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Responsiveness of Offshored Clinical Trials among Women in the Philippines

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The state of responsiveness of the offshored clinical trials in the Philippines on the health needs of Filipino women is a quantitative research using the feminist standpoint as the theoretical framework. To test for responsiveness, conditions on both offshored clinical trials and the health needs of Filipino women are the main indicators which are subcategorised by death, premature death/years of life lost (YLL), morbidity/years lived with disability (YLD), neglected tropical diseases (NTDs), maternal conditions, and specific conditions affecting Filipino women. The results and findings obtained are then analyzed on Filipino women, men, and the general population. This study used descriptive analysis describing distributions using proportions and percentages, rates and ratios, and frequencies in the data obtained from 1) ClinicalTrials.gov and 2) from the Institute for Health Metrics and Evaluation. An in-depth analysis on validating/invalidating the state of responsiveness of offshored clinical trials to the health needs of Filipino women that highlights the case '65 clinical trials on diabetes mellitus', conditions that cause death and morbidity that mostly affect Filipino women, maternal conditions, neglected tropical diseases, and female/male-specific conditions. The implication of the concept 'responsiveness' is also discussed based on the results and findings, but also as a concept itself based on the definitions attached to it by the different international organizations. The health status of Filipino women and the conditions that affect them were analyzed by incorporating the principles of feminism.

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Preface

The physician who begins from the standpoint of the patient, respecting the patient's judgments about his bodily experience, the character of his daily life, what conduces to his happiness, and the other considerations that can be brought to bear on his condition, is then able to enter into a collaboration with her patient. Working together, they can construct an understanding of what the patient is doing and thinking, and what constitutes an optimal medical response (Lindemann, 2007, p. 123).

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List of Abbreviations and Acronyms

CIOMS	Council for International Organizations of Medical Sciences
COPD	Chronic Obstructive Pulmonary Disease
DALY	Disability-Adjusted Life Year
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
HI	High Income Countries
HIV/AIDS	Human Immunodeficiency Virus infection and Acquired Immune Deficiency Syndrome
IHME	Institute for Health Metrics and Evaluation
LMICs	Low and Middle Income Countries
NBAC	National Bioethics Advisory Commission
NIH	National Institutes of Health
NLM	National Library of Medicine
NTC	Clinical Trial Registry Number
NTDs	Neglected Tropical Diseases
R&D	Research and Development
STATA	Data Analysis and Statistical Software
UNAIDS	Joint United Nations Programme on HIV and AIDS
UNDP	United Nations Development Programme
WHO	World Health Organization
WMA	World Medical Association
YLD	Years Lived with Disability
YLL	Years of Life Lost

1 Introduction

Western thought imposes the ideal health and economic status of the world (Disch & Hawkesworth, 2016; Rosenfeld, 2001). It is also not a question that regions in the developing countries became dependent on the prescription of Western worldviews on health and economics. It is thus also not surprising that health research, specifically on pharmaceutical products is also Western-centered not only in terms of the priority market but with regard to its version of how patriarchy manifested itself.

The offshoring of clinical trials in developing countries like the Philippines assumes responsiveness, i.e., that the research "*purposely aims to provide new knowledge about the best means of addressing a health condition present in that (i.e., the host's) community or region*" (Council for International Organizations of Medical Science, 2016, p. 3). Earlier research shows that clinical trials done in the Philippines respond primarily to the needs of high income countries than they do the needs of the Filipinos (Bernabe R. D., 2018). *In this study, I wish to investigate whether clinical trials in the Philippines are responsive to the health needs of Filipino women.* To achieve this analytical goal, this research thesis describes and analyzes patterns in distributions based on percentages and proportions, ratios and rates, and frequency counts of conditions from the offshored clinical trials in the Philippines with the health needs of the Filipino women using the following indicators: years of life lost (YLL), years lived with disability (YLD), maternal conditions, female/male-specific conditions, and neglected tropical diseases (NTDs) affecting women.

There are indications that responsiveness to the needs of women is a major issue. The persistent high maternal mortality rate among Filipino women in the Philippines suggests how medical advancements spurred by Western pharma and medical models have failed to address the needs of Filipino women. Closely related to the issue of responsiveness is the issue of post-trial access (Council for International Organizations of Medical Science, 2016, p. 3), i.e., that with the concerns for responsiveness is also the concern that pharmaceutical interventions are more accessible to Filipino men than they are to Filipino women. This study will primarily focus on responsiveness. The issue of post-trial access will only be brought up as a related issue in the discussion.

The Philippines is an interesting case because of its relevance in terms of clinical trials. Asia has the highest number of patients and investigator sites in terms of global/offshored clinical trials submitted to the European Medicines Agency (EMA) for marketing authorization applications among continents in the world (European Medicines Agency, 2013). Further, Asia has the largest average annual growth in terms of the number of clinical trials (Silva, Amato, Guilhem, Carvalho, & Novaes, 2016). Among these countries in Asia that belongs to the major contributors of patients in the pivotal trials, the Philippines forms the top three, along with India and China (European Medicines Agency, 2013). This trend is part of the much larger trend of offshoring of clinical trials by pharmaceutical companies, i.e., the transferring or facilitating clinical research trials from affluent countries to less affluent countries (Glickman, et al., 2009; European Medicines Agency, 2013). For instance in the EU, from 2011 up to the present, the number of patients in pivotal trials (determining trials) from the "rest of the world" (ROW)[1] submitted in marketing authorization applications to the EMA has outnumbered the number of patients from the European Union (EU) and North America, respectively (European Medicines Agency, 2013).

This study is relevant as an inquiry on a vulnerable group, specifically Filipino women. Feminist researchers and feminist practitioners in the fields of biomedical ethics, medicine, anthropology of medicine, development studies, social welfare, public and global health, and international health policy highlight this relevance by talking about the importance of having a grip on alleviating women's health (Crasnow, 2014; Annandale, 2009; Dodds, 2000; Tong, 2004). It is from a feminist perspective that I wish to investigate the issue of responsiveness of offshored clinical trials in the Philippines to the health needs of Filipino women.

[1] "Rest of the World (ROW):
- Africa;
- Middle East/Asia/Pacific;
- Australia/New Zealand;
- Central/South America;
- CIS (Commonwealth of Independent States i.e. Russia, Ukraine, Georgia etcetera);
- Eastern Europe (non EU) (e.g. Croatia, Serbia etcetera)" (European Medicines Agency, 2013, p. 7).

1.1 Aim and Research Question

The aim of this study is to determine whether the offshored clinical trials conducted in the Philippines from 2007 to 2016 are *responding* to the health needs of Filipino women. By responsiveness, this study adopts the definition by the Council of International Organizations of Medical Sciences quoted above, i.e., that the research purposely aims to "provide new knowledge about the best means of addressing a health condition present in the community or region." To test for responsiveness, I looked at the indications of the conditions on both offshored clinical trials to the health needs of Filipino women. By health needs, I used the following indicators: death, premature death / years of life lost (YLL), morbidity / years lived with disability (YLD), neglected tropical diseases (NTDs), maternal conditions, and specific conditions affecting Filipino women. The results are then compared with those of Filipino men. Secondarily, my contribution is not limited to identifying the conditions that were addressed by the offshored clinical trials. I also used the feminist standpoint in interpreting my results in my attempt to identify the underlying reasons why women's health is still compromised despite women's life longevity. *In this study, I wish to answer the question, Are offshored clinical trials in developing countries like the Philippines responsive to the health needs of the Filipino women?*

2 Theoretical framework

Since this study will use the lenses of the feminist framework, an elaboration of the feminist standpoint that I am employing in this research thesis is in order. I will do this by going through three relevant themes of said standpoint, which will be prominent in the discussion. The three themes are as follows: an intersectional approach on women's health; the feminist standpoint when it comes to the vulnerability of women; and the dismantling of Western influence in the field of health and medicine. First, a brief description of the feminist standpoint has to be given to better frame everything.

Women became recipients of the standardization of medical and clinical practices, and models; for instance, women "are diagnosed as mentally ill more often than men, perhaps because they are subject to incoherent standards of mental health" (Wolf, 1996, p. 57).

According to David Thomasma, medicine as a practice follows certain objective standards; these standards are consequence not only "from moral theory, but from the goal of healing, and from long experience in categorizing and treating illnesses" (Thomasma, 2004, p. 107), As a result, women's health conditions may be cured but this did not necessary translate into better quality of life (Wolf, 1996). What is challenging in this research is to establish new knowledge that goes beyond the norms of research by being critical of existing knowledge. *Clare Hemmings described the feminist standpoint epistemology as a recognized method of inquiry that allows the interconnectivity in the relation of ontological (reality), epistemological (knowledge), and transformative* (Disch & Hawkesworth, 2016). This will be the theoretical framework of this study. Standardizing clinical trials for both men and women might be a disadvantage for women. Susan Wolf gave several impacts of why studies enrolling women should be prioritized in advancing women's health:

- Exclusion from clinical trials hurts women in the sense that drugs that are tested only on men must have a cumulative impact on women;
- Drugs that have never been tested on women are routinely prescribed for and taken by them;
- All women, no matter what kind of health care they can pay for, suffer from the lack of knowledge about the effects of male-tested therapies in women and from the absence of basic research on primarily female health problems (Wolf, 1996, p. 219).

2.1 Intersectional Approach on Women's Health: a Feminist Perspective

Feminist standpoint is useful for this study, especially in the determination to make advancement particularly on the health needs of Filipino women. "Recent gains in serving women's health interests are not only maintained but increased, they have proposed a women's health specialty that would focus exclusively on women's health concerns, both non-reproductive and reproductive" (Tong, 2004, p. 154). Rosenfeld presented these differences in society that place women at a disadvantage, to show that women's health needs more attention than that of men (Rosenfeld, 2001). Rosenfeld stated that women's health is complex that needs to be socially, culturally, and psychologically treated; the multiplicity

however derived from evidence must be reinforced by a standpoint[2] that would provide some empirical breadth (Crasnow, 2014; Rosenfeld, 2001). In this sense, the feminist standpoint theory is an intersectional analysis that recognizes women and offers alternative ways to the hierarchical and exploitative practices in clinical trials that are reflective of the patriarchal system (Wolf, 1996). Feminist standpoint therefore was meant to promote the principles of inclusivity and justice (Disch & Hawkesworth, 2016; Crasnow, 2014). Like in the course of medical research and practice (e.g. clinical trials and medical treatment), women's participation and voice should be considered as important as physician's point of view. Wemos Foundation for example was able to document that

> A number of other news media, including the Dutch documentary television programme Netwerk, the Dutch national newspaper NRC Handelsblad and the British Channel Four have reported on the abuses surrounding clinical trials in developing countries (Wemos Foundation, 2008).

The abuses related to clinical trials are confirmed by Wemos partner organizations both in Asia and in Latin America, with abuses ranging from exposing participants to toxic experimental drugs with questionable informed consent, to lack of regulatory measures to protect the participants, and the lack of post-trial access (Wemos Foundation, 2008). The Wemos reports did not specify the gender of the participants. Feminist standpoint theory does not encourage any human being to feel violated in any form, at any time in the clinical trial process. At the same time, feminist bioethicists also suggested the vitality for medical and health practices like clinical trials to be reexamined not only for the effects of drugs and treatments in patients that are involved in the study but for patterns of discrimination, exploitation, and dominance that surround women (Wolf, 1996). It is important to understand that clinical trials are intended mostly if not all to patients who "seeks assistance (i.e. patients) and another person who freely professes to be able to heal (i.e. doctors)" (Pellegrino, 2004, p. 185). In the case of power relation between 'patient and physician' in the examples above, feminist standpoint theory provides an impartial perspective on how to protect the rights and

[2] The authors cited prominent feminist's scholars such as Harding (1986); Longino (1990); Nelson (1990); and Code (1991)

> A standpoint is not merely one's perspective in virtue of the sorts of experiences one has from a particular social location. Standpoint theorists endorse the claim, widely held by many feminist epistemologists, that the locus of knowledge is at the level of communities, rather than individuals Thus, a standpoint is something achieved by a group. Individuals may contribute to the achievement of a standpoint, but this is something that individuals cannot accomplish on their own (Disch & Hawkesworth, 2016, p. 265).

the welfare of vulnerable patients. "Starting off research from women's lives will generate less partial and distorted accounts not only of women's lives but also of men's lives and of the whole social order" (Harding, 1993, p. 56). The three basic principles of feminist standpoint as stated are

> (1) Knowledge is socially situated[3]. (2) Marginalized groups are more socially situated in ways that make it more possible for them to be aware of things and ask questions than it is for the non-marginalized. (3) Research, particularly those focused on power relations, should begin with the lives of the marginalized (Bowell, 2019; Harding, 1993).

The three basic principles of feminist standpoint are fundamentally empirical; where knowledge must be experienced for it to be valued (Cartwright & Montuschi, 2014; Moran, 2000). Pellegrino pointed out that in the encounter between patient and doctor, the experiences of the patient are more important for proper diagnosis, therapy and prognosis (Pellegrino, 2004). This perspective has the benefit to identify forms of discrimination, exploitation, and biases in an intersectional manner. For example, focusing on the patient's lived experiences and the ways in which social identity categories and societal systems of discrimination on the basis of gender, race/ethnicity, class, and others, and its intersections, affect these lived experiences. Therefore, by establishing knowledge based on the long-ignored perspective of women, the existing androcentric practices that represent inadequacies on women's health should be questioned based on empirical evidences. The evidence should not be limited to something tangible or observable; it should ideally also include the experiences of Filipino women in clinical trials, even if the study has already been completed. Further analysis shows how feminist interpretations "of female experience were used to provide evidence of patriarchy, and at the same time were used to question the truth status of some female experiences" (Disch & Hawkesworth, 2016, p. 235). My study on the responsiveness of clinical trials on Filipino women will purposely raise awareness for the improvement of their health status and their quality of life. It is carefully working on towards integrating its results to public health as an adaptable approach for the advancement of women's health in general.

[3] "Haraway named the alternative to innocence "situated knowledge" (also "feminist objectivity"), a position from which to stake a claim in a social world that acknowledges the "radical historical contingency for all knowledge claims and knowing subjects" and simultaneously commits itself to producing faithful accounts of the "real" world" (Disch & Hawkesworth, 2016, p. 125; Harraway, 1998).

2.2 Vulnerable Women and Feminist Standpoint Theory

The Philippines, because of its location, is also affected by NTDs. According to the WHO, women and children are most affected by it (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013). In this study, clinical trials must be examined and analyzed carefully especially that new therapeutic products address only 3.8% of neglected diseases; even though these diseases account for 10.5% of the global burden of disease (Doctors Without Borders, 2012). To date, we know nothing as to how responsive (or not) clinical trials are to the health needs of the population. Much less do we know how responsive clinical trials are to the health needs of vulnerable groups such as women in LMICs. The globalization[4] of clinical trials may be explained by several factors, the most prominent of which are cost savings; shorter recruitment timelines; and less stringent regulatory constraints (Seth W. Glickman, et al., 2009; Wemos Foundation, 2008). Given the other motives for the offshoring of clinical trials mentioned, these factors are not necessarily ethically problematic so long as ethical requirements are in order. By ethical requirements, we do not just refer to informed consent; as stated in guidelines such as CIOMS, it is important as well that these clinical trials conducted in the Philippines contribute to the addressing of health needs, i.e., responsive, and in increasing the accessibility of Filipino women to essential and innovative medicines. Susan Wolf gives a concrete example of the implication on women of having offshored clinical trials, she says

> The first way in which women are harmed by the barriers to their participation in clinical trials is their reduced access to genuinely new drugs and therapies not already licensed for any indication, which generally can be obtained only through protocols (Wolf, 1996, p. 218).

The primary responsibility of the feminists that is applied in this study is to challenge the inadequacy, and bad practices, traits, and values that transpired in the offshoring of clinical trials in the Philippines; where women themselves fail to see and acknowledge (Tong, 2004).

[4] Ong stated that "What was first discussed as 'globalization' has now been specified as neoliberalization that takes different forms in different parts of the world. Neoliberal governmentality reflects the infiltration of market-driven truths and calculations into the domain of politics" (Disch & Hawkesworth, 2016, p. 916).

2.3 Dismantling Western Influence in the Field of Health and Medicine

The "prevalence of an illness or condition is the number of individuals who have the condition at any moment" (World Health Organization, The Global Burden of Disease 2004 Update, 2008, p. 31). For instance, the prevalence of maternal death (which is currently at 162 per 100,000 live births) and prolonged morbidity among Filipino women could indicate that life expectancy alone does not necessarily mean that women's health is better than men's (World Health Organization, Maternal and reproductive health, 2015; Guerrero, 2011). In developing countries, maternal deaths hold for up to 99 percent (more than five hundred million) annually (Everett & Charlton, 2014). Considering that the feminist standpoint does not acknowledge the neutral standpoint, it is important for research protocols to respond to problems that are mentioned (Wolf, 1996).

