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# A review of the effects of pesticides on human health in developing Countries

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# A review of the effects of pesticides on human health in developing Countries.

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# CHAPTER ONE

## Introduction and Methodology

### 1.1 Research background

Developing countries account for only a quarter of global pesticide consumption, yet they endure the most pesticide-related deaths, which make up 99% of global pesticide-associated fatalities (UNICEF, 2018). Also, despite their inherent toxicity (Rani et al., 2021), global pesticide usage has risen by 50% compared to the 1990s (FAO, 2022a). While pesticides find application in public health, agriculture, and residential settings, their significance is particularly pronounced in the agricultural sector (Rani et al., 2021). Farmers are intensifying the use of pesticides to improve agricultural productivity and ensure food security by preventing loss before and after the harvest. The latter is especially the case in the face of climate change, rapidly growing global population and limited arable land which exacerbate food challenges. In public health, pesticides are applied in public places and residential areas to reduce vector-borne diseases including Malaria and Zika (Bonner & Alavanja, 2017). Despite their pronounced importance, pesticides carry detrimental effects on health, for both users and those indirectly exposed to them (Rani et al., 2021).

Moreover, epidemiologists and researchers from diverse disciplines are increasingly reporting on the effects of common and widely used pesticides on human health and development (Grube et al., 2011). Organophosphates (OP) and Dichlorodiphenyltrichloroethane (DDT) are specifically associated with negative effects on infant health, contributing to high infant mortality rates (Frank & Taylor, n.d.; Muñoz-Quezada et al., 2013) leading to high infant mortality (Taylor, 2022). This means, pesticide effects in developing countries, where a higher proportion of the population consists of young individuals, can have profound implications, including on the long-term development of human capital. While the further discussion on infant mortality is extended in the second chapter, adverse health effects from pesticide exposure are not limited to infant health. A wide range of literature reports on other health effects, including cancer, which is most linked to several highly toxic pesticides like DDT (Bonner & Alavanja, 2017; Carvalho, 2017; Frank & Taylor, n.d.; Taylor, 2022). Additionally, fungicides like Folpet and Dithiocarbamates have been associated with respiratory and allergic symptoms such as Rhinitis in France (Raherison et al., 2019), while Glyphosate, another widely used agricultural pesticide, is linked to impaired visual memory among farmers in Costa Rica and Uganda (Fuhrimann et al., 2021; Staudacher et al., 2020). Despite the potential hazards, there has been a surge in the production and usage of pesticides (Egbuna & Sawicka, 2019; FAO, 2022a), and there are even calls for the reintroduction of highly toxic pesticides based solely on their effectiveness (Bonner & Alavanja, 2017; Frank & Taylor, n.d.). Despite the increasing number of reports on the adverse effects of pesticides, establishing a definitive link between pesticide exposure and health effects remains a significant challenge (UNICEF, 2018).

## 1.2 Rationale

This review provides an overview of the existing knowledge and knowledge gaps concerning the effects of pesticides on human health in developing countries. Moreover, it examines the strengths, weaknesses, and replicability of selected studies that contribute to understanding the extent of this issue in developing nations. The evidence presented in this paper is derived from literature utilizing large surveys and quasi-experimental approaches to investigate the effects of pesticides on human health. While the existing literature on the topic presents substantial evidence of the associated negative health effect, narrations based on case studies from the global north dominate the discussion. Understanding further the impacts of pesticides in developing countries is vital. This is especially the case considering that in countries like China, Brazil, and India the use of pesticides is slightly lower than in the US but higher compared to the world average in 2020 (FAO, 2022b). The health risk is even higher among pesticide users in developing countries because the rapid increase in the use of pesticides is accompanied by few regulations (Snyder et al., 2018) on the sales and use of pesticides (Bonner & Alavanja, 2017), and a lack of or inadequate personal protective equipment among users (Fuhrimann et al., 2021).

### 1.3 Research significance

Although case studies conducted in developed countries have provided valuable insights into the impact of pesticides on human health, this paper aims to enhance the understanding of the extent of this problem in developing countries. This paper contributes to this understanding by proposing replicable methodological approaches that can be employed to examine the effects of pesticides in developing nations.

### 1.4 Research methodology

In this study, we employ a *selective literature review* approach to address two primary research questions. The first question focuses on exploring the documented effects of pesticides on human health as identified in the existing literature. The second question examines the extent and scope, specifically whether studies establishing a causal relationship between pesticides and health effects can be replicated at micro or macro levels to gain insights into the magnitude of the issue in developing countries.

To address the research questions, the following critical review incorporates studies that employ large surveys or quasi-experiments, as these methodologies are known for their robustness in establishing causal effects, with the latter being the most robust. In addition, this review includes a limited number of studies that adopt alternative approaches to investigating the topic, despite their deviation from the methodologies. These studies, while different in their approach, provide valuable insights that contribute to building a comprehensive case background and strengthening the foundation of the discussion.

