
# POVERTY-RELATED AND NEGLECTED DISEASES

## through a Gender Lens

DSW
Deutsche Stiftung Weltbevölkerung

youth car

# TABLE OF CONTENTS

# ACKNOWLEDGEMENTS

This study was commissioned by DSW and authored by Michaela Told at HumanImpact5 (HI5), with valuable contributions and support from Gabrielle Landry Chappuis, Uda Deshapriya, Adnan Jafferjee, and Hoi Tung Ng. DSW thanks the author for her high-quality research, thorough analysis, excellent work, and great collaboration. DSW would also like to thank the interviewees for their availability and openness to share their insights.

## ABOUT DSW

Deutsche Stiftung Weltbevölkerung (DSW) is a global development organisation that focuses on the needs and potential of the largest youth generation in history. We are committed to creating demand for and access to health information, services, supplies, and economic empowerment for youth. We achieve this by engaging in advocacy, capacity development, and reproductive health initiatives, so that young people are empowered to lead healthy and self-determined lives. With our headquarters in Hannover, Germany, DSW operates two liaison offices in Berlin and Brussels, as well as maintaining a strong presence in Ethiopia, Kenya, Tanzania, and Uganda. DSW also advocates for investment in research and innovation to fight poverty-related and neglected tropical diseases – diseases that continue to disproportionately affect women and girls.

Deutsche Stiftung Weltbevölkerung (DSW)
Avenue des Arts 43 | 1040 Brussels | Belgium
brussels@DSW.org
www.dsw.org

## ABOUT THE AUTHOR

Dr. Michaela Told is an economist, social worker, and political scientist with additional training in psycho-drama. She has more than twenty years of experience in the public sector, international organizations, the RCRC Movement, NGOs, and academia, ranging from facilitating policy development and conducting applied research studies to driving organisational development and managing humanitarian emergencies. Her thematic focus is on the interface of gender, global health, and development. She is currently teaching at the University of Geneva and is co-founder of HumanImpact5 HI5.

Author: Dr Michaela Told
Editing: Lisa Goerlitz
Design/ graphics: JHNSTL, Johannes Stoll
Graphics: HumanImpact5 HI5, Adnan Jafferjee
Cover photo: Brian Otieno, DSW

Date of publication: March 2021, © DSW

## DISCLAIMER

# ACRONYMS

| | |
|---|---|
| CDD | Community Drug Distributor |
| DALY | Disability-Adjusted Life Year |
| DSW | Deutsche Stiftung Weltbevölkerung |
| EMA | European Medicines Agency |
| EC | European Commission |
| EU | European Union |
| FDA | US Food and Drug Administration |
| FEW | Female Entertainment Workers |
| GBD | Global Burden of Disease |
| GDP | Gross Domestic Product |
| GNC | Gender Non-Confirming Adults |
| HIV | Human Immunodeficiency Virus |
| HPV | Human Papillomavirus |
| ICH | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use |
| IHME | Institute of Health Metrics and Evaluation |
| IDM | Innovative and Intensified Disease Management |
| LGBTIQ+ | Lesbian, Gay, Bisexual, Transgender, Intersex or Questioning |
| LF | Lymphatic filariasis |
| LMIC | Low- and Middle-Income Country |
| MDA | Mass Drug Administration |
| MDR | Multidrug Resistance |
| MSM | Men who have Sex with Men |
| NIH | National Institute of Health |
| NTDs | Neglected Tropical Diseases |
| PC | Preventive Chemotherapy |
| PHC | Primary Health Care |
| PRNDs | Poverty-Related and Neglected Diseases |
| R&D | Research & Development |
| R&I | Research & Innovation |
| SCH | Schistosomiasis |
| SDGs | Sustainable Development Goals |
| STDs | Sexually Transmitted Diseases |
| STH | Soil-Transmitted Helminths |
| TB | Tuberculosis |
| TDR | Special Programme for Research and Training in Tropical Diseases |
| TG | Transgender |
| UHC | Universal Health Coverage |
| UNDP | United Nations Development Programme |
| US | United States of America |
| WHO | World Health Organization |
| WoSuP | Women Susceptible to and becoming Pregnant |


Photo: Jonathan Torgovnik/Getty Images/Images of Empowerment

# TABLE OF GRAPHS, TABLES, FIGURES AND DEEP DIVES

## GRAPHS



## TABLES



## FIGURES



## DEEP DIVES

Photo: Shutterstock

# 1 INTRODUCTION

WORLDWIDE,
**2.8 BILLION**
PEOPLE ARE AFFECTED

**Worldwide, 2.8 billion people are affected by poverty-related and neglected diseases (PRNDs),** including the three major diseases of Human Immunodeficiency Virus and Acquired immunodeficiency syndrome (HIV & AIDS), tuberculosis (TB), malaria and neglected tropical diseases (NTDs)[1]. They hamper human and economic development but also make women and young people particularly vulnerable, creating a vicious cycle of poverty and poor health. Even though the burden of PRNDs has been recognised in the Sustainable Development Goals (SDGs)[2, 3] and eliminating them is seen as instrumental to achieving Universal Health Coverage (UHC)[3,4], priorities shift in the midst of a crisis. With the ongoing COVID-19 pandemic, global health progress made over recent decades towards eliminating PRNDs is at major risk of setbacks, with women and girls particularly vulnerable to lack of access to healthcare[5].

**88 MILLION**
PEOPLE MAY BE PUSHED INTO EXTREME POVERTY

Over the past 25 years, extreme poverty has been in continuous decline, but according to the World Bank, the compounded effect of COVID-19, climate change, and conflict may lead to a global poverty rate of 9.1%, **pushing an approximate 88 million people into extreme poverty and resulting in a three-year set back in the progress made so far** towards ending poverty[6]. COVID-19 will likely also cause massive setbacks in global health gains within specific disease areas, such as TB, where five to eight years of progress could be lost[7]. The fight against HIV & AIDS could lose up to ten years of progress[8]; the burden of malaria could double in one year[9]; while the impact on progress against NTDs is multi-faceted and difficult to ascertain with a singular measure[10]. Overall, no matter which disease we speak of, the economic downturn due to COVID-19 has meant that funding and implementation efforts to tackle these diseases are even more constricted by the grips of lockdowns and supply chain disruptions. Progress made over recent decades on eliminating PRNDs is thus at major risk of being reversed.

**WOMEN**
AND GIRLS ARE PARTICULARLY AFFECTED

**Women and girls are particularly affected** as they generally earn less, have less job security, are major caregivers, including caring for the elderly, and are adversely impacted by a lack of access to healthcare[5]. The latter includes exacerbated hindrances to accessing sexual and reproductive health services, and all of this is compounded by dramatic increases in domestic violence[11]. Similarly, people who face discrimination, stigmatisation, intolerance, or violence because of their actual or perceived sexual orientation, gender identity and expression, or sex characteristics are particularly at risk[12].

Therefore, **keeping a strong gender focus is key to staving off what for now is an almost silent but imminent and multifactorial global health crisis.** A strong gender lens on PNRDs in this context is all the more crucial to achieving positive health impacts. This report highlights a number of gender-related aspects of PRNDs, analysing the implications on research and innovation (R&I) needs and the role of gender-sensitive and gender-responsive approaches in fighting PRNDs.

## What are PRNDs? What is gender?

It is through the lens of the above described exacerbated economically and socially vulnerable situations for women and girls, people who identify as Lesbian, Gay, Bisexual, Transgender, Intersex or Questioning (LGBTIQ+) and for all people suffering from PNRDs, that we read the following definition, from the World Health Organization's (WHO) Global Report for Research on Neglected Diseases[13], which highlights the problematic relationship between poverty and disease. It defines **'infectious diseases of poverty'** as

> *"an umbrella term used to describe a number of diseases which are known to be more prevalent among poorer populations, rather than a definitive group of diseases. It is an overarching concept, recognising the need to focus on the poor and vulnerable, who have less power to intervene. […| Infectious diseases of poverty are not restricted to low and middle-income countries, but manifest in poor populations globally."* [13, p.13]

**POVERTY** IS ABOUT ECONOMIC STATUS BUT ALSO ABOUT **POWER**

This definition is of particular relevance because it **relates the term 'poverty' not only to income and the economic status but also to a concept of power**, and thus, also to a deprivation of capability[14]. This leads to a vicious cycle in which these diseases increase poverty but poverty in itself also increases the chances of developing these diseases[15]. Such a conceptualisation moves the attention **away from the notion of 'neglected diseases' to a notion of 'neglected populations'**, creating space for a more differentiated analysis. Diseases of poverty are, however, also 'neglected' in the sense that there is a lack of private sector interest in investing into R&I for new or improved health tools and technologies. This is the case despite the immense disease burden and the existing research and product development gaps, due to the limited market incentives for innovations targeting 'neglected populations', as well as a weak policy framework.

SEX REFERS TO BIOLOGICAL ATTRIBUTES, **GENDER IS A SOCIAL CONSTRUCT**

For the purpose of this report, **23 'diseases of poverty' will be considered** *(see Annex 1)*, including NTDs prevailing mainly in 149 low- and middle -income countries (LMICs)[16], as well as HIV & AIDS, malaria, and TB[15]. The focus will be, however, on the differential impact these diseases may have on neglected populations, among them in particular women and girls. 'Sex' refers to the biologically designated attributions at birth as male, female, or intersex person and may differ from one's gender identity and expression. Even though often related, they are distinct concepts. WHO defines 'gender' as a social construct that

> *"includes norms, behaviors, and roles associated with being a woman, man, girl or boy, as well as relationships with each other. …[It] varies from society to society and can change over time"*[17].

POLITICAL, SOCIAL, HISTORICAL, CULTURAL, AND ECONOMIC REALITIES SHAPE **GENDER NORMS,** ROLES, AND IDENTITIES

**Political, social, historical, cultural, and economic realities shape gender norms, roles, and identities.** The prescribed roles, behaviours and attitudes can be the "cause, consequence and mechanism of power relations" [18:viii]. Therefore, gender is "hierarchical and produces inequalities that intersect with other social and economic inequalities"[17]. The inequalities and discrimination that women and girls, and people with non-binary sex characteristics, gender identity and expression, or sexual orientations may face can put their health and well-being at risk and thus, make them more vulnerable, for example to the impact of PRNDs. Pregnant women and children are often even more exposed to diseases and congenital transmission can have a life-long health impact.

## What are the methods of data collection used?

The methods used to gather information are based on secondary and primary data collection. Firstly, an extensive literature search was conducted (see *Annex 2* for the search terms) with an attempt to filter relevant literature from a gender perspective. Secondly, quantitative data was extracted from the Global Burden of Disease (GBD) / Institute for Health Metrics and Evaluation (IHME) database[19] on the 23 diseases and further data extracted from the WHO[20] and G-Finder[21] websites. Relevant information from this data collection process was thereafter consolidated and integrated into the report as appropriate. Regional data has been classified according to the WHO regions and diseases with a variation between females and males of more than 20 percentage points were highlighted in the text. Thirdly, semi-structured in-depth interviews were carried out with key stakeholders. In total, 15 interviews were conducted with representatives of the following organisations (in alphabetical order), as well as key experts *(see a list of interviewed organisations in Annex 3)*. A qualitative analysis of the interviews was carried out with the help of code-and-retrieve software and has been used to substantiate the specific literature. Key stakeholders were identified through a snowball technique. Both literature review and interviews contributed to identifying case studies. All interviews were carried out remotely via different video platforms.

## What are the limitations of this study?

This study has attempted to consolidate and create a knowledge base on existing literature in regard to PRNDs, gender, and R&D needs. Even though a comprehensive literature search was conducted, restrictions had to be introduced for the search terms. In addition, diseases are not covered on an equal footing, partly because gender-specific literature was not available or not accessible for all diseases. Data on yaws and mycetoma were not available in the GBD Database for the year 2017; thus, reference is made only through the available literature. Despite these limitations, an attempt was undertaken to triangulate the information through the different interviews and the existing literature[22].

The GBD database has been criticised for various reasons, one of them being that the source data and modelling assumptions may not provide sufficient comparability[23] but also that data disaggregation is limited to the binary divide between males and females, or that source data excludes women as their disease may not be registered. The limited data and literature available on PRNDs and different sexual orientations, gender identities or sex characteristics have made it in many areas impossible to extend the analysis beyond differentiation of males and females. Much of this study therefore focuses more specifically on women and girls instead of applying a broader gender lens.

Photo: National Cancer Institute on Unsplash

# 2 GLOBAL BURDEN OF PRNDS BASED ON GENDER AND SEX-BASED DIFFERENCES

**PRNDs impact in particular on discriminated groups** that more easily find themselves in vulnerable situations, such as women and girls, LGBTIQ+, transient or minority populations, due to their different social, cultural, and economic realities, such as lack of access to education, land ownership, political power[24]. However, biological (sex-related) susceptibility is also an important influencing factor[25]. Out of these groups, this chapter hereafter mainly focuses on women and girls due to the above-mentioned limitations in data and literature availability.

PRNDS PARTICULARLY IMPACT **DISCRIMATED GROUPS**, SUCH AS WOMEN AND GIRLS

Different factors together exacerbate gender inequalities that limit women and girls' lives, opportunities, and development[26]. **The effects of PRNDs are felt by all affected individuals on multiple levels, but studies suggest that women are particularly affected** not only on physical, reproductive, sexual, and economic levels, but also on social and emotional levels[26,27]. For example, exclusion and social stigma are particularly associated with some of the diseases, such as Buruli ulcer, (cutaneous) leishmaniasis, lymphatic filariasis (LF), onchocerciasis, and trachoma and bear a much higher toll on females than males[28]. The differential impact of PRNDs is felt at the household level as women and girls may not be able to fulfil prescribed caretaking roles and men may be less able to fulfil prescribed income-earning roles[29]. These dynamics within the household, existing gender norms, and power relations consequently impact on the health seeking behaviour of women and men[30,31].

THERE IS AN IMPORTANT DIFFERENCE BETWEEN PRND **'PREVALENCE' AND 'IMPACT'**

The global burden of PRNDs on women and girls has to be considered against this background, bearing in mind the potential limitation of the GBD Database in regard to source data and implications for women and girls on prevention, treatment, and post-treatment. Considering these different factors, **it is pertinent to distinguish between PRND 'prevalence' and 'impact' and consider both when assessing PRNDs through a gender lens.** Looking at prevalence (proportion of people infected at a given time) alone would fail to paint a full picture of the burden of PRNDs on women and girls. This is an important first finding which is taken into account in the following chapters, which also consider 'impact' (e.g., in terms of direct affect on males and females in regard to wider health consequences, availability of healthcare, stigma and discrimination, financial and social consequences) and for the development of recommendations. Faramand et al. (2019) have conducted an extensive desk review on gender issues affecting NTDs and *Table 1* highlights some of their findings in regard to risk of infection and impact of diseases on women concerning LF, trachoma, onchocerciasis, soil-transmitted helminths (STH), and schistosomiasis (SCH).

Photo: Andrew Loxley, courtesy of IPM

**TABLE 1** OVERVIEW OF SELECTED NTDS, THEIR CAUSE, SYMPTOMS AND INTERSECTION WITH GENDER AND SEX

| Disease | Cause | Symptoms | NTD intersection with gender and sex | |
|---|---|---|---|---|
| | | | With risk infection | With impact of disease |
| LF | Parasitic worms transmitted by mosquitos | Damage to the lymphatic system, resulting in swelling of arms, legs, or genitals | Preventive treatments are not safe for pregnant women. Men and boys are at greater risk in many countries. | Disfigurement and disability can impact employability and marriageability of men and women differently. Hydrocele in males. Men may not seek treatment due to perception of masculinity. |
| Tracho-ma | Bacteria spread by people and houseflies; exa-cerbated by poor hygiene | Eyelid turns inward; can lead to visual impairment or irreversible blindness | Child-care and caregiving increase female risk. Preventive treatment safe for pregnant females, but often not offered. | Women are four times as likely to need eye surgery. Woman account for 86% of trichiasis cases. |
| OV | Filarial worm, transmitted by black fly bites | Visual impairment, i.e. permanent blindness; intense itching and skin disfigurement | 2/3 of water-based domestic activities are completed by females, increasing risk. Preventive treatments not safe for pregnant women. | Disfigurement and disability can impact employability and marriageability of both men and women in different ways. |
| STH | Egg ingestion from contaminated soil, poor hygiene, or skin penetration by lavae in soil | Aggravate mal-nutrition, amplify rates of anemia, and lead to cognitive impairment | Men or women working in agriculture. Gendered cultural norms, such as open defecation. Out of school children may not access deworming campaings. | Severe hookworm-related anemia in pregnant women. Low birth weight babies and/ or premature birth. Infertility (caused by hookworm) for females. |
| SCH | Parasitic larva in water | Leads to chronic ill health (e.g. damage of the bladder and urinary tract) | 2/3 of water-based domestic activities are completed by females. Exacerbates disease during pregnancy. Men's and boy's work can increase risk. | Female Genital SCH causes reproductive organ damage, infertility, and increased risk of HIV. Increased females' risk for anemia. |

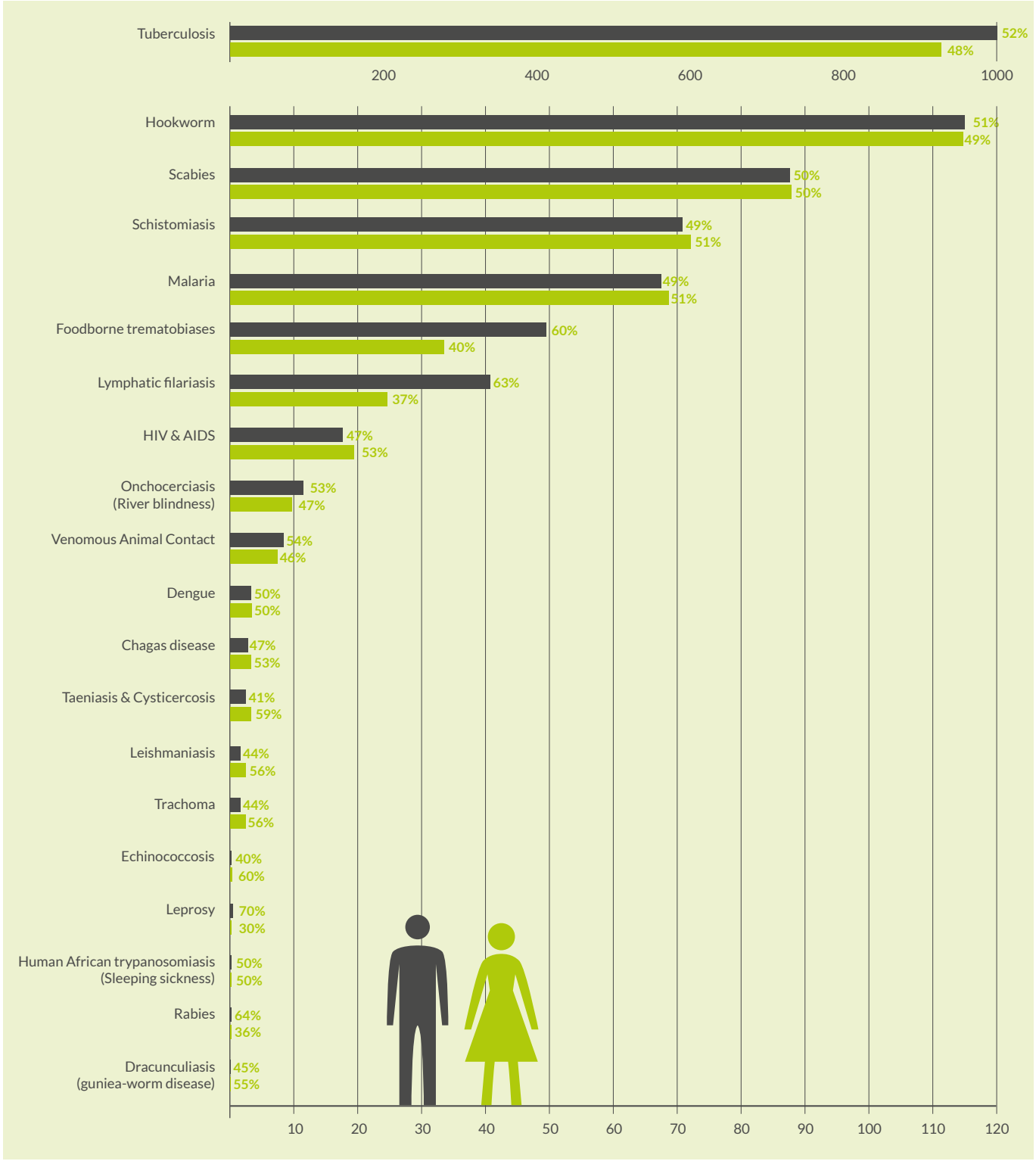
Source: Faramand T.H, Dale K. et al. (2019)[32:11], design adapted for this report

## Global and regional PRND prevalence

When considering the global prevalence rates, and without taking into consideration missing data, the disease with the highest prevalence by far is TB, with males being more affected than females, followed by hookworm disease, scabies, SCH, and malaria with only up to two percentage point difference in the global prevalence rates between females and males *(see Graph 1)*. In the context of TB, the health-seeking behaviour of women has been studied in different contexts [33-36]. Even if in theory women can often access health care similarly as men, in practice the availability of healthcare facilities, knowledge and awareness of the disease, socio-economic and cultural factors [37], and stigma associated with the disease[38] influence health-seeking behaviour and can therefore negatively impact detection and notification of TB in females [39-41].

