Association between environmental exposure to pesticides and prevalence of asthma symptoms in rural children and adolescents living in agricultural settings in the Western Cape.

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PREFACE

Plagiarism Declaration

I, Eunice Muya Tshilengu, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements 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.

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Abstract

Background: There is conflicting evidence on the association between pesticide exposure and child asthma related outcomes in agricultural settings and limited data in developing country settings.

Objectives: This study investigated the association between children's exposure to pesticides and asthma related outcomes in rural agricultural areas in Western Cape South Africa.

Methods: A cross-sectional study of 700 children from three intensive agricultural areas in the rural Western Cape in June-September 2017. Guardian reported asthma outcomes and demographic information using an abbreviated version of the International Study of Asthma and Allergies in Childhood questionnaire and self-reported pesticide exposures of children was obtained.

Results: The median age of children was 11 years. The prevalence of more than two reported asthma symptoms (current wheeze, wheeze attack, wheeze disturbing sleep, wheeze limiting speech and wheeze during exercise) was 8.5% across the sample. There were no statistically significant positive associations found between any of the three asthma related outcomes (including asthma symptoms score ≥ 2, parental reported asthma and current wheeze) and pesticide exposure variables. These included general pesticide exposure, farm activities, leisure activities and household pesticide exposure when adjusting for relevant confounders using multiple logistic regression analysis.

Conclusion: This cross-sectional study did not find evidence of an association between self-reported asthma related outcomes and pesticide exposure among rural children of the Western Cape. Longitudinal studies investigating the association using robust exposure and outcome measures are recommended.

Abbreviations

BMI	Body Mass Index
CI	Confidence Interval
DAG	Directed Acyclic Graph.
DDE	Dichlorodiphenyldichloroethylene
FENO	Fractional Exhaled Nitric Oxide
ISAAC	International Study of Asthma and Allergies in Childhood
IQR	Interquartal Range
LTE4	Leukotriene E4
OR	Odds Ratio
PPE	Personal Protective Equipment

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PART A: RESEARCH PROTOCOL

1.Literature review

1.1 Introduction

Pesticides are used primarily as a tool to kill pests and to protect produce in various agricultural sectors. They are also used as a public health tool to protect human health by eliminating vectors responsible for disease outbreak (Tarmure *et al.*, 2020). Hence, their usage in many countries around the world including South Africa, which is among the four largest importers of pesticides in the Sub-Saharan Africa with over 3000 pesticides products including 700 pesticides used for agricultural purposes (Curchod et *al*., 2020).

The agricultural sector plays an important role in South Africa, particularly in the Western Cape that contains 1.9 million of agricultural land with 70 000 households depending on it. In the recent years, the Western Cape has experienced a serious shortage of water from 2016 to 2018. This situation, resulting from the climate change crisis, had an impact on the pesticide usage level because it altered the vectors resistance to pesticides leading to a greater demand of pesticides (Curchod et *al*., 2020).

In the Western Cape, pesticides residues have been detected in food products, surface water, ground water and biological samples among rural populations (Molomo *et al.*, 2021a). Recent studies in the rural Western Cape have found agricultural pesticides in water resources above water quality standards as ("Imidacloprid, thiacloprid, chlorpyrifos and acetamiprid, terbuthylazine") and in ambient air ("Atrazine, carbaryl, chlorpyrifos or malathion"), (Fuhrimann *et al.*, 2020a).

Pesticides have been associated with several acute and chronic health effects in humans. These include neurotoxic effects, reproductive health effects, cardiovascular effects, renal effects, cancer as well respiratory effects such as asthma (Chetty-Mhlanga et *al.,* 2021, English et al, 2014, Tarmure *et al.*, 2020).

1.2 Pesticides and Asthma

Asthma is a persistent inflammatory respiratory condition characterized by bronchoconstriction, excessive mucus production, inflammation of the airways, and heightened airway responsiveness, leading to difficulties in breathing. It is the most widespread chronic non-communicable disease prevalent in children characterised by expiratory air-flow limitation and airway reversibility (Shaffo *et al.*, 2018).

According to Masekela et al (2018), South Africa has a very high rate of asthma related deaths, and it is assumed that asthma is under diagnosed and not well treated in developing countries. For example, many diagnoses are performed using questionnaires and blood tests which can reduce the reliability of the measurements. This theory suggests that asthma deaths can be higher than those reported.

Childhood asthma is the most common chronic disease among children, ranking among the top 20 conditions worldwide for disability adjusted life years in children and is characterised by issues of underdiagnosis and undertreatment in different countries. There are about a 13-fold variation of asthma symptoms in children in different countries. The cases of asthma are rising in hospitals which indicates mismanagement and poor treatment of the disease. Childhood asthma is a burden to the health care services and there is an approximately 0 to 0.7 per 100 000 death rates of asthma in children (Serebrisky et al., 2019). It affects the development of children by depriving them from attending school, affecting the child's health, and depriving them from taking part in social activities, especially in under-developed countries.

Pesticides have the capacity to increase a person's susceptibility to allergens by altering the bronchial lining through irritation, inflammation, or immune suppression (Tarmure *et al.*, 2020). For instance, organophosphate and carbamate pesticides inhibit cholinesterase activity resulting in the building up of acetylcholine, the chief neurotransmitter of the parasympathetic nervous system. The reduction of cholinesterase activity in the nervous system is associated with several symptoms such as nausea, vomiting, diarrhoea and with asthma-like symptoms such as wheezing and difficulty in breathing (Tarmure *et al.*, 2020).

Exposure to pesticides can also exacerbate asthma and trigger asthma attacks by increasing hypersensitivity of the exposed. Pesticides can cause respiratory effects among exposed populations due their small size (0.001µ.m) (Tarmure *et al.*, 2020).

Addressing childhood asthma aligns with the 2030 Sustainable Development Goal 3, which emphasizes ensuring healthy lives and well-being for all. This encompasses various health priorities such as reproductive, maternal, newborn, child, and adolescent health, as well as communicable and non-communicable diseases (UNICEF, 2024). The Goal 3.9.1 specifically targets assessing major health risks arising from exposure to outdoor and indoor air pollution, particularly from the use of polluting fuels for cooking. The pollutants emitted from industrial activities, households, and vehicles constitute a complex mixture that poses significant health

risks, with fine particulate matter being particularly detrimental. Polluting fuels include wood, coal, animal dung, charcoal, crop wastes, and kerosene (UNICEF, 2024).

1.3 Pesticide exposure among rural children

In South Africa, many children in rural areas live in poorly structured houses with poor ventilation, poor indoor air quality, and mostly overcrowded with lack of basic hygiene services as water and sanitation (Tolosana et al. 2009). It is common for children living in rural areas to inhale pesticides drifts while being at home or playing close to their houses. Additionally, children are provided with beddings covered with bed nets, exposing them to more pesticide's residue (Tolosana et al. 2009). Those whose parents, guardians or siblings work on a farm or other parts of an agricultural setting, are exposed to pesticides because those guardians can bring home their personal protective equipment's that has been sprayed with pesticides (Tolosana et al., 2009) . Exposure also occurs when children are involved in activities on the farms as picking fruits, cleaning farm utensils, helping with pesticide storage, burning of pesticides containers, and assist in spraying pesticides (Chetty-Mhlanga *et al.*, 2021a).

Inhalation of pesticide drift can occur when children assist with spraying activities (Chetty-Mhlanga *et al.*, 2021a). Many children also eat fruits or vegetables that were sprayed on and not properly washed. Children have a large oral intake of food per unit of height and weight than adults. Also, the licking of unwashed hands can cause them to ingest particles containing pesticides (Chetty-Mhlanga *et al.*, 2021a).

Children's exposure via ingestion also occurs when they are infants and breastfeeding from a mother who has been exposed to pesticides (Chetty-Mhlanga et *al*., 2018). There is also evidence that the mothers' exposure to pesticides can also be and transmitted to children in -utero or via breastfeeding. For instance, Mora et al (2020) has shown identified an association between pesticide exposure and high urinary ethylenethiourea concentrations, carbamate metabolite, during the first half of pregnancy and increased lower respiratory tract infections in infants (Odds ratio, OR = 2.45; 95% CI: 0.96, 6.26).

Dermal contact is also an important route of exposure because of the children's "hand to mouth" activities. Rural children commonly play near agricultural areas contaminated by pesticides through runoffs (Molomo *et al.*, 2021a). Children's involvement in farming activities can also lead to dermal exposure.

1.4 Review of previous epidemiological studies investigating the effect of pesticide exposure on children's respiratory health.

A systematic review of previous epidemiological studies investigating respiratory health associated with non-occupational pesticide exposure among children and adults was conducted by Mamane et al (2015a). The review identified 20 studies that included 14 on children and 6 on children all published before 2013. Out of the 14 children's studies, Seven studies investigated pre-natal pesticide exposure conducted in four countries (Canada, three in Spain, United States of America (USA) and Sweden) and 7Seven on post-natal exposure (three in the USA, one in the United Kingdom, two in Germany and one in Lebanon).

Among the six studies on adults' exposure, one study assessed pesticide exposure by using biomarkers; three studies assessed household proximity to fields or spraying areas; one study assessed pesticide exposure was by questionnaires; and in the remaining study, the exposure instrument was not clearly documented. Among the adult studies, 4 were conducted in the USA, 1 in China and 1 in Singapore.

This review found evidence of an association between pre-natal exposure to dichlorodiphenyldichloroethylene (DDE) and respiratory outcome such as asthma and wheezing among children. It was concluded that prenatal exposure to DDE can contribute to the development of childhood asthma but there is a protective effect of breastfeeding on from asthma. This information is relevant for children aged 3-6 months after birth and 7-10 years.

Overall, the evidence on the effect of current use pesticides and respiratory outcomes was limited. Seven of the studies on current use pesticides were cross-sectional in design and did not identify the specific pesticide nor provided information on the nature of pesticides to which the subjects were exposed to. For studies that provided such information, there was no detail on the frequency, duration, and intensity of exposure to pesticides. No study conducted in Africa was identified.

A literature review was conducted on the effect of exposure to current use pesticides on respiratory health outcome among children in studies published after the period of 2013 to the current year, 2021.

1.4 Search strategy

This systematic review focused on studies conducted between the years 2014 and 2021 after the review by (Mamane *et al.,* 2015a). The search was conducted using Pubmed and the

University of Cape Town's library. The following key words were used following the PECOT method: ("Pesticides") AND ("Asthma") AND ("child") and ("Pesticides" OR "Organophosphate" OR "Pyrethroid" OR "Herbicide" OR "Insecticide") AND (" Asthma" OR "Cough" OR "Wheeze" OR "Wheeze") AND ("Children" OR "Child") and ("Pesticides" OR "Organophosphate" OR "Pyrethroid" OR "Herbicide" OR "Insecticide") AND UCT library with the following key words: (" Asthma" OR "Cough" OR "Wheeze" OR "Wheeze") AND ("Children" OR "Child") AND ("Agricultural area "OR "Rural area").

With this search strategy, 103 studies were identified. After screening the titles and abstracts, 18 articles were identified. Further screening of the full length of the 18 articles, studies investigating DDT, those investigating adults and those conducted in settings other than agricultural were excluded and 8 studies were included in the review.

1.5 Summary of studies

Table 1 summarises previous epidemiological studies that investigated the effect of exposure to current used pesticides and child asthma outcomes since 2013.

In total, eights (8) studies conducted in four countries including the United States of America (California), France, Niger, and Sri Lanka were reviewed. All the studies were cross-sectional. Two of the studies investigated exposure to organophosphate pesticides using urinary DAP metabolites, one study each investigated exposure to elementary sulfur and phthalimides and dithiocarbamate fungicides, and 4 studies did not specify any pesticide.

Three studies used biomonitoring by measuring urinary levels of pesticides as an exposure measure and or pesticides in air as an exposure measure while the other five other studies used self-reported exposure or proximity to spray as an exposure measure. One study used urinary LTE4, 4 used lung function and six studies used respiratory outcomes as outcome measures.

A statistically significant association was found on adverse asthma outcomes in both studies investigating OP exposure via DAP metabolites, one on urinary LTE4, a marker of asthma exacerbation (Bukalasa *et al.*, 2018), and the other study on self-reported asthma symptoms (Raanan *et al.*, 2015a) . Increased application of elementary sulphur near children's residences was found to be significantly associated with an increased self-reported respiratory symptoms and decreased lung function in one study (Raanan *et al.*, no date). Two studies also found significantly higher prevalence of self-reported respiratory symptoms in an agricultural area compared to a non-agricultural area (Mamane et al., 2015b; Kudagammana et al., 2018a).

The other three studies did not find any association between the exposure and outcome of interest investigated. These studies examined various aspects such as the correlation between urinary ETU levels (a marker for exposure to certain fungicides) and pesticides in the air with children's respiratory symptoms and lung function (Reherison *et al*., 2018), the link between proximity to pesticide spraying and asthma symptoms (Bukalasa *et al*., 2018), and the relationship between proximity to pesticide use and lung function (Gunier *et al*., 2018).

The limitations in the studies include a small sample size, self-reported exposure and outcome measures, and lack of longitudinal data from cohort studies.

1.6 Areas for future research

The research gaps in the literature therefore include the limited number of studies especially for different types of pesticide types with no studies conducted in South Africa. There is no longitudinal data. More studies using pesticide bio-monitoring and objective outcome measures are required.

Table 1 Epidemiological studies investigating the effect of pesticide exposure in children on respiratory health.

Author (Year)	Study Population	Exposure assessment	Pesticide of interest	Health outcome measurement	Results	Limitations.
(Benka-Coker *et al.*, 2020a) *"Association of Organophosphate Pesticide Exposure and a Marker of Asthma Morbidity in an Agricultural Community Wande."*	Children (6 – 16) years, Washington State in the United States of America. **Study Sample**: 16. **Study design**: Cross-sectional study, resample of cohort study (AFARE).	Six metabolites of dialkylphosphates (DAPs) were assessed in participants by considering the limit of detection (LOD) for each specific DAP compound. This evaluation was conducted using spot urine samples to measure pesticide exposure.	Organophosphates.	Asthma exacerbation through spot urinary leukotriene E4 (LTE4)	Increased exposure to DAP was associated with increased risk of asthma morbidity. Interquartile (IQR) increase in urinary DAPs was associated with increases in urinary LTE4. (βEDE: 9.3 (95%CI: 1.7, 16.9); βEDM: 0.9 (0.3, 1.6); βEDAP: 3.9 (−0.1, 7.9).	Urine samples for exposure and outcome collected only at 6am. DAP not pesticide specific. Sample size was very small: 16 children selected.
(Raherison *et al.*, 2018) *"Pesticides Exposure by Air in Vineyard Rural Area and Respiratory Health in Children: A pilot study."*	Children (3–10 years old) from a French vineyard in rural area. **Study Sample**: 4 schools. **Study design**: Cross-sectional study.	Air monitoring involved the continuous measurement of pesticides in the outdoor air through mobile stations positioned in proximity to schools. Biological measurements included the adjustment of fungicide groups (phthalimides and dithiocarbamates) for creatinine levels. Additionally, urinary ETU levels were assessed.	Phthalimides and Dithiocarbamates	ISAAC questionnaire symptom score (0-18). Spirometry measured before and after the exercise in children over 6 years old.	No association was found between exposure to pesticides in the air and lung function, as indicated by an odds ratio (OR) of 0.73 with a 95% confidence interval of 0.20–2.72 (p=0.73). Similarly, there was no observed association between urine ETU levels and lung function, with an odds ratio of 1.52 and a 95% confidence interval of 0.24–9.55 (p=0.89).	Use of ETU: nonspecific detection of pesticides. Sample size reduced. No data provided on the selection of pesticide exposure.

(Mamane, J. F. Tessier, *et al.*, 2016) *"Increase in the Risk of Respiratory Disorders in Adults and Children Related to Crop-Growing in Niger".*	Study conducted in Niger, a desert area characterized by pastoral activity and minimal pesticide use on the limited crops cultivated, and another region benefiting from a subtropical climate conducive to crop cultivation. Age range: 7 or more. Study Sample: 471 adults and 229 children. Study design: Cross-sectional study.	Self-reported usage by study population.		The ISAAC questionnaire for adults and children confirmed by a health professional.	Children residing in the agricultural region had an elevated risk of experiencing cough without fever, with an odds ratio of 3.34 and a 95% confidence interval ranging from 1.67 to 6.66 ($p = 0.0006$).	Exposure to pesticides not assessed. Risk of selection bias between two study groups.
(Raanan *et al.*, no date) *"Elemental Sulfur Use and Associations with Pediatric Lung Function and Respiratory Symptoms in an Agricultural Community (California, USA)."*	Seven years old children living in the Salinas Valley, California. **Study design**: Cross-sectional study	Application of sulfur in agriculture in proximity to each child's dwelling calculated utilizing a Geographic Information System (GIS), with buffer radii set at 0.5, 1, and 3 km. The assessment also considered the time duration leading up to the 7-year visit, specifically 1 week, 1 month, and 12 months before the scheduled visit. Additionally, DAP metabolites were examined in the study.	Elemental Sulfur.	Maternal reports of child respiratory symptoms at age 7. International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and spirometry.	Increased respiratory outcomes associated with increased Sulfur applications indicated by the adjusted odds ratio (aOR) for respiratory symptoms, which was 1.71 with a 95% confidence interval ranging from 1.14 to 2.57.	Identification of asthmatic children based on mothers' reports can include possible recall bias. Exposure assessment using GIS can lead to possible selection bias.
(Kudagammana and Mohotti, 2018a)	The study population were children of 1 – 5	Proximity to the estate study areas.	Agrochemicals	Use of adapted ISAAC self-	Children residing in the organic estate (Haputale)	Exposure assessed according to the area

"Environmental exposure to agrochemicals and allergic diseases in preschool children in high grown tea plantations of Sri Lanka."	years conducted in Idalgashinna Bio tea project in Haputale and St Coombs estate Thalawakelle, Study conducted as a survey. Sample size: 347. Study design: Cross sectional study.		administered questionnaire, Clinical evaluation to assess childhood wheezing, eczema and allergic rhinitis.	exhibited a reduced occurrence of wheezing in comparison to their counterparts in the conventional estate (Thalawakelle), with a significance level of P<0.000. Conversely, the Thalawakelle children demonstrated a notably higher prevalence of allergic conditions, with a significance level of p< 0.0001.	children were living in. Outcome assessed by showing videos of what asthma symptoms look like. This can be source of selection bias.
(Bukalasa *et al.*, 2018) *"Associations of residential exposure to agricultural pesticides with asthma prevalence in adolescence: The PIAMA birth cohort*."	Adolescents 14 years of age. **Study sample**: 1473. **Study design**: Cross-sectional study with a prospective cohort study (PIAMA).	Selected crops area within 50, 100, 500 and 1000m of the participants' home. Crops selected based on likelihood of treatment with pesticides and being present for the least 10% of the study participants in the 1000m buffer.	Adapted ISAAC Questionnaires	No increased risk of asthma or related symptoms revealed in the crude and adjusted associations of respiratory symptoms: 0.31 (0.07, 1.32) 0.36 (0.09, 1.55) Shortness of breath: 0.61 (0.23, 1.57) 0.71 (0.27, 1.85) Dry cough. 1.26 (0.56, 2.80) 1.45 (0.65, 3.22) No associations were identified between the prevalence of asthma, shortness of breath, and dry night cough on one hand, and the existence of any crops within 500 and 1000 meters of the participants' residences on the other hand. Asthma 0.31 (0.07, 1.32), Shortness of breath: 0.61 (0.23, 1.57) and Dry cough: 1.26 (0.56, 2.80).	Pesticides selected based on assumption and not data. Small sample size Buffer estimates for exposure limits not followed.

				No correlations detected concerning the prevalence of asthma, shortness of breath, and nocturnal dry cough among the participants: 0.88 (0.54, 1.44 Shortness of breath: 1.13 (0.73, 1.74 Dry cough: 1.08 (0.66, 1.76).	
(Raanan *et al.*, 2015a) *"Early-life Exposure to Organophosphate Pesticides and Pediatric Respiratory Symptoms in the CHAMACOS Cohort."*	Children (1 – 7) years from agricultural community In California. **Study Sample**: 359 mothers and children. **Stude design**: Cross-sectional from longitudinal cohort study (CHAMOS).	Organophosphate pesticide exposure urine sample: Six nonspecific DAP metabolites.		Respiratory reports ISAAC questionnaires Maternal Report on child's prescription of asthma medication.	Concentrations of total DAPs, DEs, and DMs significantly associated with reported respiratory symptoms and exercise-induced coughing at 5 and 7 years of age (tDAPs, aOR for a 10-fold increase in concentration = 2.53; 95% CI: 1.32, 4.86, p = 0.005 for symptoms; aOR = 5.40; 95% CI: 2.10, 13.91, p < 0.001, for coughing). No significant association between the total average of DAPs and DM urinary concentrations with the reported respiratory symptoms. No correlation between increased odds of respiratory symptoms and Higher prenatal DE concentrations [adjusted odds ratio (aOR) for a 10-fold increase in	Urine samples not collected at 7 years of study participants. Respiratory outcome assessed based on mother report: child was included as having respiratory symptoms if the mother reported use of asthma controller or rescue medications, even in the absence of the above symptoms.

					concen- tration = 1.44; 95% confidence interval (CI): 0.98, 2.12, p = 0.07]	
(Gunier *et al.*, 2018a) *"Residential Proximity to Agricultural Fumigant Use and Respiratory Health in 7-year-Old Children."*	Children of 7 years old from the agricultural Salinas Valley, California **Study Sample**: 294 children. **Study design**: Cross-sectional study design from cohort study (CHAMOS).	Prenatal estimates of proximity to fumigant residence using a GIS based on child residential location and Pesticide Use Report (PUR) data.	Fumigants	FEV1, FVC and FEF25-75 measurements.	No associations found between fumigant use within 8 km of residences and lung function FEV1 (β=0.06; 95% CI: 0.0, 0.12; p=0.05) and FEF25-75 (β=0.15; 95% CI: 0.03, 0.27; p=0.01). No associations noted between the utilization of postnatal fumigants at any distance and measurements of lung function. Similarly, there were no observed associations between the use of fumigants in the year preceding the assessment and lung function measurements.	Exposure assessment suggested to recall bias. Pesticide exposure evaluation can be biased. FEV not suitable for toddlers are they have difficulty to exhale and inhale. Information on Pesticide exposure and asthma outcome was not obtained for all participants.