### *1.4.1* Keywords and databases

The literature review comprises journal articles acquired from three primary databases, namely PubMed, Science Direct, and Scopus, organized based on their relative importance. A limited quantity of grey literature, including pertinent reports, was acquired through the Google search engine and Google Scholar. Furthermore, a working paper by Tylor & Frank (Frank & Taylor, n.d.) was directly obtained from their website due to its significant importance in terms of methodological innovation for studying pesticide effects. The selection of databases was influenced by their credibility and the accessibility of relevant articles, particularly the availability of free-access articles related to the research topic. In terms of keywords, the literature review covers four key concepts as presented in Table 1 below,

Table 1: Keywords and database employed in the study.

| **Key Concepts** | **Databases** |
|---|---|
| Pesticides | PubMed |
| Pesticides exposure | Science direct |
| Health effects | Scopus |
| Developing countries | Google Scholar and Google search |

### *1.4.2* Inclusion criteria

After performing a search in the databases above using the established keywords as outlined in Table 1, the researcher applied the inclusion criteria detailed in Table 2 below to identify relevant studies. To ensure the selection of relevant articles specifically those addressing pesticides and human health effects, the researcher assessed the content of each paper. This process commenced with a review of abstracts, followed by a comprehensive examination of the entire paper, thereby determining the study's relevance.

While the primary objective of the study is to understand the health effects arising from pesticide exposure in developing countries, the inclusion criteria presented in Table 2 also encompassed studies from other country groups. This was done deliberately to explore studies that offer valuable insights into understanding both health effects and methodologies that can be replicated in developing countries.

Table 2: Inclusion criteria employed in the study.

| **Details** | **Inclusion Criteria** |
|---|---|
| Publication type | Journal articles, working papers and reports only |
| Publication date | From 2007 and beyond (Due to little number of publications) |
| Language of the publication | English language only |
| Topic | Pesticides and related health effects. |
| Geographical focus | All countries (no restriction) |
| Methodology adopted | Quasi-experiments or large surveys only (Excluded reviewed articles) |
| Article access | Open access articles |

### *1.4.3* Definition of terms

*Pesticides* **"**are substances used to prevent, destroy, repel or mitigate any pest ranging from insects, animals and weeds to microorganisms" (Grube et al., 2011). Some common classifications of pesticides include herbicides which are pesticides applied to destroy unwanted vegetation, insecticides which are applied to kill insects and fungicides which kill parasitic fungi**.**

### *1.4.4* Research gap

Despite the increase in newly generated knowledge and reports on the effects of pesticides on human health, most of the studies and reports are based on case studies in the global north, with only a few studies shedding light on what is happening in the global south.

Moreover, establishing a conclusive link between pesticide exposure and health effects is still a huge challenge (UNICEF, 2018). In particular among developing countries where management and availability of data on pesticide use, especially at the local scale, remain a considerable challenge.

### *1.4.5* Research question

To address the gap outlined above, this study aims to accommodate the following two research questions.

i. What are the potential effects of pesticides on human health reported in the literature?
ii. To what extent can studies establishing a causal link between pesticide exposure and health effects be replicated to understand the magnitude of the problem in developing countries?

# CHAPTER TWO

## Pesticides and Human Health

### 2.1 Introduction

This section presents a thorough examination of the methodologies employed in selected papers, focusing on the effects of pesticides on human health. These studies utilize either large-scale surveys or quasi-experimental designs. This analysis critically evaluates the strength and limitations of these methodologies, taking into account their applicability and potential for replication in developing countries, such as Tanzania. Our main goal is to lay the groundwork for a more profound comprehension of the extent of health effects associated with pesticides in Tanzania and other similar developing nations.

### 2.2 Pesticide effects on human health: A methodological review

Approaches to examining the health effects associated with pesticide exposure can be broadly categorized into general and specific approaches. In the general approach, researchers try to establish a causal link between pesticide applications and the general health outcomes of the exposed population. In this approach, health outcomes are mostly defined in a broader term using a broader health parameter, rather than specific diseases or health consequences manifesting among the population. For instance, several studies such as the one conducted by Frank and Tylor, which will be further discussed in subsequent paragraphs, examine changes in infant mortality rates and not specific diseases among infants following intensification in the use of pesticides in the US (Frank & Taylor, n.d.).

In contrast, studies adopting a specific approach focus on examining the effect of pesticides on specific health outcomes such as specific diseases, performance test results within specific neurological domains among children and adolescents, or by looking at the effects of pesticides on other specific health domains. This is also discussed in the later paragraphs when looking at studies adopting this methodological approach shedding light on the specific health consequences associated with pesticide exposure.

### *2.2.1* Evidence from studies adopting a general approach.

**i. Infant health parameter: *Pesticides and infant mortality***

Among studies adopting the general approach are those exploring a causal link between pesticide exposure and negative health outcomes in the infant population. A study by Frank and Tylor, introduced in the above paragraph, fits this category. In this study, the authors examine health effects among the infant population following the widespread use of Dichlorodiphenyltrichloroethane (DDT) in the US during what is referred to as the golden age of pesticides in the country. Specifically, the study explores the link between the increase in the use of DDT and rates of infant mortality in three different settings where DDT was highly in use, i.e., in cotton-producing areas, forest areas covered by the spray initiatives as part of forest management, and areas where DDT was used to control vector-borne diseases. From the three settings, they establish groups or areas where DDT was not used (as control) and those who benefited from DDT use (as treatment). A portion of data utilized by the study includes data on cotton production and annual infant mortality data (Frank & Taylor, n.d.) which can also be accessed in some developing countries like Tanzania where each death and birth is registered and designated government bodies exist for each cash crop in the country. The remaining challenge is however the availability of data on pesticide application and exposure. To overcome the latter, researchers in developing countries can utilize aggregate data and relevant proxies for pesticide exposure, including spraying seasons which represent periods of intensive pesticide application and possibly higher exposure to pesticides.

