga kwamaanyi nyo nga tosobola nakwogeera oba okussa ngabwoyogera In the past 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?	◯ resp_q17	◯	◯

Okukalubirirwa okussa: Nga tonafuna lubuto

Breathlessness: Before this pregnancy

Q18. Waliwo ekiseera wekyatukira nga tosobola nakutambula naye nga kino kiva kubulwadde obulala bwona obutakwtagana na kussa bubi?
Q18. Were you unable to walk due to a condition other than shortness of breath?

resp_q18
◯ Yee/Yes
◯ Nedda/No
◯ Simanyi/Don't know

Q19. Bwekiba nga kituufu, nyinyonyola nga bwe kyali
Q19. If YES, Please describe the condition

resp_q19 _____

		Yee/Yes	Nedda/No	Simanyi/Don't know
Q20 Wali nga okalubirirwa okussa, nga omuka obaka mubake? (bwekiba Nedda, genda ku kibuuzo nnamba 27.0.)Did you have any shortness of breath? (If NO, proceed to item 27)	resp_q20	○	○	○
Q21 Wali nga okalubirirwa okussa nga tosobola nakuva mu nyumba, okweyambaza oba okujjamu engoye?Were you too short of breath to leave the house, or short of breath on dressing or undressing?	resp_q21	○	○	○
Q22 Waliwo lwewayimirirako osobole okussa ng'obadde otambula ku musweeteDid you ever have to stop for breath after walking about 100 metres (or after a few minutes) on level ground?	resp_q22	○	○	○
Q23 Waliwo lwewayimirirako osobole okussa ng'obadde otambula ku musweeteDid you ever have to stop for breath after walking at your own pace on level ground?	resp_q23	○	○	○
Q24 Waliwo lwewesanga ng'olina okutambula e mpola nga ogerageranyiza ne sipiidi abantu bwemwenkanya emyaka kwebatambulira?Did you have to walk slower than people of your age on level ground because of shortness of breath?	resp_q24	○	○	○
Q25 Walemelerwako era n'osanga obuzibu okutambula ng'obadde olinya akasozi akatonotono oba ng'oli ku musweete?Were you troubled by shortness of breath when hurrying on the level or walking up a slight hill?	resp_q25	○	○	○

Akatundu kano kakwata ku mawugwe go nga kwotadde ebikwatagana ku bulwadde bwakafuba.
Lung health relating to tuberculosis
This section relates to your lungs and any previous history of tuberculosis

Q26 Bakukeberako nga olina obulwadde bw'akafuba/TB? (Bwekiba nedda, genda ku kibuuzo nnamba 40.0)
Q27 Have you ever been diagnosed with tuberculosis? (If NO, proceed to item 40.0)
resp_q27
◯ Yee/Yes
◯ Nedda/No
◯ Simanyi/Don't know

Q27 Wafunako obujanjabi bw'akafuba/TB emirundi emeka?
Q28 How many times have you been treated for tuberculosis
resp_q28 _____

Q28 Ddi (mu mwaka ki) lwewakeberebwako nga oyina akafuba? Omwezi
Q29 When were you diagnosed as having TB for this episode? Please state how long ago you were diagnosed in months
resp_q29_1 _____

Q29 Bitundu ki kumubiri gwo akawuka ka TB kebyakwata/kebyakosa?
Q30 What part of the body did the tuberculosis affect?
resp_q30 _____

Q30 Abasawo bakakasiza ddala nti oli mulwadde wa kafuba/TB?
Q31 Were the doctors/clinic sure that you had tuberculosis?
resp_q31
◯ Yee/Yes
◯ Nedda/No
◯ Simanyi/Don't know

Q31 Bakoozesa ngeri ki/bakebera batya okutegera nti olina akawuka akaleta akafuba?
Q32 Which tests showed that you had tuberculosis?
resp_q32 _____

Q32 Wali obaddeko ku kitanda okujjanjabibwa akafuba/TB?
Q33 Did you ever stay in hospital for treatment of TB?
resp_q33
◯ Yee/Yes
◯ Nedda/No
◯ Simanyi/Don't know

Q33 Muddwaliro wamalayo bbanga ki? (nga oli kukitanda) emyezi
Q34 How long (months) were you in the hospital (sleeping in the hospital)?
resp_q34 _____

Q34 Obujanjabi obw'empiiso oba empeke wabufuna kuva wa?(mu ddwaliro ki)
Q35 Where did you get your pills or injections for TB (which clinic)?
resp_q35 _____

Q35 Wamala banga ki (myezi emeka) nga olikubujjanjabi bwa kafuba/TB?
Q36 How long (in months) did you take treatment for?
resp_q36 _____
(less than 1 month=1)

Q36 Wamalayo obujanjabi buno? (Bwe kiba kituufu, genda ku kibuuzo nnamba 39)
Q36 Did you finish the treatment? (If YES, proceed to item 39)
resp_q37
◯ Yee/Yes
◯ Nedda/No
◯ Simanyi/Don't know

Q37 Lwakyi tewamalayo bujjanjabi?
Q38 Why did you not complete the treatment? resp_q38 _____

Q38 Okuva lwewafuna kuddagala elyo, wawulira nga otowolokose (nga oli bulungi)?
Q39 Did you feel partly or completely well again (better)
after ending treatment? resp_q39
- ◯ Yee/Yes
- ◯ Nedda/No
- ◯ Simanyi/Don't know

Q39 Omusawo yakugambako nti kati owonedde ddala
Q40 Did the clinic doctor say you were cured? resp_q40
- ◯ Yee/Yes
- ◯ Nedda/No
- ◯ Simanyi/Don't know

Q40 Walekela awo okugenda muddwaliro yadde nga tonamalayo ddagala nga bwebakugamba?
Q41 Did you stop attending the clinic before the treatment was meant to stop? resp_q41
- ◯ Yee/Yes
- ◯ Nedda/No
- ◯ Simanyi/Don't know

Kati bino byakwekebera okulaba oba olina akafuba/TB
Screening for current TB disease

		Yee/Yes	Nedda/No	Simanyi/Don't know
Q41 Obadde okolola okumala ebbanga eliweza wiiki ebbiri n'omusobyo? Wetegereze kino: eri abalwadde ba mukenenya, okukolola kwona, wadde nga wiiki ebbiri tezinawera, kusaana okwekenyebwa.Have you been coughing for 2 or more weeks? Note: For HIV positive individuals, any cough requires further assessment	resp_q42	◯	◯	◯
Q42 Ofuna omusujja ogwolutentezi nga gwezezza wiiki e bbri n'omusobyo?Have you had persistent fevers for 2 or more weeks?	resp_q43	◯	◯	◯
Q43 Owulira oba welaba nti okozze?Have you lost weight (at least 3 kilograms)?	resp_q44	◯	◯	◯
Q44 Ofuna okutuyaana enyo nga kati kuwezezza wiiki bbirir nokusoba?Have you had excessive night sweats for 3 or more weeks?	resp_q45	◯	◯	◯

Q45 Wabaddeko okumpi n'omuntu yena alina obulwadde bw' akafuba?Have you been in contact with someone with Pulmonary TB or chronic cough? resp_q46 ○ ○ ○

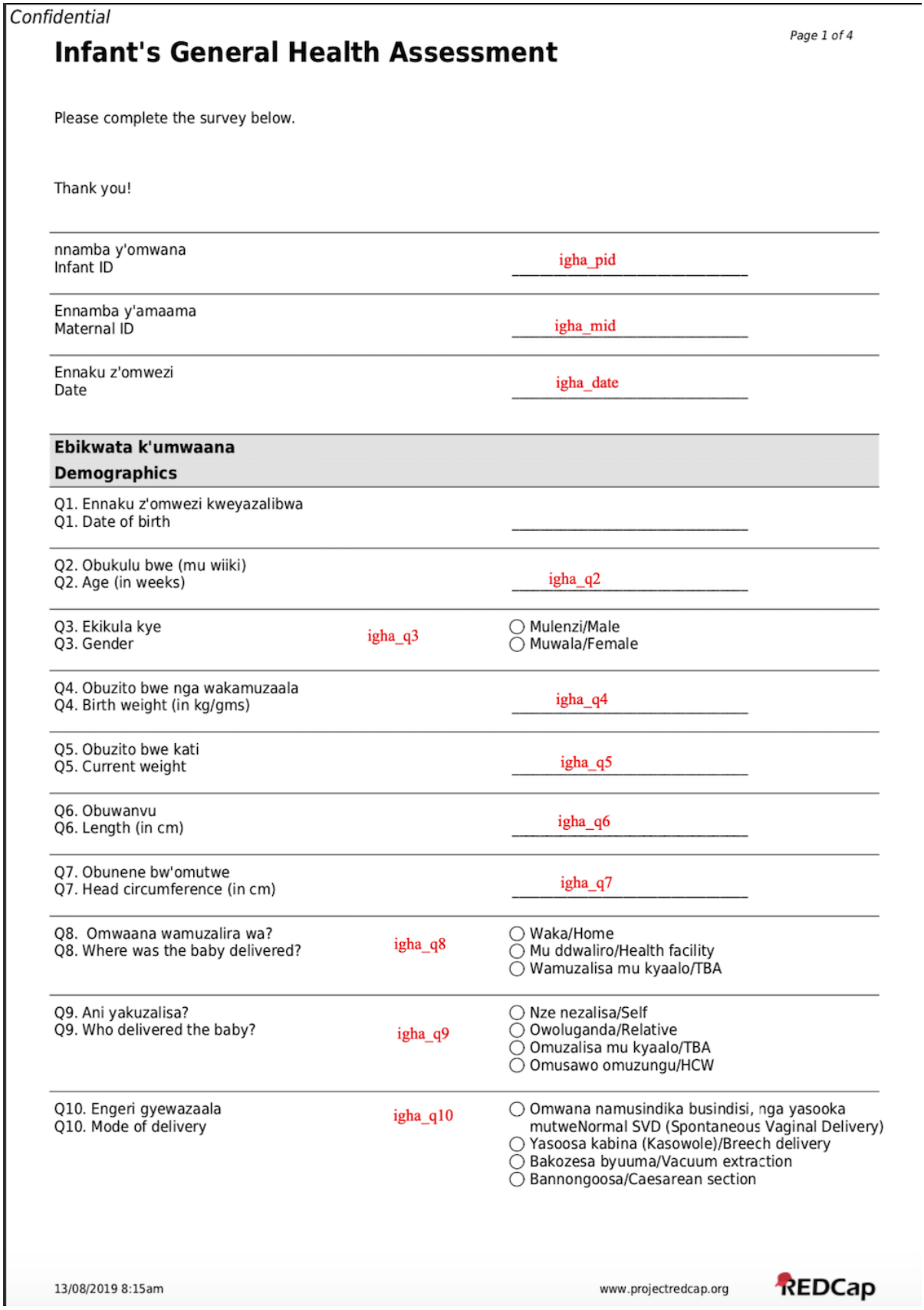
Q46 Omusawo yena yali okugambyeko nti olina obulwadde buno wammanga?
Q47 Has a doctor or other health care provider ever told you suffer from any of the following? (select all that apply) resp_q47

- ☐ None
- ☐ Chronic bronchitis
- ☐ Emphysema
- ☐ COPD
- ☐ Asima/Asthma

Q47 Wali olwaddeko obulwadde buno wammanga?
Q49 Have you ever suffered from any of the following? (select all that apply) resp_q48

- ☐ None
- ☐ Chronic bronchitis
- ☐ Emphysema
- ☐ COPD
- ☐ Asima/Asthma

CRF 2. Shows the Infant's General Health Assessment questionnaire.



