# Chapter 5
# Sexual and Gender Minority Population's Health Burden of Five Noncommunicable Diseases: Cardiovascular Disease, Cancer, Diabetes, Asthma, Chronic Obstructive Pulmonary Disease


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## 5.1 Introduction

As advances are made in precision medicine, life expectancies move steadily toward the century mark, and there is a growing expectation of living healthy lives into advanced age, there is value in comparing the health status between the sexual and gender minority (SGM) populations and heterosexual/cisgender populations. In the realm of noncommunicable diseases (NCDs), incidence and prevalence are markers of the health of a population. Evaluating these statistics between populations allows for the discovery of disparities and subsequent targeted interventions to close health gaps. Globally, factors ranging from overt discrimination, economic deprivation, and lack of access to healthcare resources may drive potential differences in NCD prevalence among SGM populations. With the intention to describe the health of SGM populations across the globe, a thorough literature review was undertaken to capture peer-reviewed manuscripts that reported on NCDs prevalence or incidence in the SGM population.

Among the 169 selected articles garnered from the literature review that addressed the five selected noncommunicable diseases (NCDs), most did not report on prevalence or incidence among SGM individuals, but rather risk factors only or as a review of studies on NCDs. Nevertheless, among these, 71% ($n$ = 119) studied the US population, with the next top five countries for the number of studies being

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the Netherlands ($n$ = 10), Australia ($n$ = 8), England/United Kingdom ($n$ = 5 each), and Italy/Canada ($n$ = 3 each). Data reported here represent 22 countries. The geographic distribution was striking, with sexual minority original research almost exclusively provided by a few "mature" countries ($n$ = 9), and only one study on CVD from Guam, a "developing" county. In contrast, studies of cancer among transgender populations are almost exclusively case studies or case series ($n$ = 48) and span the globe. For sexual minority results, except for Australia, North America, and Western European countries, limited generalizations can be made for other regions given sparse data. For studies of transgender populations, only 11 provided evidence for the population as opposed to unique aspects of individual patients as reported in the case studies and case series.

Beyond the obvious sparse data available to assess the global burden of NCDs, another important factor is the supporting role of the medical system. An in-depth discussion of this system-level factor in NCD morbidity is beyond the scope of this chapter. Briefly, however, the Economist Intelligence Unit created a healthcare index that used data from 60 countries of various income levels (The Economist Intelligence Unit, 2019). In this analysis, three categories were developed to describe the region's ability to provide appropriate health services. African and Middle Eastern countries generally scored as "emerging." In Africa, the major challenge is addressing infectious diseases, NCDs, and traumatic injuries with workforce shortages (Azevedo, 2017). In contrast, Middle Eastern countries struggle to address the increased incidence of NCDs as well as considerable variability in health service inequities due to the effects of social determinants of health (Kauth et al., 2017).

For the next group, Asia-Pacific nations and most countries in Latin America scored "developed." The challenges in these regions are divided into disparities between wealthier countries, such as Japan and Australia, and less wealthy countries, such as Afghanistan and Bolivia. In wealthier countries, the challenge is providing adequate care for historically marginalized populations, such as the Maori of New Zealand (Ellison-Loschmann & Pearce, 2006). Among the poorer countries, a challenge is delivering healthcare services to their population living on remote islands or in rural areas. Numerous studies examining healthcare access in developed countries have reported multiple barriers at both the individual and structural levels (Baptiste-Roberts et al., 2017), whereas disentangling sexual politics from healthcare to allow for safe access continues to be challenging in emerging and developed countries (Kelly-Hanku et al., 2020; Mahdavi, 2019).

The third category comprised of Europe and North America scored "mature." Although these regions, in general, provide high-quality care, there are large disparities in affordability and access to care within some countries. Compared to European countries, the United States has recently witnessed a widening of health inequalities (Mackenbach et al., 2018). Using a different metric, the Global Burden of Disease Study 2016 also described healthcare access and quality for each country in the world with similar but more nuanced findings (G. B. D. Healthcare Access and Quality Collaborators, 2018). A logical correlation between access to care and quality of care for NCDs will influence the trajectory of disease management. This trajectory can be negatively exacerbated among SGM populations.

Each section of this chapter will begin with a brief overview of the global burden of the specific NCD followed by a description of the burden in sexual minority and transgender populations, respectively. We recognize the wide diversity in both sexual orientation and gender identity across the globe. For the purposes of this chapter, we will address groups identifying as lesbian, gay, or bisexual for sections concerning sexual orientation. While we recognize that gender is not a binary construct, the existing literature broadly focuses on people identifying as transfeminine, transmasculine, and non-binary. As such, those are the groupings we will use in discussing the literature. This method of organization inherently leaves out individuals not identifying in these groups but who are still considered sexual or gender minorities.

## 5.2 Cardiovascular Disease (CVD)

CVD is a group of medical conditions that affect the heart and blood vessels. Diseases include coronary artery diseases (CADs) such as myocardial infarction (aka "heart attack"), stroke, and peripheral artery disease. Although not covered in this section, hypertension (HTN; aka high blood pressure) is also considered a CVD. HTN is often called a "silent killer" as there are rarely signs and symptoms thereby leading to substantial underreporting of this condition. Several medical conditions can lead to secondary HTN, including kidney disease, obstructive sleep apnea, thyroid problems, and adrenal gland tumors (Puar et al., 2016). Numerous concerns limit the ability to compare primary/secondary hypertension around the world that led to the decision to not report these findings since the interpretation of study results would be country-specific and more importantly year-specific.

CVD continues to be the leading cause of death in the world for both men and women (Clark, 2013). However, incidence rates for CVD vary by gender among younger cohorts. Specifically, CVD tends to develop 7–10 years later in women compared to men (Maas & Appelman, 2010). Afterward, the incidence rates are similar between men and women (Kazis et al., 2012). Among countries with greater than 15% of the population aged 65 and older (i.e., Japan and some European countries) or a projected growing aging population by 2050 (except Pakistan, Afghanistan, Yemen, Iraq, Papua New Guinea, and sub-Saharan Africa (except for Botswana)), CVD burden can be expected to persist or increase (Population Reference Bureau, 2018).

The impact of CVD on each nation's population remains high. Globally, disability-adjusted life years (DALY) for ischemic heart disease was ranked third in 1990 and almost 20 years later in 2019 remains at the same level of prevalence among 25–49-year-olds. In 2019, stroke ranked ninth for this age group. For those 50 and older, ischemic heart disease is ranked first and stroke second as a leading cause of DALY (G. B. D. Diseases and Injuries Collaborators, 2020) over the 30-year period.

### 5.2.1 Epidemiology of CVD in Sexual Minority Populations

According to our literature review, over 30 studies have been published on CVD incidence and/or risk comparing sexual minority (SM) populations to heterosexual populations. All of these studies on CVD prevalence described US residents, with a small number of studies on CVD risk from other mature countries (e.g., Sweden (Branstrom et al., 2016), Canada (Steele et al., 2009; Veenstra, 2013), and Switzerland (Wang et al., 2007)). Three systematic reviews have been completed, with one evaluating CVD prevalence among SMs using studies published from 1985 to 2015 (Caceres et al., 2017). The second included a meta-analysis and reported the prevalence of three NCDs—diabetes mellitus and cardiovascular and respiratory conditions in SM women using studies published from 2010 to 2016 (Meads et al., 2018). The third systematic review evaluated the prevalence of NCDs, including the five selected for this chapter, among SM women using studies published from 2009 to 2013 (Simoni et al., 2017). Finally, two critical reviews of the CVD prevalence literature for the SM population were completed (Caceres et al., 2017; McElroy & Brown, 2018).

Among the numerous studies, a few reported a significant increased prevalence of CVD among SMs compared to heterosexual populations. In a study comparing SM women and men to heterosexuals, Fredriksen-Goldsen and colleagues reported only lesbians and bisexual women aged 50 years and older (range 50–94 years for females) had increased CVD prevalence, defined as physician-diagnosed heart attack, angina, or stroke diagnosis (Fredriksen-Goldsen et al., 2013b). One small study completed by the Los Angeles County Health Department in California reported increased CVD prevalence for lesbians and bisexual women compared to heterosexual women (Diamant & Wold, 2003; Diamant et al., 2000).

Some studies found bisexuals at higher risk, with one study finding bisexual men, but not gay men, lesbians, or bisexual women had a higher CVD prevalence (Blosnich et al., 2014). Another study found that bisexual women had higher stroke prevalence compared to heterosexual women (Caceres et al., 2019b). With regard to age differences, Boehmer and colleagues found increased CVD prevalence among only young male and female SMs (<40 years old) compared to heterosexuals but no difference among older age groups: 40–59 years or >59 years for either sex (Boehmer et al., 2014).

Comparing race/ethnicities using the 2013–2015 US National Health Interview Survey (NHIS) data, white and Black SM women were more likely to report stroke but not heart disease compared to white and Black heterosexual women, respectively. However, in this same study, Hispanic/Latina SM women were less likely to report heart disease compared to white heterosexual women (Trinh et al., 2017).

In contrast to these handful of studies, many more studies found no difference in or even reduced CVD prevalence between SMs compared to heterosexual populations (Andersen et al., 2014; Blosnich & Silenzio, 2013; Caceres et al., 2019b; Cochran & Mays, 2007; Conron et al., 2010; Diamant & Wold, 2003; Diamant et al., 2000; Garland-Forshee et al., 2014; Matthews & Lee, 2014; Mays et al., 2002;

Patterson & Jabson, 2018; Stupplebeen et al., 2019; Swartz, 2015; Trinh et al., 2017; Valanis et al., 2000; Wallace et al., 2011; Ward et al., 2015). These null findings were supported by Meads and colleagues' meta-analysis of data from 15 CVD prevalence studies in which no difference was found between male or female SMs and their respective heterosexual counterparts for CVD prevalence (Meads et al., 2018).

Several limitations of these studies reduce the generalizability of the findings. The most striking limitation is the lack of peer-reviewed publications from any other country aside from the United States on CVD prevalence by SM status. Among the US studies, comparability was difficult due to differences in measures of CVD (e.g., self-reported, chart extraction), inclusion criteria for CVD medical conditions, and established (and adjustment for) CVD risk factors, such as alcohol consumption, smoking, and obesity. For example, in the systematic review (Caceres et al., 2017), only 7 out of 24 studies that included smoking status used a standardized measure, and only 2 included all nicotine products (Blosnich et al., 2014). Virtually all analyses used self-reported data on CVD risk factors, with less than a quarter of the studies using clinically obtained data to establish the presence of CVD (Caceres et al., 2016). Another limitation in the majority of the studies was the younger age of the SM participants compared to heterosexual participants, although some, but not all, used age-adjusted models. In addition, most studies had a median or mean age of 38–44 years for the SM participants, which is a couple of decades younger than the average age of one type of CVD, heart attack (63 years for men and 73 years for women in the United States; 62.1 years for men and 69.3 years for women globally) (Fuster & Kelly, 2010).