The analysis focuses on two significant time events, i.e., the period when DDT was extensively used by civilians (1945) and its subsequent ban in 1972 due to concerns about human health. The underlying assumption is that if DDT had any health effects, they would have been evident during its widespread use and would have declined following the ban. To examine the impact of DDT application on infant mortality, the study employs multiple identification strategies which included the use of Difference-in-Differences and Triple Difference analysis techniques. By establishing treatment and control groups in each of the above settings, the researchers were able to analyze the effects of DDT application across these settings on infant mortality rates (Frank & Taylor, n.d.).

The authors find that, compared to the baseline year of 1945, there was an 11% increase in infant mortality in the southern region of the United States following extensive DDT application in cotton production. They also find some indications of increased mortality rates in certain areas where DDT was used for forest management, but the evidence was not consistent across all regions. In areas where DDT was widely used for public health purposes, the findings were inconclusive (Frank & Taylor, n.d.).

Despite the mixed results, this study makes a significant contribution to our understanding of the health implications associated with DDT application, specifically the observed increase in infant mortality rates in certain settings. Additionally, the study sheds light on how new technologies, such as DDT in this case, can be widely embraced by the public despite limited knowledge about their potential impacts.

The findings are consistent with previous studies on pesticides, which also report higher infant mortality rates. For instance, a study conducted by Frank (2022) finds that the intensive use of insecticides among farmers in the US, following a wildlife disease outbreak that significantly reduced the population of bats, was associated with increased infant mortality. Farmers increased pesticide application because of the disruption of the ecological function of bats, i.e., natural predators for insects. Furthermore, another study by Tylor reached similar conclusions, this study examines infant mortality rates after a period of intensive pesticide application in apple production, caused by a mass emergence of cicadas (insects that attack trees) across the eastern half of the US (Taylor, 2022).

While knowledge from medical science can help to explore the underlying mechanisms for the reported high infant mortality, these studies establish a causal link between pesticides and higher infant mortality rates. Moreover, they highlight the implication and importance of understanding ecological disruptions and the need to mitigate the associated consequences.

***Application of the Infant health parameter in developing countries.***

Understanding the health consequences of pesticides does not necessarily depend on having precise data on actual exposure. The cited paper demonstrates that even in a developed country like the US, some studies on pesticide-related health effects utilize indirect measures of exposure, such as examining the ban of a pesticide in specific areas and timeframes as outlined above. This approach holds relevance, particularly in developing countries where obtaining data is even more challenging. It represents a potential pathway to further comprehend the effects of pesticides in such contexts.

Utilizing such approaches becomes even more feasible in developing countries like Tanzania, where the extensive DHS data provides valuable insights into health, particularly for children under the age of 5. While the availability of pesticide data remains scarce, researchers can leverage DHS data and employ relevant indirect approaches, similar to those utilized in various papers such as those by Frank and Taylor, including the aforementioned study on infant mortality. This will lead to a deeper understanding of the health effects of pesticide exposure among infants and the establishment of causal links. Additionally, these studies offer valuable insights and experiences in employing robust quasi-experiments to investigate infant health parameters, bringing researchers in developing countries closer to comprehending the magnitude of the health effects due to pesticides in their respective contexts.

Moreover, while existing research presents other possibilities for addressing data challenges related to pesticide exposure and application in developing countries, including the use of proxies, the selection of a suitable proxy depends on various factors, such as the scale of pesticide effects being examined (micro or macro level). For instance, if pesticide import data is used as a proxy for pesticide application or consumption, it primarily allows for macro-level studies on pesticide effects. However, if researchers aim to investigate infant mortality at the micro level in countries like Tanzania where cash crops are prevalent, an alternative proxy could be to utilize pesticide spraying seasons, which reflect periods of intensive pesticide application and possibly high exposure to pesticides. Another relevant proxy for pesticide exposure applicable to many countries in Sub-Saharan Africa, is the nationwide Malaria programs, as discussed later.

In conclusion, when opting to utilize indirect measures of pesticide exposure or other relevant proxies, researchers need to consult existing literature carefully. This ensures the selection of indirect measures and proxies that are most relevant to their specific context and align with the scope of their examination of the health effects of pesticides.

**ii. Pregnancy outcome parameter:** ***Pesticide (pyrethroids) and pregnancy outcomes***

Malaria is one of the major causes of infant mortality in Sub-Saharan Africa, including Tanzania. When pregnant women contract the malaria parasite it poses significant health risks for both them and their unborn babies. One of the risks is the increased likelihood of low birth weight (LBW) and stillbirth occurrences (Desai et al., 2007). Nationwide mosquito net campaigns are among the earliest and most popular approaches to control Malaria. In most cases, households have access to both piperonyl butoxide (PBO) treated and non-treated mosquito nets. However, little is known regarding the long-term impacts and health effects associated with the application of PBO whose function is to enhance the ability and effectiveness of Pyrethroids in controlling insects such as Mosquitos.