Historical events in the medical field show how biases and its standardization had a tremendous impact on women's health. Cases of maternal and infant mortality in some regions of the world like the Philippines stay high, which is comparable to the case in Europe hundreds of years ago (Everett & Charlton, 2014). Prior to the 17th century, Western knowledge introduced binary thinking, i.e., social and biological, mind and body, reason and emotion, rational and irrational, active and passive, culture and nature, rich and poor, and etcetera (Plumwood, 1993; Wolf, 1996; Disch & Hawkesworth, 2016). Everett and Charlton stated regarding the Western influence in biology as well as in medicine about gender distinction as logically inherent. They further explained that

> Some have pointed out that not until relatively late in Western history did the dualism found in both sex and gender distinctions come to dominate our thinking and, therefore, our expectations (Everett & Charlton, 2014, p. 13).

This binary thought reveal the constructed position of women: women are designated at home and are prohibited from engaging in public / social life, education, and job opportunities such as being philosophers, physicians, academicians, theologians, etcetera (Annandale, 2009). Annandale added that as an effect of this binary thought, in the 18th and 19th century, women from the upper class (bourgeoisie) became eligible patients of the rational male physicians, as women were perceived to be unescapably (biological/natural) unhealthy (Annandale, 2009, p. 5). Western binary thought was also expanding its influence in mitigating the fiscal

difficulties of their respective countries and the countries they colonized. It suggested that the economic status of a country was inversely proportional to its fertility rate (Banerjee & Dulfo, 2011). Feminist writers such as "Mary Astell and Mary Wollstonecraft not only stressed that women's oppression was socially rather than biologically caused but did so in the name of health and body politics" (Annandale, 2009, p. 4). In the early 19th century, "health and illness was a sensitive political barometer of socially troublesome gender identities, which feminists were able to press into the service of challenging the dualisms that nourished patriarchy" (Annandale, 2009, p. 5). In fact, it was in this period that male physicians were engrossed with labelling human organs and systems; henceforth, female reproductive function was critically associated with the general health and disease courses (Kuh & Hardy, 2002). In mid-19th century, the first female entered the male arena in medicine in the United States and became the first female physician (Office on Women's Health, 2002). Women by then were not anymore limited to being nurses and midwives. In the beginning of the twentieth century, health investment was pronounced through clean water and sanitation; mortality rate in general plunged dramatically specifically for infants and women during and post-birthing even before antibiotic was introduced (Banerjee & Dulfo, 2011; Office on Women's Health, 2002). Women's natural condition such as pregnancy became medicalized: "women's health was then primarily equated with maternal health and women's role as mothers" (Office on Women's Health, 2002). The advancement of the male-centered medical field became a barrier on women's participation that underrepresented them in the knowledge formation. On the positive end, nurses and midwives began to have formal training in their particular fields to regulate, and to improve their competency (Office on Women's Health, 2002). Further, due to economic, political, and social circumstances, "women were more likely to be accepted in medical school, since physicians were scarce" (Office on Women's Health, 2002, p. 2). However, society must still unlearn the Western androcentric and capitalistic foundation of knowledge in the medical field. Detecting the possible risks of this knowledge and studying these risks will reduce or avoid detrimental results; also, detection is "needed to explore how these early risk factors shape exposure and sensitivity to later risk, and conversely how early risk may be by later experiences" (Kuh & Hardy, 2002, p. 397). There have been several theoretical studies on responsiveness but none of them have ever been from the perspective of the feminist standpoint. Jana Everett and Sue Ellen M. Charlton attempt to analyze development and globalization under the feminist lenses, stating that

> Feminist research has focused on the origins and evolution of these distinctions in an effort to confront what might be called biological determinism—that is, the assumption of a natural and inescapable inevitability to the categories of male and female. Feminists have long argued that this kind of determinist thinking sustains a hierarchical order in which girls and women are always subordinate (Everett & Charlton, 2014, p. xi).

As such, it may be that existing literature is blind to the assumed Western androcentric and capitalistic foundation that women's health in particular may be subjected to, especially given the disadvantaged position of vulnerable women, such as women in the Philippines.

3 Literature Review

Clinical trials are increasingly offshored in developing regions and in the case of the EU, among the Rest of the World (ROW) countries, Asia has the most number of the patients and investigator sites, as well as the continent with the largest average annual growth in terms of number of clinical trials (Glickman, et al., 2009; Silva, Amato, Guilhem, Carvalho, & Novaes, 2016). India, the Philippines, and China were the major Asian country contributors in terms of the number of patients in pivotal trials[5] submitted for marketing authorization applications to the EMA (Silva, Amato, Guilhem, Carvalho, & Novaes, 2016). This means that developing countries such as the Philippines are vessels for developing new clinical trials that may or may not be responsive on the health needs of women. Clinical trials in developing countries such as the Philippines are supposed to be examined based on national regulations, ethical guidelines such as the Declaration of Helsinki, CIOMS, and other regional or national instruments. CIOMS also states that "if the knowledge to be gained from the research is intended for use primarily for the benefit of populations other than those involved in the research, the responsiveness requirement is violated" (Council for International Organizations of Medical Science, 2016, p. 4). Responsiveness therefore reinforces the importance of justice which is the equitable distribution of benefits and burdens of research (Council for

[5] "Usually a phase III study which presents the data that the FDA uses to decide whether or not to approve a drug. A pivotal study will generally be well-controlled, randomized, of adequate size, and whenever possible, double-blind" (Center Watch, 2019).

International Organizations of Medical Science, 2016). Despite the concrete explanation on how responsiveness must be observed by clinical trials conducted in developing countries such as the Philippines, the ambiguous notion of responsiveness has created disparities and ethical issues for not providing practical guidance (Shah, Wolitz, & Emanuel, 2013). Below are the different conceptions of responsiveness that Shah, Wolitz, and Emanuel provided (Shah, Wolitz, & Emanuel, 2013, p. 152)

Conception of Responsiveness	**What it requires**	**Proposed by**
Responsiveness to Health Needs	Research question must address a health need, not necessarily a health priority.	National Bioethics Advisory Commission (NBAC)
Responsiveness to Health Priorities	Research question must address a health priority or urgent health need.	Nuffield, London and Kimmelman; Council for International Organizations of Medical Sciences (CIOMS); National Bioethics Advisory Commission (UNAIDS)
Adding Reasonable Availability	Research question must address a health need or health priority and successful interventions must be made reasonably available.	CIOMS; UNAIDS; World Medical Association (WMA)

Within the literature, several reasons are provided why there is a shift of clinical trials away from the traditional Western countries towards developing regions, among which are the following

1.) Cost savings, as the typical cost report in these Asian countries is 1/10th the cost compared to the United States; 2.) shorter recruitment timelines as research participants are easier to find considering the large populations of Asian countries, many of the patients being treatment-naive; 3.) less stringent regulatory constraints; 4.) initiatives of the Asian governments to attract offshored clinical trials for the potential economic benefits; and 5.) a relatively workable healthcare infrastructure conducive to clinical trials (European Medicines Agency, 2013) (Glickman, et al., 2009) (Wemos Foundation, 2008).

Offshored clinical trials that are conducted for these reasons are not necessarily ethically problematic and a violation of human rights if, aside from the usual ethics requirements of informed consent and ethics committee review, these trials contribute to increased access to essential medicines in the region. Specifically, this means that trials are responsive to the health needs of the host country and that post-trial access is in place. In the current state of the country, the people, and the health care system, 80% (8 out of 10) of Filipinos have been deprived to undergo medical checkup or physical examination in their lifetime (Van Gijsel, 2016). As a result, 28% of Filipino women give birth without the assistance of a skilled birth or medical attendant (Van Gijsel, 2016). Filipino women therefore are susceptible to complications that are linked to child birth due to the current state of Filipino women's access to health care system. As such, benefits for Grady should be linked to responsiveness and thus, she gave examples of several benefits that clinical trials can be responsible for (Grady, 2006, pp. 237-238)

- Therapeutic benefits to study participants
- Useful and generalizable knowledge for the community
- Infrastructure and capacity building
- The addition of needed public health measures
- Training of research and clinical staff
- Ancillary medical benefits to participants or others
- The post-trial benefit of new drugs and other products
- Economic benefits
- Increased business, employment.

Despite the possible benefits that could be linked to responsiveness of clinical trials in the host countries, responsiveness is also linked to possible exploitation (Grady, 2006). Exploitation can be due to the lack of awareness of the patients or the participants; however, it is the prime responsibility of the regulatory agencies to ensure possible benefits to the patients and protect them from conceivable harm and exploitation. She clearly provided observations on how investigators in developing countries such as the Philippines perceived the possible "benefit" from research that the study population must have. Investigators in the survey that Grady cited gave several examples such as interventions must be provided after doing interventional studies; nevertheless, more than 50% "of the respondents who were conducting observational or descriptive studies[6] that focus on "responsiveness" and on making products available provide no guidance about appropriate benefits for these studies" (Grady, 2006, p. 238). The questionable part of conducting observational research that aims for "responsiveness", which that should form part of the core objective of research, is likely connected to the findings and results that have been enumerated in the next paragraph.

In the current research of the UiO investigator in UiO, Rosemarie Bernabe (Bernabe R. D., 2018) who looks at the state of affairs of responsiveness and post-trial access in the Philippines, and she has found that

- Due to volume and the general lack of access to healthcare, clinical trials are now considered as sources of healthcare, albeit very random and temporary;
- that the medicines being studied in the country only partially address the leading causes of mortality and morbidity: the studied pharmaceutical products address >50% of the leading causes of morbidity/mortality in the country, while addressing the majority of the leading causes of mortality and morbidity in high income nations; and
- that after marketing authorization, the medicines are inaccessible due to price, especially considering that medicines are most of the time availed out of pocket. These findings are reflective of the current state of affairs in offshored clinical trials and global health.

[6] "Non-experimental, open label, uncontrolled study, usually done in phase iv (post-marketing observational study); they may be useful to study how doctors actually practice, and how drugs actually perform because patient selection in controlled clinical trials often limits generalization of results; such observational studies (o.s.) are indicated when practical or ethical considerations render randomized clinical trials infeasible, e.g. in surgery; objections made frequently are that results provided by such a design can easily be manipulated" (Nahler, 2009, p. 125)"

These findings are in agreement with international trend such as the following:

- new therapeutic products address only 3.8% of neglected tropical diseases, even though these diseases account for 10.5% of the global burden of disease (Doctors Without Borders, 2012);
- in some countries such as India, the clinical trials conducted are "not in consonance with healthcare needs" (Mansi Chaturvedi, 2017);
- the availability of essential medicines is on average 35% for the public sector and 66% in the private sector in low and middle income countries (LMICs) (Zaidi & Nishtar, 2011);
- the cost of access is usually born out-of-pocket by households, with almost 10% the expenditures of low and middle income (LMIC) households allocated to medicines (Wirtz, et al., 2017);
- access to medicines is hampered by prices, for example, a month of treatment of three common chronic non-communicable diseases (gastric ulcer, asthma, and type 2 diabetes) "was not affordable to large segments of the population when purchased in the private sector" (Wirtz, et al., 2017).

Considering the aforementioned, the increased number of offshored clinical trials barely do justice to the health needs of the host countries and are not in compliance with the normative requirements United Nation Member States have committed themselves to follow with regard to responsiveness and the sharing of benefits resulting from scientific research. This study explores the first requirement, i.e., the requirement of responsiveness. Specifically, it will look at the state of responsiveness of clinical trials to the health needs of women in the Philippines.

Lastly, the study mentioned above on the case of India where clinical trials conducted in the country "are not in consonance with healthcare needs" (Mansi Chaturvedi, 2017, p. 175) seems to be only published study so far on this issue. Aside from this, we know of no other study that looks at the empirics of responsiveness. Instead, what we have are ethical guidelines and general recommendations based on ethical guidelines (i.e., ethical reflections on guidelines). These general recommendations have barely reached the ground, i.e., in spite of the increased number of clinical trials in low middle income countries (LMICs), these

studies, some of which are innovative, are barely responsive to healthcare needs. As such, there is sparse literature that we know of that looks at the responsiveness of clinical trials to the healthcare needs of women, especially economically vulnerable women. This study wishes to contribute towards a genuine sustainable responsive solution.

4 Data and Methods

4.1 Data

The study utilized data from ClinicalTrials.gov and the IHME, which are both accessible online. From ClinicalTrials.gov, I used data on clinical trials conducted in the Philippines from 2007 to 2016. "The ClinicalTrials.gov is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH)" (US National Library of Medicine, 2018) which allows all clinical trials around the world to register and provide the information from the onset of the study until results are delivered. From the IHME, I used data on conditions that affect females and males in the Philippines from 2007 to 2016. The IHME is an independent body where the data are contributed by the post-graduate fellows from different parts of world to come up with data on global health trends (The Institute for Health Metrics and Evaluation, 2018). This study will look into the state of 'responsiveness' by associating the data extracted from the ClinicalTrials.gov and the health needs of Filipino women extracted from the IHME.

The data from ClinicalTrials.gov provided 568 offshored clinical trials from the period 2007 to 2016, when excluding the four withdrawn, i.e. trials were not able to commence and therefore was not able to recruit participants. The dataset provides information on identification of clinical trial (NTC), conditions, interventions, enrollment, sex, age group, study results, status, and phases.

The IHME data contains information on conditions based on death, Years of Life Lost (YLL), and Years Lived with Disability (YLD) by country, sex, and year. Because YLL measures the incident stream of lost years of life due to deaths, an incidence perspective has also been taken for the calculation of YLD in the original Global Burden of Disease Study for year 1990 and

in subsequent WHO updates for years 2000 to 2004 (World Health Organization, Health statistics and information systems: , 2019).

The IHME dataset is composed of aggregated information on 152 conditions. In the data, each condition has designated death, YLL, and YLD rates. The IHME reports each condition by sex, and rate. Death and YLL have the same set of conditions that combined all together with the conditions that comprised the YLD. In this study, the health needs of Filipino women are defined as the top 10 death and YLL, YLD, and NTDs.

By comparing the frequency of trials conducted for specific condition with the prevalence rate of the same condition, possible validation can be done whether trials are responsive to the health needs of Filipino women. Categorizing the data based on conditions female-specific condition, male-specific conditions, NTDs, death, YLL, YLD, and sex (females and males) provide comparative results that create new data that could identify possible relevant phenomena.

4.2 Coding

Table 1 below is a summary of the clinical trials data using Data Analysis and Statistical Software (STATA). It shows the different variables being used to validate responsiveness by assigning values if possible and applicable. The dash (-) in each variable suggests that no possible value can be obtained given the minimum and maximum value available for each variable. The variables below are assigned for each condition that was identified in the data set obtained from ClinicalTrials.gov. The complete dataset is available online, https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k .

4.2.1 Table 1. Summary of the ClinicalTrials.gov Data

Variable	Observations	Min	Max
Enrollment	568	5	27564
Sex	568	0.00	2
Age	568	0.00	5
Study Results	568	0.00	1

Status	568	0.00	5
Phases	568	1	7
Gastric Ulcer/Duodenal Ulcer/Ulcerative Colitis	3	1	1
NTDs	15	1	1

Note: *The summary indicates the different variables with designated number of observations for each assigned variables.*

Some studies address more than one condition. As such, all conditions are coded '0 = without' and '1 = with' (the condition) to measure whether the different conditions are being studied in the 568 offshored clinical trials. Table 1 shows the summary of the data where the min and the max indicate the lowest and the highest observed value. The number of subjects enrolled for each offshored clinical trial is indicated under the enrollment. The sex indicates the following value labels such as all, male, and female as 0, 1, and 2 respectively. While the value labels for the variables on the different age groups are as follows: 0 for Child, Adult, Older Adult; 1 for Child, 2 for Child, Adult; 3 for Adult; 4 for Adult, Older Adult; and 5 for Older Adult. Under the study results, 0 indicates no results available; 1 indicates has results. Under status, 0 means unknown status; 1 means terminated; 2 means withdrawn; 3 means active, not recruiting; 4 means recruiting; and 5 means completed. The study phases has assigned 1 as early phase 1; 2 for phase 1; 3 for phases 1 and 2; 4 for phase 2; 5 for phases 2 and 3; 6 for phase 3; and 7 for phase 4. Therefore, the generated values from the data are numbers assigned for each variable. Each observation in the data may reflect more than one condition or disease. For NTDs[7], observations are identified for conditions that presence of NTDs and then combined in one variable. NTDs are comprised of 15 incidences and have 5 variations in 568 offshored clinical trials. For the complete results of the data, please refer to Table 2.

