Non-communicable lung disease in Nairobi, Kenya: from burden and early life determinants to participatory inter-disciplinary solutions

The TUPUMUE Study

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List of abbreviations and acronyms

AHRC	Arts and Humanities Research Council
AIR	Air Pollution Interdisciplinary Research
BOLD	Burden of lung disease
CLD	chronic lung disease
COPD	chronic obstructive pulmonary disease
FEV1	Forced expiratory volume 1 second
FVC	Forced Vital Capacity
HICs	High Income Countries
ICT	Information Communication Technology
IMPALA	International Multidisciplinary Programme to Address Lung Health in Africa
ISAAC/GAN	International study of Asthma and Allergies in Childhood/Global Asthma Network
KEMRI	Kenya Medical Research Institute
LMICs	Low- to middle-income countries
LSTM	Liverpool School of Tropical Medicine

1. SUMMARIES

1.1 Synopsis

Short title	*Tupumue*
Full title	Non-communicable lung disease in Nairobi, Kenya: from burden and early life determinants to participatory inter-disciplinary solutions.
Funding	Kenya: National Research Fund, UK: Medical Research Council
Organisations	KEMRI Centre for Respiratory Disease Research, Several UK Universities (see list of contributors)
Investigators	Dr Chakaya Muhwa, Dr Evans Amukoye, Dr Hellen Meme
Rationale	In recent years many studies of adults in Africa have shown that long term lung diseases not caused by infections such as TB and pneumonia are common. These diseases (e.g. asthma & COPD) cause much suffering and early death. It is not clear why African adults have so much lung disease but there is increasing evidence from Europe and America that many lung problems in adults start during childhood. This study will investigate the lung health of Kenyan children to see if this could explain the high rate of lung problems in adults. This study will also see if the lung health of Kenyan children is affected by air pollution and early life factors.
Aims	1) To involve all of the local stakeholders in the design, conduct and dissemination of the study. 2) To co-create and deliver a comprehensive sensitisation programme to raise awareness of the Tupumue study in Mukuru and Buruburu. 3)To investigate the lung health of children aged 5-18 yrs attending school in Mukuru or Buruburu. 4) To investigate whether indoor and outdoor air pollution, birth weight, and early life chest infections affect children's lung health. 5) To measure the air pollution exposure of children from 200 households. 6) To explore community knowledge about what damages lungs and the lived experience of air pollution and lung health
Study design	A mixed methods cross-sectional study.
Number of participants	Sensitisation: 145 adults/children Mukuru, 145 adults/children Buruburu Quantitative: 1000 children (+parents) attending Mukuru schools, 1000 children (+parents) attending Buruburu schools. Qualitative: 300 children attending Mukuru schools, 300 children attending Buruburu schools.
Description of procedures	1. All appropriate permissions will be obtained. 2. A programme of three workshops and community sensitisation activities/events will be conducted at key locations within Murkuru/Buruburu. 3. 3-4 primary schools and 1-2 secondary schools in each area will be initially identified, the number of classes in each year to approach will be estimated. 4. Parents/guardian will be asked to provide consent and the children asked to provide assent. 5. For 2000 children (1000 Mukuru, 1000 Buruburu) 5.1) Parents/guardian will be asked to complete a respiratory health questionnaire about the study child that includes also enquires about possible sources of air pollution. 5.2) Parents/guardian will be asked to allow sections of the child's health card to be copied 5.3) Lung function of children will be assessed using blowing tests (spirometry) before and after 6 minutes of running. 4. Air pollution measurements will be made in the homes of 200 children (100 Mukuru, 100 Buruburu) together with measurements in strategic areas where children spend time. 5. About 600 primary school children (300 Mukuru, 300 Buruburu) will use storytelling/ drawing/artefact collection to describe their experiences of air pollution and lung health. 6. 40-60 older children (15-18 years) with lung health issues (20-30 Mukuru, 20-30 Buruburu) will take part in walking interviews to describe their experiences of air pollution and lung health.
Duration of study	This study started in January 2019 and will last for three years. 2019: study design, community consultations, permissions, community sensitisation 2020: Recruitment of children, collection of measurements 2021: Analysis of data, reporting of results.

1.2 Scientific summary

Background: Studies in Africa reveal a high prevalence of chronic obstructive pulmonary disease (COPD) and abnormal lung function in adults that cannot be attributed to tobacco smoking. The Kenya National Strategy for the prevention and control of non-communicable diseases highlights the impact of non-communicable lung diseases and makes their prevention and control national priorities. Although it is generally accepted that COPD in Africa is driven by pollution from the burning of biomass fuels, the evidence is conflicting. There is a growing consensus in high income countries that asthma and COPD originate in early life, being manifestations of reduced childhood lung function tracking into later life. It remains to be seen in Africa whether the high prevalence of reduced lung function observed in adults is a consequence of tracking of reduced childhood lung function and if so, what factors influence childhood lung function.

The aims of the Tupumue study are to determine and compare the respiratory health status of children living in two contrasting communities in Nairobi and to investigate the early life origins and potential drivers of chronic lung disease (CLD) including indoor and outdoor air pollution, low birth weight and early life respiratory infections.

Methods and design: this is a mixed methods cross sectional study conducted in two communities in Nairobi, the first, the informal settlement of Mukuru, the second, the adjacent affluent area of Buruburu. A participatory approach will involve community participants in study design, conduct and dissemination. The design of the study has been determined by a 3 day community engagement workshop in May 2019.

Community sensitisation: strategies will be co-developed with local communities to raise residents' awareness of the Tupumue study and research procedures to support recruitment and active engagement in the study. The need for a widespread campaign of community sensitisation to promote engagement with the study and enhance recruitment and local buy-in was identified during project inception workshops in Mukuru and Buruburu earlier this year. A parallel programme of sensitisation will be conducted to inform members of the education system, parents and children.

Quantitative: A total of 2000 children aged 5-18 years and their parents/guardian will be recruited from primary and secondary schools (1000 Mukuru, 1000 Buruburu), the samples will be age and sex stratified. Fieldworkers will administer questionnaires to ascertain respiratory symptoms, demographics, and indoor/outdoor air pollution sources. Birth weight and early life respiratory tract infection data will be obtained from Child Health Cards. Spirometry will be conducted before and after a 6-minute run. In 100 representative children from each community. Exposure to air pollution will be assessed using direct measurements within home settings and a mixture of measurements made at fixed sites where children spend time (e.g. schools and other settings). Pollution exposures for all children will be modelled using these direct measurements coupled to questionnaires. The lung function, questionnaire and health card data of children in Mukuru and Buruburu will be compared and associations with air pollution, birth weight, and early life respiratory tract infections will be investigated.