Confidential

Infant's General Health Assessment

Please complete the survey below.

Thank you!

nnamba y'omwana Infant ID		igha_pid
Ennamba y'amaama Maternal ID		igha_mid
Ennaku z'omwezi Date		igha_date
Ebikwata k'umwaana **Demographics**		
Q1. Ennaku z'omwezi kweyazalibwa Q1. Date of birth		
Q2. Obukulu bwe (mu wiiki) Q2. Age (in weeks)		igha_q2
Q3. Ekikula kye Q3. Gender	igha_q3	◯ Mulenzi/Male ◯ Muwala/Female
Q4. Obuzito bwe nga wakamuzaala Q4. Birth weight (in kg/gms)		igha_q4
Q5. Obuzito bwe kati Q5. Current weight		igha_q5
Q6. Obuwanvu Q6. Length (in cm)		igha_q6
Q7. Obunene bw'omutwe Q7. Head circumference (in cm)		igha_q7
Q8. Omwaana wamuzalira wa? Q8. Where was the baby delivered?	igha_q8	◯ Waka/Home ◯ Mu ddwaliro/Health facility ◯ Wamuzalisa mu kyaalo/TBA
Q9. Ani yakuzalisa? Q9. Who delivered the baby?	igha_q9	◯ Nze nezalisa/Self ◯ Owoluganda/Relative ◯ Omuzalisa mu kyaalo/TBA ◯ Omusawo omuzungu/HCW
Q10. Engeri gyewazaala Q10. Mode of delivery	igha_q10	◯ Omwana namusindika busindisi, nga yasooka mutweNormal SVD (Spontaneous Vaginal Delivery) ◯ Yasoosa kabina (Kasowole)/Breech delivery ◯ Bakozesa byuuma/Vacuum extraction ◯ Bannongoosa/Caesarean section

Q10.2 Lwaki bakulongoosa? wandiika ensonga
Q10.2 If YES for Caesarean section, specify indication
igha_q10_2 _____

Q11. Apgar score (kebera ku bbaluwa y'okuzalibwa)
Q11. Apgar score (enter value from birth record if available)
igha_q11 _____

Q12. Omwana watandika okumuyonsa mu ssawa esooka nga wakamuzaala?
Q12. Breastfeeding initiated within one hour after birth? igha_q12
◯ Yee/Yes
◯ Nedda/No

Q13. Kati omuliisa/omugabirira otya?
Q13. Current feeding practices igha_q13
◯ Ayonka buyonsi, tewali kirala kyona kyemuwa/Exclusively breastfeeding
◯ Ayonka naye muwa nebintu ebirala/Mixed feeding
◯ Tayonka/Replacement feeding

Q13.1 Bwaba nga ayonka wamu n'okunywa ebintu ebirala, menya ebyo byona byakozesa
Q13.1 If MIXED FEEDING, specify foods
igha_q13_1 _____

Q13.2 Bwaba nga tayonka, menya ebyokunywa/byokulya by'omuwa
Q13.2 If REPLACEMENT FEEDING, specify foods
igha_q13_2 _____

Q14. Omwaana yali alwaddeko okuva lwewamuzaala?
Q14. Any history of illnesses since birth? igha_q14
◯ Yee/Yes
◯ Nedda/No

Q15. If YES, which of the following illnesses did the baby have? igha_q15
☐ Okulemererwa okuyonka/Failure to breastfeed
☐ Okukalubirirwa okussa/Breathing difficulties
☐ Okufuuka kyenvu/Yellow discolouration
☐ Okufuna omuliro/Fever
☐ Okukaaba ennyo/Excessive crying
☐ Okwesika/Convulsions
☐ Ebirala (wandiika)/Others (specify)

Q15.1 Please specify
igha_q15_1 _____

Q16. Olina/Maama w'omwaana alina akawuka ka mukenenya? igha_q16
Q16. Is the baby HIV-Exposed?
◯ Yee/Yes
◯ Nedda/No

Q17. Bwekiba nga kituufu, yafuna eddagala eriziyiza akawuka erya Niverapine? igha_q17
Q17. If YES, did s/he receive Nevirapine?
◯ Yee/Yes
◯ Nedda/No

Q18. Mu kiseera wewazaalira, walina ku ndwadde zino wammanga (Laga buli bulwadde bwamenya)
Q18. Around the time of labour and delivery, did the mother have any of these conditions? (Tick all that apply)

igha_q18

- ☐ Ensuulwe okwabika nga tonafuna bias/PROM (Premature Rupture of Membranes)
- ☐ Ensuulwe okwabika nga olubuto telunnatuusa kuzaala/PPROM (Preterm Premature Rupture of Membranes)
- ☐ Okuvaamu amazzi oba ebiserera mu bitundu ebyekyama/Abnormal vaginal discharge
- ☐ Amazzi g'ensuulwe nga gawunya bubi/Foul-smelling liquor
- ☐ Omusujja/omuliro/Fever
- ☐ Okukozesa oba okufuna obujjanjabi bwa antibioticsUse of antibiotics

Physical Examination

Q19. General Condition — igha_q19

- ◯ Active
- ◯ Weak
- ◯ Lethargic

Q20. Physical abnormalities — igha_q20

- ◯ Yes
- ◯ No

Q20.1 If YES, please describe

igha_q20_1 _____

Q21. Temperature (axillary)

igha_q21 _____

Q22. Pallor — igha_q22

- ◯ Normal
- ◯ Mild
- ◯ Moderate
- ◯ Severe

Q23. Jaundice — igha_q23

- ◯ Normal
- ◯ Mild
- ◯ Moderate
- ◯ Severe

Q24. Cyanosis — igha_q24

- ◯ Normal
- ◯ Mild
- ◯ Moderate
- ◯ Severe

Q25. Dehydration — igha_q25

- ◯ Normal
- ◯ Mild
- ◯ Moderate
- ◯ Severe

Respiratory system

Q26. Respiratory rate (breaths per minute) igha_q26

Check for features of distress

		Yes	No
Q27 Severe chest in-drawing	igha_q27	○	○
Q28 Nasal flaring	igha_q28	○	○
Q29 Grunting	igha_q29	○	○
Q30 Chest deformities	igha_q30	○	○

Q30.1. If Yes (Chest deformities), describe igha_q30_1

Q31. Any other systemic findings (list) igha_q31

B. MANUSCRIPT

Title: Air pollution exposure during pregnancy among rural Ugandan women

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Keywords: Air pollution exposure, Carbon Monoxide, Particulate Matter, Mothers, Infants, Measurements, Uganda

Journal: American Journal of Epidemiology (AJE)

Manuscript word count (excluding tables, figure legends, abstract and references) = 3013

Abstract = 255

Tables: 6

Figures: 4

Abstract

Introduction: Air pollution monitoring of pollutants such as CO and PM aids in the control of emissions in the environment. This study described air pollution exposure during pregnancy among rural Ugandan women. We described the relationships between air pollution exposure (CO and PM 2.5), respiratory symptoms and birth weight. All available data from the parent study were used in this analysis.

Methods: A cohort study design was used, and 562 mothers with their infants (562) were recruited into the study. The study was over a four-year period. Monitors were used to measure PM 2.5 in households, while CO was measured at two different points at the Health Demographic Surveillance Site (HDSS) once a week. Boxplots were used to compare the relationship between air pollution exposures (CO and PM 2.5) and respiratory symptoms. Boxplots were used to compare the relationship between air pollution exposure and infant birth weight. A multiple logistic regression model was used to test the association between air pollution exposures and infant birth weight.

Results: Our findings suggest that mothers who presented no respiratory symptoms had lower levels of air pollution exposure compared to mothers who presented one or more symptoms. Our findings also showed that exposure to CO and PM 2.5 may not be a risk factor for low birth weight.

Conclusion: There is a positive relationship between air pollution exposure and respiratory symptoms. Solutions that are relevant to Africa are needed to reduce indoor and outdoor air pollution, which will in turn reduce the risk of respiratory diseases within the population.