1.7 Significance and relevance

Pesticides are used worldwide and in South Africa for vector control, crop protection and disease prevention. However, these substances have been associated with adverse health effects on exposed populations.

Data on childhood asthma, a significant contributor to the global burden of disease, is limited in African settings despite high potential exposures in these settings especially among children.

2 Research aims and objectives.

The aim of this study is to investigate the association between children's exposure to pesticides and asthma-related outcomes in rural Western Cape in South Africa

The objectives are:

- To describe the demographics and, socio-economic factors and co-exposures among the study population.
- To determine the pesticide exposures among the participants
- To report the prevalence of asthma-related outcomes in the study population
- To assess the association between pesticide exposure and asthma-related outcomes controlling for confounding.

3. Research question

Is there an association between exposure to pesticides and asthma-related outcomes among children and adolescent living in and near agricultural settings in the Western Cape?

4. Hypothesis

Exposure to pesticide among children living in and near agricultural settings is associated with increased risk of asthma-related symptoms.

5. Methods

5.1 Study population and design

This study is a cross-sectional study that was part of a longitudinal cohort study of 1002 school children aged 9 -18 years. This study aimed to investigate the adverse reproductive health and neurobehavioral effects of pesticide exposure in children and adolescent boys and girls living in rural areas of the Western Cape. The baseline measurements on children were conducted at six schools in 2017 and the follow-up in 2019. During this period, caregivers were also interviewed at homes. This current sub-study includes 680 school children who participated in the baseline study and whose caregivers were interviewed. The data for this study includes exposure data collected in the child questionnaire (APPENDIX 2: Participant questionnaire) and the child asthma-related outcomes and other data in the caregiver's questionnaire (APPENDIX 2: Participant questionnaire).

The study areas included: The Hex River Valley (grape farming), Grabow (apple farming) and Piketberg (wheat and fruit). These areas were selected according to three characteristics (Chetty-Mhlanga *et al.*, 2018a): the large number of agricultural activities present requiring the use of high volume of pesticides, the usage of pesticides that were once detected in the environment, and evidence of pesticide metabolites detected in workers on the farm and people living around those areas.

5.2 Sampling

Schools in the three study areas was the sampling frame in the main study. To avoid a loss to follow-up due to children leaving high school, only primary, intermediate, and combined schools were approached (n = 32). Seven schools agreed to participate after contacting the principals and governing bodies of the schools (APPENDIX 5: Permission letter to school principal and board). The parents or guardians of all school children in grades two to nine were sent information sheets about the research and the role of the school, along with permission letters (APPENDIX 5: Permission letter to school principal and board).

All parents or guardians that responded positively to the study invitation were visited at their homes to obtain consent (APPENDIX 6: Caregiver consent form). Participants were then selected to obtain an approximate equal number of children by area, age, sex, those living on farms and those in the nearby town. Stratified random sampling was used to select the children where the

number of consenting parents or guardians exceeded the number of children targeted for a particular category.

5.3 Sample size calculation

A two sample-test for proportions was used comparing participants in 2 groups with study power of 80% and a 95% Confidence Interval. The study by Mamane et al., (2016) reports that the frequency of wheezing in children exposed to pesticides in agricultural area (32.0%) was higher than those exposed in residential setting (12.0%). Using these variables and a sample size of 600 children, we could estimate that a minimum sample power of 90% could be achieved with a significance level of 0.05.

5.4 Study Instruments

5.4.1 Participant and Parent Questionnaire

The participant questionnaire (APPENDIX 2: Participant questionnaire) was administered to school children during the baseline study on the school premises by trained interviewers using the Open Data Kit software uploaded on cellular phones. The parents were likewise interviewed at their homes, the interview information was captured onto the phones from where it was uploaded onto a server. Interviews were conducted in the interviewees language of preference and translated back to English. The questionnaires were based on those used previously among these communities. This was done to reduce social desirability bias, information bias, recall bias.

The participants questionnaires administered to the parents/guardians of the children included sections on basic demographic information, and ever, recent, and current pesticide exposures (including currently living on a farm or not, pesticide contact including: seeing and smelling pesticides, swimming in nearby dams or rivers and eating crops from the vineyard and working on farms such as involvement with farming activities like picking fruit, spraying, cleaning, or burning containers) (Chetty-Mhlanga et al., 2018a).

The guardian questionnaires included sections on the child's demographics information, birth weight, general medical history, lifetime environmental and household exposure to pesticides, the child's nutritional intake and asthma-related symptoms. Additionally, there were items on the mothers' personal habits during pregnancy including questions on alcohol consumption, smoking, diet, and possible exposure to environmental/occupational exposure to pesticides. The

section on pesticides exposures included place of residency, years of residence, domestic use of pesticides, domestic water sources, use of empty containers and pesticide exposure through diet. The asthma-related symptoms and medication questionnaire were an abbreviated version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.

6.Statistical analysis

6.1 Exposure and outcome variables

Exposure variables: Pesticide exposure proxies previously developed (Chetty-Mlanga et al, 2021) based on the participant questionnaire were used in this study. Briefly these included dichotomous variables (Yes/No) on 1) exposure farm activities; 2) eating crops directly from the field; 3) contact with surface water around the field; and 4) seen and smelt pesticide spraying activities.

Farm activities included picking fruits in the field/vineyard/orchard; cleaning farm equipment; pesticide storage; burning any pesticide or chemical containers and pesticide or chemical spraying, mixing, or loading. Long-term exposure proxies ("ever" exposures) were used, as the previous study found considerable overlap with short-term exposure (current exposure and exposure "in the last 7 days"). An exposure variable for all exposures could not be created as virtually all the participants would be exposed and there would be no exposure contrast.

Outcome variable: The ISAAC standardised questionnaire was administered to the parents/guardian of the participants. Information on the child current wheeze or wheeze symptoms during the past 12 months and any occurrence of asthma was collected. An asthma score was developed from the responses of the participants to the ISSAC questionnaire. The asthma-related outcomes will include three variables.

The one dichotomous variable was based on a yes or no response to self-reported asthma including doctor diagnosed asthma (has your child ever had asthma?) and parental reported wheeze (current wheeze). The third asthma variable was based on an asthma symptom score calculated from the sum of responses to (0=negative response, 1=positive response) to six questions previously validated by Sunyer *et al.*, (2007).

The asthma score was given following responses to: Amount of attacks of wheezing the child had in the past 12 months, whether the child had asthma, whether the child had a dry cough at night apart from a cough associated with a cold or chest infection and whether the child's chest

sounded wheezy during or after exercise with one or more attack of wheezing. A score ≥ 2 was labeled as “more likely” and ≤2 was labelled ‘less likely’.

Confounding variable: Data on potential confounders were collected by trained interviewers while collecting data on child exposure to pesticides. Information on the childbirth history, residential history, household exposure and diet were collected. The potential confounders were age, body mass index (BMI), history of allergy or family history of allergy (as a marker for atopy), passive smoking, child current smoking, previous history of lung disease, Low Birth Weight.

6.2 Data analysis.

The collected data was analysed using the latest version of a statistical software R (RStudio Desktop 3.6.2), through the RStudio Desktop 3.6.2 interface. Firstly, the data was explored, and any missing data coded as “NA” for the covariate’s categorical variables and any implausible data for continuous variables. The data was analysed for the main exposure and outcome of interest, for any missing information and the data custodian was consulted before deciding on how these will be handled. A univariate analysis was used to describe the demographic representation, exposure and outcome of interest prevalence and medical history of the study participants.

For our initial analysis between exposure and outcome of interest, a bivariate analysis was conducted using a simple logistic regression analysis between the exposure of interest and outcome of interest (doctor diagnosed asthma, current wheeze, and asthma score). Thereafter the association between the outcome of interest with the identified confounders as age, sex, maternal smoking, born on a farm, family history of allergy (as a marker for atopy) and lung infection was assessed. Information on the residential history, household exposure and diet were collected and analysed with the outcome of interest as well.

A multivariate analysis between the exposure of interest and outcome of interest (doctor diagnosed asthma, current wheeze, and asthma score) was done adjusting for confounders that were associated with the outcome at a p-value of 0.1 and other confounders identified a priori. A stratified analysis by sex was be done to represent the group of children.

Additional analysis using the directed acyclic graphs (DAGs) was done to ascertain the sensitivity of the models (based on apriori confounders and those selected from bivariate

analysis) to the covariates adjusted for. The end point of asthma related outcome was determined using asthma scores from the selected ISAAC questionnaires to each of these symptoms.

Table 2 Dummy table of demographics and socioeconomic factors by study area.

Characteristics	The Hex River valley (n)	Grabow (n)	Piketberg (n)	All areas (n)
Demographics				
Age (years)				
Weight (Kg)				
Height (cm)				
Bmi				
Birth history				
Gestational age (weeks)				
Low birth weight				
Childbirth length				
Child head circumference				
Mother smoking during pregnancy				
Live on a farm				
Pre-existing conditions				
Family history of allergy (as a marker of atopy)				
Child passive smoking (mother or siblings smoking)				
Child ever or currently smoking				
Previous history of lung disease				
Child diagnosed with tuberculosis (TB)				
Household exposure n (%)				
Housemates working in agriculture.				
Washing PPE				
Usage of pesticides inside home for gardening or pest control.				
Child pesticide poisoning				
Living on a farm				
Time of the year sprayed pesticides come into the house				
Sources of water from unprotected source				
Child diet and nutrition n (%)				
Soya milk				
Fruits				
Vegetables				
Meat				
Categorical variables: n (%)				
Continuous variables: median (IQR)				

Table 3: Dummy table of Respiratory symptoms and asthma outcome by four study areas

Characteristics	The Hex River valley n, (%)	Grabow n,	Piketberg n,	All areas, n
Current wheeze				
Ever had asthma (q5.22)				

Asthma scores n (%)			
Score 0			
Score 1			
Score >= 2			

Table 4: Dummy table of exposure proxies by four study areas

	The Hex River Valley (N) n (%)	Grabow (N) n (%)	Piketberg (N) n (%)
Current wheeze ever had asthma in the last 7 days.			
Exposure to farm activities			
Eating crops directly from the field			
Contact with surface water around the field			
Seen and smelt pesticide spraying activities			

Table 5: Dummy table of rude and multivariate associations between pesticide exposures and asthma outcomes

	Crude associations			Adjusted associations		
	Current wheeze	Ever had asthma	Asthma scores	Current wheeze	Ever had asthma	Asthma scores
Exposure farm activities						
Eating crops directly from the field						
Contact with surface water around the field						
Seen and smelt pesticide spraying activities						

7. Ethical procedures

Permission was first obtained from the Department of Education (APPENDIX 4: Approval letter from Department of Education) for the main study to be conducted in schools. The main

study obtained ethical approval from the University of Cape Town Human Research Ethics Committee (234/2009) and was conducted in accordance with the Declaration of Helsinki of the 25th world Medical Assembly (Chetty-Mhlanga *et al.*, 2018a). Caregivers consented for their children to participate in the study (APPENDIX 6: Caregiver consent form) and these were provided in the language spoken by the study participant. Assent were obtained from the learners who participated in the study APPENDIX 7: Child assent form.

This study delt with vulnerable populations (women and children) and the ethical issues include the following:

Respect of persons: All details concerning the study participants were securely stored and kept confidential at a protected location. Furthermore, only the research team had permission to access the data, and the findings were reported in aggregate, maintaining the anonymity of individual participants.

Privacy: The privacy of the participants was respected in that the guardian interview took place in their homes, a place they felt most comfortable in. When not at their homes, it will take place in a private environment at the study sites set aside for research purposes. No external person aside from the researcher administering the questionnaire, the participant with a family member/guardian.

Confidentiality: The study ensured confidentiality of the participants by keeping all the information and data on the study participants in strict confidentiality in records and locked in filing cabinets at the University of Cape Town. Participants were given identifier information, which were only seen by the staff nominated personnel involved with the triangulation analysis. The individual results with personal identifiers were to be shown to the parents, participants and their physicians if authorised in writing. Additionally, the contact information forms were not stored with confidential information, they were kept in a separate locked file cabinet.

Beneficence: The study will be advantageous for the community, as the insights gained from the analysis will contribute to the development of strategies and potential formulation of health policies. This aims to ensure the future protection of farm workers, residents, and their children from the detrimental effects of pesticide exposure impacting their respiratory systems.

Non-maleficence: During the data collecting process, minimal harm will be done to the participants except the needle pricking while taking blood samples on the children. Consequently, a male nurse was assigned to male students, while a female nurse was designated for female students to conduct examinations in a private setting to ensure acceptability and confidentiality. Moreover, interviewers were directed to prioritize the emotional well-being of participants, both guardians/parents and children, during the interview process. Participants had the freedom to refrain from answering questions they found uncomfortable and were allowed to withdraw from the study at any point.

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PART B: MANUSCRIPT

Preparation for submission

Journal: Prepared to be submitted for publication in the peer-reviewed journal, International Journal of Hygiene and Environmental Health **apart from** the cover page with co-author details which are not included in the dissertation paper.

Title: Association between environmental exposure to pesticides and prevalence of asthma symptoms in rural children and adolescents living in agricultural settings in the Western Cape.

Competing financial interest declaration: None

Abstract

Background: There is conflicting evidence on the association between pesticide exposure and child asthma related outcomes in agricultural settings and limited data in developing country settings.

Objectives: This study investigated the association between children's exposure to pesticides and asthma related outcomes in rural agricultural areas in Western Cape South Africa.

Methods: A cross-sectional study of 700 children from three intensive agricultural areas in the rural Western Cape was conducted in June-September 2017. Guardian reported asthma outcomes and demographic information using an abbreviated version of the International Study of Asthma and Allergies in Childhood questionnaire and self-reported pesticide exposures of children was obtained.

Results: The median age of children was 11 years. The prevalence of more than two reported asthma symptoms was 8.5% across the sample. There were no statistically significant positive associations found between any of the three asthma related outcomes (including asthma symptoms score ≥ 2, parental reported asthma and current wheeze) and pesticide exposure variables. These included general pesticide exposure, farm activities, leisure activities and household pesticide exposure when adjusting for relevant confounders using multiple logistic regression analysis.

Conclusion: This cross-sectional study did not find evidence of an association between self-reported asthma related outcomes and pesticide exposure among rural children of the Western Cape. Longitudinal studies investigating the association using robust exposure and outcome measures are recommended.

Keywords: childhood asthma, pesticides, symptoms, rural, adolescent, South Africa

Highlights

- High prevalences of self-reported pesticide exposures were found.
- Pesticide exposures included farm activities, leisure activities, eating crops, domestic exposures, and other general exposures.
- Several asthma related symptoms were reported.
- No associations were found between self-reported pesticide exposure and guardian reported asthma related outcomes.

Abbreviations

- **BMI** Body Mass Index
- **CI** Confidence Interval
- **DAG** Directed Acyclic Graph.
- **DDE** Dichlorodiphenyldichloroethylene
- **FENO** Fractional Exhaled Nitric Oxide
- **ISAAC** International Study of Asthma and Allergies in Childhood
- **IQR** Interquartal Range
- **LTE4** Leukotriene E4
- **OR** Odds Ratio
- **PPE** Personal Protective Equipment

1. Introduction

Pesticides are commonly used in many countries around the world including South Africa, which is among the four largest importers of pesticides in Sub-Saharan Africa. Over 3000 pesticide products are imported in South Africa, including 700 pesticides used for agricultural purposes (Degrendele *et al.*, 2022). Recent years have seen an increase in pesticide usage due to the intensification of agricultural production. This is expected to increase in the future and could affect children's exposure to pesticides in South Africa (Degrendele *et al*., 2022).

The rural Western Cape is one of the most important agricultural areas in South Africa. Several recent studies have found the presence of many currently used pesticides in environmental media such as water, soil, and air and among rural children in the rural Western Cape in South Africa (Curchod *et al.*, 2020; Fuhrimann *et al.*, 2020b, 2021, 2022; Chetty-Mhlanga *et al.*, 2021b; Molomo *et al.*, 2021b; Degrendele *et al.*, 2022; Veludo *et al.*, 2022, 2024; Chow *et al.*, 2023)

Asthma is of concern to the healthcare system, specifically it's prevalence in children. Childhood asthma is the most common chronic disease among children worldwide, ranking among the top 20 conditions worldwide for disability-adjusted life years in children (Serebrisky and Wiznia, 2019). Childhood asthma constitutes a burden to the health care services and there are approximately 0 to 0.7 per 100 000 death rates of asthma in children globally (Serebrisky and Wiznia, 2019). It is characterised by issues of underdiagnosis and undertreatment in different countries and can be exacerbated by pesticides because they can increase a person's susceptibility to allergens by altering the bronchial lining through irritation, inflammation, or immune suppression (Serebrisky and Wiznia, 2019).

Children's exposure to pesticides occurs in multiple forms. One such way, is living near agricultural settings which leads to being exposed to pesticides via many routes including spray drift from spraying, ingestion of sprayed crops, contact with contaminated surfaces and domestic exposures (Molomo *et al.*, 2021c). Other exposure from living on farm include working on farms, being involved in activities on the farms as picking fruits, cleaning farm utensils, helping with pesticide storage, burning of pesticides containers, and assisting in spraying pesticides (Chetty-Mhlanga *et al.*, 2021a).

Although several studies have investigated the association between pesticide exposure and child asthma related outcome in agricultural settings, the evidence is conflicting with no previous study conducted in Africa (Buralli et al., 2020). This study aims to investigate the association between exposure to agricultural pesticides and asthma-related symptoms among children residing in the rural Western Cape of South Africa

2. Material and methods

2.1 Study design and population

This study is a cross-sectional study that is part of a longitudinal cohort study of 1002 school children aged from 9 to 18 years. The baseline measurements on children were conducted in six schools in 2017 with a follow-up in 2019 and caregivers were also interviewed at homes. This current sub-study includes 670 school children who participated in the baseline study and whose caregivers were interviewed. The data for this study includes exposure data collected in the child questionnaire (APPENDIX 2: Participant questionnaire) the child's asthma-related outcomes and demographic data in the caregiver's questionnaire (APPENDIX 2: Participant questionnaire).

2.2 Sampling

The areas included in the main study were the Hex River Valley (grape farming), Grabow (predominantly apple farming) and Piketberg (wheat and fruit farming). Schools in these three study areas were the sampling frame in the main study. Seven schools agreed to participate after contacting the principals and governing bodies of the schools (APPENDIX 5: Permission letter to school principal and board). To avoid a loss to follow-up due to children leaving high school, only primary, intermediate, and combined schools were approached (n = 32).

The parents or guardians of all school children in grades two to nine were sent information sheets about the research and the role of the school, along with permission letters (APPENDIX 5: Permission letter to school principal and board). All parents or guardians that responded positively to the study invitation were visited at their homes to obtain consent (APPENDIX 6: Caregiver consent form). Participants were then selected to obtain an approximate equal number of children by area, age, sex, those living on farms and those in the nearby town. Stratified random sampling was used to select the children where the number of consenting parents or guardians exceeded the number of children targeted for a particular category.

2.3 Participant and Parent Questionnaire

The participant questionnaire (APPENDIX 2: Participant questionnaire) was administered to school children during the baseline study. This was done on the school premises by trained interviewers using the Open Data Kit software uploaded on cellular phones. The interview information was captured onto phones from where it was uploaded onto a server. Interviews were conducted in the interviewee's language of preference and translated back to English. The parents were likewise interviewed at their homes.

The participants' questionnaires administered to the parents/guardians of the children included sections on basic demographic information, and ever, recent, and current pesticide exposures. The information included (currently living on a farm or not, pesticide contact including seeing and smelling pesticides, swimming in nearby dams or rivers and eating crops from the vineyard and working on farms such as involvement with farming activities like picking fruit, spraying, cleaning, or burning containers), (Chetty-Mhlanga et al., 2018a).

The guardian questionnaires included sections on the child's demographic information, birth weight, general medical history, lifetime environmental and household exposure to pesticides, and asthma-related symptoms. Additionally, there were items on the mothers' habits during pregnancy including questions on alcohol consumption, smoking, diet, and possible exposure to environmental/occupational exposure to pesticides. The section on pesticide exposures included place of residency, years of residence, domestic use of pesticides, domestic water sources, use of empty containers and pesticide exposure through diet. The asthma-related symptoms and medication questionnaire was an abbreviated version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.

2.4 Exposure and Outcome variables

Exposure variables: Pesticide exposure proxies used in this study were previously developed by (Chetty-Mhlanga *et al.*, 2018b) based on the participant questionnaire. Briefly, these include dichotomous variables (Yes/No) on 1) farm activities; 2) eating crops directly from the field; 3) contact with surface water around the field; and 4) seeing and smelling pesticide spraying activities. Farm activities include helping with picking fruits in the field/vineyard/orchard;

helping with cleaning farm equipment; assisting in pesticide storage; helping with burning any pesticide or chemical containers and helping with pesticide or chemical spraying, mixing, or loading. An exposure variable for all exposures could not be created as virtually all the participants would be exposed and there would be no exposure contrast. Due to the overlap with short-term exposure (current exposure and exposure “in the last 7 days”) found in previous studies, long-term exposure proxies (“ever” exposures) were used in this study.