Qualitative: The lived experience of lung health and air pollution of about 600 children (300 Mukuru, 300 Buruburu) of primary school age (100 per 5-7, 8-10, 10-14 age group in each community) will be investigated through a combination of storytelling/drawing/artefact acquisition, visual mapping and focus groups. A cross-section of older children (aged 15-18, n=20-30 in each community) that take part in the quantitative respiratory questionnaire and lung function measurements will be chosen to take part in a walking interview. The walking interviews will explore lived experiences of air pollution and lung health through place-based discussion.

It is anticipated that Tupumue will quantify the burden and impact of non-communicable lung disease in Kenyan children living in two communities in Nairobi, and in addition identify possible early life and environmental determinants.

1.3 Lay Summary

The lung diseases asthma and chronic obstructive pulmonary disease (COPD) are very common. Around the world 300 million people have asthma and 200 million have COPD. Low- to middle-income countries (LMICs), such as Kenya, shoulder the burden of asthma and COPD. These diseases interfere with the lives of people, they stop people working and cost them money. The diseases also hold back countries from developing. The Kenyan Government has highlighted asthma and COPD as national priorities. Research from high income countries shows that the process of developing asthma and COPD starts early in life during childhood, or even earlier. Although research has shown that many adults in Africa have reduced lung function, no one has looked to see if this starts early in life.

The aim of the Tupumue study is find out how many children have lung problems and to explore children's experiences of lung problems and air pollution. In addition, we will see if the lung diseases seen in African adults start during childhood and what causes lung problems in children. We are particularly interested to look at the effects of indoor and outdoor air pollution, birth weight and early life chest infections.

This study will recruit children and young adults aged 5 to 18 years and their parents/guardian in two areas in Nairobi. The first is an informal settlement (Mukuru) and the second a better-off area (Buruburu). These two areas are very close but very different in terms of their environments. Community members are being involved in all stages of the study to ensure that it is directly relevant to community members.

To help raise the profile of the study, around 10 community awareness raising events will be held in key locations in Mukuru and Buruburu. The type and locations of the events will be decided after discussions with local community members in a series of co-creation workshops.

In total, 1300 children in Mukuru and 1300 children in Buruburu will be studied. The children and young adults will be recruited through their primary and secondary schools. Parents will be asked to give permission for their children to take part.

For 1000 children/young adults in each community we will ask questions about lung symptoms, sources of indoor air pollution and any known lung problems. We will ask mothers if we can look at the Child Health Card that records birth weight, childhood weights and chest infections. We will measure the lung function of the young people using a simple blowing test called spirometry. We will do this before and after they run for 6 minutes, a simple way of looking for a form of asthma. To look at the effect of air pollution we will measure air pollution experienced in the homes of 100 young people in each community together with measurements made at a number of places where children spend time including outdoors and at school. The results of this monitoring will be used with the questionnaires to estimate exposure to air pollution for all those taking part.

To get an idea of the everyday experiences of lung problems and air pollution, we will ask around 300 primary school children (5-14 years) in each community to draw their stories or bring in items that they link to lung problems. We will also ask them to show us on a map where their stories or items come from and discuss what these activities tell us with smaller groups of children from each class. For older children (15-18 years) about 20-30 in Mukuru and 20-30 in Buruburu will be asked to take part in walking interviews around their community to help us better understand what living in the community is like, their experiences of lung health, their understanding of air pollution and their future aspirations.

The information collected will be used to compare the children of Mukuru and Buruburu and to see if more children than expected have reduced lung function and at what age this appears. We will also see if air pollution, birth weight and early life chest infections affect the lung function of children, and the extent to which the experiences of children the two communities differ. This has not been done before in Africa. The study is large enough to make fairly accurate estimates of prevalence and to look for associations. The results of this study will be fed back to the two communities in ways they feel are easy to understand, including through the use of creative methods (e.g. theatre, storytelling, T-shirts, posters/banners, puppetry, games, music, arts festival).

2 INTRODUCTION

2.1 Background

Although non-communicable diseases (NCDs) are the leading causes of morbidity and mortality worldwide, most of the burden of NCDs is in low- and middle-income countries (LMICs) where they drive and perpetuate poverty.[1,2] NCDs are barriers to economic and social development and WHO has identified their prevention and control as an urgent development issue.[3] The commonest non-communicable lung diseases are asthma and chronic obstructive pulmonary disease (COPD): both characterised by airflow obstruction.[4-8] In LMICs the prevalence of asthma and COPD is increasing; COPD is projected to be the third leading cause of death in LMICs by 2030[9,10]. Africa has the highest rates of severe asthma and asthma mortality globally.[11]

In recent years high rates of abnormal lung function have been reported in African countries with low cigarette consumption.[12,13] In contrast to high income countries (HICs), tobacco smoking appears not to be the main driver of lung disease in LMICs with COPD mortality in these countries not being associated with cigarette smoking.[14,15] There is considerable interest in the role of air pollution including biomass smoke in the aetiology of lung disease in LMICs. However, the ongoing Burden of lung disease (BOLD) study, a high-quality prevalence survey of adults (>40 years), surprisingly and against expectations found no association between solid fuel use and spirometric evidence of airflow obstruction casting doubt on the role of household air pollution from biomass fuels during adult life as a risk factor for COPD[16]. In a further contrast with HICs, BOLD studies have shown that the predominant pattern of abnormal lung function in LMICs is restrictive (low forced vital capacity (FVC)) whereas in HICs the predominant abnormality is obstructive. These findings suggest that the development and natural history of non-communicable lung diseases in LMICs is different to that of high-income countries (HICs) necessitating further investigation.[15]

Emerging evidence from HICs provides some insights into the origins of asthma and COPD in Kenya and Africa and the failures to demonstrate associations between household air pollution/ biomass smoke and COPD in adults. There is a building consensus in HICs that asthma and COPD have their origins in early life, being manifestations of children developing sub-optimal lung function early in life, during vital periods of lung development, including in utero, that subsequently 'tracks' such that their lung function is sub-optimal for the rest of their lives.[17-19] It remains an unanswered question as to whether the pattern of reduced lung function so widely prevalent in African adults develops during adult life or is a manifestation of suboptimal lung function originating during childhood, tracking through adolescence into adult life, and if so at what age this is first evident. In Africa, plausible drivers of impaired childhood lung development and subsequent asthma and COPD include early life exposure to air pollution, respiratory tract infections (especially if <2 years) and low birth weight[18] and changes in risk exposure during adolescence (e.g. smoking).