**TB IS THE MOST PREVALENT PRND GLOBALLY**, MALES ARE MORE AFFECTED THAN FEMALES

**GRAPH 1** GLOBAL PREVALENCE OF PRNDS

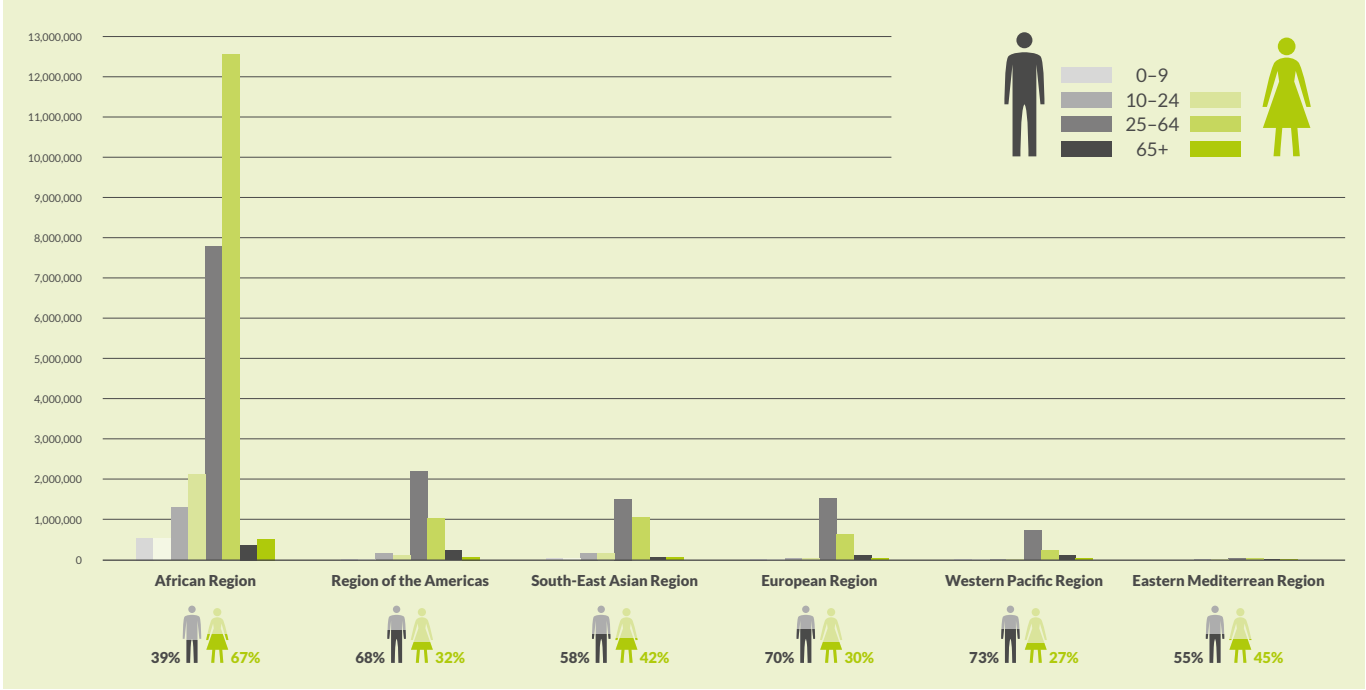



Source of data: Global Health Data Exchange (GHDx) 2017

The overall **global prevalence of PRNDs may not always correspond to the regional prevalence** rates as evident in the example of HIV. The global prevalence of HIV shows a prevalence rate of 53% among females vs. 47% among males. If data is disaggregated regionally, the prevalence rates paint a significantly different picture *(see Graph 2)*. Prevalence generally is highest in Africa, but also the prevalence of HIV in females (61%) is much higher than in males. All other regions not only have lower prevalence in general but also the prevalence in males is higher than that of females, with the Americas, Europe, and the western Pacific regions having a difference of 40 – 45 percentage points.

HIV PREVALENCE IS HIGHEST IN AFRICA, WITH A **HIGHER PREVALENCE IN FEMALES**

**GRAPH 2** REGIONAL PREVALENCE OF HIV

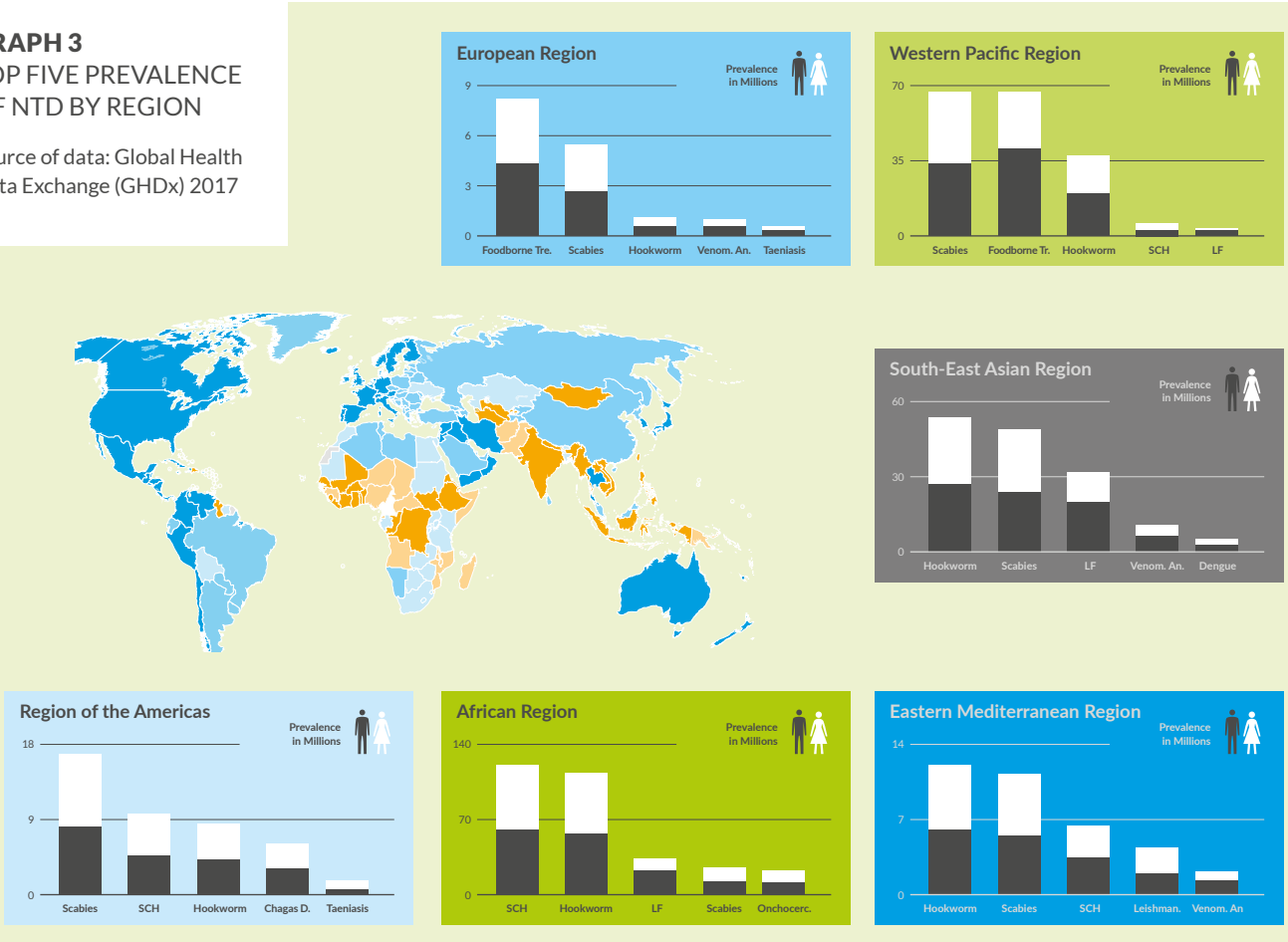



Source of data: Global Health Data Exchange (GHDx) 2017

A comparison of the regional prevalence rates of NTDs (without HIV, TB, Malaria) show that in five regions of the world (except Europe) **hookworm, scabies, and SCH are among the top five ranked NTDs** *(see Graph 3)*. In Europe and the western Pacific, both foodborne trematodiases and scabies are the two most prevalent diseases, whereas in South-East Asia and the eastern Mediterranean, hookworm and scabies are most prevalent. In the African region, SCH is ranked first followed by the hookworm disease and in the Americas, scabies has the highest prevalence followed by SCH.

**GRAPH 3**
TOP FIVE PREVALENCE OF NTD BY REGION

Source of data: Global Health Data Exchange (GHDx) 2017



CHAGAS DISEASE
GUINEA-WORM DISEASE
ECHINOCOCCOSIS
LEISHMANIASIS
RIVER BLINDNESS
SCHISTOSOMIASIS
TAENIASIS & CYSTICERCOSIS
TRACHOMA
HIV & AIDS

**disproportionately affect women and girls**

## Diseases that disproportionately affect women and girls

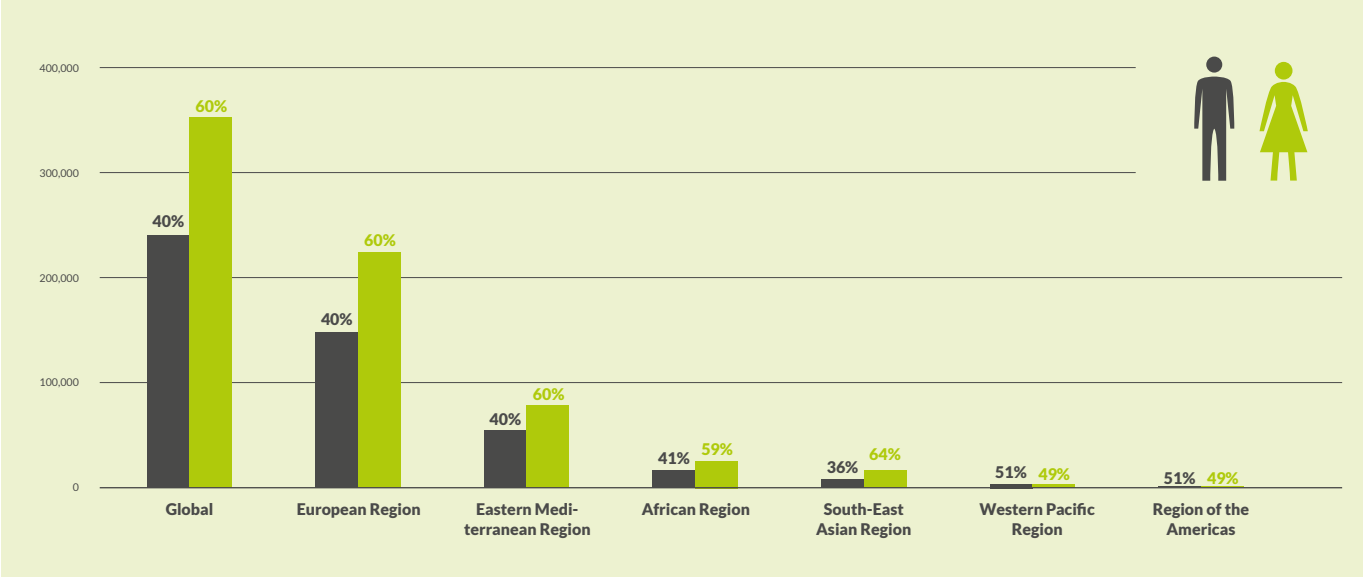
**Chagas disease, dracunculiasis (Guinea-worm disease), echinococcosis, leishmaniasis, onchocerciasis (river blindness), SCH, taeniasis & cysticercosis, trachoma, and HIV & AIDS are the nine diseases with a higher global prevalence among females** than males. *Graph 3* illustrates the prevalence rates among males and females across regions with little striking difference among the top five NTDs per region. It is thus of greater importance to consider the gendered impact of these diseases.

**Schistosomiasis takes a heavy toll on females** as it promotes horizontal transmission of HIV & AIDS[42] and is also interlinked with cervical cancer[43]. In addition, 40 million women of childbearing age suffer from female genital SCH and having the disease during pregnancy is yet another concern, especially in regard to anaemia, miscarriage, preterm labour, and in regards to the ability to become pregnant. Exact numbers of pregnant and breastfeeding women affected by SCH, however, are missing[26].

Similar to SCH, **echinococcosis is a zoonotic disease (tapeworm infections) that has a disproportionately high prevalence rate among females**, globally and in most regions of the world (except the Americas and western Pacific). The highest prevalence is in the European region followed by the eastern Mediterranean region, in both cases with a prevalence rate that is 20 percentage points higher among females than males *(see Graph 4)*.

**GRAPH 4** GLOBAL AND REGIONAL PREVALENCE OF ECHINOCOCCOSIS

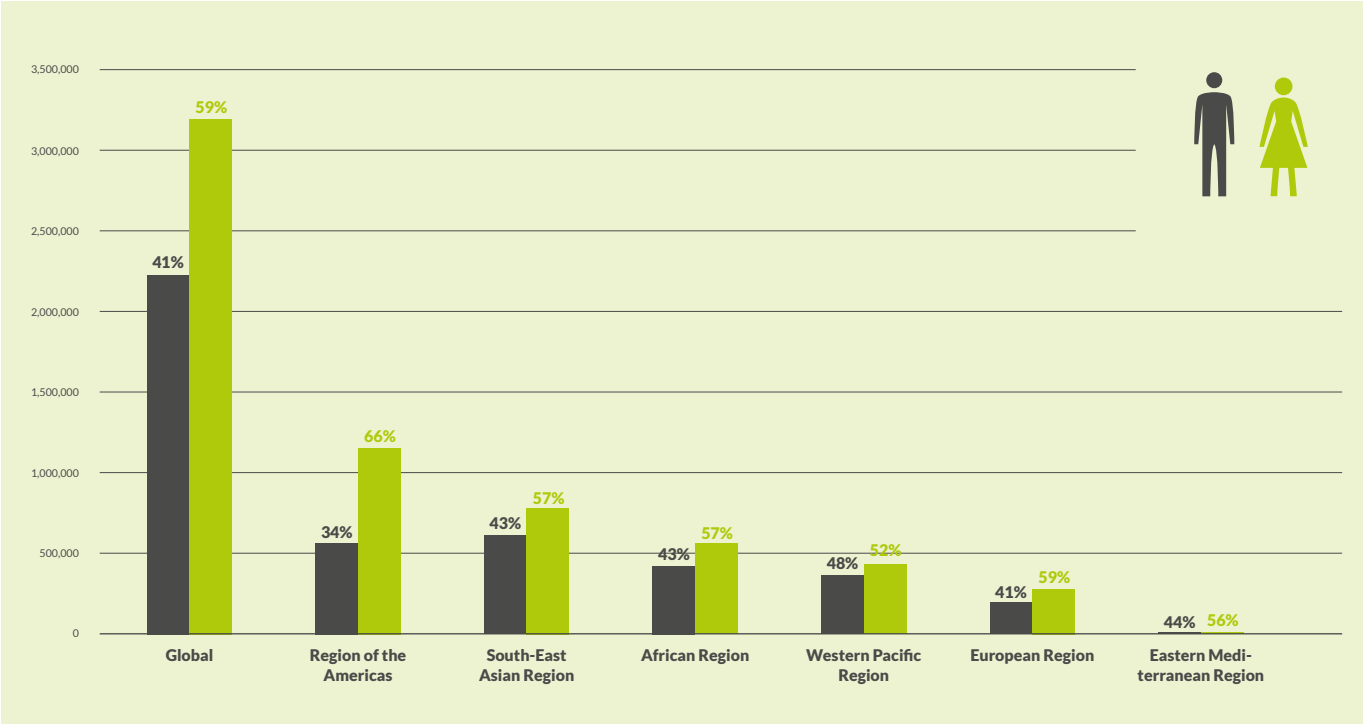
Source of data: Global Health Data Exchange (GHDx) 2017




Studies on echinococcosis are few, and if available mostly focus on countries in the Middle East[44–46] a few in Europe[47]. Sex-disaggregated data is generally very limited. The **higher prevalence rates in females are – if mentioned – directly related to gender roles in the household** in predominantly rural settings. Women and girls more often take care of the dogs or other animals (whose faeces can be contaminated with tapeworm eggs), undertake the gardening, and prepare the food, all of which enhance the likelihood of transmission of this zoonotic tapeworm[45, 46, 48]. As symptoms are developed on average over a period of ten years, medical care rates are usually much lower, also influenced by the (un-)availability of financial resources to pay for the treatment[48].

The prevalence rate of taeniasis (another tapeworm infection) is similar to echinococcosis, thus higher among females than males around the globe. In the Americas, the most endemic region, **the burden of taeniasis in females is 32 percentage points higher than in males.** South-East Asia and Africa also remain considerably affected regions *(see Graph 5)*. Transmission takes place through the tapeworm eggs, linked to rearing livestock, especially pigs, and is exacerbated by a lack of hygiene and sanitary measures[49, 50]. The reviewed literature[50–52] does not provide information on the gendered nature of the disease but similarities to echinococcosis exist in as far as gender roles in the household are likely to play a crucial role and may provide some explanation for the disease burden in females.

**GRAPH 5** GLOBAL AND REGIONAL PREVALENCE OF TAENIASIS & CYSTICERCOSIS




Source of data: Global Health Data Exchange (GHDx) 2017

(Cutaneous) Leishmaniasis has a top five ranked prevalence rate in the eastern Mediterranean region, which is also reflected in the available literature (e.g. Yemen [53], Tunisia [54], Iraq [55]). Common to the different studies across regions – independent of the prevalence rates – is the higher disease burden in women due to reduced health care access [56] and the socio-aesthetic impact of the cutaneous form of the disease, resulting in increased professional exclusion and social isolation, even within the family [53, 57].

**Trachoma, Guinea-worm, and Chagas disease all have a global prevalence rate between 12 and 16 percentage points higher among females** than males *(see Table 2)*, yet, the consequences of these diseases may go beyond what figures portray.

**TABLE 2** GLOBAL PREVALENCE OF TRACHOMA, GUINEA-WORM, AND CHAGAS DISEASE

| | |
|---|---|
| **Trachoma** | 56% 44% |
| **Guinea-worm disease** | 55% 45% |
| **Chagas disease** | 53% 47% |

Source of data: Global Health Data Exchange (GHDx) 2017

The **risk factors for developing trachoma are embedded in women and girls' ascribed household-related gender roles**, such as the responsibility for water collection and household sanitation [58], as well as for childcare [59-62]. In endemic countries, trichiasis might be prevalent in girls between one to nine years already [61, 63] and may then lead to higher prevalence rates of trachoma at an adult age [64]. Blindness as an effect of trachoma, however, means more than just not being able to see, it also affects women's ability to care for children, to earn an income, and to get married [26]. The reduced ability to look after their children is also one of the described consequences of Guinea-worm disease [65], a disease that also impacts negatively on married life and the ability to work in agriculture or generate an income [66, 67].

Even though Chagas disease has a higher overall global prevalence in females, the picture is more differentiated across age groups. Young males and females have an equal prevalence rate but the prevalence rate in females between 40 – 60 years of age is higher, reflecting the higher mortality rate of males. **Men suffer from higher morbidity from Chagas disease**, reflected in a more frequent evolution of a chronic form, resulting in higher mortality. Even though the chronic form of the disease is much milder in women, the higher morbidity and mortality rates in men place women under physical, psychological, and financial stress [68].

## Diseases with similar prevalence rates between women and men

HOOKWORM
DENGUE
MALARIA
SCABIES
SLEEPING SICKNESS

**have similar prevalence in females and males**

Some diseases, namely hookworm, dengue, malaria, scabies, and sleeping sickness have balanced global prevalence rates and do not show significant variations at first sight between females and males. Nevertheless, some of them do have considerable gendered impact: hookworm morbidity is higher among females as they need more iron than males and thus, are predisposed to iron deficiency anaemia caused by hookworm. For women of reproductive age, especially pregnant and breastfeeding women, this can be aggravated and cause stillbirth, miscarriage, or infertility [27, 67].