Outcome variable: The ISAAC standardised questionnaire was administered to the parents/guardians of the participants, which collected information on the child's current wheeze or wheeze symptoms during the past 12 months and any occurrence of asthma. The asthma-related outcomes included three variables. The one dichotomous variable was based on a "yes" or "no" response to self-reported asthma including doctor-diagnosed asthma (has your child ever had asthma?) and current asthma (asthma attack in the past 12 months). The third asthma variable was based on an asthma symptom score calculated from the sum of responses (0=negative response, 1=positive response) to six questions previously validated by Sunyer *et al.*, (2007).

An asthma score was developed from the responses of the participants to the ISAAC questionnaire. The asthma score was created from the given responses to: attacks of wheezing the child had in the past 12 months, whether the child had asthma, whether the child had a dry cough at night apart from a cough associated with a cold or chest infection and whether the child’s chest sounded wheezy during or after exercise with one or more attack of wheezing. A score ≥ 2 was labelled as "more likely", and ≤ 2 was labelled 'less likely'.

2.5 Statistical analysis

The data was analysed using R version 4.3.2. The data was taken from the codebook containing all the responses to the questionnaire in the main study. The variables selected for the analysis were cleaned. Univariate analysis was conducted, and the descriptive statistics was stratified by sex. Bivariate analysis was done using a simple logistic regression analysis between exposure variables and outcome of interest (Doctor diagnosed asthma, current wheeze, and asthma score.

Multivariate analysis was conducted using multiple logistic regression to evaluate the association between the exposure and outcome variables and adjusting for confounding. Confounding variables were selected *apriori* namely (age, sex, history of allergy, born on farm)

based on known confounders in the literature and on a positive bivariate association ($p < 0.01$) with the outcome of interest (wheeze, asthma, asthma score >2). The multivariate analysis model was adjusted for age, sex, maternal smoking, born on a farm, family history of allergy and lung infection.

To ascertain the sensitivity of the models (based on apriori confounders and those selected from bivariate analysis) to the covariates adjusted for, a direct acyclic graph (DAG) was created, using the DaGitty software, of the model to identify the minimal variables to adjust for and to identify additional potential confounders. The DAG analysis confirmed that the correct model was used.

2.6 Ethics consent

This study obtained ethical consent (HREC 155/2022) from the Human Research Ethics Committee and the main study obtained ethical approval from the University of Cape Town Human Research Ethics Committee (234/2009) and was conducted by the Declaration of Helsinki of the 25th world Medical Assembly (Chetty-Mhlanga et al., 2018). Caregivers consented for their children to participate in the study (APPENDIX 6: Caregiver consent form) and these were provided in the language spoken by the study participant. Assent was obtained from the learners who participated in the study (APPENDIX 7: Child assent form).

3. Results

3.1 Demographic characteristics, anthropometric measurements, exposures at birth and medical history

Table 1 summarises the prevalence in demographic characteristics, anthropometric measurements, exposures at birth and medical history of children residing in rural Western Cape province. There was an even distribution of girls (47.9 %) and boys (52.0%) in the study sample with the same median age (11 years) and similar BMI (17.12 kg/m2 and 16.28 kg/m2, respectively). Nearly 40% of the participants were born on a farm including nearly two-thirds of girls and more than a third of boys.

The reported prevalence of tuberculosis (2.4%), lung infection (0.4%) and Fatal Alcohol Syndrome (1.3%) was below 3% among both boys and girls while family history of allergies was above 30% among both groups. More than a third of mothers smoked during pregnancy while about 2.5% worked on farms during pregnancy. About 14.2% of participants reported ever smoking in their lifetime and the households of about 16% used alternative fuels to electricity including coal or wood, gas, and paraffin (kerosene) as energy sources for cooking.

Table 1: Demographic Characteristics, anthropometric measurements, exposures at birth and medical history of children residing in rural Western Cape province.

	Overall		Female		Male	
	N*	# Summary statistic	N1 **	#Summary statistic	N2***	# Summary statistic
Demographic/Host Characteristics						
Age median (IQR)	670	11.00 (2.00)	321	11.00 (2.00)	349	11.00 (2.00)
Weight (kg) - median (IQR)	670	34.00 (14.00)	321	36.00 (14.00)	349	33 (14.00)
Height (cm) - median (IQR)	670	142.0 (16.8)	321	143.0 (16.0)	349	140 (17)
BMI (kg/m2) - median (IQR)	670	16.75 (3.93)	321	17.12 (4.39)	349	16.28 (3.67)
Medical history n (%)						
Tuberculosis	666	16 (2.4)	318	9 (2.9)	348	7 (2)
Lung infections	667	3 (0.4)	318	1 (0.3)	349	2 (0.6)

Fetal alcohol syndrome	668	9 (1.3)	320	4 (1.3)	348	5 (1.4)
Family History of Allergy	670	213 (31.8)	321	96 (29.9)	349	118 (33.5)
Antenatal exposures n (%)						
Being Born on a farm	670	258 (38.5)	321	197 (61.3)	349	124 (35.5)
Mother smoking during pregnancy	656	240 (36.6)	315	109 (34.6)	341	131 (38.4)
Mother working on a farm	661	15 (2.3)	318	8 (2.5)	343	7 (2.0)
Substance abuse and exposure to fossil fuel n (%)						
Participant ever smoking	670	95 (14.2)	321	46 (14.3)	349	49 (14.0)
Cooking sources: Electricity Others*	670	561(83.9) 109 (16.1)	321	275 (85.7) 46 (14.3)	349	286 (82.0) 63 (18.0)

Other sources of cooking* include coal, coke, or wood (solid fuel), gas (from the mains), paraffin (kerosene), gas (from bottles or other non-mains sources) and other sources.

3.2 Participant's self-reported exposures to pesticides

About 45% of the participants reported taking part in a farm activity namely picking fruit, pesticide application (spray, mixing or loading), burning pesticides, and storage of pesticides, with exposures higher among boys than girls. Less than 14% of participants who reported that they picked fruit, wore PPE with the prevalence less among girls (8.4%) compared to boys (18.2%).

More than three-quarters (75.2%) of participants reported that they took part in a leisure activity that could expose them to pesticides such as entering fields after spraying, recreational activities (playing, swimming, and bathing in water bodies) and eating produce from sprayed fields with the first two exposures higher among boys. Of those who reported that they eat produce from sprayed fields, about half reported that they do not wash it before eating.

Household pesticide exposures included using pesticides (70.8%), smelling pesticide sprayed on the farm in homes (52.7 %), a household member bringing PPE home (32.1%) and a household member being a farm worker.

Table 2 Participant's self-reported exposures to pesticides

	Overall		Female		Male	
Pesticide exposure	**N***	**[#] Summary statistic**	**N1 ****	**[#]Summary statistic**	**N2*****	**[#] Summary statistic**
			General pesticide exposure			
Currently living on a farm	670	306 (45.4)	321	145 (45.2)	349	161 (46.1)
			Farm activities			
Picking fruit in the field	670	155 (23.1)	321	50 (14.6)	348	105 (30.2)
Wearing protective gear (PPE)	668	90 (13.7)	321	27 (8.4)	347	63 (18.2)
*Picking fruits in the field with Personal Protective Gear	668		321		347	
• Low		514 (76.9)		271 (84.4)		243 (70)
• Moderate		90 (13.5)		27 (8.4)		63 (18.2)
• High		64 (9.6)		23 (7.2)		41 (11.8)
Spraying, mixing, loading	666	43 (6.5)	318	13 (4.1)	348	30 (8.6)
Cleaning farm equipment	667	148 (22.8)	320	58 (18.1)	347	90 (25.9)
Assisting in pesticide storage	667	138 (20.6)	318	61 (19.2)	349	77 (22.1)
Burning pesticide containers	666	43 (6.4)	318	7 (2.2)	348	36 (10.3)
Taking part in any farm activity**	670	300 (45)	321	121 (37.7)	349	179 (51.3)
			Leisure activities			
Entering the farm after spraying	667	116 (17.6)	319	44 (13.8)	348	72 (20.7)
Playing, swimming, and bathing in water bodies	670	329 (49.1)	321	129 (40.2)	349	200 (57.3)
Eating produce from sprayed fields	667	362 (54.3)	320	174 (54.4)	347	188 (54.2)

Washing produces before eating	667	334 (50.1)	320	160 (50)	347	174 (50.1)
Exposure from eating produce***: • Low • Moderate • High	670	308 (45.9) 334 (50.3) 28 (4.2)	321	147 (45.8) 160 (49.8) 14 (4.4)	349	161 (46.1) 174 (49.9) 14 (4.0)
****Taking part in any leisure activity	664	499 (75.2)	318	230 (72.3)	346	269 (77.7)
Household exposure						
Using household chemicals for pests	641	454 (70.8)	306	219 (71.6)	335	240 (71.6)
Pesticide odour in the home	660	348(52.7)	316	166 (52.5)	344	182 (52.9)
Household members bring PPE home	667	214 (32.1)	319	107 (33.5)	348	107 (30.7)
Any family members living with the participant working on a farm	525	126 (24)	256	64 (25)	269	62 (23.0)

Taking part in any farm activity*: Yes: Taking part in Any farm activity mentioned (burning, storing, spraying, mixing, loading pesticides). Picking fruits in the field with personal protective gear**: Low: "Not picking fruits = 0" Moderate: Picking fruits and wearing protective gear = 1; High: Picking fruits and not wearing protective gear = 2, ***Washing produce before eating: Low: “Not Eating produce = 0” Moderate: Eating produce = and washing before eating = 1; High: Eating produce and not washing before eating = 2. Taking part in any leisure activity****: Entering farm after spraying, Playing, swimming, and bathing in water bodies, eating produce from sprayed fields and washing produces before eating.

3.3 Asthma-related symptoms and outcomes reported in the past year for children residing in rural Western Cape province.

Table 3 shows that 6.5% of guardians reported that participants had previously been diagnosed with asthma and several wheeze-related symptoms in the previous 12 months that varying in prevalence between 1.6 – 7.2%. About 14% (13.8%) also reported a dry cough not associated with a cold or chest infection. All symptoms were more prevalent among boys. An asthma symptom score > = 2 calculated from the sum of positive responses (yes = 1) to 6 main asthma symptom questions (current wheeze, wheeze attacks, wheeze disturbing sleep, wheeze limiting speech and wheeze during exercise) was 8.5% with a higher prevalence among boys (10.3%) than girls (6.5%).

Table 3 Asthma-related symptoms and outcomes reported in the past year for children residing in rural Western Cape province.

	Overall		Female		Male	
Asthma-related outcome	**N***	**# Summary statistic**	**N1 ****	**# Summary statistic**	**N2*****	**# Summary statistic**
Parental-reported lifetime asthma	664	43 (6.5)	319	15 (4.7)	345	28 (8.1)
Parental-reported lifetime wheezing	670	48 (7.2)	321	20 (6.2)	349	28 (8.02)
Current wheeze*	670	38 (5.7)	321	16 (4.9)	349	22 (6.3)
Wheeze attacks*	670	41 (6.1)	321	15(4.7)	349	26 (7.4)
Wheeze disturbing sleep *	670	32 (4.7)	321	12 (3.7)	349	20 (5.7)
Wheeze limiting speech *	670	11 (1.6)	321	5 (1.6)	349	6 (1.7)
Wheeze during exercise *	670	43(6.4)	321	18 (5.6)	349	25 (7.1)
Dry cough at night not associated with a cold or chest infection*	670	92 (13.8)	321	38 (11.8)	349	54 (15.5)
Asthma Symptom Score**						
• >=2	670	57 (8.5)	321	21(6.5)	349	36 (10.3)

Asthma Symptom Score >=2**: Having more than one reported asthma symptom* (1= yes) namely current wheeze, wheeze attacks, wheeze disturbing sleep, wheeze limiting speech, wheeze during exercise and dry cough at night not associated with a cold or chest infection.

3.4 Association between reported asthma-related outcome and pesticide exposure

Table S1 summarises the bivariate associations between asthma-related outcomes and demographic and other exposures. There was a statistically significant positive association found between parental reports of child wheezing and mother smoking during pregnancy (OR: 2.30, CI: 1.24 - 4.24) and family history of allergy (OR: 4.07, CI: 1.20-13.85). Being born on a farm (OR: 0.40, CI: 0.19 -0.85) was negatively associated with parental-reported asthma indicating a protective effect.

There were no statistically significant positive associations found between any of the three asthma-related outcomes and pesticide exposure variables including general pesticide exposure, farm activities, leisure activities and household pesticide exposure in adjusted

models (Tables 4 and 5). There was, however, a negative association found between eating produce from sprayed fields (OD:0.38, CI: 0.16 - 0.90), and asthma symptom score >=2.

Additional analysis showed that living on farms was consistently associated with farm activities but further analysis including living on farm in the models and stratifying by living on farms (Tables S3 – S7) did not find consistent positive associations between asthma-related outcomes and other self-reported exposures.

Table 4 Association between reported asthma-related outcome and pesticide exposure on farms and farm-related activities in adjusted and unadjusted regression models.

	N*	Models	Asthma symptom score>=2	Parental reported asthma	Current Wheeze
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
			General Pesticide exposure		
Currently living on a farm	670	Unadjusted	1.62 (0.91-2.89)	**0.38 (0.19- 0.78)**	1.00 (0.55 - 1.81)
		Adjusted	2.24 (0.58 - 8.61)	1.39 (0.26 – 7.23)	0.97 (0.17 – 5.32)
			Farm activities		
Picking fruit in the field	670	Unadjusted	0.50 (0.22 - 1.14)	0.63 (0.27 - 1.46)	0.75 (0.35 - 1.58)
		Adjusted	0.66 (0.23 - 1.88)	1.46 (0.36 - 5.91)	0.84 (0.29 – 2.47)
*Picking fruits in the field with Personal Protective Gear • Low (ref) • Moderate • High	514	Unadjusted	1 0.62(0.24-1.63) 0.34 (0.08 - 1.45)	1 0.47 (0.14 - 1.56) 0.87 (0.30 - 2.55)	1 1.02 (0.44 - 2.37) 0.39 (0.09 - 1.66)
 • Low (ref) • Moderate • High		Adjusted	1 0.71 (0.19 - 2.57) 0.60 (0.12 - 2.82)	1 0.76 (0.08 - 6.50) 2.75 (0.49 -15.28)	1 1.26 (0.38 - 4.12) 0.35 (0.04 - 2.89)
Spraying, mixing, loading	666	Unadjusted	0.27 (0.03 - 2.02)	0.68 (0.16 - 2.93)	0.61 (0.14 - 2.61)
		Adjusted	0.51 (0.06 - 4.14)	NC	0.57 (0.06 – 4.70)
	667	Unadjusted	0.53 (0.23 - 1.21)	0.92 (0.43 - 1.98)	0.79 (0.37 - 1.68)

Cleaning farm equipment		Adjusted	0.41 (0.13 - 1.28)	1.44 (0.35 - 5.91)	0.52 (0.16 - 1.64)
Assisting in pesticide storage	667	Unadjusted	0.69 (0.31 - 1.51)	0.47 (0.18 - 1.24)	1.15 (0.57 - 2.32)
		Adjusted	1.00 (0.39 - 2.56)	1.43 (0.34 - 5.88)	0.97 (0.35 - 2.69)
Burning pesticide containers	666	Unadjusted	0.89 (0.26 - 3.01)	1.52 (0.51-4.47)	0.96 (0.28 - 3.23)
		Adjusted	0.34 (0.04 - 2.80)	2.07 (0.38 -11.06)	0.37 (0.04 - 3.08)
Taking part in any farm activity**	670	Unadjusted	0.62 (0.34 - 1.13)	0.61 (0.32 - 1.18)	0.91 (0.50 - 1.66)
		Adjusted	0.68 (0.30 - 1.55)	1.30 (0.40 - 4.14)	0.64 (0.26 - 1.55)

NC: Non-computable statistical output due to non-convergence of the model
Bold: Statistically significant output with p-value <0.05
Model adjusted for Age, Sex, Maternal smoking, born on a farm, family history of allergy and lung infection. Taking part in any farm activity*: Yes: Taking part in Any farm activity mentioned (burning, storing, spraying, mixing, loading pesticides). Picking fruits in the field with Personal Protective Gear**: Low: "Not picking fruits = 0" Moderate: Picking fruits and wearing protective gear = 1; High: Picking fruits and not wearing protective gear = 2

Table 5 Association between reported asthma-related outcome and exposure from leisure and household activities in adjusted and unadjusted regression models.

	N*	Models	Asthma symptom score>=2	Parental reported asthma	Wheeze
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
			Leisure activities		
Entering the farm after spraying	667	Unadjusted	1.01 (0.48 -2.15)	1.09 (0.48 - 2.12)	1.86 (0.95 - 3.63)
		Adjusted	1.38 (0.52 - 3.64)	1.95 (0.47 - 7.97)	1.88 (0.69 - 5.16)
Playing, swimming, and bathing in water bodies	670	Unadjusted	0.99 (0.56 - 1.76)	0.81 (0.43 - 1.51)	1.03 (0.57 - 1.86)
		Adjusted	0.92 (0.41 - 2.06)	1.01 (0.33 - 3.14)	0.65 (0.27 - 1.56)
Eating produce from sprayed fields	667	Unadjusted	0.61 (0.34 - 1.09)	1.08 (0.58 - 2.01)	0.99 (0.55 - 1.79)
		Adjusted	**0.38 (0.16 - 0.90)**	NC	0.81 (0.34 - 1.97)
Exposure from eating produce***	308	Unadjusted	1	1	1
• Low (ref)			0.64 (0.35 – 1.15)	1.08 (0.57 – 2.04)	0.96 (0.52 - 1.76)
• Moderate			0.35 (0.04 - 2.71)	1.16(0.25 - 5.28)	1.56 (0.43 - 5.57)
• High					

• Low (ref) • Moderate • High		Adjusted	1 0.42 (0.18 – 0.99) NC	1 1.11 (0.34 - 3.55) NC	1 0.90 (0.37 – 2.16) NC
Taking part in any leisure ****activity	664	Unadjusted	0.77 (0.41 - 1.45)	0.96 (0.47 - 1.97)	1.12 (0.55 - 2.25)
		Adjusted	0.58 (0.24 - 1.37)	1.11 (0.31 - 3.92)	0.70 (0.27 - 1.78)
Household pesticide exposure					
Using household chemicals for pests	641	Unadjusted	1.66 (0.81 - 3.40)	0.67 (0.35 - 1.29)	1.57 (0.76 - 3.22)
		Adjusted	1.95 (0.74 - 5.12)	0.45 (0.13 - 1.47)	1.28 (0.49 - 3.32)
Pesticide odour in a home	660	Unadjusted	**2.28 (1.22 - 4.25)**	0.68 (0.36 - 1.28)	**1.87 (1.00 - 3.48)**
		Adjusted	2.00 (0.79 - 5.02)	0.65 (0.20 - 2.04)	0.91 (0.36 - 2.26)
Bringing PPE home_ Guardian (Mother and Father).	667	Unadjusted	0.87 (0.46 - 1.63)	0.63 (0.30 - 1.31)	0.68 (0.35 - 1.35)
		Adjusted	0.98 (0.41 - 2.31)	1.52 (0.46 - 4.96)	0.84 (0.32 - 2.16)
Any family members living with the participant working on a farm	525	Unadjusted	0.50 (0.22 -1.16)	**0.17 (0.04 - 0.73)**	1.59 (0.81 - 3.12)
		Adjusted	0.73 (0.25 - 2.1)	2.54 (0.28 - 22.8)	1.21 (0.32 - 4.50)

NC: Non-computable statistical output
Bold: Statistically significant output with p-value <0.05
Model adjusted for Age, Sex, Maternal smoking, born on a farm, family history of allergy and lung infection. Washing produce before eating: Low***: "Not Eating produce = 0" Moderate: Eating produce = and washing before eating = 1; High: Eating produce and not washing before eating = 2, Taking part in any leisure activity****: Entering farm after spraying, Playing, swimming, and bathing in water bodies, eating produce from sprayed fields and washing produces before eating.

4. Discussion

In this study of children residing in agricultural settings in the Western Cape, South Africa, no significant associations were found between the three guardian-reported asthma-related outcomes and several self-reported long-term pesticide exposure indices based on questionnaire responses. These indices include general pesticide exposure to spraying on a farm, performing farm activities, performing leisure activities and household pesticide exposure following adjustment for relevant confounders. There was also no association found between pesticide exposure and asthma-related outcomes in both boys and girls. Living on farms was however correlated with other reported exposures but did not influence the associations observed.

Conflicting findings were found in a recent literature review conducted by (Buralli et al., 2020) that identified 12 post-natal epidemiological studies that investigated the association between current use of agricultural pesticide exposure in rural areas and asthma-related outcomes in children. Studies varied in design, sample size, exposure and outcome measures employed.

The review included both longitudinal and cross-sectional investigations with varying sample sizes (16-13977 participants), with studies conducted predominantly in the United States of America, including England, France, Sri Lanka, and Lebanon. Seven of the studies in the review by Buralli et al. (2020) found positive associations between pesticide exposure and asthma-related outcomes of which four used objective measures of exposure and/or outcomes (Salameh et al., 2003; Meng et al., 2016; Dayasiri et al., 2017a; Kudagammana et al., 2018b; Benka-Coker et al., 2019, 2020b; Raherison et al., 2019) . However, five studies did not find an association between pesticide exposure and asthma-related outcomes, with three of the five studies using various objective measures of exposure and/or outcomes (Weselak, Arbuckle and Foster, 2007; Cupul-Uicab *et al.*, 2014; Perla *et al.*, 2015; Raanan *et al.*, 2015b; Gunier *et al.*, 2018b). Furthermore, a study by Bukalasi et. al. (2018) did not find an association between residential proximity to pesticide usage and asthma-related outcomes.