Air pollution exposure is a growing environmental health issue globally and is a major contributing factor to various adverse health outcomes. Respiratory health is one of the aspects of human health that is adversely affected by air pollution exposure.[1] Cumulative exposure to high levels of air pollution is known to decrease life years and the quality of life experienced by people globally.[2] CO and PM are some of the problematic air pollution toxins that affect human lung function negatively as they are associated with respiratory symptoms.[3] Records show that PM 2.5 concentrations in Sub-Saharan Africa (SSA) regions are estimated to be around 100 $\mu g/m^3$ compared to an estimated <20 $\mu g/m^3$ in most European and North American regions.[4] Low-middle-income countries such as those in SSA experience a greater burden of morbidities and mortalities compared to high-income countries as the air pollution exposure in low-middle-income countries is greater than that of high-income countries.[5]

In 2012 the global annual rate of preventable mortality due to outdoor air pollution exposure was estimated to be 4.2 million, and a large proportion of those deaths (91%) occurred in low- and middle- income countries.[6] Continuous exposure to air pollution as part of daily living is a known risk-factor for morbidities that are attributable to various non-communicable diseases (NCDs) such as chronic obstructive lung diseases (COPD), stroke and cardiovascular diseases.[6] In 2016, the WHO reported that 18% of premature outdoor air pollution-related mortalities were due to respiratory diseases, and 6% were attributed to lung cancer.[6]

The deterioration of air quality which has been noted in sub-Saharan Africa is attributed to the rapid urbanization that is also occurring.[5] Rapid industrial expansion and the exponential growth of the population contribute to the worsening of air pollution as vehicle ownership and the use of fossil fuels increases.[5] Outdoor activities that contribute to the deterioration of air quality include automobile emissions, stationary power generating plants and emissions from industrial and agricultural activity.[7]

In addition to outdoor air pollution, indoor air pollution exposure can be a major contribution to total air pollution exposure. WHO has estimated that 3.8 million mortalities occur across the globe every year due to indoor air pollution.[8] It has been reported that these estimated global mortalities are linked to the "inefficient use of solid fuels and kerosene for cooking within households". [8] The WHO has estimated that 3 billion people still make use of solid fuels and kerosene for cooking purposes. These cooking practices are commonly found among people in low-income households.[8] Consequently, inhalation of health-damaging pollutants occurs daily

in these homes, which often compromises the health of mothers and children the most as they spend more time indoors compared to men.[8] Air pollution exposure affects human health negatively, *in utero* and in all other stages of life.[1] Studies show that air pollution exposure *in utero* is associated with long term lung function implications, as this is a sensitive period of growth and development for the lungs. [1]

The rate at which CO and PM are absorbed into the lungs is determined by the duration of the exposure, the level of exposure concentration as well as minute ventilation.[9] The measurement of these toxins in the environment is helpful to researchers in that they are able to detect whether exposure to these toxins is above the threshold for human inhalation, and to detect which symptoms arise from air pollution exposure. In this study CO and PM are measured. A cohort study of pregnant women in rural Uganda with air pollution exposure measurements pre- and post-natal period provides the opportunity to investigate air pollution exposure in a rural low-income context.

METHODS

Study location and characteristics

The study location is the Kyamulibwa Health Demographic Surveillance Site (HDSS), with a total population size of 22,000. The HDSS is situated in the Kyamulibwa sub-county, Kalungu district, Southwestern Uganda. The HDSS has a total of 25 rural villages, including a small township that also falls within the Kyamulibwa Town Council. Agriculture in Kyamulibwa is the main contributor to economic productivity. Agricultural activities in this area include small-scale farms for crop production and farming of animals. The study region has five health care facilities that provide basic medical care; however, antenatal care (ANC), deliveries and postnatal care (PNC) services are only provided at three of the five health care facilities.

Study population and sampling

The study population consisted of 562 pregnant women who consented and were enrolled into the study, including their household members, as well as their new-born infants. No population sampling or randomization was undertaken, as this is a secondary data analysis study.

Recruitment and enrolment

Eligible pregnant women and their infants were recruited at clinics during regular antenatal care by trained study staff and then consented. This analysis is a subset of the full cohort, only including women with valid measurements of either CO or PM during the antenatal period.

Study design

A cohort study design was used to conduct the study.

Research procedures and data collection methods

Research assistants were employed to collect data periodically through questionnaires. Data collection was conducted during four time points: 1) during one clinic visit when a woman visited the clinic for routine antenatal care; 2) one pre-delivery visit at the home of the pregnant woman; 3) during one health-clinic visit for a post-natal appointment (at week 6 since birth), and 4) one visit at the home of the pregnant woman, during the postnatal period (week 5-6 post-delivery). The study team monitored the community and individual air-quality at times that would coincide with home visits.

Study Measures

Self-reported exposure was measured through a series of questionnaire instruments that were given to participants. Maternal respiratory symptoms and infant outcomes were measured by questionnaire and medical record extraction. Birthweight measures were extracted from hospital record files. Personal monitoring tools were used to measure and monitor CO and PM 2.5 exposure levels. Details of device measurement and data preprocessing can be found in the Supplement.

Lascar instruments were used to monitor CO levels for a one-week period. CO monitors were set to take measurements every 60 seconds. Total available measurement time per file was split into 24-hour periods and summary measures (mean, median, quantiles, standard deviation, geometric mean) calculated per 24-hour period. In addition, the number of minutes per period, the duration above and below the limit of detection were summarized.

Household air pollution was monitored by using Dylos instruments, which were used to measure PM2.5 concentrations for three days during the antenatal and postnatal period. Instruments were installed at households based on timing relative to delivery and by logistics due to limitations caused by the number of instruments available for use in the study. Similar to CO levels, 24-hour period summaries were calculated.

Household energy use

The household energy source and use were measured from questionnaire. The energy sources included in the questionnaire were electricity, generator, diesel or gasoline. The type of stove used in a household is a determining factor for indoor air pollution; therefore, the questionnaire included types of stoves used, which included electric, Liquefied petroleum gas (LPG), kerosene, wood/sawdust burning, charcoal, efficient wood burning, other biomass burning and open fire. Furthermore, the questionnaire explores what sources each household uses for cooking, lighting, heating and space cooling. The sources included firewood, dung, crop residue, kerosene, LPG, charcoal, solar and electricity. We also used the questionnaire to find out the quantity of the sources used in the households.

Analytical methods

Data

All descriptive analysis pertaining to air pollution exposure variables as well as maternal and infant outcomes were summarized by median (interquartile range), mean (standard deviation) or frequency (percent) as appropriate. Data analysis for each study objective was conducted through the aid of tables and figures. Descriptive analysis of air pollution exposures (mean and standard deviation) was articulated through a table showing clinical characteristics of individuals. Boxplots that show relationships between air pollution exposures, symptoms and birthweight were included. Boxplots were used to explore relationships between a set of risk factors, symptoms experienced by women, and infant characteristics. This applied to relationships between respiratory symptoms experienced by the pregnant women and air pollution exposure. This also applied to relationships between infant birth weight and air pollution exposure. A multiple regression model was used to explore the associations between air pollution exposures and infant birth weight. There were missing data; however, this did not

have a significant effect on the results of the study. Furthermore, for the variable household energy use, the participants could select more than one type of household energy use, which resulted in more than 562 responses.

RESULTS

Characteristics of participants

The study enrolled n= 562 mothers who also had completed air pollution measurements and are included in this analysis. The demographic characteristics of the individuals are shown in Table 1. The median (IQR) age in years of the mothers was 25 (15-46). A slightly larger proportion of the infants were male (52.2%). The vaginal mode of birth delivery was higher (89.2%) compared to caesarean (10.5%) and vacuum delivery (0.2%). The birthweight of infants was predominantly within the normal range (84.1%). Infants with a low birthweight were 45 in total (11.9%).

Table 1. Demographic and exposure characteristics of mothers and infants, Kyamulibwa, Uganda, 2020.

Variable	Value	Total
Observations (N**)**	562	
Maternal age (years) [Median (IQR)]	25 (10)	
Birth weight [N (%)]		**337**
Low birthweight (< 2.5 kg)	45 (11.9)	
Normal birthweight (2.5-4.0)	317 (84.1)	
High birthweight (> 4.0 kg)	15 (4.0)	
Gender [N (%)]		**446**
Male	233 (52.2)	
Female	13 (47.8)	
Mode of delivery [N (%)]		**446**
Vaginal delivery	398 (89.2)	
Caesarean section	47 (10.5)	
Vacuum extraction	1 (0.2)	
Household energy use [N (%)]		**799**
Use of charcoal	157(19.6)	
Use of crop residue	160(20)	
Use of firewood	481(60)	
Use of LPG	1(0.1)	
Particulate Matter PM 2.5 24hr exposure (N/m^3)		
Mean of PM 2.5 [Mean (sd)]	12,745 (20,433)	
Carbon monoxide 24hr exposure (N/m^3)		
Mean of CO [Mean (sd)]	2.6 (4.9)	

A typical example of CO and PM 2.5 exposure measurements for one individual is shown below in Figure 1, which shows that the CO exposure measured was < 50 ppm daily on average. The measurements displayed also show that all log10 PM 2.5 measurements were < 5 N/m^3.

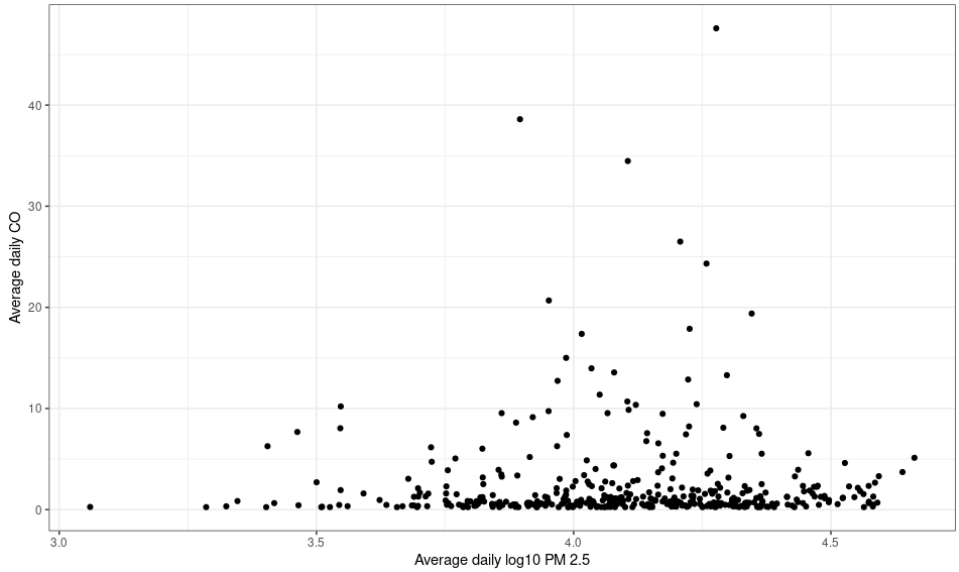


Figure 1. Scatterplot of CO vs log10 PM 2.5 (N/m^3) daily average exposure measurements of an individual, Kyamulibwa, Uganda, 2020.

Symptoms identified

The respiratory symptoms of interest are included in Table 2. The symptom that was most prevalent among mothers was wheezing limits speech (24.0%); in contrast, history of TB had the lowest prevalence (0.4%). Other symptoms that were experienced by more than 1% of mothers were cough (9.8%), recurrent cough (2.1%), shortness of breath (1.6%) and wheezing (4.3%). The rest of the symptoms were experienced by less than 1% of mothers.

Calculations are performed for respiratory symptoms (cough, recurrent cough, wheezing, wheezing limits speech, phlegm, shortness of breath, suffered asthma, persistent fever and tuberculosis) by frequency and percentage. Wheezing limits speech was only answered by those who answered yes to wheezing. Phlegm was only answered by those who answered yes to recurrent cough.