Globally, the prevalence rate of malaria is balanced between females and males, sometimes with a slightly higher prevalence among males due to their increased exposure to the transmitting mosquitoes. However, malaria can pose a gendered burden on mothers and wives as they need to look after the sick children or husband. Women also commonly postpone their own treatment in order to give priority to other sick family members or to care for them despite sickness. In addition, females' immune reaction can weaken during pregnancy, leaving them to contract malaria more easily.[68]

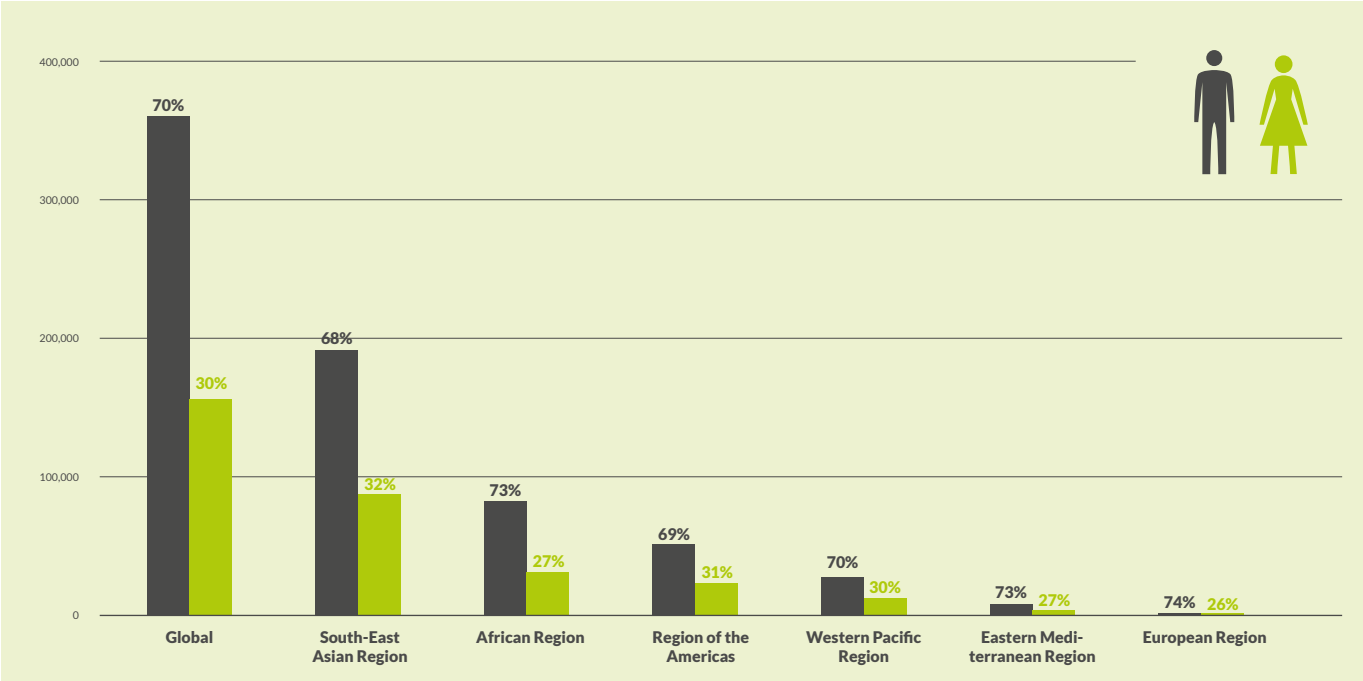
## Diseases that disproportionately affect men

LEPROSY
LYMPHATIC FILARIASIS
RABIES

**show higher prevalence in males**

Traditional male occupational roles, for example in agriculture or in fishing, expose them to some diseases with higher risk [29]. Among the 23 diseases, there are three which show a much higher prevalence among males than females, namely leprosy, LF, and rabies. Even though males have higher prevalence rates in these diseases [69], the gendered impact on females can be quite significant. The global prevalence rate of leprosy is for males 40 percentage points higher than for females and these higher rates are seen across all regions of the world *(see Graph 6)*.

**GRAPH 6** GLOBAL AND REGIONAL PREVALENCE OF LEPROSY

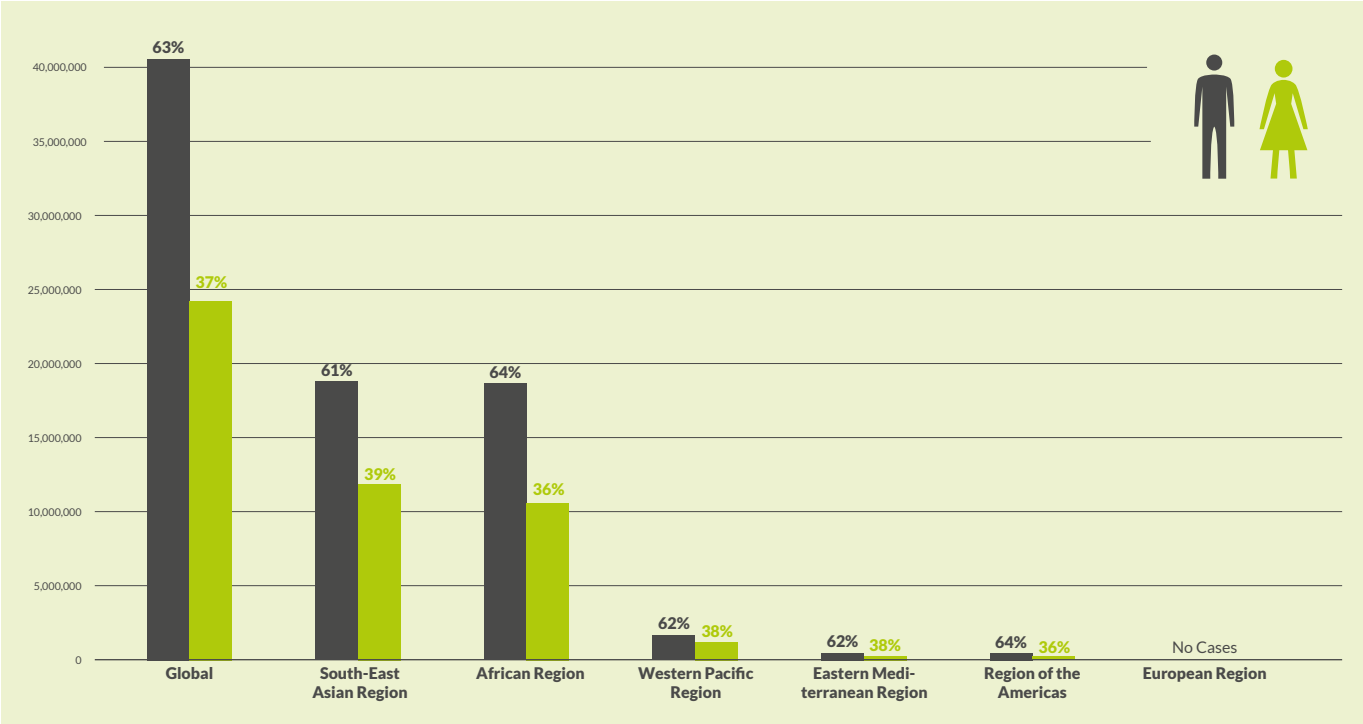



Source of data: Global Health Data Exchange (GHDx) 2017

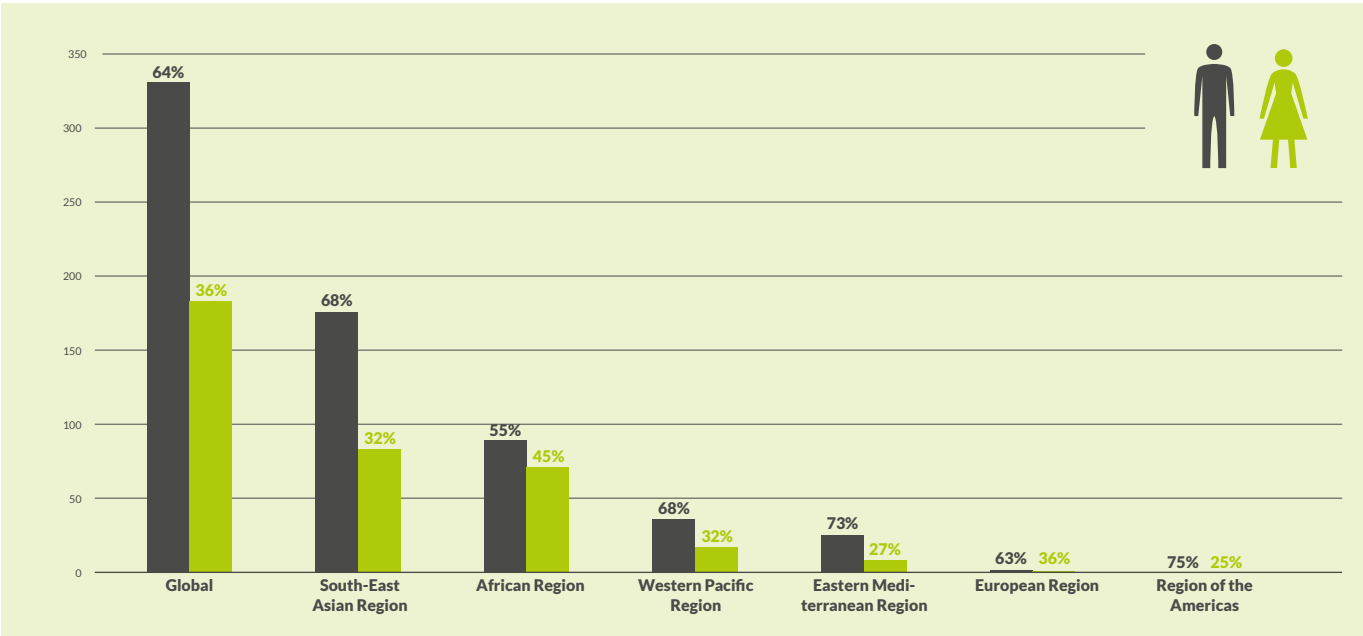
**South-East Asia has the highest regional prevalence of leprosy with 68% in males and 32% in females**, followed by the African region with 73% in males and 27% in females. In both regions, the difference between male and female prevalence rates amounts to 46 percentage points. The stigma and isolation associated with leprosy are felt both by males and females, but a number of studies and systematic reviews have highlighted the more severe impact on females[70-78]. In addition, Varkevisser et al.[74] in case studies from Nepal, Indonesia, Brazil, and Nigeria pointed out that females with the disease are underreported because of their low status, limited mobility, and poor educational levels.

LF is among the top five ranked NTDs in the western Pacific, in South-East Asia, and the African region and results in social stigma and isolation that can go as far as losing jobs and wages, or being abandoned by family[79]. LF has a higher prevalence rate among males *(see Graph 7)* but the social impact is felt by both males and females. **Men may experience the disease as a 'silent burden'[80], whereas women may face a double burden** as their role and identity in society depend upon marriage and the associated ability to bear children[81]. If unmarried young women develop the disease, they may not be able to continue any education and are unable to marry and with this, enter into a spiral of distress, anxiety, shame, and exclusion[82].

**GRAPH 7** GLOBAL AND REGIONAL PREVALENCE OF LF




**GRAPH 8** GLOBAL AND REGIONAL PREVALENCE OF RABIES

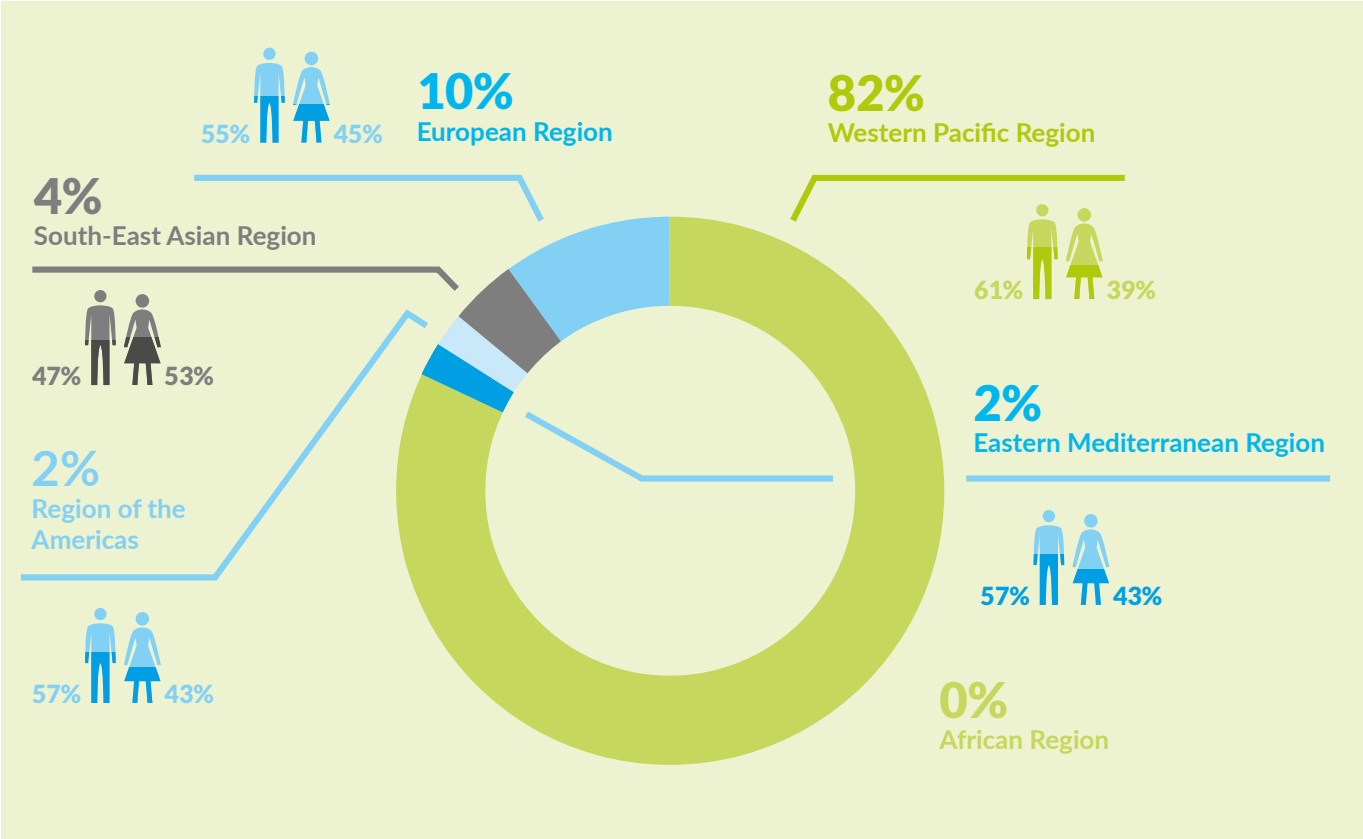



Source of data (GRAPH 8 ,9) : Global Health Data Exchange (GHDx) 2017

**Rabies is a zoonotic disease that disproportionately affects males** with a global prevalence rate of 64% in males vs. 36% in females. South-East Asia has the highest burden followed by the African region. All regions except Africa have a 45 to 50 percentage point difference in the prevalence between males and females. Africa has the lowest male – female gap with only ten percentage points *(see Graph 8)*. A number of Knowledge, Attitude and Practices (KAP) surveys [83-86] exist, which do not have an explicit gender focus but mention the differences between males and females with males usually having more awareness about the disease than females.

A number of other diseases do not have variations beyond 20 percentage points and thus, are not specifically investigated, even if **stark regional differences exist, such as in the case of foodborne trematodiases** *(see Graph 9)*. The African region has no recorded cases, whereas the western Pacific Region has a prevalence rate of 82% with 61% in males and 39% in females.

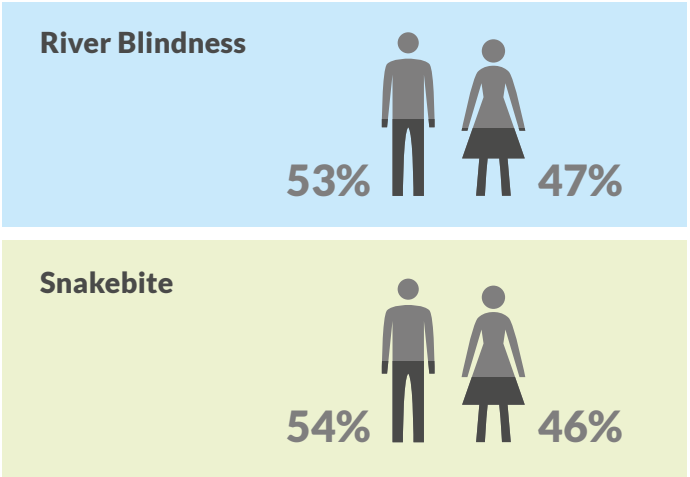
**GRAPH 9** REGIONAL PREVALENCE OF FOODBORNE TREMATODIASES




Source of data: Global Health Data Exchange (GHDx) 2017

**Onchocerciasis (River Blindness) and snakebite** have both a slightly higher global prevalence rate in males *(see Table 2)*. The GBD database does not provide any data on Buruli ulcer, a skin infection, which places a social and economic burden on the affected person and the family as a whole[87].

**TABLE 3** GLOBAL PREVALENCE OF RIVER BLINDNESS AND SNAKEBITE




Source of data: Global Health Data Exchange (GHDx) 2017

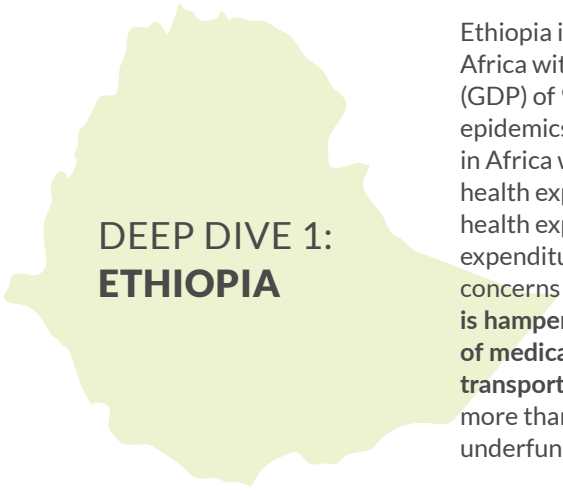
## How do (certain) PRNDs affect LGBTIQ + individuals?

Research into PRNDs and sex/ gender is limited and - if conducted and depending on the disease – very often focusses on the consequences of a disease on women. **Where data is disaggregated, it mostly distinguishes between males and females without taking into account people with non-binary sex characteristics, gender identity and expression, or sexual orientations. The wider gender impact of PRNDs is therefore much less examined**[31]. In the literature search conducted for this report, studies concerned mainly HIV & AIDS and the North American context (with few exceptions, e.g. Fearon[88], Silva-Santisteban[89], Pal[90]). The thematic focus across all of these studies, however, varies.

**Among others, existing studies investigate:**

- **the HIV and sexually transmitted diseases (STDs) risk among LGBTIQ+ individuals in abusive relationships**[91]**, as well as among male to female transgender individuals**[92]**;**
- **testing and care behavior, for example of HIV-negative men who have sex with men (MSM) and transgender individuals (TG) in South Africa**[88] **or of MSM, transgender women and female entertainment workers in Cambodia**[90]**;**
- **the epidemiology of HIV and TB (among others) of transgender individuals in prisons**[93]**;**
- **the access/ barriers to care for transgender and gender non-confirming adults (GNC)**[94]**, as well as access to treatment for MSM**[95]**;**
- **the project funded by the National Institute of Health (NIH) to address the needs of LGBTIQ+ populations**[96]**;**
- **the Sexual Orientation and Gender Identities Strategy of the Global Fund to Fight AIDS, Tuberculosis and Malaria to meet the needs of the LGBTIQ+ community**[97]**;**
- **the prevention of HIV among transgender women in Latin America**[89]**.**

One study addressed knowledge, attitudes, and practices among transgender people in Sao Paolo in Brazil and concludes that health educational activities insufficiently reach the transgender population[98]. The conclusions of the research studies in HIV and LGBTIQ+ individuals are similarly grim, in so far as **LGBTIQ+ individuals face either disadvantaged access, lack knowledge, or face more stigma, discrimination and violence**, and most of them call for more research, collaboration or better programming to address their needs. This is also coherent with the United Nations Development Programme (UNDP) Discussion Paper that states that "[h]ealth outcomes for transgender people are generally poorer than for cisgender (i.e. not transgender) men and women'[31:3] and further notes that 'sex- and gender-disaggregated data are often collected for binary, mutually-exclusive categories only, leaving out important insights about the health of transgender and intersex people"[31:16]. The present study and literature confirm this observation. In addition, the GBD database does not provide data along those lines. The collection of valid, reliable, and accurate data on different gender identities and sexual orientations may not only be very difficult but also dangerous in some contexts.



### DEEP DIVE 1: **ETHIOPIA**

Ethiopia is a landlocked country in eastern Africa, positioned in the Horn of Africa with more than 110 million inhabitants and a gross domestic product (GDP) of 96 billion USD[99]. The country is regularly hit by crises, such as droughts, epidemics, displacements, and armed conflict[100]. It is one of the poorest countries in Africa with 8% of its population living in multidimensional poverty[101]. The health expenditure per capita is at 3.5% of the GDP and the general government health expenditure per capita amounts to 0.87% of the GDP. 34% of the health expenditure is paid out-of-pocket and 53% of the current health expenditure concerns domestic private health expenditure[99]. **The access to health services is hampered by a limited number of health institutions, inefficient distribution of medical supplies, disparities between urban and rural areas and poor transportation infrastructure** with more than half of the population living more than ten km away from the nearest health facility, as well as by general underfunding of the health sector[100].

## The 'big three'

**Malaria, TB and HIV & AIDS, together with maternal mortality, acute malnutrition, and lack of access to clean water and sanitation are the main health concerns**. Even though Ethiopia is considered a low-to-moderate transmission intensity country for malaria, climate change impacts on the transmission cycle of vector-borne infectious diseases [102]. According to the GBD database, **malaria is almost equally common in males (51% prevalence) and in females (49% prevalence)**, nevertheless, it is particularly serious for pregnant women and can lead to death.