### *5.2.2 Epidemiology of CVD in Transgender and Non-binary Populations*

About the same number of studies as have been done for the SM population have also been completed with transgender populations ($n = 30$). 22 studies were located in eight countries: Belgium, China, Germany, Italy, the Netherlands, Spain, Thailand, and the United States. They characterized changes in biological markers of CVD risk (e.g., total cholesterol, weight, endothelin levels, etc.) following gender-affirming hormone therapy (GAHT) initiation (Bunck et al., 2006; Chandra et al., 2010; Deutsch et al., 2015; Emi et al., 2008; Fisher et al., 2016; Giltay et al., 2004; Jacobeit et al., 2007, 2009; Mueller et al., 2006, 2007; Pelusi et al., 2014). Studies comparing the incidence or risk of CVD between transgender and cisgender populations ($n = 8$) described populations in four countries: Germany, Guam, the Netherlands, and the United States. The five studies not conducted in the United States focused on transgender populations initiating GAHT (Asscheman et al., 1989; Bazarra-Castro et al., 2012; Ott et al., 2010; van Kesteren et al., 1997; Wierckx et al., 2013), whereas US-based studies largely did not account for this

characteristic (Alzahrani et al., 2019; Meyer et al., 2017; Nokoff et al., 2018). Two Europe-based cohorts (Sweden and the Netherlands) assessed CVD-related mortality among transfeminine populations (Asscheman et al., 2011; Dhejne et al., 2011). One US-based study explored CVD among gender non-binary individuals, comprised of both those assigned female at birth (AFAB) as well as those assigned male at birth (AMAB) (Nokoff et al., 2018).

Five reviews have been published to synthesize the evidence concerning CVD among transgender populations (Gooren et al., 2014; Irwig, 2018; Maraka et al., 2017; Streed et al., 2017; Velho et al., 2017). Two scoping reviews of publications from 1989–2011 and 1997–2017 stratified by GAHT use and CVD health outcomes or risk factors (Gooren et al., 2014; Irwig, 2017). Streed et al. conducted a narrative review of literature published 1989–2016 focused on CVD health events among transmasculine and transfeminine populations receiving GAHT and focused distinctly on clinical guidelines for GAHT regimes (Streed et al., 2017). Maraka et al. conducted the only meta-analysis to quantify changes in lipid profile, venous thromboembolism, CVD health events, and mortality among transgender adults receiving GAHT from studies published in 1989–2016 (Maraka et al., 2017). Finally, Velho et al. conducted a systematic review of studies published in 2004–2016 and focused on changes in BMI, blood pressure, and routine blood test results (such as lipid panels) of transmasculine populations following testosterone therapy (Velho et al., 2017). The length of follow-up of these studies ranged from 4 months to 2 years after GAHT initiation.

A number of studies focused on characterizing CVD risk factor changes after initiation of GAHT among transgender populations. The underlying assumption seems to be that the hormonal milieu specific to sex is linked to CVD risk given that among similarly aged men and women, men experience more CVD events; after menopause, more women experience CVD events; and hyperandrogenism in women confers a higher CVD risk (Kannel, 2002; Liu et al., 2001; Wild et al., 2000). However, current thinking explores the multifactorial understanding of CVD risk beyond the hormonal milieu, including genomic and nongenomic effects (Vitale et al., 2010). Findings from these and additional studies will be discussed below.

#### 5.2.2.1 Transfeminine Population

##### 5.2.2.1.1 CVD Risk Factors

Among transfeminine individuals, CVD risk factor changes included increases in weight (Elbers et al., 2003; Giltay et al., 1998, 1999; Gooren et al., 2014; Quiros et al., 2015), body mass index (Klaver et al., 2020; Suppakitjanusant et al., 2020), total body fat (Elbers et al., 2003; Gooren & Giltay, 2014), visceral fat (Giltay et al., 1998), triglycerides (Giltay et al., 1998, 1999; Klaver et al., 2020), fibrinolysis (Elbers et al., 2003; Giltay et al., 1998), and endothelin levels (Polderman et al., 1993). Mixed results among transfeminine individuals were seen for changes in low-density lipoprotein (LDL) cholesterol (Elbers et al., 2003; Gooren & Giltay,

2014; Klaver et al., 2020; Kulprachakarn et al., 2020), blood pressure (Elbers et al., 2003; Giltay et al., 1999; Klaver et al., 2020; Kulprachakarn et al., 2020; Quiros et al., 2015), and markers of inflammation (measured by IL-4, IFN-γ, and C-reactive protein (CRC)) (Giltay et al., 2003; Gooren & Giltay, 2014; Kulprachakarn et al., 2020). No effects among transfeminine individuals were seen in total cholesterol (Elbers et al., 2003; Giltay et al., 1999; Gooren & Giltay, 2014; Klaver et al., 2020; Kulprachakarn et al., 2020), very low-density lipoprotein (VLDL) (Elbers et al., 2003), heart rate (Giltay et al., 1999), or arterial stiffness (measured by distensibility and compliance coefficients of the carotid, femoral, and brachial arteries) (Giltay et al., 1999). Two studies noted an increase in high-density lipoprotein (HDL) cholesterol (Elbers et al., 2003; Gooren et al., 2014). A meta-analysis by Maraka et al. found statistically significant changes only for triglycerides after ≥24 months of follow-up subsequent to GAHT initiation. In this meta-analysis, other lipid measures assessed (i.e., LDL, HDL, and total cholesterol) had no statistically significant change after GAHT initiation (Maraka et al., 2017) (see Table 5.1).

One known risk factor for dangerous clot formation that can lead to CVD events in cisgender women is exogenous estrogen supplementation (Laliberte et al., 2011; Vinogradova et al., 2019). A similar finding of pulmonary embolism and venous thromboembolism was also described in four cohort studies among transfeminine individuals (Asscheman et al., 1989; Getahun et al., 2018; Goodman & Nash, 2019; van Kesteren et al., 1997). One narrative review considered evidence of the association between specific GAHT regimens and venous thromboembolism and pulmonary embolism and suggested that clinicians should favor "low-dose transdermal estrogen and oral bioidentical estrogens (such as 17β-estradiol, estrone, and estriol) and limiting the use of high-dose oral ethinyl estradiol" (Streed et al., 2017, p. 261). Outside of analyses reporting results, this is one of the only sources to suggest specific clinical guidance based on the limited evidence available.

#### 5.2.2.1.2 CVD Prevalence

Mixed results are seen for CVD prevalence when comparing transfeminine individuals with cisgender men across an array of events and conditions including myocardial infarction, congestive heart disease, and stroke (Alzahrani et al., 2019; Bazarra-Castro et al., 2012; Getahun et al., 2018; Nokoff et al., 2018). The largest studies to assess CVD among transfeminine persons compared to cisgender men ($n$ = 3477 and $n$ = 4394) found equivalent incidence of myocardial infarctions and increased incidence of stroke (Goodman & Nash, 2019). Two other studies found no difference in incidence rate (Getahun et al., 2018) or prevalence (Wierckx et al., 2013) of myocardial infarction when comparing transfeminine individuals using GAHT to cisgender men.

Much of the literature focuses on CVD events (stroke, myocardial infarction, venous thromboembolism, and pulmonary embolism) with less attention paid to CVD conditions that lead up to those events such as hyperlipidemia, hypercholesterolemia, and hypertension. One of the larger studies to assess CVD health did not

**Table 5.1** CVD risk profile changes in transfeminine individuals following GAHT initiation

| CVD risk factor | Change after GAHTinitiation | CVD risk profile status | References |
|---|---|---|---|
| Weight | Increase | Increase | Gooren et al. (2014), Elbers et al. (2003), Giltay et al. (1998, 1999) and Quiros et al. (2015) |
| Total body fat | Increase | Increase | Elbers et al. (2003) and Gooren and Giltay (2014) |
| Visceral fat | Increase | Increase | Giltay et al. (1998) |
| Triglycerides | Increase | Increase | Giltay et al. (1998, 1999), Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Fibrinolysis | Increase | Increase | Elbers et al. (2003) and Giltay et al. (1998) |
| Endothelin levels | Increase | Increase | Polderman et al. (1993) |
| LDL (low-density lipoprotein) cholesterol | Mixed evidence | NA | Elbers et al. (2003), Gooren and Giltay (2014), Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Blood pressure | Mixed evidence | NA | Elbers et al. (2003), Giltay et al. (1999), Quiros et al (2015), Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Inflammatory markers (CRP, IFN-γ, IL-4) | Mixed evidence | NA | Gooren and Giltay (2014), Kulprachakarn et al. (2020) and Giltay et al. (2003) |
| Total cholesterol | Mixed evidence | NA | Elbers et al. (2003), Giltay et al. (1999), Gooren and Giltray (2014), Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Very low-density lipoproteins | No changes | Null | Elbers et al. (2003) |
| Heart rate | No changes | Null | Giltay et al. (1999) |
| Arterial stiffness | No changes | Null | Giltay et al. (1999) |
| HDL (high-density lipoprotein) cholesterol | Mixed evidence | NA | Gooren et al. (2014), Elbers et al. (2003), Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Heart rate | No changes | Null | Kulprachakarn et al. (2020) |
| Ankle-brachial index (ABI) | Decrease | Increase | Kulprachakarn et al. (2020) |
| Pulse wave velocity | No changes | Null | Kulprachakarn et al. (2020) |
| Cardio-ankle vascular index (CAVI) | No changes | Null | Kulprachakarn et al. (2020) |
| Carotid intima-media thickness (CIMT) | No changes | Null | Kulprachakarn et al. (2020) |
| Fasting plasma glucose | No changes | Null | Kulprachakarn et al. (2020) and Klaver et al. (2020) |
| Body mass index (BMI) | Increase | Increase | Suppakitjanusant et al. (2020) and Klaver et al. (2020) |

stratify by GAHT use and found no difference in adjusted odds of hypertension when comparing transfeminine individuals ($n = 369$) to cisgender men ($n = 60{,}009$) or cisgender women ($n = 78{,}548$) (Nokoff et al., 2018).

Many of the studies accounting for GAHT are limited by their short duration of post-GAHT follow-up. One may expect that extended use of GAHT among transfeminine individuals may change the hormonal profile-attributable aspects of cardiovascular risk. Without extensive follow-up, this dynamic cannot be understood. Even among individuals using GAHT, which presumably mimics the female hormonal milieu, the CVD risk profile of transfeminine individuals may be closer to that of cisgender men, who share their sex assigned at birth, than that of cisgender women. Additional research is needed to deepen our understanding of genomic and non-genomic factors associated with CVD risk.

#### 5.2.2.2 Transmasculine Populations

##### 5.2.2.2.1 CVD Risk Factors

Among transmasculine individuals initiating GAHT, decreases in HDL cholesterol were observed (Chandra et al., 2010; Deutsch et al., 2015; Giltay et al., 1998, 1999; Klaver et al., 2020; Mueller et al., 2007, 2010). Increases were seen for triglycerides (Emi et al., 2008; Giltay et al., 1998; Klaver et al., 2020; Quiros et al., 2015) and weight (Giltay et al., 1998, 1999, 2004; Gooren & Giltay, 2014). Mixed changes were observed in blood pressure (Elbers et al., 2003; Emi et al., 2008; Giltay et al., 2003; Gooren & Giltay, 2014; Klaver et al., 2020). No effect was seen on arterial stiffness (Giltay et al., 1999), fibrinolysis (Giltay et al., 1998), total cholesterol (Elbers et al., 2003; Gooren & Giltay, 2014; Gooren et al., 2014; Klaver et al., 2020), or BMI (Klaver et al., 2020; Suppakitjanusant et al., 2020). Comparing transmasculine individuals receiving GAHT to cisgender women in routine blood test results for CVD risk factors (such as cholesterol) did not find any difference (Asscheman et al., 1989, 2011; Bazarra-Castro et al., 2012; van Kesteren et al., 1997; Wierckx et al., 2013) (see Table 5.2).