Among the few studies which examine the health effects of using PBO-treated mosquito nets and their impact on pregnancy outcomes, i.e., changes in low birth weight (LBW) and stillbirth incidences, is a study in Uganda. The researchers employ a cluster randomized controlled trial, randomly assigning different health subdistricts (HSDs) into treatment and control groups. Five HSDs received PBO-treated long-lasting insecticidal nets (LLINs), six HSDs received non-PBO LLINs, and one group consisted of a combination of treated and untreated LLINs. Birth registry data was collected 29 months before the campaign as a baseline and nine months after. The researchers utilize interrupted time-series analyses to assess monthly changes in pregnancy outcomes, specifically focusing on changes in low birth weight (LBW, less than 2500g) and stillbirth incidences. Additionally, they employ the Difference-in-Difference technique to measure the overall impact of using treated LLINs on pregnancy outcomes in Uganda (Roh et al., 2022).

Interestingly, unlike most studies on pesticides and human health that often report negative effects, this study reports positive outcomes associated with the use of treated mosquito nets. Within nine months after the PBO LLINs campaign in Uganda, they observed a 26% reduction in stillbirth incidences and a 15% decrease in the incidence of low-birth-weight cases. Although the study did not specifically investigate the link between the prevalence of malaria and the use of PBO-treated nets, it reports a 26% lower malaria prevalence among children aged 2 to 10 years who used PBO-treated nets, compared to a 15% reduction in the control group, six months after the distribution of PBO-treated nets. These findings suggest a potential for PBO-treated nets to effectively reduce malaria prevalence when compared to non-treated mosquito nets (Roh et al., 2022). Therefore, considering the documented impact of malaria on pregnancy outcomes in existing literature (Desai et al., 2007), this implies that PBO nets may have contributed to improving pregnancy outcomes by reducing malaria incidences among pregnant women in the treatment group. Therefore, it is important to note that this also implies that the overall effect of using treated nets might be positive, without necessarily suggesting that pesticides are good for health.

Further examination is warranted regarding the impact of pesticides on pregnancy outcomes. This is not only because the current study only assesses limited parameters of pregnancy outcomes, but also because other studies utilize different approaches and report negative effects of increased pesticide application on birth outcomes, particularly in countries like the US. For example, Jones (2020) conducted a natural experiment study which utilized an instrumental variable approach to examine birth outcomes following an increase in the use of insecticides and fungicides to control invasive species in the US and found that a 10% increase in the use of insecticide and fungicide was associated with a 0.18 and 0.15 percentage point increase in infant prematurity, as well as a 0.08 and 0.08 percentage point increase in instances of low birth weight, respectively. (Jones, 2020).

***Application of the pregnancy outcome parameter in developing countries***

This approach is highly relevant for examining the effects of pesticides on infant health in developing countries like Tanzania where national anti-Malaria programs, including the distribution of treated mosquito nets, have been implemented on a large scale. Researchers, particularly those in the Ministry of Health, often have easy access to both published and unpublished data on these campaigns which present a good opportunity to conduct similar studies.

However, it is important to note that the study in Uganda, which reports a positive impact of pesticide application on pregnancy outcomes, focuses solely on two parameters: stillbirth and low birth weight (LBW). Therefore, these outcomes represent only immediate health effects associated with exposure to pyrethroids (PBO) in these two domains of infant health (Roh et al., 2022). Therefore, the observed positive effects can likely be attributed to PBO-treated nets being more effective than non-PBO-treated nets in reducing malaria which exacerbates LBW and stillbirth incidences (Desai et al., 2007)., leading to a positive net effect which does not imply that PBO pesticides are good for health. Therefore, while these results are interesting, they provide only a glimpse of the potential effects as there is a limited understanding of the effects of PBO on other aspects of infant health, which presents an opportunity for further research.

Moreover, in countries like Tanzania, where long-standing malaria programs have been implemented and comprehensive data is available on other variables such as in the birth and death registry, school enrolment, and student performance in national exams, this approach is applicable and relevant for examining various health parameters beyond pregnancy outcomes. Researchers can leverage these programs and available data to investigate potential links between pesticides and factors such as infant mortality and neurobehavioral performance among youth and school children.

In situations where individual-level data is scarce or where randomization at the individual level is impractical or ethically challenging, researchers can employ alternative approaches such as cluster randomization, as done in this study. Cluster randomization offers benefits such as minimizing contamination, which is an important consideration when randomizing at the individual level.

### *2.2.2* Evidence from Studies adopting a specific approach.

**i. Neurobehavioral performance outcomes: *Pesticides and neurobehavioral outcomes.***

Studies on pesticides have also explored the connection between pesticide exposure and specific neurobehavioral outcomes in young individuals, as well as neurological health outcomes in adults. A notable study in this area is the work conducted by Fuhrimann et al. (2021), which provides valuable insights into this issue within the global south. Specifically, the study focuses on examining the neurobehavioral outcomes associated with exposure to multiple pesticides among 288 farmers in Uganda. This study is relevant for developing countries including Tanzania in particular for several reasons. Firstly, a significant portion of the population in developing nations, particularly in Sub-Saharan Africa, is engaged in agricultural activities. Additionally, existing literature emphasizes the increasing use of pesticides in agriculture and the concerning fact that pesticide exposure is more common and not exceptional among farmers. Lastly, it is worth noting that farmers in these countries often lack sufficient protective equipment, which highlights the importance of investigating the potential health effects associated with pesticide exposure in the agricultural sector.