The boxplot method of analysis in Figure 2 shows the relationships between respiratory symptoms and the mean of CO exposure measurements. This method displays the exposure levels of mothers who presented symptoms in contrast to those who did not present symptoms. Mothers who indicated yes for symptoms such as wheezing that limits speech, history of tuberculosis and suffered asthma had been exposed to higher CO concentration levels compared to mothers who indicated no for symptoms (Figure 2). The boxplots also show that the CO concentration data of mothers who indicated no for wheezing limits speech and suffered asthma had less variability compared to mothers who indicated yes for these symptoms (Figure 2). Table 3 also shows that mothers who had one or more respiratory symptoms had been exposed to higher levels of CO and PM compared to mothers who had no respiratory symptoms.

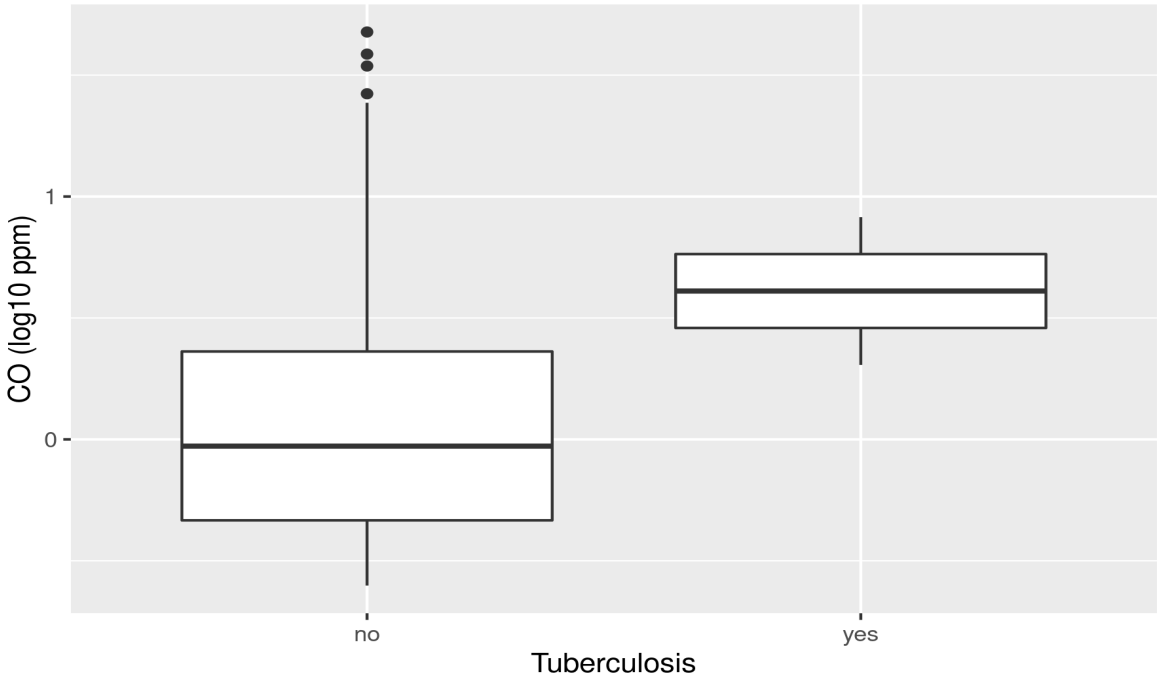
Table 2. Respiratory symptom profile of mothers in antenatal period, Kyamulibwa, Uganda, 2020.

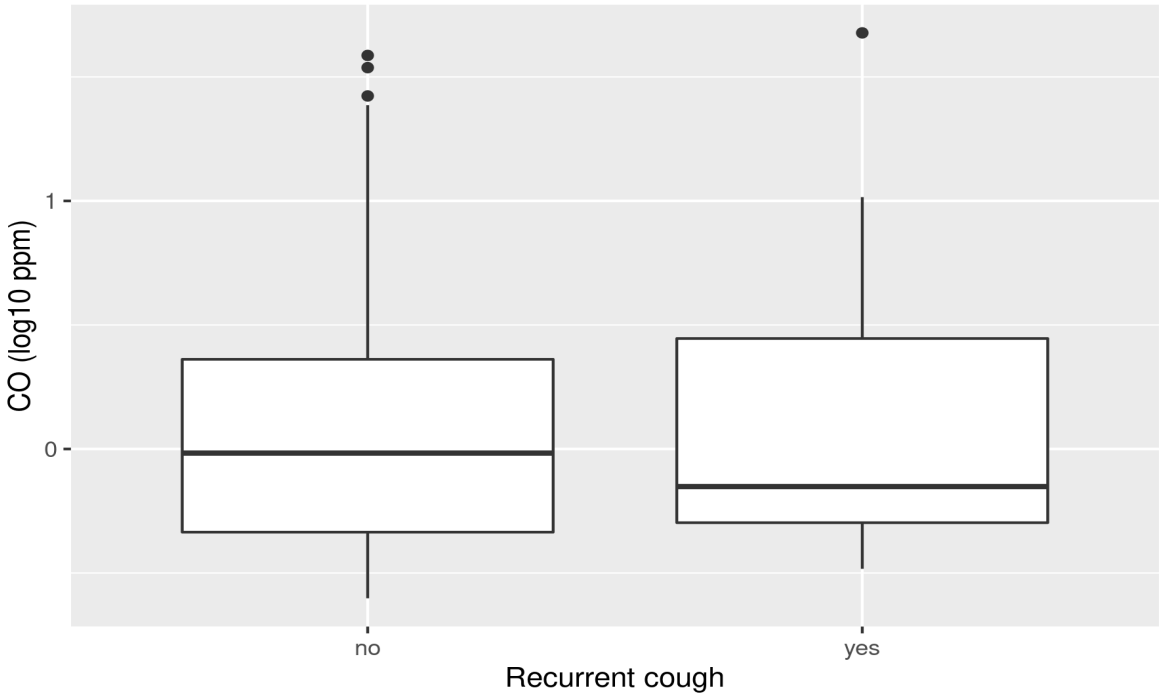
Characteristics	N(%)	Total (N)	Missing data (NA)
Observations (N)	562		
Cough		561	1
Yes	55 (9.8)		
No	506 (90.2)		
Recurrent cough		561	1
Yes	12 (2.1)		
No	549 (97.9)		
Wheezing		558	3
Yes	24 (4.3)		
No	534 (95.7)		
Wheezing limits speech		25	537
Yes	6 (24.0)		
No	19 (76.0)		
Phlegm		518	44
Yes	4 (0.8)		
No	514 (99.2)		
Shortness of breath		554	8
Yes	9 (1.6)		
No	545 (98.4)		
History of Asthma		561	0
Yes	4 (0.7)		
No	557 (99.3)		
History of TB		558	1
Yes	2 (0.4)		
No	556 (99.3)		
Don’t know	2 (0.4)		
Persistent Fever		560	1
Yes	3 (0.5)		
No	557 (99.5)		

Table 3. CO and PM 2.5 exposure levels of mothers with no symptoms compared to mothers with one or more symptoms, Kyamulibwa, Uganda, 2020.

Variable	No Symptoms	1 or more Symptoms
PM 24hr exposure [Mean (sd)]		
PM 2.5 (N/m^3)	14,940 (8,546)	16,462 (8,926)
CO 24hr exposure [Mean (sd)]		
CO (N/m^3)	2.4 (4.4)	9.95 (8.0)

The relationship between the mean of PM 2.5 and respiratory symptoms is displayed in Figure 3. In the case of all the symptoms displayed, women who presented symptoms had been exposed to higher levels of PM 2.5. Figure 3 also shows that mothers who have suffered asthma and those who have a history of tuberculosis had less variance of PM 2.5 exposure levels compared to mothers who have not suffered asthma as well as those who do not have a history of tuberculosis. It is also noticeable that mothers who answered no for phlegm had less variance of PM 2.5 exposure levels compared to mothers who answered yes for phlegm (Figure 3).