##### 5.2.2.2.2 CVD Prevalence

The largest analysis of transmasculine individuals to date ($n = 2893$) was a US-based cohort that found no difference in venous thromboembolism, myocardial infarction, or stroke when compared to cisgender women ($n = 63{,}855$) (Goodman & Nash, 2019). With the exception of one US-based study that did not account for GAHT usage (Alzahrani et al., 2019), the current evidence does not support an elevated CVD morbidity among transmasculine populations for myocardial infarction, stroke, venous thromboembolism, pulmonary embolism, or hypertension (Asscheman et al., 1989, 2011; Getahun et al., 2018; Goodman & Nash, 2019; van

**Table 5.2** CVD risk profile changes in transmasculine individuals following GAHT initiation

| CVD risk factor | Change after GAHT initiation | CVD risk profile status | References |
|---|---|---|---|
| HDL (high-density lipoprotein) cholesterol | Decrease | Increase | Chandra et al. (2010), Deutsch et al. (2015), Giltay et al. (1998, 1999), Mueller et al. (2007, 2010), Emi et al. (2008) and Klaver et al. (2020) |
| LDL (low-density lipoprotein) | Increase | Increase | Klaver et al. (2020) |
| Triglycerides | Increase | Increase | Giltay et al. (1998), Emi et al. (2008), Quiros et al. (2015) and Klaver et al. (2020) |
| Weight | Increase | Increase | Giltay et al. (1998, 1999, 2004) and Gooren and Giltay (2014) |
| Blood pressure | Mixed evidence | NA | Emi et al. (2008), Gooren and Giltay (2014), Elbers et al. (2003), Giltay et al. (2003) and Klaver et al. (2020) |
| Arterial stiffness | No changes | Null | Gitay et al. (1999) |
| Fibrinolysis | No changes | Null | Giltay et al. (1998) |
| Total cholesterol | Mixed evidence | NA | Gooren and Giltay (2014), Elbers et al. (2003), Gooren and Wierckx (2014) and Klaver et al. (2020) |
| Body mass index (BMI) | Mixed evidence | NA | Suppakitjanusant (2020) and Klaver et al. (2020) |

Kesteren et al., 1997; Wierckx et al., 2013). This assessment is greatly limited by the younger average age of transgender populations in these studies.

#### 5.2.2.3 Gender Non-binary Populations

One general US population-based study accounted for gender non-binary individuals in their analyses (Behavioral Risk Factor Surveillance Study: BRFSS). BRFSS is an annual national study with probabilistic sampling for each state to provide data on health-related risk factors, health outcomes, and healthcare utilization for individual states. Each state had the option of including the Centers for Disease Control and Prevention's approved question on sexual orientation and gender identity (SOGI) beginning in 2014. However, some states included their own version of a SOGI question as early as 2001 (Baker & Hughes, 2017). Comparison groups were selected based on natal sex. In adjusted analyses of non-binary individuals (AFAB, $n = 61$), no differences were found in odds of obesity, overweight status, myocardial infarction, angina/CHD, or stroke when compared to cisgender females ($n = 78{,}548$). Among non-binary individuals (AMAB, $n = 68$), no differences were seen for myocardial infarction or angina/CHD when compared to cisgender males ($n = 60{,}009$). Non-binary individuals with male natal sex were found to have higher odds of obesity/overweight status and lower odds of stroke (Nokoff et al., 2018).

The generalizability of the existing data is limited due to a narrow geographic scope and small sample size. Differences in comparison groups for transgender populations also make comparison of study results challenging. While some smaller studies from the Netherlands indicated specific GAHT regimens, few large-scale studies noted GAHT regimen or duration. This lack of information presents an interpretation challenge when trying to assess the effect that GAHT may have on CVD prevalence. It is also of note that recommended GAHT formulations have changed over the years with potential concomitant health effects. In addition, there is likely a cohort effect due to this change that would need to be considered in comparing studies. Another challenge is that many samples of transgender individuals skew younger, notably in some of the early studies with smaller sample sizes. Younger samples make it more difficult to draw conclusions about CVD outcomes, which have strong relationships with age. Additionally, the mean age reported by a study may not reflect the distribution of the data. Analytically, if a sample has a low number of older transgender individuals and is not a random sample, then selection bias may be introduced, and simply applying statistical adjustments for age may not be a sufficient analytic approach. Among the larger cohort studies represented, the median age was usually in the 40–50-year age bracket (Caceres et al., 2019a; Getahun et al., 2018; Meyer et al., 2017; Nokoff et al., 2018). This is an important context for any discussion of NCDs where age is strongly related, particularly CVD.

## 5.3 Cancer

Approximately 5% of the world's population are cancer survivors (43.8 million), with 20% and 16% of men and women, respectively. In 2018, there were an estimated 18.1 million new cancer cases and 9.6 million cancer deaths. India, China, and other East and Central Asian countries make up approximately half of new cancer cases (American Cancer Society, 2019). Lung, female breast, and colorectal cancers dominate worldwide, together comprising one-third of the cancer burden (Bray et al., 2018). The global picture of cancer incidence shows a mosaic of 23 individual cancer sites that describe 90% of the cancer incidence burden (Bray et al., 2018). By 2040, these numbers are expected to double due to growth and aging populations as well as changes in the prevalence of established cancer-related risk factors such as overweight/obesity, unhealthy diet, physical inactivity, tobacco use, alcohol use, and air pollution (World Health Organization, 2018). The increased prevalence is also expected to be the most pronounced in emerging and developing countries due to an expected shift from cancers related to poverty and infections to cancers associated with lifestyles more typical of mature countries (International Agency for Research on Cancer, 2018; Omran, 2005).

Cancer burden can be described in three ways: incidence, prevalence, and mortality. For this chapter, both incidence and prevalence will be described. Incidence data means the number of all new cancer cases, either overall or for a specific

cancer, typically defined over a year period for the population at risk for that cancer, whereas prevalence includes both newly diagnosed and survivors of cancer.

A frequent statistic used is that 4 in 10 cancer diagnoses are preventable since many cancers are strongly or causally linked to modifiable lifestyle behaviors or treatable/avoidable exposures. The top risk factors are cigarette smoking; secondhand smoke exposure; excess body weight; drinking alcohol; eating red and processed meat; diets low in fruits and vegetables, dietary fiber, and dietary calcium; physical inactivity; ultraviolet (UV) radiation from the sun or indoor tanning; and cancer-associated viruses, including helicobacter pylori, hepatitis B virus (HBV), hepatitis C virus (HPC), human herpes virus type 8 (HHV8), human immunodeficiency virus (HIV), and human papillomavirus (HPV) (Islami et al., 2018). The majority of studies that address cancer burden among the SM population inevitably suggest a disparity in many of the aforementioned established risk factors compared to heterosexual populations (Boehmer & Elk, 2015; Mansh et al., 2015; Meads & Moore, 2013; van der Zee et al., 2013; Ward et al., 2014). However, little is known about the prevalence of most of these risk factors by SM status for the majority of the world's population.

### *5.3.1 Epidemiology of Cancer in Sexual Minority Populations*

The preponderance of studies that describe cancer in SM populations assesses cancer risk with established cancer-related risk factor data and possibly cancer screening behavior. Most of these studies report an increased cancer risk for SMs compared to heterosexual populations. Because of the lack of SM identity in established data systems, such as cancer registry data, a handful of studies have used geography to evaluate cancer risk. For example, San Francisco, California in the United States is known to have a large SM population. Using this knowledge, compared to the state of California's age-adjusted anal cancer incidence rates, San Francisco county had higher rates, attributed to the higher proportion of men who have sex with men (Cress & Holly, 2003).

To our knowledge no country in the world systematically collects SM demographic data as part of the patient's medical record and/or for a cancer registry data element. The consequence of this omission is that incidence data cannot be ascertained reliably for any country or for comparison among countries or regions. For example, the Behavioral Risk Factor Surveillance Study (BRFSS), a national survey in the United States, does not include SOGI data from all 50 states, which results in an "incomplete picture" of both the nationwide health needs and cancer disparities among LGBTQ+ people (National LGBT Cancer Network, 2021, p. 1).

Less than a dozen unique studies have been published on cancer comparing SM populations to heterosexual populations with the caveat that studies focusing on HIV/AIDS were excluded (see Chap. 7). Studies that compare overall cancer prevalence include three from the United States and one from England (which also described individual cancers) (Blosnich et al., 2016; Patterson & Jabson, 2018;

Saunders et al., 2017; Trinh et al., 2017). Incidence data calculated among SM cohorts of a longitudinal study were described in one Australian study for any cancer; one Danish study for both overall and individual cancer incidence; and one US study of SM female participants (Brown et al., 2015; Frisch et al., 2003; Valanis et al., 2000). Two more studies from the United States evaluated individual cancers of the skin and breast among SMs (Cochran et al., 2001; Mansh et al., 2015).

The preponderance of aforementioned studies described no statistical difference in overall cancer prevalence or incidence between SM males/females and heterosexuals (Blosnich et al., 2016; Brown et al., 2015; Frisch et al., 2003; Patterson & Jabson, 2018; Saunders et al., 2017; Valanis et al., 2000). The one exception for overall cancer was the US National Health Interview Survey (NHIS). This national surveillance survey, conducted yearly, included a sexual orientation question since 2013. Pooled data (2013–2015) stratified by race/ethnicity and using direct standardization for age reported an increased cancer prevalence for white SM women but not Latina, whereas Black SM women were at a reduced cancer prevalence compared to white heterosexuals. Among SM men, only white SM men were at an increased cancer prevalence compared to white heterosexuals (Trinh et al., 2017). In the second NHIS study using pooled data (2013–2016) and adjusting for demographic and socioeconomic factors, gay men and bisexual women had a higher prevalence of any cancer than their respective heterosexual counterparts. This finding was more pronounced among those aged 65 years and older (Gonzales & Zinone, 2018).

Machalek and colleagues' systematic review reported on anal HPV infection and cancer among men who have sex with men (Machalek et al., 2012). They stratified studies by HIV status (Chaturvedi et al., 2009; D'Souza et al., 2008; Dal Maso et al., 2009; Franceschi & De Vuyst, 2009; Frisch et al., 2003; Koblin et al., 1996; Piketty et al., 2008; Silverberg et al., 2009; van Leeuwen et al., 2009). Neither of the two studies of HIV-negative men who have sex with men reported an increased anal cancer incidence (D'Souza et al., 2008; Koblin et al., 1996). In Machalek's meta-analysis of these studies, the incidence of anal cancer was significantly higher in HIV-positive men compared to HIV-negative men (Machalek et al., 2012). Van der Zee and colleagues also reported similar findings of a significantly increased standardized incidence ratio for anal cancer in HIV-positive men who have sex with men (van der Zee et al., 2013). Similarly, other studies have shown no increased cancer prevalence among HIV-negative gay men (Frisch et al., 2003; Lyter et al., 1995). It is noteworthy to mention that neither of the NHIS studies described above that reported an overall increased cancer prevalence for gay men and bisexual women adjusted for HIV/AIDS infection (Gonzales & Zinone, 2018; Trinh et al., 2017).