The data gathered from IHME consists of Philippine death, YLL, and YLD rates within the ten-year period (2007 – 2016). The rates used in the data are expressed per 100,000 people. In

[7] "The neglected tropical diseases (NTDs) in the Institute for Health Metrics and Evaluation list that affects the Philippines are the following: malaria, leishmaniasis, schistosomiasis, cysticercosis, lymphatic filariasis, dengue, rabies, ascariasis, hookworm disease, food-borne trematodiases, leprosy, and other neglected tropical diseases" (The Institute for Health Metrics and Evaluation, 2018).

total, the data consists of 152 conditions that cause death, YLL and YLD on females and males. In Table 2, variables are based on death, mortality, and morbidity for females and males. The female average death rate variables are results from averaging the yearly rates for each condition (2007-2016); while male average death rate variables are results from averaging the yearly rates for each condition (2007-2016). The female average YLL rate variables are results from averaging the yearly rates for each condition (2007-2016); while male average YLL rate variables are results from averaging the yearly rates for each condition (2007-2016). The female average YLD rate variables are results from averaging the yearly rates for each condition (2007-2016); while male average YLD rate variables are results from averaging the yearly rates for each condition (2007-2016). Table 2 illustrates the different variables used whose designated values are based on rate as the standard of measurement.

4.2.2 Table 2. Summary of the Institute for Health Metrics and Evaluation (IHME) Data

Variable	Observations	Min	Max
Female average death rate	152	0.00	168.9319
Male average death rate	152	0.00	217.9962
Female average YLL rate	152	0.00	3566.054
Male average YLL rate	152	0.00	5828.584
Female average YLD rate	152	0.00	730.6897
Male average YLD rate	152	0.00	725.9808

Note: *The summary indicates the different variables with designated number of observations and values based on rates provided in the data from IHME.*

4.3 Methods

To achieve the general and specific objectives of this study, the four (4) sub-sections below are specified in details:

1. Collected and collated the data on offshored clinical trials done in the Philippines from 2007 to 2016;

   The data used for collecting and collating the offshored clinical trials done in the Philippines within the defined period belongs to the ClinicalTrials.gov that is accessible online. This offshored clinical trials' registry archives all the clinical trials done worldwide. I restricted the sample to clinical trials which were registered as "interventional", conducted in the Philippines, were in "Phase I to Phase IV", conducted in years 2007 to 2016", "industry sponsored", "academic sponsored", and "U.S. government sponsored" are very important (US National Library of Medicine, 2018). The data gathered are formatted in the excel spread sheet to identify the conditions and diseases to be created as dummy variables. The dummy variables are coded with '0' as 'without the condition' and '1' as 'with the condition'. The assigned scale of 0 to 1, determines the frequency of each dummy variable assigned for each condition and the NTDs variable which is consists of 5 conditions present in the 568 offshored clinical trials. The clinical trial conducted within the period of ten (10) years is adequate to identify what conditions are involved in the offshored clinical trials being tested in the Philippines and which among these conditions belong to the top most clinically-tested diseases. The data will provide results and analyses whether the offshored clinical trials respond or do not respond to the health need of women in the Philippines. Hence, it is important obtain data that can establish relationship such as conditions for validating and invalidating the responsiveness of offshored clinical trials to the conditions that cause death, YLL, YLD, NTDs, and diseases that are female-specific including maternal diseases and conditions; which are presented in the next paragraph.

2. To understand the health needs of Filipino women, what accounts for most death, most premature death (YLL), most disabling (YLD), the neglected tropical

diseases, and diseases that are female-specific have identified through the data from Institute for Health Metrics and Evaluation (IHME);

IHME provides a complete database for the causes of death, YLL, YLD, female specific and maternal conditions, and the NTDs. The data collection from the IHME is obtained through the "GDB Results Tool" page which requires certain information such as "Location", "Year", "Context", "Age", "Metric", "Measure", "Sex", and "Cause". These information narrows down the data based on the information provided for the study. For instance, the study focus on the Philippines and the parts being filled are "recruitment status" , "condition/disease" , "other terms" and "Country" (US National Library of Medicine, 2018). The ClinicalTrials.gov is comprised of "273,543 research studies in all 50 states and in 204 countries" (US National Library of Medicine, 2018).

The data illustrate the frequency, percentage, and the average rates for each dummy variable such as the female average death rate, male average death rate, female average YLL rate, male average YLL rate, female average YLD rate, and male average YLD rate. Table 2 illustrates these different variables with designated values based on rate as the standard of measurement. All the said variables produced two sets; i.e. conditions causing death and premature death (YLL) are the same and combined with the set of conditions causing YLD. It identifies and categorizes the conditions based on the results generated. The study will focus on the top 10 conditions that affect Filipino women and men based on top 10 causes of death, YLL, YLD, NTDs, maternal conditions, and female/male-specific conditions. Conditions belong to the top 10 causes of death, YLL, YLD, and NTDs are identified whether it affects females, males, and the general population i.e. the average rates among the categories mentioned for each condition. It is important to understand that conditions vary from each variable aside from death and YLL that consist of the same set of conditions. Therefore, a condition could either cause death, YLL, and YLD, cause death and YLL, or only cause YLD. Appendices for all the conditions, link: https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k .

Identifying the top 10 conditions based on the average rate from the aforementioned categories are put together by sexes (females, and males) and on general population. Maternal conditions are also identified from the IHME data and presented in Figure 7, the same with the results of the top 10 conditions that cause death, YLL, and YLD on females. The results are then arranged in descending order (from highest to lowest) in all categories that are presented in Tables and figures.

3. The findings and results from #1 and #2 are paired to investigate how responsive offshored clinical trials are to the needs of women in the Philippines;

I have done all the coding and tabulations first in Excel and then in STATA. This research used univariate descriptive analysis using proportions and percentages, rates and ratios, and frequencies. An analysis between the conditions from offshored clinical trials and conditions that are considered as health needs based on what cause death, YLL, and YLD on NTDS, female/male-specific conditions, and maternal conditions to scrutinize the contrasts. Findings and results are being extended to Filipino male and to the general population. The data is cautiously reviewed and analyzed for identifying major trends, unusual phenomenon, and subgroup and context descriptions. This stage will explore the relationship of one variable to other variables mentioned at the same time pairing two data that are parallel based on conditions. Findings and results generated will be used to validate or invalidate the responsiveness of offshored clinical trials to the health needs of Filipino women. Therefore, in this part of the study, analyzing the trends and subcategories from merging the conditions based on the results from the clinical trials and IHME through rates, proportions, ratios, frequencies, and percentages. Determining the statistical significant results from both data gathered from ClinicalTrials.gov and IHME whether the state of responsiveness of the offshored clinical trials meet the needs of women. Additionally, I looked at the data for descriptive analysis based on sex. It is important to know that the

frequency (number of clinical trials) in some conditions is a combination of different conditions found in clinical trials data. Here are the following conditions:

- For cerebrovascular diseases

Atherosclerosis
Atherothrombosis
Intracranial Hemorrhages
Ischemia
Stroke
Cerebral Infarction
Transient Ischemic Attack

- For digestive diseases

Stool composition and gastric ulcer
Duodenal ulcer
Ulcerative colitis

- For nutritional deficiencies:

Anemia
Children under-nutrition
Iron deficiency
Iron absorption
Hypothyroidism

- For neglected tropical diseases:

Dengue
Schistosomiasis
Rabies
Malaria
Leprosy

- For maternal conditions:

Maternal hemorrhage
Maternal hypertensive disorders
Other maternal disorders
Maternal abortion, miscarriage, and ectopic pregnancy
Maternal sepsis and other maternal infections
Indirect maternal deaths
Genital prolapse
Maternal obstructed labor and uterine rupture
Late maternal deaths
Maternal deaths aggravated by HIV/AIDS

- For female-specific conditions *(maternal conditions and conditions enumerated below)*:

Cervical cancer
Endometriosis
Female infertility
Other gynecological diseases
Ovarian cancer

Polycystic ovarian syndrome	Uterine cancer
Premenstrual syndrome,	Uterine fibroids
Trichomoniasis	Breast cancer

- For male-specific conditions:

Benign prostatic hyperplasia	Prostate cancer
Male infertility	Testicular cancer

The rest of the subcategories that are relevant in analyzing the data are reflected in the appendices online. Link, https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k .

4. The results are then being discussed based on the feminist standpoint theory; and interpreted for the conclusion which will reflect the interest, theories and framework, ideas, and concepts that encourage the subject of inquiry. Persistent and unusual results are then used to support certain claims that are considered vital.

4.4 Ethics

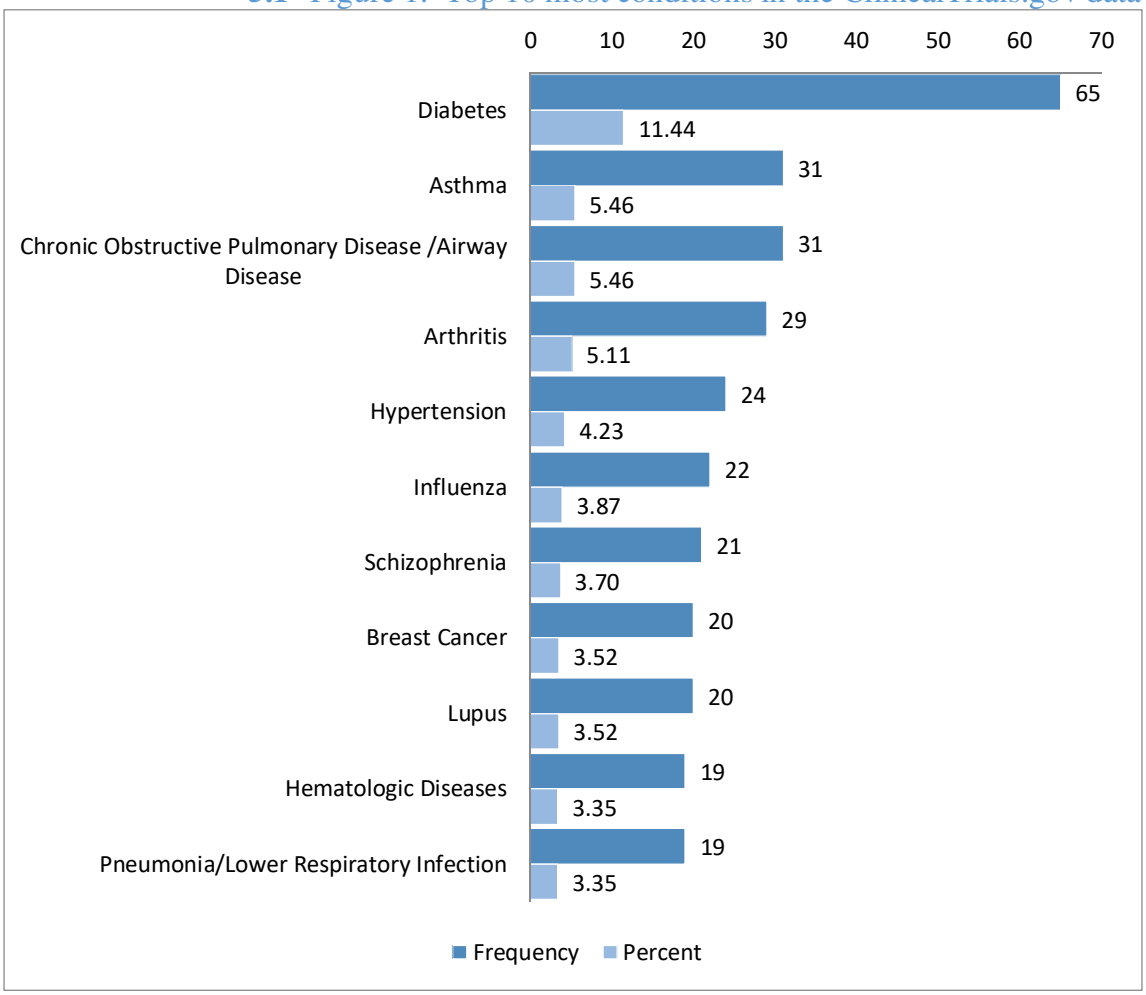
Since this study uses publicly accessible database and no personal information was gathered in any way, this study does not require a review from a research ethics committee nor from the Norwegian Centre for Research Data. Ethical considerations will be reflected in the discussion within the context of this research based on the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS), and Feminist bioethics[8].

5 Results

The conditions in Figure 1 are the top 10 most allocated conditions by clinical trials in the Philippines which taken from ClinicalTrials.gov within 2007-2016.

[8] "A feminist bioethics is not a separate bioethics for women. It is a bioethics that sees oppression based on gender as a serious wrong and critically investigates the workings of power and gender" (Wolf, 1996, p. 8).

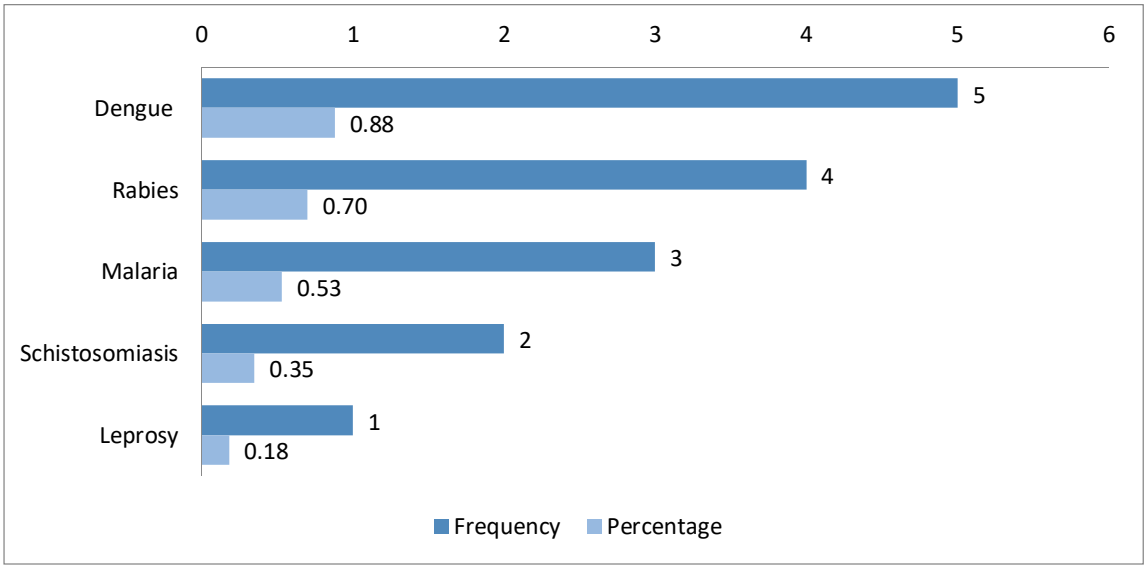
5.1 Figure 1. Top 10 most conditions in the ClinicalTrials.gov data



Note: *Frequency and percentage are measured based on the 568 observations that represent the number of clinical trials that were conducted in the Philippines from 2007 to 2016.*

Figure 1 indicates values in percentage and frequency for the top 10 most conditions being trialed in the Philippines based on the 568 offshored clinical trials from 2007 to 2016. It shows that out of 568 offshored clinical trials, 11.44% were on diabetes mellitus that made it to the top 1 condition among the 151 different conditions that are studied in the Philippines for a 10-year period. This was followed by diseases such as chronic obstructive pulmonary/airway disease (5.46%), asthma (5.46%), arthritis (5.11%), hypertension (4.23%), influenza (3.87%), schizophrenia (3.70%), lupus (3.52%), breast cancer (3.52%), hematologic diseases (3.35%), and pneumonia / lower respiratory infection (3.35%) that summed up to 53.01%. Meaning, the remaining 46.99% is for the 140 conditions.

5.2 Figure 2. Clinical trials on neglected tropical diseases (NTDs)



Note: *The NTDs in the data consist of dengue, rabies, malaria, schistosomiasis, and leprosy.*

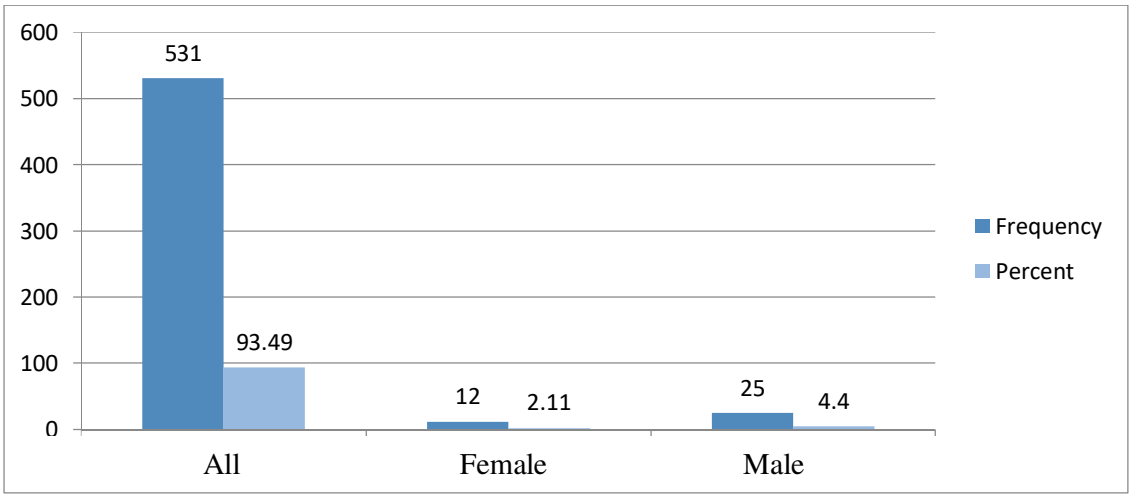
The NTDs obtained 15 clinical trials out of the 568 offshored clinical trials in the Philippines. This accounts to dengue which obtained five incidences, followed by rabies with four incidences, malaria with three incidences, schistosomiasis with 2 incidences, and leprosy/Hansen's disease with 1 incident. Among these clinical trials on NTDs, schistosomiasis requires female subjects solely and the remaining NTDs required both sexes. No particular clinical trial in the NTDs required male subjects solely.