The researchers collected self-reported data on pesticide use, including Glyphosate, from farmers for 12 months before the survey. The study sample consists of two groups: a randomly selected group of farmers using synthetic pesticides and a group of farmers using organic pesticides (snowball sampled) in at least one crop. To assess the level of pesticide exposure, they use a semi-quantitative exposure algorithm. This algorithm enables them to estimate the yearly pesticide exposure intensity score, reflecting the level of pesticide exposure experienced by farmers throughout the year. To establish the relationship between exposure to 14 different pesticide-active ingredients and neurobehavioral outcomes among the farmers, the researchers employ Bayesian Model Averaging (BMA) techniques, and they assess outcomes on five pre-identified neurobehavioral domains, i.e., attention, language, executive function, memory, and motor function (Fuhrimann et al., 2021).

The study's findings highlight that a minimum of 72% of farmers in Uganda utilized pesticides that contained at least one active ingredient. Moreover, the study reveals that overall pesticide exposure, including Glyphosate, was linked to several neurobehavioral outcomes. These outcomes encompass impaired visual memory, language skills, perceptual-motor function, and complex attention problems (Fuhrimann et al., 2021). While this study focuses on the detrimental effects observed in the adult population, other studies exploring the neurological impacts of pesticide exposure provide further evidence that these harmful outcomes are not limited to adults.

Another study examines the neurobehavioral performance outcomes among children in the famous floricultural industry area of Pichincha province in Ecuador, where plantations use multiple pesticides including Organophosphates. In this area, pesticide application intensifies in periods shortly before the harvest season known as the Mother's Day Flower Harvest (MDH) season. In their study (Espinosa da Silva et al., 2022) utilize the MDH season to examine the effects of pesticide exposures during different periods on various neurobehavioral development domains among more than 1000 examined children and adolescents. They analyzed three different periods starting in 2008, April 2016, and July to October 2016. In the 2008 examination, 313 participants were chosen from the prior Access and Demand survey conducted in 2004. They employed two selection criteria which involved selecting a child who had lived with a floriculture worker for at least one year or choosing a child who had never been in a household with a floriculture worker or pesticide storage. For the 2016 examination, 316 new participants were selected from the 2004 survey list. Additionally, 238 participants from the 2008 examination were reexamined, and 124 additional volunteers recruited through village office advertisements were examined (Espinosa da Silva et al., 2022).

Similar to the previous study, this research also assesses five different neurobehavior performance domains including social perception, language, memory/learning, attention/inhibitory control and visuospatial processing. The researchers employ linear regression and generalized linear mixed models to analyze the cross-sectional and longitudinal relationships between the examination date (measured in days after the MDH) and neurobehavioral outcomes in children and adolescents. The results show that children and adolescents exhibited lower neurobehavioral performance immediately after the harvest period. The authors conclude that periods with intensive pesticide application (MDH) are negatively affecting neurobehavioral development among children and adolescents and that these effects decline during the periods when farmers apply fewer pesticides (Espinosa da Silva et al., 2022). These findings are consistent with the previously discussed study on neurobehavioral development and are further supported by other studies utilizing different methodologies. These include a systematic review study that examined longitudinal studies on prenatal exposure to Organophosphate (OP), which reports several neurological deficits among infants, including cognitive deficits, behavioural deficits, and motor deficits (Muñoz-Quezada et al., 2013).

***Application of the Neurobehavioral parameter approach in developing countries.***

These two studies provide researchers in Tanzania and other developing countries with a comprehensive methodology for assessing the effects of pesticides on various domains of neurobehavioral performance, specifically those discussed in the two studies (Espinosa da Silva et al., 2022; Fuhrimann et al., 2021). What makes these studies particularly relevant and applicable to developing countries is the fact that they do not rely on pre-existing data on neurobehavioral performance. Instead, neurobehavioral performance can be assessed as needed. Furthermore, this approach is not overly complex and can be learned or overcome through interdisciplinary collaboration with experienced researchers, even though analyzing the neurobehavioral outcomes requires specific skills.

Moreover, the utilization of a period of intensive pesticide application as practised in Ecuador represents another way researchers in developing countries may use proxies to address the absence of data on pesticide use among farmers to examine the health effects associated with pesticides in their context.

While both case studies benefit from large sample sizes, which should improve their statistical power, the use of self-reporting data in the study in Uganda (Fuhrimann et al., 2021) could, if not properly handled, compromise the credibility of the research due to associated challenges of self-reported data. However, when self-reporting data is carefully planned and organized, it can successfully tackle issues related to the availability of microdata on pesticide use in developing countries.

Lastly, when adopting the approaches used in these two studies (Espinosa da Silva et al., 2022; Fuhrimann et al., 2021), it's crucial to focus on strengthening the methodologies to enhance their robustness, establish causal relationships, and gain deeper insights into pesticide effects.

In the Uganda study, the quasi-experiment approach employed (Fuhrimann et al., 2021) showcased its effectiveness. However, it's important to note that the selection of participants for the control group, particularly organic farmers, utilized a non-random method—namely, snowball sampling. While this approach can effectively overcome data collection challenges with organic farmers, it's important to be aware of its limitations, including potential selection bias. Furthermore, the study in Uganda did not explore the joint effects of multiple active pesticide ingredients. Future research could expand upon this aspect by investigating the joint effects, considering that farmers often encounter and use various pesticide-active ingredients in their daily work.

As for the study in Peru (Espinosa da Silva et al., 2022), it remains unclear whether participant selection was conducted randomly or through other means. For forthcoming studies adopting a similar approach, integrating a random sample selection procedure would be beneficial. Additionally, researchers could explore alternative methodologies that provide solutions for associated limitations when the use of a random sampling procedure is impractical.