2.2 Justification

The optimal study design to investigate these issues would be a longitudinal birth cohort study, however such a study would be costly and take at least 15 years to conduct. The Tupumue study is a Medical Research Council (MRC)/ Kenya National Research Fund (NRF) funded mixed methods cross-sectional study of children and adolescents aged 5-18 years in two contrasting populations in Kenya: the informal settlement Mukuru and a wealthier adjacent urban area Buruburu. The study will determine whether the observed impairments of lung function in African adults are present in African children, the age at which they are evident and whether they are associated with air pollution, low birth weight and early life respiratory tract infections. Following the study, additional funding would be sought for further follow-up and evaluation of the well-characterised children participating in Tupumue, providing potential for the current project to contribute to provision of unique longitudinal data in an African context.

The study and comparison of two contrasting communities will not only optimise our ability to identify associations with environmental exposures but will also indicate if informal settlements such as Mukuru have poorer lung health than in more affluent areas, and why.

Children and young adults aged 5 to 18 years will be studied, at 5 years of age about 75% of children can reliably perform spirometry.[20-22] Spirometry will be measured before and after 6 minutes of free running because many children with asthma have normal resting lung function;[23] this is a well described challenge test has been shown to 'reveal' asthma and to be acceptable to Kenyan children.[24] Assessment of outdoor and household air pollution will enable associations with lung function to be identified. Data on important confounders e.g. HIV and TB will be collected.

Information about birth weight, place of birth and early life respiratory tract infections will be available for many children because these data are routinely documented in the child health card provided to every Kenyan mother on the birth of a child. In recent years it has been government policy to include these data and other health record data in the electronic educational records of each child upon entering the school system.

Exposure to air pollution will be assessed using direct measurements within home settings for a sub-sample of children and a mixture of measurements made at fixed sites where children spend time (e.g. schools and other settings). Pollution exposures for all children will be modelled using these direct measurements coupled to questionnaires.

The age group 5-18 years can be a difficult to engage in studies.[25,26] To address this issue, a comprehensive programme of community engagement and sensitization will be conducted before data collection commences. The need for such a programme emerged from a series of workshops in both Mukuru and Buruburu in May 2019. The aim of these study inception workshops was to support representatives of the local communities to input into the design and conduct of the Tupumue fieldwork. A clear message throughout the workshops was that sensitisation should be widespread and accessible to local communities including the target population. It was therefore suggested that creative methods (e.g. theatre, storytelling, T-shirts, posters/banners, puppetry, games and music) would be appropriate and could be co-designed and delivered by local community artists. A community participatory approach will also be taken to dissemination of the study findings to promote engagement and to ensure that the outputs are relevant to the communities.

In order to gain a holistic insight into lung health, the lived experience of lung health and air pollution of children in the two communities will be investigated through a combination of storytelling, drawing, artefact collection, focus groups and walking interviews.

3.AIMS and OBJECTIVES

3.1 Aim

To use an interdisciplinary, collaborative, participatory approach to determine and compare the burden of non-communicable lung diseases in children living in two communities in Nairobi and to investigate the role of early life factors and air pollution.

3.2 Specific Objectives

1. To design and evaluate a Tupumue sensitization strategy designed and implemented by the communities in the two contrasting sites in Nairobi, Kenya

2. To determine and characterise the clinical characteristics and lung function of children aged 5-18 years in the two sites.
3. To determine the early life origins, and potential drivers of non-communicable lung diseases (including indoor and outdoor air pollution, birth weight, early life respiratory tract infections)
4. To estimate daily air pollution exposure which the study groups are exposed to in the two communities.
5. To explore local children's lived experiences of air pollution and lung health.

4. METHODS

4.1 Study design

This study will adopt a mixed methods design. An initial sensitisation phase will use a collaborative co-design process and qualitative methods (reflective diaries, interviews, participant observation and group discussions) to design, implement and evaluate the impact (in raising awareness of and supporting recruitment to the main study) of a creative arts-based sensitisation process. In the main study, a two-centre cross-sectional design using respiratory outcome and exposure questionnaires, spirometry and air pollution monitoring will be used in the quantitative component whereas the participatory qualitative research component will comprise recorded interviews, storytelling, drawings, artefacts, focus groups and maps to gain an insight into the experience of children in each community. Whenever available, Child Health Cards will be used to capture early life data. For both components a co-created citizen science approach is being used that involves community participants in the research design, methods, data collection and dissemination. Many of the findings of a three-day workshop held in May 2019 with the communities of Mukuru and Buruburu are included in this protocol.

4.2 Setting

The study will be conducted in two contrasting settings in Nairobi, Kenya:

(1) Mukuru slum is one of the largest informal settlements in Kenya occupying 450 acres, it stretches along the Nairobi Ngong river and is situated on waste lands in the industrial area of Nairobi. About 600,000 people live in Mukuru, poverty is almost universal, biomass is widely used for cooking. In addition to being overcrowded Mukuru is heavily polluted by the dumping and burning of household and commercial waste. There is generally poor sanitation, congestion and lack of basic amenities including inadequate access to clean water, electricity and health facilities. Mukuru is faced by myriad of health issues, but there is a paucity of data on NCDs. A large number of hospital attendees are reported to present with respiratory complaints. The Mukuru Promotion Centre (MPC) runs clinics that look after 1800 patients a month, 80% of whom have respiratory complaints.[27]

(2) Buruburu is a large middle-class residential area in the Eastlands part of Nairobi. It is a planned neighbourhood comprising of 5 phases developed in the 1970s and 1980s with finance from the commonwealth development corporation as an owner-occupier housing project consisting of 5000 three-bedroom single dwelling units. To date it remains largely owner-occupied. Some parts have however been extended for rental purposes. Buruburu is inhabited by Kenyan business people, government officials, and professionals. Although there is some burning of household waste, traffic emissions are the main source of air pollution.[28]

4.3 Participants

For the sensitisation programme around 20 Mukuru/Buruburu community members, artists, teachers and 10 Kenyan/UK researchers will attend co-creation workshops to develop a sensitisation programme that will be implemented within Murkuru/Buruburu. Up to 270 adults and children will be recruited for interviews/discussions to assess the impact of the sensitisation activities.