Dengue being the top NTD that is clinically trialed in the Philippines is still not considered as part of the top 10 most clinically trialed condition in the Philippines. This applies to the rest of the NTDs, i.e., schistosomiasis, rabies, malaria, and leprosy. It shows that out of 568 clinical trials, 0.88% went to dengue, 70% went to rabies, 0.53% went to malaria, 0.35% went to schistosomiasis, and 0.18% went to leprosy. Therefore, only 2.64% of the 568 clinical trials was conducted for NTDs that comprised of 5 conditions.

Figure 3 below shows the number of offshored clinical trials that are conducted to female-specific, male-specific, and all (combining both sexes) subjects. The 568 offshored clinical trials are comprised of three sex categories such as A (ALL) which is equivalent to 531

offshored clinical trials (93.49%), M (Male) which is equivalent to 12 offshored clinical trials (2.11%), and F (Female) which is equivalent to = 25 offshored clinical trials (4.40%).

5.3 Figure 3. Distribution of Clinical Trials among Sexes

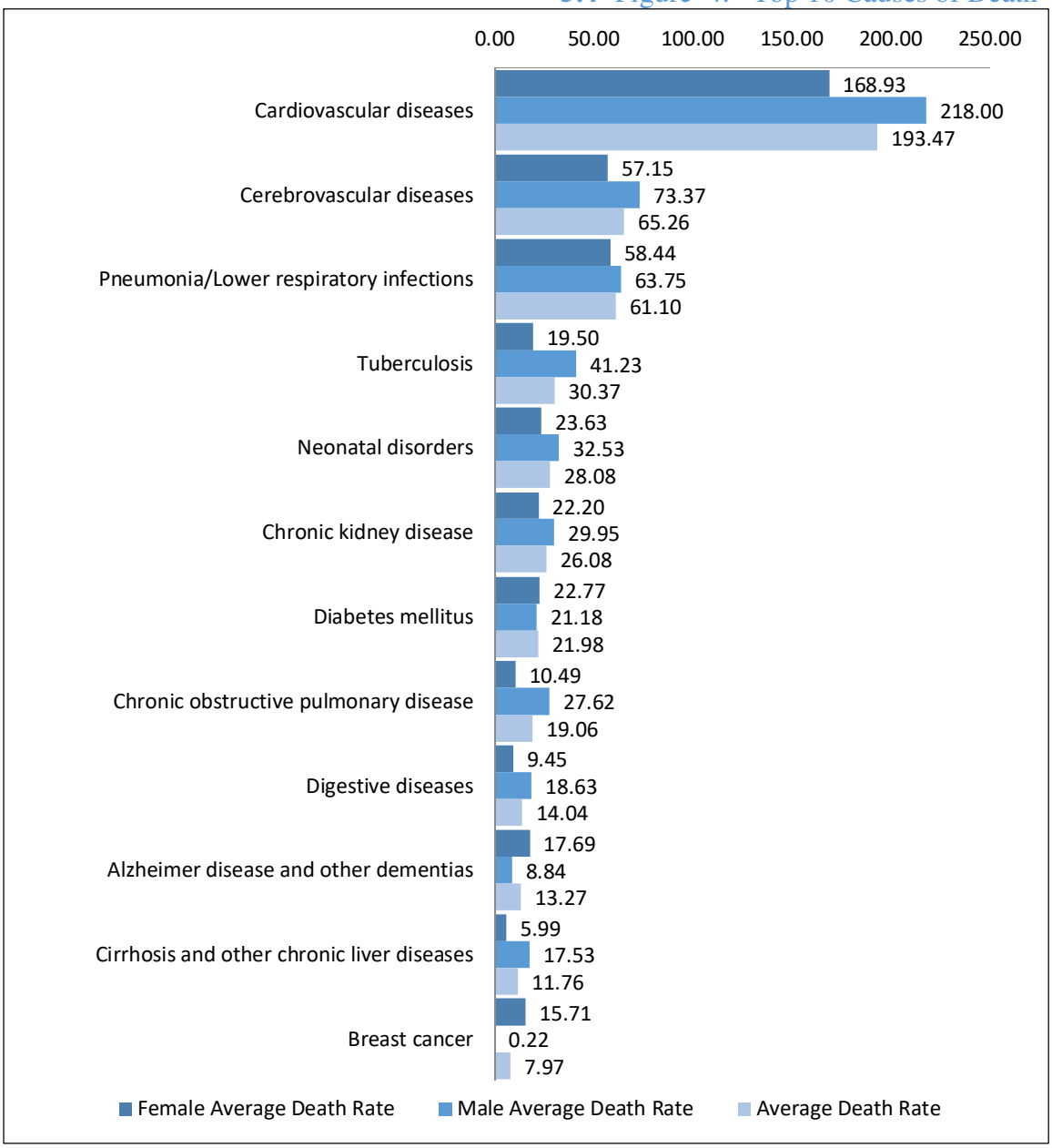


Note: *All (both female and male), Female, and Male*

The graph shows that clinical trials administered to 'ALL' (both female and male) got the majority of clinical trials in the Philippines which was 93.49% out of 568 offshored clinical trials. This was followed by clinical trials administered on 'Female' subjects or patients with 4.4%, and clinical trials administered to male subjects or patients with 2.11%.

Below are Figures 3, 4, and 5 that illustrate the top 10 conditions that cause death, YLL, and YLD for females, males, and the general population; and Figure 7, maternal conditions that affect Filipino women based from the IHME. The measurement used on these Figures is expressed in rates. The rate values for death, YLL, and YLD are per 100,000 people. As an overview, among the 152 conditions in the data, 20 conditions (13.16%) are female-specific and 4 conditions (2.63%) male-specific.

5.4 Figure 4. Top 10 Causes of Death

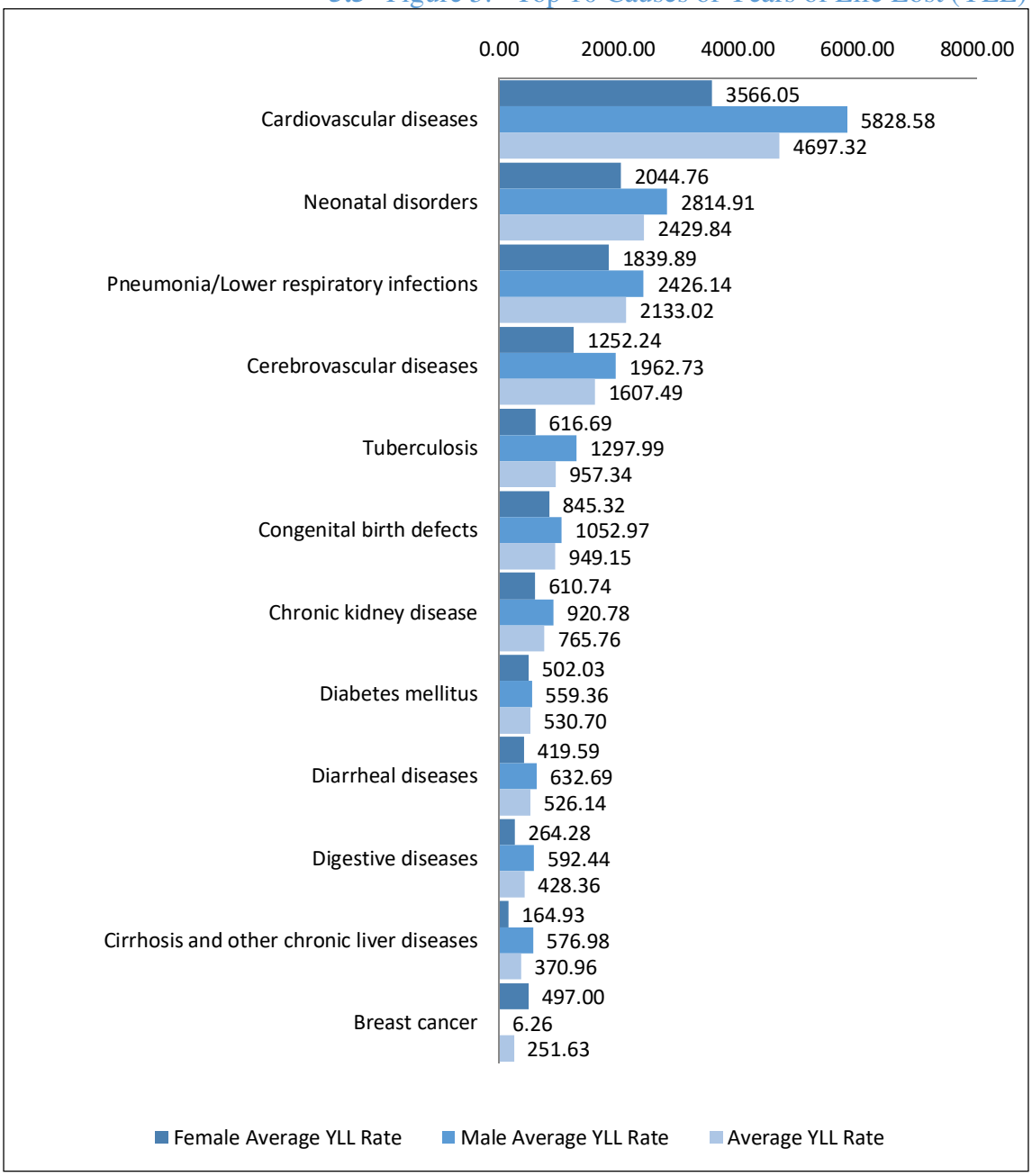


Note: *The conditions in Figure 4 are comprised of the top 10 conditions that cause death on females and on males in contrast with the top 10 conditions that cause death on general population i.e. by extracting the average rate from female and male death rates for each condition. This applies to the rest of the conditions in Figures 4, 5, 6, and 7. See Appendix online for the complete results. Link, https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k*

In Figure 4, all the results of the top 10 conditions that cause death on females, males, and on general population are put together. Breast cancer that is a female-specific condition is part of the top 10 conditions that cause premature death among Filipino women; and, not part of the top 10 conditions that cause death on general population. Alzheimer disease and other dementias also belong to the top 10 conditions that cause death among Filipino women, which is considered as part of the top 10 conditions that cause death on the general population. However, Alzheimer and other dementias are not part on the top 10 conditions that cause death on Filipino men. Cirrhosis and other chronic liver diseases belong to the top 10 conditions that cause death among Filipino men, but, not part of the top 10 conditions that cause death on Filipino women and on general population. The rates of the top 10 conditions that cause death on the general population are affecting both sexes and it turned out that males have higher rates compared to females.

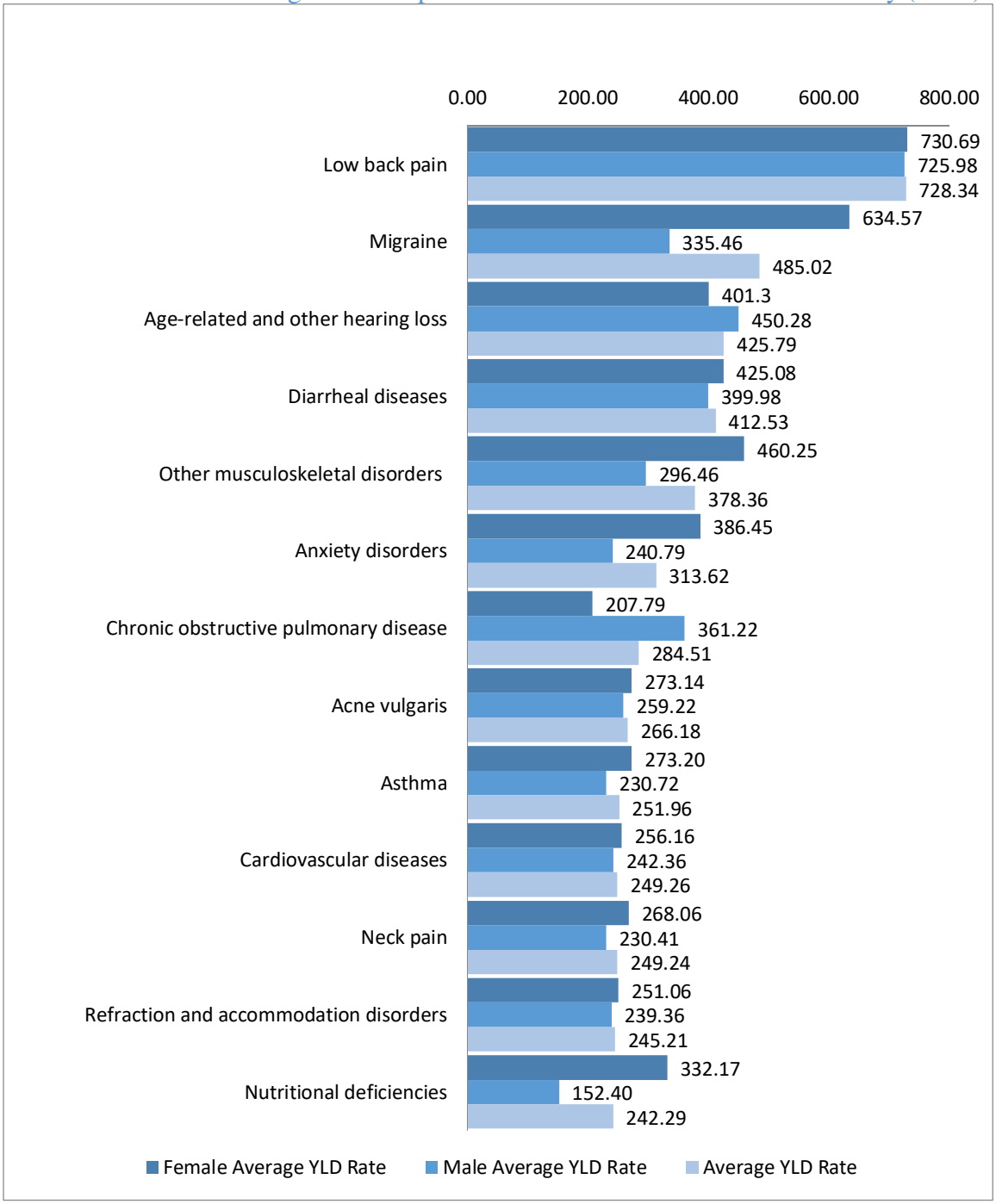
In Figure 5, all the results of the top 10 conditions that cause premature death on females, males, and on general population are put together. Breast cancer that is a female-specific disease is part of the top 10 conditions that cause premature death among Filipino women and not part of the top 10 conditions that cause premature death on the general population. Cirrhosis and other chronic liver diseases belong to the top 10 conditions that cause premature death among Filipino men, but not part of the top 10 conditions that cause premature death on Filipino women and on the general population. Rates of the top 10 conditions that cause premature death on the general population show that all conditions affecting both sexes, Filipino men have higher rates compared to Filipino women.