MALARIA, TB, AND HIV & AIDS ARE AMONG THE MAIN HEALTH CONCERNS IN ETHIOPIA

In regard to TB, Ethiopia is one of the 22 high burden countries [102, 103] and has similar prevalence rates among males (51%) and females (49%) as in malaria. The disease remains one of the leading causes of mortality with a rate of 64% in males and 36% for females [19]. **TB detection rates among males are higher than in females** [102], which suggests that decentralised diagnostic and treatment services need to be enhanced in order for females to access these services [104]. In addition, 13% of all new TB cases are HIV coinfected [102], bringing along stigma and mental health problems for both women and men [104]. In addition, the country has a high level of multidrug resistant (MDR) TB. According to a national TB resistance surveillance report, 2.3% of new TB cases and 17.8% of previously treated TB cases were estimated to have MDR-TB [102], requiring expensive and more toxic drugs [105].

HIV & AIDS **PREVALENCE IN ETHIOPIA IS 60% IN FEMALES** AND 40% IN MALES

As in many African countries, **the prevalence of HIV & AIDS in Ethiopia is 60% in females and 40% in males.** Even though awareness about the disease has increased within the country, married women especially still remain disproportionately susceptible to HIV infection. Even though marriage was believed to be a protective factor against HIV, this does not seem to be the reality [106]. HIV & AIDS awareness and the ability to negotiate safer sex is associated with higher education and higher socioeconomic status [106]. Co-infection with TB is more likely to occur among the poor, less-educated population, suggesting that further efforts are needed to reach out to this strata of society, and in particular to women and girls [107].

## NTDs in Ethiopia

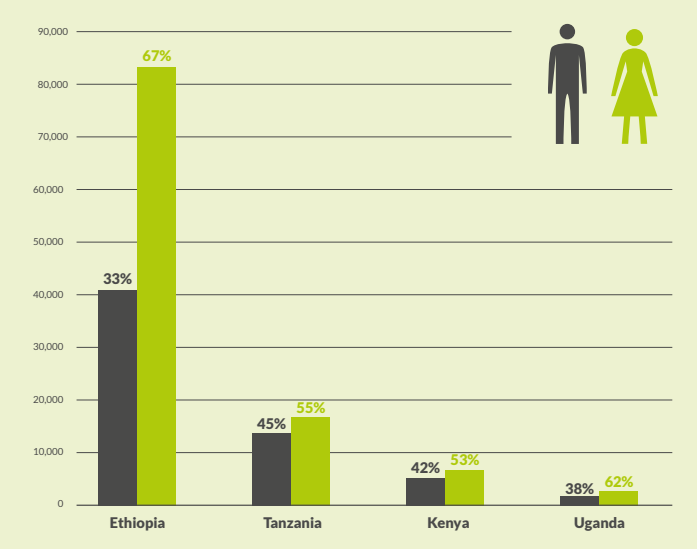
Ethiopia bears a significant burden of NTDs in Africa [102]. Hookworm, schistosomiasis, scabies, river blindness, snakebite, and trachoma are the top six NTDs prevalent in the country. The below *table 4* shows the overall prevalence rates among males and females in the country *(see Table 4)*.

**TABLE 4** SIX MOST PREVALENT NTDS IN ETHIOPIA

| | Polulation Affected | Female Prevalence | Male Prevalence |
|---|---|---|---|
| **Hookworm** | 23.9 mio | 49% | 51% |
| **SCH** | 20.6 mio | 50% | 50% |
| **Scabies** | 3.40 mio | 51% | 49% |
| **River Blindness** | 0.58 mio | 45% | 55% |
| **Snakebite** | 0.16 mio | 51% | 49% |
| **Trachoma** | 0.12 mio | 67% | 33% |

Source of data: Global Health Data Exchange (GHDx) 2017

**GRAPH 10** PREVALENCE OF TRACHOMA IN EAST AFRICA




Source of data: Global Health Data Exchange (GHDx) 2017

This disproportionally **high prevalence in females can be explained through their roles in caring for infected children** through whom they themselves get infected. The high prevalence among children between age 1 and 9 is often associated with risk factors including access to water and latrine facilities [63]. Females' greater exposure and less access to treatment and care results in them being two to three times more likely to become permanently blinded by the disease than males [26,60]. Similarly to what was outlined earlier, the impact of blindness on social, economic, and family life is often felt more strongly by females.

In addition, a recent qualitative study on the gender-related factors affecting health-seeking behavior for NTDs [109] highlights that **women may delay care seeking or may not seek care at all because of reservations about disclosing diseases affecting 'hidden' ('private') body parts** as in the case of schistosomiasis. Men may also delay seeking care if they are affected by hydrocele, scrotal swelling as in the case of lymphatic filariasis. This confirms the complex and multi-layered impact of NTDs and the need to adopt a differentiated gendered approach to NTDs.

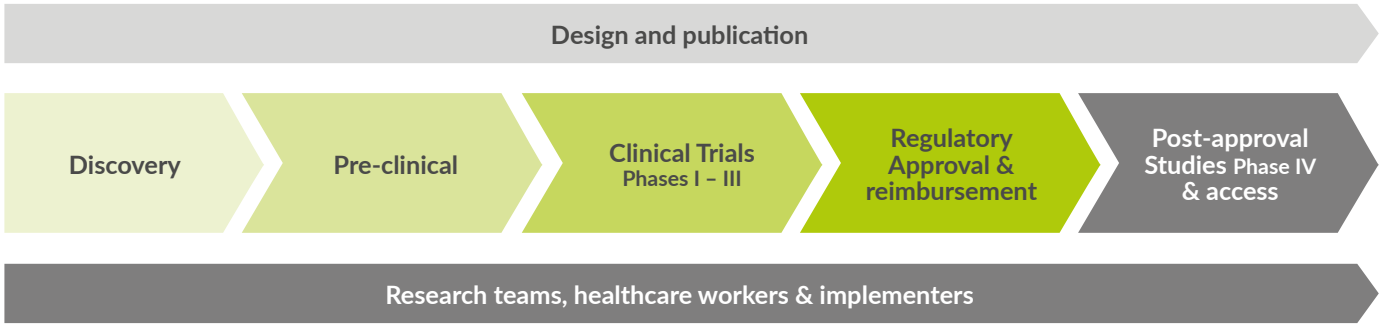
# 3 PRND RESEARCH AND INNOVATION NEEDS TO ENSURE GENDER EQUITY IN HEALTH

In the midst of COVID-19, R&I needs for diagnostics, treatments, and vaccines receive unprecedented attention globally. However, often overlooked, and more so in times of a global pandemic, the **differences in biological susceptibility**[25] **as well as the broader gender dimensions in R&I have significant impacts on health outcomes**, with an increasingly robust evidence base. The biological differences between women and men, or people with non-binary sex-characteristics, are simply not considered in clinical research, and **a number of 'blind spots', 'knowledge gaps'**[110] **and even 'knowledge biases' exist**. Nevertheless, diseases may have a differential impact on different genders, and treatment efficacy, for example, could benefit from capturing differences at biological and social levels. The lack of gender specificity begins at the earliest research stages and sometimes persists throughout the entire R&I process[111]. This chapter provides an overview of the ongoing debates on sex and gender aspects within the R&I process and identifies the resulting PRND R&I needs that ought to be tackled to contribute to greater gender equity in health. Even though diagnostics, drugs, and vaccines require distinct R&I processes, for the purpose of this study a generalised view will be provided, and illustrative examples will highlight the gendered dimensions of the R&I process.

THERE ARE A NUMBER OF 'BLIND SPOTS', 'KNOWLEDGE GAPS', AND EVEN **'KNOWLEDGE BIASES' IN CLINICAL RESEARCH**

*Figure 1* illustrates in generic terms the R&I pipeline, alongside a number of identified needs, challenges, and dilemmas. This illustration differs from other commonly used pipeline representations as it integrates the crosscutting and integral activities of research design and publication, carried out throughout the R&I process. It also recognises that research teams, health workers, and implementers collaborate throughout the process.

**FIGURE 1** RESEARCH & INNOVATION PROCESS




Source: Adapted from TDR (2016)[112] by Told & Landry Chappuis, HumanImpact5 HI5.

While knowledge of gender specific R&I needs and gaps exists in different institutions and organisations working in this field, **a holistic view on gender mainstreaming and gender analysis throughout the entire R&I cycle is still missing.** Research and publications addressing sex and gender in an integrated continuum across the R&I cycle are scant. The existing literature focuses mainly on the following distinct areas: data disaggregation, pregnant and breastfeeding women, diagnostics and screening, clinical trials in humans, regulatory approval processes, and access and delivery. The vast majority of publications specifically address the challenges in conducting clinical trials in pregnant and breastfeeding women, and the issues of access and delivery.

## Design and publication/ research teams, health care workers & implementers

CLARITY ON THE CONSTRUCTION OF SEX AND GENDER IS A PREREQUISITE FOR THE DESIGN AND REPORTING OF HEALTH RESEARCH STUDIES

Health research attempts to address a wide range of factors that affect population health and clinical and biomedical research evaluates the safety and efficacy of medications (including drugs and vaccines), medical devices, diagnostic procedures, and treatment regimens for preventing, treating, diagnosing, monitoring, or alleviating symptoms of a disease[113]. Both sex and gender considerations are increasingly recognised as important factors influencing health inequities and related health outcomes. Conceptual clarity on the construction of sex and gender, as well as its multi-facetted intersections are important prerequisites for both the design and reporting of health research studies [114]. An increasing number of literature and specific training modules for health researchers provide clarity and guidance to increase and improve sex and gender considerations in research[115]. **An understanding of the disease or condition, its gender specific prevalence, and its gender specific impact is needed at an early stage** in order to meaningfully design and engage in research that incorporates sex and gender dimensions and hence has the potential to develop knowledge and tools that work – better - for everyone.

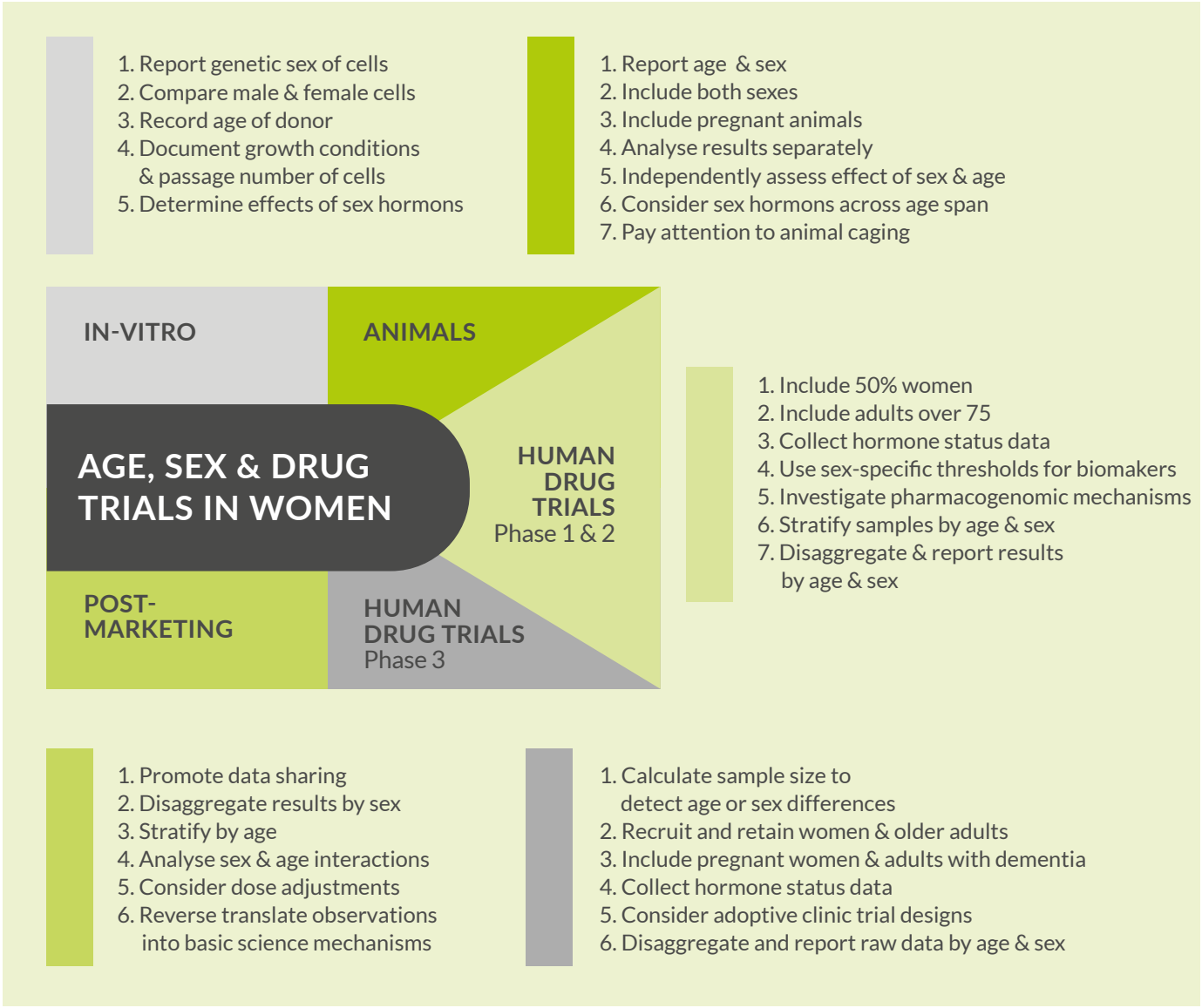
Research study design and knowledge translation activities carried out along the R&I continuum are inextricably linked. The sharing of research results through a sex and gender lens is only possible if sex and gender considerations are integrated into research projects from the very beginning in order to produce more accurate, rigorous, and valid results[116]. **The consistent uptake of sex and gender aspects across health research publications is, however, generally missing.** In order to address these 'blind spots', health research journals should incentivise the production and dissemination of sex-disaggregated health research evidence, for example through editorial policies that enforce disaggregated outcome reporting[114, 117].

Studies [117, 118] show that **women are underrepresented in positions of power, are less likely to lead a research team or be the head of a laboratory**, which then means that they are also less likely to appear as first author in high impact journals. The greater representation of women in leadership and decision-making within research teams is particularly important because they are more likely to consider and report sex-differentiated outcomes[117]. Key decisions made by the research teams but also implementers in the process are crucial – or detrimental - to sex- and gender-sensitive research[119]. Science that works for women, thus also means science that works with (e.g. is developed and led by) women.

Furthermore, publications that integrate recommendations for intersectional issues such as age and sex considerations along the full R&I process *(see Figure 2 from Tannenbaum and Day[120])* are far too rare. **Literature otherwise mainly focusses on a specific research phase or specific aspects within a research phase, thus lacking integral approaches.**

Photo: Jonathan Torgovnik/Getty Images/Images of Empowerment

**FIGURE 2** SEX AND AGE CONSIDERATIONS IN CLINICAL TRIALS




Source: Tannenbaum and Day (2017)[120], design adapted for this report

## Discovery

This phase of the process includes, for example for drug development, the target identification and screening of molecules to find one or more lead compounds that show activity against the pathogen eliciting the intended biochemical or physiological changes for which the research is conducted. This phase should include experiments on both genetically male and female cells in order to be able to identify early the sex differences [117, 120, 121]. Differences at the cellular level can lead to differences on how PRNDs and treatments affect women and men[111]. However, **up to 75% of the research articles do not report on the sex of the cells used. Where cell sex is specified, studies show that female cells account for only 5%** [122]. Inclusion of male and female cells to identify the sex differences at this early stage of research is needed and to compare, analyse and report data by sex for subsequent research stages[111, 120].

UP TO 75% OF RESEARCH ARTICLES DO NOT REPORT ON THE SEX OF CELLS USED IN STUDIES

## Pre-clinical stage




The pre-clinical stage involves laboratory and animal studies to evaluate efficacy and potential risks involved in the usage of the identified compounds: plans for clinical trials are also developed and applications to the regulatory authorities are prepared in this phase[117]. Sex and even gender play a role in animal research, and sex-gender interaction is significant in the specific context of this phase of research. For example, through the caging conditions and dynamics of male and female animals, or through the way the sex of research personnel interacts with hormonal, genetic, reproductive, and stress factors of the animals. Animal studies should include male and female study animals. However, **females are generally underrepresented, and a major gap exists in the reporting of the sex of the animals**[117, 123–125]. A survey conducted in 2000 found that 80% of animal studies had a male bias[126] and in 2016, 70% of the biomedical research did not report sex; among those studies reporting sex, less than half have included both sexes in the study sample[127]. This can result in gaps to examine the safety and efficacy of the therapeutic agents for women, ultimately leading to, for example, **unsafe dosage recommendations and adverse drug reactions in women** that originate from the insufficient attention given to the sex-specific pharmacokinetic variations during this phase[117].

## Clinical trials (phases I – III)

PHASE I CLINICAL STUDIES TEND TO BE SKEWED TOWARDS MEN




The different phases of this research stage concern trials on humans to identify the suitable dosage ranges, product efficacy, and side effects. Phase I usually concerns testing of the molecules in a small group of people, usually healthy human volunteers, in order to test the safety of a drug, for example, and to establish a maximum tolerated dose of a drug. **Studies at this stage are generally skewed towards men (approx. 67%)**[122]. Phase II entails trials with a patient pool of about 100 or more persons who carry the disease. It is focused on the safety and short-time side effects of the developed drug and on finding the optimal dosage[128]. The design of phase I and II trials is based on the evidence received from the pre-clinical stage. The data required before initiation of the trials and the inclusion of women are defined in the Guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) [129, 130]. This data concerns, for example, the reproductive toxicity and carcinogenicity but also safety considerations, yet are entirely dependent upon existing knowledge of the product, type, and indication[130]. The more robust the sex- and gender-differentiated knowledge database, both from pre-clinical data but also epidemiological data (e.g. disease prevalence in different sexes) and disease or condition impact data on different genders, the more reliable the clinical research will be. Phase III aims to confirm on a large-scale the efficacy and the safety of the drug and if successful, preparations are made for the approval of the drug with the regulatory authorities.

**While women are more likely to be included in phase III studies, they are still generally underrepresented in all the phases of clinical trialling**, despite recommendations, and in some cases regulations, to include sex and gender considerations in study design to ensure better outcomes, even at the early clinical study phases[131]. A meaningful inclusion of women, analysis of outcomes by sex, and reporting is yet to be fully achieved [117, 132]. More recent guidelines suggest that women should be represented in trials in proportion to the prevalence rate of the disease[133]. As outlined in the previous chapter, however, prevalence rates do not sufficiently capture the gendered impact of a disease, and thus its impact on women and girls.

REGULATORY AUTHORITIES PLAY AN IMPORTANT ROLE IN INCREASING INCLUSION OF WOMEN IN CLINICAL TRIALS

**Regulatory authorities have an essential role to play in increasing the inclusion of women, and people with non-binary sex characteristics in clinical trials.** For example, the NIH Revitalization Act recognises that women's exclusion from clinical trials has led to deficits in the understanding of women's health and sex-based differences[134]. The challenge remains that if no distinct, sex-disaggregated analysis is carried out, study conclusions could be either misleading or erroneous in regards to detecting sex and gender differences of pharmaceutical and non-pharmaceutical interventions[135]. Consequently, women's health care can be compromised due to lack of sex-specific information about drug dosage and unique use of drugs[136]. Adaptive design can be a useful tool to allow for making planned changes to the course of an ongoing trial on the basis of accumulated data from the trial itself. This could then lead to the adaptation or discontinuation of a drug dosage, for example[130]. Furthermore, the current bias in research can be addressed not only by reporting the sex of the animals, cells, or cell culture models used[135] in early research phases, but also by including women in all phases and by regular monitoring of the studies[136].

A recent publication by Couderc-Pétry et al. (2020)[130] proposes to **include women susceptible to and becoming pregnant (WoSuP) in NTD clinical trials** from an ethical and regulatory standpoint. The authors outline the following conditions so that such clinical trials can happen:

- Women receive "prior and complete information on potential risks and benefits of treatment for themselves, their unexpected but potential pregnancy, and resultant offspring and their fertility.
- Research is relevant to the healthcare needs of WoSuP; and
- Pre-clinical trials in animals have provided sufficient reliable results in regard to 'risks for reproductive toxicity and genotoxicity". [130:5]

**ETHICAL CONSIDERATIONS** ARE AN IMPORTANT COMPONENT WITHIN THE CLINICAL TRIAL STAGE

Finally, **ethical considerations are an important component within the clinical trial stage**[137]. Ample literature exists on clinical trials, ethics, and pregnant women *(see Deep Dive 2)* and less but still some on breastfeeding women. Excluding pregnant, breastfeeding, and menopausal women from trials may also slow down the recruitment rate and delay the availability of a helpful drug, for example, for these population groups[130]. Fair inclusion of pregnant women in clinical trials requires, on the one hand, that eligible pregnant women are not excluded from the trials only due to their pregnancy and, on the other hand, that research interests of pregnant women receive more attention. Depending on the research, this **could also necessitate oversampling of WoSuP, or promoting separate trials in pregnant women**[138]. This implies that there is an ethical aspect to including WoSuP and that they should be able to make informed decisions about participation in trials, aware of the potential risks. They should also have the liberty of withdrawing voluntarily from the trial at any time or to terminate pregnancy if legally allowed and wished so by the woman herself. This would nonetheless require a guaranteed medical follow up and the availability of contraceptives[130]. Contraceptives may not always be widely available, socially or culturally accepted, or even effective in preventing pregnancy, calling yet again for a differentiated understanding of the social, cultural, religious, and legal conditions.