For the quantitative and qualitative components participants will be children and young adults aged 5-18 years of both sexes in Mukuru and Buruburu and their parents. The intention is to recruit 1300 children from each community (figure 1).

For the quantitative components initially age, sex stratified samples of >1000 in each community will be identified from 3-4 local primary schools (5-14 years) and 1-2 local secondary schools (15-18 years). To facilitate recruitment the number of classes per year group in each school to be approached will be identified. Schools will be asked to provide data on children who have left the education system in the previous four years so that these children can be incorporated into the stratified sampling process. Additional schools may be included in the sampling if required to achieve the target sample size of 1000 in each community.

For the qualitative components, three classes with children aged 5-7, 8-10 and 10-14 in participating primary schools will be approached, (these will be different to the classes approached for the quantitative component of the study). The aim will be to recruit about 300 children in each community (100 per age group), with a sub-set (n~120, 6-8 in each class) being invited to take in a focus group discussions. Additional schools/classes may be included if required to achieve the target sample size of 100 in each age group. From the 1000 children that take part in the quantitative part of the study, 20 – 30 young adults (aged 15 – 18 years) in each community will be selected to participate in walking interviews.

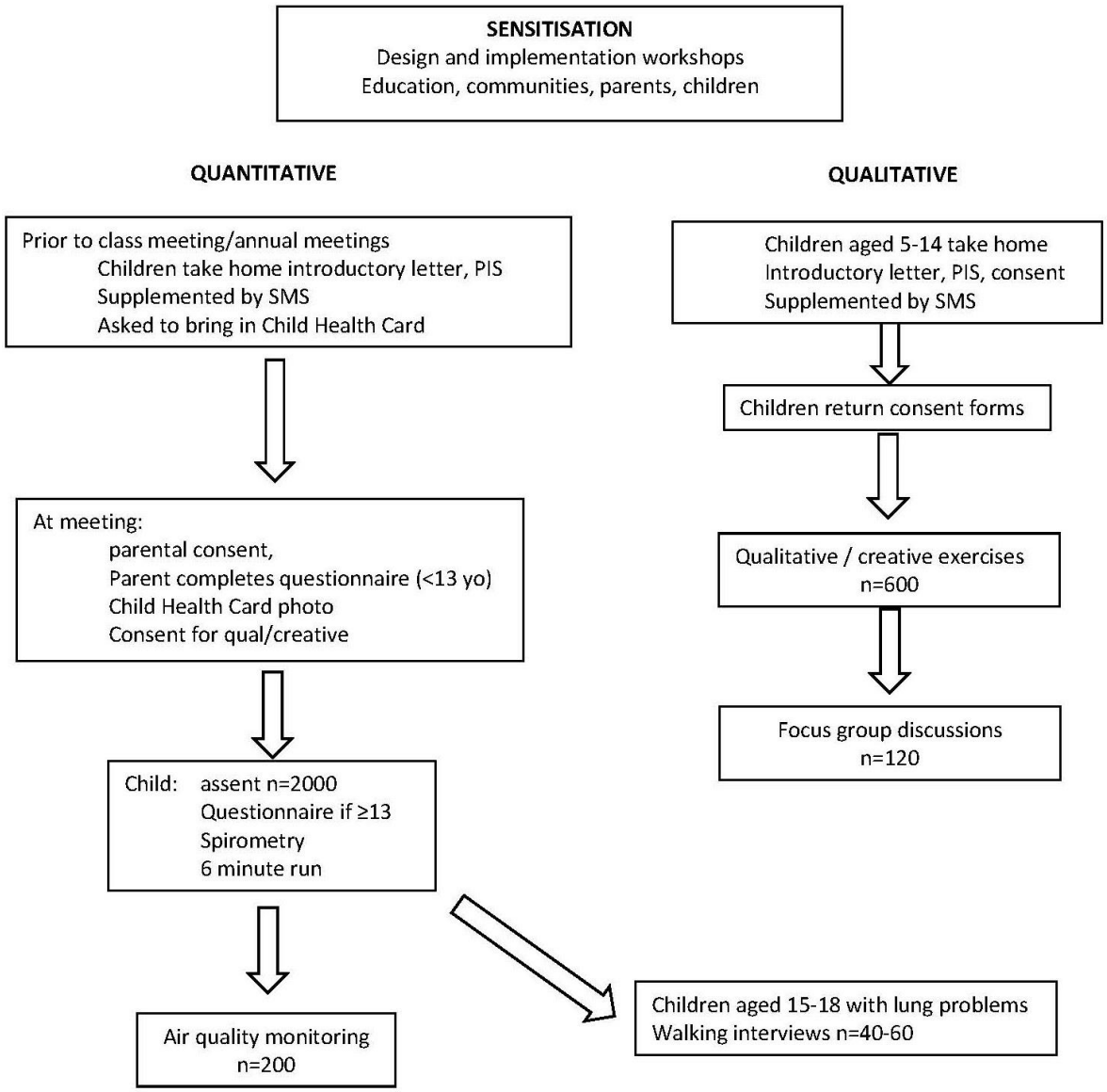

Figure 1: Outline of study

4.4 Eligibility criteria

Sensitisation: the sensitisation events will target adults and children 5-18 years who live in Mukuru and Buruburu. Parental consent and child assent will be obtained for the research components.

For the quantitative and qualitative components

4.4.1 Inclusion criteria

1. Age 5-18years.
2. Parental consent and participant assent.
3. Attending participating schools in Mukuru and Buruburu.
4. Older children resident in Mukuru/Burburu no longer attending participating schools.

4.4.2 Exclusion criteria

1. No parental consent or assent from potential participant.

2. Children in whom spirometry is contraindicated: presence of respiratory tract infection (e.g. influenza); coughing up blood; pneumothorax; aneurysm; recent thoracic, abdominal or eye surgery; nausea, vomiting; current chest or abdominal pain; current treatment for tuberculosis (TB).