Evaluating the literature on participants living with HIV and/or HPV and cancer is beyond the scope of this chapter. However, a brief comment is warranted. Six cancers have been identified with strong evidence of a causal cancer relationship with HPV: cervix, penis, vulva, vagina, anus, and oropharynx (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2012). Similarly, an International Agency for Research on Cancer (IARC) working group indicated a

causal role of HIV infection for Kaposi sarcoma, non-Hodgkin's lymphoma, Hodgkin's lymphoma, as well as cancer of the cervix, anus, and conjunctiva (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2012; International Agency for Research on Cancer). Some of these HIV-related cancers are the most prevalent in several African counties. From a global perspective, HPV and HIV-related cancer may be less associated with SM status in many countries where the transmission route is predominantly among heterosexual contacts, such as sub-Saharan Africa (Forman et al., 2012; Gayle & Hill, 2001; Williamson, 2015). In the two studies in which individual cancer incidence was described, SM men were over-represented among men with Kaposi's sarcoma, penile cancer, anal cancer, and/or non-Hodgkin's lymphoma (Frisch et al., 2003; Saunders et al., 2017). In one of these two studies, SM women were over-represented among women with oropharyngeal cancer (Saunders et al., 2017).

The most striking limitation to understanding the global burden of cancer among SM populations is no peer-reviewed publication on national cancer incidence for the SM population exists. Data to evaluate cancer prevalence or incidence (from longitudinal studies) were also limited to four countries—all mature countries. Until SM status is systematically collected, it will be difficult to definitely determine whether or not SM populations are at increased cancer risk.

### *5.3.2 Epidemiology of Cancer Among Transgender Populations*

Population-level data does not exist with respect to cancer incidence or prevalence for transgender populations. Broadly, the literature falls into the categories of case studies ($n$ = 48) and incidence and prevalence measures of cancers in cohorts of transgender patients ($n$ = 8).

Case studies form the majority of literature and chronicle a single or up to five patients with a given cancer. The case studies have the most geographic variation compared to cohort studies with 17 countries represented: Australia ($n$ = 2), Belgium ($n$ = 1), Brazil ($n$ = 1), Canada ($n$ = 1), Czech Republic ($n$ = 2), France ($n$ = 1), Germany ($n$ = 3), Italy ($n$ = 2), Japan ($n$ = 1), the Netherlands ($n$ = 5), Serbia ($n$ = 1), Singapore ($n$ = 1), Spain ($n$ = 3), Switzerland ($n$ = 2), Thailand ($n$ = 1), the United Kingdom ($n$ = 8), and the United States ($n$ = 15). Among the 48 publications, 59 cases were detailed, as some publications described more than one case. Among the 59 case reports, transfeminine individuals comprised 71% ($n$ = 42). Cancer incidence and prevalence studies ($n$ = 9) using cohorts comprised less geographic diversity, including populations from Belgium, the Netherlands, and the United States.

#### 5.3.2.1 Case Studies

Among transfeminine individuals, case studies were found describing testicular (Chandhoke et al., 2018), anal (Caricato et al., 2009), neovaginal (Fernandes et al., 2014; Harder et al., 2002), prostate (Dorff et al., 2007; Markland, 1975; Miksad

et al., 2006; Nguyen & O'Leary, 2018; Thurston, 1994; Turo et al., 2013; van Haarst et al., 1998), and breast cancers (Chotai et al., 2019; Dhand & Dhaliwal, 2010; Ganly & Taylor, 1995; Gooren et al., 2015; Grabellus et al., 2005; Maglione et al., 2014; Pattison & McLaren, 2013; Pritchard et al., 1988; Sattari, 2015; Symmers, 1968; Teoh et al., 2015), as well as meningiomas (Bergoglio et al., 2013; Cebula et al., 2010; Deipolyi et al., 2010; Gazzeri et al., 2007) and prolactinomas (Bunck et al., 2009; Cunha et al., 2015; Garcia-Malpartida et al., 2010; Gooren et al., 1988; Kovacs et al., 1994; Mueller & Gooren, 2008). For transmasculine individuals, case studies were found for uterine (Urban et al., 2011), breast (Burcombe et al., 2003; Nikolic et al., 2018; Shao et al., 2011), cervical (Dizon et al., 2006), ovarian (Dizon et al., 2006; Hage et al., 2000), and endometrial cancers (Urban et al., 2011). Most of the case studies identified individual cases associated with reproductive organs (testicular, uterine, cervical, ovarian, endometrium), breast cancer, hormone-associated masses (prolactinomas and meningiomas), as well as prostate and anal cancers. The majority of cases were among individuals who had initiated GAHT. Little information was provided on sexual behavior. Although these case studies are important for exploring pathophysiology, treatment, and prognosis, they do not appropriately characterize population-level cancer burden (see Appendix).

#### 5.3.2.2 Transgender Cohort Studies

In total, eight cohort studies were found that assessed cancer among transgender populations (see Table 5.3). One of the larger cohorts of transgender persons (1578 transfeminine individuals and 3557 transmasculine individuals) was from a US-based cohort of military veterans. The mean age of transfeminine and transmasculine individuals in the study was 56 years. This study found a decreased incidence of breast cancer and an increased incidence of prostate cancer among transfeminine individuals compared to the group of cisgender male and female individuals combined (10,671 cisgender men and 4734 cisgender women), after adjusting for established risk factors (Brown & Jones, 2016). Another large US-based cohort found an elevated risk of endocrine gland cancers (i.e., thyroid, adrenal, pituitary, and pineal gland cancers) and reduced risk of prostate cancers when comparing transfeminine individuals ($n$ = 2793) to cisgender males ($n$ = 63,813) who were enrolled in a private health insurance plan over 8 years of follow-up and were age-matched for analyses (Goodman & Nash, 2019). In this sample of transfeminine individuals, 47% were ≥36 years, and 14% were >55 years. The same study also found the equivalent risk of intestinal, lymphatic, smoking-related (i.e., lung/bronchus, trachea, esophagus, larynx, cervix, stomach, pancreas, urinary bladder, kidney, and renal pelvis), and viral infection-induced (i.e., anus, base of tongue/tonsil, oropharynx, nasopharynx, pharynx, liver, Kaposi sarcoma, non-Hodgkin's lymphoma, and Hodgkin's lymphoma) cancers comparing the two populations. In the same cohort, no differences were noted between transmasculine participants ($n$ = 2099) and cisgender women ($n$ = 63,855) for incidence of breast, cervical, smoking-related, or viral infection-induced cancers over 8 years of follow-up (Goodman & Nash, 2019). In this

**Table 5.3** Cohort studies assessing cancer among transgender populations

| Study | Transgender Population | Comparison Group | Elevated | Equivalent | Lower | Study Measure | Cohort Description | Country |
|---|---|---|---|---|---|---|---|---|
| Brown, 2016 | 5135 (1578 TF, 3557 TM) | 15405 (4734 CW, 10671 CM) | Prostate | – | Breast | Odds ratio | US military veterans | United States |
| Braun, 2016 | 354 transgender individuals | CM, number not specified | Anal, breast, Kaposi sarcoma, non-Hodgkin's lymphoma | Tongue, pharynx, colorectal, kidney, liver, lung, pituitary, bladder | Melanoma | Proportional incidence ratio | US National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database | United States |
| | | CW, number not specified | Anal, Kaposi sarcoma, liver, lung, non-Hodgkin's lymphoma, bladder | Colorectal, kidney, pituitary | Breast, melanoma | | | |
| De Blok, 2019 | 2260 TF individuals using GAHT | 2260 age-matched CM | Invasive breast and noninvasive breast cancers | – | – | Standardized incidence ratio | VU University Medical Centre in Amsterdam patients matched with the Nationwide Network and Registry of Histopathology and Cytopathology in the Netherlands (PALGA) | Netherlands |
| | | 2260 age-matched CM | – | – | Invasive breast and noninvasive breast cancers | | | |
| | 1229 TM individuals using GAHT | 1229 age-matched CM | Invasive breast cancer | – | – | | | |
| | | 1229 age-matched CW | – | – | Invasive breast cancer | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Nash, 2018 | 805 transgender individuals | 10,928,591 CW | Anal, tongue, colorectal, esophageal, hematopoietic, Hodgkin's lymphoma, Kaposi sarcoma, laryngeal, liver, lung, non-Hodgkin's lymphoma, bladder, and vaginal cancers | Brain, kidney, melanoma, ovarian, pancreatic, pituitary, stomach, and thyroid cancers | Breast, cervical, and endometrial cancers | Proportional incidence ratio | North American Association of Central Cancer Registries (NAACCR) database | United States |
| | | 10,896,000 CM | Anal, breast, Kaposi sarcoma, and non-Hodgkin's lymphoma cancers | Tongue, brain, colorectal, esophageal, hematopoietic, Hodgkin's lymphoma, kidney, laryngeal, liver, lung, pancreatic, pituitary, stomach, thyroid, and bladder cancers | Melanoma, prostate, and testicular cancers | | | |

(continued)

**Table 5.3** (continued)

| Study | Transgender Population | Comparison Group | Elevated | Equivalent | Lower | Study Measure | Cohort Description | Country |
|---|---|---|---|---|---|---|---|---|
| Goodman, 2019 | 2793 TF | 63183 CW | Lymphatic and hematopoietic cancers | Endocrine gland cancers[a], intestinal, melanoma of the skin, smoking-related cancer[b], colorectum, viral-infection induced[d] | – | Adjusted hazard ratio | Commercially insured patients under Kaiser Permanente | United States |
| | | 63855 CM | Endocrine gland cancers[a] | Intestinal, melanoma of the skin, lymphatic, smoking-related cancer[b], colorectum, viral-infection induced[d] | Prostate cancer, screening-detectable cancers[c] | | | |
| | 2099 TM | 63855 CM | Breast, smoking-related[b], screening-detectable cancers[c] viral-infection induced[d] | – | – | | | |
| | | 63183 CW | – | Breast, cervical, smoking-related[b], screening-detectable cancers[c] viral-infection induced[d] | – | | | |
| | 4266 TF | 42660 CM | – | Colorectal, lung, melanoma of the skin, liver, kidney, bladder cancers | Prostate cancer | | US military veterans | |
| | | 42660 CW | – | Colorectal, lung, melanoma of the skin, liver, kidney, bladder cancers | – | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Wierkx, 2013 | 214 TF | 640 age-matched CM | – | Any cancer | – | Prevalence | Patients at the Center for Sexology and Gender Problems at the Ghent University Hospital | Belgium |
| | | 619 age-matched CW | – | Any cancer | – | | | |
| | 138 TM | 414 age-matched CM | – | Any cancer | – | | | |
| | | 414 age-matched CW | Any cancer | – | – | | | |
| Brown, 2015 | 138 transgender individuals | 188 cisgender individuals | – | Prostate and breast cancer | – | Odds ratio | US military veterans | United States |
| Brown, 2015 | 1579 TF | 10671 CM | Breast cancer | – | – | Standardized incidence ratio | US military veterans | United States |
| | | 4734 CW | – | Breast cancer | – | | | |
| | 3566 TM | 10671 CM | Breast cancer | – | – | | | |
| | | 4734 CW | – | Breast cancer | – | | | |

Abbreviations: *TM* transmasculine, *TF* transfeminine, *CM* cisgender men, *CW* cisgender women

[a]Includes cancers of the thyroid gland, adrenal gland, pituitary gland, and pineal gland

[b]Includes cancers of the lung/bronchus, trachea, esophagus, larynx and other head/neck, cervix, stomach, pancreas, urinary bladder, kidney, and renal pelvis

[c]Includes cancers of the colorectum, melanoma of the skin, and prostate; the analyses are natal-sex specific. 6 Includes cancers of the cervix, breast, colorectum, and melanoma of the skin; the analyses are natal-sex specific

[d]Includes cancers of the anus, base of tongue/tonsil, oropharynx, nasopharynx, pharynx, liver, and Kaposi sarcoma, non-Hodgkin's lymphoma, and Hodgkin's lymphoma. 6 Includes cancers of the cervix, breast, colorectum, and melanoma of the skin; the analyses are natal-sex specific

[e]All cancers of the cervix

sample of transmasculine individuals, 24% were ≥36 years and only 4.2% were >55 years. Another US-based cohort of transfeminine veterans ($n$ = 4394) found a reduced risk of prostate cancer when compared to cisgender males ($n$ = 14,431) and an equivalent risk of colorectal, lung, skin (melanoma), liver, kidney, and bladder cancers over 17 years of follow-up with a median study population age of 46–55 years (Goodman & Nash, 2019).