There are potential exposures to pesticide among the participants that are worth noting in this study. The data on pesticide exposures to spraying, farm activities, leisure activities and household pesticide exposures highlight the multiple pesticide exposure routes that rural children in these settings experience. About 45% of the participants reported taking part in farm activities such as picking fruit, pesticide application, burning pesticides, and storage of pesticides, with exposures being higher among boys than girls. More than 75% of participants reported that they took part in a leisure activity that could expose them to pesticides. Previous studies in these settings have found high levels of urinary levels of pesticide metabolites among children compared to other settings (Fuhrimann et al. 2022; Molomo et al., 2021; Veludo et al., 2023, 2024). No comparative data on self-reported pesticide exposures via different routes of exposure could be found.

The mechanisms underlying the association between pesticides exposure and asthma-related outcomes are still being investigated. Pesticides are thought to cause asthma by increasing a person's susceptibility to allergens by altering the bronchial lining through irritation, inflammation, or immune suppression (Tarmure et al., 2020). Pesticides also inhibit cholinesterase activity resulting in the building up of acetylcholine, the chief neurotransmitter

of the parasympathetic nervous system. The reduction of cholinesterase activity in the nervous system is associated, among others, with asthma-related symptoms such as wheezing and difficulty in breathing (Tarmure *et al.*, 2020). Exposure to pesticides can also exacerbate asthma and trigger asthma attacks by increasing hyperreactive responses to the exposure. However, there was a contrary association observed in this study.

For example, an unexpected finding in the study was the negative association between eating produce from sprayed fields (OR:0.38, 95% CI: 0.16 - 0.90), and asthma symptom score >=2 which indicates a protective effect. The negative effect of this association might be attributed to the fact that eating produce from sprayed field may not adequately capture pesticide exposure through ingestion as it was self-reported and recall bias could have been introduced in the data collection process. Although, eating produce from field have been found to be one of the primary sources of exposure to pesticides and ingestion is considered the most frequent route of pesticide poisoning in children (Dayasiri et al, 2017b) There was also no additional information on the frequency of eating crops from the sprayed field to determine the dose-response effect in this current study.

The lack of objective exposure and outcome measures could have limited the study in detecting plausible exposure-outcome relationships. The non-statistical significance of some of the positive associations between pesticide exposure and asthma-related outcomes found in the study could have resulted due to recall bias from self-reported exposures leading to misclassification of exposure, and thus skewing the associations towards the null. Although the questionnaire incorporated multiple exposure routes. The lack of data on the frequency of pesticide exposure could also have resulted in a null association, as dose-response relationship could not be investigated.

In addition to the limitations mentioned above, the cross-sectional study design of the study is a limitation as it precludes determining the temporality of the associations observed. The lack of an objective exposure measures such as biomonitoring as well as not identifying specific pesticides, is another limitation as it could result in exposure misclassification driving associations towards the null. Additionally, the lack of objective outcome measures such as lung function indices and forced exhaled nitric oxide measurement, is also a limitation. The reporting of smoking, alcohol consumption and substance abuse could introduce social desirability bias, but standardised questionnaires were used. The use of parent/guardian-

reported family history of allergy instead of assessing atopic status objectively is also an important limitation of the study.

Hence, it is imperative that more longitudinal studies of similar populations using objective indices and measures for both exposure and asthma outcomes. As the current study is to our knowledge, the only study to investigate the association between current use of agricultural pesticide exposure and childhood asthma in a rural agricultural setting in Africa.

The strengths of the study include a good sample size of 700 children with good representation by gender, age, area and farm/non-farm residence, adjustment for co-exposures and sampling in three intensive agricultural areas.

5. Conclusions

The study found that children form rural areas of the Western Cape are exposed to agricultural pesticides via many different routes. However, this cross-sectional analysis did not observe evidence of an association between self-reported asthma-related outcomes and pesticide exposure among the rural children. This study has laid the groundwork for future studies as it was the first study conducted in Africa looking at rural children's exposure to pesticides and asthma outcomes. It demonstrated the exposure routes of children in the Western Cape who are residing in an agricultural setting.

A longitudinal study investigating this association using robust and objective exposure and outcome measures is recommended. Interventions and policy to guide the usage of pesticide in agriculture and inform regulations on children’s participation in farm activities and reduce pesticide exposures among rural children should be implemented and improved.

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SI 1 Association between reported asthma-related outcomes and demographic characteristics and other exposures using simple logistic regression, n=670

	N* 670	Asthma symptom score>=2	Parental reported asthma	Wheeze
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic/Host Characteristics				
Age median (IQR)	670	1.08 (0.92 - 1.27)	0.85 (0.70 - 1.03)	1.02 (0.86 - 1.20)
Sex	670	0.68 (0.38 - 1.22)	0.55 (0.29 – 1.06)	0.76 (0.42_ 1.38)
BMI - median (IQR)	670	0.92 (0.84 - 1.01)	0.93 (0.84 - 1.02)	0.94 (0.86 - 1.03)
Medical history				
Tuberculosis	666	0.76 (0.00 - NC)	0.95 (0.12 - 7.41)	1.87 (0.413 - 8.50)
Lung infections	667	0.73 (0.00 – NC)	**NC**	7.92 (0.00 – NC)
Fetal alcohol syndrome	668	0.76 (0.00 – NC)	0.90 (0.00- NC)	0.81 (0.00 – NC)
Family History of Allergy	670	2.61 (0.97- 7.0)	7.5 (0.99 – 58.11)	**4.07 (1.20 – 13.85)**
Antenatal exposures and medical history				
Mother smoking during pregnancy	656	**2.07 (1.15 - 3.72)**	0.95 (0.12 – 7.40)	**2.30 (1.24 - 4.24)**
Mother working on a farm	661	1.91 (0.42 - 8.74)	1.12 (0.14- 8.81)	2.05 (0.44 - 9.38)
Being born on a farm	670	1.59 (0.89 - 2.82)	**0.40 (0.19 – 0.85)**	1.15 (0.63 – 2.09)
Substance abuse and exposure to fossil fuel				
Smoking	670	0.63 (0.24 -1.65)	0.78 (0.30 - 2.05)	0.85 (0.35 -2.07)
Cooking sources: Electricity (Ref) Others	670	1.461 (0.72-2.94)	0.51 (0.18 - 1.47)	1.20 (0.56 - 2.56)

Supplementary Information

NC: Non-computable statistical output. **Bold**: Statistically significant output with p-value <0.05

SI 2 Association between reported asthma-related outcome and exposure variable in adjusted and unadjusted analysis stratified by sex.

			Female				Male		
	N*	**Models**	**Asthma symptom score>=2**	**Parental reported asthma**	**Wheeze**	**N***	**Asthma symptom score>=2**	**Parental reported asthma**	**Wheeze**
Exposure variable	**321**		**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**349**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
		General Pesticide exposure							
		Farm activities							
Taking part in any farm activity**	121	Unadjusted	0.88 (0.34 - 2.27)	0.58 (0.18 - 1.89)	1.38 (0.55 - 3.43)	179	0.49 (0.22 - 1.05)	0.58 (0.26 - 1.29)	0.69 (0.31 - 1.50)
		Adjusted	1.29 (0.35 - 4.7)	1.23 (0.19 - 7.60)	1.33 (0.33 - 5.39)		0.45 (0.15 - 1.34)	1.00 (0.17 - 5.9)	0.43 (0.13 - 1.42)
		Leisure activities							
Exposure from eating produce***: Low Moderate High	411	Unadjusted	1 0.51 (0.19 - 1.34)	1 1.25 (0.42 - 3.70)	1 0.91 (0.41 - 2.04)	335	1 0.74 (0.35 - 1.55)	1 1.00 (0.45 - 2.21)	1 0.91 (0.41 - 2.04)
		Adjusted	1 0.59 (0.16 - 2.1) 0.00 (0.00 – N)	1 1.45 (0.25 - 8.23) 0.00 (0.00 – NC)	1 1.33 (0.35 - 5.05) 0.00 (0.00 – NC)		1 0.34 (0.10 - 1.07) 0.00 (0.00 – NC)	1 0.84 (0.15 - 4.53) 0.00 (0.00 – NC)	1 0.64 (0.19 - 2.18) 0.00 (0.00 – NC)
	230	Unadjusted	1.40 (0.87 - 2.25)	0.91 (0.53 - 1.54)	1.00 (0.63 - 1.58)	269	0.97 (0.40 - 2.36)	1.07 (0.41 - 2.74)	1.05 (0.41 - 2.69)

Taking part in any leisure ****activity		Adjusted	0.65 (0.18 - 2.26)	1.207 (0.20 - 7.28)	0.86 (0.44 - 1.70)		0.50 (0.15 - 1.65)	0.00 (0.17 - 5.95)	0.45 (0.13 - 1.55)

NC: Non-computable statistical output. **Model adjusted for** Age, Maternal smoking, born on a farm, family history of allergy and lung infection.

SI 3 Association between reported asthma-related outcome and pesticide exposure on farms and farm-related activities in unadjusted and adjusted regression models including living on farms in the models.

	N*	Models	Asthma symptom score>=2	Parental reported asthma	Current Wheeze
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
General Pesticide exposure					
Farm activities					
Picking fruit in the field	670	Unadjusted	0.50 (0.22 - 1.14)	0.63 (0.27 - 1.46)	0.75 (0.35 - 1.58)
		Adjusted	**0.42 (0.18 - 0.9)**	0.61(0.26 -1.45)	0.67 (0.31 - 1.45)
*Picking fruits in the field with Personal Protective Gear • Low (ref) • Moderate • High	514	Unadjusted	1 0.62(0.24-1.63) 0.34 (0.08 - 1.45)	1 0.47 (0.14 - 1.56) 0.87 (0.30 - 2.55)	1 1.02 (0.44 - 2.37) 0.39 (0.09 - 1.66)
• Low (ref) • Moderate • High		Adjusted	1 0.53 (0.20 - 1.41) 0.27 (0.06 - 1.18)	1 0.43(0.12 - 1.46) 0.91(0.30 - 2.73)	1 0.93 (0.40 - 2.19) 0.34 (0.08 - 1.49)
Spraying, mixing, loading	666	Unadjusted	0.27 (0.03 - 2.02)	0.68 (0.16 - 2.93)	0.61 (0.14 - 2.61)
		Adjusted	0.24 (0.03 - 1.85)	0.65 (0.15 -2.83)	0.57 (0.13 - 2.48)
Cleaning farm equipment	667	Unadjusted	0.53 (0.23 - 1.21)	0.92 (0.43 - 1.98)	0.79 (0.37 - 1.68)
		Adjusted	0.43 (0.19 - 1.01)	1.07 (0.48 -2.38)	0.75(0.35 - 1.63)
Assisting in pesticide storage	667	Unadjusted	0.69 (0.31 - 1.51)	0.47 (0.18 - 1.24)	1.15 (0.57 - 2.32)
		Adjusted	0.56 (0.25 - 1.26)	0.59 (0.22 - 1.59)	1.12(0.54 - 2.32)
Burning pesticide containers	666	Unadjusted	0.89 (0.26 - 3.01)	1.52 (0.51- 4.47)	0.96 (0.28 - 3.23)
		Adjusted	0.77 (0.22 - 2.63)	1.37 (0.45 -4.16)	0.86 (0.25 - 2.94)
Taking part in any farm activity**	670	Unadjusted	0.62 (0.34 - 1.13)	0.61 (0.32 - 1.18)	0.91 (0.50 - 1.66)
		Adjusted	**0.53 (0.28 - 0.98)**	0.69 (0.35 - 1.36)	0.89 (0.48 - 1.64)

NC: Non-computable statistical output due to non-convergence of the model**. Bold:** Statistically significant output with p-value <0.05**. Model adjusted for** Age, Sex, being born on a farm, and living on a farm.

SI 4 Association between reported asthma-related outcome and exposure from leisure and household activities in unadjusted and adjusted regression models including living on farms in the models.

	N*	Models	Asthma symptom score>=2	Parental reported asthma	Current Wheeze
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Leisure activities					
Entering the farm after spraying	667	Unadjusted	1.01 (0.48 - 2.15)	1.09 (0.48 - 2.12)	1.86 (0.95 - 3.63)
		Adjusted	0.88 (0.41 - 1.89)	1.21(0.53 -2.76)	1.80 (0.91 - 3.58)
Playing, swimming, and bathing in water bodies	670	Unadjusted	0.99 (0.56 - 1.76)	0.81 (0.43 - 1.51)	1.03 (0.57 - 1.86)
		Adjusted	0.86 (0.47 - 1.55)	0.83 (0.44- 1.59)	0.99 (0.54 - 1.81)
Eating produce from sprayed fields	667	Unadjusted	0.61 (0.34 - 1.09)	1.08 (0.58 - 2.01)	0.99 (0.55 - 1.79)
		Adjusted	0.55 (0.30 – 1.00)	1.24 (0.65 - 2.35)	0.96 (0.53 - 1.76)
Exposure from eating produce*** • Low (ref) • Moderate • High	308	Unadjusted	1 0.64 (0.35 – 1.15) 0.35 (0.04 -2.71)	1 1.08 (0.57 – 2.04) 1.16(0.25 - 5.28)	1 0.96 (0.52 - 1.76) 1.56 (0.43 - 5.57)
• Low (ref) • Moderate • High		Adjusted	1 0.57 (0.31 - 1.05) 0.35 (0.04 - 2.72)	1 1.26 (0.65 - 2.42) 1.2 (0.25 - 5.55)	1 0.93 (0.50 - 1.72) 1.56 (0.43 - 5.65)
Taking part in any leisure ****activity	664	Unadjusted	0.77 (0.41 - 1.45)	0.96 (0.47 - 1.97)	1.12 (0.55 - 2.25)
		Adjusted	0.68 (0.35 - 1.30)	1.07 (0.52 - 2.22)	1.07 (0.53 - 2.19)
Household pesticide exposure					
Using household chemicals for pests	641	Unadjusted	1.66 (0.81 - 3.40)	0.67 (0.35 - 1.29)	1.57 (0.76 - 3.22)
		Adjusted	1.63 (0.79 - 3.35)	0.72 (0.37 - 1.40)	1.58 (0.77 - 3.26)
Pesticide odour in the home	660	Unadjusted	**2.28 (1.22 - 4.25)**	0.68 (0.36 - 1.28)	**1.87 (1.00 - 3.48)**

		Adjusted	**2.09 (1.08 - 4.05)**	0.92 (0.47 - 1.79)	**2.00 (1.03 - 3.87)**
Bringing PPE home_ Guardian (Mother and Father).	667	Unadjusted	0.87 (0.46 - 1.63)	0.63 (0.30 - 1.31)	0.68 (0.35 - 1.35)
		Adjusted	0.81 (0.43 - 1.53)	0.73 (0.35 - 1.55)	0.67 (0.34 - 1.33)
Any family members living with the participant working on a farm	525	Unadjusted	0.50 (0.22 -1.16)	**0.17 (0.04 - 0.73)**	1.59 (0.81 - 3.12)
		Adjusted	0.62 (0.25 - 1.50)	0.49 (0.18 - 1.34)	**0.39 (0.15 - 0.98)**

NC: Non-computable statistical output**. Bold:** Statistically significant output with p-value <0.05**. Model adjusted for** Age, Sex, being born on a farm, and living on a farm.

SI 5 Association between reported asthma-related outcome and farm activities stratified by living on farms.

			Living on farm			Not living on a farm		
	N*	**Models**	**Asthma symptom score>=2**	**Parental reported asthma**	**Asthma symptom score>=2**	**Parental reported asthma**	**Current Wheeze**	**Current Wheeze**
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
General Pesticide exposure								
Farm activities								
Picking fruit in the field	670	Unadjusted	0.36 (0.08 - 1.61)	0.61 (0.13 - 2.92)	0.60 (0.19 - 1.84)	0.36 (0.08 - 1.61)	0.71 (0.26 - 1.91)	0.91 (0.33- 2.50)
		Adjusted	0.35 (0.08- 1.58)	0.66 (0.24 - 1.82)	0.88 (0.31 - 2.47)	0.35 (0.08 - 1.58)	0.66 (0.24 - 1.82)	0.88 (0.31 - 2.47)
*Picking fruits in the field with Personal Protective Gear • Low (ref) • Moderate • High	514	Unadjusted	1 0.61 (0.17 - 2.13) 0.50 (0.11 - 2.24)	1 0.56 (0.06- 4.58) NC	1 1.12 (0.24 - 5.12) NC	1 0.61 (0.13 - 2.70) NC	1 1.11 (0.31 - 3.92) NC	1 0.89 (0.25 - 3.11) 0.94 (0.21 4.25)
• Low (ref) • Moderate • High		Adjusted	1 0.50 (0.14 - 1.77) 0.40 (0.08 - 1.84)	1 1.19 (0.26 - 5.47) 0.67 (0.08- 5.34)	1 0.99 (0.31 - 3.15) NC	1 0.60 (0.13 - 2.71) NC	1 0.42 (0.09 - 1.87) 1.07 (0.29 - 3.89)	1 0.86 (0.24 - 3.07) 0.91 (0.20 - 4.18)
Spraying, mixing, loading	666	Unadjusted	0.43 (0.05 - 3.33)	NC	NC	NC	1.08 (0.24 - 4.86)	0.63 (0.08 - 4.90)
		Adjusted	0.38 (0.04 - 3.01)	NC	0.52(0.06 - 4.14)	NC	1.01 (0.22 - 4.66)	0.59 (0.07 - 4.65)
	667	Unadjusted	0.51 (0.20 - 1.30)	1.19 (0.34 - 4.19)	0.78 (0.22 - 2.77)	0.28 (0.03 - 2.20)	1.22 (0.44 - 3.34)	0.82 (0.23 - 2.84)

Cleaning farm equipment		Adjusted	0.48 (0.18 - 1.24)	1.12 (0.32 - 3.97)	0.72 (0.27 - 1.92)	0.29 (0.03 - 2.29)	1.06 (0.38 - 2.97)	0.82 (0.23 - 2.88)
Assisting in pesticide storage	667	Unadjusted	0.66 (0.27 - 1.62)	0.79 (0.20 - 3.07)	1.89 (0.69 - 5.14)	0.34 (0.04 - 2.65)	0.47 (0.11 - 2.07)	1.42 (0.46 - 4.35)
		Adjusted	0.63 (0.26 - 1.56)	0.78 (0.20 - 3.08)	0.95 (0.37 - 2.45)	0.35 (0.04 - 2.70)	0.44 (0.10 - 1.93)	1.43 (0.46 - 4.40)
Burning pesticide containers	666	Unadjusted	0.94 (0.21 - 4.27)	NC	NC	0.75 (0.09 - 5.93)	1.07 (0.23 - 4.84)	0.63 (0.08 - 4.88)
		Adjusted	0.75 (0.16 - 3.49	NC	1.12 (0.23 - 5.30)	0.81 (0.10 - 6.59)	1.09 (0.23 - 5.03)	0.65 (0.08 - 5.22)
Taking part in any farm activity**	670	Unadjusted	0.72 (0.33 - 1.55)	0.65 (0.19 - 2.17)	1.38 (0.55 - 3.43)	0.38 (0.12 - 1.15)	0.81 (0.37 - 1.77)	1.13 (0.49 - 2.58)
		Adjusted	0.65 (0.29 - 1.42)	0.59 (0.17 - 2.03)	0.69 (0.29 - 1.68)	0.36 (0.11 - 1.12)	0.75 (0.33 - 1.67)	0.11 (0.48 - 2.58)

NC: Non-computable statistical output due to non-convergence of the model**. Bold:** Statistically significant output with p-value <0.05**. Model adjusted for:** Age, Sex and being born on the farm.

SI 6 Association between reported asthma-related outcome and exposure from leisure and household activities stratified by living on farms.