CO (log10 ppm)
1
0
no
yes
Tuberculosis


CO (log10 ppm)
1
0
no
yes
Recurrent cough

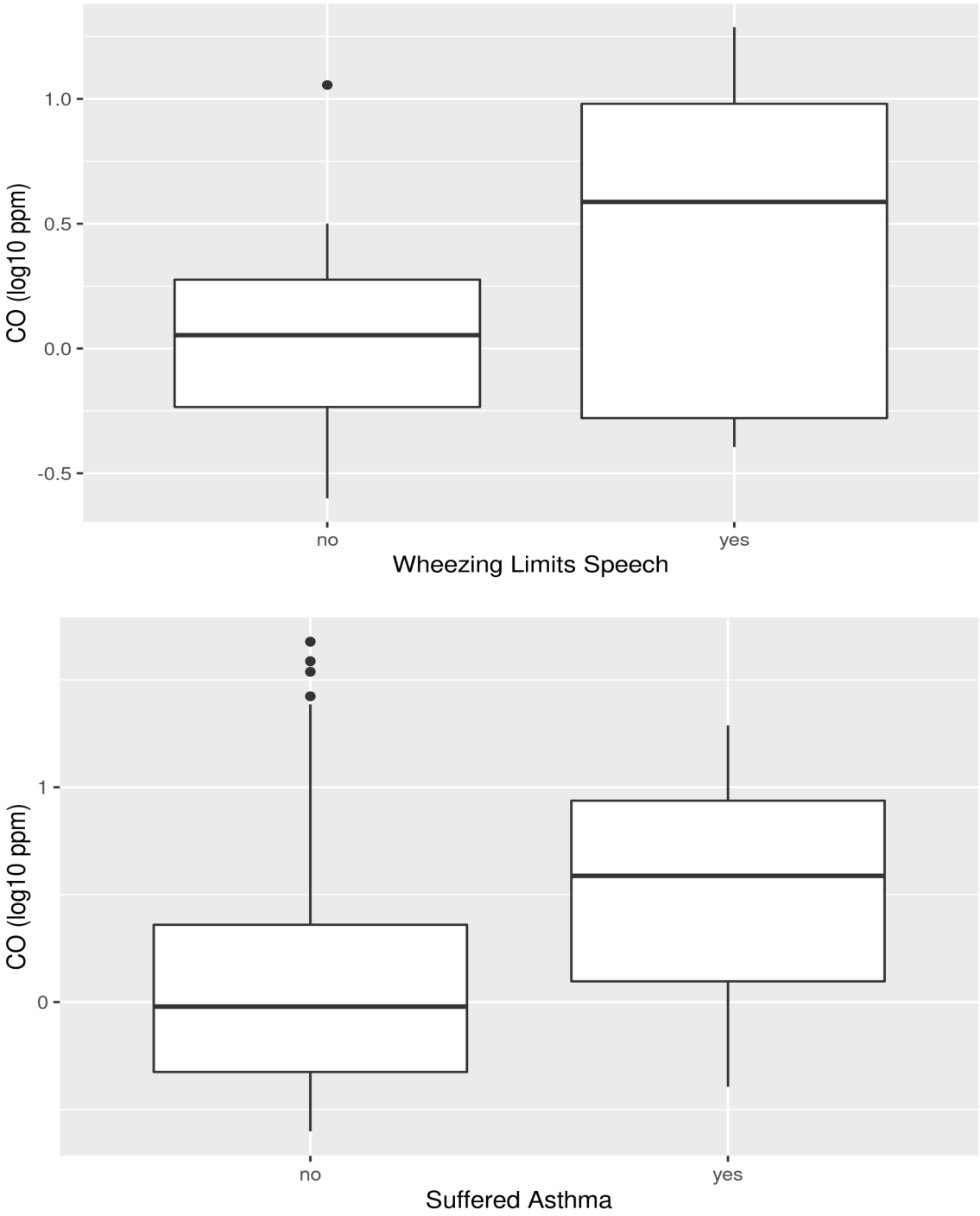
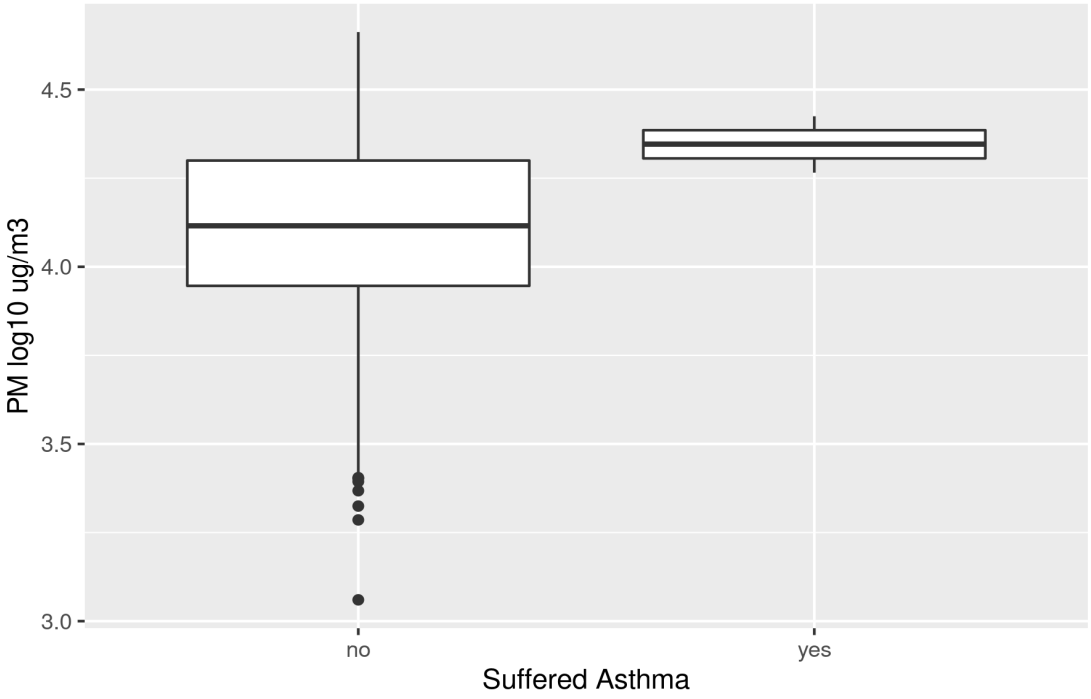
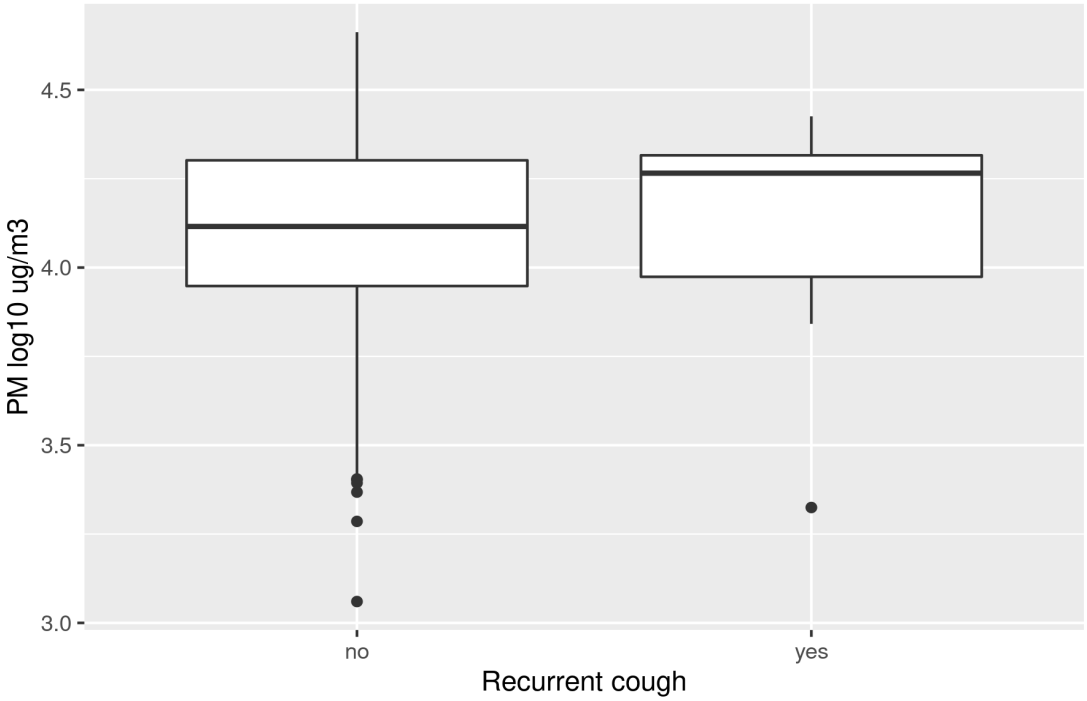


Figure 2 Boxplots for the correlations between the mean of Carbon Monoxide (mg/m^3) and respiratory symptoms, Kyamulibwa, Uganda, 2020.

The bolded line within the box represents the median value. The upper and lower border lines of the box represent the 75th and 25th percentiles, respectively. The whiskers represent the range for the 95% confidence interval (CI). The small black circles indicate the outliers.


4.5
4.0
3.5
3.0
PM log10 ug/m3
no
yes
Suffered Asthma


4.5
4.0
3.5
3.0
PM log10 ug/m3
no
yes
Recurrent cough

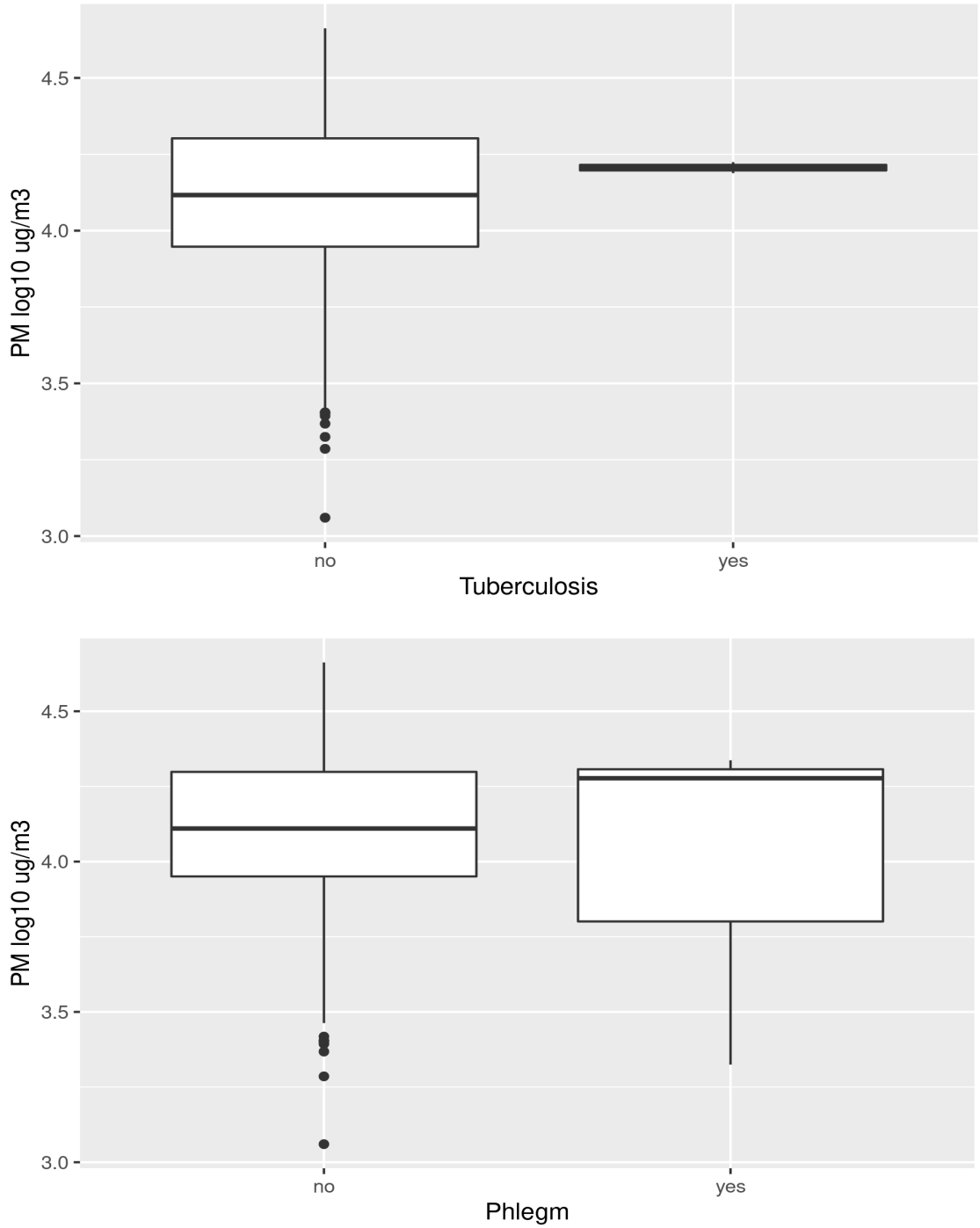


Figure 3 Boxplots for the correlations between log10 PM 2.5 (µg/m^3) and respiratory symptoms, Kyamulibwa, Uganda, 2020.