4.5 Data collection and procedures

4.5.1 Recruitment

Participants for the sensitisation co-creation workshops will largely be drawn from participants in the Tupumue project inception workshops earlier this year. If needed, additional community participants will be identified through word of mouth. Researchers will be existing members of the Tupumue project team and local researchers identified by KEMRI as being integral to the conduct of the Tupumue study.

Community sensitisation activities will be held at locations identified in the co-creation workshops and may include barazas (Chiefs, elders), health clinics (community health volunteers), community-based organisations (CBOs), and faith-based organisations, as well as youth groups and local community meeting places. Sensitisation of the local education system will start from the Ministry of Education and cascade down through the head Teachers, teachers, parents and pupils.

It is likely that the actual process of recruitment to the study will differ between schools and will be decided upon after close consultation with the teaching staff and Boards of Management. Recruitment will follow the principle that parents/guardian will be informed of the study and then provide written informed consent for their child to be approached, children will only participate if they subsequently provide assent. The qualitative and quantitative components of the study will, on the whole, study different groups of children.

Wherever possible advantage will be taken of routine meetings between the school and parents/ guardian e.g. Annual General Meetings, scheduled class meetings, to inform the parents/guardian of the study and for the parents/guardian to provide consent. Wherever possible and with the support of schools, prior to these meetings children can be sent home with a letter of invitation notifying parents/guardian that at the forthcoming meeting they will be invited to consent to their child taking part in a research study, a participant information sheet (PIS) and for the quantitative component, a request to bring the Child Health Card to the meeting. In some schools it will be possible to reinforce this by bulk SMS messaging to parental mobiles.

Special efforts will be made to recruit children included in the sample who have left the school system, at age ≥14 years. Community Health Volunteers will be asked to take letters of invitation from schools and participant information sheets to the children and their parents/guardian.

4.5.2 Time compensation

Parents/guardian will be offered 500 Ksh/half day to compensate them for lost earnings in participating (attending the school to complete questionnaire). An additional 300 Ksh will be offered to those parents who are selected to take part in the air pollution measurement program and for whom two home visits will be required.

Adult participants in the sensitisation workshops will receive Ksh 1,000-3,000 per day to cover any inconvenience or loss of work time or other related expenses.

4.5.3 Consent & assent

Informed consent to participate in the study will be sought and received according to Good Clinical Practice (GCP) guidelines by an appropriately trained individual listed on a delegation log.

4.5.3.1 Sensitisation component

The sensitisation component will be led by social science and arts and humanities researchers, therefore informed consent will be required for all activities. Participants in the workshops (and parents of any under 18 years) will receive sensitisation information sheets prior to providing written informed consent. If necessary, the participant information sheet will be read out to participants/parents, and they will apply their mark witnessed by an independent person. Children taking part will be provided with age appropriate sensitisation information sheets and asked to give assent. Attendees at community sensitisation events will be informed of the presence of researchers and that participant observations will be undertaken, but that no-one will be identifiable. Those taking part in group discussions/interviews will receive sensitisation information sheets and written informed consent/assent taken as described above.

4.5.3.2 Quantitative and qualitative components

Parents/guardian of potential participating children will receive a copy of the participant information sheet prior to providing written informed consent. If necessary the participant information sheet will be read out to the parent(s) and if agreeable the parent(s) will apply their mark(s), this will be witnessed by an independent person. As part of the informed consent process, parents/guardian will be made aware of all aspects of the study, including potential risks and that their child's participation is entirely voluntary, they will be given opportunity to ask questions and to have these answered before giving consent. The documentation will be provided in English and Kiswahili. 18 year olds will be asked if they wish to provide consent instead of assent.

There will be no minimum time that parents/guardian will be given to decide whether or not to allow their child to participate in the study: parents/guardian will be given sufficient time, and as long as they themselves want, to accept or decline their child's involvement. It will be emphasised that non-participation will not detrimentally affect the parents/guardian or children in any way.

Parents/guardian of participants will be asked to consent to be approached about their child participating in the air pollution monitoring and qualitative components. They will also be asked if they would consent to receive invitations for ethically approved ancillary studies relevant to the study child, e.g. further phases of follow up.

For the quantitative component, children for whom parental consent has been provided will be introduced to the study team by their teacher(s). Children will be provided with age appropriate participant information sheets, if necessary, the participant information sheet will be read to the child. If the child expresses a wish to participate in the study they will be asked to sign/apply mark to an age appropriate assent form, if necessary, this will be witnessed by an independent person.

For the qualitative component children aged 5-14 years will be asked to complete storytelling/drawing/artefact collection exercises as part of a routine class educational activity. Researchers will only be allowed to access to the material from the children for whom parental/guardian consent has been obtained (this will prevent non-participating children from being treated differently in class to participating children). Children with parental consent will also be asked to read an age appropriate information sheet and provide assent. A sub-sample (n=6-8) from each class will be invited to take part in focus group discussions. Older children (15-18 years) who take part in quantitative

component will be invited to participate in walking interviews if they fulfil the criteria provided in 4.5.4.2.2.

4.5.4 Data collection

4.5.4.1. Community Sensitisation

Short verbal or written reflective exercises during the co-creation workshops will explore community members' ownership and confidence to implement the creative sensitisation strategies, and researchers' understandings of using creative sensitisation for research. As well as documenting attendance at sensitisation events/activities, we will use participant observation and fishbowl discussions (up to 10, each with up to 20 participants and lasting an hour) to describe changes in attendees' awareness of air pollution and lung health, and their attitudes towards the Tupumue study. Participant observation/individual interviews (N~20-30 interviews, each lasting 20-30 minutes) during sensitisation events/activities will explore children/youths' response and attitudes towards becoming Tupumue participants/citizen scientists. During the Tupumue study, structured discussions with citizen scientists (N~120) will also assess the impact of the sensitisation campaign. Finally, interviews with ~10 community/researcher workshop participants (each lasting 30-40 minutes) will assess what worked well/less well during the sensitisation campaign. Reflective exercises, discussions and interviews will be audio-recorded and detailed notes taken. These will then be written up electronically.

4.5.4.1 Quantitative data

Parents/guardian of children ≤12 years will be asked to complete questionnaires administered by field workers using an electronic tablet device, parents/guardian will also be asked to bring the Child Health Card of the study child. All participating children will be asked to undergo spirometry pre and post 6 minutes of free running. Children ≥13years of age will be asked to complete questionnaires on the electronic tablet, a field worker will be on hand to provide clarification about any questions. Subsamples of children will be asked to undertake 24-hour air quality monitoring or (for those aged 15-18) to participate in walking interviews.