While much of what is outlined above applies to any disease or condition, some specific PRND considerations are noteworthy. In addition, studies conducted in LMIC settings may need to give specific attention to the capacity for clinical data management and building of capacities at the local research sites[139].

There are also some disease-specific particularities, examples of which are listed in *table 5* and *Deep Dive 2* provides a more in-depth discussion on the link of clinical trials and pregnant women.

**TABLE 5** EXAMPLES OF DISEASE-SPECIFIC IMPACTS ON PREGNANT WOMEN

| | |
|---|---|
| **Malaria** | has a high prevalence among pregnant women and can pose a risk for both mother and foetus because females' immune reaction can weaken during pregnancy, increasing the risk of contracting malaria[130]. In addition, malaria may cause anaemia in pregnant women[140]. |
| **Chagas disease** | bears the risk of vertical transmission of the disease to the foetus[130], and certain drugs are contraindicated in at least the first trimester of pregnancy[130]. |
| **Hookworm** | may cause anaemia in pregnant women[140]. |
| **Leishmaniasis** | decreases the fertility rates of women and impacts the perception of women in society. |
| **LF** | may increase susceptibility in infants and children to the infection, despite treatment of the mother[141]. |
| **Sleeping sickness** | bears the risk of vertical transmission of the disease to the foetus[130], and decreases the fertility rates of women, impacting the perception of women in society. |

## DEEP DIVE 2: **CLINICAL TRIALS AND PREGNANT WOMEN**

The development of safe and effective diagnostic tools or treatment requires prior knowledge as to whether NTDs affect women with the potential to fall pregnant in the same way as other adult populations[130]. Despite existing guidelines, particularly the ICH guidelines[142], pregnant women, breastfeeding women or women who potentially can become pregnant are frequently excluded from clinical trials[129] due to ethical and safety considerations. This may then lead to no treatment or treatment with medication for which little data on efficacious dosing during pregnancy or safety and effectiveness is available[143]. Some PRNDs could be treated in pregnancy, such as soil-transmitted helminths or schistosomiasis, but pregnant women do not receive treatment, for example, due to lack of pregnancy safety trials[26]. Other PRNDs cannot be treated at all in pregnant women, such as lymphatic filariasis, or treatment is contraindicated, such as in onchocerciasis[67].

### PREGNANT OR BREASTFEEDING WOMEN ARE FREQUENTLY EXCLUSDED FROM CLINICAL TRIALS

Interviewees suggest that the exclusion of pregnant or breastfeeding women from clinical trials needs to be addressed, as testing a drug in a (healthy, non-pregnant, potentially mainly male) sample of volunteers is not representative of the average health and risk profile of the entire population, and does not allow to assess safety for pregnant women. It may also mean that drugs are developed for men only, leaving out a large percentage of the population from access to treatment, protecting the fetus but having nevertheless major implications for women's health. A critical balance needs to be found here. The US Food and Drug Administration (FDA) refers to this in explaining the purpose of the 2018 draft Guidance Note on 'Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials' in the following way:

> *"to support an informed and balanced approach to gathering data on the use of drugs and biological products during pregnancy through judicious inclusion of pregnant women in clinical trials and careful attention to potential fetal risk"*[144].

A milestone was reached when the 'Common Rule', the US federal regulations governing research in humans, was revised to remove the category of "pregnant women" as a "vulnerable population" of research participants. This revision came into effect on 1 January 2019 and now allows, under certain conditions, pregnant women to participate in clinical research[143]. According to the draft European Medicines Agency (EMA) guideline on good pharmacovigilance practices on product- and population- specific considerations, "pregnant and breastfeeding women are considered vulnerable, or special populations"[171].

Most progress in this regard was made in the development of antimalarials. On the one

GENDER CONSIDERATIONS SHOULD BE INCLUDED IN REGULATORY HARMONISATION EFFORTS

hand, vaccines developed that can serve as a preventive measure before pregnancy and clinical trials have shown positive results, even though they did not include pregnant women as volunteers in the clinical trials[145, 146]. On the other hand, **a number of initiatives are ongoing that actively recruit pregnant women into the clinical trials** in order to develop new drugs that can be effective and safe during pregnancy itself. Alongside these efforts, networks are established to include pregnant women in clinical trials[147]. In addition, data is collected among pregnant women on existing drugs, and pregnancy registries are established that can inform their use during pregnancy[147].

These activities, however, require an active involvement of ethical review committees and regulatory authorities, such as the FDA, the EMA or national pharmacovigilance centres[138]. Regulatory authorities' participation and ownership in the research needs to be established early on in the R&I cycle in order for them to support the clinical trial phase. An extra layer of complexity is added here through the heterogeneity of country regulations and the need to receive national approval in each country **suggesting the need for including gender considerations in regulatory harmonisation efforts** between countries and regions.

## Regulatory approval and reimbursement

THE REGULATORY APPROACH TO SEX AND GENDER REMAINS FRAGMENTED AND UNENFORCED

During phase III of clinical trials usually, the application for regulatory approval is already prepared. In this approval stage, trial data is submitted to the regulatory authorities for approval for the specific use of the drug, vaccine, or diagnostic[117]. While progress has been made to include women in clinical study phases, **the regulatory approach to sex and gender remains fragmented and unenforced**, with the US and Canada being the most stringent in this respect. Few regulatory agencies have requirements around the provision of sex- and gender- related information[148]. Where guidelines do exist, entities engaged in R&I often insufficiently adapt their models to account for sex- and gender-related differences[117].

Reimbursement policies and drug or diagnostic formularies are other aspects in this phase but often lack sex and gender data, although sex-disaggregated cost-effectiveness analysis could prove critical to evaluate the usefulness of the inclusion in national or insurance benefits lists. This lack of data may lead to missing out on interventions that could be highly impactful and cost-reducing for health systems, or to including interventions that might not be impactful or cost-effective for parts of the population. **Therefore, there is a clear need to use regulatory enforcement, penalties, and incentives to foster the inclusion of sex and gender data in drug evaluation**. It would be useful to set up sex- and gender-disaggregated global performance indicators, for example through WHO's global benchmarking tool for the evaluation mechanisms of national regulatory systems. This could be an important area for collaboration and harmonisation efforts among regulatory agencies between different countries and regions. Other international strategies to foster the application of a gender lens can concern the research design support, fee waivers, expedited reviews and regulatory penalties for insufficient sex- and gender data disaggregation[117].

## Post-approval studies and access

THE IMPACT OF DISEASES ON DIFFERENT SEXES AND GENDERS NEEDS TO BE CONSIDERED IN ANY POST-APPROVAL RESEARCH

**Interventions that work in small-scale pilot studies, too often fail when rolled out in larger scale or national strategies.** Once health tools are approved and used in real-life settings, sex and gender are (next to other factors) therefore crucial to understanding the gendered impact of health interventions[149]. A differentiated understanding of prevalence rates and of the (physical and mental health, social, economic, etc.) impact of diseases on different sexes and genders as outlined in *chapter 2* thus needs to be applied to any post-approval research undertaken (such as epidemiological, modelling and pharmacoeconomic, or post-marketing surveillance studies). These aspects will be relevant regarding access and delivery of the diagnostic, drug, or vaccine to the population, in particular to women and girls. Knowledge gained in the phase of implementation research can then also feedback into the earlier phases of the R&I process.

WHO defines five main intervention strategies to access populations affected by NTDs and deliver treatment, namely preventive chemotherapy (PC), innovative and intensified disease management (IDM), vector ecology and management; veterinary public health services, and the provision of safe water, sanitation and hygiene (WASH)[150]. PC and IDM are further elaborated and analysed in the context of this study, even if the other intervention areas would also merit an analysis through a gender lens.

MANY PRNDS REQUIRE INNOVATIVE AND INTENSIFIED DISEASE MANAGEMENT (IDM)

**Many PRNDs, such as Buruli ulcer, Chagas disease, leishmaniasis, sleeping sickness, and yaws, require the use of IDM because cost-effective control tools either do not exist or their large-scale use is limited.** IDM uses different interventions, from medicine to surgery, to relieve symptoms and to treat the patients[150]. Diseases to which IDM is applied share several common characteristics that influence access and delivery, such as costly management concerning diagnosis, treatment, and follow-up, difficult access to the affected population, and a lack of understanding of the burden of disease and its social consequences[151]. All of these aspects are likely to negatively impact women and girls, and people who face discrimination because of their sex characteristics, gender identity, and expression, or sexual orientation. Availability of treatment, its pricing, and protocols further influence access. Many other factors determine the access of medical tools for women and girls, such as cultural norms and practices, economic and social status, power relations and decision-making structures within the household, but also the educational level of health care personnel, the availability of infrastructure and health care facilities. IDM requires not only an intersectional gender analysis that considers all these factors and their influence upon each other but also draws conclusions for the R&I cycle.

IN EVERY PHASE IF THE R&I CYCLE THE GENDERED IMPACT OF ACCESS AND DELIVERY NEEDS TO BE KEPT IN MIND

Indeed, **in every phase of the R&I cycle – from design to post-approval studies - scientists and researchers have to keep in mind the gendered impact of access and delivery modes.** Even if drugs that are safe and effective for women and children are developed, these efforts only bear fruit if, for example, women and girls can travel the distance to distribution points, receive the permission to get treatment from their partner and receive the drug prescribed by the health workers.

An effective intervention for PRNDs is PC or mass drug administration (MDA)[150]. However, it can only be used for some PRNDs against which the relevant tools exist, such as LF, SCH, trachoma, and a group of STH[152], and is usually implemented in endemic areas to prevent and alleviate symptoms and morbidity[153]. MDA is …

> *"a means of delivering safe and inexpensive essential medicines based on the principles of preventive chemotherapy, where populations or sub-populations are offered treatment without individual diagnosis".* [153:1]

## THE SUCCESS OF MDA DEPENDS ON THE THE **EQUAL INCLUSION OF WOMEN AND GIRLS**

MDA will therefore be distributed to every person or a defined population – unless contraindicated – in a specific geographical area. Where vaccines exist and can be applied, mass vaccine programmes may be carried out to reach a wide coverage, such as in school-based campaigns [154]. However, MDA can also be contested because of its compulsory nature, the potential development of drug resistance, and the missing follow-up with patients.

The success of MDA, usually carried out by ministries of health, depends on the reach of the targeted population. Depending on the intensity of transmission and the objective of the outreach campaign, usually more than 80% coverage is needed for it to be effective. This requires a high level of community engagement, correct and full completion of the treatment, high acceptance of the intervention in the population, willingness to participate by the individual [155], and hence presupposes equal inclusion of women and girls.

However, **MDA programmes, including vaccination programmes, entail several specific challenges for women and girls, particularly pregnant and breastfeeding women.** As a result of the exclusion of women in the clinical trial phase and the unknown safety profile for some medication during pregnancy, pregnant and breastfeeding women are regularly excluded from treatment. It also occurs that community drug distributors (CDDs) withhold the drug from pregnant and breastfeeding women due to erroneous safety concerns [157]. As women often face serial pregnancies in some low-income settings, new strategies need to be devised to consistently and safely include them in MDA campaigns whenever and wherever safe and possible [26].

Oral drugs and rapid tests that can be delivered at primary health care (PHC) clinics are critical for ensuring women's equal access. If there is a delivery at home, men might miss out on the treatment as they are away from home due to their occupational role. Another gendered challenge concerning MDA programmes is that in some cultural contexts, older men refuse to take the medicines offered by younger women as CDDs, or in other contexts, women living alone can only receive the medicines from female CDDs [158]. The confidence in and competence of the CDDs thus play a crucial role here [156], and competencies need to include gender-sensitive approaches, considering the cultural, social or other barriers women and girls might be facing in participating in MDA campaigns.

A recent study examining gender equity of MDA for NTDs across 16 countries (2019) [152] highlighted the importance of sex- and gender-disaggregated data. Even though the coverage of MDA programmes is gender-equal at the national level, differences exist at the sub-national level where sex-, gender- and age-disaggregated data are often missing or (if collected) are not communicated upstream [159]. The study [152] pointed out that while females, in general, have not necessarily lower coverage rates, the gendered barriers to coverage need to be investigated with location-specific knowledge in order to understand the differences among males and females. *Table 6* by Theobald et al. (2017) [158] gives an overview of different elements of and approaches to MDA, the extent to which data is disaggregated, and poses questions concerning gender.

Photo: Shutterstock

**TABLE 6** APPROACHES TO MDA AND WHY GENDER MATTERS

| Approach to MDA | Data sex disaggregated | Questions for programme managers to consider from a gender perspective |
|---|---|---|
| House to house Community drug distributors CDDs/ others visit households to register the household members and distribute drugs | Routinely reported data may be sex disaggregated at community level but frequently not cascaded to national level | • Who is chosen to distribute the drugs and why?<br>• How are they chosen and who is involved?<br>• Are they remunerated?<br>• Does this influence who is involved?<br>• At what time are drugs distributed?<br>• If it is in the evenings is it acceptable/ does it prompt security concerns?<br>• If daytime, does this affect the involvement of those who have activities outside the home?<br>• Does this access influence individual, household and community adherence?<br>• Who has the power to decide whether the medicines are taken or not?<br>• Who has the power to provide consent for household members under the age of 18?<br>• Do power relations at the community level also shape this? |
| Fixed point approaches: health post clinic/ distribution point Drugs are distributed by CDD or health workers at a fixed point | Routinely reported data may be sex disaggregated at facility level but frequently not cascaded to national level | • How and to whom is information communicated about the distribution – how does this affect the needs of migrants, inhabitants of informal settlements, women, men, people of other genders?<br>• How does it reflect the literacy levels?<br>• Who is able to attend the distribution? How do livelihoods, gender, power and autonomy affect this?<br>• Does the location of distribution points influence distribution of medicines, what is the impact on community coverage or the coverage of any specific group within the community? |
| Child (under 5) health/ special events Particularly common in the African context, drugs are provided with these gatherings | Routinely reported data may not be sex disaggregated at national level with the possible exception of nutrition | • How and to whom is information communicated about the distribution – to what extent does this reflect the needs of women, men, people of other genders, migrants, inhabitants of informal settlements?<br>• Who is able to attend the distribution? How do livelihoods, gender, power and autonomy affect this?<br>• Who has the power to provide consent for the treatment of those under 18 years of age? |
| School-based programme Teachers and/ or others distribute drugs in the schools | Routinely reported data may be sex disaggregated at school level but frequently not cascaded to national level | • Who attends school?<br>• How is this linked to gender and poverty?<br>• How is informed consent negotiated?<br>• What happens to those who do not attend school on a regular basis?<br>• What happens to those who drop-out of schools/ do not complete primary education? |
| Coverage improvement activities for example, mop up. Additional 'pro-equity' activities undertaken to try to ensure everyone is covered | No sex disaggregated information and limited documentation on types of approaches | • What are the 'coverage improvements' strategies?<br>• Who decided on them?<br>• What baseline/ census material do they relate to and who might be potentially excluded from these?<br>• Where appropriate how can we ensure women who are pregnant (and unable to take certain drugs) do access them at a later more appropriate date? |

Source: Theobald S., MacPherson E.E. (2017)[158:3]

Even though the above *table 6* may neither be exhaustive nor applicable to all settings, it can be a useful entry point to develop a deeper understanding of gender issues in MDA. Such gender frameworks create awareness and better understanding. They are useful tools to trigger action on the gendered dimensions of PRNDs. The following chapter provides an overview of such frameworks that either have been specifically developed for PRNDs or may be usefully applied to PRNDs.

# 4 GENDERED APPROACHES TO ADDRESSING PRNDS

## GENDER MAINSTREAMING IS STILL TODAY A VALID TOOL TO ADDRESS WOMEN'S SPECIFIC HEALTH NEEDS

Many different approaches towards women and girls in vulnerable or disadvantaged situations exist and this chapter will focus on highlighting some of the most relevant existing frameworks.

Rights-based approaches[29] and other integrated 'pro-poor' approaches [160] as very generic approaches, addressing the vulnerable situation in which women and girls live, can be applied to PRNDs, even if such approaches often lack the gender specificity needed.

In a publication from 2002, WHO has examined 17 existing tools and their usefulness for gender analysis in health[161]. The publication describes the approach taken by different donors and focuses on gender mainstreaming in health, which was the predominant approach at the time. Gender mainstreaming is still today a valid tool to address women's specific health needs through the identification of the differences and disparities between males and females. It also allows integrating a gender perspective within an organisation and/ or within an ongoing process, for example, as outlined earlier in the R&I process. Gender mainstreaming includes decision-making processes, aims at triggering change, and ultimately targets the achievement of gender equality.

Nearly ten years later, WHO has published a facilitator's guide on 'Gender mainstreaming for health managers: a practical approach' (2011)[162]. This publication not only addresses gender mainstreaming but specifically addresses the process involved to achieve this. It focuses on creating awareness, conducting (gender) analysis, and finally acting in a gender-responsive way. It introduces a **gender assessment scale, allowing projects or research to be classified from gender-unequal, gender-blind to gender-sensitive, and gender-specific to gender-transformative.** Even though the publication does not specifically focus on PRNDs, it remains a useful resource. The network on Research in Gender and Ethics (RinGs) describes ten gender analysis tools (2015), their key dimensions and intended audience[163]. This document highlights among others the 'UNAIDS Gender Assessment Tool: Towards a Gender-Transformative HIV Response' [164]. Research in this area on PRNDs is limited but in recent years, some specific studies and reports have been published referring specifically to women and gender [18, 25, 27, 30-32, 37, 73, 158, 165-167], often offering an analytical framework but hardly ever considering the specificities in the R&D cycle.

## ROOT CAUSES OF INEQUITIES AND POWER RELATIONS ARE IN FOCUS WITHIN GENDER TRANSFORMATIVE APPROACHES

The field has developed since then, and addressing the root causes of gender inequities and power relations are now much more in focus within gender transformative approaches. *Figure 3* reproduces the adapted gender framework by Morgan et al. (2016) and is geared towards addressing gender power relations. It is a tool that allows addressing the gendered dimensions of PRNDs in a holistic, systematic way and is applicable in all settings.