The bolded line within the box represents the median value. The upper and lower border lines of the box represent the 75th and 25th percentiles, respectively. The Whiskers represent the range for the 95% confidence interval (CI). The small black circles indicate the outliers.

Figure 4 and Table 4 displays the difference in distribution of air pollution exposure for different infant birthweight categories. There is no evidence of differences in CO exposure between low birth weight and normal birthweight.

Boxplots in figure 4 display the relationship between PM and birth weight as well as the relationship between CO and birth weight. Infants born with low birth weight had household measures of PM that were on average lower than infants born with normal and high birthweight respectively. In addition, table 4 shows that infants born with low birthweight had been exposed to less PM compared to infants born with normal and high birth weight. Figure 4 and Table 4 also demonstrate that on average, there was no large difference for CO exposure measurements between infants with low birthweight compared to infants with normal birth weight.

Table 4. shows the CO and PM 2.5 24-hour exposure levels of infants with low birth weight, normal birth weight and high birth weight, Kyamulibwa, Uganda, 2020.

Variable	**Low bw (<2.5 kg)**	**Normal bw (2.5-4.0 kg)**	**High bw (>4.0 kg)**
PM 2.5 [Mean (sd)]			
PM (N/m^3)	12,788 (7,481)	15,164 (8,611)	16,165 (10,591)
CO [Mean (sd)]			
CO (N/m^3)	1.64 (2.42)	2.57 (5.1)	4.57 (8.49)

Table 5. shows associations between air pollution exposures (PM 2.5 and CO) and birth weight (low and not low birth weight)

Predictors	Odds ratio	CI	*p*
Intercept	1.3	0.1 - 15.0	0.8
Age	1.1	1.0 - 1.2	0.2
PM 2.5	1.0	1.0 - 1.0	0.1
CO	1.6	0.7 - 7.9	0.5

The results from table 5 show that the odds ratio for PM 2.5 is 1, therefore there is no association between PM 2.5 exposure and low birth weight. However, the p value is greater than 0.05, which shows that the result is not statistically significant.

Table 6. shows associations between air pollution exposures (PM 2.5 and CO) and respiratory symptoms (one, or more than one) respiratory symptoms

Predictors	Odds ratio	CI	*p*
Intercept	0.1	0.01 – 2.2	0.2
Age	1.1	1.0 - 1.2	0.3
PM 2.5	1.0	1.0 - 1.0	0.3
CO	1.9	1.1 – 4.4	0.05

The results from table 6 show that the odds ratio for PM 2.5 is 1. However, the p value is greater than 0.05, which shows that the result is not statistically significant.

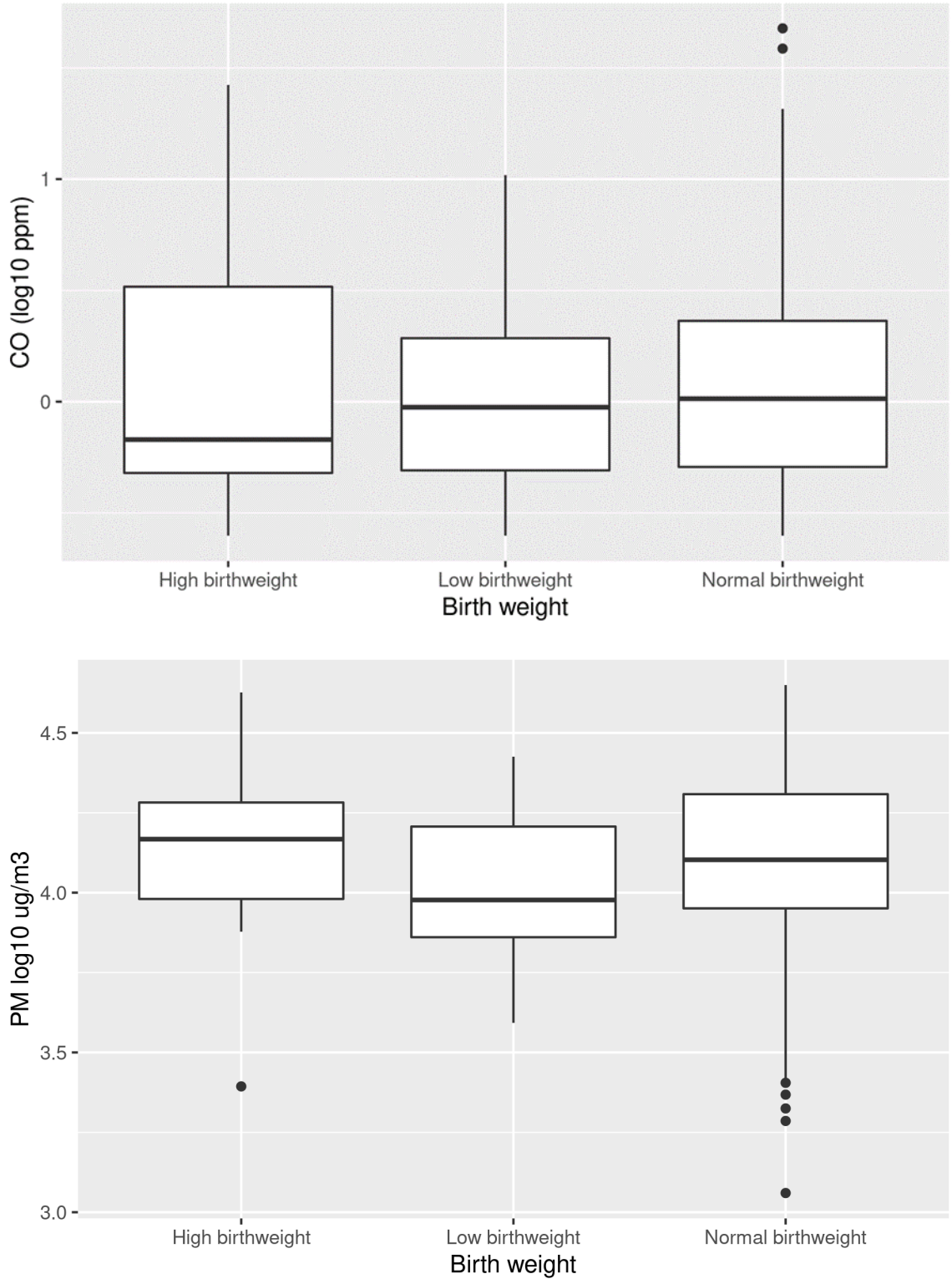


Figure 4 Boxplots for the correlations between air pollution exposures (geometric mean) and infant birthweight (kilograms) below, Kyamulibwa, Uganda, 2020.

The bolded line within the box represents the median value. The upper and lower border lines of the box represent the 75th and 25th percentiles, respectively. The whiskers represent the range for the 95% confidence interval (CI). The small black circles indicate the outliers.

DISCUSSION

The analysis carried out here demonstrates that even in rural settings in Uganda, measured 24-hour exposure to air pollution is high. WHO guidelines recommend that 24-hourly mean concentrations for CO should not exceed 4 mg/m^3.[6] WHO guidelines also recommend that the annual mean for PM 2.5 concentrations should not exceed 5 $\mu g/m^3$, and the 24-hourly mean should not exceed 15 $\mu g/ m^3$.[6] Furthermore, the WHO recommended limits for CO exposure levels are 9-10 ppm for a maximum of 8 hours, 25-35 ppm for a maximum of 1 hour, and 90-100 ppm for a maximum of 15 minutes.[6] Figure 1 shows the daily CO and PM 2.5 exposure levels as measured by monitors; the CO measurements were at an average of 0.9 ppm per day, while log10 PM 2.5 were at an average of 3.9 N/m^3 per day. These daily levels of air pollution exposure pose a risk to the lung health of mothers and their unborn babies.

This study described relationships between 24-hour air pollution exposures measured in households of pregnant women, along with nine respiratory symptoms and infant birthweight for individuals. Our study demonstrates a relationship between air pollution exposures (CO and PM) and respiratory symptoms that were experienced by mothers during the antenatal period. The measurements of the CO and PM 2.5 exposure were only recorded during the antenatal period. The findings demonstrate that mothers that experienced respiratory symptoms had been exposed to higher levels of PM 2.5 compared to mothers that did not experience those symptoms. Furthermore, mothers that had experienced the respiratory symptoms had been exposed to higher CO compared to mothers that did not experience those symptoms. Our findings are consistent with previous studies. A study conducted on a cohort of Taiwanese adults aged 20 years and above demonstrated decreased lung function and an increased incidence of respiratory disease among adults who have been exposed to PM 2.5 over a prolonged period of time.[10] Furthermore, a study conducted among Australian women that assessed exposure to air pollutants including CO and PM 2.5, PM10, NOx, and SO2 showed an increased risk of compromised lung function due to respiratory illness among women who were exposed to these pollutants over a long time period.[11] However, it has also been noted that it is not clear whether significant respiratory impairment is due to exposure to a single

exposure pollutant or the combination of the pollutants, and whether this occurs in an additive or synergistic way. [11]

The findings of our study do not show any large difference between the relationship between CO and low birth weight, relative to the relationships between CO and the other birth weight categories (normal and high birth weight). The analysis demonstrates that CO exposure is not a risk factor for low birthweight. There is sparce data on the association between CO exposure during pregnancy and low birthweight. However, there are previous studies that suggest that exposure to CO during pregnancy may be a risk factor for low birth weight. A study conducted by Salam et al[(12)] observed that a 1.4 ppm difference in first trimester CO exposure was associated with 21.7g lower birth weight.[(12,p.1638)] Our findings show that there is a noticeable difference between PM 2.5 and low birth weight, relative to the relationships between PM 2.5 and the other birth weight categories. When comparing the boxplot dispersions and skewness of PM 2.5 and infant birth weight, the relationship between PM 2.5 and low birth weight showed a positive relationship, which was not seen between PM 2.5 and the other birth weight categories. This difference however displays higher PM 2.5 exposure measurements for mothers who gave birth to infants with high birth weight compared to mothers who gave birth to infants with low and normal infant birth weight.