There is some evidence of an increased risk of breast cancer among transfeminine individuals as compared to cisgender men (Braun et al., 2017; de Blok et al., 2019; Gooren et al., 2013). Other studies among transfeminine individuals compared to cisgender male populations detected increased incidence of anal, Kaposi-Sarcoma, non-Hodgkin's lymphoma, prostate, and HPV-induced cancers after adjusting for age at diagnosis (Braun et al., 2017; Brown & Jones, 2015; Nash et al., 2018). Though statistically significant differences in cancer incidence exist, the relatively small number of cases (4–15) for any single cancer among transfeminine participants does not allow for population-level inferences. Instances of decreased cancer levels were isolated to invasive breast, noninvasive breast, prostate, and colorectal cancers as well as melanoma of the skin comparing transfeminine individuals to cisgender men and invasive breast cancer when comparing transmasculine individuals to cisgender women (de Blok et al., 2019; Goodman & Nash, 2019; Nash et al., 2018).

As described above, the eight cohort studies used different comparison groups to calculate estimates including cisgender women, cisgender men, or combined cisgender persons (both cisgender men and women together) for the transfeminine group as well as for the transmasculine group. Consequently, comparing the results from the nine cohort studies cannot be reasonably done given different comparison groups. Another major issue in understanding cancer incidence among transgender populations is the relatively small number of cases within even the largest cohorts of transgender patients. Assessing cancer risk is complicated further by a lack of data concerning medical gender affirmation treatments for transgender individuals, preventing analyses from stratification on this basis. GAHT in particular has raised concerns related to the risk of some cancers, as has been the focus of case studies, especially given some cancers are hormone-dependent, such as breast cancer (Wierckx et al., 2013). None of the largest studies of cancer among transgender populations accounted for GAHT use. As mentioned in the SM section, HIV-positive status is associated with certain cancers. In the United States among transgender populations, the estimate of the prevalence of HIV is 14% (Becasen et al., 2019). HIV status is another factor not considered in the studies that estimated cancer incidence. Of note is that some of the top global cancers (lung and colorectal) are sparsely mentioned in the literature for transgender populations. This distinction is particularly germane for hormone-dependent cancers, where multiple comparison groups (i.e., cisgender women and cisgender men separately) may be needed to most appropriately draw conclusions.

## 5.4 Diabetes Mellitus

Diabetes mellitus (DM) is a medical condition in which glucose (i.e., blood sugar) levels are abnormally high because the body is not properly using or does not make the hormone insulin. Insulin is made in the pancreas and allows the body to use glucose from consumed foods or to store glucose for future use. Insulin helps keep glucose levels from getting too high or too low (Palicka, 2002).

Approximately 7–12% of DM cases in mature countries are Type 1 (formerly known as juvenile or insulin-sensitive DM in which the body does not produce (enough) insulin) (International Diabetes Federation, 2019; Olokoba et al., 2012). The majority of cases, where data are available, are attributed to Type 2 diabetes (formally known as non-insulin dependent, insulin-insensitive, or adult-onset DM, which indicates that the cells in the body do not respond well to insulin and therefore cannot use glucose for energy) (D'Adamo & Caprio, 2011; Gale, 2002; Klonoff, 2009; Motala et al., 2003; Olokoba et al., 2012). Significant and alarming increases in Type 2 diabetes among children and adolescents have been described in Europe, New Zealand, Oceanic, and Asian countries (Pinhas-Hamiel & Zeitler, 2005). Almost all surveillance studies about NCDs make no distinction between Type 1 and Type 2 DM. Consequently, if not specified, the term diabetes refers to the combination of both Type 1 and Type 2.

Diabetes has emerged as a leading cause of disability globally, ranking as the fourth leading cause of age-standardized years of life disabled (YLDs) in 2017 up from a ninth position in 1990 (Institute for Health Metrics and Evaluation, 2018). This increased burden was observed across all levels of economic development (G. B. D. Risk Factor Collaborators, 2018).

### *5.4.1 Epidemiology of Diabetes Mellitus in Sexual Minority Populations*

As with surveillance data on DM globally for the general population, the prevalence of DM reported in the studies with SM populations does not differentiate between Type 1 and Type 2. Consequently, it is assumed that prevalence data reflect a combination of both types. Over 30 studies, virtually all completed by US respondents, reported DM prevalence or adjusted odds ratios comparing SM populations to heterosexual populations. The data consistently demonstrate no difference in DM between lesbians or gay men and their heterosexual counterparts (Beach et al., 2018; Blosnich et al., 2016; Boehmer et al., 2014; Conron et al., 2010; Diamant & Wold, 2003; Dilley et al., 2010; Jackson et al., 2016; Newlin Lew et al., 2018a, b; Patterson & Jabson, 2018; Wallace et al., 2011; Wang et al., 2007).

For bisexual males and females, among the 13 studies that reported bisexual female statistics, all but three (Diamant et al., 2000; Dilley et al., 2010; Newlin Lew et al., 2018b) reported no difference in DM prevalence (Beach et al., 2018; Boehmer

et al., 2014; Clark et al., 2015; Conron et al., 2010; Diamant & Wold, 2003; Jackson et al., 2016; Patterson & Jabson, 2018; Wallace et al., 2011; Ward et al., 2015) compared to heterosexual females. Among the three studies, two showed increased and one decreased DM prevalence. The increased DM prevalence was among studies of specific places in the United States: Los Angeles, California (data collected in 1997), and Washington state (data collected in 2003–2006). For bisexual men, half of the studies indicated significantly increased DM prevalence (Beach et al., 2018; Dilley et al., 2010; Farmer et al., 2013; Newlin Lew et al., 2018a; Wallace et al., 2011), and the other half indicated no difference (Boehmer et al., 2014; Clark et al., 2015; Conron et al., 2010; Jackson et al., 2016; Patterson & Jabson, 2018; Ward et al., 2015) compared to heterosexual men. It is not clear what unique risk factors support the finding of a possible increased risk of diabetes for bisexual men. Nor is it clear why half of the studies found bisexual men at no increased risk but the other half identified an increased risk.

Among the US studies, one-third used BRFSS. Of the 10 BRFSS studies exploring DM, 4 focused on older age or age groups, and all found no difference between SM and heterosexual populations (Boehmer et al., 2014; Fredriksen-Goldsen et al., 2013a; Garland-Forshee et al., 2014; Matthews & Lee, 2014).

Two studies carefully considered weight status (i.e., underweight-healthy weight (<25.0 body mass index (BMI)) as a reference category, and three increasing weight categories) and diabetes (Eliason et al., 2017; Stupplebeen et al., 2019). Each overweight category compared to a reference weight category demonstrated an increased likelihood of DM among SM men and women and heterosexual men and women independently. However, for both SM men and women, the increased likelihood of DM was much stronger compared to their heterosexual counterparts (Eliason et al., 2017; Stupplebeen et al., 2019). Further, a strong positive DM trend was also reported with increasing weight. Corliss and colleagues support this finding (Corliss et al., 2018). The implication of this remains to be determined, but current work explores inflammation pathways in obesity, diabetes prevention, and diabetes management (Monteiro & Azevedo, 2010; Tsalamandris et al., 2019).

A severe limitation to understanding the global burden of DM, or lack thereof, among SM populations is virtually nonexistent data on this topic, globally. Evidence exists for only the US Patterns of DM prevalence or risk cannot be generalized beyond US borders. Even within the United States, the literature on DM typically mixes Type 1 and Type 2. With the increase in Type 2 DM among children and adolescents globally, disentangling information from participants on the type of DM will become increasingly important.

### *5.4.2 Epidemiology of Diabetes Mellitus in Transgender and Non-binary Populations*

The studies ($n$ = 11) assessing DM among transgender populations are represented by Belgium (Defreyne et al., 2017), the Netherlands (Elbers et al., 2003; Giltay et al., 1999; Nokoff et al., 2018; Polderman et al., 1993; Wierckx et al., 2013), and

the United States (Alzahrani et al., 2019; Caceres et al., 2019a; Dragon et al., 2017; Herman et al., 2017; Nokoff et al., 2018). Three studies from the Netherlands assessed changes in biomarkers for DM risk following the initiation of GAHT among small cohorts of transgender individuals (Elbers et al., 2003). Five studies compared the prevalence of DM among transgender populations to cisgender populations (Alzahrani et al., 2019; Caceres et al., 2019a; Dragon et al., 2017; Herman et al., 2017; Wierckx et al., 2013), four of which were general population samples. The fifth study specifically compared transgender populations that were elderly (age over 65 years) or experiencing disability to their cisgender counterparts (Dragon et al., 2017). One study assessed the prevalence of DM in a cohort of transgender individuals but did not have a comparison group (Defreyne et al., 2017). Another general US population study (using BRFSS data) compared the odds of DM status among transmasculine, transfeminine, and non-binary populations to cisgender comparator groups (Nokoff et al., 2018). Only one of the studies on DM stratified estimates by GAHT use (Defreyne et al., 2017). Unlike DM studies among sexual minority populations, two studies among the transgender population differentiated between Type 1 and Type 2 DM (Defreyne et al., 2017; Wierckx et al., 2013).

The three studies assessing biomarkers for diabetes before and after GAHT initiation were relatively small with 12–20 transfeminine individuals and 12–17 transmasculine individuals (Elbers et al., 2003; Giltay et al., 1999; Polderman et al., 1993). One study found reduced insulin sensitivity among transfeminine individuals and no change among transmasculine individuals following GAHT (Elbers et al., 2003). The second study found decreased endothelin levels among transfeminine individuals and increased endothelin levels among transmasculine individuals following GAHT initiation (Polderman et al., 1993). The third study noted no change in insulin levels among transmasculine individuals and an increase among transfeminine individuals following GAHT initiation (Giltay et al., 1999). Notably, these studies were published over two decades ago and standard GAHT formulations have changed in the interim.

The largest general population surveillance study to date on DM used data from a US state-based study with BRFSS data. This study contained 829 transmasculine individuals, 1373 transfeminine individuals, and 570 gender non-binary persons compared separately to cisgender women ($n$ = 368,220) and cisgender men ($n$ = 291,911) (Caceres et al., 2019a). The breakdown of birth-assigned sex for the gender non-binary individuals in the study was not provided. No statistically significant difference was seen in adjusted DM prevalence when comparing transmasculine, transfeminine, or gender non-binary persons to cisgender men or among transmasculine or gender non-binary individuals compared to cisgender women. Transfeminine individuals were found to have a higher adjusted DM prevalence when compared to cisgender women. Analyses were adjusted for the state of residence, age, survey year, race/ethnicity, income, education, marital status, employment status, self-rated health, healthcare coverage, delayed care, routine checkup, current tobacco use, heavy drinking, and exercise but not obesity status.