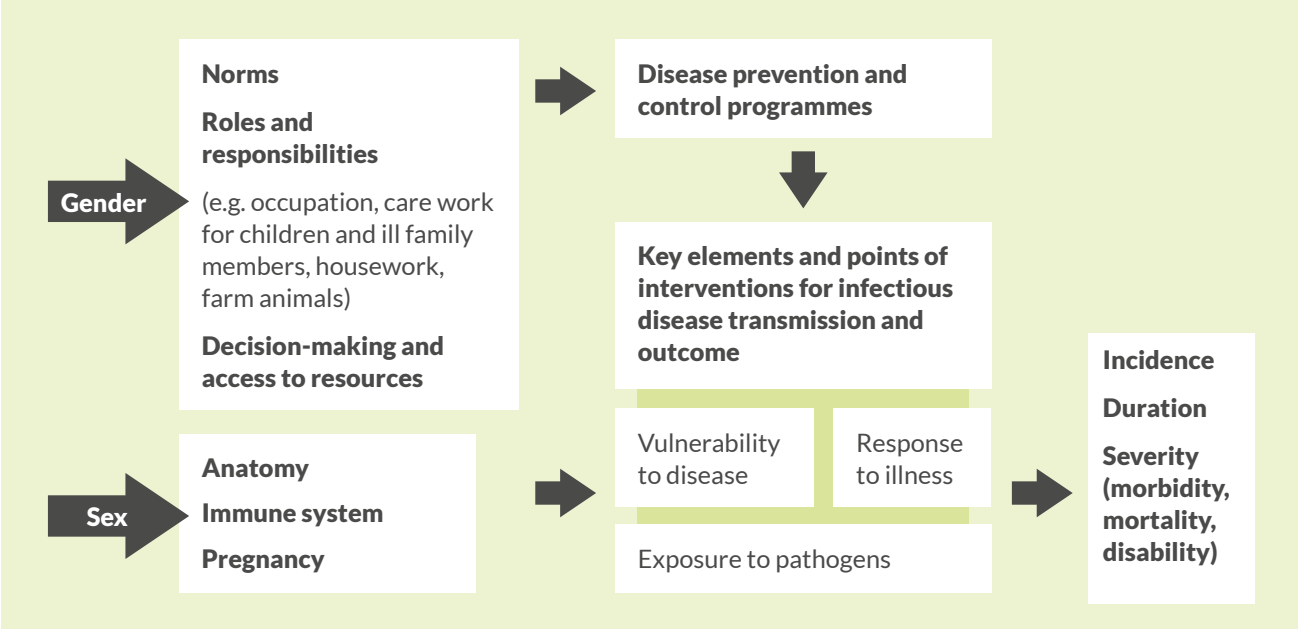
**TABLE 6** APPROACHES TO MDA AND WHY GENDER MATTERS

| | |
|---|---|
| **Who has what?**<br>Access to education, information, skills, income, employment, services, benefits, time, space, social capital, etc. | **Who does what?**<br>Division of labour within and beyond the household and everyday practices |
| **How are values defined?**<br>Social norms, ideologies, beliefs and perceptions | **Who decides?**<br>Rules and decision-making (formal and informal) |
| **How power is negotiated and changed?**<br>Critical consciousness, acknowledgement, agency/ apathy, interests, historical and lived experiences, resistance or violence | **Structural/ environmental conditions?**<br>Legal and policy status, institutionalization within planning and programmes, funding, accountability mechanisms |

Source: Adapted from Morgan et al. (2016) in UNDP (2019) [31:20]

The WHO Regional Office for the Western Pacific (2011) has created a useful tool that helps to analyse the influence of sex and gender differences on emerging infectious disease prevention and control programs. In doing so, the proposed analytical framework describes differential sex and gender effects on vulnerability, exposure, response to the infection, and public health interventions. *Figure 4* illustrates this relationship that can be transformed into a gender analysis matrix in which each row corresponds to one of the elements of the framework. The overall framework applies to several disease groups and social and geographical environments. [168]

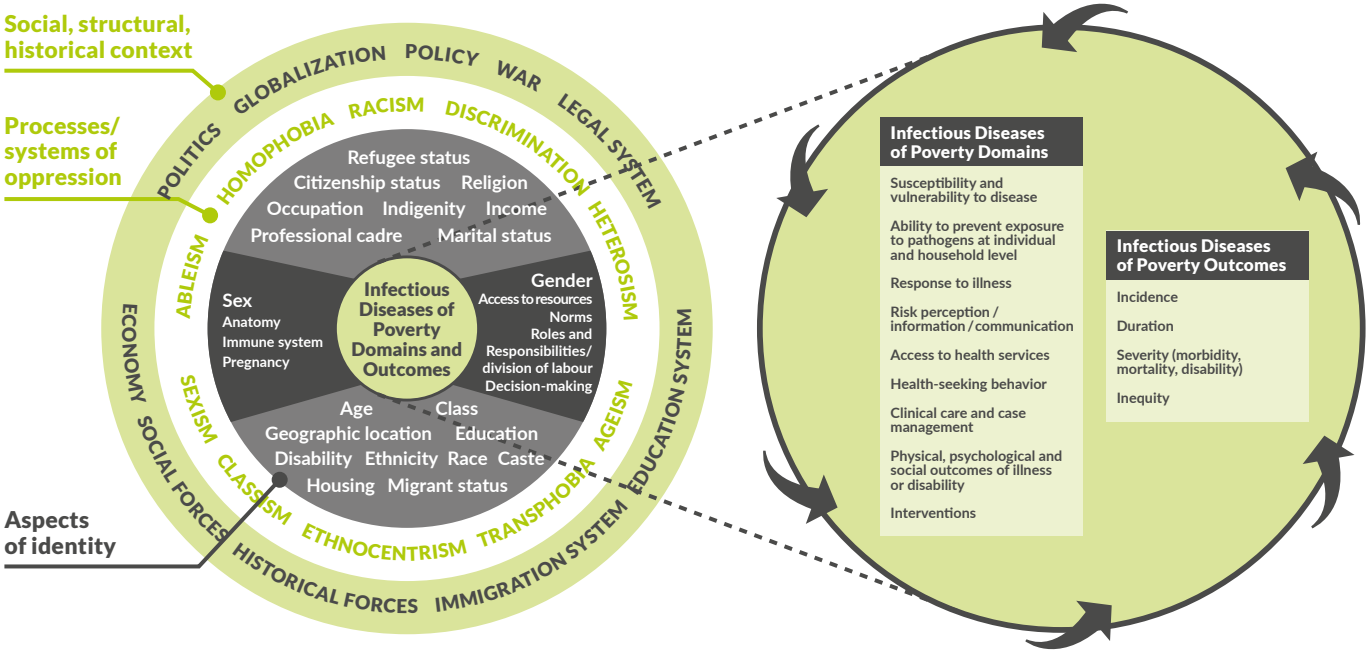
**FIGURE 4** FRAMEWORK FOR SEX AND GENDER AND EMERGING INFECTIOUS DISEASES




Source: WHO Western Pacific Region (2011)[168:8], design adapted for this report

Expanding on the gender dimensions of power relations and specifically applying it to health research, TDR (2020) has published an interactive toolkit entitled "Incorporating Intersectional Gender Analysis into Research on Infectious Diseases of Poverty"[18]. The interface of gender power relations with other stratifiers, such as age, class, gender, sex, ability, disability, ethnicity, sexuality, etc., are at the core of intersectional gender analysis. *Figure 5* illustrates the many factors that influence and that need to be considered and combines it with the framework presented in *Figure 4*.

**FIGURE 5** FRAMEWORK FOR SEX AND GENDER AND EMERGING INFECTIOUS DISEASES




Source: TDR (2020)[19:37], design adapted for this report

The TDR publication not only focuses on an intersectional gender analysis but also targets specifically researchers of infectious diseases of poverty. Hence, it provides detailed advice on how to conduct an intersectional gender analysis within the four stages of the research process, namely:

1. **design and development of research, including the development of research protocol,**
2. **data collection,**
3. **data analysis, and**
4. **dissemination and reporting.**[18]

These specific gender frameworks are just some of the most frequently used tools that can be applied to analysing the gendered dimensions of the R&I cycle. More generic approaches used for PRNDs, such as multisectoral or integrated approaches [43], can enhance these specific gender frameworks and can be considered as complementary.

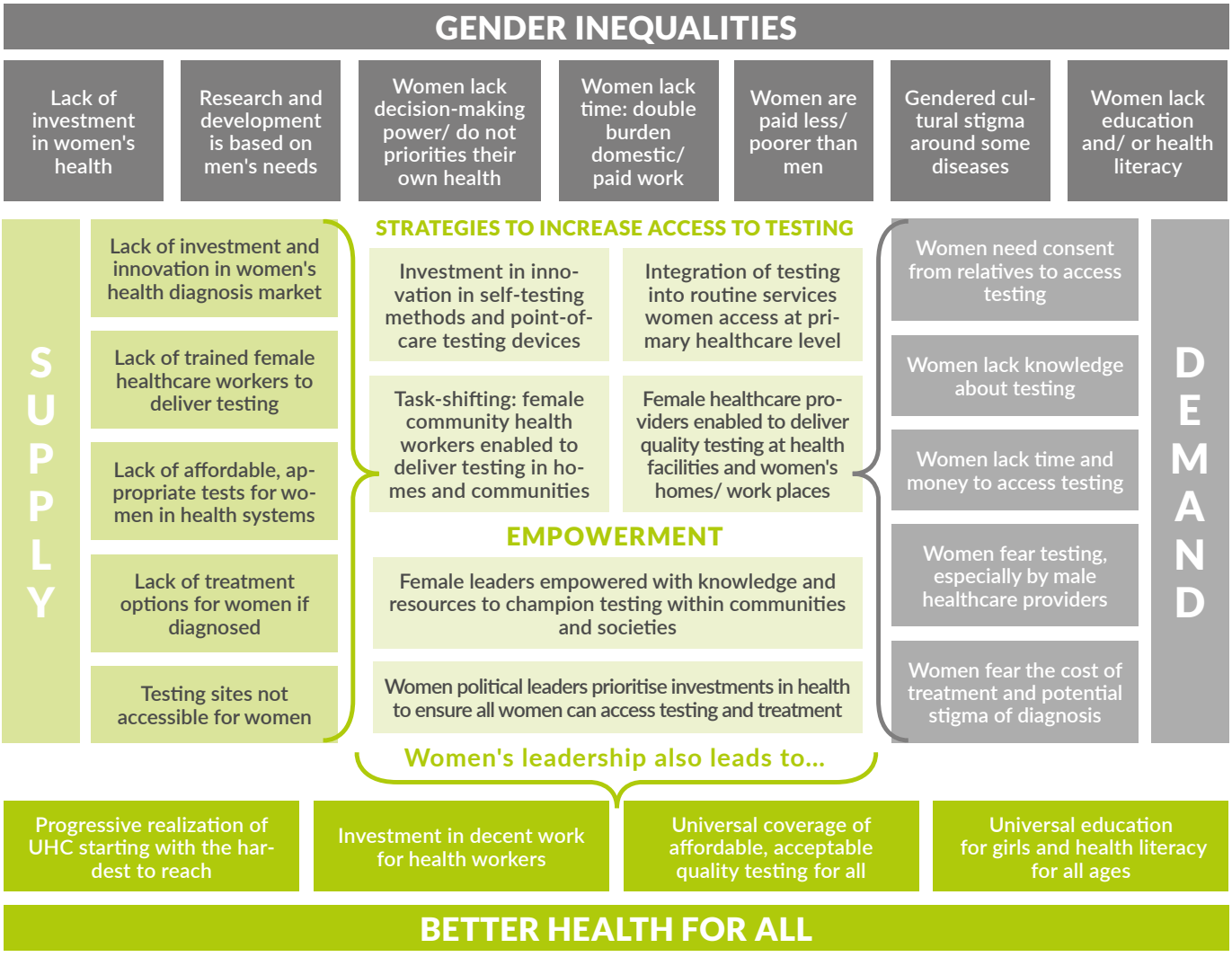
As mentioned throughout the report, **a major prerequisite for the systematic integration of the gender dimensions in medical research and thus for all the above-outlined approaches is the continuous disaggregation of data by sex and gender.** This not only refers to greater equality of male and female research subjects as outlined earlier but also to the use of methodological tools that do not show any gender bias. For example, the use of the disability-adjusted life year (DALY), even though disaggregated in the database has been criticised to underrepresent the burden on women. This highlights the much larger problem that the interconnectedness of women's health problems is not sufficiently captured, and the cumulative complexity not necessarily sufficiently represented in the measuring tools [169].

**DISAGGREGATION OF DATA IS A CRUCIAL PREREQUISITE** FOR ALL GENDERED APPROACHES TO ADDRESSING PRNDS

Data is mostly collected based on sex only, broader gender aspects are not yet part of a standardised data collection process, even if awareness around this is increasing. In addition, data on some PRNDs are totally missing, for example, neither DALY nor prevalence rates are available for Buruli ulcer and yaws in the GBD, or specific aspects are missing, with, for example, data on SCH in pregnant women unavailable [26]. Even if sex- and gender-disaggregated data is collected at the local level, this data has to be reflected in the available reporting systems and information flow needs to be ensured, for example to the regional or national level, for data to be captured in national databases and reports. Missing this provides a distorted picture of the reality and neither interventions nor research priorities will be able to adequately address the needs of women and girls. As an example, the over-reliability on 'evidence' and hard data as a basis of intervention, and **overlooking the social, cultural, and psychological factors that influence the impact of an intervention can cause major diagnostic delays**[35]. A recent report by FIND and Women in Global Health (2020)[170] showcases how a gender lens can be applied to a concrete medical need (increase women's access to testing) and how a comprehensive understanding of women's realities – both in terms of supply & demand - is essential. *Figure 6* provides a comprehensive analysis of gender inequalities that exist in testing and outlines some strategies to remedy these gaps.

OVERLOOKING THE SOCIAL, CULTURAL, AND PSYCHOLOGICAL FACTORS THAT INFLUENCE THE IMPACT OF AN INTERVENTION CAN HAVE SERIOUS NEGATIVE EFFECTS

**FIGURE 6** GENDER INEQUALITIES IN TESTING AND REMEDIAL STRATEGIES




Source: FIND & Women in Global Health (2020) [170:11], design adapted for this report

# 5 CONCLUSIONS

This study highlights several gender-related aspects of PRNDs, in particular, the global prevalence of PRNDs in relation to their impact. It draws conclusions regarding the R&I needs to better address PRNDs in women and girls. It also provides some insights to existing gender frameworks and their usefulness and briefly outlines challenges for pregnant women and selected knowledge gaps. The study does not deliver a comprehensive analysis but provides evidence on key messages from the scoped literature. A more detailed analysis about age groups and geographical distribution would be necessary to get more differentiated insights on the issues outlined.

## Key findings

The main messages of the two analytical *chapters 2 and 3* of this report are summarised in *Table 7* and *Figure 7*.

The analysis has identified a number of diseases that have significantly higher prevalence rates in females than in males and has shown that when looking at prevalence, both biological susceptibility and non-biological factors that contribute to infection need to be taken into account. More importantly, however, the study found that applying a gender lens on PRNDs necessitates a full-fledged analysis of the conditions and lived experiences by different genders to consider the determinants of health in all dimensions. The first key finding depicted in *Table 7* thus is, that it is crucial to distinguish between PRND 'prevalence' and 'impact' and consider both when assessing PRNDs through a gender lens. Prevalence rates alone are an insufficient indicator for understanding the gendered dimension of a disease, for example in terms of wider health consequences, availability of healthcare, stigma, and discrimination, financial and social consequences. Decision-making on R&I or programmes addressing the diseases cannot and should not rely on such figures alone.

**TABLE 7** OVERVIEW OF GLOBAL PREVALENCE AND IMPACT ON FEMALES AND MALES

| | Global Prevalence Females > Males | Global Prevalence Males = Females | Global Prevalence Males > Females | Global Prevalence No information |
|---|---|---|---|---|
| Specific impact on women and girls (as identified in *chapter 2*) | • Dracunculiasis (Guinea worm disease)<br>• Echinococcosis<br>• Leishmaniasis<br>• SCH<br>• Trachoma | • Hookworm<br>• Malaria | • Leprosy<br>• Lymphatic filariasis<br>• TB | • Buruli ulcer |
| Specific impact on men (as identified in *chapter 2*) | • Chagas disease | | | |

**A differentiated understanding of the gendered realities inherent in PRNDs is thus a prerequisite to further delve into the R&I needs of women and girls.** The existing literature points to a number of knowledge gaps and blind spots when it comes to considering biological and non-biological differences between women and men, or people with non-binary-characteristics in medical research. Each phase of the R&I process involves certain challenges and considerations that specifically concern women and girls. Research (re-)design and publication, and all the stakeholders involved in the process influence each phase. Therefore, the second key finding is **the need for the consistent application of a gender lens throughout the entire R&I cycle. Integrating a gender perspective in R&I needs to happen with due respect to all ethical considerations, and needs to be incentivised or mandatory**, despite potential resource implications. *Figure 7* translates some of the key findings of each phase into a checklist tool applicable to the entire R&I cycle for health. Some modifications may be worth considering for the distinct diagnostic, drug, and vaccine development processes. This suggested checklist is not an endpoint but a means to trigger and inspire further holistic thinking on the gendered nature of the R&I process and thus, should be considered as a dynamic and evolving tool.

As highlighted throughout the report, the lack of data makes it difficult to conclude on the impact of PRNDs on people with non-binary sex characteristics, gender identity or expression, and sexual orientation. The needs of the LGBTIQ+ population are only selectively mentioned throughout the literature, with the HIV & AIDS community being the most vocal to consider their needs specifically. Some agencies and organisations have, however, undertaken steps to more coherently integrate a broader gender perspective in their medical research.

## Policy and funding recommendations

This study aims to provide a more holistic and gendered understanding of PRNDs and the R&I process around PRNDs. The report identified several recommendations which can be summarised in the below eight key points aiming to contribute to and strengthen the implementation of a gendered approach in R&I for PRNDs.

**Legislators when setting the relevant rules, governments, and more specifically R&I and PRND programmes agencies in their funding requirements and funding allocation priorities, regulators, and research teams should in collaboration:**



1. **Integrate both female and male sex in all phases of research and product development**
From discovery to post-approval studies on PRNDs all relevant elements depicted in *Figure 7* need to be considered, for example by including male and female cells in in-vitro studies, males and females in animal studies, taking into account the sex and gender of research and laboratory team members, and including man and women in clinical trials. Misleading or erroneous conclusions in regards to sex and gender differences of pharmaceutical and non-pharmaceutical interventions need to be avoided and differences at biological and social levels need to be captured to improve treatment efficacy, efficiency, and safety. A gender lens needs to be applied to any post-approval research undertaken (such as epidemiological, modelling and pharmacoeconomic, or post-marketing surveillance studies).



2. **Foster greater representation of women in science**
Women need to be part of leadership and decision-making within research teams to facilitate the better integration of sex- and gender considerations at all levels.

LGBTIQ+

3. **Consider all people beyond the binary focus on males and females**
Further research is needed to understand – within the often restrictive political and legal environments – the impact of PRNDs on the entire gender identity spectrum, particularly the needs of the LGBTIQ+ population, and the resulting implications for the R&I process.



4. **Move beyond the biomedical focus and introduce a holistic approach**
Going beyond the traditional biomedical model that relies primarily on quantitative, medical data will require research to systematically integrate a gender perspective, rooted in a contextual (local) analysis based on sociology, political sciences, and anthropology. This calls for studies contributing to understanding the gender-specific impact (and not only prevalence) of diseases and conditions, and more socio-behavioural and implementation research. Gender mainstreaming and inter-sectional gender analysis can be useful tools that need to be solidified and mandatory in the R&I process beyond the generic requirements of 'ticking the gender box' in project proposals. It implies, for example, establishing impact indicators specifically on gender.



5. **Disaggregate data by sex and gender at each step and at each level**
The call for disaggregating data by sex and gender has been made many times, and yet, it needs to be reiterated once again because it is – together with a more holistic approach – an important prerequisite to be able to consider gendered dimensions in the R&I process. This disaggregation needs to start at the very beginning of the chain and information collected at every phase has to be captured, reported, analysed, and delivered to the appropriate entities in order to fully take the information into account in the decision-making processes at different phases of R&I. The data disaggregation chain has to be ensured horizontally and vertically.

**6. Address the lack of pregnancy safety trials and redefine existing concepts**

Following the example of the US' Common Rule, women should no longer be defined as a 'vulnerable population'. Pregnant women or breastfeeding women need to be included in the research process, for example, in clinical trials - in a safe and ethically sound way. It might be necessary to oversample pregnant women or WoSuP, or to conduct specific separate trials. The reconceptualisation of women as equal participants who face conditions that can render them more vulnerable is crucial for more gender-sensitive research. It also implies that priorities have to be newly set, not only focussing on women as part of a process but also as separate research subjects. Moreover, as women often face serial pregnancies in some low-income settings, new strategies need to be devised to consistently and safely include them in MDA campaigns whenever and wherever safe and possible.



**7. Adopt a gender-sensitive approach in medical regulation and international regulatory harmonisation efforts**

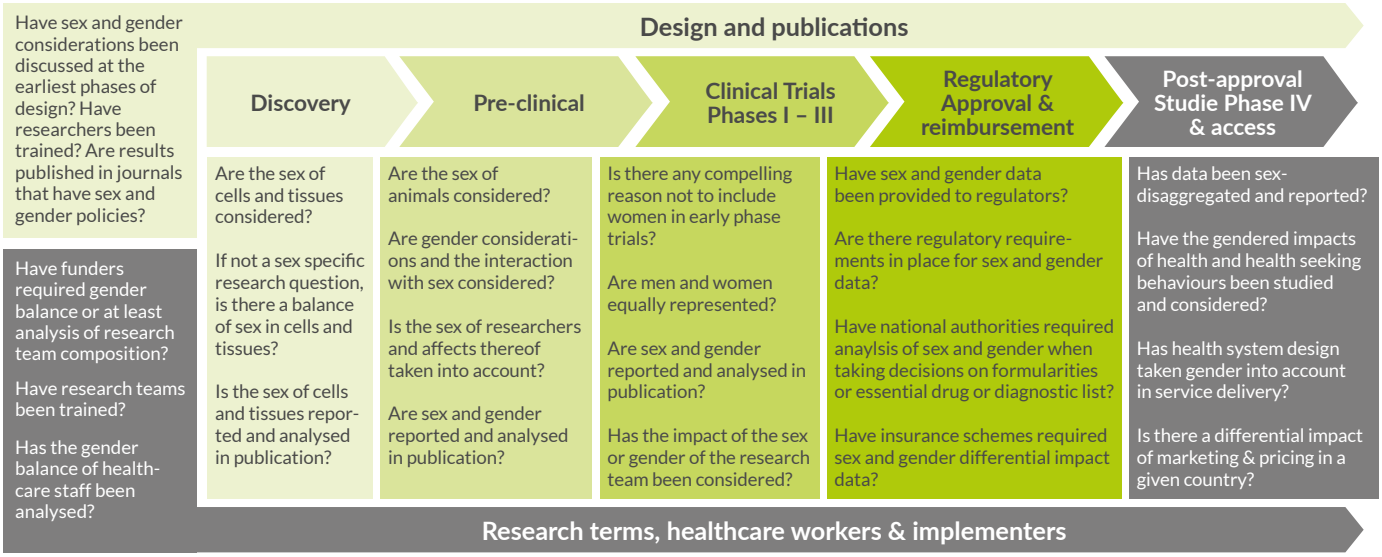
There is a clear need to use regulatory enforcement, penalties, incentives, and other tools (such as research design support, fee waivers, expedited reviews, etc.) to foster the inclusion of sex and gender data in drug evaluation. National ethics committees' and regulatory authorities' understanding of integrating a gender perspective needs to increase, allowing for the necessary guidelines, regulations, and directives to be set. International regulatory collaboration and harmonisation efforts should include this field of work. It would be useful to set up sex- and gender-disaggregated global performance indicators, for example through WHO's global benchmarking tool for the evaluation mechanisms of national regulatory systems. It is important to build on existing regulations and committees and inject new parameters on gender in their work. Existing governance structures can be expanded, for example, through the establishment of pregnancy committees and pregnancy investigation plans if the diagnostic tool, drug, or vaccine is to be used by pregnant women. Sex-disaggregated cost-effectiveness analysis needs to be taken into account in the evaluation of the inclusion in national or insurance benefits lists.