4.5.4.1.1 Questionnaires

The following questionnaires will be administered by fieldworkers and entered directly into an electronic database

1. Demographics, school, date, date of birth, sex, number older/younger sibs, place of birth (Mukuru, Buruburu, number of years Mukuru, Buruburu), wealth score (0–10) based on household assets.[29]
2. The ISAAC core questions for wheezing and asthma, the Global Asthma Network core questions on trouble with breathing, management of asthma and use of health services for breathing problems, history of measles, TB, whooping cough or HIV.[30,31]
3. Environmental exposures including exposure to traffic and domestic sources of dusts, vapours and fumes, including burning of domestic waste, developed and validated as part of the MRC GCRF 'Lung health across the life course in Africa' programme.[32]
4. Household energy use questions that comprehensively explore household heating, cooking and ventilation practices.[32]
5. Cigarette smoking.[32]

4.5.4.1.2 Child Health Card

Parents/guardian will be asked to bring the Child Health Card of the study child, this will be photographed to provide data on birth weight, gestational age at birth, serial weights and any serious illnesses. Efforts will be made to retrieve information from parents/guardian who may have forgotten the child health card, e.g home visits, emailing of photos of pages.

4.5.4.1.3 Spirometry

Spirometry training, including exercise challenge testing, will take place over 7 days to include theory, practical demonstration/practice in the classroom and pilot in the field.

Spirometry will then be measured in accordance with international guidelines using the NDD EasyOne spirometer employing an on-screen incentive.[33] For all participants, the best of three technically acceptable (or usable) and repeatable efforts out of eight attempts will used for interpretation. Should less than three acceptable (or usable) tests be recorded, the best two acceptable (or usable) and repeatable efforts will be used for interpretation.

Two readers (1 internal and 1 external) will independently inspect all curves recorded for each participant in the EasyOne Connect software to ensure accuracy of precision of recorded spirometric data.

Standard operating procedures (SOPs) established in partnership with the Pan African Thoracic Society and Spirometry Training Services Africa will apply for spirometry data collection, data quality assurance and over-reading.

Spirometry will be performed pre- and post-exercise (6 minutes running). Children will be asked to run in pairs outdoors for six minutes at a jogging pace aiming to achieve a heart rate of more than 170 beats/min. Spirometry will be conducted 5 and 10 minutes after running. The highest FEV1 from at least three acceptable (or usable) and repeatable forced exhalation manoeuvres at 0, 5 and 10 minutes after exercise will be recorded.[34,35] Children with ≥15% bronchoconstriction will receive 200ug salbutamol via spacer with spirometry repeated 10 minutes later, if still evidence of >15% bronchoconstriction then a further 200ug salbutamol will be administered using a spacer with spirometry repeated 10 minutes later. In the event of persisting bronchoconstriction 80ug ipratropium will be administered by spacer device. If this fails Dr Amukoye will be available by phone or an ambulance will be called paid for by the study. The exercise test will not be conducted if FEV1 <70% predicted.[37]

Children using asthma medication will continue to take their medication, we will note if any medications have been taken in the previous 24 hours.

Height will be recorded within 0.5cm using the Frankfort positioning with a stadiometer and weight within 0.5kg with a calibrated weight scale.

4.5.4.1.4 Exposure Measures:

Our approach to the assessment of exposure to air pollution has been informed by discussions with community partners at the May 2019 project meeting. A central outcome of these discussions was the view that 24h personal exposure measurement using wearable air pollution devices was not a practical option for children within the study communities due to the potential personal safety risks.

Our revised methodology uses a combination of time-activity diary, GPS loggers and static exposure measurement in a range of 'micro-environments' to generate data that can be used to estimate 24h personal exposure to air pollution.

Drawing on the sub-set of participants who indicate on the consent form that they are happy to take part in the exposure measurement element of the study, we will identify a sub-sample of 200 children/households that are broadly representative of the wider 2000 cohort in terms of gender, age, school, household smoking, household fuel use and travel mode to school. A further subsample of 20 of these 200 will be selected for an additional time-activity study described below.

Approximately 20 children (10 from each community) will be asked to wear a GPS tracking instrument for 24h and to complete a time activity diary for this period (checked by fieldworker at interview at end). These data will be gathered once during the dry season and again once during the wet season. These diary and GPS data will enable generation of estimates for the time spent in each microenvironment by children in each of the two centres. The GPS instruments are small (size of a USB stick) and can be placed inside the children's school bag so that they are not visible during use.

The 200 participants selected for the pollution measurements will have a low-cost particle counter installed in their home for a period of 24 hours. This will involve a visit to the home by one of the research team: first to install the device and then, 24 hours later, to collect the instrument. The participating child in the home will also be asked to wear a Lascar Carbon Monoxide (CO) monitor during the time they are at home during the day of the measurement. These CO data will provide a broad indication of duration of exposure to Household Air Pollution (HAP) typically from burning solid fuel indoors and will be utilised in exploring differences in exposure by age, gender and study site.

Measurements will also be made using the Purple Air-II-SD particle monitor in the most common microenvironments where children spend time. In addition to home and school we will capture concentration data for the journey to/from school plus a selection of other indoor/outdoor settings informed by analysis of the GPS data. These measurements will either be made by a project fieldworker carrying a portable Purple Air device, or from fixed classroom and outdoor school playground sites in collaboration with the schools involved in the study. The Purple Air monitor will be compared to a 'gold standard' gravimetric method for measuring particles. This will be done to ensure that the Purple Air values are appropriately calibrated for local conditions. This will be done in microenvironments that are representative of the ones we will be measuring (e.g. outdoors, school, inside homes). The calibration work will be carried out in home settings of the study team and fieldworkers and will not be done in the participants' homes.

It is our intention to repeat measurements at both wet and dry seasons to capture seasonal variability. Further to this we aim to have four schools operate a Purple Air pollution monitor continuously for the 12 month period of 2020 to provide detail on background outdoor air pollution concentrations.