Another large cohort study using BRFSS data found no differences in the prevalence of DM comparing transfeminine individuals ($n$ = 1788) or transmasculine individuals ($n$ = 1267) separately to cisgender men ($n$ = 306,046) or cisgender

women ($n$ = 410,828). These were unadjusted analyses, with each group having a similar average age (Alzahrani et al., 2019). A smaller study ($n$ = 369 transfeminine individuals, $n$ = 239 transmasculine individuals, $n$ = 78,548 cisgender women, and $n$ = 60,009 cisgender men) using BRFSS data had similar findings comparing transfeminine and transmasculine individuals to cisgender women and men. The only comparison to note a difference was lower adjusted odds of DM comparing transmasculine individuals to cisgender women (Nokoff et al., 2018). Adjusted odds of DM were not statistically significantly different when comparing gender non-binary (AFAB) ($n$ = 61) to cisgender women or gender non-binary (AMAB) ($n$ = 68) to cisgender men.

A study analyzing the prevalence of Type 2 DM among transfeminine individuals ($n$ = 214) and transmasculine individuals ($n$ = 138) in Belgium used age-matched control groups. The transfeminine cohort was compared, separately, to age-matched cisgender men ($n$ = 640) and cisgender women ($n$ = 619). Similarly, the age-matched comparator groups for transmasculine individuals had cisgender men ($n$ = 414) and cisgender women ($n$ = 414) (Wierckx et al., 2013). Higher prevalence of DM was found when comparing transfeminine individuals to cisgender men and to cisgender women. Similarly, a higher prevalence of Type 2 DM was found when comparing transmasculine individuals to cisgender women. Transmasculine individuals did not have a statistically significant difference in Type 2 DM prevalence when compared to cisgender men (Wierckx et al., 2013).

Four studies used general population samples and showed mixed evidence of DM among transfeminine, transmasculine, and gender non-binary individuals in the United States and Belgium compared to cisgender men and cisgender women (Alzahrani et al., 2019; Herman et al., 2017; Wierckx et al., 2013). Two high-quality studies noted higher prevalence of DM among transgender women compared to cisgender women, and one found a higher prevalence compared to cisgender men (Alzahrani et al., 2019; Caceres et al., 2019a; Wierckx et al., 2013). All other studies noted no difference in DM prevalence compared to either cisgender men or women. Among transmasculine patients, one study noted a higher prevalence when compared to cisgender women and men separately, but all other studies found no difference (Wierckx et al., 2013). Studies assessing changes in DM risk profile following GAHT initiation among transfeminine individuals had mixed results, with two studies noting increases in DM risk profile (based on insulin sensitivity and insulin levels) and one noting a reduced risk profile (by endothelin levels). Among transmasculine individuals, one study found an elevated DM risk profile (based on endothelin) following GAHT initiation, and two others found no significant changes. Notably, the samples for these studies were relatively small (less than 30) (Elbers et al., 2003; Giltay et al., 1999; Polderman et al., 1993).

There does not seem to be substantial evidence to suggest a difference in DM comparing transmasculine individuals to cisgender men or women. With mixed evidence concerning transfeminine individuals, more high-quality research is needed to make a conclusion on DM risk compared to cisgender populations. Too few high-quality studies have been conducted stratifying by GAHT status to make meaningful recommendations. A single study with a small sample size explored

DM among gender non-binary individuals, so no conclusions can be drawn here either. No studies address DM among transgender populations outside of the United States, Belgium, and the Netherlands, and similarly they do not incorporate consideration of diabetes risk factors. Some studies controlled for age, while others relied on similarly distributed age or did not account for it in their analysis, presenting challenges with drawing population-level conclusion given DM's strong association with age.

## 5.5 Asthma

Among chronic respiratory diseases, asthma is the most common. Asthma is sometimes reported as a "lifetime" diagnosis; in other words, ever diagnosed with asthma. "Lifetime" diagnosis includes childhood asthma, which is "outgrown" by adulthood in more than two-thirds of patients (Sears et al., 2003). In other studies, current asthma includes both adult-onset asthma and unresolved childhood asthma (de Nijs et al., 2013). For international studies, the accepted gold standard question is "wheezing in the last 12 months" as the response to determine the prevalence of asthma or diagnosed by physicians (Masoli et al., 2004; Pearce et al., 2000). However, there is no single test or clinical feature that defines the presence or absence of asthma. As a result, the prevalence of current asthma symptoms is not equivalent to the prevalence of clinically diagnosed asthma.

Worldwide, approximately 339 million people have asthma (Marks et al., 2018). Globally, asthma is ranked 16th among the leading causes of years lived with disability and 23rd among the leading causes of burden of disease, as measured by disability-adjusted life years (DALYs) in 2015 (G. B. D. Chronic Respiratory Disease Collaborators, 2017). Established risk factors for asthma include smoking and chemical irritants in the workplace, whereas other strongly suspected exposures include indoor pollutants, outdoor allergens such as pollens and molds, and air pollution (G. B. D. Chronic Respiratory Disease Collaborators, 2017; World Health Organization, 2019). Sparse surveillance data are available on older and elderly populations globally. Overall, a U-shaped pattern exists between asthma prevalence and country income, with emerging and mature countries both facing the greatest asthma burden (Sembajwe et al., 2010).

### *5.5.1 Epidemiology of Asthma in Sexual Minority Populations*

About two dozen studies describe asthma prevalence in SM, with only three studies restricted to current asthma diagnosis only. Among the studies that separated lesbians and bisexual females, the majority reported an increased asthma prevalence for both populations compared to heterosexual populations (Blosnich et al., 2014; Boehmer et al., 2014; Conron et al., 2010; Dilley et al., 2010). Similarly, in

a meta-analysis of nine studies, Meads and colleagues reported an increased asthma risk for lesbians and bisexual women compared to heterosexual women (Meads et al., 2018). However, the only study conducted outside of the United States in Australia reported asthma prevalence among their four groups of participants: exclusively heterosexual, mainly heterosexual, bisexual, and lesbian. Among these four groups, bisexual and mainly heterosexual females had a statistically increased asthma prevalence. When the model controlled for current smoking, the difference was found to be nonsignificant for current smokers but remained significant for those who had never smoked or were former smokers by sexual identity (McNair et al., 2011).

Studies comparing gay or bisexual men to their heterosexual counterparts generally found similar asthma prevalence between the two groups (Blosnich et al., 2014, 2016; Boehmer et al., 2014; Cochran & Mays, 2007; Conron et al., 2010; Dilley et al., 2010; Kim & Fredriksen-Goldsen, 2012; Stupplebeen et al., 2019). In the BRFSS studies described under the diabetes section that focused on older populations, asthma was similar between SM men and women compared to their respective heterosexual groups (Boehmer et al., 2014; Fredriksen-Goldsen et al., 2013b, 2017; Matthews & Lee, 2014).

To evaluate the heterogeneity in the published literature regarding the role of obesity in asthma incidence, Beuther and colleagues completed a meta-analysis that included seven studies (sexual orientation was not noted) (Beuther & Sutherland, 2007). A dose-response effect of elevated BMI on asthma incidence was observed in both men and women (Beuther & Sutherland, 2007). Obesity status and asthma were evaluated in three studies (Blosnich et al., 2013; Eliason et al., 2017; Stupplebeen et al., 2019). For example, in Blosnich and colleagues' study, overweight/obese status was a significant predictor of both current and lifetime asthma diagnosis among same-sex partners as well as opposite-sex partners for women but not for men. Some risk factors for asthma, such as smoking and obesity, were much higher among lesbians compared to heterosexual females (Garland-Forshee et al., 2014).

Smoking is also considered a risk factor for adult onset of asthma. In a Finnish case-control study, both workplace and total environmental tobacco exposures (combining both workplace and home exposure) during a 12-month period were significantly related to general population adult-onset asthma diagnosis (Jaakkola et al., 2003). As higher smoking rates have been consistently noted for SM populations compared to heterosexual populations, this is an important component in understanding asthma risk among SMs. See Chap. 6 (Substance Use) for more details on smoking among the SM populations. Most of the studies controlled for smoking by adding this variable to the models to assess asthma risk. However, the definition of smoking varied (current versus ever), and none considered environmental tobacco exposure, thereby limiting the comparability among studies.

Similar to diabetes, virtually no studies have been published on asthma risk for the SM population beyond the United States. This dearth of information limits the generalizability of findings. It also does not provide an assessment of the global

burden of asthma in other places where triggers and links to asthma may be considerably different than in the United States.

### 5.5.2 *Epidemiology of Asthma in Transgender and Non-binary Populations*

A limited number of studies ($n = 5$) have assessed the prevalence of asthma in transgender populations, all of which were based in the United States. Three of the studies were national samples (Dai & Hao, 2019; Downing & Przedworski, 2018; Dragon et al., 2017), while the fourth (Herman et al., 2017) was limited to the state of California. Each used varying comparison groups for transfeminine and transmasculine individuals. One study that accounted for non-binary individuals did not conduct comparative analyses (Dai & Hao, 2019).

Data from the 2014 BRFSS survey found no statistically significant differences in the prevalence of asthma comparing 206 transmasculine individuals to 60,485 cisgender men and 351 transfeminine individuals to 85,739 cisgender women after adjusting for age, race, ethnicity, education, income, employment status, and depression. The study calculated the prevalence for the 112 gender-nonconforming persons but did not conduct analyses comparing them to cisgender populations (Dai & Hao, 2019). The proportion of participants aged 45 years and older was similar across the groups, ranging from 59% among transfeminine individuals to 51% among gender non-binary individuals (Dai & Hao, 2019). The breakdown of sex assigned at birth for individuals identifying as gender non-binary was not included in the study. Another study of 85 transgender persons in California showed a similar prevalence of asthma to a sample of 32,142 cisgender individuals at 8% (Herman et al., 2017). This estimate is nearly identical to CDC estimates for the prevalence of asthma in the general population in the United States (Asthma and Allergy Foundation of America, 2019).

Data from the 2014 to 2016 BRFSS surveys analyzed 1073 transfeminine individuals, 699 transmasculine individuals, and 449 non-binary individuals. The breakdown of sex assigned at birth for individuals identifying as gender non-binary was not included in the study. Each of these groups was compared independently to samples of 297,810 cisgender women and 218,021 cisgender men. Transfeminine individuals in the study had a lower adjusted odds ratio (aOR) of having asthma as compared to cisgender females after adjustment for age, race/ethnicity, relationship status, educational attainment, health insurance coverage, and state of residence. All other comparisons were not statistically significantly different (Downing & Przedworski, 2018).

In contrast, two studies reported an increased prevalence of asthma among transgender populations. The first study focused on two mutually exclusive groups: US residents aged 65 or older (age-entitled Medicare beneficiaries) and disability-entitled Medicare beneficiaries using a large claims database from a

government-funded health plan (Dragon et al., 2017). All of the analyses presented were unadjusted for relevant covariates, such as age. This is particularly relevant for the disability-entitled Medicare beneficiaries, where the transgender population was statistically significantly younger. The age distribution in the three groups (18–44, 45–54, and 55–64 years) are almost exact opposites with about 50% of transgender individuals in the youngest age group and 50% of cisgender individuals in the oldest age group. The study found higher prevalence estimates of asthma among 2133 transgender individuals (transfeminine and transmasculine combined) as compared to 32,588,061 combined cisgender individuals (cisgender women and men combined) who were age-entitled Medicare beneficiaries and for the 5321 transgender disability-entitled Medicare recipients compared to 6,548,168 combined cisgender disability-entitled Medicare recipients (mean age 44.9 and 51.3, respectively). In unadjusted estimates, a prevalence of 20.9% was found among transgender age-entitled Medicare beneficiaries compared to 12.7% among cisgender age-entitled Medicare beneficiaries. Among the disability-entitled Medicare beneficiaries, the unadjusted prevalence was 33.2% among transgender individuals and 18.0% among cisgender individuals (Dragon et al., 2017). However, this analysis did not adjust for any risk factors, such as smoking status, indoor air pollution, or family history of asthma due to the limitation of these data and included only individuals who have this health plan. The second study was a quantitative needs assessment among transmasculine individuals ($n$ = 73) in the United States and also reported elevated age-standardized asthma prevalence of 33.3% compared to the CDC-reported age-standardized estimate for all US males of 11.0% (Reisner et al., 2013).