The median values for the PM readings were not very different between low and normal infant birth weight, which suggests that there is no strong relationship between PM exposure and low infant birth weight. These results are supported by other previous research that also suggest that CO and PM are not risk factors for low birthweight. Laurent et al[(13)] investigated associations between low birth weight and air pollution exposures, including primary PM. Their findings showed that although there were significant associations between low birth weight and other air pollution exposures such as elemental carbon, nitrates and ammonium, there was no significant association observed between low birth weight and primary PM.[13]

Data from the air pollution monitoring tools and questionnaires has potential for further research concerning the effects of air pollution on various aspects of human health. The boxplots have been a useful way of comparing how air pollution affects human health among people with different exposure measurement levels. Analysis from the boxplots has been useful in demonstrating that CO and PM may not be among the pollutants that are risk factors for low birthweight. Further research would be useful to further understand distribution and burden of disease associated with air pollution exposure in the African context. This will help in finding

solutions that are relevant for low-middle-income countries such as those in sub-Saharan Africa.

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Online supplement to: [INSERT TITLE ETC]
Methods detail of handling of exposure measure

Household PM monitoring

PM monitoring devices were set to provide one measurement every 60 seconds, and PM2.5 values were calculated taking the difference between the censor reported values ("large" particles, and "small" particles). The censor provides PM measurements in particles per cubic foot and these were converted to particles per cubic metres by dividing by 35.315. Total available measurement time per file was split into 24-hour periods and summary measures (mean, median, quantiles, standard deviation, geometric mean) calculated per 24-hour period. In addition the number of minutes per period, the duration above and below the limit of detection were summerised. Measurements exceeding the upper limit of measurement were set to the upper limit. Measurements where the count of "large" particles exceeded the count of "small" particles were excluded. PM monitor files with less than 20 hours of measurement were excluded. Each period of monitoring over 20 hours was split into multiple 24-hour periods, as with the CO monitoring files. If the final period was less than 20 hours in duration, it was excluded, and only periods of 20 hours or greater were retained. The total minutes above the upper limit of measurement per 24-hour period was calculated, and any files with >20% of observation time above the upper limit were excluded. Files with incorrect data based on graphs and outlying values (malfunctioning monitors) were removed. PM measurements for each individual 24-h period were summarised using arithmetic mean, standard deviation, maximum, geometric mean, and geometric standard deviation (SD) resulting in a single value for each 24-h monitoring period. These values were then summarised as mean (SD), and median (IQR). 24-hour PM2.5 estimates were transformed to log10 for modelling and some visualisation purposes, although described in text and tables as parts per cubic meter (ppm3).

Personal carbon monoxide monitoring

CO monitors were set to take measurements every 60 seconds. Total available measurement time per file was split into 24-hour periods and summary measures (mean, median, quantiles, standard deviation, geometric mean) calculated per 24-hour period. In addition the number of minutes per period, the duration above and below the limit of detection were summarised.

CO monitor files with less than 20 hours of measurement were excluded. Measurements exceeding the upper limit of measurement (LOM) of the instrument were set to the upper limit (1000 parts per million (ppm)), and the total minutes above LOM per 24-hour period calculated. Any files with >14 minutes of observation above the upper limit of measurement were excluded. Values below the lower limit of detection (LOD, CO = 0.5 for this data) were set to 0.5*LOD. Each period of monitoring over 20 hours was split into multiple 24-hour periods, the first from 0 – 24-hours, the second from 24 – 48 hours, the third from 48 - 72 hours, etc and labelled period "A", "B", "C". If the final period was less than 20 hours in duration, it was excluded, and only periods of 20 hours or greater were retained. Files with incorrect data based on graphs and outlying values (malfunctioning monitors) were removed. CO measurements for each individual 24-hour period were summarised using arithmetic mean, standard deviation, maximum, geometric mean, and geometric standard deviation (SD) resulting in a single value for each 24-hour monitoring period. We also calculated the minutes above the limit of measurement and below the instrument LOD. These estimates per 24-hour period were then summarized as mean (SD) and median (interquartile range, IQR). 24-hour CO estimates were transformed to log10 for modelling and some graphical display purposes, although described in text and tables in parts per million (ppm) units.

C. APPENDICES

Appendix A. Ethics Approval for study

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

06 July 2021

HREC REF: 367/2021

Prof M Lesosky
Division of Epidemiology & Biostatistics
Falmouth Building-FHS
Email: maia.lesosky@uct.ac.za
Student: mhlhar004@myuct.ac.za

Dear Prof Lesosky

PROJECT TITLE: AIR POLLUTION EXPOSURE DURING PREGNANCY AMONG RURAL UGANDAN WOMEN-MASTERS' CANDIDATE-MISS HARMONY MAHLABA

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 30 July 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: - Miss Harmony Mahlaba will also be involved in this study.

Please quote the HREC REF 367/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

HREC/REF 367/2021sa

Appendix B. Instructions to Authors

Instructions to authors

Below are instructions for submitting original manuscripts and revisions to the *American Journal of Epidemiology (AJE)*. If you have any questions, please contact the editorial office at AJEADMIN@jhu.edu.

Table of Contents

Initial Submission

Manuscript Submission Guidelines

We at the *AJE* appreciate the time and effort our authors expend to prepare manuscripts for publication. We will consider for publication articles submitted in any format and reference style. Our only text requirements are the following:

1. Articles must be blinded (i.e., no authors, affiliations, or disclosures/conflicts of interest listed within the article.
2. Abstracts must be provided for those articles types that require them (see below).
3. Word counts must fall within the prescribed limits (see below). Note that word counts should not include the abstract, references, tables, or figure legends.

Please visit ScholarOne to submit. Please follow this link for instructions on how to submit your manuscript online.

If your paper is a new version of a previously rejected one, please include the original article number and a detailed explanation of why it is being resubmitted as a new paper in the cover letter.

Correspondence

The author who submits the manuscript will remain the contact author throughout the entire publishing process. At the time of submission, the corresponding author must confirm that all authors meet the authorship criteria and have seen and approved of the paper. When the final revision of the manuscript has been accepted, the senior author must sign a Publication Agreement (see "Copyright") and a statement accepting responsibility for publication charges.

Manuscripts

The *AJE* considers manuscripts for which copyright has not been assigned, that do not essentially duplicate already published material, and that are not being simultaneously considered for publication elsewhere. We do accept manuscripts that have been published on preprint servers (see below). If the submitted manuscript is based on the findings of an article that is in press or if such an article is cited in support of current findings, a copy of the article should be uploaded along with the submitted manuscript.

Descriptions of manuscript types and associated word counts are available in the table below. Although we typically follow the author's suggested section, the editorial board reserves the right to change the section in which the paper will be published if it is found to be acceptable for publication. Editors can request that authors shorten their papers further. Lengthy, encyclopedic tables should be avoided.

Abstracts are limited to 200 words and should be unstructured. For Original Contributions and Practice of Epidemiology articles, abstracts should state concisely the research question that was asked, the methods used, and the results and conclusions of the research. For opinion pieces, it should include a brief summary of the arguments being presented. Because the abstract is used by abstracting services such as MEDLINE and must make sense when read alone, it should not include citations of the scientific literature or figures or tables. However, it should include the study year(s), location, and population studied, if applicable.

Manuscript Type	Description	Word Count	Abstract?
	ORIGINAL RESEARCH ARTICLES		
Original Contribution	Reports of original research comprising laboratory, field, clinical, or mathematical modeling studies of conditions that impact the population's health, as well as studies of statistical or methodological issues. We encourage methodological contributions aimed at improving the design and analysis of epidemiologic studies. Although we recognize that such papers may require a technical level above that of the typical original contribution published in the *Journal*, we encourage authors of methodological papers to make them as comprehensible as possible by using examples based on epidemiologic studies and by relegating highly technical material to appendices.	4,000	Yes
Practice of Epidemiology and Methodology	Papers dealing with the practical application of epidemiologic or statistical methods (such as the implementation of statistical techniques or the evaluation of interview strategies).	4,000	Yes

Study Design	Manuscripts that describe designs, methods, and procedures of specific epidemiologic studies, particularly large and/or multicenter studies.	4,000	Yes
Systematic Reviews and Meta- and Pooled Analysis	In-depth reviews and analyses on both substantive subject areas and methodologic aspects of epidemiology.	4,000	Yes
The *AJE* Classroom	Short articles in which basics of epidemiologic methods are explained.	1,500	No
Research Letter	Articles presenting new data (often preliminary) that are not of sufficient length to warrant an Original Contribution. Only 1 figure and 1 short table are permitted.	1,500	No
	OPINION ARTICLES		
Commentary	Opinion piece about either an epidemiologic topic or a previously published *AJE* article.	2,000	Yes
Data-Driven Commentary	Article in which authors present the state of knowledge on a topic along with their opinions on the topic. The purpose is to effectively synthesize the available data while also commenting on the current state of affairs	4,000	Yes
Point–Counterpoint	Groups of 2 articles in which authors present different sides of a discussion.	2,000 each	Yes

Editorial	A short opinion piece written by an editor/editors of the *AJE*. Similar articles written by those who are not editors should be submitted as commentaries.	1,500	No
Letter to the Editor	Brief response to an article recently published in the *AJE*. The authors of the original paper will be invited to respond. Note that letters to the editor are not blinded.	500–600	No
Erratum	A brief article detailing necessary corrections to a previously published *AJE* article. They must include a description of the error, the corrected text, and a reference to the original article.	No limit	No

Authorship

Authorship credit should be based on criteria developed by the International Committee for Medical Journal Editors (ICMJE): 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or reviewing it and, if appropriate, revising it critically for important intellectual content; 3) final approval of the version to be published. Authors should meet all conditions. In addition, each author must certify that he or she has participated sufficiently in the work to believe in its overall validity and to take public responsibility for appropriate portions of its content. Author names should be listed in ScholarOne and author contributions should be detailed in the cover letter (e.g., "Author A designed the study and directed its implementation, including quality assurance and control. Author B helped supervise the field activities and designed the study's analytic strategy. Author C helped conduct the literature review and prepare the Methods and the Discussion sections of

the text.") Neither names nor contributions should appear in the blinded manuscript.

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At the point of submission, *AJE* policy requires that each author reveal any financial interests or connections, direct or indirect, or other situations that might raise the question of bias in the work reported or the conclusions, implications, or opinions stated—including pertinent commercial or other sources of funding for the individual author(s) or for the associated department(s) or organization(s), personal relationships, or direct academic competition. This information should be entered into ScholarOne at initial submission. When considering whether you should declare a conflicting interest or connection, please consider the conflict of interest test: Is there any arrangement that would embarrass you or any of your coauthors if it was to emerge after publication and you had not declared it?