Microenvironment	Duration	N
School (indoor)	168h/ 1 week continuous data (repeated at wet and dry season)	10 (5 at each site)
Homes	24h (repeated at wet and dry season)	200 (100 at each site) – mix of fuel types; adult smoking; child age (5-11/12-17)
Travel to and from school	10-90 minutes depending on journey	20 (based on GPS data). Worn by fieldworkers walking or travelling with study participants from home to school. Mix of am/pm to/from school
Other outdoor/indoor locations	2-3h measurements representing time children spend at each setting (repeated at wet and dry season)	10 (5 at each site) At a range of locations where children spend time outside the home/school (e.g. art centre; near to football field; bike shops etc). The selection of locations will be informed by the GPS data logs
Ambient air	12 month	4 (2 schools at each site). Longer term outdoor school measurements.

* Dry seasons generally from June to October and from late-December to mid-March. Wet seasons Nov/Dec and April/May.

These measurements will provide typical microenvironment air pollution concentrations that will then be married to individual household and questionnaire data to estimate each child's exposure.

4.5.4.2 Qualitative data

4.5.4.2.1: 5-14 year-olds class work

The lived experience of lung health and air pollution of around 100 primary school children in each of 5-7, 8-10, 10-14 age groups in each community will be investigated through a combination of storytelling/artefact acquisition, visual mapping and focus groups. Schools involved in the project will be asked to select appropriate classes to either draw stories of children's lung health and air pollution or collect relevant artefacts. Children in each class will also be asked to mark on a map of the local area where their story takes place/artefact was obtained. These activities will run through normal school lesson timetables themed to relevant subject areas. Around six to eight volunteers from each class will be selected to act as citizen scientists to organise data collection (with the help of their teachers) and to analyse the data collected (with training from the Tupumue research team). They will then take part in a focus group, where experienced Tupumue qualitative researchers (who will also have analysed the data) will ask them about their findings and how these relate to their own experiences of lung health and air pollution. Focus groups will be audio recorded.

4.5.4.2.2: 15-18 year-olds walking interviews

A selection of older children (aged 15-18, n=20-30 in each community) will be selected from the 1000 children that participate in the quantitative part of the study to participate in a walking interview. Those selected will – at the quantitative consent stage – have said that they would be willing to be contacted for an interview. During the interview, they will lead an experienced Tupumue qualitative researcher around their local area, showing them areas in which they like to spend their time which they identify as

having good or poor air quality. During this walk, they will be asked open-ended questions to explore community life, their experiences of lung health, their experiences of air pollution in the community and their future aspirations. A GPS device will track their location throughout the interview, so we can map experiences to location precisely. The researcher will also wear a personal air pollution exposure monitor (Purple Air) during the interview to measure air pollution along the route. Interviews will be recorded (audio and video). Video recordings will be used by the research team to add context to the discussions and air pollution measurements – no footage that includes people will be included in any project outputs. Interviews are expected to last 45 minutes – 1 hour depending on the distances walked and the depth of discussion.

5. STATISTICAL CONSIDERATIONS

5.1 Sensitisation

Audio recordings and field notes taken during sensitisation workshops and community activities will be written up electronically, and together with any written reflections, subjected to a thematic analysis using an adapted framework approach and NVivo software to code, organise and chart the data.

5.1 Quantitative

5.1.1 Sample size and study power

In each community we will recruit 1000 children aged 5-18 allowing us, after accounting for refusals and inability to provide acceptable spirometry measurements, to estimate the prevalence of reduced lung function in the full sample with a full dataset (n ~1600) with a precision (95% CI; 90% power) of ±4.0% (assuming a prevalence of 40%).

Allowing for unequal gender distributions, refusals and inability to provide acceptable spirometry, a sample of 800 participants in one community will provide an estimate of prevalence in this community with a precision (95% CI; 81% power) of ±5.0% (again assuming a prevalence of 40%).

The representative sample of 10% of participants (n=200) invited to participate in the sub-study to gather exposure data is a pragmatic sample size based on feasibility and experience.

5.1.2 Statistical analysis plan

Lung function data will be converted to age, gender, height and ethnicity adjusted z scores using GLI2012.[38] Reduced lung function will be defined as less than lower limit of normal LLN. All measures will be subject to comprehensive numeric and graphical descriptive analysis. Symptoms and lung function outcome prevalence (95% confidence intervals) will be estimated for the full data set and for pre-specified strata (site, gender, age). Univariable and multivariable analyses will compare lung function outcomes in Mukuru and Buruburu and investigate associations with symptoms, air pollution, birth weight, early life respiratory tract infections s with adjustment for potential confounding factors. Sensitivity analyses will use continuous lung function outcomes in linear and quantile multivariable regression models. Continuous covariates such as age and air pollution measures that may have non-linear associations with lung function outcomes will be evaluated in sensitivity analyses utilising natural B-splines and/or generalised additive models. All models will be evaluated for appropriateness related to statistical assumptions.

Linear multivariable regression models attain 95% power to estimate an association explaining 5% of overall variance with a total sample size of 176 in a model with no more than 8 predictors that account for less than 50% of the total variance. Logistic multivariable regression models attain that same power

at a total sample size of 674, to estimate an odds ratio not smaller than 1.5. With an expected sample size of 1600, we have sufficient power to demonstrate small- to moderate effect sizes depending on the choice of model and stratum. Sensitivity analyses and exploratory modelling will be presented as such. Correction for multiple testing will be applied as required by the method of Benjamini and Hochberg.[39]

5.1.3 Missing data

Analyses will be carried out on complete case data if the proportion of missing data is small (<3%), else multiple imputation will be utilised to generate complete data sets and will be presented as the primary analysis. Complete case analysis will then be presented as a sensitivity analysis.

5.2 Qualitative

The sample sizes for the qualitative components are informed by similar work conducted by members of the project team in schools in Mukuru, where 150 children were recruited across three classes for an air pollution storytelling exercise. The slightly lower estimate in the current study, allows for the drawings of children without parental consent to be excluded.

The children's stories/drawings/collected artefacts will be subjected to a content analysis to produce a quantitative summary of ways in which lung health and air pollution are represented.[40,41] Audio recordings of the focus groups and walking interviews will be transcribed into English and analysed thematically using a framework approach and NVivo software to code, organise and chart the data.[42] The qualitative research team will read a subset of transcripts independently before meeting to determine a common coding scheme. The full datasets will then be coded by experienced qualitative researchers, with double coding of representative samples to ensure data fidelity. The videos of the walking interviews will be used by the research team to support data analysis by providing context to discussions. As part of our citizen science approach, we will form groups of local people (including children) within the communities where the studies are taking place to help finalise the core focus group and walking interview topic guides and aid interpretation of our emerging findings in relation to the local context. Children's personal experiences of lung health and air pollution within Mukuru and Buruburu will be compared, and spatial information (including air pollution) mapped to identify what and where the children see as sources of lung health issues in their area.