In summary, the one probabilistic-based study reported no difference in asthma prevalence when comparing transgender populations to their cisgender counterparts (Herman et al., 2017). None of the studies indicated whether they inquired specifically about lifetime, adult-onset, or current asthma. Conflating these would have direct implications, as many people have asthma during childhood that does not persist into adulthood. Given evidence only existing for US populations, limited generalizations can be made as to the burden of asthma in transgender populations globally. Finally, studies that do not evaluate transfeminine and transmasculine populations separately have limited value in understanding their asthma burden since these groups have unique asthma-related risk factors (Naeem & Silveyra, 2019). Additionally, disability status is highly correlated with NCDs, and assessment of disability status has received focused attention recently. As indicated in the Dragon et al.' (2017) study described above, disability may disproportionally affect the transgender population and therefore warrants further investigation. The Washington Group on Disability Statistics has validated a six-item question in all regions of the world that provides a standardized instrument to characterize disability status (Groce & Mont, 2017).

## 5.6 Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a medical condition characterized by incompletely reversible chronic obstruction of lung airflow that interferes with normal breathing (Viegi et al., 2007). This occurs as a response to inflammation. COPD has been associated with inhalation of toxins from cigarette smoke, combustion of biomass for cooking and heating, and environmental pollution (Global Initiative for Chronic Obstructive Lung Disease, 2018). A population-based US study estimated that the fraction of COPD attributable to workplace exposure was 19.2% in smokers and 31.1% in nonsmokers (Hnizdo et al., 2002). Household air pollution from exposure to smoke from the combustion of solid or biomass fuels is a frequently reported COPD risk factor in nonsmoking populations (Gnatiuc & Caramori, 2014; Gordon et al., 2014; Mortimer et al., 2012; Salvi et al., 2012). Other COPD risk factors include age, genetics, socioeconomic status, and lung growth and development (Chinai et al., 2019).

Unlike the term asthma that has been used for over 3000 years, the term COPD has only been used since the mid-twentieth century. Prior to the adoption of the term COPD, American physicians used the term 'emphysema,' whereas British physicians used the term "chronic bronchitis" for the same condition (Petty, 2006). Describing the global burden of COPD is hampered for several methodological reasons (Salvi et al., 2012; Soriano & Lamprecht, 2012) as well as 72–92% of COPD cases being underdiagnosed (Casas Herrera et al., 2016).

Globally, COPD is projected to rank seventh in 2030, up from the 11th position in 2002, in DALYs (Mathers & Loncar, 2006). This translates into approximately 168 million men and 160 million women worldwide (Vos et al., 2012). COPD accounted for 5% of all deaths worldwide in 2015, with more than 90% of COPD deaths occurring in emerging and developed countries (World Health Organization, 2017). The prevalence of COPD is around 10%, but considerable variation in prevalence by country exists (Buist et al., 2007; Halbert et al., 2006; Menezes et al., 2005).

### *5.6.1 Epidemiology of Chronic Obstructive Pulmonary Disease in Sexual Minority Populations*

Given the methodological issues in ascertaining the global burden of COPD, it is not surprising that very limited studies are available to describe the global burden of COPD among the SM population (Salvi et al., 2012; Soriano & Lamprecht, 2012). The Geneva Gay Men's Study indicated that gay men were much more likely to be treated for bronchitis in the previous 12 months than heterosexual men (Wang et al., 2007). Similarly, Patterson and colleagues also found an increased risk for chronic bronchitis in the United States among gay men but not bisexual men or heterosexuals who have a history of opposite-sex sexual behavior (Patterson & Jabson, 2018). In contrast, two other US-based studies did not find an increased risk for

emphysema or COPD, respectively, for SM men (Blosnich et al., 2016; Ward et al., 2015).

The two studies that reported on COPD for SM women produced mixed results. One study reported no difference in COPD prevalence between lesbians and bisexual women compared to heterosexual women (Ward et al., 2015). The second study only reported an increased risk for chronic bronchitis among lesbians but not bisexuals, lifetime lesbians or bisexual females, or those self-identified as SM with or without same-sex sexual behavior (Patterson & Jabson, 2018).

Smoking is the most common risk factor for COPD (Global Initiative for Chronic Obstructive Lung Disease, 2018). A family history of asthma is another significant risk factor (Silva et al., 2004; Vonk et al., 2003). SMs have an increased smoking prevalence, and SM women may also have an increased asthma prevalence. (See Chap. 6 (Substance Use) on smoking prevalence among SMs.) No studies have been published that evaluate the additional risk factors associated with COPD for the SM population.

### *5.6.2 Epidemiology of Chronic Obstructive Pulmonary Disease in Transgender and Non-binary Populations*

COPD is a growing cause of morbidity and mortality in countries at all levels of economic development (Buist et al., 2008; Mannino & Buist, 2007). Similar to the SM section on COPD, sparse data are available for the transgender population. This may reflect a global issue of the younger age of participants who provide data, whereas COPD is considered a disease of the elderly (Holm et al., 2014). Only two studies were found that explored the prevalence of COPD among transgender populations, both of which focused on US-based cohorts. One study focused on transgender individuals with government-provided health insurance noted in the prior section on asthma also explored COPD prevalence (Dragon et al., 2017). In unadjusted analyses, the prevalence of COPD was higher among transgender individuals among both age-entitled and disability-entitled Medicare beneficiaries compared to similarly defined cisgender beneficiaries. The unadjusted prevalence of COPD among patients older than 65 was 30.4% in transgender patients (transmasculine and transfeminine patients combined) as compared to 20.7% in cisgender beneficiaries (cisgender women and men combined). Among disability-entitled Medicare beneficiaries, the unadjusted prevalence of COPD was 26.1% among transgender patients as compared to 21% among cisgender patients. No adjusted analyses were presented.

Similarly, in the 2014 BRFSS study also described in the asthma section, no differences in unadjusted COPD prevalence were found when comparing transmasculine individuals to cisgender women, transfeminine individuals to cisgender men, and gender non-conforming individuals to both cisgender men and women (Dai & Hao, 2019). Adjusted analyses comparing COPD prevalence among the three aforementioned transgender populations to gay cisgender men also showed no differences.

With only two studies, both in the United States, exploring COPD among transgender populations and one of these two studies not evaluating the prevalence separately for transfeminine and transmasculine participants, generalizations cannot be drawn as to the global burden of COPD in transgender populations. However, given that smoking is the leading cause of COPD, and smoking prevalence among transgender populations has been reported at higher rates than either the SM or cisgender heterosexual populations (Buchting et al., 2017; McElroy et al., 2011; Tamí-Maury et al., 2020), the prevalence of COPD would be expected to be much higher in transgender populations. This higher prevalence would be particularly noticeable in countries with high tobacco smoking prevalence (Reitsma et al., 2017).

## 5.7 Conclusion

In the scoping review of SGMs and the top five NCDs, 11% of the countries in the world were represented. A note of caution should be at the forefront when considering the global burden of NCDs represented in this chapter given the clear overrepresentation of data from one country. Specifically, the United States contributed almost three-quarters of research articles. Further, findings from only a few and mostly mature countries as described in this chapter limits the generalizability given the lack of representation of many countries and regions of the world. With that being said for the SM population, the literature suggests an increased burden only for asthma among lesbians and bisexual women. Little evidence exists of an increased burden among SMs for cancer, COPD, diabetes mellitus, or CVD. This is in stark contrast to established risk factors for NCDs, such as increased weight (SM women), smoking, excess alcohol consumption, and minority stress (see Chap. 2 on Stigma and Chap. 6 on Substance Use for a more in-depth exploration of these factors).

There is minimal evidence of any differential burden of cancer, COPD, diabetes mellitus, or asthma among transgender populations. Too few studies exist to draw conclusions specific to GAHT use for these NCDs. Among transfeminine populations, there is some evidence of elevated CVD risk, with notable increases in venous thromboembolism and pulmonary embolism across multiple studies associated with GAHT use (Getahun et al., 2018; van Kesteren et al., 1997; Wierckx et al., 2013). Large-scale studies centered on transgender populations infrequently accounted for GAHT use, regimen, or duration. The lack of these data drastically inhibits conclusions that may be drawn concerning NCDs among transgender populations given the diversity of various medical and physical gender affirmation processes that individuals may pursue. Smaller studies tended to focus explicitly on NCDs among transgender persons using GAHT, often excluding those who may choose not to pursue GAHT and limiting conclusions that may be drawn.

A very limited understanding of the influence of multiple identities that each person embodies beyond gender is reflected in this research. For example, racial/ethnic minority populations within the SGM community are rarely captured. In Thailand, one such population is the SGM Malay Muslims (Minority Rights Group International, 2018), whereas in the United States, SGM Native Americans comprise another such population. In addition, socio-cultural characteristics such as marriage/co-habitation among same-sex couples or economic position are not commonly considered in these studies. This lack of consideration of important characteristics also restricts the generalizability of findings to the SGM population within any one country and across countries.

Another characteristic reflected in the SGM population is the fluidity of identification over one's life course. This fluidity can be experienced by both sexual minority individuals as well as transgender individuals and is not uncommon (Dickson et al., 2013; Katz-Wise et al., 2014, 2016). The practical implications of this fluidity are unclear. A parallel construct is marital status. At any moment in time, marital status may change but is considered a core socio-demographic characteristic captured in medical records, health-related surveys, and countries' censuses. A rich and deep level of research continues to explore this social behavior, and, going forward, a similar depth and breadth of research is warranted to understand sexual and gender fluidity.

A notable limitation to drawing conclusions concerning NCD incidence and prevalence among SGM populations is that the average age in many studies skews younger. This is most noteworthy in studies with transgender populations, where many have average ages under 50. Some studies dealt with this dilemma by generating estimates adjusting for age or using age-matched samples. Many studies did not account for differences in age structure. This gap in study recruitment prevents strong conclusions given the strong associations between age and disease onset for CVD, cancer, DM, and COPD. Unlike the other NCDs discussed in this chapter, age is not strongly associated with asthma (American Lung Association, 2020; Centers for Disease Control and Prevention, 2021).

In conclusion, the limited data representing a global perspective hint at the possibility of a similar burden for CVD, cancer (excluding HIV/AIDS-related cancers), diabetes mellitus, COPD, and asthma (among SM men and transgender populations) compared to heterosexual and/or cisgender populations with some evidence of an increased asthma risk among SM women and elevated CVD risk among transfeminine populations. Research on long-term use of GAHT is needed since little is known about the influence of these exogenous hormones on the biological system.

The exponential increase in publications over the last two decades on SGM health concerns, albeit with the United States dominating the field, illustrates a promising trend. Increasing research from the 21 other countries who have already contributed to the literature as well as other countries joining this research agenda will undoubtedly provide valuable evidence-based insight into the influence of SGM status on the global burden of NCDs. For this to happen, adding SGM identity questions to national surveillance studies as well as capturing these identities within

healthcare records and in cohort studies would significantly improve our ability to evaluate NCDs as well as other health outcomes among the SGM population.