			Living on farm			Not living on a farm		
	N*	**Models**	**Asthma symptom score>=2**	**Parental reported asthma**	**Current Wheeze**	**Asthma symptom score>=2**	**Parental reported asthma**	**Current Wheeze**
Exposure variable			**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Leisure activities								
Entering the farm after spraying	667	Unadjusted	1.08 (0.44 - 2.64)	1.28 (0.33 - 4.97)	**2.94 (1.06 - 8.12)**	0.67 (0.15 - 2.96)	0.29 (0.47 - 3.54)	2.21 (0.83 - 5.83)
		Adjusted	0.95 (0.38 - 2.37)	1.16 (0.29 - 4.56)	1.50 (0.58 - 3.89)	0.68 (0.15 - 3.04)	1.26 (0.45 - 3.52)	2.26 (0.85 - 6.02)
	670	Unadjusted	1.02 (0.47 - 2.21)	1.46 (0.41 - 5.10)	1.23 (0.49 - 3.06)	0.85 (0.35 - 2.05)	0.74 (0.35 - 1.56)	1.26 (0.57 - 2.81)

Playing, swimming, and bathing in water bodies		Adjusted	0.89 (0.40 -1.96)	1.29 (0.36 - 4.63)	0.76 (0.31 - 1.86)	0.82 (0.33 - 2.01)	0.70 (0.32 - 1.51)	1.22 (0.54 - 2.76)
Eating produce from sprayed fields	667	Unadjusted	0.52 (0.24 - 1.14)	0.65 (0.19 - 2.19)	1.02 (0.41 - 2.55)	0.72 (0.30 - 1.71)	1.34 (0.64 - 2.82)	1.45 (0.64 - 3.29)
		Adjusted	0.45 (0.20 - 1.02)	0.65 (0.18 - 2.27)	0.60 (0.24 - 1.47)	0.7 (0.29 - 1.68)	1.56 (0.73 - 3.33)	1.47 (0.64 - 3.37)
Exposure from eating produce*** • Low (ref) • Moderate • High	308	Unadjusted	1 0.56 (0.25 - 1.21) NC	1 0.69 (0.20 - 2.32) NC	1 1.02 (0.40 - 2.59) NC	1 0.71 (0.29 - 1.76) 0.64 (0.07 - 5.27)	1 1.36 (0.64 - 2.91) 1.35 (0.28 - 6.50)	1 1.32 (0.56 - 3.10) NC
• Low (ref) • Moderate • High		Adjusted	1 0.48 (0.21 - 1.08) NC	1 0.69 (0.19 - 2.41) NC	1 0.63 (0.26 - 1.56) NC	1 0.71 (0.29 - 1.76) 0.64 (0.07 - 5.27)	1 1.58 (0.73 - 3.42) 1.63 (0.33 - 7.98)	1 1.35 (0.57-3.19) NC
Taking part in any leisure ****activity	664	Unadjusted	0.91 (0.37 - 2.23)	NC	1.15 (0.40 3.28)	0.61 (0.25 - 1.52)	0.79 (0.36 - 1.73)	1.23 (0.48 - 3.17)
		Adjusted	0.79 (0.31 - 2.00)	NC	0.95 (0.33 - 2.73)	0.59 (0.23 - 1.48)	0.86 (0.38 - 1.91)	1.23 (0.47 - 3.20)
Household pesticide exposure								
Using household chemicals for pests	641	Unadjusted	2.18 (0.73 - 6.53)	0.61 (0.17 - 2.15)	1.20 (0.42 - 3.42)	1.24 (0.47 -3.26)	0.75 (0.35 - 1.60)	1.58 (0.61 - 4.05)
		Adjusted	2.26 (0.75 - 6.83)	0.62 (0.17 - 2.23)	1.66 (0.53 - 5.12)	1.27 (0.48 - 3.36)	0.78 (0.36 - 1.67)	1.63 (0.63 - 4.19)
Pesticide odour in the home	660	Unadjusted	1.22 (0.50 - 2.98)	0.65 (0.18 - 2.30)	1.38 (0.54 - 3.48)	**3.30 (1.34 - 8.10)**	1.03 (0.49 - 2.19)	**3.64 (1.57 - 8.43)**
		Adjusted	1.26 (0.51 - 3.11)	0.67 (0.18 - 2.38)	0.78 (0.30 - 2.02)	**3.33 (1.35 - 8.19)**	1.06 (0.49 - 2.26)	**3.69 (1.59 - 8.56)**
Bringing PPE home_ Guardian (Mother and Father).	667	Unadjusted	0.65 (0.27 - 1.52)	0.66 (0.17 - 2.56)	0.50 (0.17 - 1.39)	1.16 (0.45 - 2.93)	0.67 (0.28 - 1.62)	0.90 (0.36 - 2.21)
		Adjusted	0.62 (0.26 - 1.47)	0.66 (0.17 -2.59)	0.48 (0.17 - 1.37)	1.12 (0.43 - 2.89)	0.78 (0.32 - 1.89)	0.90 (0.36 - 2.25)

Any family members living with the participant working on a farm	525	Unadjusted	0.75 (0.2 - 2.22)	0.65 (0.18 - 2.30)	0.35 (0.09 - 1.31)	0.37(0.10 - 1.35)	0.62 (0.19 - 2.02)	0.30 (0.09 - 0.96)
		Adjusted	0.97 (0.30 - 3.07)	0.23 (0.023 -2.41)	0.65 (0.15 - 2.70)	0.38 (0.10 - 1.41)	0.62 (0.19 - 2.03)	**0.31 (0.09 - 0.99)**

NC: Non-computable statistical output**. Bold:** Statistically significant output with p-value <0.05**.** Model adjusted for: Age, Sex and born on the farm.

PART C: APPENDICES

Note: The sections highlighted (Yellow) in the questionnaires are the questions that will be used for this study.

APPENDIX 1: Parental/Guardian Questionnaire

THE CHILD HEALTH AGRICULTURAL STUDY IN SOUTH AFRICA (CAPSA) 2017 - 2019

We will be following up with the schools for an update on all the referrals that we initiated during the study. From this point going onwards the following activities will be undertaken by the study 2018 – 2019:

- Home visits to conduct interviews with the guardians of the children (now – April 2018)
- 3 Follow-up urine samples from a proportion of the cohort to assess pesticide seasonal variations (2018)
- The follow-up study to repeat all the measurements done in the baseline study for comparison and also to assess how children have developed (January – June 2019)

Introduction: Interviewer Reads to Respondent

The purpose of this questionnaire is to collect information about your child's possible exposure to pesticides and their potential health effects. There is also a section collecting information on your child's development from their time of birth to date and any difficulties they may have had or are having currently. Your answers will help us figure out the levels of exposure you and your child may be experiencing from pollutants in the environment and how it is affecting your child's health. To do this we need to know quite a lot of information and therefore this will take 1 hour of your time with 9 sections of information to cover. If you need a break, please stop me and we can take one. If there is a question you do not want to answer, please let me know and we can skip it. All your responses are confidential and will not be shown to anyone outside the study team without your written consent.

Please enter the following consistently throughout the interview:

- 96 – other
- 97 – not applicable
- 98 – don't know/ don't remember
- 99 – missing

Before proceeding with interview, it is crucial that fieldworker fill in the consent form (labelled "Guardian Consent" on ODK) with the guardian.

1. GENERAL INFORMATION

Introduction: Interviewer Reads to Respondent

This section will focus on general details about the child and his/her family structure for example, where they live and with whom they live.

1.1.	Study ID Number:	
1.2.	Are you the primary caregiver of the **child** or the person most familiar with any health problem(s) the **child** has or had in the past?	☐$_1$ Yes ☐$_2$ No
Make all effort to interview the mother for the questionnaire, if not available reschedule or interview one most knowledgeable about the mother and the child.		
1.3.	How are you related to the **child**?	☐$_1$ Mother ☐$_2$ Father ☐$_3$ Grandmother ☐$_4$ Grandfather ☐$_5$ Aunt ☐$_6$ Uncle ☐$_{96}$ Other: **1.3.1. Specify** _____
1.4.	Study Area:	☐$_1$ Grabouw ☐$_2$ Piketberg ☐$_3$ Hex River Valley
1.5.	Is the household located on the property of a farm?	☐$_1$ Yes ☐$_2$ No
1.6.	If yes (to **1.5.**), what is the name of the farm?	
1.7.	If yes (to **1.5.**), what crops are produced on the farm?	☐$_1$ Apple and pears (stone fruits) ☐$_2$ Table grapes ☐$_3$ Wine grapes ☐$_4$ Wheat ☐$_5$ Citrus ☐$_6$ Other:**1.7.1. Specify:**_____

1.8.	Name of Interviewer:	☐$_1$ Wisdom ☐$_2$ Phillancia ☐$_3$ Phumla ☐$_4$ Maritza ☐$_5$ Denise ☐$_6$ Belinda ☐$_7$ Felicia ☐$_8$ Mereldine ☐$_{96}$ Other: **1.8.1 Specify:** _____
1.9.	What is the ethnicity of the parent / guardian?	☐$_1$ White ☐$_2$ Coloured ☐$_3$ Black ☐$_4$ Asian
1.10.	What is the ethnicity of the child?	☐$_1$ White ☐$_2$ Coloured ☐$_3$ Black ☐$_4$ Asian
1.11.	What is your first / home language?	☐$_1$ Afrikaans ☐$_2$ IsiXhosa ☐$_3$ English ☐$_4$ IsiZulu ☐$_5$ SeSotho ☐$_6$ IsiNdebele ☐$_7$ SiSwati ☐$_8$ Xitsonga ☐$_9$ Sepedi ☐$_{10}$ Tshivenda ☐$_{11}$ Setswana ☐$_{96}$ Other: **1.11.1 Specify**_____
1.12.	Does the **child** have any biological siblings or biological half-siblings?	☐$_1$ Yes ☐$_2$ No → **go to 2.1**
1.13.	How many brothers and sisters (both biological and half-siblings) does the **child** have?	**1.13.1** |__| Siblings **1.13.2** |__| Half-siblings
1.14.	Please give the ages of your children from the oldest to youngest: **(and indicate with a √ whether they live in this household)**	**1.14.1** 1st – Age |___| **1.14.2** 2nd – Age |___| **1.14.3** 3rd – Age |___| **1.14.4** 4th – Age |___| **1.14.5** 5th – Age |___|

		1.14.6 6th – Age |___| **1.14.7** 7th – Age |___| **1.14.8** 8th – Age |___| **1.14.9** 9th – Age |___| **1.14.10** 10th – Age |___|

2. SOCIO-DEMOGRAPHIC INFORMATION

Introduction: Interviewer Reads to Respondent

This section will focus on questions about work, income and education for the parent and child.

2.1. What is the highest level of education completed by the **child's** mother/female guardian?	☐0 No schooling ☐1 Primary education ☐2 Secondary education ☐3 Tertiary education
2.2. What is the highest level of education completed by the **child's** father /male guardian?	☐0 No schooling ☐1 Primary education ☐2 Secondary education ☐3 Tertiary education
2.3. What is the child's mother and father's marital status?	☐1 Married/Cohabiting ☐2 Widowed ☐3 Divorced/Separated ☐4 Never married/Never Lived together
2.4. Has this **child's** mother/ female guardian been employed in the last 12 months?	☐1 Yes ☐2 No ☐98 Don't Know
2.5. If yes (to 2.4), was this long-term/	☐1 Long-term / permanent work

permanent for 12 months, or contract /seasonal work? *(Choose one)* *(Hint: contract / seasonal work is short-term for only a few months or perhaps they move from one short-term job to another short-term job)*	**2.5.1.** For how long? _____ (months) ☐$_2$ Contract / seasonal work **2.5.2.** For how long? _____ (months)
2.6. If, yes (to **2.4**), what kind of paid work did the mother/ female guardian do?	☐$_1$ Worked on a farm **2.6.1** Specify crops: ☐$_1$ Apple & pears (stone fruits ☐$_2$ Table grapes ☐$_3$ Wine grapes ☐$_4$ Wheat ☐$_5$ Citrus ☐$_{96}$ Other: **2.6.1.1 Specify:** _____ ☐$_2$ Worked outside a farm but agricultural **2.6.2** Specify crops: ☐$_1$ Apple & pears (stone fruits ☐$_2$ Table grapes ☐$_3$ Wine grapes ☐$_4$ Wheat ☐$_5$ Citrus ☐$_{96}$ Other: **2.6.2.1 Specify:** _____ ☐$_3$ Non-farm related work _____
2.7. Has this **child's** father/ male guardian been employed in the last 12 months?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't Know

2.8. If yes (to 2.7), was this long-term/ permanent for 12 months, or contract /seasonal work? *(Choose one)* *(Hint: contract / seasonal work is short-term for only a few months or perhaps they move from one short-term job to another short-term job)*	☐1 Long-term / permanent work **2.8.1.** For how long? _____ (months) ☐2 Contract / seasonal work **2.8.2.** For how long? _____ (months)
2.9. If, yes (to **2.7**), what kind of paid work did the father/ male guardian do?	☐1 Worked on a farm **2.9.1** Specify crops: ☐1 Apple & pears (stone fruits ☐2 Table grapes ☐3 Wine grapes ☐4 Wheat ☐5 Citrus ☐96 Other: **2.9.1.1 Specify:** _____ ☐2 Worked outside a farm but agricultural **2.9.2** Specify crops: ☐1 Apple & pears (stone fruits ☐2 Table grapes ☐3 Wine grapes ☐4 Wheat ☐5 Citrus ☐96 Other: **2.9.2.1 Specify:** _____ ☐3 Non-farm related work_____
Does your **child** do any of the following activities in the field/vineyard/orchard with you or independently?	
2.10. Harvesting crops	☐1 Yes ☐2 No ☐98 Don't Know

2.11. Picking fruit	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't Know
2.12. Pesticide spraying, mixing or loading	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't Know
2.13. Cleaning of farm equipment	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't Know
2.14. Assist in a pesticide store	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't Know
The following set of questions is on household socio-economic position	
2.15. How many people live in this household?	_____
2.16. How much money or income does your household receive every month after tax? *(including. money from work, pension, informal business etc.)*	☐$_0$ No income ☐$_1$ R1 – R400 ☐$_2$ R401 – R800 ☐$_3$ R801 – R1600 ☐$_4$ R1601 – R3200 ☐$_5$ R3201 – R6400 ☐$_6$ R6401 – R12800 ☐$_7$ R12801 – R25600

	☐8 25601 or more ☐9 Refused to answer ☐98 Dont know
2.17. Do you or anyone in your household receive any of the following? *(Tick all that apply)*	☐1 Child Support Grant ☐2 Government grant ☐3 State old age pension ☐4 Disability grant ☐5 Care dependency grant ☐6 Foster care grant ☐96 Other: **2.17.1 Specify**_____

3. CHILDHOOD DEVELOPMENT

Introduction: Interviewer Reads to Respondent

To understand pesticide exposure, we need to know what other difficulties the child may have had during their development during the stages of pregnancy, birth and up to their school year.

Note: The following few questions are about your **child's** development from birth *(Hint: Ask for their child's Road to Health Card and mother's Ante-natal care clinic card - show them samples)*	
3.1 How many weeks were you pregnant when you found out you were expecting a baby?	☐1 0-4 weeks ☐2 5-8 weeks ☐3 9-12 weeks ☐4 13 or more weeks
3.2 Did you have any complications during your pregnancy?	☐1 Yes

	☐2 No → go to **3.4**
3.3 If yes (to **3.2**), please specify complication?	☐1 Diabetes ☐2 High Blood Pressure ☐3 Bleeding ☐96 Other: **3.3.1 Specify:** _____
3.4 When did you give birth (estimate) compared to your due date? *(Hint: Tick only one option, Do not read the options aloud)*	☐1 Weeks before _____ ☐2 Days before _____ ☐3 Due date ☐4 Days after _____ ☐98 Don't know/ Don't remember
3.5 How did you give birth?	☐1 Normal Vertex Delivery ☐2 Planned Caesarean ☐3 Emergency Caesarean ☐**98** Don't know
3.6 Was a vacuum extractor or forceps used to help the delivery?	☐1 Yes, forceps ☐2 Yes, vacuum extractor ☐3 No ☐**98** Don't know
3.7 Did you have any complications during birth?	☐1 Yes ☐2 No ☐98 Don't know

3.8 Did your baby have to stay in a hospital after birth for more than four (4) days?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
3.9 Did you have to stay in a Kangaroo Care Unit with your baby while in hospital?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
3.10 Was your baby put under lights because his/her skin was a yellow colour?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
3.11 Did you breastfeed your baby?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know/ Don't remember
3.12 How many months in total did you exclusively breastfeed? *(Hint: If a period is less than one month, state one month)*	|__|__| months ☐$_{98}$ Don't know/ Don't remember

3.13 Did your baby do any of the following at the same time as most other babies? *(Choose one)*	
3.13.1 Crawling?	☐$_1$ About the same time ☐$_2$ Rather earlier ☐$_3$ Rather later ☐$_{98}$ Don't know
3.13.2 Walking?	☐$_1$ About the same time ☐$_2$ Rather earlier ☐$_3$ Rather later ☐$_{98}$ Don't know

3.13.3 Talking?	☐$_1$ About the same time ☐$_2$ Rather earlier ☐$_3$ Rather later ☐$_{98}$ Don't know
3.14 In comparison to other children at the same age as your **child**, would you say your **child's** physical development is:	☐$_1$ Much earlier ☐$_2$ Somewhat earlier ☐$_3$ About the same time ☐$_4$ Somewhat later ☐$_5$ Much later ☐$_{98}$ Don't know/ Don't remember
3.15 Did your **child** attend pre-school?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
3.16 Did your **child** repeat any grades during primary school?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
3.17 Has your child ever received or been referred for learning support from any of the following professionals?	☐$_1$ Learner Support Teacher ☐$_2$ Occupational Therapist ☐$_3$ Speech Therapist ☐$_4$ Physiotherapist ☐$_5$ Educational Psychologist ☐$_{96}$ Other: **3.17.1 Specify:** _____

4. CHILD'S STRENGTHS AND DIFFICULTIES

Introduction: Interviewer Reads to Respondent

This section continues from the previous section about the difficulties that the child may have had during their development. These difficulties focus on social factors including behavior and emotion of your child.

Note: For each item, please mark the box for not true, somewhat true, or certainly true. It would help us if you answered all items as best you can even if you are not absolutely certain or the item seems daft! Please give your answers on the basis of the child's behaviour over the last six months. *(Hint: show the time line and the not true – certainly true cheat sheet)*		
4.1	Considerate of other people's feelings	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.2	Restless, overactive, cannot stay still for long	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.3	Often complains of headaches, stomach-aches or sickness	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.4	Shares readily with other children (treats, toys, pencils, games, music, etc.)	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.5	Often has temper tantrums or hot tempers	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.6	Rather solitary, tends to play alone	☐$_1$ Not true

	☐$_2$ Somewhat true ☐$_3$ Certainly true
4.7 Generally obedient, usually does what adults request	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.8 Many worries, often seems worried	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.9 Helpful if someone is hurt, upset or feeling ill	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.10 Constantly fidgeting or squirming	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.11 Has at least one good friend	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.12 Often fights with other children or bullies them	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.13 Often unhappy, down-hearted or tearful	☐$_1$ Not true

	☐$_2$ Somewhat true ☐$_3$ Certainly true
4.14 Generally liked by other children	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.15 Easily distracted, concentration wanders	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.16 Nervous or clingy in new situations, easily loses confidence	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.17 Kind to younger children	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.18 Often lies or cheats	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.19 Picked on or bullied by other children	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.20 Often volunteers to help others (parents, teachers, other children)	☐$_1$ Not true

	☐$_2$ Somewhat true ☐$_3$ Certainly true
4.21 Thinks things out before acting	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.22 Steals from home, school or elsewhere	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.23 Gets on better with adults than with other children	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.24 Many fears, easily scared	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.25 Sees tasks through to the end, good attention span	☐$_1$ Not true ☐$_2$ Somewhat true ☐$_3$ Certainly true
4.26 Overall, do you think that your child has difficulties in one or more of the following areas: emotions, concentration, behaviour or being able to get on with other people?	☐$_1$ Yes – minor difficulties ☐$_2$ Yes – definite difficulties ☐$_3$ Yes – severe difficulties ☐$_4$ No
If you have answered "Yes" **(to 4.26)**, please answer the following questions about these difficulties:	
4.27 How long have these difficulties been present?	☐$_1$ Less than a month

	☐$_2$ 1-5 months ☐$_3$ 6-12 months ☐$_4$ Over a year
4.28 Do the difficulties upset or distress your child?	☐$_1$ Not at all ☐$_2$ Only a little ☐$_3$ Quite a lot ☐$_4$ A great deal
4.29. Do the difficulties **(**in **4.26)** interfere with your child's everyday life in the following areas?	
4.29.1 Home life	☐$_1$ Not at all ☐$_2$ Only a little ☐$_3$ Quite a lot ☐$_4$ A great deal
4.29.2 Friendships	☐$_1$ Not at all ☐$_2$ Only a little ☐$_3$ Quite a lot ☐$_4$ A great deal
4.29.3 Classroom learning	☐$_1$ Not at all ☐$_2$ Only a little ☐$_3$ Quite a lot ☐$_4$ A great deal
4.29.4 Leisure activities	☐$_1$ Not at all ☐$_2$ Only a little ☐$_3$ Quite a lot

	☐4 A great deal
4.29.5 Do the difficulties put a burden on you or the family as a whole?	☐1 Not at all ☐2 Only a little ☐3 Quite a lot ☐4 A great deal

5. GENERAL MEDICAL HISTORY OF THE CHILD

Introduction: Interviewer Reads to Respondent

This section is quite detailed on the health and medical history of the child and family. If you have the Road to Health Card of the child and the maternal records with information on the pregnancy please avail them so that we can refer to them.