**ii. Urine biomarkers approach (*Urinary concentrations of pesticide metabolites*).**

The effects of pesticides on human health extend beyond those presented in the approaches discussed earlier. One popular and widely used approach among epidemiologists involves measuring biomarkers and metabolites present in body fluids, specifically urine. This approach allows researchers to study the metabolic process and gather valuable information that helps to understand the health status of individuals exposed to pesticides (Sabbioni et al., 2022). By utilizing this technique, researchers can examine the level and types of pesticide chemicals to which a person is exposed and establish a causal link to commonly known diseases. Several studies have employed this approach to investigate the effects of pesticides on human health. Focusing on different health aspects the following are some of these studies,

- **Urine biomarkers approach*: Pesticide exposure and children's respiratory health***

Employing the urine biomarkers approach, Raherison et al. (2019) conducted a large survey in a rural area of a French vineyard to investigate the link between pesticide exposure (specifically dithiocarbamates fungicides) in the air and respiratory health among young children. The study surveyed 281 schoolchildren aged 3 to 10 years from four schools and examine symptoms of common respiratory health outcomes such as Asthma and Rhinitis, associated with pesticide exposure.

To assess pesticide exposure, the researchers measure the presence and variation of 56 different pesticides in the ambient air of the four schools. Measurements were taken during two periods, i.e., winter, when pesticide levels are typically low or absent, and summer, when pesticide application is intensive, and levels are high. The researchers also collected urine samples from the children to measure the concentration of dithiocarbamates fungicides, which are commonly used in agriculture and horticulture to control fungal diseases in crops. In addition, the children underwent a Peak Expiratory Flow (PEF) test, which measures the speed at which a person can forcefully exhale air. This test provides an indication of lung function. In the end, they construct quantitative symptoms score for each child (Raherison et al., 2019).

They analyze the collected data using a logistic regression model to investigate the relationship between pesticide exposure and children's respiratory health. The study finds a significant presence of fungicides, specifically folpet and dithiocarbamates (89.3%), in the air surrounding the schools. Additionally, the researchers report the presence of certain insecticides (10.6%) (Raherison et al., 2019).

The study does not find evidence linking pesticide levels around the school to the symptom scores of the children during summer. However, they establish an association between urinary concentration of pesticides and Asthma and Rhinitis among children. The researchers conclude that the risk of exposure to pesticides is higher during the summer due to intensive pesticide application on farms compared to the winter period (Raherison et al., 2019). One possible explanation for these contradictory results could be that the children were not necessarily exposed to pesticides in the school surroundings but rather during extracurricular activities, which the study did not take into consideration. This is something future studies in developing countries should take into consideration while designing the methodology using this approach.

***Application of the urine biomarker approach to examining children's respiratory health in developing countries.***

Although many studies that employ the urine biomarker approaches often rely on large surveys and observational techniques instead of quasi-experiments, this method remains highly advantageous, especially in developing countries where challenges of obtaining data on pesticide application and exposure prevail. With this approach, researchers can construct comprehensive assessments of pesticide levels, types, and exposure by analyzing both ambient air and urine biomarkers. This eliminates the need for finding appropriate proxies and allows for localized examination of pesticide effects.

However, when adopting the urine biomarker approach presented in this study, researchers in Tanzania and beyond are encouraged to incorporate additional techniques to address potential bias and methodological limitations that may arise from relying solely on large surveys and observational techniques. One option is to incorporate quasi-experiments or (quasi-)natural experiments. For instance, in addition to surveying the population residing in areas with intensive pesticide application (treatment group), researchers can also survey a neighbouring community with similar observable characteristics but minimal or no pesticide application and exposure (control group).

However, it is important to note that both quasi-experiments and (quasi-)natural experiments lack random assignment, which can also lead to bias. To minimize potential bias, researchers can incorporate techniques such as matching, which can allow them to create more comparable groups based on observable characteristics. This reduces the impact of confounding factors, enhances internal validity, and strengthens both the robustness of their methodology and results. Also, by implementing these strategies, researchers can confidently establish causal effects. The discussion on addressing these challenges continues in chapter three.

- **Urine biomarkers Approach*: Pesticide exposure and sperm quality***

The application of the urinary biomarker approach to examine health effects due to exposure to pesticides is not limited to the young population as presented in the study above. Examination of the link between pesticides and sperm quality among male adults is another parameter gaining importance. This is due to increasing reports on adverse effects associated with insecticides such as organophosphorus and pyrethroids on sperm quality (Perry et al., 2007; Radwan et al., 2015).

In a comprehensive survey conducted in Poland Radwan et al. (2015) explore the relationship between environmental exposure to Pyrethroids, another widely used pesticide, and the presence of abnormal chromosome numbers in sperm cells, referred to as sperm chromosomes disomy. Sperm chromosome disomy is an issue because males are likely to pass sperm chromosome disomy to their offspring during fertilization. Further, this condition can lead to various genetic disorders and conditions including Down syndrome (Trisomy 21), Klinefelter syndrome (XXY) and

Turner syndrome (45, X) (Butler, 2009; Iwarsson et al., 2015). In their study, a non-random selection approach was used to choose 195 study participants from a total of 344 men who were undergoing infertility tests at a clinic.