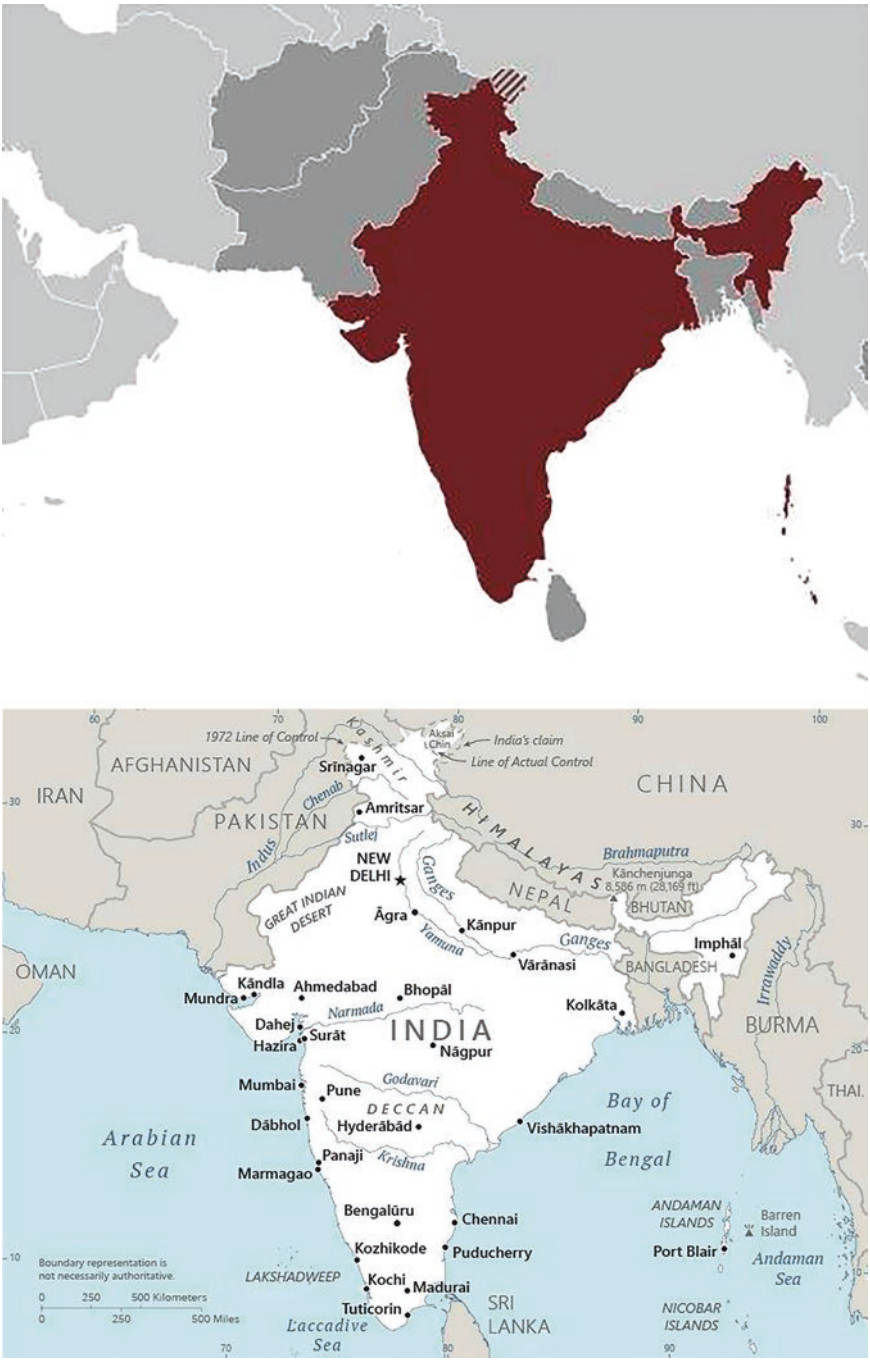
## 5.8 Case Study: Noncommunicable Diseases Among Men Who Have Sex with Men and Transgender Women in India

The research on cancer and other noncommunicable diseases (NCDs) among sexual and gender minorities (SGM) in India is limited. The one comprehensive literature review of research on SGM people in India identifies one of the major gaps in research as the topic of noncommunicable diseases (Chakrapani et al., 2023). This dearth of research is likely due to multiple factors including the lack of some legal rights and anti-discrimination protections for SGMs in the country. Fear of stigmatization from healthcare providers and other communities can also play a role, preventing SGMs from seeking the routine and appropriate medical care they need and hindering the ability of epidemiologists to track their chronic illness patterns (Patel et al., 2012). Of the research on SGM in India on all topics related to health, there is virtually no research on lesbian women and transmasculine people, with just 4% and 2% of the research, respectively, focusing on these identity groups (Chakrapani et al., 2023). However, there are some studies that allow insight into NCDs among transgender people and illnesses related to HIV-positive status and high-risk human papilloma virus (HPV) infection among men who have sex with men (MSM) in India.

### *5.8.1 NCDs Among Transgender Populations*

The research on the risk and prevalence of NCDs among SGMs in India is scarce; however, there is an emerging body of research exploring risk and disease prevalence for transgender people. One study analyzed data on 200 transgender people, the vast majority of whom were transfeminine, from Puducherry, India, and found that their prevalence of risk factors, such as high blood pressure, obesity, physical inactivity, and unhealthy dietary practices, were significantly higher than the general population (Madhavan et al., 2020). Another study found that among transgender people surveyed in Mumbai, two-thirds suffered from NCDs including diabetes (40%), hypertension (11%), and other musculoskeletal disorders like arthritis (Gupta & Sivakami, 2016).

Transgender women often receive GAHT as part of their gender affirmation journey, and research shows that such transgender women in India are at an increased risk of developing breast cancer when compared to cisgender men (Majumder et al.,




Map of India showing major cities as well as parts of surrounding countries and the Indian Ocean. (Source: Central Intelligence Agency, 2021)

2020). Additionally, the presence of estrogen receptors in prostate tissue raises concern for prostate cancer among transgender women (Majumder et al., 2020). Although prevalence estimates for India are not available for these cancers in transgender women, data collected outside of India showing the increased risk of breast cancer during a relatively short duration of hormone treatment can be extrapolated to this population (Majumder et al., 2020).

### *5.8.2 HIV-Related Cancers Among MSM*

When examining the risk for other NCDs, it becomes apparent that MSM are at increased risk of cancer if they are living with HIV due to the way HIV compromises their immune systems. Globally, HIV status contributes to the risk of certain cancers, specifically called AIDS-defining malignancies, as well as non-AIDS-defining cancers such as those of the anus and oral cavity/pharynx (National Cancer Institute, 2017). One study examined malignancies in over 2500 people with HIV in India in an antiretroviral clinic, of which almost 70% were males (Sharma et al., 2015). With MSM prevalence of HIV higher among MSM, it is likely that some or many of these participants were MSM. Results of a retrospective analysis of patients registered at this clinic found that the frequency of malignancies was higher in the study group than in the general population, suggesting an important connection between their HIV status and these malignancies (Sharma et al., 2015).

When examining sexual behaviors in Indian men living with HIV in relation to cancer risk and incidence, another study screened 126 male patients living with HIV who were accessing antiretroviral therapy. Although 91% were married to female partners, almost 40% of those gave a positive history of anal sex with other men (Gautam et al., 2018). Researchers found that 60% of patients screened had a variety of cytological abnormalities, all of which were precursors to anal cancer (Gautam et al., 2018). Risk factors for these lesions included a history of anal intercourse (Gautam et al., 2018). Finally, one study compared the prevalence of abnormal anal cytology in Indian MSM living with and without HIV. Researchers established that MSM living with HIV had higher rates of abnormal anal cytology than HIV-negative MSM (Arora et al., 2014).

### *5.8.3 HPV-Related Cancers Among MSM*

While there is no national prevalence data on HPV infection in MSM in India, researchers who examined it within West Bengal, an eastern province in India, found that the prevalence of HPV infection among MSM was almost 70% in that region (Ghosh et al., 2012), as compared to 26% in men overall (Bruni et al., 2019). While HPV itself is not cancer, there is overwhelming evidence that certain high-risk strains of HPV cause cancer (Frisch et al., 1997; Hoots et al., 2009). In one

systematic review, high-risk strains of HPV were found in 71% of invasive anal cancer cases (Hoots et al., 2009). Globally, nearly 90% of anal cancers can be attributed to HPV infection, occurring more frequently in males in lower-income countries such as India (de Martel et al., 2017). In one study in India, HPV-attributable cases of penile cancer were almost as frequent as anal cancer in males, which suggests a higher burden of disease for MSM who are at higher risk of contracting HPV (de Martel et al., 2017).

### *5.8.4 Health Advocacy for SGM Populations in India*

There are multiple organizations in India that are working to both advocate for better health services and change stigmatizing social beliefs about LGBTQ+ people. One of these organizations is Naz, which has an initiative dedicated to fighting for LGBTQIA+ individuals (Naz India, 2020). They empower LGBTQIA+ people to access their rights, including medical care, safer sex information, and HIV testing (Naz India, 2020). Earlier access to appropriate medical care can decrease the risk of cancer going undetected and untreated (World Health Organization, 2020). Additionally, LGBTQ+ people's ability to receive information regarding safer sex and regular HIV testing as well as preventative screening and treatment for illnesses like diabetes and heart disease can reduce the risk for SGM and allow them to get the appropriate treatment should they need it.

Another organization that is fighting for the rights of LGBTQ+ people in India is the Humsafar Trust. This organization has been doing outreach to LGBTQ+ people within the Mumbai metropolitan and surrounding areas for over 25 years (Humsafar Trust, 2020a). Their health-related projects include three targeted interventions among MSM and transfeminine/koti/hijra communities surrounding Mumbai: reduce transmission of HIV, promote access to healthcare for the community, and reduce stigma against these individuals (Humsafar Trust, 2020b). The Humsafar Trust also does research about the LGBTQ+ community in India (Humsafar Trust, 2020c). Their focus is on behavioral health research, which is necessary as mental and behavioral health are inextricably intertwined with chronic illness and physical health outcomes. One example of a research study they are currently conducting is regarding the impact of stigma on depression and sexual risk behavior of MSM and transgender women in India (Humsafar Trust, 2020c). Findings will be able to inform interventions to reduce stigma and discrimination, both of which are associated with physical and sexual health outcomes related to HIV prevention for these populations (Humsafar Trust, 2020c).

Finally, there is an advocacy organization called Swatantra whose mission is to advocate for transgender working-class Indians (Global Human Rights, 2018). They advocate for more inclusive laws and policies on all levels of the Indian government, conduct research on issues impacting the transgender community, and lead community outreach campaigns to support transgender people (Global Human Rights, 2018). All these actions can support the legal protections for and

destigmatization of transgender people in India, ultimately supporting their access to and utilization of healthcare to improve their health outcomes.

The lack of research on the burden of NCDs among SGMs in India is striking and needs to be remedied. While research on HIV- and HPV-related cancer among this population can be connected to inferences about cancer, and there is some research on general health outcomes for transgender people, without research focused on specific conditions such as cancers, CVD, or diabetes, it is not possible to fully understand the scope of the problem. It is necessary to have an epidemiological understanding of NCDs among these populations to feasibly allocate funding for intervention or prevention work. The three organizations described above, Raz, the Humsafar Trust, and Swatantra, are key starting places for further exploration of NCDs among SGM.

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