5.1 What is the mother's date of birth?	_____ (dd/mm/yyyy)
5.2 What is the mother's age?	_____ (years)
5.3 Which health facility (MOU) did the mother attend during her pregnancy with this participant?	_____
5.4 What was the weight of the mother during pregnancy? *(Hint: refer to maternal health records if available)*	_____ (kg) ☐98 Don't know
5.5 What was the height of the mother during pregnancy? *(Hint: refer to maternal health records if available or measure the current height of mother)*	_____ (cm) ☐98 Don't know
5.6 What was the weight of the mother at the birth of the participant? *(Hint: refer to maternal health records if available)*	_____ (kg) ☐98 Don't know
5.7 What was the duration of pregnancy (gestational age) at the birth of the child? *(Hint: refer to Road to Health card if available)*	_____(weeks)

5.8 What was the **child's** birth weight (grams)? *(Hint: refer to Road to Health card if available)*	_____(g)
5.9 What was the **child's** birth length (cm)? *(Hint: refer to Road to Health card if available)*	_____(cm)
5.10 What was the **child's** birth head circumference (cm)? *(Hint: refer to Road to Health card if available)*	_____(cm)
5.11 What was the **child's** APGAR score? *(Hint: refer to Road to Health card if available)*	_____(1 min) _____(5 min)
5.12 During the 1st and 2nd trimester of the mother's pregnancy, did she carry a heavy load >5 kg?	☐1 Yes ☐2 No ☐98 Don't Know
5.13 If yes (to **5.11**), how frequently were you involved with the task of carrying a load >5kg?	☐1 Seldom ☐2 Sometimes ☐3 Often ☐98 Don't Know
5.14 Currently, how would you rate your **child**'s health in general?	☐1 Poor ☐2 Fair ☐3 Good ☐4 Very good ☐5 Excellent

5.15 Has your **child** ever been diagnosed by a doctor to have / have had any of the following conditions?

Condition/Illness	**Response**	**If Yes, age of child when diagnosed**
5.15.1 Diabetes	☐1 Yes	**5.15.1.1**_____ (years)

	☐$_2$ No ☐$_{98}$ Don't know	
5.15.2 Obesity/Overweight	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.2.1**_____ (years)
5.15.3 Cancer	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.3.1**_____ (years)
5.15.3.2 If Yes (to **5.15.3.)**, what was the type of cancer?		_____
5.15.4 Fits/Epilepsy/Seizures	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.4.1**_____ (years)
5.15.5 Foetal Alcohol Syndrome (FAS)	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.5.1**_____ (years)
5.15.6 Heart problems	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.6.1**_____ (years)
5.15.7 Back problems	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know	**5.15.7.1**_____ (years)

5.15.8 Attention Deficit Hyperactivity Disorder (ADHD)	☐1 Yes ☐2 No ☐98 Don't know	**5.15.8.1** _____ (years)
5.15.9 Autism	☐1 Yes ☐2 No ☐98 Don't know	**5.15.9.1** _____ (years)
5.15.10 Tuberculosis	☐1 Yes ☐2 No ☐98 Don't know	**5.15.10.1** _____ (years)
5.15.11 High Blood Pressure	☐1 Yes ☐2 No ☐98 Don't know	**5.15.11.1** _____ (years)
5.15.12 Mumps	☐1 Yes ☐2 No ☐98 Don't know	**5.15.12.1** _____ (years)
5.15.13 Thyroid condition - Hyper/Hypothyroidism	☐1 Yes ☐2 No ☐98 Don't know	**5.15.13.1** _____ (years)
5.15.14 Any Lung infections	☐1 Yes ☐2 No ☐98 Don't know	**5.15.14.1** _____ (years)

5.15.15 Was your **child** born with an abnormality in their reproductive organ/ have they been diagnosed by a doctor with a reproductive health problem?	☐$_1$ Yes ☐$_2$ No (go to **5.15.19.**) ☐$_{98}$ Don't know (go to **5.15.19.**)
5.15.16 If yes (to **5.15.15.**), what was/is the name of the condition?	
5.15.17 If yes (to **5.15.15.**), did your **child** go for an operation for the abnormality?	☐$_1$ Yes ☐$_2$ No
5.15.18 If yes (to **5.15.15.**), did your **child** receive medication for the abnormality?	☐$_1$ Yes ☐$_2$ No
5.15.19 Has your **child** ever experienced an injury, resulting in a swelling of the reproductive organ area that has this been diagnosed by a doctor?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
If the child is male, go to question 5.17	
5.16 If the child is a female, complete the following questions with the mother / female guardian:	
5.16.1 Has your daughter started menstruating?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.16.2 If yes (to **5.16.1)**, at what age did she start menstruating?	_____ (years)
5.16.3 What is your daughter's average menstrual cycle length?	☐$_1$ 24 days or less ☐$_2$ 25–30 days ☐$_3$ 31–35 days ☐$_4$ 36–42 days

	☐$_5$ 43 days or more ☐$_6$ Too irregular to say ☐$_{98}$ Don't know
5.16.4 Has your child ever been diagnosed by a doctor with any of the following reproductive conditions? *(Tick all that apply)*	☐$_1$ Polycysitc Ovarian Syndrome ☐$_2$ Premature Ovarian Failure ☐$_3$ Endometriosis ☐$_4$ Uterine Fibroids ☐$_{98}$ Don't know
5.16.5 During the past 12 months, did you (the mother) ever go for 6 weeks or more without a menstrual period? *(Hint: Do not count times when you were pregnant, breast-feeding, or using birth control pills)*	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.16.6 During the past 12 months, did you ever bleed or spot between menstrual periods? *(Hint: Do not count spotting at the beginning or end of your period)*	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.17 Has your **child** ever had wheezing or whistling in the chest at any time in the past?	☐$_1$ Yes ☐$_2$ No → go to **5.22** ☐$_{98}$ Don't know
5.18 If yes (to **5.17**), has your **child** had wheezing or whistling in the chest in the past 12 months?	☐$_1$ Yes ☐$_2$ No → go to **5.22** ☐$_{98}$ Don't know
5.19 If yes **(**to **5.17)** how many attacks of wheezing has the **child** had in the past 12 months?	☐$_0$ None ☐$_1$ 1 to 3 times

	☐$_2$ 4 to 12 times ☐$_3$ >12 times ☐$_{98}$ Don't know
5.20 In the past 12 months, how often on average, has your **child's** sleep been disturbed due to wheezing?	☐$_0$ Never woken with wheezing ☐$_1$ Less than one night per week ☐$_2$ One or more nights per week ☐$_{98}$ Don't know
5.21 In the past 12 months, has the wheezing ever been serious enough to limit your **child's** speech to only one or two words at a time between breaths?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.22 Has your **child** ever had asthma?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.23 In the past 12 months, has your **child's** chest sounded wheezy during or after exercise?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.24 In the past 12 months, has your **child** had a dry cough at night, apart from a cough associated with a cold or chest infection?	☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Don't know
5.25 Does the **child** have/had any other illness diagnosed by a doctor that needs you to attend the clinic regularly for medication (≥ 3 months) apart from those listed above (in **5.15**)?	☐$_1$ Yes ☐$_2$ No → go to **5.27** ☐$_{98}$ Don't know → go to **5.27**

5.26 If yes (to **5.25**), specify condition? *(Hint: if they don't know, look in clinic card and write down diagnosis or specific clinic they attend)*	_____ __ _____ __
5.27 Has your **child** taken any daily medication during the last three months?	☐1 Yes ☐2 No → go to **5.31** ☐98 Don't know
5.28 Was the medication prescribed by a doctor?	☐1 Yes ☐2 No
5.29 What is the name of the medication? *(Hint: if they don't know, ask for the medication box and write down the information)*	
5.30 Specify the frequency of taking this medication? *(Hint: if they don't know, ask for the medication box and write down the information)*	
5.31 Does anyone in the biological family have any of the following allergic diseases? (*Tick all that apply)*	☐1 Asthma ☐2 Eczema ☐3 Hayfever (Rhinitis) ☐4 Food allergy ☐98 Don't know

6. PESTICIDE AND HOUSEHOLD EXPOSURE

Introduction: Interviewer Reads to Respondent

This section will focus on the possible history and current exposure to pesticides during pregnancy, work and residential location. There will also be questions on other possible chemical exposures to the child, such as indoor exposures.

Past exposures will focus on the period during the mother's pregnancy with the child participant. This section starts off asking questions about the mother and then about the father.	
6.1 Where did the mother of the child live when she was pregnant?	☐1 On a farm **6.1.1** Specify crops grown: ☐1 Apple & pears (stone fruits ☐2 Table grapes ☐3 Wine grapes ☐4 Wheat ☐5 Citrus ☐96 Other: **6.1.1.1 Specify:** _____ ☐2 Outside a farm (surrounding town/Village/Hamlet) **6.1.2** Specify crops grown ☐1 Apple & pears (stone fruits ☐2 Table grapes ☐3 Wine grapes ☐4 Wheat ☐5 Citrus ☐96 Other: **6.1.2.1 Specify:** _____ ☐3 Non-farm area _____
6.2 Was the mother a farm worker?	☐1 Yes ☐2 No → go to **6.6**
6.3 If yes (to **6.2.**), did she spray/mix/load pesticides?	☐1 Yes ☐2 No → go to **6.6** ☐98 Don't know

6.4 If yes (to **6.3**), for how long in a 12-month period did the mother spray/mix/load pesticides?	☐$_1$ 1-4 weeks (about a month) ☐$_2$ 5-8 weeks (about 2 months) ☐$_3$ ≥9 weeks (3 months or more) ☐$_{98}$ Don't know
6.5 How often did the mother bring work clothing (PPE) home to get washed with the rest of the washing? *(Hint: overalls, boots, masks, respirator, gloves goggles)*	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
6.6 Did the mother enter in the field/ vineyard/ orchard while there was pesticide spraying? *(Hint: this includes work/non-work related purposes)*	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always

These questions are about the father/partner who was present during the mother's pregnancy with the participant. If the biological father was absent, the questions are about the mother's partner who was present.

6.7 Did the father/partner live with the mother during her pregnancy with the participant?	☐$_1$ Yes ☐$_2$ No (go to **6.10**)
6.8 Did the father/partner do farm work as a pesticide sprayer/mixer/loader?	☐$_1$ Yes ☐$_2$ No → go to **6.10** ☐$_{98}$ Don't know
6.9 How often did the father's/partner's work clothing (PPE) get washed with the rest of the washing at home where the mother lived?	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes

	☐3 Always
Current work exposure: for mother/female guardian The following section will inquire about the current mother's/female guardian's work	
6.10 Is the mother/female guardian a farm worker?	☐1 Yes ☐2 No → go to **6.17**
6.11 What crops does the mother/female guardian grow or work on?	☐1 Apple and pears (stone fruits) ☐2 Table grapes ☐3 Wine grapes ☐4 Wheat ☐5 Citrus ☐96 Other: **6.11.1 Specify:** _____
6.12 If yes (to **6.10.**), what is the mother/ female guardian's job title? (*Tick all that apply*)	☐1 Supervisor ☐2 Sprayer/Mixer/Loader ☐3 Non-sprayer farm worker
6.13 Since when has she been working in the job of **6.12**?	☐0 Never ☐1 1-5 years ago ☐2 5-10 years ago ☐3 >10 years ago ☐98 Don't know
6.14 Does the mother/ female guardian take work clothes / personal protective equipment (PPE) home after work? *(Hint: overalls, boots, masks, respirator, gloves goggles)*	☐1 Yes ☐2 No

6.15 If yes (to **6.14**), does their work clothing (PPE) get washed with the rest of the washing at home?	☐$_1$ Yes ☐$_2$ No
6.16 How often does the mother/ female guardian take produce (crops/fruit) home after entering a treated field/vineyard/orchard?	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
6.17 How often does the mother/ female guardian come into contact with empty pesticide containers? *(Hint: for domestic purposes like water storage and for disposal like burning)*	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
Current work exposure: for the father/ male guardian *(Hint: In this case, the male guardian could be the mother's partner who is not the biological parent, but is involved with caring for the participant).*	
6.18 Is the father/male guardian a farm worker?	☐$_1$ Yes ☐$_2$ No → go to **6.25**
6.19 What crops does the father/male guardian grow or work on?	☐$_1$ Apple and pears (stone fruits) ☐$_2$ Table grapes ☐$_3$ Wine grapes ☐$_4$ Wheat ☐$_5$ Citrus ☐$_{96}$ Other: **6.19.1 Specify:** _____
6.20 If yes (to **6.18**), what is the father/ male guardian's job title? (*Tick all that apply*)	☐$_1$ Supervisor

	☐$_2$ Sprayer/Mixer/Loader ☐$_3$ Non-sprayer farm worker
6.21 Since when has he been working in the job from **6.20**?	☐$_0$ Never ☐$_1$ 1-5 years ago ☐$_2$ 5-10 years ago ☐$_3$ >10 years ago ☐$_{98}$ Don't know
6.22 Does the father/ male guardian take work clothes or personal PPE home after work? *(Hint: overalls, boots, masks, respirator, gloves goggles)*	☐$_1$ Yes ☐$_2$ No
6.23 If yes (to **6.22**), does their work clothing (PPE) get washed with the rest of the washing at home?	☐$_1$ Yes ☐$_2$ No
6.24 How often does the father/ male guardian take produce (crops/fruit) home after entering a treated field/vineyard/orchard?	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
6.25 How often does the father/ male guardian come into contact with empty pesticide containers? *(Hint: for domestic purposes like water storage and for disposal like burning)*	☐$_0$ Never ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
Household Exposure:	

The following section enquires about any pesticide exposure in the house. We will ask you on the specific details about the type of application and who other than the mother or father may be involved with applying or using pesticides.	
6.26 Besides the male and female guardians, how many other people in the household work in agriculture? *(Hint: write down the number)*	_____ If 0 → go to **6.28**
6.27 Does this other person/s bring work clothes or personal protective clothing or even pesticides, home after work? *(Hint: overalls, boots, masks, respirator, gloves, goggles)*	☐1 Yes ☐2 No
6.28 Do you use any pesticides inside/ outside your house for gardening or pest control? (*Hint: show picture for household pesticides)*	☐1 Yes ☐2 No **go to 6.30**
Reasons for chemical application or spraying may include the following: • *Insects include: mosquitoes, flies, cockroaches, fleas, moths, bees, wasps, ants, beetles, crickets, lice, spiders, termites, bedbugs and ticks* • *Weeds* • *Mammals include: Rats, Mice, Squirrels* • *Plant disease: mould, mildew, leaf spot, root rot, viruses*	
6.29 What are your reasons for the indoor/outdoor application/spraying of chemicals? (*Tick all that apply*) *(Hint: Show cheat sheet for pests)*	☐1 Insects ☐2 Weeds ☐3 Mammals ☐96 Other **6.29.1 Specify**_____
6.30 What pests do you have in your home?	_____
6.31 What are the names of the products that you used in the past year to control pests or for gardening? *(Name the pest and product used)* *(Hint: Interviewer to ask for consent to take a picture of the house and the pesticide products at this household)*	_____ _____
6.32 Who applies pesticides/ chemicals in the house? (*Tick all that apply*)	☐1 Respondent or any adult in household

	☐2 Children ☐3 External company/contractor (go to **6.34)** **6.32.1** Specify company name: _____
6.33 In the past 12 months, how often did you or another family member apply pesticides in the house? *(Hint: Show cheat sheet of time frame months and spraying seasons which occur in these months)*	☐1 Once a year ☐2 Once a month ☐3 Once a week ☐4 Twice a week ☐5 More than twice a week
6.34 In the past 12 months, how often did an external company or a contractor came to your house to apply pesticides in the house? *(For e.g.: to fumigate for household pests like fleas)*	☐1 Once a year ☐2 Once a month ☐3 Once a week ☐4 Twice a week ☐5 More than twice a week
6.35 In what form is the chemical/pesticide usually applied/sprayed? (*Tick all that apply)* *(Hint: Show cheat sheet for the different forms of pesticides)*	☐1 Spray ☐2 Liquid ☐3 Granules ☐4 Fogger ☐5 Powder ☐6 Bait/Trap ☐7 Moth balls ☐8 Dip ☐9 Collar

	☐10 Pet shampoo
6.36 If you use chemicals, where do you get them from? (*Give examples of sources*)	_____ _____
6.37 Do you ever buy chemicals to control pests from informal traders? (*for e.g. street vendors)*	☐1 Yes ☐2 No
6.38 Has there been mould or mildew on any surface inside the home in the last 12 months?	☐1 Yes ☐2 No ☐98 Don't know
6.39 Within the last 12 months have you had wet or damp spots on surfaces inside your home other than in the basement? *(for e.g. on walls, wall paper, ceilings or carpet)* *(Hint: This could be due to for example leaks, burst pipe, flooding)*	☐1 Yes ☐2 No ☐98 Don't know
6.40 Which of the following do you mostly use for cooking or heating?	☐1 Coal, coke or wood (solid fuel) ☐2 Gas (gas from the mains) ☐3 Electricity ☐4 Paraffin (Kerosene) ☐5 Gas (from bottles or other non-mains sources) ☐96 Other **6.40.1 Specify**:_____
Child Pesticide Poisoning: The next questions will focus on the potential poisonings with the pesticides and chemicals mentioned above	
6.41 Has the **child** ever had pesticide poisoning? *(Hint: Show cheat sheet of pesticide poisoning symptoms)*	☐1 Yes ☐2 No ☐98 Don't know

6.42 Has your **child** ever experienced any unusual signs or symptoms (that they usually don't suffer from) after exposure to pesticides? *(Hint: dizziness, skin irritation, vomiting, blurry vision etc)*	☐1 Yes ☐2 No → go to **7.1** ☐98 Don't know → go to **7.1**
6.43 If yes **(**to **6.41),** was the pesticide poisoning confirmed by a doctor?	☐1 Yes ☐2 No
6.44 If yes **(**to **6.41),** specify the hospital or clinic the **child** was taken to?	_____
6.45 When did the last episode of pesticide poisoning happen?	_____
6.46 How many times has pesticide poisoning occurred?	_____

7. CHILD RESIDENTIAL HISTORY

Introduction: Interviewer Reads to Respondent

Please answer the following questions regarding the places where your child has lived: In the case where the current residence is short-term, meaning the child has only lived here for a year or less, we would need to know the exposure in both their current and previous residence. In this case, please answer both sections on current residence AND the section after on previous residence.

Pesticide exposure related to the child in their current residence	
7.1 Where does the **child** currently live?	☐1 On a farm **7.1.1** Name of farm: _____ ☐2 Next to a farm (Town/Village/Hamlet <1000m) ☐3 Non-Farm area
7.2 For how long has the child been living there?	|__ | years |__ | months

7.3 Does the pesticide spraying that happens on the farm or on the nearest farm come into your home? *(Hint: was it detectable by the sense of smell)*	☐$_1$ Yes ☐$_2$ No (go to **7.6**) ☐$_{98}$ Don't know
7.4 During which time of the year do pesticides which are sprayed (in **7.3**) come into the house? *(Tick all that apply)*	☐$_1$ January - March ☐$_2$ April - June ☐$_3$ July - September ☐$_4$ October - December
7.5 How often does the pesticide spraying come into the house during the spraying period?	☐$_1$ Almost every day ☐$_2$ 2-3 times per week ☐$_3$ Once per week ☐$_4$ Once per month
7.6 Are you informed by the farm management on your farm or the closest farm, when pesticides are being sprayed?	☐$_0$ Never (go to **7.8**) ☐$_1$ Rarely ☐$_2$ Sometimes ☐$_3$ Always
7.7 If rarely, sometimes or always, is there any advice provided on how to behave or protect your family from pesticide exposure?	☐$_1$ Close the windows during the day ☐$_2$ Close the windows at night ☐$_3$ Close the windows during the spraying ☐$_4$ That you and your family members should not access the sprayed area for a certain time after the spraying ☐$_5$ That you and your family members should not pick fruits from the field for a certain time after the spraying ☐$_{96}$ Other measures you take as soon as you realize that there are pesticide sprayed?

	7.7.1. Other measures: _____
7.8 Do you do any preventive action to protect your family from pesticide exposure?	☐$_1$ Close the windows during the day ☐$_2$ Close the windows at night ☐$_3$ Close the windows during the spraying ☐$_4$ That you and your family members should not access the sprayed area for a certain time after the spraying ☐$_5$ That you and your family members should not pick fruits from the field for a certain time after the spraying ☐$_{96}$ Other measures you take as soon as you realize that there are pesticide sprayed? **7.8.1.** Other measures: _____
7.9 What are the sources of drinking water in the household?	☐$_1$ Municipality water scheme/Tap water ☐$_2$ Borehole ☐$_3$ Spring ☐$_4$ Rain water tank ☐$_5$ Dam/pool/stagnant water ☐$_6$ River/stream ☐$_7$ Water vendor ☐$_8$ Water tanker ☐$_{96}$ Other: **7.9.1 Specify:** _____
7.10 What are the sources of water for using inside the house? *(Hint: this may be the same as the drinking source, or perhaps they use different sources for washing dishes or clothes for example)*	☐$_1$ Municipality water scheme/Tap water ☐$_2$ Borehole ☐$_3$ Spring ☐$_4$ Rain water tank ☐$_5$ Dam/pool/stagnant water ☐$_6$ River/stream ☐$_7$ Water vendor

	☐8 Water tanker ☐96 Other: **7.10.1 Specify:** _____

Pesticide exposure related to the child in their previous residence These questions will attempt to capture possible exposure if you changed residence in the last years. They will be a repeat of the questions asked above but will be referring to your previous residence.	
7.11 Did the **child** live in a different home from the current one since he / she was born?	☐1 Yes ☐2 No (go to **8.1)**
7.12 During which years did the child live there?	Date: _____ **7.12.1** _____ years/ months (calculated from above)
7.13 Where did the **child** live?	☐1 On a farm **7.13.1** Name of farm: _____ ☐2 Next to a farm (Town/Village/Hamlet <1000m) ☐3 Non-farm area: _____
7.14 Did the pesticide spraying that happened on the farm or on the nearest farm come into your home? *(Hint: was it detectable by the sense of smell)*	☐1 Yes ☐2 No → **go to 7.17** ☐98 Don't know/ Don't remember
7.15 What time of the year did pesticides which were sprayed (from **7.14**) come into the house? *(Tick all that apply)*	☐1 January - March ☐2 April - June ☐3 July - September

	☐4 October - December
7.16 If yes (to **7.14),** how often did the pesticide spraying come into the house during the spraying period?	☐1 Almost every day ☐2 2-3 times per week ☐3 Once per week ☐4 Once per month
Pesticide exposure related to the child in their previous residence (2) These questions will attempt to capture possible exposure if you changed residence in the last years. They will be a repeat of the questions asked above but will be referring to your previous residence.	
7.17 Did the **child** live in a different home from the current one, since he / she was born?	☐1 Yes ☐2 No go to **8.1**
7.18 During which years/months did the child live there?	Dates: _____ 7.18.1 _____ years/ months (calculated from above)
7.19 If yes (to **7.17**), where did the **child** live?	☐1 On a farm **7.19.1** Name of farm: _____ ☐2 Next to a farm (Town/Village/Hamlet <1000m) ☐3 Non-Farm area _____
7.20 Did the pesticide spraying that happened on the farm or the nearest farm, come into your home? *(Hint: was it detectable by the sense of smell)*	☐1 Yes ☐2 No → go to **8.1**
7.21 What time of the year did pesticides which were sprayed (from **7.20**) come into the house? *(Tick all that apply)*	☐1 January - March ☐2 April - June ☐3 July - September

	☐4 October - December
7.22 If yes (to **7.20**), how often did the pesticide spraying come into the house during the spraying period?	☐1 Almost every day ☐2 2-3 times per week ☐3 Once per week ☐4 Once per month

8. CHILD'S DIET AND NUTRITION

Introduction: Interviewer Reads to Respondent

This is a short section on the child's daily eating pattern, what type of food they eat and how regular they eat this food type.