The researchers collected urine samples and examined four Pyrethroids Metabolites, i.e. cis-3-(2,2-dichloro vinyl)-2,2-dimethyl cyclopropane carboxylic acid (CDCCA), 3-phenoxy benzoic acid (3PBA), cis-2,2-dibromovinyl-2,2- dimethyl cyclopropane-1-carboxylic acid (DBCA) and trans-3-(2,2-dichloro vinyl)-2,2-dimethyl cyclopropane carboxylic acid (TDCCA) using a validated gas chromatography ion-tap mass spectrometry method. They also collected semen samples and performed semen analysis (sperm counts and percentage of sperm motility) using a computer-aided semen analysis (CASA). To examine the relationship between the observed level of pyrethroids in the urine and sperm chromosome disomy, they employ a negative binomial regression modelling and a generalized linear mixed model with a Poisson distribution. While their results show that CDCCA is associated with disomy of chromosome 18 and positively associated with the urinary level of 3PBA, the level of TDCCA in urine is related to XY disomy and disomy of chromosome 21. Also, Urinary 3PBA level 650 has an association with disomy of sex chromosomes (XY disomy, Y disomy, disomy of chromosome 21 and total disomy). With these results, they conclude that pyrethroids may be one factor contributing to an abnormal number of chromosomes in the sperm cells (sperm aneugens) (Radwan et al., 2015).

Negative health effects on semen quality due to exposure to pesticides are also reported in another study in China which adopted a similar approach in examining exposure among men of reproductive age to a distinct set of insecticides, i.e., pyrethroid and organophosphorus. While this study looks at a different aspect of semen quality, i.e., sperm concentration or count (Perry et al., 2007), it also involves a random sampling approach which is not the case in the previous study. Eighteen (18) urine samples were randomly chosen from a reproductive male cohort consisting of 202 men.

Along with the urine samples, semen samples were also collected, and both were analyzed in the laboratory to evaluate pesticide exposure and semen count. To ensure the reliability of the findings, the laboratory analysts were unaware of the individual characteristics of the sample as well as of the study's objective. The analysis of urine samples for non-persistent pesticides involved a screening method that utilized mass spectrometry and quantification through isotope dilution (ID) calibration. The targeted pesticides for analysis included organophosphates, triazine herbicides, chloroacetanilide herbicides, phenoxyacetic acid herbicides, and pyrethroid (Perry et al., 2007).

Among the pesticides examined, the research findings reveal higher levels of organophosphates and pyrethroids metabolites implying a significantly greater exposure to these two pesticides among the participants under study. Moreover, when comparing the exposure levels of these pesticides in China to those observed in the general US population, the study participants in China exhibit even higher levels of exposure. Further analysis of the existing link between the level of exposure and sperm concentration reveals that participants with higher-level metabolites also had a lower level of sperm count (Perry et al., 2007).

***Application of the urine biomarker approach examining sperm quality in developing countries.***

The studies mentioned above provide valuable and relevant methodological insights for investigating the health effects associated with pesticide exposure in developing countries like Tanzania, with a specific focus on male reproductive health.

In contrast to the research conducted in Poland (Radwan et al., 2015), which utilized a non-random sampling approach but maintained a relatively substantial sample size of 195 participants, lending it strong statistical power, the study undertaken in China (Perry et al., 2007) has a smaller sample size that could potentially compromise its internal validity. Researchers adopting the latter approach are advised to consider increasing the sample size to enhance the statistical power.

Nevertheless, despite its smaller sample size, the study in China possesses several strengths over the Polish study. For instance, the use of random sampling and a blind strategy in the Chinese study helps mitigate selection bias, enhancing its overall rigour and robustness. Another interesting aspect of this study is the selection and characteristics of study participants. Instead of studying the directly exposed population or those living in pesticide-intensive areas, the researchers study urban dwellers who occasionally visit their families in rural China (Perry et al., 2007). The assumption here is that participants are exposed to pesticides during visits to their hometowns.

The frequency of urban dwellers visiting rural areas in some developing countries may vary, but the common occurrence of visiting rural areas other than one's homeland can be a valuable phenomenon for researchers to consider when planning their approach. For instance, in Tanzania, it is well-known that the Chagga tribe, residing in urban areas, place significant importance on travelling to their rural villages in the Kilimanjaro region from October to December annually for traditional rituals, ceremonies, and family gatherings. Researchers could take advantage of this practice, similar to the strategy discussed in the aforementioned study in China and conduct comparable studies.

Moreover, while the methodology adopted by the study in China is interesting, researchers, when deciding to adopt this approach for future studies, have room to further improve the analysis by including the control group which can be urban dwellers with similar characteristics but not periodically visit rural or other agricultural areas. By doing so researchers ensure that they exclude the effect of other confounding factors which are likely to affect the semen count among men of reproductive age and they can therefore claim the casual relationship.

# CHAPTER THREE

## Conclusion and Recommendation

### 3.1 Conclusion

This study contributes to our understanding of pesticide effects on human health in developing countries through an extensive literature review and examining the replicability of methodologies employed in selected studies. The review reveals several key findings and knowledge gaps.

Firstly, previous studies have employed diverse methodological approaches, which this study has classified as general and specific. General approaches focus on broader health outcomes such as infant mortality rates and pregnancy outcomes in populations exposed to pesticides, while specific approaches examine pesticide effects on health outcomes using parameters like neurobehavioral performance and urinary pesticide metabolite concentrations.