5.5 Figure 5. Top 10 Causes of Years of Life Lost (YLL)



Note: *The conditions in Figure 5 are comprised of the top 10 conditions that cause YLL on females and on males in contrast with the top 10 conditions that cause YLL on the general population, i.e., by extracting the average rate from female and male YLL rates for each condition.*

5.6 Figure 6. Top 10 Cause of Years Lived With Disability (YLD)



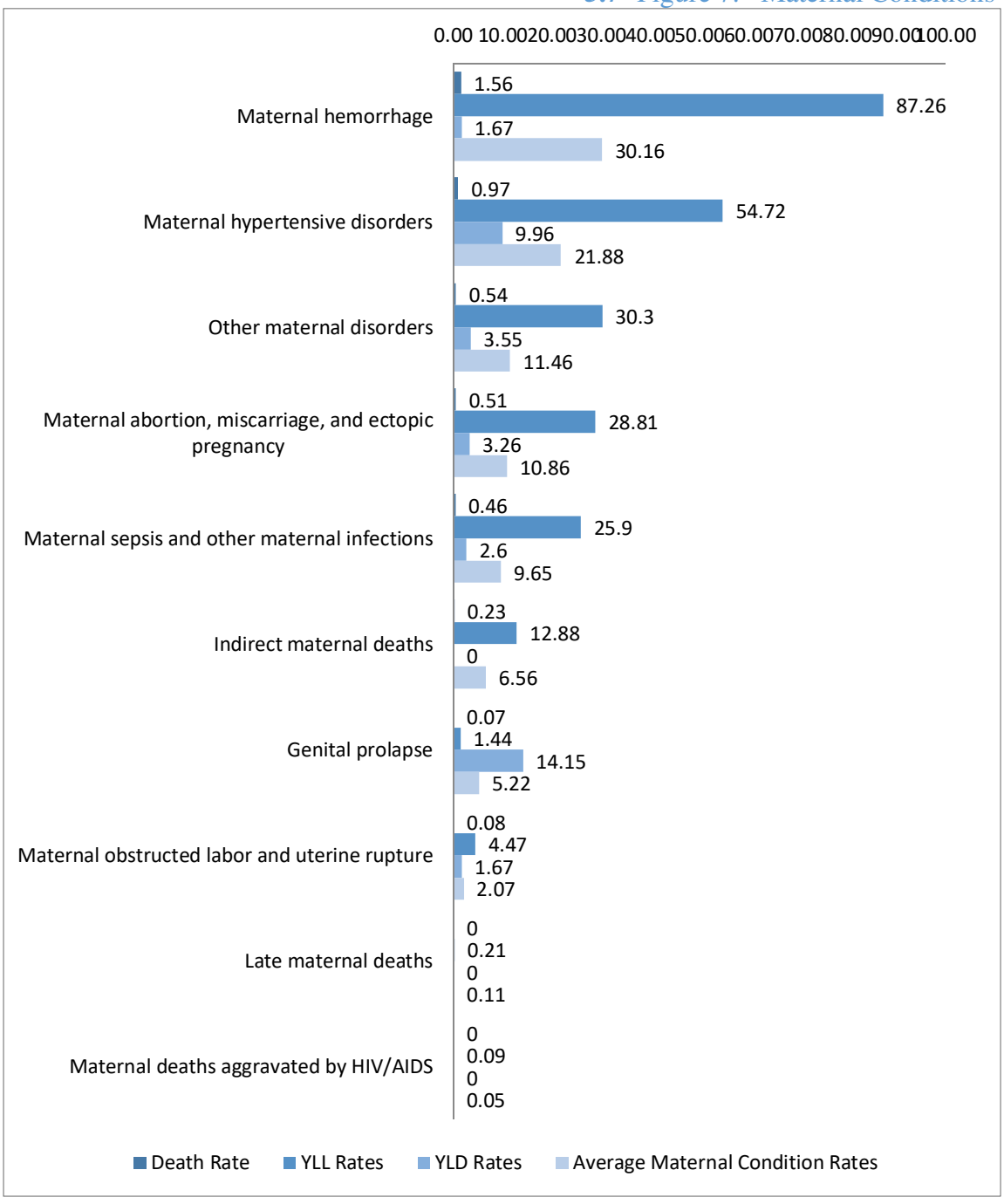
Note: *The conditions in Figure 6 are comprised of the top 10 conditions that cause YLD on females and on males in contrast with the top 10 conditions that cause YLD on general population, i.e., by extracting the average rate from female and male YLD rates for each condition.*

In Figure 6, all the results of the top 10 conditions that cause YLD on females, males, and on general population are put together. Neck pain and nutritional deficiencies are part of the top 10 conditions that cause morbidity among Filipino women, but not part of the top 10 conditions that cause morbidity on males and on the general population. Refraction and accommodation disorders belong to the top 10 conditions that cause morbidity among Filipino men, but not part of the top 10 conditions that cause morbidity on Filipino women and on the general population. Neck pain, refraction and accommodation disorders, and nutritional deficiencies are the three conditions that are not part of the top 10 conditions that cause morbidity on the general population. However, neck pain and nutritional deficiencies are part of the top 10 conditions that cause YLD on women and not for men. On the other hand, refraction and accommodation disorders belong to the top 10 conditions that cause YLD among men alone. Rates of the top 10 conditions that cause morbidity on general population shows that all conditions that affect both sexes, Filipino women have higher rates compared to Filipino men.

Out of the 152 conditions from the IHME data that causes of death, YLL, and YLD, there are 145 conditions under death and YLL and 110 conditions under YLD. Among the 152 conditions, 20 conditions are female-specific, other than breast cancer which came out to have insignificant result on men which is next to nothing and 4 conditions are male-specific only. The conditions that are female and male-specific are available in appendices online, https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k .

In Figure 7, indirect maternal deaths, late maternal deaths, and maternal deaths aggravated by HIV/AIDS are maternal conditions that cause death and premature death (YLL), even if late maternal deaths, and maternal deaths aggravated by HIV/AIDS have zero (0) incidence of death.

5.7 Figure 7. Maternal Conditions



Note: *The conditions in Figure 7 are comprised of the maternal conditions that cause death, YLL, and YLD on Filipino women.*

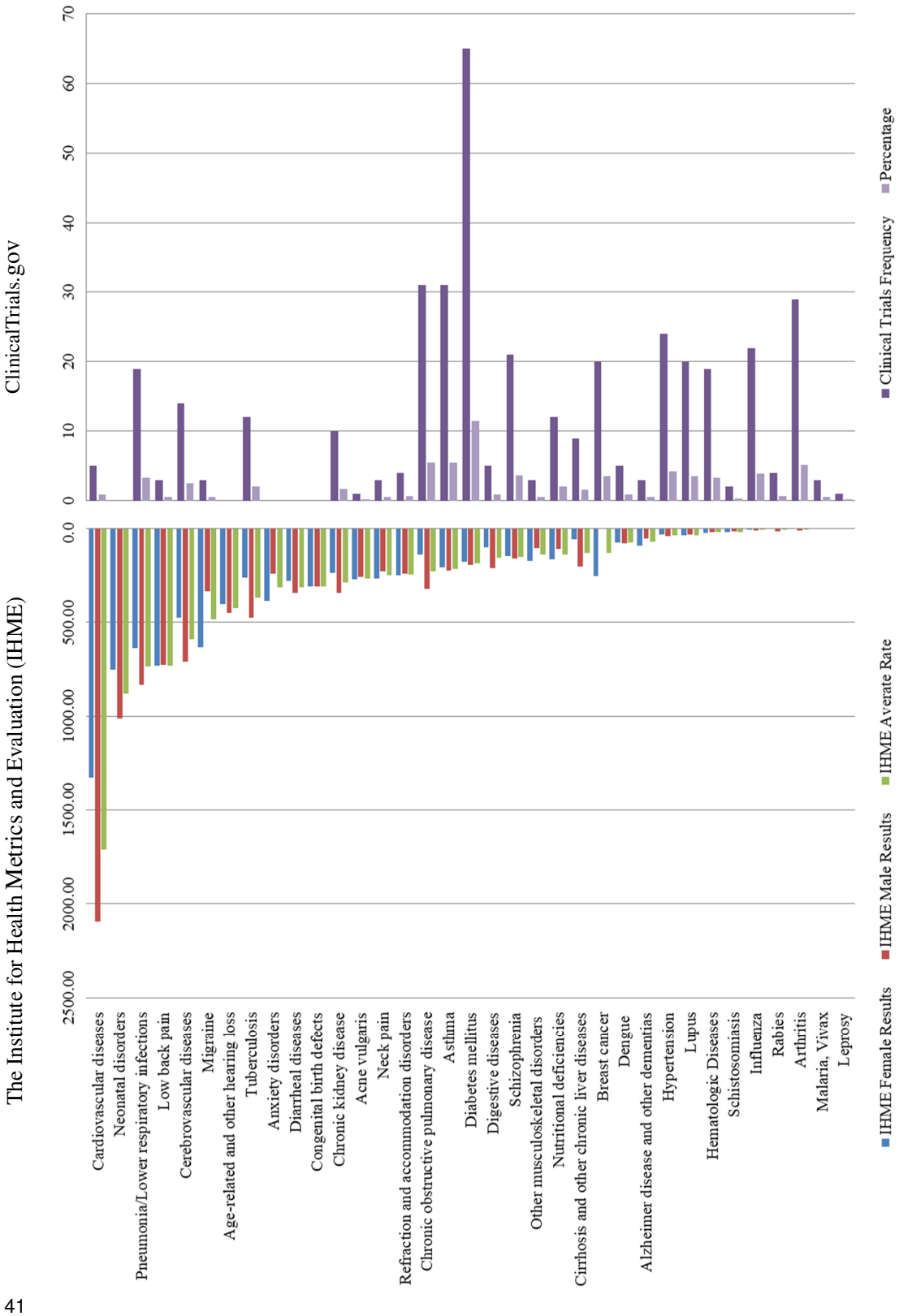
5.8 Descriptive Results in ClinicalTrials.gov and the Institute for Health Metrics and Evaluation (IHME)

This section has Figures 8 and 9. The contrast of the results of two data sets from ClinicalTrials.gov and the Institute for Health Metrics and Evaluation (IHME) is important to analyze and identify patterns in results that might provide evidential support to claims in relation to the status of the responsiveness of offshored clinical trials to the needs of Filipino women. The results are arranged in accordance to the results that were gathered, i.e., from highest to lowest rates of the conditions that are obtained from IHME. Results from ClinicalTrials.gov are then associated to find out the trend in the conditions from both data sets. The conditions in Figures 8 and 9 are arranged in descending order (highest to lowest) based on the results from IHME. For the complete results, refer to appendix 1.

Figure 8 is comprised of all the conditions that belong to the top 10 causes of "death", "Years of Life Lost (YLL)", and the "Years of Lived with Disability (YLD)" combined with the top 10 conditions that were clinically trialed in the Philippines from 2007 to 2016. The Figure is divided into two parts which shows the proportion of the conditions that are considered as the needs of the population by combining all the rates for each condition on both sexes in death, YLL, YLD and NTDs in contrast with the frequency and percentage of each condition based from the results gathered in ClinicaTrials.gov. It suggests that among the consolidated top 10 conditions that cause death, premature death, and morbidity on Filipino women, men, and the general population, neonatal disorders, congenital birth defects, age-related and other hearing loss, diarrheal diseases, and anxiety disorders are among the conditions that clinical trials are not responsive at all. No single offshored clinical trial responded on these conditions. Out of the 5 conditions, 3 conditions affect children, i.e., neonatal disorders, congenital birth defects, and diarrheal diseases. These diseases cause death, premature death, and morbidity on children. Additionally, a disabling condition, i.e., anxiety disorders, which affects Filipino women more than men, is not clinically trialed as well. Age-related and other hearing loss conditions that affect the aging population is not clinically trialed also; it affects Filipino men than women, and belongs to the top 10 conditions based on the general population health needs.

The response of the offshored clinical trials on the top 10 conditions that cause death, YLL, and YLD resulted to 5 clinical trials (0.88%) on cardiovascular diseases, none on neonatal disorders, 19 clinical trials (3.35%) on pneumonia / lower respiratory infections, 3 clinical trials (0.53%) on low back pain, 14 clinical trials (2.46%) on cerebrovascular diseases, 3 clinical trials (0.53%) on migraine, none on age-related and other hearing loss, 12 clinical trials (2.11%) on tuberculosis, and none on anxiety disorders and diarrheal diseases. These summed up to 9.86% of the 568 offshored clinical trials. Five among the top 10 conditions i.e. cardiovascular diseases, neonatal disorders, cerebrovascular diseases, tuberculosis, and diarrheal diseases mostly affect men on death and YLL and mostly affect women on YLD (5.45%). One out of the top 10 conditions i.e. pneumonia / lower respiratory infections mostly affect men on death, YLL, and YLD (5.45%). Three out of the top 10 conditions i.e. low back pain, migraine, and anxiety disorders mostly affect women on YLD-specific conditions (1.06%). And finally, 1 among the top 10 conditions i.e. age-related and other hearing loss mostly affect men on YLD-specific conditions (0).

5.8.1 Figure 8. Joined Results from the Institute for Health Metrics and Evaluation (IHME) and the ClinicalTrials.gov



5.8.2 Figure 9. Joined Results of Neglected Tropical Diseases (NTDs) from the Institute for Health Metrics and Evaluation (IHME) and the ClinicalTrials.gov

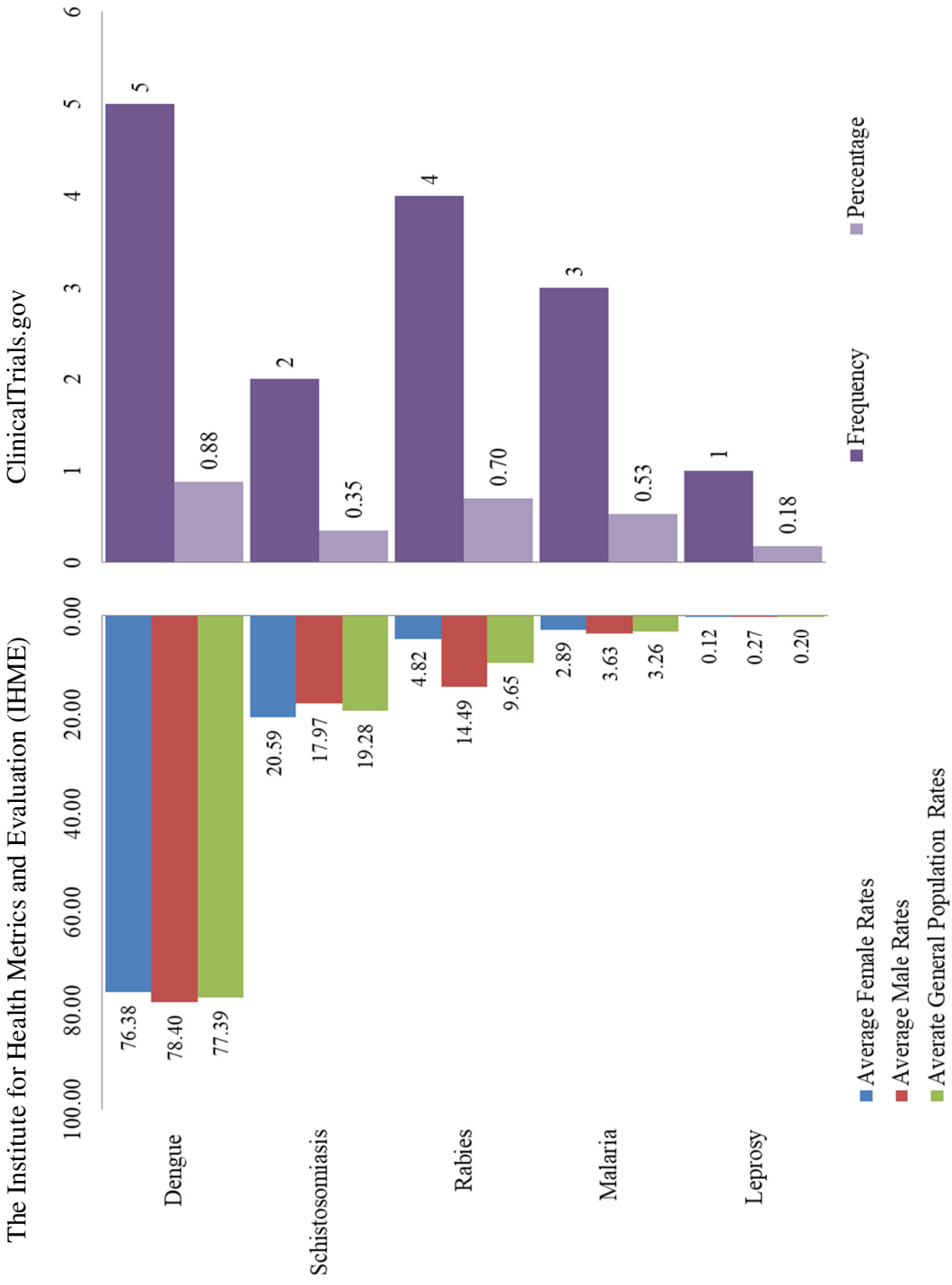


Figure 9 above is comprised of neglected tropical diseases (NTDs) that affect Filipino women and men. The rates used are the average IHME rate for each condition based on the death, YLL, and YLD rates. The results from IHME are combined with the results from ClinicalTrials.gov based on frequency and its percentage. Dengue which can be life threatening condition among children received clinical trials the most. This was followed by rabies, malaria, schistosomiasis, and leprosy. Among the neglected tropical diseases that cause death to Filipino women, men, and the general population are dengue, schistosomiasis, rabies, and malaria.