8.1 How would you describe the **child's** appetite?	☐1 Poor ☐2 Fair ☐3 Good
8.2 As an infant/ toddler/ young child, was the child given soya milk formula?	☐1 Yes ☐2 No ☐98 Don't know
8.3 On average, how many servings of the following foods does your child have in a week?	
8.3.1 Fruits?	☐0 Never ☐1 Rarely (1-3 times) ☐2 Sometimes (4-6 times) ☐3 Always (everyday)
8.3.2 Vegetables (excluding potatoes)?	☐0 Never ☐1 Rarely (1-3 times)

	☐$_2$ Sometimes (4-6 times) ☐$_3$ Always (everyday)
8.3.3 Red meat such as beef and lamb?	☐$_0$ Never ☐$_1$ Rarely (1-3 times) ☐$_2$ Sometimes (4-6 times) ☐$_3$ Always (everyday)
8.4 What type of milk does your **child** usually drink?	☐$_0$ Does not drink milk ☐$_1$ Full cream milk ☐$_2$ Low or fat free milk ☐$_3$ Unpasteurized milk ☐$_4$ Soya milk
8.5 How often does your **child** drink cow's milk or soya milk in a week?	☐$_1$ Rarely (1-3 times) ☐$_2$ Sometimes (4-6 times) ☐$_3$ Always (everyday)
8.6 How many times a week does your **child** eat fast food like Steers, KFC, Nando's, Chicken Licken, etc.?	☐$_0$ Never ☐$_1$ Rarely (1-3 times) ☐$_2$ Sometimes (4-6 times) ☐$_3$ Always (everyday)

9. SMOKING AND ALCOHOL CONSUMPTION

Introduction: Interviewer Reads to Respondent

To understand pesticide exposure, we need to know what other exposures the child may have had. This is a section on the smoking and alcohol exposure that the child may have had before, during and after pregnancy.

(HINT: If the biological mother is NOT answering the questions, please phrase them accordingly)

Note: Now I am going to ask you some questions about drinking alcohol

9.1 Does the mother currently drink alcohol?	☐$_0$ Never ☐$_1$ Less than 1 glass a day ☐$_2$ About 1 glass a day ☐$_3$ More than 1 glass a day
9.2 Did the mother drink alcohol during pregnancy?	☐$_0$ Never ☐$_1$ Less than 1 glass a day ☐$_2$ About 1 glass a day ☐$_3$ More than 1 glass a day
9.3 Has the mother ever drank alcohol in the past?	☐$_0$ Never **(go to 9.8)** ☐$_1$ Less than 1 glass a day ☐$_2$ About 1 glass a day ☐$_3$ More than 1 glass a day
9.4 Who is the responder on the mother's smoking and alcohol consumption?	☐$_1$ Mother ☐$_2$ Guardian

Note: For Questions **9.5. – 9.11.**: Please, complete the **correct option** as indicated.

9.5 **CURRENT DRINKING** **9.5.1** (*Hint: Question for the mother)* Have you ever felt that you should cut down on your drinking? **9.5.2** (*Hint: Question for the guardian)* Has she (the mother) ever felt that she should cut down on her drinking?	**Mother:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know	**Guardian:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know
9.6 **CURRENT DRINKING** **9.6.1** (*Hint: Question for the mother)*		

Have people annoyed you by criticizing your drinking? **9.6.2** (*Hint: Question for the guardian)* Have people annoyed her (the mother) by criticizing her drinking?	**Mother:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know	**Guardian:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know
9.7 CURRENT DRINKING **9.7.1** (*Hint: Question for the mother)* Have you ever felt bad or guilty about your drinking? **9.7.2** (*Hint: Question for the guardian)* Has she (the mother) ever felt bad or guilty about her drinking?	**Mother:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know	**Guardian:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know
9.8 CURRENT DRINKING **9.8.1** (*Hint: Question for the mother)* Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover? **9.8.2** (*Hint: Question for the guardian)* Has she (the mother) ever had a drink first thing in the morning to steady her nerves or to get rid of a hangover?	**Mother:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know	**Guardian:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know
9.9 PAST DRINKING **9.9.1** (*Hint: Question for the mother)* When you did drink alcohol, did you ever feel that you should cut down on your drinking? **9.9.2** (*Hint: Question for the guardian)* When she (the mother) did drink alcohol, did she ever feel that she should cut down on her drinking?	**Mother:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know	**Guardian:** ☐$_1$ Yes ☐$_2$ No ☐$_{98}$ Do not know

9.10 PAST DRINKING **9.10.1** (*Hint: Question for the mother)* When you did drink alcohol, did people annoy you by criticizing your drinking? **9.10.2** (*Hint: Question for the guardian)* When she (the mother) did drink alcohol, did people annoy her by criticizing her drinking?	**Mother:** ☐1 Yes ☐2 No ☐98 Do not know	**Guardian:** ☐1 Yes ☐2 No ☐98 Do not know
9.11 PAST DRINKING **9.11.1** (*Hint: Question for the mother)* When you did drink alcohol, did ever feel bad or guilty about your drinking? **9.11.2** (*Hint: Question for the guardian)* When she (the mother) did drink alcohol, did she ever feel bad or guilty about her drinking?	**Mother:** ☐1 Yes ☐2 No ☐98 Do not know	**Guardian:** ☐1 Yes ☐2 No ☐98 Do not know
9.12 PAST DRINKING **9.12.1** (*Hint: Question for the mother)* When you did drink alcohol, did you ever have a drink first thing in the morning to steady your nerves or to get rid of a hangover? **9.12.2** (*Hint: Question for the guardian)* When she (the mother) did drink alcohol, did she ever have a drink first thing in the morning to steady her nerves or to get rid of a hangover?	**Mother:** ☐1 Yes ☐2 No ☐98 Do not know	**Guardian:** ☐1 Yes ☐2 No ☐98 Do not know
9.13 Did the mother smoke during pregnancy?	☐0 Never ☐1 Less than 1 cigarette a day ☐2 1-5 cigarettes a day ☐3 6-20 cigarettes a day ☐4 More than a packet a day	

9.14 Does anyone in the household currently smoke or ever smoked at home?	☐$_0$ None ☐$_1$ One ☐$_2$ Two ☐$_3$ More than two
9.15 Has the mother ever taken any recreational drugs during pregnancy eg: Tik, Marijuana? *(Hint: Interviewer to record the name(s) of the drug(s) used)*	☐$_1$ Never ☐$_2$ Less than 1 times a week ☐$_3$ 1-6 times a week ☐$_4$ Once a day ☐$_5$ More than once a day

Signature: ..... Date: .....

Mother/Father/Other (please specify:)_____

Thank you

APPENDIX 2: Participant questionnaire

Assent: It is crucial for the fieldworker to have gained assent (permission) from the child to go ahead with the data collection before beginning the interview.

Intro: It is essential that the fieldworker informs the learner before starting with questions:
This interview will be about our study on pesticides which are the sprays that you may have heard or seen or smelt or all of these, while you are living around and or on the farm vineyards. [Show picture of the pesticide spraying on vineyard].
Explain that the study we are doing is to find out if this spraying may be harmful to their health and learning and so our questions we ask will be about the pesticides, their activities outdoors and indoors so activities on social media use, their health and learning.

Serial measurements and cell phone use questionnaire

Your answers will be treated strictly confidential and only analysed anonymous

(Hint: Fill information for question a to i out according to the information in the participant envelope, and remember to fill the individual station from in parallel)

a. Study number: _____

b. Physical Address: _____

c. Participant Grade: _____

d. Participant Age: _____

e. Date seen: ___/_____/_____
Day Month Year

f. What is the name of your school:

1. Glen Elgin
2. De Rust Combined
3. Kathleen Murray Primary
4. Van Cutsem Combined
5. FJ Conradie Primary
6. Groenvlei Primary
7. Steynville Primary
8. Steynville Secondary
9. Hex Vallei Secondary
10. Hex River High School
11. Groenberg Secondary

g. Participant first/home language:

1. Afrikaans
2. isiXhosa
3. English
4. Other (**h.** Specify: _____)

i. Interviewed by:

1. Wisdom Basera
2. Phillancia Januarie
3. Chad Dirks
4. Zanele Gwanya
5. Althea Claasen
96. Other (**j.** Specify: _____)

SECTION A: Pesticide Exposure The following section is about possible contact with pesticides.	
1.1. Are you currently living on a farm?	0. No 1. Yes
1.1.1. Please specify the name of the farm?	
1.2. Is any one of your family members who lives with you working on a farm?	0. Nobody works on a farm 1. Mother 2. Father 3. Siblings 4. Grandparents 5. Other
1.2.1. Please specify the name of the farm or farms if there is more than one?	
Since the last time we saw you for the urine sample and questionnaire	
1.3. Did you see any of these spraying activities happening on the field/vineyard/orchard close to you? **Hint**: show spraying activities cheat sheet 1	0. Never 1. Aeroplane spraying 2. Tractor spraying 3. Knapsack spraying
1.3.1. Specify how many times you saw aeroplane spraying? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.3.2. Specify how many times you saw tractor spraying? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.3.3. Specify how many times you saw knapsack spraying? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
Since the last time we saw you for the urine sample and questionnaire	
1.4. How often could you smell the pesticides that were being sprayed on the nearest field/vineyard/orchard? Even if you did not see that they were sprayed?	0. Never 1. One day a week 2. Two days a week

Hint: show cheat sheet 2.2 point out days in the week	3. Three or more times a week
1.5. How often did you go into field/vineyard/orchard after pesticides were sprayed? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.6. How often did you play/swim/bath in the nearest dam/river/or any other water body? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
In the past seven (7) days, how often did you do the following	
1.7. How many days did you eat crops *(including fruits)* from the field/vineyard/orchard that were sprayed?	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.7.1. Did you wash the crops/fruits you ate?	0. No 1. Yes
1.7.2. Specify which crop/fruit it was? **Hint**: show cheat sheet 2.2 point out days in the week	1. Table grapes 2. Apples or pears 3. Citrus fruits such as oranges 96. Other (1.7.2.1. Specify: _____)
1.7.3. Eat Table grapes **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.7.4. Apples or pears **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.7.5. Citrus fruits such as oranges or lemons **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.7.6. Any other fruit **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
Since the last time we saw you for the urine sample and questionnaire	
1.8. How often were chemicals or pesticides used in your home (indoors or outdoors) to control fleas, cockroaches, ants, termites, or other insects and weeds? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week

Section B Farming activities The next few questions will be about how often you helped with activities or work on the farms since the last time we saw you for the urine sample and questionnaire	
1.9. Picking fruits in the field/vineyard/orchard? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.9.1. When helping with picking fruit, were you given any protective clothes like clothes or boots? **Hint**: show PPE cheat sheet	0. No 1. Yes
1.10. Pesticide or chemicals spraying mixing or loading (this could be transporting the pesticides in any way)?	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.11. Helped with cleaning farm equipment? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.12. Assist in pesticide storage? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
1.13. Help with burning any pesticide or chemical containers? **Hint**: show cheat sheet 2.2 point out days in the week	0. Never 1. One day a week 2. Two days a week 3. Three or more times a week
Section 3: Injury and exposure to drugs The following questions are about possible injury and other activities you may be involved in since the last time we saw you for the urine sample and questionnaire.	
1.14. Have you ever had an accident while playing/working where you fell and hit your head very badly?	0. No 1. Yes 99. Don't know
1.15. If yes (to 1.25), did you have any serious bleeding to your head that you had to go to the hospital?	0. No 1. Yes 99. Don't know
1.16. How long were you in the hospital for?	1. 1-6 days 2. 1-4 weeks 3. >1 month

1.17. Did you experience vomiting or losing consciousness or maybe confused, not sure where you were at the time of the accident? *(define to participant passing out/fainting)*	0. No 1. Yes 99. Don't know
1.18. Please tell us how often this happens to you since the last time we saw you for the urine sample and questionnaire **Hint**: show never, rarely, sometimes, always cheat sheet	
1.18.1. Difficulty in falling asleep at night?	0. Never 1. Rarely 2. Sometimes 3. Always
1.18.2. Agitated during your sleep at night?	0. Never 1. Rarely 2. Sometimes 3. Always
1.18.3. Waking up during your sleep at night?	0. Never 1. Rarely 2. Sometimes 3. Always
1.18.4. Waking up too early in the morning?	0. Never 1. Rarely 2. Sometimes 3. Always
1.19. Have you ever tried to smoke? *(If participant has said they only tried once, then tick never; otherwise we want to recall regular smokers)* **Hint**: show cigarette amount cheat sheet	0. Never 1. 1-2 cigarettes a week 2. 3-4 cigarettes a week 3. More
1.20. Have you ever tried to drink alcohol? *(If participant has said they only tried once, then tick never; otherwise we want to recall regular drinkers)* **Hint**: show alcohol amount cheat sheet	0. Never 1. 1-2 glasses a week 2. 3-4 glasses a week 3. More
1.21. Have you ever tried taking recreational drugs *(for e.g. tik, marijuana)*? *(If participant has said they only tried once, then tick never; otherwise we want to recall regular drug issues)* **Hint**: show amount cheat sheet	0. Never 1. 1-2 times a week 2. 3-4 times a week 3. More

Hint: The next 4 SETS are validated questionnaires: this means these questions should be asked as written.

GERoNiMO: **G**eneralised **E**MF **R**esearch using **N**ovel Meth**O**ds

With this section, we would like to obtain information about your use of mobile phones and other communication technologies before and during the days you the days we see you for the study. Some of the questions are quite difficult but *I will use some pictures to help you*.

(Hint: Refer to cheat sheet)

Section D: GERoNiMO: Generalised EMF Research using Novel MethOds	
1.22. Do you **use** mobile phones for calling, texting or for the internet normally at least once per week? *(This question is not about owning. Still fill out if they USE their mothers, sisters, friends etc, phones)*	0. No 1. Yes
1.23. Do you use a smart phone? *(This question is not about owning. Still fill out if they USE their mothers, sisters, friends etc, phones)*	0. No 1. Yes 99. Don't know
1.24. How long do you call with a mobile phone on average per day (incoming and outgoing calls)? (**HINT**: please use the minutes' scale cheat sheet 10)	1. less than once a day 2. 1-5 minutes per day 3. 6-15 minutes per day 4. 16-30 minutes per day 5. 31-60 minutes per day 6. >1 hour per day
1.25. How many text messages (including WhatsApp-, Viber, iMessage, etc) do you send on average from a mobile phone? (**HINT**: please use the messages cheat sheet 8)	1. None 2. up to 10 per day 3. 10-30 per day 4. 30-100 per day 5. >100 per day
1.26. Are you sometimes woken up in the night by a message or call on your mobile phone or on another mobile phone in your sleeping room? (**HINT**: please use the frequency scale cheat sheet 9)	1. Never 2. less than once a week 3. 1-2 times per week 4. 3-5 times a week 5. almost every night
1.27. How much time per day do you actively spend with a mobile phone on the internet (WhatsApp, google, Facebook, YouTube, internet dependent apps, news sites, surfing in general, etc.) on average? *(If they do not understand the word surf, use "search" or "google")* (**HINT**: please use the minutes' scale cheat sheet 10)	1. I do not use internet/apps that connect to the internet on a mobile phone → **go to 1.40** 2. <10 minutes per day 3. 10-30 minutes per day 4. 31-59 minutes per day 5. 1-1.5 hours per day 6. >1.5 hours per day

1.28. If you are on the internet with the phone, what are you doing and for how long each day on average?

Item	**1=Yes 2=No** *Write the appropriate code in the box*	Average minutes per day		
1.28.1 Watching videos	**1.28.1.**		**1.28.2**	
1.28.3 Reading news and other internet sites	**1.28.3.**		**1.28.4.**	
1.28.5 Being active in social media	**1.28.5.**		**1.25.6.**	
1.28.7. Playing online games	**1.28.7.**		**1.28.8.**	
1.28.9. Listening to music (streaming)	**1.28.9.**		**1.28.10**	

1.29. Do you use a computer / laptop / tablet PC (e.g. iPad)/ game console? If so, for how long?

Item	**1= Yes 2=No** *Write the appropriate code in the box*		Average minutes per day	
1.29.1. Computer	**1.29.1**		**1.29.2**	
1.29.3. Laptop	**1.29.3.**		**1.29.4.**	
1.29.5. Table PC (iPad, Tablet etc.) (HINT: this does not include using the ipad for the CANTAB today)	**1.29.5.**		**1.29.6**	
1.29.7. Handheld game (eg (eg: Sony or Nintendo game as shown in cheat sheet)	**1.29.7.**		**1.29.8.**	
1.29.9. Video game (eg: joystick, playstation or Wii)	**1.29.9.**		**1.29.10.**	

1.30**.** For the devices below, do you connect to the internet and if so, what are you doing and for how long?

1= Watching videos **2**= Reading news and other internet sites **3**= being active in social media **4**= playing online games **(HINT: Refer to cheat sheets)**

Write the appropriate code in the box

Computer				
Item	**1=Yes 2=No** *Write the appropriate code in the box*	Average minutes per day		
1.30.1. Watching videos	**1.30.1.**		**1.30.2**	
1.30.3. Reading news and other internet sites	**1.30.3.**		**1.30.4.**	
1.30.5. Being active in social media	**1.30.5.**		**1.30.6.**	
1.30.7. Playing online games	**1.30.7.**		**1.30.8.**	
1.30.9. listening to music (streaming)	**1.30.9.**		**1.30.10.**	
Laptop				
Item	**1= Yes 2=No** *Write the appropriate code in the box*	Average minutes per day		
1.31.1. Watching videos	**1.31.1.**		**1.31.2.**	
1.31.3. Reading news and other internet sites	**1.31.3.**		**1.31.4.**	
1.31.5. Being active in social media	**1.31.5.**		**1.31.6.**	
1.31.7. Playing online games	**1.31.7.**		**1.31.8.**	
1.31.9. listening to music (streaming)	**1.31.9.**		**1.31.10.**	
Table PC (iPad, Tablet etc.)				
Item	**1=Yes 2=No** *Write the appropriate code in the box*	Average minutes per day		
1.32.1. Watching videos	**1.32.1.**		**1.32.2.**	
1.32.3. Reading news and other internet sites	**1.32.3.**		**1.32.4.**	
1.32.5. being active in social media	**1.32.5.**		**1.32.6.**	
1.32.7. playing online games	**1.32.7.**		**1.32.8**	
1.32.9. listening to music (streaming)	**1.32.9.**		**1.32.10.**	

The following 10 questions are only asked if the learner has said yes to using mobile phones stated from the question **1.22** above:

Section E

PROBLEMATIC MOBILE PHONE USE QUESTIONNAIRE

For each item, please mark the box which fits best for you from these options:

1 ‘‘Not true at all’’ to 10 ‘‘Extremely true

HINT: Fieldworker to please use a colour version of the cheat sheet and explain to participant: I am going to ask you 10 questions about your phone-you might think the question is not true at all (point to 1 on the scale) or very true (point to 10 on the scale) or you might think it’s only half true (point to the 5). You can decide where your answer fits from 1-10.

1.33. I have used my mobile phone to make myself feel better when I was feeling down	1	2	3	4	5	6	7	8	9	10
1.34. When out of range for some time, I become preoccupied with the thought of missing a call.	1	2	3	4	5	6	7	8	9	10
1.35. If I don’t have a mobile phone, my friends would find it hard to get in touch with me.	1	2	3	4	5	6	7	8	9	10
1.36. I feel anxious if I have not checked for messages or switched on my mobile phone for some time	1	2	3	4	5	6	7	8	9	10
1.37. My friends and family complain about my use of the mobile phone	1	2	3	4	5	6	7	8	9	10
1.38. I find myself engaged on the mobile phone for longer periods of time than intended	1	2	3	4	5	6	7	8	9	10
1.39. I am often late for appointments because I’m engaged on the mobile phone when I shouldn’t be	1	2	3	4	5	6	7	8	9	10
1.40. I find it difficult to switch off my mobile phone.	1	2	3	4	5	6	7	8	9	10
1.41. I have been told that I spend too much time on my mobile phone	1	2	3	4	5	6	7	8	9	10
1.42. I have received mobile phone bills I could not afford to pay	1	2	3	4	5	6	7	8	9	10

Section F **KIDSCREEN**	
This questionnaire will ask you about your health in different areas of your life. **INSTRUCTIONS : To complete, please tick one answer for each question** **(HINT: PLEASE USE CHEAT SHEET 5)**	
1.43. Have you felt fit and well?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.44. Have you felt full of energy?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.45. Have you felt sad?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.46. Have you felt lonely?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.47. Have you had enough time for yourself?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.48. Have you been able to do the things that you want to do in your free time?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always

1.49. Have your parent(s) treated you fairly?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.50. Have you had fun with your friends?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.51. Have you got on well at school?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
1.52. Have you been able to pay attention?	1. Never 2. Seldom 3. Quite Often 4. Very Often 5.Always
Section G **HIT-6-questionnaire**	
This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches. **INSTRUCTIONS: To complete, please tick one answer for each question.** **(HINT: please answer even if the participant says they have never had a headache-you can tick NEVER but the child might start remembering they had a headache as you ask about it)**	
1.53. When you have headaches, how often is the pain severe?	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always
1.54. How often do headaches limit your ability to do usual **daily activities** including household work, school, or social activities?	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always
1.55. When you have a headache, how often do you wish you could lie down?	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always

1.56. In the past 4 weeks, how often have you felt too tired to go to school, do home-work or daily activities because of your headaches?	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always
1.57. In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always
1.58. In the past 4 weeks, how often did headaches limit your ability to **concentrate** on work ordaily activities? (HINT: Not the same as above question, this one involves concentrating)	1. Never 2. Rarely 3. Sometimes 4. Very Often 5. Always
1.59. Do you have any question or comments to the questionnaire or the procedure?	