**8. Allocate (additional) dedicated funding and set new standards**

The implementation of all of the above recommendations will require that funding is made available to fill knowledge, research, product, and regulatory gaps, and to increase gender capacities within responsible authorities, organisations, research teams, etc. Standards and requirements for project funding proposals need to be re-defined, including through setting relevant indicators that can support the mainstreaming of sex-, and gender considerations in PRND R&I, rule out 'gender blindness' of the funded research, and serve as an incentive for relevant stakeholders and organisations to make the necessary efforts. But there is also a need for additional/ dedicated funding and calls for proposals that specifically address some of the knowledge gaps, invest in further developing and implementing gender transformative approaches, and recognise women and girls, LGBTIQ+ people, transient, or minority populations as priority populations.

**FIGURE 7** RESEARCH & INNOVATION NEEDS THROUGH A GENDER LENS




Source: Told & Landry Chappuis, HumanImpact5 HI5 (2020)

# 6. ANNEXES

## Annex 1: Overview of Poverty-Related and Neglected Diseases

The below list of diseases defines the scope of this study.
WHO definitions are used [20].

- **Buruli ulcer:** A debilitating mycobacterial skin infection causing severe destruction of the skin, bone and soft tissue.
- **Chagas disease:** A life-threatening illness transmitted to humans through contact with vector insects (triatomine bugs), ingestion of contaminated food, infected blood transfusions, congenital transmission, organ transplantation or laboratory accidents.
.
- **Dengue**: A mosquito-borne infection causing flu-like illness that may develop into severe dengue and cause lethal complications.
- **Dracunculiasis (Guinea-worm disease):** A nematode infection transmitted exclusively by drinking-water contaminated with parasite-infected water fleas.
- **Echinococcosis:** Infection caused by the larval stages of tapeworms forming pathogenic cysts in humans and transmitted when ingesting eggs most commonly shed in faeces of dogs and wild animals.
- **Foodborne trematodiases**: Infection acquired by consuming fish, vegetables and crustaceans contaminated with larval parasites; clonorchiasis, opisthorchiasis and fascioliasis are the main diseases.
- **Human African trypanosomiasis (sleeping sickness):** A parasitic infection spread by the bites of tsetse flies that is almost 100% fatal without prompt diagnosis and treatment to prevent the parasites invading the central nervous system.
- **Human Immunodeficiency Virus (HIV) & Acquired Immunodeficiency Syndrome (AIDS):** An infection that attacks the body's immune system, specifically the white blood cells called CD4 cells. HIV destroys these CD4 cells, weakening a person's immunity against infections such as TB and some cancers. If the person's CD4 cell count falls below 200, their immunity is severely compromised. Someone with a CD4 count below 200 is described as having AIDS.
- **Malaria:** A disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes. There are five parasite species that cause malaria in humans, and two of these species – Plasmodium falciparum and Plasmodium vivax – pose the greatest threat.
- **Leishmaniases:** Disease transmitted through the bites of infected female sandflies that in its most severe (visceral) form attacks the internal organs and in its most prevalent (cutaneous) form causes face ulcers, disfiguring scars and disability.
- **Leprosy:** A complex disease caused by infection mainly of the skin, peripheral nerves, mucosa of the upper respiratory tract and eyes.
- **Lymphatic filariasis:** Infection transmitted by mosquitoes causing abnormal enlargement of limbs and genitals from adult worms inhabiting and reproducing in the lymphatic system.
- **(Mycobacterium) Tuberculosis:** A bacterial infection most often affecting the lungs and spread through the air when people with lung TB cough, sneeze or spit. A person needs to inhale only a few germs to become infected.
- **Mycetoma** is a chronic, progressively destructive inflammatory skin disease which usually affects the lower limbs. Infection is thought to be caused by the inoculation, through a thorn prick or skin damage, of fungi or bacteria into the subcutaneous tissue.
- **Onchocerciasis (river blindness):** Infection transmitted by the bite of infected blackflies causing severe itching and eye lesions as the adult worm produces larvae and leading to visual impairment and permanent blindness.
- **Rabies:** A preventable viral disease transmitted to humans through the bites of infected dogs that is invariably fatal once symptoms develop.
- **Schistosomiasis:** Trematode infections transmitted when larval forms released by freshwater snails penetrate human skin during contact with infested water.
- **Soil-transmitted helminthiases:** Nematode infections transmitted through soil contaminated by human faeces causing anaemia, vitamin A deficiency, stunted growth, malnutrition, intestinal obstruction and impaired development.
- **Taeniasis & cysticercosis:** An infection caused by adult tapeworms in human intestines; cysticercosis results when humans ingest tapeworm eggs that develop as larvae in tissues.
- **Trachoma:** A chlamydial infection transmitted through direct contact with infectious eye or nasal discharge, or through indirect contact with unsafe living conditions and hygiene practices, which left untreated causes irreversible corneal opacities and blindness.
- **Yaws:** A chronic bacterial infection affecting mainly the skin and bone.

## Annex 2: Search Terms

**Neglected Tropical Diseases / NTDs**

… and gender
… among females
… among women
Impact of …. on women / girls
Sex differentials of ….
… among LGBT communities / transgender people
Gender-sensitive approaches to …
… and gender and innovation
… and gender and funding
Clinical trials on …
Financing / Funding / Health Systems / SDGs / UHC & …
Gender sensitive clinical trials on …
Gender related findings from clinical trials on …
Financing / Funding / Health Systems / SDGs / UHC, and
… and gender
… and access to medicines
… and women's /girls' access to medicines
… and access to medicines of transgender communities / of LGBT communities
UHC for women / transgender people / LGBT communities and …
Gender and diagnostics of …
Diagnostics of … in women / girls
Diagnostics of … among transgender people / LGBT communities
Case studies on …

**Buruli ulcer**
**Chagas disease**
**Dengue**
**Chikungunya**
**Dracunculiasis**
**Guinea worm disease**
**Echinococcosis**
**Foodborne trematodiases**
**Foodborne trematodiases**
**Human African trypanosomiasis**
**Leprosy**
**Leishmaniasis**
**Lymphatic filariasis**
**Mycetoma, chromoblastomycosis and other deep mycoses**
**Onchocerciasis**
**River blindness**
**Rabies**
**Scabies and other ectoparasites**
**Schistosomiasis**
**Soil-transmitted helminthiases**
**Snakebite envenoming**
**Taeniasis/Cysticercosis**
**Trachoma**
**Yaws**

… and gender
… among females / women
Impact of …. on women / girls
…among LGBT communities / transgender people
Sex differentials of ….
Gender-sensitive approaches to …
…and gender and poverty and funding
…and gender and poverty and innovation
Case studies on ...

## Annex 2: Search Terms

**HIV**

… and gender
… among females
… among women
Impact of …. on women
Impact of …. on girls
Sex differentials of ….
… among LGBT communities
… among transgender people
Gender-sensitive approaches to …
… and gender and innovation
… and gender and funding
… and gender and poverty and funding
… and gender and poverty and funding and Kenya /Uganda / Tanzania / Ethiopia
… and gender and funding and Kenya / Ethiopia
… and gender and Tanzania / Ethiopia
Case studies on …
Clinical trial/ Financing/ research and innovation/ access to medicines / SDGs / UHC / Health systems /diagnostics /case studies and gender and …
Case studies on ...

**Malaria**
**Tuberculosis**

… and gender
… among females / women
… among LGBT communities / transgender people
Impact of … on women/ girls
Sex differentials of …
Gender-sensitive approaches of …
… and gender and poverty and innovation
… and gender and poverty and funding
… and gender and poverty and funding and Kenya / Uganda
… and gender and funding and Uganda
… and gender and Uganda / Tanzania /Ethiopia / Kenya
Case studies on …
Clinical trials / Financing / R&D / research and innovation / access to medicines / SDGs / UHC / Health systems / diagnostics / case studies and gender and …

**Clinical trials**
**Diagnostics**

Gender and …
Gender sersitive … on NTDs
Gender bias in …

**DATA BASE USED**

**1. Global Health Data Exchange (GHDx) – Global Burden of Disease Results Tool**
http://ghdx.healthdata.org/gbd-results-tool

**2. WHO website and sources**
https://www.who.int/ or https://apps.who.int/

**3. G-Finder – Policy Cures Research Database**
https://gfinderdata.policycuresresearch.org/pages/data-visualisations

## Annex 3: List of Interviewed Organisations

1. **Drugs for Neglected Disease initiative (DNDi)**
2. **European & Developing Countries Clinical Trials Partnership (EDCTP)**
3. **Foundation for Innovative New Diagnostics (FIND)**
4. **Medicines for Malaria Venture (MMV)**
5. **PATH**
6. **TB Alliance**
7. **The Global Fund to fight AIDS, Tuberculosis and Malaria**
8. **Tuberculosis Vaccine Initiative (TBVI)**
9. **University College, London**
10. **WHO**

# 7. REFERENCES


1. Institute of Health Metrics and Evaluation. Global Health Data Exchange. 2017 [cited 2020 13.10.]; Available from: http://ghdx.healthdata.org/gbd-results-tool.
2. WHO. NTD and SDGs. Available from: https://www.who.int/neglected_diseases/global-partners-meeting/NTD-and-SDG/en/.
3. Fitzpatrick, C. and D. Engels, Leaving no one behind: a neglected tropical disease indicator and tracers for the Sustainable Development Goals. International Health, 2016. 8(suppl_1): p. i15-i18.
4. United to Combat Neglected Tropical Diseases, Reaching a Billion: Ending Neglected Tropical Diseases: A gateway to Universal Health Coverage. Available from: https://unitingtocombatntds.org/reports/5th-report/
5. UN WOMEN. In Focus: Gender equality matters in COVID-19 response. 2020; Available from: https://www.unwomen.org/en/news/in-focus/in-focus-gender-equality-in-covid-19-response.
6. The World Bank, Reversals of Fortune. 2020, Washington: The World Bank. Available from: https://openknowledge.worldbank.org/bitstream/handle/10986/34496/9781464816024.pdf
7. Stop TB Partnership, The devastating effect of Covid-19 pandemic on the TB response. 2020. Available from: http://www.stoptb.org/assets/documents/covid/Covid%20impact%20on%20TB%20Modeling_Key%20Messages_FINAL.pdf
8. UNAIDS, Seizing the Moment. Tackling entrenched inequalities to end epidemics. 2020, Geneva: UNAIDS. Available from: https://aids2020.unaids.org/report/
9. Sherrard-Smith, E., et al., The potential public health consequences of COVID-19 on malaria in Africa. Nature Medicine, 2020. 26(9): p. 1411-1416.
10. Molyneux, D.H., et al., COVID-19 and neglected tropical diseases in Africa: impacts, interactions, consequences. International Health, 2020. 12(5): p. 367-372.
11. UN, The Impact of COVID-19 on Women. 2020, UN: New York. Available from: https://www.un.org/sexualviolenceinconflict/wp-content/uploads/2020/06/report/policy-brief-the-impact-of-covid-19-on-women/policy-brief-the-impact-of-covid-19-on-women-en-1.pdf
12. UN General Assembly, Report of the Independent Expert on portection against violence and discrimination based on sexual orientation and gender identity. Violence and discrimination based on sexual orientation and gender identity during coronavirus disease (COVID-19) pandemic. A/75/258. 2020, New York: UN General Assembly.
13. WHO, Global Report for Research on Infectious Diseases of Poverty. 2012, WHO, : Geneva. Available from: http://whqlibdoc.who.int/publications/2012/9789241564489_eng.pdf?ua=1
14. Sen, A., Development as Freedom. 2001, New Dehli: Oxford University Press.
15. Singh, A.R. and S.A. Singh, Diseases of poverty and lifestyle, well-being and human development. Mens sana monographs, 2008. 6(1): p. 187-225.

16. WHO. Neglected tropical diseases. Available from: https://www.who.int/neglected_diseases/diseases/en/.

17. WHO. Gender. 2020 [cited 2020 15.10.2020]; Available from: https://www.who.int/health-topics/gender#tab=tab_1.

18. TDR, W.a., Incorporating intersectional gender analysis into research on infectious diseases of poverty: a toolkit for health researchers. 2020, WHO: Geneva. Available from: https://www.who.int/tdr/publications/year/2020/tdr-intersectional-gender-toolkit/en/

19. Global Health Data Exchange. Global Burden of Disease Results Tool. 2019 [cited 2020 19 September 2020]; Available from: http://ghdx.healthdata.org/gbd-results-tool.

20. WHO. Neglected tropical diseases - Summary. 2020 [cited 2020 13.10.]; Available from: https://www.who.int/neglected_diseases/diseases/summary/en/.

21. G-Finder. Policy Cures Research. 2020 [cited 2020 20 September 2020]; Available from: https://gfinderdata.policycuresresearch.org/.

22. Leung, L., Validity, reliability, and generalizability in qualitative research. Journal of family medicine and primary care, 2015. 4(3): p. 324-327.

23. Cislaghi, B., et al., Gender equality and global health: intersecting political challenges. Journal of global health, 2020. 10(1): p. 010701-010701.

24. McQueston, K., The Known Unkown: Estimating the Global Burden of Disease, in Commentary and Analysis, C.f.G. Development, Editor. 2014.

25. von Philipsborn, P., et al., Poverty-related and neglected diseases – an economic and epidemiological analysis of poverty relatedness and neglect in research and development. Global Health Action, 2015. 8(1): p. 25818.

26. McDonald, M.C., Neglected Tropical and Zoonotic Diseases and Their Impact on Women's and Children's Health, in The Causes and Impacts of Neglected Tropical and Zoonotic Diseases: Opportunities and Integratd Intervention Strategies, Institute of Medicine (US) Forum on Microbial Threats, Editor. 2011, National Academies Press: Washington (DC).

27. Hotez, P.J., Empowering women and improving female reproductive health through control of neglected tropical diseases. PLoS neglected tropical diseases, 2009. 3(11): p. e559-e559.

28. Hofstraat, K. and W.H. van Brakel, Social stigma towards neglected tropical diseases: a systematic review. International Health, 2016. 8(suppl_1): p. i53-i70.

29. Sun, N. and J.J. Amon, Addressing Inequity: Neglected Tropical Diseases and Human Rights. Health and human rights, 2018. 20(1): p. 11-25.

30. Dean, L., et al., Neglected tropical disease as a 'biographical disruption': Listening to the narratives of affected persons to develop integrated people centred care in Liberia. PLOS Neglected Tropical Diseases, 2019. 13(9): p. e0007710.

31. UNDP, The Gender Dimensions of Neglected Tropical Diseases. Discussion Paper. 2019, United Nations Development Programme: New York. Available from: https://adphealth.org/upload/resource/2523_ADP_Discussion_Paper_NTDs_211119_web.pdf

32. Faramand, T.H., et al., Desk Review on gender Issues Affecting Neglected Tropical Diseases. 2019, RTI International: Washington DC.

33. Onifade, D.A., et al., Gender-related factors influencing tuberculosis control in shantytowns: a qualitative study. BMC Public Health, 2010. 10(1): p. 381.

34. Mhalu, G., et al., Explaining patient delay in healthcare seeking and loss to diagnostic follow-up among patients with presumptive tuberculosis in Tanzania: a mixed-methods study. BMC Health Services Research, 2019. 19(1): p. 217.

35. Wang, J., et al., Gender difference in knowledge of tuberculosis and associated health-care seeking behaviors: a cross-sectional study in a rural area of China. BMC public health, 2008. 8: p. 354-354.

36. Karim, F., et al., Gender differences in delays in diagnosis and treatment of tuberculosis. Health Policy and Planning, 2007. 22(5): p. 329-334.

37. Hudelson, P., Gender differentials in tuberculosis: The role of socio-economic and cultural factors. Tubercle and Lung Disease, 1996. 77(5): p. 391-400.

38. Miller, C., et al., 'It makes the patient's spirit weaker': tuberculosis stigma and gender interaction in Dar es Salaam, Tanzania. Int J Tuberc Lung Dis, 2017. 21(11): p. 42-48.

39. Connolly, M. and P. Nunn, Women and tuberculosis. World Health Stat Q, 1996. 49(2): p. 115-9.

40. Borgdorff, M.W., et al., Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. The International Journal of Tuberculosis and Lung Disease, 2000. 4(2): p. 123-132.

41. Thorson, A.E., Gender differences in tuberculosis. International Journal of Infectious Diseases, 2014. 21: p. 65-66.

42. Hotez, P.J., et al., Female genital schistosomiasis and HIV/AIDS: Reversing the neglect of girls and women. PLOS Neglected Tropical Diseases, 2019. 13(4): p. e0007025.

43. Engels, D., et al., Integration of prevention and control measures for female genital schistosomiasis, HIV and cervical cancer. Bulletin of the World Health Organization, 2020. 98: p. 615-624.

44. Khalkhali, H.R., et al., Prevalence of cystic echinococcosis in Iran: a systematic review and meta-analysis. Journal of Helminthology, 2018. 92(3): p. 260-268.

45. El Berbri, I., et al., Knowledge, attitudes and practices with regard to the presence, transmission, impact, and control of cystic echinococcosis in Sidi Kacem Province, Morocco. Infectious Diseases of Poverty, 2015. 4(1): p. 48.

46. Abdulhameed, M.F., et al., Neglected Zoonoses and the Missing Opportunities for One Health Education: The Case of Cystic Echinococcosis among Surgically Operated Patients in Basrah, Southern Iraq. Diseases, 2019. 7(1).

47. Gołąb, E. and M.P. Czarkowski, Echinococcosis and cysticercosis in Poland in 2012. Przegl Epidemiol, 2014. 68(2): p. 279-82, 379-81.

48. Budke, C.M., et al., A Systematic Review of the Literature on Cystic Echinococcosis Frequency Worldwide and Its Associated Clinical Manifestations. The American Journal of Tropical Medicine and Hygiene, 2013. 88(6): p. 1011-1027.

49. PAHO. Taenia solium Taeniasis/ cysticercosis. 2020 [cited 2020 15.10.]; Available from: https://www.paho.org/en/topics/taenia-solium-taeniasiscysticercosis.

50. Prasad, K.N., et al., Prevalence and associated risk factors of Taenia solium taeniasis in a rural pig farming community of north India. Trans R Soc Trop Med Hyg, 2007. 101(12): p. 1241-7.

51. de Kaminsky, R.G., Taeniasis-cysticercosis in Honduras. Transactions of The Royal Society of Tropical Medicine and Hygiene, 1991. 85(4): p. 531-534.

52. Garcia-Noval, J., et al., Epidemiology of Taenia solium Taeniasis and Cysticercosis in Two Rural Guatemalan Communities. The American Journal of Tropical Medicine and Hygiene, 1996. 55(3): p. 282-289.

53. Al-Kamel, M.A., Impact of leishmaniasis in women: a practical review with an update on my ISD-supported initiative to combat leishmaniasis in Yemen (ELYP). International Journal of Women's Dermatology, 2016. 2(3): p. 93-101.

54. Chahed, M.K., et al., Psychological and Psychosocial Consequences of Zoonotic Cutaneous Leishmaniasis among Women in Tunisia: Preliminary Findings from an Exploratory Study. PLOS Neglected Tropical Diseases, 2016. 10(10): p. e0005090.

55. Al-khayat, Z.A.Y., N.F.S. Agha, and K.I.F. Alharmni, Gender differences in the severity and features of lesions among Cutaneous Leishmaniasis patients. Journal of Contemporary Medical Sciences; Vol 5 No 6 (2019): November-December 2019, 2020.

56. Jayakumar, B., et al., "It's just a fever": Gender based barriers to care-seeking for visceral leishmaniasis in highly endemic districts of India: A qualitative study. PLOS Neglected Tropical Diseases, 2019. 13(6): p. e0007457.

57. Hotez, P.J., Stigma: The Stealth Weapon of the NTD. PLOS Neglected Tropical Diseases, 2008. 2(4): p. e230.

58. Shoemaker, E.A., et al., Gender and neglected tropical disease front-line workers: Data from 16 countries. PLOS ONE, 2019. 14(12): p. e0224925.

59. Hotez, P.J. and A. Kamath, Neglected Tropical Diseases in Sub-Saharan Africa: Review of Their Prevalence, Distribution, and Disease Burden. PLOS Neglected Tropical Diseases, 2009. 3(8): p. e412.

60. Cevallos, V., et al., Association of Conjunctival Bacterial Infection and Female Sex in Cicatricial Trachoma. Investigative Ophthalmology & Visual Science, 2012. 53(9): p. 5208-5212.

61. Courtright, P. and S.K. West, Contribution of Sex-linked Biology and Gender Roles to Disparities with Trachoma. Emerging Infectious Diseases, 2004. 10(11).