Note: *Each condition in Figures 8 and 9 are associated with three (3) categories based on the average female rates, average male rates, and average general population rates from IHME which correspond with the frequency and percentage of clinical trials done on that particular condition. The reference data can be accessed online. Link,* *https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k*

6 Discussion

The theoretical concept 'responsiveness' that is used in this study should be reexamined for impacts it brought to Filipino women specifically. Especially those international organizations such as World Health Organization (WHO), Council for International Organizations of Medical Sciences (CIOMS) and World Medical Association (WMA) established the concept to serve as a guide in researches like clinical trials for the pursuit of advancing matters related to public health (Council for International Organizations of Medical Science, 2016).

This is somehow linked to the development of the ethics guidelines of CIOMS in 1992 where the present formulation of 'responsiveness' is rooted (Council for International Organizations of Medical Science, 2016). As stated in the introduction, CIOMS defines responsiveness as *the research purposely aims to "provide new knowledge about the best means of addressing a health condition present in the community or region" where the trial is being hosted* (Council for International Organizations of Medical Science, 2016, p. 3).

Neglect to respond the health needs of the vulnerable groups such as Filipino women, are apparent in the results of this study as well as the ongoing inferior status of women in the

Philippine society. The World Medical Association (WMA) created the Declaration of Helsinki in 1964 as a code of ethics to act as a guideline by medical doctors in doing research (Fisher, 2009). In accordance to the Declaration of Helsinki's ethical principle, vulnerable groups such as women "may have an increased likelihood of being wronged or of incurring additional harm" (World Medical Association, 2018). Number six (6) of the Declaration of Helsinki states that

> The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality (World Medical Association, 2018).

This particular general principle explicitly defines how clinical trials in the locality such as the Philippines should provide new knowledge in developing researches such as clinical trials that will respond to the Filipino women's health needs. Amendments in public health policies and regulations for the safety, protection, and best interest of women in clinical trial procedures should be strengthened. However, women in reality are seldom asked or engaged in the process of improving what is best and suitable for them (Grand, 2007). Drug and medical interventions, discoveries, and researches, and the privatization and unregulated healthcare services are more likely to neglect women which made healthcare unavailable and inaccessible to those economically deprived group of individuals i.e. women. As we saw above in the results, having a ratio of offshored clinical trials that is equivalent to 1:3 where 1 is the number of clinical trial responding to Filipino women's health needs and 3 is the number of clinical trials responding to Filipino men's health needs, 3 times more likely of the offshored clinical trials in the Philippines are responsive to male conditions than to female conditions. Existing unresolved biases, prejudices, exploitation, and discrimination in health care services, platform, policies, and drug & pharmaceutical research (e.g. offshored clinical trials) that are patriarchal and capitalistic have to be reexamined in such a way that encourages women's inclusion in the process of formulating new knowledge and how this knowledge affect them individually and as a group. In the results, it is clear that the health needs of Filipino women and men are not the same; extending its variations in terms of quality of life, to more specific conditions that cause death, premature death, and morbidity. Given the results and findings of this study regarding the state of responsiveness of offshored

clinical trials to the health needs of Filipino women, feminist standpoint's principle of involving vulnerable and marginalized women's lived experiences is strongly recommended (Harding, 1993; Tong, 2004; Bowell, 2019). This follows the importance of women's participation on proper diagnosis, therapy and prognosis (Pellegrino, 2004). Feminist standpoint therefore reassures that researches such as clinical trials that embrace the lives and health needs of women in the locality will produce "less partial and distorted accounts not only of women's lives but also of men's lives and of the whole social order" (Harding, 1993, p. 56)

In the results and findings of the research I conducted on the responsiveness of clinical trials on the health needs of Filipino women, we saw the difference in the of the top causes of deaths, mortality, and morbidity on Filipino women and men, which tells us how the standardization of drugs works differently in terms of safety and efficacy. In top diseases that caused death, mortality and morbidity among women, tested drugs and interventions should work on their survival at least if not to prevent them. Interventions on diabetes mellitus exceed more than twice the number of clinical trials on asthma, chronic obstructive pulmonary disease, arthritis, hypertension and etcetera. Top diseases causing death, mortality and morbidity like cardiovascular diseases, pneumonia/lower-respiratory infections, cerebrovascular diseases, diabetes mellitus, and etcetera mostly affect men; therefore, diseases that affect women alone like ovarian cancer, other gynecological diseases, and maternal conditions and disorders have in the end insufficient amount of research.

6.1 In Sickness and in Health: The Status of Women in the Philippines

As we saw above, among the 20 different conditions that are female-specific, only 3 conditions have been responded by offshored clinical trials, which are cervical cancer (1 clinical trial), breast cancer (20 clinical trials), and cervical dystonia (1 clinical trial). While among the 4 conditions that are male-specific, there are 2 conditions that have been responded by offshored clinical trials, which are benign prostatic hyperplasia (1 clinical trial), and prostate cancer metastatic (1 clinical trial). The ratio of the conditions that are female-specific and male-specific only from the offshored clinical trials that were studied in the Philippines from 2007 to 2016 appeared to be 1:3 (which is 15% of clinical trials responded to female conditions, and 50% of clinical trials responded to male conditions). Meaning, it is 3 times

more likely that the offshored clinical trials are responsive to male conditions than to female conditions. The saving factor for this instance in terms of the number of clinical trials that were studied for breast cancer alone i.e. 20 clinical trials which made it to the top 10 conditions responding to the conditions that are female-specific only. Based on the 20 breast cancer clinical trials, 9 clinical trials are administered in ALL (female and male subjects) and 11 clinical trials are administered on female subjects solely. The 20 clinical trials are comprised of phase 2[9] (confirm safety and start efficacy) and phase 3[10] (confirm efficacy and safety). It could also mean that Filipino women who are suffering from breast cancer are more likely to have drug and/or treatment options; but, breast cancer patients in the Philippines are diagnosed in an advanced stage. This is in line with women's economic, medical, and educational constraints; additionally, breast cancer does not show any symptoms or pain at an early stage (Mitchell, 2009). In fact, if detected at an early stage, survival rate of breast cancer is much higher. The offshored clinical trials therefore may seem to respond to breast cancer condition that Filipino women are experiencing compared to other female conditions that have significant number of prevalence[11]. Further investigation on breast cancer should be encouraged especially that several factors may attribute other than the 5 to 10% genetic

[9] "These trials can be for people who all have the same type of cancer, or for people who have different types of cancer. Phase 2 trials aim to find out:

- if the new treatment works well enough to be tested in a larger phase 3 trial
- which types of cancer the treatment works for
- more about side effects and how to manage them
- more about the best dose to use

These treatments have been tested in phase 1 trials, but you may still have side effects that the doctors don't know about. Treatments can affect people in different ways. Phase 2 trials are usually larger than phase 1. There may be up to 100 or so people taking part. Sometimes in a phase 2 trial, a new treatment is compared with another treatment already in use, or with a dummy drug (placebo). Some phase 2 trials are randomized. This means the researchers put the people taking part into treatment groups at random" (Cancer Research UK, 2019).

[10] "Phase 3 trials aim to find out:

- which treatment works better for a particular type of cancer
- more about the side effects
- how the treatment affects people's quality of life

They may compare standard treatment with:

- a completely new treatment
- different doses of the same treatment
- having the same treatment more, or less, often
- a new way of giving a standard treatment (radiotherapy for example)

Phase 3 trials usually involve many more patients than phase 1 or 2. This is because differences in success rates may be small. So, the trial needs many patients to be able to show the difference. Sometimes phase 3 trials involve thousands of people in many different hospitals and even different countries. Most phase 3 trials are randomized. This means the people taking part are put into treatment groups at random (Cancer Research UK, 2019).

[11] "The number of subjects, at a single point in time, with a specific attribute (disease) divided by the total number of subjects (total population)" (Nahler, 2009, p. 146).

tendency i.e. hormonal, environmental, diet, and lifestyle (Office on Women's Health, 2002; Rosenfeld, 2001; Wolf, 1996). The inadequacy of the government in facilities e.g. cheap or free breast screening, breast self-examination, and routine mammograms by health professionals are big issues that put women's life at stake. In a clinical study, paclitaxel (Taxol®) for instance was reported to increase the survival rate of women suffering from breast cancer (Lee, Lee, Wu, Lee, & Chen, 2006). In line with the positive results brought by paclitaxel (Taxol®) decades ago, inaccessibility by the majority of Filipino women diagnosed with breast cancer is still an issue. Other than insufficient health facilities, high pricing is another hindrance for early detection of breast cancer. Post-trial access, which as we saw in the introduction is an ethical issue closest to responsiveness, is an ethical issue for interventions that are clinically trialed in the Philippines. Therefore, ratifying policies that protect and provide patients' post-trial access is not alone an ethical responsibility of the host country but other agencies that are involved in research and development (R&D) of clinical trials. In fact, pharmaceutical companies like Johnson & Johnson deliberately strategizes for equitable pricing:

> Policies and takes measures to ensure its clinical trials are conducted ethically. Its policies are strong: they include measures on scientific requirements, research protocols and provisions for post-trial access to investigational medicines (Access to Medicine Foundation, 2016, p. 86).

In the 152 conditions in the data, there are 110 conditions that cause death and Years of Life Lost (YLL); majority of these conditions affect women than men. But if we settle on the values that combines all diseases we could not see the huge gap between female and male conditions. 98.18% of the conditions (108 conditions) affect women and 84.55% of the conditions (93 conditions) affect men. An overlap in the results of the number of conditions is possible; due to other conditions affect both sexes. In the conditions that cause the Years Lived with Disability (YLD), there are 145 conditions in total. 97.24% of the conditions (141 conditions) affect women and 88.28% of the conditions (128 conditions) affect men. However, if the results to be analyzed are number of conditions that are female/male-specific, 15.45 % (17) of the conditions that causes death and YLL affect women, and 1.82% (2) of the conditions affects men. In addition, the numbers of conditions that cause YLD are composed of 145 conditions. 11.72% (17) of the conditions affect women alone and 2.76% (4) of the

conditions affect men alone. In the latter presentation, the difference among the conditions that affect death, YLL, and YLD on women and men show a notable gap which is more than 4 times the number of conditions that affect men are affecting women. Given these results on the conditions that affect women over men, Table 3 shows how offshored clinical trials seem to be responsive to the needs of women than men. In 568 offshored clinical trials that supposedly are responsive to the needs of women and men, 25 clinical trials (25/568 = 4.40%) are responsive to women alone and 12 clinical trials (12/578 = 2.11%) are responsive to men alone. Other than that, the difference of the clinical trials that are assigned to men alone is almost half of the number of clinical trials that are assigned to women alone, even if the number of diseases that are female-specific in death, YLL, and YLD is multiple times higher than the number of diseases that are male-specific.

In the Philippines, where abortion is completely banned and the mother is criminalized if she does undergo an abortion, there is a soaring rate of maternal mortality,[12] which is 162 deaths/100,000 live births due to infections, bleeding, complications during pregnancy and from delivery UNSAFE abortion furthermore has been a constant struggle of women in developing regions such as the Philippines (Republic of the Philippines, 2018; Guerrero, 2011). Despite health advancement in general, there are still significant number of unreported women's deaths in the Philippines which are connected to pregnancy and childbirth; complications brought about by unskilled birth attendance and unsafe and/or self-induced abortion procedure (Van Gijsel, 2016; Tadiar, 2002). Figure 7 shows that among the 10 maternal conditions that cause death, 2 or 20% have zero (0) death record in the length of 10 years (2007-2016). On the issue of abortion, it became a moral subject rather than health. For instance, the rate on maternal abortion, miscarriage, and ectopic pregnancy in Figure 7 is reported to have 0.51 on death, 28.81 on YLL, and 3.26 on YLD. It shows that death rate on maternal abortion, miscarriage, and ectopic pregnancy is the lowest rate than YLL, and YLD.

[12] "(…) is the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes. To facilitate the identification of maternal deaths in circumstances in which cause of death attribution is inadequate, a new category has been introduced: Pregnancy-related death is defined as the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death" (World Health Organization, World Health Organization: Health statistics and information systems, 2019).

This may support the claim of the unreported cases of death especially that abortion is illegal and perceived by Filipino culture as a moral than a women's health issue.

Gender gaps on wages are also a big factor for Filipino women to rather stay home besides the fact that our bodies require us to stay home sometime during pregnancy, delivery and post-delivery childcare. Tadiar also give several social services that appears to care for women in the Philippines but actually the contrary

> Maternal Health Services, particularly prenatal care, are focused on ensuring the birth of a healthy infant. (…) Motherhood Programs have tended to concentrate more on improving technical competencies and biomedical interventions. Family Planning Programs, particularly "birth spacing" and "natural" methods of family planning, are believed by health providers to be primarily for increasing the chances of having healthier babies, rather than for enabling a woman to achieve and maintain physical, emotional, and social well-being during her lifetime (whether or not she wants or chooses to become pregnant and be a mother) (Tadiar, 2002, pp. 91-92).

The World Health Organization therefore, encourages the Philippine government to improve maternal health programs, along with breast feeding and child health platforms due to the lack of national social investments that would certainly alleviate preventable deaths of women and children (UNICEF, 2017). However, international against maternal health in the Philippines proved how women are unconsciously and consistently not prioritized at all by simply interpreting on the intention of its own promotion by stating

> UNICEF, WHO urges Philippine government to improve public investment in support for breastfeeding, child and maternal health programmes: *Investment in newborns is critical to avoid huge economic burden and to ensure far reaching gain* (UNICEF, 2017).

This form of social negligence should be reexamined properly; researchers, regulatory agencies, and policy makers must work together when it comes to the advancement of women's health, quality of life, and wellbeing. In addition to heterosexual norms that are mentioned, women's body is seen by "capitalist ventures" as simply a manufacturer of human beings for labor market, fashion industry, 'pharmaceutical industry' (contraceptive methods specifically), and prostitution (Estrada-Claudio, 2002). Also, "Women are still, to a certain extent, expected to value children and taking care of the home and family as a priority;

women who deviate from this convention are often viewed with judgment and derision" (Martin, 2010, p. 29). Women in the developing countries like the Philippines for instance are much more affected with the occupational status or unemployment due to the pervasiveness of the androcentric value system that confines women to perform reproductive work rather than to enjoy and to benefit from opportunities outside the home. According to UNDP,

> Shortfalls in basic human development among various groups often persist because of discrimination. Women are particularly discriminated against with respect to opportunities and end up with disadvantaged outcomes. In many societies women are discriminated against with respect to productive assets, such as the right to land and property. As a result only 10–20 percent of landholders in developing countries are women ((UNDP), 2016, p. 5).

The Filipino women's health for this apparent reason is not a priority in institutional levels in the international, national, or within the locality. The constant disengagement of women from society and the biases that women are persistently experiencing validate that the reality, knowledge, and conclusions that were formulated in relation to women are questionable. Mainly because women's body changes during pregnancy which result to the progression of most diseases that women suffer. The ethical foundation and legal aspects of researches including clinical trials should require an in-depth scrutiny to address the heterosexual norms that inevitably encourage biases and gender inequality (assuming similarity and equality of men and women, and hence, applied clinical results using male models/samples to general population and women) that put women's health and wellbeing in jeopardy. Kathy Davis is quoted on how women's embodied experiences are essential not only for empowering women but in questioning the truth about women's bodies which states

> OBOS was a lively and accessible manual on women's bodies and health. It was full of personal experience and contained useful information on issues ranging from masturbation (how to do it) to birth control (which methods were available and how to use them) to vaginal infections, pregnancy, and nursing. It combined a scathing critique of patriarchal medicine and the medicalization of women's bodies with an analysis of the political economies of the health and pharmaceutical industries. But above all, OBOS validated women's embodied experiences as a resource for challenging medical dogmas about women's bodies and, consequently, as a strategy for personal and collective empowerment (Disch & Hawkesworth, 2016, p. 636).

Discrimination is a concern that acts as barrier in promoting equitable[13] and efficient[14] opportunities in society specifically in rendering healthcare services. The Figures that are discussed above prove the unseen discrimination against women in providing appropriate drugs and treatments concerning diseases that Filipino women have been suffering for a long time. It is assumed as always that equity and equality create the same results; however, it is not correct when applied to the allocation of resources and apparently, even in responding to the needs of women. There are instances when what was spent or distributed equally actually may not be equitable especially in the context of health economics such as the distribution on the demands of the number of the patients, investigator sites, and clinical trials that are created in countries like the Philippines (Glickman, et al., 2009). Another example is the effect on women and men suffering from the same illnesses (e.g. depression, cardiovascular disease, pneumonia) and are treated in an equal manner with the same medical treatment regardless of the fact that women react differently with medication compared to men (Whitley & Lindsey, 2009). This fact is still is in practice in medical arena since current models, data and knowledge about women are still fully focused and determined by a male model (Disch & Hawkesworth, 2016; Wolf, 1996). To some extent, the lives of women are not handled well with the right treatment that they should receive from doctors and/or health professionals. Almost if not all medical procedures, treatments, and drugs enables discriminatory practices due to the lack of sufficient data and involvement of women patients and participants in the early phases of the clinical trials. For instance, "investigators and pharmaceutical companies have been hesitant to include women of childbearing age in research; presumably because of a fear of litigation should potential offspring be harmed" (Faden, Kass, & McGrow, 1996, p. 261). As a result, information obtained from clinical trials involving men are basically meant to address health issues concerning men. As a response, Vanessa Merton proposes that

> (…) at a minimum, pharmacokinetic[15] screens of all new drugs should be conducted in women and men, and animal studies should include female as well as male animals.