Secondly, this research identified valuable insights into the adverse health effects associated with pesticide exposure. Despite the pronounced benefits of pesticides in improving agricultural productivity and in public health (controlling vector-borne diseases), they also carry substantial risks to human health, including but not limited to increased infant mortality, respiratory and allergic symptoms, and impaired vision and cognitive function (Frank & Taylor, n.d.; Fuhrimann et al., 2021; Grube et al., 2011; Muñoz-Quezada et al., 2013; Rani et al., 2021; Staudacher et al., 2020; Taylor, 2022). Although a study in Uganda reports positive pregnancy outcomes associated with the use of pyrethroid-treated mosquito nets (Roh et al., 2022), further investigation of additional health parameters related to pregnancy outcomes is necessary for a comprehensive understanding of the effects.

Thirdly, although case studies from developed countries have provided valuable insights on methodologies and health effects, there remains little knowledge regarding the health effects of pesticides in developing countries. Moreover, the applicability of these methodologies to the context of developing countries hinges on data availability, particularly regarding pesticide use and exposure, which often presents challenges. Researchers in these settings are encouraged to employ innovative methodologies and thoughtfully select appropriate proxies to address data limitations.

Lastly, researchers can opt to adopt some of the methodologies presented and consider the highlighted recommendations to advance understanding and research on pesticides and their health effects in developing countries. Furthermore, the recommendations offer potential solutions to the obstacles hindering a rigorous analysis of pesticide-related health effects in developing country settings.

## 3.2 Recommendations

The following recommendations are put forth for policymakers, researchers, and relevant stakeholders involved in addressing knowledge gaps, mitigating health risks associated with pesticides, and promoting sustainable pesticide use in developing countries.

### *3.2.1* Emphasis to conduct quasi-experiment studies.

Many of the current studies on pesticide effects primarily rely on large surveys and observational studies. While some of these studies adopt large sample sizes which should improve their statistical power, internal validity can still be questioned. Researchers should consider moving to adopt quasi-experiments to establish a causal link between pesticide exposure and health effects. Moreover, these approaches will enhance robustness in terms of methodology and generate evidence to support claims for a causal relationship between pesticides and health effects. Some of the common quasi-experiment approaches are mentioned in the paragraph below (see 3.2.2).

### *3.2.2* Adopting methods that mitigate bias in the absence of randomization.

Randomized Control Trials (RCTs) are widely acknowledged as the gold standard of experimental designs due to their ability to reduce bias and enhance research validity. However, there are instances where randomization may not be practically or ethically feasible. This is particularly evident in the study of pesticides, where exposing individuals to these substances solely for research purposes is not viable. Furthermore, pesticide exposure is non-random, occurring through various channels such as residential, occupational, and food contamination. These inherent limitations in pesticide research pose potential biases, including selection bias.

Building on the quasi-experiments argument presented above, researchers can incorporate approaches such as Difference in Difference (DiD), Propensity Score Matching, and Regression Discontinuity Design to address these challenges. By utilizing these methods, researchers can enhance the methodological robustness of their studies and contribute to a better understanding of the effects of pesticides in developing countries.

### *3.2.3* Promote interdisciplinary collaboration among researchers.

Collaboration among researchers in the fields of pesticides and human health along with experts from diverse disciplines such as public health, economics, toxicology, agriculture, and epidemiology, is essential for the successful transition towards quasi-experiments. This interdisciplinary approach enables a comprehensive understanding of the health effects linked to pesticide exposure and promotes the exchange of research knowledge. It also facilitates the adoption of more rigorous research methodologies. Furthermore, such collaboration plays a vital role in designing effective mitigation strategies to address the health effects associated with pesticide exposure.

### *3.2.4* Foster international collaboration

The existing literature highlights the disparity in knowledge generation and proactive policies on pesticide regulations between developed and developing countries. To address this gap, international collaboration plays a crucial role by complementing the recommendations above. Such collaboration enables the transfer of knowledge, experience, best practices, and resources among researchers, policymakers, and organizations. Furthermore, through collaborative efforts, countries can attain a deeper understanding of the effects of pesticides on human health.

### *3.2.5* Strengthen regulations, enforcement and raise awareness.

The presence of departments dedicated to chemicals and pesticide regulation in various developing countries is well acknowledged. However, existing literature highlights a concerning trend in developing countries, where the use of pesticides is on the rise without adequate regulatory measures in place which is likely to exacerbate the associated health effects (Bonner & Alavanja, 2017; Fuhrimann et al., 2021; Snyder et al., 2018). There is an urgent necessity to strengthen the capacity of these departments in terms of their regulatory practices, particularly regarding robust regulations governing the sales, distribution, and usage of pesticides.

Additionally, governments, communities and public health agencies should prioritize awareness campaigns aimed at informing users and the public about the potential risks associated with pesticide exposure and promoting best practices in pesticide handling. These measures are crucial for addressing the current challenges and mitigating the adverse effects of pesticide use in developing countries.

### *3.2.6* Improve data collection and management.

While this is easier said than done, developing countries face ongoing challenges in improving data availability in the field of pesticides and beyond. It is crucial to continuously work on addressing these challenges as they significantly impact various socioeconomic aspects, including pesticide research. To address this issue, further efforts should be directed towards generating comprehensive data on pesticide production, imports, and application across different sectors. A durable solution could be to strengthen collaborations in data management among government agencies, research institutions, and relevant stakeholders. This can facilitate the establishment of robust data collection systems and enable data sharing across sectors, ultimately enhancing the research capacity of investigating the effects of pesticides in developing countries.

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