62. Cromwell, E.A., et al., The excess burden of trachomatous trichiasis in women: A systematic review and meta-analysis. Transactions of The Royal Society of Tropical Medicine and Hygiene, 2009. 103(10): p. 985-992.

63. Golovaty, I., et al., Access to Water Source, Latrine Facilities and Other Risk Factors of Active Trachoma in Ankober, Ethiopia. PLOS ONE, 2009. 4(8): p. e6702.

64. Munoz, B., et al., Incidence estimates of late stages of trachoma among women in a hyperendemic area of central Tanzania. Tropical Medicine & International Health, 1997. 2(11): p. 1030-1038.

65. Watts, S.J., W.R. Brieger, and M. Yacoob, Guinea worm: An in-depth study of what happens to mothers, families and communities. Social Science & Medicine, 1989. 29(9): p. 1043-1049.

66. Guthmann, J.P., et al., Guinea worm disease in Ayod, Upper Nile Province, southern Sudan: a cross-sectional study. Tropical Medicine & International Health, 1996. 1(1): p. 117-123.

67. Okwa, O.O., Tropical Parasitic Diseases and Women. Annals of African Medicine, 2007. 6(4): p. 157-163.

68. Pinto Dias, J.C., Tropical Diseases and the Gender Approach. Bulletin of PAHO, 1996. 30(3): p. 242-260.

69. Michelson, E.H., Adam's rib awry? Women and schistosomiasis. Social Science & Medicine, 1993. 37(4): p. 493-501.

70. Zodpey, S.P., R.R. Tiwari, and A.D. Salodkar, Gender differentials in the social and family life of leprosy patients. Lepr Rev, 2000. 71(4): p. 505-10.

71. Dijkstra, J.I., W. Brakel, and M.V. Elteren, Gender and leprosy-related stigma in endemic areas: A systematic review. Leprosy Review, 2017. 88: p. 419-440.

72. Oliveira, M.H.d., The effects of leprosy on men and women: a Gender Study. 1997, Geneva: WHO.

73. Vlassoff, C., S. Khot, and S. Rao, Double jeopardy: women and leprosy in India. World Health Stat Q, 1996. 49(2): p. 120-6.

74. Varkevisser, C.M., et al., Gender and leprosy: case studies in Indonesia, Nigeria, Nepal and Brazil. Lepr Rev, 2009. 80(1): p. 65-76.

75. Rao, S., et al., Gender differentials in the social impact of leprosy. Leprosy Review, 1996. 67: p. 190-199.

76. Ramos, J.M., et al., Gender differential on characteristics and outcome of leprosy patients admitted to a long-term care rural hospital in South-Eastern Ethiopia. International Journal for Equity in Health, 2012. 11(1): p. 56.

77. Mastrangelo, G., et al., Leprosy reactions: the effect of gender and household contacts. Memórias do Instituto Oswaldo Cruz, 2011. 106: p. 92-96.

78. Le Grand, A., Women and leprosy: a review. Lepr Rev, 1997. 68(3): p. 203-11.

79. Perera, M., et al., Neglected Patients with a Neglected Disease? A Qualitative Study of Lymphatic Filariasis. PLOS Neglected Tropical Diseases, 2007. 1(2): p. e128.

80. Dreyer, G., J. Norões, and D. Addiss, The silent burden of sexual disability associated with lymphatic filariasis. Acta Trop, 1997. 63(1): p. 57-60.

81. Wynd, S., et al., Understanding the community impact of lymphatic filariasis: a review of the socialculture literature. Bulletin of the World Health Organization, 2007. 85(6): p. 421-500.

82. Person, B., et al., "Can It Be That God Does Not Remember Me": A Qualitative Study on the Psychological Distress, Suffering, and Coping of Dominican Women With Chronic Filarial Lymphedema and Elephantiasis of the Leg. Health Care for Women International, 2008. 29(4): p. 349-365.

83. Ali, A., E.Y. Ahmed, and D. Sifer, A Study on Knowledge, Attitude and Practice of rabies among residents in Addis Ababa, Ethiopia. African Journals Online, 2013. 17(2).

84. Kabeta, T., et al., Knowledge, Attitudes and Practices of Animal Bite Victims Attending an Anti-rabies Health Center in Jimma Town, Ethiopia. PLOS Neglected Tropical Diseases, 2015. 9(6): p. e0003867.

85. Kiffner, C., et al., Comparative knowledge, attitudes, and practices regarding anthrax, brucellosis, and rabies in three districts of northern Tanzania. BMC Public Health, 2019. 19(1): p. 1625.

86. Palamar, M.B., et al., Assessing Rabies Knowledge and Perceptions Among Ethnic Minorities in Greensboro, North Carolina. The Journal of Wildlife Management, 2013. 77(7): p. 1321-1326.

87. Debacker, M., et al., Mycobacterium ulcerans disease: role of age and gender in incidence and morbidity. Tropical Medicine & International Health, 2004. 9(12): p. 1297-1304.

88. Fearon, E., et al., HIV testing, care and viral suppression among men who have sex with men and transgender individuals in Johannesburg, South Africa. PLOS ONE, 2020. 15(6): p. e0234384.

89. Silva-Santisteban, A., et al., HIV prevention among transgender women in Latin America: implementation, gaps and challenges. J Int AIDS Soc, 2016. 19(3 Suppl 2): p. 20799.

90. Pal, K., et al., Acceptability Study on HIV Self-Testing among Transgender Women, Men who Have Sex with Men, and Female Entertainment Workers in Cambodia: A Qualitative Analysis. PLOS ONE, 2016. 11(11): p. e0166129.

91. Heintz, A.J. and R.M. Melendez, Intimate Partner Violence and HIV/STD Risk Among Lesbian, Gay, Bisexual, and Transgender Individuals. Journal of Interpersonal Violence, 2006. 21(2): p. 193-208.

92. Melendez, R.M. and R. Pinto, 'It's really a hard life': Love, gender and HIV risk among male-to-female transgender persons. Culture, Health & Sexuality, 2007. 9(3): p. 233-245.

93. Poteat, T.C., M. Malik, and C. Beyrer, Epidemiology of HIV, Sexually Transmitted Infections, Viral Hepatitis, and Tuberculosis Among Incarcerated Transgender People: A Case of Limited Data. Epidemiologic Reviews, 2018. 40(1): p. 27-39.

94. Gonzales, G. and C. Henning-Smith, Barriers to Care Among Transgender and Gender Nonconforming Adults. The Milbank Quarterly, 2017. 95(4): p. 726-748.

95. Hubach, R.D., et al., Barriers to Access and Adoption of Pre-Exposure Prophylaxis for the Prevention of HIV Among Men Who Have Sex With Men (MSM) in a Relatively Rural State. AIDS Education and Prevention, 2017. 29(4): p. 315-329.

96. Coulter, R.W.S., et al., Research Funded by the National Institutes of Health on the Health of Lesbian, Gay, Bisexual, Ωand Transgender Populations. American Journal of Public Health, 2014. 104(2): p. e105-e112.

97. Seale, A., A. Bains, and S. Avrett, Partnership, sex, and marginalization: Moving the Global Fund sexual orientation and gender identities agenda. Health Hum Rights, 2010. 12(1): p. 123-35.

98. Ferreira Júnior, S., P.M.S.B. Francisco, and P.A. Nogueira, Conhecimento, atitudes e práticas sobre tuberculose entre transgêneros na cidade de São Paulo, Brasil. Ciência & Saúde Coletiva, 2019. 24: p. 3025-3036.

99. The World Bank. DataBank. 2020 [cited 2020 14 November 2020]; Available from: https://databank.worldbank.org/reports.aspx?source=2&country=ETH.

100. WHO. Health Action in Crises: Ethiopia. 2020 [cited 2020 14 November 2020]; Available from: https://www.who.int/hac/donorinfo/callsformobilisation/ethiopia_resmob.pdf?ua=1.

101. UNDP, Global Multidimensional Poverty Index 2019: Illumanting Inequalities. 2019, New York: UNDP and Oxford Poverty and Human Development Intiat. Available from: http://hdr.undp.org/en/2019-MPI

102. WHO. Ethiopia. 2020 [cited 2020 14.11.2020]; Available from: https://www.afro.who.int/countries/ethiopia.

103. Teklu, T., et al., Latent tuberculosis infection and associated risk indicators in pastoral communities in southern Ethiopia: a community based cross-sectional study. BMC Public Health, 2018. 18(1): p. 266.

104. Deribew, A., et al., Tuberculosis Burden in Ethiopia from 1990 to 2016: Evidence from the Global Burden of Diseases 2016 Study. Ethiopian journal of health sciences, 2018. 28(5): p. 519-528.

105. Shenoi, S., et al., Multidrug-resistant and extensively drug-resistant tuberculosis: consequences for the global HIV community. Current opinion in infectious diseases, 2009. 22(1): p. 11-17.

106. De Coninck, Z., et al., Improved HIV Awareness and Perceived Empowerment to Negotiate Safe Sex among Married Women in Ethiopia between 2005 and 2011. PLOS ONE, 2014. 9(12): p. e115453.

107. Gebremichael, D.Y., et al., Gender difference in health related quality of life and associated factors among people living with HIV/AIDS attending anti-retroviral therapy at public health facilities, western Ethiopia: comparative cross sectional study. BMC Public Health, 2018. 18(1): p. 537.

108. Deribe, K., et al., The burden of neglected tropical diseases in Ethiopia, and opportunities for integrated control and elimination. Parasites & Vectors, 2012. 5(1): p. 240.

109. Wharton-Smith, A., et al., Gender-related factors affecting health seeking for neglected tropical diseases: findings from a qualitative study in Ethiopia. PLOS Neglected Tropical Diseases, 2019. 13(12): p. e0007840.

110. Epstein, H.M., Medicine's Biggest Blind Spot Women's Bodies. Society to Improve Diagnosis in Medicine, 2019. Online.

111. Sánchez-Serrano, I., Gender-Specific Medicine's Imminent Coming of Age. Gender and the Genome, 2017. 1(4): p. 1-7.

112. TDR, Health Product Research and Development Fund. A Proposal for Financing and Operation. 2016, Geneva: TDR / WHO.

113. Schiebinger, L. Designing Health & Biomedical Research. Gendered Innovations in Science, Health & Medicine, Engineering, and Environment 2020 [cited 2020 13 November 2020]; Available from: https://genderedinnovations.stanford.edu/methods/health.html.

114. Gahagan, J., K. Gray, and A. Whynacht, Sex and gender matter in health research: addressing health inequities in health research reporting. International Journal for Equity in Health, 2015. 14(1): p. 12.

115. Canadian Institutes of Health Research. Integrating Sex & Gender in Health Research. Online Training Module. Available from: https://cihr-irsc.gc.ca/e/49347.html 2020

116. Johnson, J.L., L. Greaves, and R. Repta, Better science with sex and gender: Facilitating the use of a sex and gender-based analysis in health research. International Journal for Equity in Health, 2009. 8(1): p. 14.

117. Ravindran, T.S., et al., Making pharmaceutical research and regulation work for women. BMJ, 2020. 371: p. m3808.

118. Filardo, G., et al., Trends and comparison of female first authorship in high impact medical journals: observational study (1994-2014). BMJ, 2016. 352: p. i847.

119. Greaves, L., Why Put Gender and Sex Into Health Research?, in Designing and Conducting Gender, Sex, and Health Research, J.L. Oliffe and L. Greaves, Editors. 2012, Sage: London. p. 3-14.

120. Tannenbaum, C. and D. Day, Age and sex in drug development and testing for adults. Pharmacological Research, 2017. 121: p. 83-93.

121. McMarthy, M. Measuring and Manipulating Sex Hormones in Laboratory Animals. Meet the Methods Series 2020; Available from: https://cihr-irsc.gc.ca/e/52107.html.

122. Song, M.M., et al., Development of a PubMed Based Search Tool for Identifying Sex and Gender Specific Health Literature. Journal of women's health (2002), 2016. 25(2): p. 181-187.

123. Beery, A.K. and I. Zucker, Sex bias in neuroscience and biomedical research. Neuroscience and biobehavioral reviews, 2011. 35(3): p. 565-572.

124. McCullough, L.D., et al., NIH initiative to balance sex of animals in preclinical studies: generative questions to guide policy, implementation, and metrics. Biology of sex differences, 2014. 5: p. 15-15.

125. Schiebinger, L., et al. Animal Research 2: Analyzing How Sex and Gender Interact. Gendered Innovations in Science, Health & Medicine, Engineering, and Environment 2020.

126. Zucker, I. and A.K. Beery, Males still dominate animal studies. Nature, 2010. 465(7299): p. 690.

127. Sugimoto, C.R., et al., Factors affecting sex-related reporting in medical research: a cross-disciplinary bibliometric analysis. The Lancet, 2019. 393(10171): p. 550-559.

128. Goldmann, B.J., A Drug Company Report: What is the Same and What is Changing with Respect to Inclusion/Exclusion of Women in Clinical Trials. Food and Drug Law Journal, 1993. 48(2): p. 169-174.

129. Ruiz Cantero, M.T. and M.A. Pardo, European Medicines Agency policies for clinical trials leave women unprotected. Journal of Epidemiology and Community Health (1979-), 2006. 60(11): p. 911-913.

130. Couderc-Pétry, M., et al., Inclusion of women susceptible to and becoming pregnant in preregistration clinical trials in low- and middle-income countries: A proposal for neglected tropical diseases. PLOS Neglected Tropical Diseases, 2020. 14(6): p. e0008140.

131. Franconi, F., et al., Sex-Gender Variable: Methodological Recommendations for Increasing Scientific Value of Clinical Studies. Cells, 2019. 8(5): p. 476.

132. Avery, E. and J. Clark, Sex-related reporting in randomised controlled trials in medical journals. Lancet, 2016. 388(10062): p. 2839-2840.

133. Scott, P.E., et al., Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs. J Am Coll Cardiol, 2018. 71(18): p. 1960-1969.

134. Liu, K.A. and N.A. Mager, Women's involvement in clinical trials: historical perspective and future implications. Pharm Pract (Granada), 2016. 14(1): p. 708.

135. Ingersoll, M.A., Sex differences shape the response to infectious diseases. PLOS Pathogens, 2017. 13(12): p. e1006688.

136. Prout, M.N. and S.S. Fish, Participation of women in clinical trials of drug therapies: a context for the controversies. Medscape Womens Health, 2001. 6(5): p. 1.

137. Rosser, S.V., Re-visioning Clinical Research: Gender and the Ethics of Experimental Design. Hypatia, 1989. 4(2): p. 125-139.

138. van der Graaf, R., et al., Fair inclusion of pregnant women in clinical trials: an integrated scientific and ethical approach. Trials, 2018. 19(1): p. 78.

139. Ravinetto, R., et al., Clinical Research in Neglected Tropical Diseases: The Challenge of Implementing Good Clinical (Laboratory) Practices. PLOS Neglected Tropical Diseases, 2016. 10(11): p. e0004654.

140. Simon, G.G., Impacts of neglected tropical disease on incidence and progression of HIV/AIDS, tuberculosis, and malaria: scientific links. Int J Infect Dis, 2016. 42: p. 54-57.

141. Bal, M., et al., Maternal Infection Is a Risk Factor for Early Childhood Infection in Filariasis. PLOS Neglected Tropical Diseases, 2015. 9(7): p. e0003955.

142. ICH. Search the Index of ICH Guidelines. 2020 [cited 2020 16.11.2020]; Available from: https://www.ich.org/page/search-index-ich-guidelines.

143. Payne, P., Including Pregnant Women in Clinical Research: Practical Guidance for Institutional Review Boards. Ethics & Human Research, 2019. 41(6): p. 35-40.

144. Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research, Guidance Document Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials. FDA-2018-D-1201. 2018, Food and Drug Administration. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pregnant-women-scientific-and-ethical-considerations-inclusion-clinical-trials

145. Rogerson, S.J. and E.H. Aitken, Progress towards vaccines to protect pregnant women from malaria. EBioMedicine, 2019. 42: p. 12-13.

146. Gallagher, G.M. Malaria Vaccine for Pregnant Women Safe in Phase 1 Trial. 2020 [cited 2020 5.10.2020]; Available from: https://www.contagionlive.com/view/promising-phase-1-results-in-malaria-vaccine-for-pregnant-women.

147. Venture, M.f.M., Malaria in Mothers and Babies. 2020, Geneva: MMV. Available from: https://www.mmv.org/newsroom/publications/mimba-malaria-mothers-and-babies

148. Fisher, J.A. and L.M. Ronald, Sex, gender, and pharmaceutical politics: From drug development to marketing. Gender Medicine, 2010. 7(4): p. 357-370.

149. CIHR IRSC, What a Difference Sex and Gender Make. 2012, Ottawa: CIHR IRSC. Available from: https://cihr-irsc.gc.ca/e/documents/What_a_Difference_Sex_and_Gender_Make-en.pdf

150. WHO, Integrating Neglected Tropical Diseases into Global Health and Development. 2017, Geneva: WHO. Available from: https://www.who.int/neglected_diseases/resources/9789241565448/en

151. WHO. Innovative and Intensified Disease Management (IDM). 2020 [cited 2020 29.11.2020]; Available from: https://www.who.int/neglected_diseases/disease_management/Innovative_Intensified_Disease_Management/en/.

152. Cohn, D.A., et al., Gender equity in mass drug administration for neglected tropical diseases: data from 16 countries. International Health, 2019. 11(5): p. 370-378.

153. Webster, J.P., et al., The contribution of mass drug administration to global health: past, present and future. Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 2014. 369(1645): p. 20130434-20130434.

154. Bethony, J.M., et al., Vaccines to combat the neglected tropical diseases. Immunological reviews, 2011. 239(1): p. 237-270.

155. WHO, Mass drug administration for falciparum malaria. A practical field manual. 2017, Geneva: WHO. Available from: https://www.who.int/malaria/publications/atoz/9789241513104/en/

156. Gyapong, J.O., et al., Integration of control of neglected tropical diseases into health-care systems: challenges and opportunities. The Lancet, 2010. 375(9709): p. 160-165.

157. Rilkoff, H., et al., Exploring Gender Dimensions of Treatment Programmes for Neglected Tropical Diseases in Uganda. PLOS Neglected Tropical Diseases, 2013. 7(7): p. e2312.

158. Theobald, S., et al., 20 years of gender mainstreaming in health: lessons and reflections for the neglected tropical diseases community. BMJ global health, 2017. 2(4).

159. Mbabazi, P., Medical Epidemiologist, Department of Control of NTDs, WHO, in Interview, M. Told, Editor. 2020.

160. Holveck, J.C., et al., Prevention, control, and elimination of neglected diseases in the Americas: Pathways to integrated, inter-programmatic, inter-sectoral action for health and development. BMC Public Health, 2007. 7(1): p. 6.

161. WHO, Gender analysis in health: A review of selected tools. 2002, Geneva: WHO. Available from: https://www.who.int/gender-equity-rights/knowledge/9241590408/en

162. WHO, Gender mainstreaming for health managers: a practical approach. 2011, Geneva: WHO. Available from: https://www.who.int/gender-equity-rights/knowledge/health_managers_guide/en

163. Research in Gender and Ethics (RinGs). Ten Gender Analysis Frameworks & Tools to Aid with Health Systems Research. 2015; Available from: https://www.ringsgenderresearch.org/wp-content/uploads/2018/07/Ten-Gender-Analysis-Frameworks-and-Tools-to-Aid-with-HSR.pdf.

164. UNAIDS, UNAIDS Gender Assessment Tool: Towards a gender-transformative HIV response. 2014 (updated 2018), Geneva: UNAIDS. Available from: https://www.unaids.org/sites/default/files/media_asset/unaids-gender-assessment-tool_en.pdf

165. Pastrana, N.A., C. Somerville, and L.S. Suggs, The gender responsiveness of social marketing internventions focused on neglected tropical diseases. Global Health Action, 2020. 13(1).

166. Degnan Kambou, S., et al., Power, pleasure, pain, and shame: Assimilating gender and sexuality into community-centred reproductive health and HIV prevention programmes in India. Global Public Health, 2007. 2(2): p. 155-168.

167. Ozano, K., et al., A call to action for universal health coverage: Why we need to address gender inequities in the neglected tropical diseases community. PLOS Neglected Tropical Diseases, 2020. 14(3): p. e0007786.

168. WHO Western Pacific Region, Taking sex and gender into account in emerging infectious disease programmes: An analytical framework. 2011, Geneva: WHO. Available from: https://iris.wpro.who.int/handle/10665.1/7977

169. Doyal, L., Sex and Gender: The Challenges for Epidemiologists. International Journal of Health Services, 2003. 33(3): p. 569-579.

170. FIND and Women in Global Health, Health in Their Hands: Testing & Women's Empowerment Means Better Health For All. 2020, Geneva: FIND. Available from: https://c8fbe10e-fb87-47e7-844b-4e700959d2d4.filesusr.com/ugd/ffa4bc_507919addd1541d-4902129365c9a8dd1.pdf

171. Draft Guideline on good pharmacovigilance practices (GVP) - Product- or Population-Specific Considerations III: Pregnant and breastfeeding women, 2019, p.3. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-good-pharmacovigilance-practices-product-population-specific-considerations-iii_en.pdf

DSW
Deutsche Stiftung
Weltbevölkerung

youth
can