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If the manuscript is published, conflict of interest information will be communicated in a statement in the published paper.

Crossref Funding Data Registry

In order to meet your funding requirements authors are required to name their funding sources, or state if there are none, during the submission process. For further information on this process or to find out more about CHORUS, visit the CHORUS initiative.

CONSORT Guidelines

For papers in which results of randomized trials are reported, the *Journal* encourages authors to follow the CONSORT guidelines. Please note that the CONSORT guidelines help to guarantee that the paper has the information necessary for the integration of the trial into meta-analyses and systematic reviews.

Multipart Papers

The *Journal* strongly discourages the submission of multipart papers. If submitted, multipart papers should be prepared so they can be assigned to different editorial board members and independent outside expert reviewers.

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If your article has Web material, please note that we cannot guarantee that it will be peer reviewed. Please see below for Web material guidelines for accepted manuscripts.

Revisions

Revisions should be submitted online to ScholarOne using the same "Contact Author" account that was used for the original submission. At this site, authors will find a link to the current paper and instructions on how to upload the revisions. Authors

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Revisions should include the following (note that all but the references should appear on the first page(s)):

Author names: Note that degrees are not required.

Acknowledgments section: Provide an ordered list of material that may be included: 1) author affiliations; 2) statement about authors contributing equally to the work; 3) grants and/or financial support; 4) data-availability statement; 5) thank-you's (in this part only, "Dr." should precede the name of each person with a medical and/or doctoral degree (e.g., "The authors thank Dr. Penny Kerkovich for his contributions to this study."); do not thank reviewers or study subjects; 6) members of a study group; 7) presentation at a meeting, report number in a series, or student prize paper; 8) preprint information; 9) disclaimer; and 10) conflict of interest statement.

Author affiliations: These should be listed in a single paragraph. If an author is associated with more than 1 department or institution, that name should be listed after each relevant affiliation. Each affiliation should be as detailed as possible (e.g., section, unit, department; division; school at the university; university name; city and state/province or country). Write out names of states, provinces, and countries. Sample: Author affiliations: Department of Epidemiology, Villanueva School of Public Health, Solano University, Baltimore, Maryland, United States (Janet Mendoza, Rebecca Chan, and Joshua G. Serrano); Department of General Medicine, Villanueva School of Public Health, Solano University, Baltimore, Maryland, United States (Rebecca Chan, Michael Shellstrop, Jane Williams); and Department of Internal Medicine, School of Medicine, Public University, Newark, Delaware, United States (Darryl Proctor, Jacob Boyle, and Eleanor A. Hartz).

Funding information: The sentence should begin: "'This work was supported by....'" The full official funding agency name should be given rather than the abbreviation. Grant numbers should be complete, accurate, and provided in parentheses. Multiple grant numbers should be separated by a comma. Agencies should be separated by a semicolon (plus "and" before the last funding agency). If individuals need to be specified for certain sources of funding, the following text should be added after the relevant agency or grant number: "to [author initials]." Example: "This work was supported by the National Institutes of Health (grants P50 CA098252 and CA118790 to E.S.A.); and the Alcohol & Education Research Council (grant HY GR667789)."

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Keywords: Please include a list of 3–8 keywords. Stand-alone adjectives are not permitted (e.g., longitudinal), but phrases that include adjectives are (e.g., longitudinal study).

Abbreviations: Include a list of all abbreviations used in the text and their definitions. Avoid excessive use of abbreviations solely to limit the word count. At its first appearance in the abstract and text, an abbreviated term should be written out in full, with the abbreviation in parentheses immediately following.

References: References in revisions should be formatted in basic *AMA* style; that is, numbered references cited chronologically in text.

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Once the editor(s) handling your paper have determined that it is suitable for publication in the *AJE*, it will be moved to the "accept with technical review" phase. You will receive from the editorial office a customized list of necessary changes that must be made to the text, table, figures, and/or Web material before final acceptance. However, for citation purposes, you can consider articles at this stage as "in press."

Text Guidelines

Below are text, figure, table, reference, and Web material requirements, along with some *AJE* style points. These do not have to be implemented in the original submission but may be required in revisions or at conditional acceptance. Our dedicated copy editors will implement our style when editing your article; the information below is only intended to provide guidance on a few specific points. If you have questions about *Journal* style after reading the following instructions, please contact the *Journal* office at AJEADMIN@jhu.edu.

Text Format and Style

Refer to a current issue of the *Journal* if you have concerns about the correct format and style. It should be used in conjunction with the *AMA Manual of Style, 10th Edition*, published by Oxford University Press. Use American English spelling. Follow *Webster's Third New International Dictionary or Merriam Webster's Collegiate Dictionary, 11th Edition*, for spelling and word division. Follow the *Merck Index* and *Stedman's Medical Dictionary, 26th Edition*, for spelling of chemical names and medical terms.

Usage

The *Journal* discourages the use of the word "effect(s)" as a proxy for "association(s)" in reports of single observational studies. There are many exceptions to this guideline, such as use of the expression "effect modification" as a proxy for "heterogeneity" and in papers focused on methods. The use of the word "effect" is also warranted when discussing the parameters the authors are trying to estimate. (For example:

"The effect we are trying to estimate is the difference in 5-year risk/incidence curves.") In general, authors should make a good case for why they believe that the use of the word "effect" is justified. Please refer to the editorial "Associations Are Not Effects" (Am J Epidemiol. 1991;133(2):101–102).

Text headings: *The main headings* used in Original Contributions are METHODS, RESULTS, and DISCUSSION. (These headings may not apply to statistical papers.) Do not use "Introduction" as a heading. Do not number the sections of the paper.

Trade names: For products used in experiments or methods (particularly those referred to by a trade name), give the manufacturer's full name and location (in parentheses). When possible, use generic names of drugs.

Footnotes to text: Do not use footnotes to the text. Instead, incorporate such material into the text (e.g., in parentheses).

Metric system: The *Journal* strongly encourages authors to use the metric system for all measurements. Where US measurements must be used (e.g., when reporting original measurements used in the study), metric equivalents *must* be given in parentheses.

***P* values:** In cases in which *P* values should be reported, please note style for probability: $P < 0.01$, with an uppercase italic letter *P*. *P* values should not be bolded. Avoid reporting an excessive number of digits beyond the decimal for estimates, especially when the estimate has a wide confidence interval. If *P* values are given, they should be reported to, at most, 2 digits beyond any leading zeros. They may alternatively be reported as less than some specified value (e.g., $P < 0.05$ or $P < 0.001$). Indicate whether *P* values are 1 sided or 2 sided.

Statistical notation: Equations can appear within the text or displayed. Whenever possible, mathematical equations should be written on a single line, as $a/(a + b)$ and $\exp(x)$. With proper use of braces, brackets, parentheses, and exponents, even complicated expressions can be put into this form. However, any mathematical expression that contains a character taller than a line of type should be displayed and numbered as an

equation. If your manuscript is submitted in Microsoft Word, please ensure that all math is editable with either the Word Math Editor or MathType. If your manuscript is submitted in LaTex, please be sure to include the .tex file.

When referring to an equation in the text, use, for example, "equation 6."

For multiplication, use a times sign (×) rather than an asterisk or centered dot. For +, ≤, and ≥, do not use an underline. The underline may be lost during software conversion, changing the meaning of the data from what the authors intended and leading to inaccurate representation.

Regression analyses: When presenting results of regression analyses, regression coefficients should usually be converted into more generally meaningful terms (e.g., relative odds instead of β coefficients). Note that because regression coefficients are unit dependent for continuous variables and category dependent for discrete or ordinal variables, the *Journal* strongly encourages statements specifying the units or categories, that is, as parenthetical statements in the text or in table footnotes or figure legends.

Table Format and Style

Tables should be submitted in the main manuscript file at the end of the document, after the references. Each table must be formatted by using the table feature in Word, and each entry must be in a separate cell. Tables should be numbered (Arabic numerals) in the same consecutive sequence in which they are mentioned in the text. They should be concise and self-explanatory. Avoid internal headings whenever possible. Column headings should be clearly delineated, with straddle rules over pertinent columns to indicate subcategories. Data in vertical columns should have the same unit of measurement. Divide overly long tables into 2 or more tables. Multipart tables (e.g., Table 2A and 2B) are not acceptable. For files submitted in LaTex, tables should be included in the PDF and follow the guidelines listed above.

Table titles should give details on the place of the study, the time of the study, and the study population (if applicable). Example, "Baseline Characteristics of Infants With Initial and Follow-up Screening, London, United Kingdom, 2001–2003." In the table body, leave blank spaces for no entry; avoid using dashes. Order of footnotes: 1) Abbreviations: (no footnote symbol, listed alphabetically, separated by semicolons); 2) other footnotes as necessary, each preceded by a superscript lowercase letter. Footnotes must be cited in order when reading from left to right and top to bottom.

Requirements for Figures

General figure requirements are provided below. These guidelines have been compiled to ensure maximum clarity and readability in both the full-text XML and PDF versions of the article. However, we are happy to work with authors to determine the format that makes the most sense for each specific figure.

Please format figures so that when they are reduced for print publication, the smallest type size is 8 pt. Note that figures set in portrait mode cannot be wider than 7 inches; those set in landscape mode cannot be wider than 9 inches. The maximum height depends on the length of the legend. We discourage the publication of figures set in landscape mode unless absolutely necessary. Figures should be scaled appropriately for the content.

Authors should submit their figures with the manuscript. The charge per color figure is £350/$600/€525. If you wish to avoid that fee, please submit the figures in gray scale or move them to the Web material.

If your figures were created in Word, Excel, or PowerPoint, please submit in that format. For all other programs, please save these figures directly to EPS, PDF, or TIFF files and submit in that format with accompanying PDFs. Vector files are preferred.

On maps, add a scale bar (in kilometers or meters) and an arrow indicating which direction is north.

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Standard journal article with a published correction/erratum

Korpi A, Mantyjarvi R, Rautiainen J, et al. Detection of mouse and rat urinary aeroallergens with an improved ELISA [published correction appears in *J Allergy Clin Immunol*. 2004;113(6):1226]. *J Allergy Clin Immunol*. 2004;113(4):677–682.

Journal article with digital object identifier (article not yet in print)

Sturmer T, Gefeller O, Brenner H. A computer program to estimate power and relative efficiency to assess gene-environment interactions in flexibly matched case-control studies [published online ahead of print August 10, 2005]. *Comput Methods Programs Biomed.* (doi:10.1016/j.cmpb.2003.08.003).

Article in an online-only journal that accounts for the lack of a page range

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