6. ETHICAL AND REGULATORY CONSIDERATIONS

All study staff and investigators will be appropriately trained and will conduct the study in accordance with the principles of Good Clinical Practice (GCP). Internal quality control monitoring will be conducted to ensure: understanding of protocol and standard operating procedures, protocol and Good Clinical Practice compliance and source document verification. Written informed consent will be obtained from parents/guardian and wherever possible assent from the children will be obtained, the age of majority in Kenya is 18 years.

6.1 Ethical Review

Favourable ethical opinions will be obtained from LSTM Research Ethics Committee and Kenya Medical Research Institute Scientific and Ethics Review Unit prior to commencement of the study. If necessary approvals will be obtained from the Kenyan Ministry of Education and School Boards of Management.

Amendments to the protocol must be submitted in writing to the appropriate REC and will not be implemented until the REC grants a favourable opinion. Amendments to other documentation will not be implemented until appropriate approvals are in place.

6.2 Participant safety

The investigations proposed are considered safe and have been used widely in epidemiological studies of children.

Spirometry occasionally results in symptoms typical of hyperventilation, if these occur, spirometry will be stopped, the child will be sat down and allowed to recover.

Children with ≥15% reduction in FEV1 after 6 minutes of exercise will receive 200ug salbutamol via spacer and only allowed back to class when FEV1 within 5% of the baseline. Salbutamol is an extremely safe widely used inhaled medication, potential side effects are short term (<4 hours) and mild e.g. tremor, headache.

The potential risks to the children participating in the exposure monitoring components of the study have been mitigated by the choice of monitoring equipment used, after extensive discussion with the communities and the implementation of a wide ranging programme of sensitisation in both communities that will sensitise the education system, the communities and parents/children.

The protocol for the walking interviews will be refined through discussion with community members, and if making a video recording is considered unsafe, only audio recording will be used. To reduce any safety risks relating to collecting personal exposure measurements, the research assistant will monitor air pollution exposure along the route while wearing a rucksack that contains the instrument. Again, if through discussion with community members this is deemed unsafe, this part of the walking interviews will not be undertaken.

Data from children identified as possibly having respiratory diseases not already under follow-up, symptomatic on questionnaire and positive exercise test (>15% reduction in FEV1 upon exercise) will be reviewed by Dr Evans Amukoye, a consultant paediatrician, who will inform the parents/guardian and arrange onward referral, if needed, to local (free to access) health services.

6.3 Peer review

This study has undergone internal and external peer review as part of the funding process.

All reports of work arising from Tupumue including conference abstracts should be peer reviewed by the Project Management Group prior to submission.

6.4 Public and Patient Involvement

A Community Advisory Board will be established and comprise stakeholders from the Ministry of Education, Ministry of Health, schools, parents, community workers. Local artists and community members will lead community sensitisation events, which will empower local children/youth, parents and teachers to become fully informed participants in the main Tupumue study. A citizen science approach will be adopted in the school classroom drawing, storytelling and artefact collection activities, with ~6-8 children in each class leading data collection and analysis before feeding back to the research team as part of the focus group discussions.

6.5 Intellectual Property

Intellectual property (IP) generated by community collaborators will remain with the individuals who generate the IP subject only to the generation of IP that may result in a patented output. In this case the consortium will seek to enter into an IP agreement with the community collaborators to the effect that should any financial benefit be generated through exploitation of patentable project outputs then the community will be eligible for a fair and equitable share in the benefits. Any copyright and trademarks arising from the co-created methods chosen for the sensitisation events (such as copyright in photo stories; videos; songs) the IP will reside wholly with the community creator(s) who may exploit the outcomes as they wish subject only to attributing the project. The Tupumue project will seek a CC-BY (Creative Commons Attribution Only) licence from the owners of this intellectual property for the right to use the works for any purposes connected to Tupumue, the research and dissemination of outcomes. The project will obtain agreement to use the copyright outputs for research reports, presentations, websites and other outputs for non-commercial purposes.

6.6 Indemnity

LSTM holds and maintains insurance policies, which will provide appropriate compensation.

6.7 Data

All Investigators and study site staff involved with this study must comply with the requirements of the General Data Protection Regulation (or subsequent legislation), with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. All study staff and investigators will protect the rights of the study's participants to confidentiality and will have received formal Good Clinical Practice (GCP) training prior to study initiation. LSTM and KEMRI Ethics Committee approved processes will be followed throughout.

6.7.1 Managing, storing and curating data.

Hard copies with participant identifiable data, e.g. consent forms will be stored in KEMRI in locked filing cabinets in secure premises. Access to these data will be restricted to local investigators with a duty of confidentiality.

All electronically stored data will be in a will be in a linked-anonymised form, any transmitted data will be in a linked-anonymised form. Consent will be obtained to store and process data. Electronic fieldnotes from the sensitisation activities and audio transcriptions of interviews will be anonymised and stored. Audio recordings will be deleted after transcription. Drawings or other physical outputs produced by participants or community members will be photographed and the physical artefacts and images stored without identifying data unless the creator specifically requests that they be credited in any outputs.

Published results will not contain any personal data that could allow identification of individual participants.

Data will be captured electronically and stored on a password protected central study computer at Kenya Medical Research Institute (KEMRI) and backed-up on a secure off-site server. KEMRI data management will be responsible for managing and curating the collected data. Data will be collated into a study database, and into an analysis dataset using the appropriate software tools. The analysis dataset will be used as the source for statistical analysis and reporting.

7. WORKPLAN

ACTIVITY	**DURATION**
Proposal Development/Ethical Approval	January 2019 to November 2019
Staff Recruitment	August 2019 to October 2019
Training Study Staff	November 2019 to December 2019
Sensitisation Activities	December 2019 to August 2020
Data Collection	January 2020 to December 2020
Data Analysis/Dissemination	January 2021 to December 2021

8. **BUDGET**

	In Kenyan Shillings	**In UK Pounds**	**Budget Justification**
Kenya funding	32,322,720	238,203	
UK funding	65,235,913	476,693	
Total funding	97,558,633	714,896	

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