[13] The notion of equity "is inextricably linked to the notions of fairness and justice" and importantly understand the difference of the idea of equality" (Phillips, 2005, s. 10).

[14] "The concept of efficiency embraces inputs (costs) and outputs and/ or outcomes (benefits) and the relationship between them, with a society being judge in efficiency terms by the extent to which it maximizes the benefits for its population, given the resources at its disposal" (Phillips, 2005, s. 8)

[15] "Science dealing with the absorption, distribution, metabolism, and excretion (adme) of drugs in the body, usually conducted as single dose studies or steady state study; population pharmacokinetics takes into account that drugs behave differently in different populations" (Nahler, 2009, p. 137).

Moreover, reproductive studies must be conducted in animals prior to clinical studies in human subjects, and those studies should investigate adverse reproductive outcomes mediated through male and female parents (Merton, 1996, p. 235).

6.2 The Corporation of Culture and Health: The Third world Perspective

In the clinical trials that were conducted in the Philippines from 2007 to 2016, the top most studied disease is 'diabetes mellitus' which obtained 11.44% (65 out of 568 clinical trials). And according to the data in Figure 8, diabetes mellitus is ranked 18. The results in Figure 8 shows that diabetes mellitus mostly affects women on death and morbidity; while it mostly affects men on premature death. Therefore, it appears that more women suffer longer and died more than men due to diabetes mellitus. However, if you analyze the data for the top 10 causes of death, YLL, and YLD separately among sexes, diabetes mellitus does not belong to the top 5 causes of death and YLD, and top 8 for YLL on Filipino women. For men, diabetes mellitus is top 8 for death and top 3 for YLD; and does not belong on the top 10 diseases that men suffer on YLL. Still, among the conditions in Figure 8 that cause death, YLL, and YLD on women, diabetes mellitus is ranked 18, while it ranked 20 on conditions that cause death, YLL, and YLD on men. In this case, offshored clinical trials on diabetes mellitus seems to be responsive to the needs of the population and women; but obviously, being the most clinically trialed condition in the Philippines, these clinical trials may have other underlying reasons other than responding to the needs of the population especially to Filipino women. Clinical trials on diabetes mellitus in the Philippines were generally rendered to ALL (both sexes) but one study among the 65 clinical trials was designed and administered to female patients.

In the global burden of disease, diabetes mellitus is part of the top 10 causes of death among middle-income and high-income countries (World Health Organization, The Global Burden of Disease 2004 Update, 2008). Globalization is the core component of the business models of pharmaceutical companies. Clinical trials are questioned on their integrity on research regarding economics and ethics of clinical practice with the application of the study results to clinical practice (Glickman, et al., 2009). In clinical trials where the trend is focused on the biological and genetic bases of the diseases, feminist's scholars are concerned of the other aspects of disease i.e. biology, psychology, sociology, and economics that influence the researches and the results (Asch & Geller, 1996). It was noted that "studies were being run in developing countries without concerns regarding adherence to the international ethical

principles contained in the 1947 Nuremburg Code and in the 1964 Helsinki Declaration" (Silva, Amato, Guilhem, Carvalho, & Novaes, 2016, p. 2). Given that diabetes mellitus have been given much resources and priority based on the number of clinical trials (more than double the number of the next disease being trialed i.e. asthma, and Chronic Obstructive Pulmonary/Airway Disease/COPD in the Philippines), it seems to be excessively responsive to Filipino women's needs and to the general population. Nevertheless, there are other diseases with soaring rates that cause more death, more premature mortality, and more disabling to Filipino women than diabetes mellitus i.e. cardiovascular diseases, neonatal disorders, pneumonia/lower respiratory infections, low back pain, cerebrovascular diseases, etcetera (see Figure 8). There are several perspectives on analyzing the state of responsiveness of clinical trials to the host population; yet, it is important to remind us that responsiveness should always work on a resolution by finding and providing new knowledge in countering a disease of the host country in the best means possible (Council for International Organizations of Medical Science, 2016). Being known that pharmaceutical companies reduce its cost in clinical trials by targeting 10 to 50% cheaper for having it done in developing countries, it is not surprising that the clinical trials done on diabetes mellitus in the Philippines are more responsive to the needs of middle and high-income countries (World Health Organization, The Global Burden of Disease 2004 Update, 2008; Wemos Foundation, 2008). LMICs are the target of pharmaceutical companies in research and developing medicines and also for diagnostics (Access to Medicine Foundation, 2016). As a result, pharmaceutical companies like Merck KGaA primarily focus their portfolio on non-communicable diseases that includes diabetes mellitus (Access to Medicine Foundation, 2016).

Based on the results of the unpublished study conducted by Bernabe on the responsiveness of offshored clinical trials in the Philippines from 2006-2017 on the top 20 causes of death, YLL, and YLD in the Philippines, US, and high –income countries (HI) (excluding diseases that were common between the Philippines, the US, and/or HI), offshored clinical trials in the Philippines turned out to be less responsive to diseases that cause death, and unresponsive to the diseases that cause morbidity compare to US and HI (Bernabe R. , 2019). Countries like the Philippines have regulations that are not strictly monitored. Thus, procedures and results can be ethically and economically problematic and exploitative (Glickman, et al., 2009; Wemos Foundation, 2008). Clinical trials held in developing countries are usually founded on corporate values (profit) and, as such, these trials are purposely situated in countries where

there are treatment-naïve subjects/patients (not exposed to any treatment). Treatment-naïve patients are not resistant to any drugs and/or treatment; thus, reactions of patients to drugs are not influenced by any factor that may impact the results. In women, diabetes mellitus[16] is a disease that could arise during pregnancy. In a country like the Philippines where the number of registered live births is in the millions from 2006 up to the present, the likelihood for Filipino pregnant women with diabetes mellitus is higher compared to any developed country ((UNDP), 2016). Given that the results of death and morbidity of diabetes mellitus on Filipino women is higher than men, and pregnant women are most likely to develop the condition, this shows that clinical trials that operate in the Philippines does not respond to the needs of Filipino women who are pregnant. This is especially important since clinical trials usually exclude pregnant women, as Brody explained it:

> Women of child bearing potential and pregnant women were in the past often excluded from participation in clinical trials out of fear that the intervention being tested might have a negative impact upon fetuses. This denied the potential women subjects the benefits, if any, of participating in the trials (Brody, 2000, p. 342).

This then qualifies the question, is responsiveness measured by the occurrence of clinical trials for a specific condition or is it insufficient to prove that clinical trials are responsive given the numbers alone? In one of the study in diabetes mellitus with low income users in Karachi, patients participating in a clinical trial were basically not complying with the terms of treatment due to expenses requirement; hence, noncompliance was due to unaffordability (Zaidi & Nishtar, 2011). In a developing country like the Philippines (where women are second to the poorest sectors), Filipino women will be most likely to be noncompliant to treatment than men. The state of responsiveness of clinical trials does not consider the individual situation of the patient that participates. Up to this date, data regarding completion and noncompliance of patients participating in clinical trials in the Philippines are not available.

[16] "(…) the most prevalent endocrine disease, diabetes mellitus is a metabolic disorder that is generally diagnosed by the characteristic symptoms of polydipsia, polyuria, and polyphagia in correlation with exceeded blood glucose levels more than 200 mg/dL. It causes hyperglycemia due to a defect of insulin secretion, that insulin has an effect on the regeneration of bone matrix. In a diabetic patient, hyperglycemia reduces clot quality, number of osteoclasts, and collagen production, which are the keys of bone regeneration" (Akay & Arısan, 2018).

The key concept 'responsiveness' used in this research is tied to clinical trials brought to countries like the Philippines to validate or invalidate the availability of a new knowledge in addressing a health condition in the best possible way (Council for International Organizations of Medical Science, 2016). Responsiveness, therefore, can't stand alone in providing efficient and equitable policies in securing the health needs of Filipino women. It is important to see other relevant factors such as sexual and gender norms, socio-economic, political, and health implications that may result to or expose patients to exploitation, violence, injury, and death. And what requires an individual to be a subject in clinical trial is basically a confirmation of global norms. Women's involvement in health and economics underwent unbearable circumstances which made the lives of many women in the past tormented and sacrificial in the field of medicine and economics (Rosenfeld, 2001; Banerjee & Dulfo, 2011; Annandale, 2009). Dehumanizing women for centuries such as the 'burning of witches', using women for medical experimentations, were sold, and women's unfavorable status in society which forced women to marry another man or to move to another family for survival, are few of the many tragic circumstances women underwent to be recognized and to survive (Banerjee & Dulfo, 2011; Faden, Kass, & McGrow, 1996; Shang, 2008). These circumstances provide us the impacts of standardizing biotechnological advancement and economic development have resulted to uncertainties in terms of benefits in responding to the health needs of women. The fact that health issues encompass personal, education, social, sexuality, diseases, drug development, and biotechnology, it became the new challenges this era has to address on top of the previous unresolved issues of women. The government's lack of mediation in regulating the research and development of clinical trials in developing countries like the Philippines (which if left on its own encourages free competition), could seemingly unresponsive to the health needs of Filipino women. Thus, feminists are steadily and enthusiastically making effort to confront and to take women out from all forms of oppression and discrimination particularly in women's health. In fact, according to Rosenfeld, it was also 20 to 40 years ago that health economics started to consider the discourse on women's health as vital (Rosenfeld, 2001). It is alarming that health and economic development that influences the standards of clinical trials are systemically positioned of women as disadvantaged (Disch & Hawkesworth, 2016). "In a society which has long practiced systematic discrimination against women, for example, women may not be dissatisfied with their unjustly disadvantaged state, including the health differences that result

from that discrimination" (Brock, 2004, p. 361). Exploitation of participants in developing countries is possible especially for vulnerable population like women. Richard Chin for instance states the following

> You can also exploit a vulnerable population when you withhold something that they want unless they participate in the study. Examples of coercive inducements include offering significant money to an indigent population, entry into a particular social group, promises of job promotions or good grades, freedom for a prisoner or servant, or promises of cure for a disease. Of course, many patients will participate in a trial because they are seeking a cure for their ailment. Promising a cure and not mentioning alternative treatments is coercion. Clearly stating the risks and benefits of participating and making no promises is not coercion (Chin & Lee, 2008, p. 25).

In the Philippines where healthcare is universal but semi-privatized and government resources are scarce, people are looking for any means that could provide them medical treatment. Charitable institutions and NGOs are options for Filipinos in time of health crisis. The presence of clinical trials in the Philippines is somehow appearing for Filipinos as an opportunity for free treatment because of inaccessibility to interventions. Women being in a vulnerable position and lacking financial autonomy always ends up in a hopeless situation. In consequence, women are most likely to be exploited especially in desperate situation when life is at stake. This situation is widespread in the Philippines as more than 80% of the working Filipinos belong to informal sector; which means, they have limited or no access to healthcare. To supplement the claim, statistics show that "of the 101.5 Filipinos, more than 70 million are of working age and, according to the Philippine Statistics Authority (PSA), the labor force consists of 42.5 million, of which 40.7 million are supposedly employed. Of the 40.7 million employed, only 7.7 million are in the formal sector, while 33 million are in the informal sector" (Cecilia, 2018). Taking into account the factors affecting women's health could be insufficient by not engaging the women themselves to be part of theorizing their empirical experiences and knowledge about their own body, situation, environment, and behaviors directly to the clinical trial sponsors. Emphasizing not solely in the participation of women in clinical trials but also the involvement of women patients and participants in theorizing is necessary. By allowing women's desires, needs, experiences, and thoughts is an empowering act to identify the impacts of a health system that tolerates clinical trials. This

observation is essential especially if clinical trials in developing countries are increasing and the health and values of the population are still striving towards women's empowerment. Rosemarie Tong explicitly challenge the issues that involve women's health and bioethics, she stated that

> Despite such strides in women's health, power-focused feminist bioethicists have not rested content. In an effort to make certain that recent gains in serving women's health interests are not only maintained but increased, they have proposed a women's health specialty that would focus exclusively on women's health concerns, both non-reproductive and reproductive. Interestingly, this recommendation has not met with feminist bioethicists' universal approval (Tong, 2004, p. 154).

6.3 Filipino Women and 'Responsiveness': WHAT is the Priority?

By looking at the Figures 8 and 9, it is apparent that the results being paired on both data are not consistent to each other. The needs of the general population, Filipino women, or men based on the average death, YLL, and YLD rates, the ratio of the average rate and the frequency in a disease is not proportional. For conditions that on the top list that clinical trials are not responsive at all (zero (0) clinical trials) based on the results from 2007 to 2016 are neonatal disorders (2nd in rank for women , 2nd men, & 2nd general population), age-related and other hearing loss (9th women, 7th men, & 9th general population), congenital birth defects (11th women, 8th men, & 10th general population), diarrheal diseases (16th women, 13th men, & 14th general population), and anxiety disorders (10th for women, 15th for men, & 12th general population). The conditions that offshored clinical trials are not responsive to are diseases that primarily affect the vulnerable groups which are children and women. In a short time frame, the conditions that are mentioned a forehand are long way suffered by vulnerable groups in vulnerable population in poor countries. This follows the dichotomized association that Lindstrand, and Elstad explained about partiality in attachment of diseases to individuals that are considered disadvantaged, primitive, unsuccessful, unintelligent, undesirable, insufficient, and inferior (Lindstrand, et al., 2006; Elstad, 2000).

In Figure 9 NTDs that affect Filipinos based on the IHME data i.e. ascariasis, cysticercosis, dengue, leishmaniasis, leprosy/Hansen's disease, malaria, rabies, schistosomiasis, and other neglected tropical diseases, more than half of (5 NTDs) which are included in the top 10 conditions that causes death, YLL, and YLD among women, and men. This proved how

NTDs are unaddressed or treated inefficiently by health models and programs provided mainly by World Health Organization (WHO) and World Bank (WB) through the results of the global burden of diseases using Disability-Adjusted Life Year (DALY)[17] (World Health Organization, The Global Burden of Disease 2004 Update, 2008). Some of the NTDs are chronic diseases and are even ancient diseases (some are mentioned biblically) and thus, are simply prolonged the agony of individuals having been affected by these diseases. These are obviously the best example of how international financial/research institutions both private and public, pharmaceutical and biotechnical companies, non-governmental organizations (NGOs), the academia, and foreign countries (especially the developed) give so little attention to these diseases that caused millions of death in countries affected for ages. It is a fact that some NTDs got higher ratio in the global burden of disease (GBD) such as dengue and leprosy/Hansen's disease which are both affect the Filipinos (dengue being the highest and leprosy/Hansen's disease as the lowest among the NTDs that affect Filipinos in general (refer to Figure 9). In WHO report on neglected tropical diseases, it states

> In 2012, dengue ranked as the most important mosquito-borne viral disease with an epidemic potential in the world. There has been a 30-fold increase in the global incidence of dengue during the past 50 years, and its human and economic costs are staggering. The world needs to change its reactive approach and instead implement sustainable preventive measures that are guided by entomological and epidemiological surveillance (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013).

Additionally, Lao People's Democratic Republic was reported in 2013 to have high incidence of dengue; however, Philippines is reported to have most cases as well as death (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013). NTDs which affects solely developing countries are stagnant (not improving) and less prioritized as oppose to tropical diseases such as TB (considered NTD before), rabies, and malaria which are given much attention and mitigated when the developed countries were also affected with it. This

[17] "One DALY can be thought of as one lost year of "healthy" life. The sum of these DALYs across the population, or the burden of disease, can be thought of as a measurement of the gap between current health status and an ideal health situation where the entire population lives to an advanced age, free of disease and disability" (World Health Organization, Health statistics and information systems: , 2019).

trend reflect how clinical trials done in the past on these NTDs have brought positive results in developed countries based on the GBD (World Health Organization, The Global Burden of Disease 2004 Update, 2008). Up to this date, NTDs that affect Filipinos other than dengue (5 clinical trials) are, schistosomiasis (2 clinical trials), rabies (4 clinical trials), malaria vivax (3 clinical trials), and leprosy/ Hansen's disease (1 clinical trials) which are all responded by offshored clinical trials at the same time (refer to Figure 9). Rabies is described by the same report as improving in terms of control (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013). In the case of schistosomiasis, the platform for its elimination was restarted after new cases were reported in areas like Cagayan and Negros Occidental which are considered as endemic (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013). Studies show that most NTDs are proven to extremely affect women and children, WHO provide reports on women stating

- Biological sex and age to the outcomes of infections can be young mothers can reactivate leprosy;
- Nerve damage from leprosy is accelerated in pregnant and lactating women, 45% of whom develop silent neuritis, including those on chemotherapy and those considered cured;
- Women who have urogenital schistosomiasis are three times to four times more likely to become infected with HIV;
- The development of dengue hemorrhagic fever and dengue shock syndrome, and secondary-type antibody response, are affected by age and sex; the incidences are higher in young children and females than in males, particularly in Asia (World Health Organization, Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, 2013, pp. 21-22).