APPENDIX 3: Farm manager questionnaire

Q1. Date:	_____/_____/_____ Day Month Year		
Q2. Study Area:	☐1 Grabouw ☐2 Piketberg ☐3 Hex River Valley.		
Q3. What is your current occupation at the farm?	_____		
Q4. What type of crops do you farm with?	**Q4.1** Crop 1: _____ **Q4.2** Crop 2: _____ **Q4.3** Crop 3: _____ **Q4.4** Crop 4: _____ **Q4.5** Crop 5: _____		
Q5. What types of pests do you encounter while farming these crops?	Crop 1	**Q5.1.1** Pest 1	**Q5.2.1** Pest 2
	Crop 2	**Q5.1.2** Pest 1	**Q5.2.2** Pest 2
	Crop 3	**Q5.1.3** Pest 1	**Q5.2.3** Pest 2
	Crop 4	**Q5.1.4** Pest 1	**Q5.2.4** Pest 2
	Crop 5	**Q5.1.5** Pest 1	**Q5.2.5** Pest 2
Q6. What types of weeds do you encounter while farming these crops?	Crop 1	**Q6.1.1** Weed 1	**Q6.2.1** Weed 2
	Crop 2	**Q6.1.2** Weed 1	**Q6.2.2** Weed 2
	Crop 3	**Q6.1.3** Weed 1	**Q6.2.3** Weed 2
	Crop 4	**Q6.1.4** Weed 1	**Q6.2.4** Weed 2
	Crop 5	**Q6.1.5** Weed 1	**Q6.2.5** Weed 2
Q7. What chemicals/pesticides do you use for these pests?	Pesticide Name		Physical aspect (liquid, solid, gas, powder)
	Q7.1.1 Pesticide 1		**Q7.2.1** Form
	Q7.1.2 Pesticide 2		**Q7.2.2** Form
	Q7.1.3 Pesticide 3		**Q7.2.3** Form
	Q7.1.4 Pesticide 4		**Q7.2.4** Form
	Q7.1.5 Pesticide 5		**Q7.2.5** Form
	Pesticide Name		Physical aspect (liquid, solid, gas, powder)

Q8. What chemicals/pesticides do you use for these weeds?	**Q8.1.1** Pesticide 1	**Q8.2.1** Form
	Q8.1.2 Pesticide 2	**Q8.2.2** Form
	Q8.1.3 Pesticide 3	**Q8.2.3** Form
	Q8.1.4 Pesticide 4	**Q8.2.4** Form
	Q8.1.5 Pesticide 5	**Q8.2.5** Form
Q9. What is the most frequently used method of pesticide application?	***1= 1st most frequent*** ***2= 2nd most frequent*** ***3= 3rd most frequent*** ***4= 4th most frequent*** a. Airplane ☐ b. Tractor with boom sprayer ☐ c. Tractor with persons with back packs ☐ d. Tractor with persons with hand packs ☐	
Q10. Interviewer to ask for a description of the predominant methods of spraying and classify according to attached descriptions attached to this questionnaire	**Q10.1.1** Method 1 classification	
	Q10.1.2 Method 2 classification	
	Q10.1.3 Method 3 classification	
Q11. What month of the year do you apply the first treatment?		
Q12. What month of the year do you apply the last treatment?		
Q13. What is the frequency of continuous spraying per week and per month?	**Q13.1** days/week	
	Q13.2 weeks/month	
Q14. Are there farming records that inform of any changes in the use of chemicals over the years?	☐1 Yes ☐2 No	
If available, interviewer to ask for a record of the pesticides sprayed and quantities for the past decade		
Q15. Have you or do you currently use any of the following pesticides?		

Pesticide	**Have** 1= Yes 2= No	**Use** 1= Yes 2= No
Q15.1 Endosulfan	☐	☐

Q15.2 Dichlorodiphenyltrichloroethane	☐	☐
Q15.3 Chlordane	☐	☐
Q15.4 Heptachlor	☐	☐
Q15.5 Diedrin	☐	☐
Q15.6 Endrin	☐	☐

APPENDIX 4: Approval letter from Department of Education

Audrey.wyngaard@westerncape.gov.za

tel: +27 021 467 9272

Fax: 0865902282

Private Bag x9114, Cape Town, 8000

wced.wcape.gov.za

REFERENCE: 20150629-846

ENQUIRIES: Dr A T Wyngaard

Prof Aqiel Dalvie
School of Public Health and Family Medicine
Health Sciences Faculty
Anzio Road
Observatory
7729

Dear Prof Aqiel Dalvie

RESEARCH PROPOSAL: REPRODUCTIVE HEALTH EFFECTS DUE TO PESTICIDE EXPOSURE AMONGST CHILDREN IN THE RURAL WESTERN CAPE IN SOUTH AFRICA

Your application to conduct the above-mentioned research in schools in the Western Cape has been approved subject to the following conditions:

1. Principals, educators and learners are under no obligation to assist you in your investigation.
2. Principals, educators, learners and schools should not be identifiable in any way from the results of the investigation.
3. You make all the arrangements concerning your investigation.
4. Educators' programmes are not to be interrupted.
5. The Study is to be conducted from **20 July 2015 till 30 September 2017**
6. No research can be conducted during the fourth term as schools are preparing and finalizing syllabi for examinations (October to December).
7. Should you wish to extend the period of your survey, please contact Dr A.T Wyngaard at the contact numbers above quoting the reference number?
8. A photocopy of this letter is submitted to the principal where the intended research is to be conducted.
9. Your research will be limited to the list of schools as forwarded to the Western Cape Education Department.
10. A brief summary of the content, findings and recommendations is provided to the Director: Research Services.
11. The Department receives a copy of the completed report/dissertation/thesis addressed to:

The Director: Research Services
Western Cape Education Department
Private Bag X9114
CAPE TOWN
8000

We wish you success in your research.

Kind regards.

Signed: Dr Audrey T Wyngaard
Directorate: Research
DATE: 01 July 2015

APPENDIX 5: Permission letter to school principal and board

Date: _____/_____/_____

Dear Principal

Re: An epidemiological cohort study of school-going children investigating reproductive and neurobehavioral effects due to environmental pesticide and cell phone use in the Western Cape, South Africa

We would like to ask for your permission to include Grade 4 – 9 learners at your school in the important study above conducted by the University of Cape Town, Centre for Environmental Health and Occupation Research.

This study will investigate the reproductive and neuro-behavioural health effects that pesticides and radiation from cell-phone usage may have on children. This will be of benefit to people who make use of cell-phones and those exposed to pesticides in the environment that can be absorbed through the skin, breathed in and ingested through contaminated drinking water. The learners will undergo free medical testing and will benefit educationally from participation in the study.

This is a 3-year study, starting in 2017 and ending in 2019. Our sample population is 510 boys and 510 girls from 3 different farmland areas so we will require 340 learners from each area and about ±55 learners from each grade. In the 1st year, the learner will be required to complete a questionnaire at their home on demographic details, health and pesticide exposure and they will be required to perform the following tests at school: produce a urine and blood sample, undergo a physical examination of the genital area; perform a neurobehavioural test on a computer and complete a short questionnaire on pesticide exposure and cellphone use. These tests will be repeated in 2019. The tests will cause minimal disruption as it will last for only 2 hours at most. Additionally, a urine sample will be collected from each learner and a short questionnaire on pesticide exposure administered at school every 3 months during 2017-2019

Participation by your school involves identification of Grade 4-9 classes at the school, making available a copy of the class lists and their birth certificates if possible, distributing letters to all Grade 4-9 parents (copy enclosed) asking them for permission to include their child in the study and arranging an appropriate venue at the school on the days of testing during 2017-2019.

We would like to ensure that you, the learner and their guardian/parent offer your consent to participation before we conduct the study.

The results of the study will help to inform regulations to reduce harmful environmental exposures in residential areas in the Western Cape.

The survey has the approval of the Department of Education and Research Ethics Committee of the University of Cape Town.

Yours sincerely

Associate Professor MA Dalvie (Principle Investigator)

Cell phone number: 0827863781

APPENDIX 6: Caregiver consent form

Consent to participate in a study investigating reproductive and neurobehavioral effects due to environmental pesticide and cell phone use exposure in the Western Cape

1. **Title of research project**

   An epidemiological cohort study of school-going children investigating reproductive and neurobehavioral effects due to environmental pesticide and cell phone use exposure in the Western Cape, South Africa

2. **Names of researchers**

   Mohamed Aqiel Dalvie (BSc, Honours, MSc, PhD)

   Wisdom Basera (HBMLS, MPH)

   Shala Mhlanga (BSc (Hons), MSc)

3. **Purpose of the research project**

   This study will investigate the reproductive and neuro-behavioural health effects that pesticides and radiation from cell-phone usage may have on children. This study will be of benefit to communities who make use of cell-phone use and those exposed to pesticides in the environment that can be absorbed through the skin, breathed in and ingested through contaminated drinking water. Your child will undergo free medical testing and will benefit educationally from participation in the study.

4. **Description of the research project**

   This is a 3-year study, starting in 2017 and ending in 2019. In the 1st year, you will be required to complete a questionnaire at your home on your child's demographic details, health and pesticide exposure and your child will be require to perform the following tests at school: produce a urine and blood sample, undergo a physical examination of the genital area; perform a neurobehavioural test on a computer and complete a short questionnaire on pesticide exposure and cellphone use. These tests will be repeated in 2019. The tests will cause minimal disruption as it will last for only 2 hours at most. Additionally, a urine and hair sample will be collected from your child and a short questionnaire on pesticide exposure administered at school every 3 months during 2017-2019.

   The following are more detailed explanations of what each assessment will entail:

a) **Guardian Questionnaire:** A member of our study team will interview you to fill out a ±1hour questionnaire. You will be asked questions about general information about your child, his/her

general medical health, genital health history, development, cell-phone usage and lifetime environmental exposure to pesticides.

b) **Urine and hair samples:** Your child has to produce a urine sample (in privacy) voiding into a plastic container and give it to the nurse. The nurse will also draw a few strands of hair or shave a small amount of hair from your child The samples will be analysed for the presence of pesticides.

c) **Blood sample:** A study nurse will draw 10 ml blood from a vein on your child's arm. The blood will be analysed for reproductive hormone levels.

d) **Physical examination:** A nurse will assess your child's reproductive health and development by examining their genital area.

e) **Participant Questionnaire:** A member of our study team will administer a 20-minute questionnaire to your child. It has questions on whether they have a cell-phone and about their experience with using cell-phones and any other technical equipment linked to an internet source. There are a few questions on their leisure activities to determine their exposure to pesticides and electro-magnetic fields (internet etc.) that we are studying.

f) **Behavioural Assessment:** This is a 30-40 minutes assessment to test brain functions like reaction and memory, to be administered by a member of our study team. Your child will be given a tablet, with a program that will ask them to follow instructions and respond through touch-screen, similar to a computer game.

5. Risks and discomforts of the research

i. **From the blood tests:** A single needle stick will be felt when the blood is taken. Sometimes a small bruise may occur from the needle stick, but this is minor and will heal quickly. The total amount of blood taken is quite small and the body will quickly replace it. Blood samples will be used only to measure reproductive hormones and will be disposed of at the end of the study.

ii. **From the urine and hair samples:** There will be no discomfort as the urine sample is done privately by the participant themself in the toilet facility. Only a small amount of hair will be collected. The urine and hair sample will only be used to measure any evidence of metabolised pesticides and will be disposed of after this laboratory test.

iii. **From the physical examination:** This examination will have some discomfort for the participant as it requires them to reveal their genital area. However, this exam will be done in a private setting with the use of a curtained zone and in a professional manner by a nurse. In addition the exam is observational and therefore will be done quite briefly.

iv. **From the questionnaires:** There are minimal risks associated with completing the questionnaires. The only risk is a loss of confidentiality about personal information about personal information but the data will be seen only by study personnel. All reports will present data in which individuals will not be identifiable by name but by their study number.

v. **From the behavioural assessment:** There is no risk in completing this assessment. It has been specifically adapted to accommodate children and their ability in this age group.

6. **Expected benefits to you and others**

i. A doctor/nurse will examine your child's reproductive health.

ii. Refreshments will be provided as compensation for the time spent participating in the study.

iii. This study on the reproductive health effects of pesticides will benefit children living in farming areas and those exposed from the environment. Steps can be taken to reduce or prevent exposure or the pesticides can be selected for further investigation and subsequent banning. The findings from the blood and the urine samples can be used to develop ways in which the amount of pesticides in your body can be monitored in people exposed such as yourself.

iv. The assessment on your child's neurobehavioral status will provide you with information about the child's functioning/coping in their daily activities for school tasks, home tasks and social interaction.

7. **Costs from participation in the study.**

The study is offered to you at no cost.

In the event a problem is discovered and you wish to be seen by a doctor for it, we can recommend someone for you to see. However, the study cannot pay for these additional medical visits or treatments.

The University of Cape Town (UCT) has insurance cover for the event that research-related injury or harm resulting from your child's participation in the study. The insurer will pay all reasonable medical expenses in accordance with the South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI) in the event of an injury or side effect resulting directly from your participation in the study. You will not be required to prove fault on the part of the University.

The University **will not be liable** for any loss, injuries and/or harm that your child may sustain where the loss is caused by:

The use of unauthorised medicine or substances during the study.

- Any injury that results from your child not following the protocol requirements or the instructions that the study-nurse may give.
- Any injury that arises from inadequate action or lack of action to deal adequately with a side effect or reaction to the study medication.
- An injury that results from negligence on your child's part.

By agreeing to participate in this study, you do not give up your right to claim compensation for injury where you can prove negligence, in separate litigation. In particular, your right to pursue such a claim in a South African court in terms of South African law must be ensured. Note, however, that you will usually be requested to accept that payment made by the University under the SA GCP guideline 4.11 is in full settlement of the claim relating to the medical expenses. An injury is

considered study-related if, and to the extent that, it is caused by study activities. You must notify the study nurse immediately of any side effects and/or injuries during the study, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your child's injury came about because your child chose not to follow the instructions that your child was given while taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected.

8. Confidentiality of information collected

Study participants will not be personally identified in any of the study reports. The records will be kept confidential to the extent provided by law. The records, including any identification information, will be destroyed after the data collected has been fully analysed.

9. Documentation of the consent

One copy of this document will be kept together with our research records. A second copy will be given to you to keep.

10. Contact person

You may contact the following persons for answers to further questions about the research, your rights, or any injury you may feel is related to the study:

Principal Investigator: Professor Mohamed Aqiel Dalvie	Telephone #: 021 4066610
Researcher: Mr Wisdom Basera	Telephone #: 082 5802776
Researcher: Mrs Shala Mhlanga	Telephone #: 072 3308540
Ethics Administrator: Lamees Emjedi	Telephone #: 021 4066338

Nature of participation

The participation in this project is voluntary (assent from your child) subsequent to your consent, you may refuse your child to participate or withdraw from the study at any time without penalty or loss of benefits to which you may otherwise be entitled.

Consent of the Parent/Guardian

I have read the information given above. I understand the meaning of this information. I hereby consent my child, _____ to participate in the study.

_____ _____ _____ Printed

name of Parent/Guardian Signature Date

Date: _____

APPENDIX 7: Child assent form

The Western Cape Pesticides and Cellphone use study

Introduction

Introduction

Hi [child's name]! My name is_____ and I would now like to talk to you about your health. Before I begin, I want to assure you that we have your parent or guardian's permission to approach you. You now have the right to refuse to participate, after I explain to you what we want to do.

1. **Title of research project**

Reproductive and neurobehavioral effects due to environmental pesticide exposure and cell phone use in the Western Cape, South Africa

2. **Purpose of the research**

People have done research on the pesticides that farmers use to protect their crops from insects and how they affect our health. There is very little research done in SA on how these pesticides are harmful to children, so with your help, our study will be one of the very few done so far. Through The University of Cape Town, we are going to be looking at 2 important areas of health that may be affected from being exposed to the pesticides used on the farm and EMF through cell-phone usage. This will help other children living in farming areas who are exposed to pesticides by ensuring that farmers cannot use those harmful chemicals. Pesticides can spread from the environment by the wind that disperses it to drinking water, to skin and may be breathed in. Cell phones are also another area with little research done so far. so we hope to find out more on the effects of mobile phones through this study.

3. **Description of the research project**

This is a 3-year study. The study will be done in the 1st year, 2017 and then again in the 3rd year, 2019. In each of these years, we will need you for one day to do some tests and answer some questionnaires. In between the 2 years, a nurse will visit you every 3 months for a urine sample, hair sample and a short questionnaire on pesticide exposure related activities.

If you agree to participate, you will be asked to complete:

a) Questionnaire:

I want you to know that the answers you give me to the questions I ask about your health and cell phone usage will be private and we won't share your answers with other kids or with your parents. Only project members of this study will see the answers and they will use these answers to help you improve your health. There are no right or wrong answers to these questions I will ask you. We want to know how you feel. Also, if you do not want to answer one particular question or if you want to stop at any time and not answer any more questions, you can do that by telling me you don't want to continue. Nothing will happen to you if you decide not to answer these questions. But your participation is important and will help us understand health problems in children and this will help other children who might have similar health problems in the future.

This is a 10-15 minute questionnaire, administered by a member of our study team. It has questions on whether you have a cell-phone and about your experience with using cell-phones and any other technical equipment linked to an internet source.

There are a few questions on your leisure activities to determine your exposure to pesticides and cell phone use (internet etc.) that we are studying.

b) Urine and hair sample: We will collect a urine sample and a hair sample from you to test for chemicals.

c) Blood sample: A nurse will draw a small blood sample from you to check the level of your hormones.

d) Physical examination: A nurse will do a very brief body assessment by examining your genital area.

e) Behavioural Assessment: This is a 30-40 minutes assessment to test your brain functions like reaction and memory, to be administered by a member of our study team. Your will be given a tablet, with a program that will ask you to follow instructions and respond through touch-screen, similar to a computer game.

4. **Confidentiality of information collected**

Your name will not appear in any reports on this study. The records of questionnaires, assessments, blood samples, urine samples and examination, will be kept completely confidential at the University of Cape Town and will be seen only by our study team.

5. **Contact person**.

You may contact one of the following persons for answers to further questions about the research, your rights, or any injury you may feel is related to the study. You may also contact these persons for questions related to your child's rights or any injury you may feel is related to the study.

Principal Investigator: Professor Mohamed Aqiel Dalvie Telephone#: 021 4066610

Researcher: Mr Wisdom Basera Telephone#: 082 5802776

Researcher: Mrs Shala Mhlanga Telephone#: 072 3308540

Ethics Administrator: Lamees Emjedi Telephone#: 021 4066492

6. **Assent for your participation**

The information above has been read to me. I understand the meaning of this information

Dr./Mr./Ms. _____has offered to answer any questions concerning the study. By signing this form, I agree to participate in the study. I also understand that I am free to withdraw from the study at any time without penalty.

_____ _____

Printed name of child Signature, Mark, or Thumb Print

_____ _____

Interviewer's name (Print) Signature

_____ _____

Witness (Print) Signature

DATE: _____

APPENDIX 8: Physical examination for girls – Tanner staging

Study Number: _____

Date: _____

Physician/Nurse: _____

Measures/evaluations of height, weight, breast size, areola development and papilla formation performed with the girl/woman in standing position.

Evaluation of pubic hair should be according to the stages of Tanner, for which illustrations have been provided.

Characteristic	**Response**		
1. Height (cm)			
2. Weight (kg)			
3. Birth weight (kg)			
Genital region			
4. Any visible scaring due to surgery	☐$_1$ Yes → *describe in "other remarks" below* ☐$_2$ No		
5. Pubic Hair: Tanner stage	☐$_1$ 1 ☐$_2$ 2 ☐$_3$ 3 ☐$_4$ 4 ☐$_5$ 5		
Breast morphology	Size	Areola	Papilla *1 = Yes* *2 = No*
6. Breasts		☐	☐
7. Other remarks			

APPENDIX 9: Physical examination for boys – Tanner staging

Study Number: _____

Date: _____

Physician/Nurse: _____

Measures/evaluations of height, weight, testes disposition, varicocele and hydrocele have been performed with the man in standing position.

Evaluation of pubic hair should be according to the stages of Tanner, for which illustrations have been provided.

For evaluation of testes size, the orchidometer provided has to be used.

Characteristic	**Response**		
8. Height (cm)			
9. Weight (kg)			
10. Birth weight (kg)			
Genital region			
11. Scars due to surgery	☐$_1$ Yes → *describe in "other remarks" below* ☐$_2$ No		
12. Pubic Hair and penis: Tanner stage	☐$_1$ 1 ☐$_2$ 2 ☐$_3$ 3 ☐$_4$ 4 ☐$_5$ 5		
13. Penis	☐$_1$ Normal ☐$_2$ Abnormal → *describe in "other remarks" below*		
Testiscular morphology	Size (ml)	Consistency *N = Normal (1)* *S = Soft (2)* *H = Hard (3)*	Abnormality *1 = Yes* *2 = No*
14. Left testes		☐	☐

APPENDIX 10: Methods of Application

To get the best result using the least amount of pesticide applicators need to think through the application process carefully. Different application methods are appropriate for different crop and pest types, but the method of application should always be consistent with the label directions.

Application methods include:

Band application	Applying a pesticide in parallel strips or bands, such as between rows of crops rather than uniformly over the entire field.
Basal application	Directs herbicides to the lower portions of brush or small trees to control vegetation.
Broadcast application	The uniform application of a pesticide to an entire area or field.
Crack and crevice application	The placement of small amounts of pesticide into cracks and crevices in buildings, such as along baseboards and in cabinets, where insects or other pests commonly hide or enter a structure.
Directed Spray Application	Specifically targets the pests to minimize pesticide contact with non-target plants and animals.
Foliar application	Directs pesticide to the leafy portions of a plant.
Rope-wick or wiper treatments	Is wiped onto weeds taller than the crop, or wiped selectively onto individual weeds in an ornamental planting bed.
Soil application	Places pesticide directly on or in the soil rather than on a growing plant.
Soil incorporation	The use of tillage, rainfall, or irrigation equipment to move the pesticide into the soil.
Soil injection	The application of a pesticide under pressure beneath the soil surface.
Space treatment	The application of a pesticide in an enclosed area.
Spot treatment	The application of a pesticide to small, distinct areas.
Tree injection	The application of pesticides under the bark of trees.