In the rates of dengue on death and premature death (YLL) Filipino men are more affected than women; while on the morbidity rate (YLL) Filipino women have suffered longer than men.

The results in Figures 4, 5, and 6 show the top conditions affecting both sexes that cause death, premature death, and disability demonstrate a trend in terms of the number Filipinos affected by sexes. The trend demonstrates that conditions causing death and premature death (YLL) affect Filipino men mostly based on number of incidence on each condition; while morbidity or disabling conditions affect Filipino women mostly than men. In line with this, women suffer longer carrying the burden of the disease/s than men. Despite of the detailed monitoring and evaluation categories of the WHO on the universal healthcare system in each country globally, women's access to healthcare system and services has been the underlying problem and issue. In the Philippines, women are utilizing traditional medicine and treatment over Western medicine in dealing with reproductive, maternal, and other health issues. Ignorance on women's experiences is basically detrimental for all women and the society in general.

Pre-assigned identifiers of illnesses are not usually exact and therefore it is essential to include the self-perceived health of the individual to come up with a more realistic picture of the status of health (including women's health) of that particular person (Elstad, 2000; Brock, 2004). On the other end, if women will be part of the modelling process of the healthcare system, then women will have space for discussion and could be part of the solution which will produce substantive benefits to all. Susan Wolf gives a very good point on the importance of communication in healthcare practices/system. She states

> In evaluating the ethical standing of a practice, we must go beyond stated objectives and anticipated consequences to analyze the actual effects of the practice on real women and their interests. Moreover, we must determine those consequences not only for each individual woman but for women as a group (Wolf, 1996, p. 217).

This explains how important the participatory approach is in the process of evaluation in healthcare practices/system is, but also to look for patterns of "discrimination, exploitation, and dominance" that women experience (Wolf, 1996, p. 218; Annandale, 2009; Funnell & Rogers, 2011).

While research and development (R&D) is dichotomized according to men/women, healthy/unhealthy, west/east, rich/poor, developed/developing; this dichotomy is associated unfairly with prescribed statuses of certain group of individuals as disadvantaged, primitive,

unsuccessful, unintelligent, and inferior (Elstad, 2000; Lindstrand, et al., 2006). The large disparity among populations through these dichotomies not only represents the consumption of an average human being, but again, by two opposite poles that show the partiality in the distribution of resources which reflects the hierarchy in health status that affects human productivity and condition (Lindstrand, et al., 2006; Elstad, 2000). The results in Figure 8 shows that the top 10 conditions that affect the general population i.e. by the average rate from death, YLL, and YLD, Again, from the beginning of the discussion, this research viewed women as disadvantaged and poor. The 'social comparisons' that Elstad pointed out could imply and aggravate "frustrations, inadequacy, inferiority, and anxiety" (Elstad, 2000, p. 43). At the same time, the presence of epidemiology became very influential in today's developmental research to quantify and to assign terms which are used to label different groups of individuals and concepts that imply 'justice', 'ethical' and 'strategic' (Friedman, 1974; Disch & Hawkesworth, 2016). But we should not overlook that "health is not usually a matter of doctors, social services and hospitals, but an issue of social justice" (Lindstrand, et al., 2006, p. 61). Clinical trials that are poured on developing countries like the Philippines are considered beneficial but can also be detrimental.

7 Study Limitations

This research covers clinical trials that were conducted in the Philippines only. Therefore, the researcher exercised caution in generalizing the state of responsiveness of other offshored clinical trials. This study utilizes data gathered from ClinicalTrials.gov and the Institute for Health Metrics and Evaluation (IHME) from 2007 to 2016. It only considered clinical trials with the following statuses: completed, active, not recruiting, recruiting, terminated, and unknown status. The number of participants provides an important factor in determining which clinical trials did or did not proceed with providing the experimental and the control interventions. However, I was not able to validate the results of either the clinical trials or the YLL, YLD, and NTDs from any Philippine agency as information from the Philippines were incomplete, and as such were unreliable. Further, conditions that are not relevant to the Philippines from the data gathered from the IHME were not included. The results obtained will use descriptive analysis in context, and univariate descriptive analysis to look for patterns in describing and comparing distributions using proportions and percentages, rates and ratios,

and frequencies. Lastly, the study uses the feminist standpoint to address the biases that afflict the health needs of Filipino women based on the results and findings.

8 Conclusion

Based on the results and the in depth analysis performed in this study, responsiveness is a concept that can be quantified and qualified on specific conditions and group of conditions. The phenomenon that transpired in the case of 65 clinical trials on diabetes mellitus came out to be responsive to the health needs of Filipino women, aside from patients who are lactating and/or pregnant. Since the trends and patterns on the rates of conditions that cause death and morbidity mostly affect Filipino women, it is not impossible that women who are lactating and/or pregnant will have a high risk of death and longer suffering compared not only to men but also to women who are not in the same case. In the case of maternal conditions, not a single case in 568 offshored clinical trials responded to women's maternal health needs. The lack of involvement of Filipino pregnant and lactating mothers is in fact detrimental on the lives of women in general. This applies in the case of neglected tropical diseases such as dengue, leprosy, schistosomiasis, malaria, and rabies, which turned out that offshored clinical trials respond so little compared to other diseases that do not belong to the top 10 conditions that causes death, YLL, and YLD; with the exemption of dengue cases where offshored clinical trials in the Philippines are completely banned despite being responsive to the health needs of the Filipinos, including women. In the event of neonatal disorders, anxiety disorders, and diarrheal diseases, offshored clinical trials are totally unresponsive (no clinical trial) to the health needs of Filipino female patients. These are conditions that affect females more than males in terms of morbidity (YLD). There is also a trend that Filipino women suffer from disabling conditions more than men, while Filipino men are more affected by conditions on death and premature death. On female/ male specific conditions, offshored clinical trials tend to respond 3 times more to male-specific conditions than women; therefore, responsiveness of clinical trials on female specific conditions may be considered poor despite the high number of clinical trials put on breast cancer patients. From a feminist standpoint, it was argued that the ambiguity of the concept of 'responsiveness' can also be strategically contributing to the inadequacies and loopholes wherein offshored clinical trials neglect the gravest needs of Filipino women. Because of this, the health status of Filipino women and the

conditions that affect them are still considered irrelevant and/or not a priority. By incorporating the principles of feminist standpoint theory in medical practices and clinical researches, solution to end exploitation, discrimination, and biases are favorable not only to women but to everyone.

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10 Appendices

10.1 Appendix 1. Combined data from Institute for Health Metrics and Evaluation (IHME) and from ClinicalTrials.gov

Summary of conditions that belong to the top 10 cause of death, premature death (YLL), morbidity (YLD), and NTDs on female, male and the general population.

Conditions	Female Average Death Rates	Male Average Death Rates	Average Death Rates	Female Average YLL Rates	Male Average YLL Rates	Average YLL Rates	Female Average YLD Rates	Male Average YLD Rates	Average YLD Rates	Average Female Rates	Average Male Rates	Average General Population Rates	Frequency of Clinical Trials	Percentage of Clinical Trials
Cardiovascular diseases	168.93	218.00	193.47	3566.05	5828.58	4697.32	256.16	242.36	249.26	1330.38	2096.31	1713.35	5	0.88
Neonatal disorders	23.63	32.53	28.08	2044.76	2814.91	2429.84	184.86	180.88	182.87	751.08	1009.44	880.26	0.00	0.00

Migraine	Cerebrovascular diseases	Low back pain	Pneumonia/Lower respiratory infections	Conditions
0.00	57.15	0.00	58.44	Female Average Death Rates
0.00	73.37	0.00	63.75	Male Average Death Rates
0.00	65.26	0.00	61.10	Average Death Rates
0.00	1252.24	0.00	1839.89	Female Average YLL Rates
0.00	1962.73	0.00	2426.14	Male Average YLL Rates
0.00	1607.49	0.00	2133.02	Average YLL Rates
634.57	112.71	730.69	6.87	Female Average YLD Rates
335.46	91.25	725.98	7.84	Male Average YLD Rates
485.02	101.98	728.34	7.36	Average YLD Rates
634.57	474.03	730.69	635.07	Average Female Rates
335.46	709.12	725.98	832.58	Average Male Rates
485.02	591.58	728.34	733.82	Average General Population Rates
3	14	3	19	Frequency of Clinical Trials
0.53	2.46	0.53	3.35	Percentage of Clinical Trials

Diarrheal diseases	Anxiety disorders	Tuberculosis	Age-related and other hearing loss	Conditions
0.00	0.00	19.5	0.00	Female Average Death Rates
0.00	0.00	41.23	0.00	Male Average Death Rates
0.00	0.00	30.37	0.00	Average Death Rates
419.59	0.00	616.69	0.00	Female Average YLL Rates
632.69	0.00	1297.99	0.00	Male Average YLL Rates
526.14	0.00	957.34	0.00	Average YLL Rates
425.08	386.45	148.73	401.3	Female Average YLD Rates
399.98	240.79	81.81	450.28	Male Average YLD Rates
412.53	313.62	115.27	425.79	Average YLD Rates
281.56	386.45	261.64	401.30	Average Female Rates
344.22	240.79	473.68	450.28	Average Male Rates
312.89	313.62	367.66	425.79	Average General Population Rates
0.00	0.00	12	0.00	Frequency of Clinical Trials
0.00	0.00	2.11	0.00	Percentage of Clinical Trials

Neck pain	Acne vulgaris	Chronic kidney disease	Congenital birth defects	Conditions
0.00	0.00	22.20	10.3	Female Average Death Rates
0.00	0.00	29.95	12.75	Male Average Death Rates
0.00	0.00	26.08	11.53	Average Death Rates
0.00	0.00	610.74	845.32	Female Average YLL Rates
0.00	0.00	920.78	1052.97	Male Average YLL Rates
0.00	0.00	765.76	949.15	Average YLL Rates
268.06	273.14	75.55	72.83	Female Average YLD Rates
230.41	259.22	80.74	126.23	Male Average YLD Rates
249.24	266.18	78.15	99.53	Average YLD Rates
268.06	273.14	236.16	309.48	Average Female Rates
230.41	259.22	343.82	311.59	Average Male Rates
249.24	266.18	289.99	310.54	Average General Population Rates
3	1	10	0.00	Frequency of Clinical Trials
0.53	0.18	1.76	0.00	Percentage of Clinical Trials

Diabetes mellitus	Asthma	Chronic obstructive pulmonary disease	Refraction and accommodation disorders	Conditions
22.77	9.93	10.49	0.00	Female Average Death Rates
21.18	13.81	27.62	0.00	Male Average Death Rates
21.98	11.87	19.06	0.00	Average Death Rates
502.03	332.99	200.39	0.00	Female Average YLL Rates
559.36	430.64	572.20	0.00	Male Average YLL Rates
530.70	381.82	386.30	0.00	Average YLL Rates
13.89	273.20	207.79	251.06	Female Average YLD Rates
0.16	230.72	361.22	239.36	Male Average YLD Rates
7.03	251.96	284.51	245.21	Average YLD Rates
179.56	205.37	139.56	251.06	Average Female Rates
193.57	225.06	320.35	239.36	Average Male Rates
186.57	215.22	229.95	245.21	Average General Population Rates
65	31	31	4	Frequency of Clinical Trials
11.44	5.46	5.46	0.70	Percentage of Clinical Trials

Nutritional deficiencies	Other musculoskeletal disorders	Schizophrenia	Digestive diseases	Conditions
4.92	1.36	0.00	9.45	Female Average Death Rates
4.05	0.51	0.00	18.63	Male Average Death Rates
4.49	0.94	0.00	14.04	Average Death Rates
156.74	63.70	0.00	264.28	Female Average YLL Rates
175.18	20.27	0.00	592.44	Male Average YLL Rates
165.96	41.99	0.00	428.36	Average YLL Rates
332.17	460.25	148.29	26.33	Female Average YLD Rates
152.40	296.46	159.09	28.87	Male Average YLD Rates
242.29	378.36	153.69	27.60	Average YLD Rates
164.61	175.10	148.29	100.02	Average Female Rates
110.54	105.75	159.09	213.31	Average Male Rates
137.58	140.43	153.69	156.67	Average General Population Rates
12	3	21	5	Frequency of Clinical Trials
2.11	0.53	3.70	0.88	Percentage of Clinical Trials

Alzheimer disease and other dementias	Dengue	Breast cancer	Cirrhosis and other chronic liver diseases	Conditions
17.69	2.48	15.71	5.99	Female Average Death Rates
8.84	2.70	0.22	17.53	Male Average Death Rates
13.27	2.59	7.97	11.76	Average Death Rates
200.80	190.41	497.00	164.93	Female Average YLL Rates
119.36	200.47	6.26	576.98	Male Average YLL Rates
160.08	195.44	251.63	370.96	Average YLL Rates
56.79	36.26	0.00	9.15	Female Average YLD Rates
31.71	32.02	0.00	10.34	Male Average YLD Rates
44.25	34.14	0.00	9.75	Average YLD Rates
91.76	76.38	256.36	60.02	Average Female Rates
53.30	78.40	3.24	201.62	Average Male Rates
72.53	77.39	129.80	130.82	Average General Population Rates
3	5	20	9	Frequency of Clinical Trials
0.53	0.88	3.52	1.58	Percentage of Clinical Trials

Schistosomiasis	Hematologic Diseases	Lupus	Hypertension	Conditions
0.11	1.02	2.33	2.51	Female Average Death Rates
0.17	1.07	1.43	2.75	Male Average Death Rates
0.14	1.05	1.88	2.63	Average Death Rates
3.47	40.80	77.42	75.18	Female Average YLL Rates
5.85	45.80	62.61	94.83	Male Average YLL Rates
4.66	43.30	70.02	85.01	Average YLL Rates
58.20	26.69	33.79	19.15	Female Average YLD Rates
47.89	17.66	35.40	22.22	Male Average YLD Rates
53.05	22.18	34.60	20.69	Average YLD Rates
20.59	22.84	37.85	32.28	Average Female Rates
17.97	21.51	33.15	39.93	Average Male Rates
19.28	22.17	35.50	36.11	Average General Population Rates
2	19	20	24	Frequency of Clinical Trials
0.35	3.35	3.52	4.23	Percentage of Clinical Trials

Malaria, Vivax	Arthritis	Rabies	Influenza	Conditions
0.16	0.00	0.18	0.27	Female Average Death Rates
0.21	0.00	0.49	0.38	Male Average Death Rates
0.19	0.00	0.34	0.33	Average Death Rates
7.80	0.00	9.46	19.71	Female Average YLL Rates
9.98	0.00	28.48	28.59	Male Average YLL Rates
8.89	0.00	18.97	24.15	Average YLL Rates
0.70	4.99	0.00	4.88	Female Average YLD Rates
0.69	13.66	0.00	5.25	Male Average YLD Rates
0.70	9.33	0.00	5.07	Average YLD Rates
2.89	4.99	4.82	8.29	Average Female Rates
3.63	13.66	14.49	11.41	Average Male Rates
3.26	9.33	9.65	9.85	Average General Population Rates
3	29	4	22	Frequency of Clinical Trials
0.53	5.11	0.70	3.87	Percentage of Clinical Trials

Conditions	Female Average Death Rates	Male Average Death Rates	Average Death Rates	Female Average YLL Rates	Male Average YLL Rates	Average YLL Rates	Female Average YLD Rates	Male Average YLD Rates	Average YLD Rates	Average Female Rates	Average Male Rates	Average General Population Rates	Frequency of Clinical Trials	Percentage of Clinical Trials
Leprosy	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.27	0.20	0.12	0.27	0.20	1	0.18

Note: In the frequencies and percentages of clinical trials columns, some conditions are combinations of diseases/conditions in the data; the following are:

- Cerebrovascular diseases include atherosclerosis, atherothrombosis, intracranial hemorrhages, ischemia, stroke / cerebral infarction, and transient ischemic attack.
- Digestive diseases include, stool composition, and gastric ulcer / duodenal ulcer / ulcerative colitis.
- Nutritional deficiencies include anemia, children under-nutrition, iron deficiency, iron absorption, and hypothyroidism
- Neglected tropical diseases include dengue, schistosomiasis, rabies, malaria, and leprosy.

10.2 Appendix 2. Data from ClinicalTrials.gov

10.3 Appendix 3. Complete list of conditions extracted from the IHME data

Note: Appendix 2 and appendix 3 are accessible online.

Link: *https://1drv.ms/b/s!AtaY1Q1OSnqx5ghpIAh6eAtPEb8k*