# Sex, Gender, Race and Ethnicity Matter in Limb Preservation in North America

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Sex as a biological attribute and gender as a social construct are crucial considerations in relation to health care. Sex and gender issues affect, among other things, patients' incomes, resource availability, access to health services, commitment to their health, and relationships with health and social services providers and caregivers.<sup>1</sup> Similarly, *race*, a social construct based on shared physical traits, and *ethnicity*, a cultural expression of identification, also have impacts. The causes of sex, gender, racial and ethnic disparities in health care are multifactorial and reflect differences in biological vulnerability to disease as well as differences in social resources, environmental conditions and health-care interventions.<sup>2</sup>

These factors are well known to influence the fate of people with diabetes-related foot complications such as diabetic foot ulcer, infection and amputation, and are important considerations for healthcare professionals, especially with the diversity of Canada's population.<sup>3</sup> In this paper we discuss the important concepts of health equity, equality and disparity in relation to the impact of sex, gender, race and ethnicity on limb preservation.

#### **Health Equity**

The difference in health status between populations is closely linked to social and demographic factors such as socioeconomic status, health insurance status, literacy level, sexual orientation and disability. Health equity applies the concept of social justice to the realm of health care to ensure social and environmental factors do not limit a person's access to high-quality health care.<sup>4</sup> Further, health equity aims to ensure no person is denied the possibility of good health as the result of belonging to a group that has historically been economically or socially disadvantaged.

*Health inequity* is therefore defined as difference in health status that is avoidable, unfair and unjust.<sup>5</sup> Some examples of health inequity include racial and ethnic discrimination, lack of access to high-quality education, income and/or wealth gaps, inadequate or absent housing, or an unsafe environment.

#### **Health Disparity**

Health disparities are the differences in health care—including access, patient factors and clinical outcomes—between populations related to social or demographic factors.<sup>6</sup> Health disparity is a metric used to measure progress toward achieving health equity. These disparities are modifiable factors that systematically and negatively impact less advantaged groups and compromise heath-care systems. Health disparities are preventable and signal gaps in the quality of care.

#### **Equality in Health**

*Equality* in health care refers to what is fair and equitable. It means that everyone receives the same standard of care, regardless of their specific needs and contexts.<sup>7</sup> The patient-centred care and holistic approaches can therefore be compromised with a very rigid application of health equality. However, patient-centred care can result in a higher degree of equality in health when there is an equal patient-provider relationship.<sup>8</sup>

## **Social Determinants of Health and Limb Preservation**

The World Health Organization (WHO) defines social determinants of health as conditions or circumstances in which people are born, grow, live, work, and age (see Figure 1). These conditions are shaped by political, social, and economic forces.<sup>9</sup>

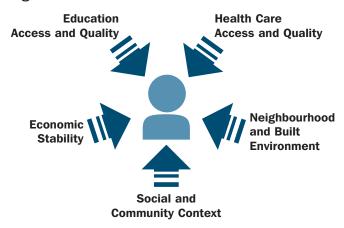


Figure 1: Social Determinants of Health

Diabetes leads to 65% of all non-traumatic lower-extremity amputations (LEA) in Canada.<sup>10</sup> The precursor event is the diabetic foot ulcer (DFU), with an incidence of 2–4% per annum. The prognosis of DFU is poor, especially with concomitant infection and peripheral arterial disease (PAD).<sup>10–12</sup> **Dr. Virginie Blanchette** is the first podiatrist PhD in Québec and has been an associate professor in the podiatric medicine program at Université du Québec at Trois-Rivières since 2014. Her research specialty is prevention and management of diabetic foot ulcers and their complications, with a limb preservation approach within patient-oriented research. She is mentored by David G. Armstrong (Keck School of Medicine, University of Southern California) and is currently a Diabetes Action Canada trainee. She joined the Diabetic Foot Canada Task Force in 2019, is a member of the scientific committee of the Limb Preservation Symposium and a member of the Wounds Canada board of directors.

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Indeed, PAD is another leading cause of LEA in Canada.<sup>12–14</sup> A recent study from Ontario showed that 94% of those who had an LEA had also PAD.<sup>12</sup> As a result, over 80% of LEAs in Canada are attributable to the presence of both conditions. In high-income countries like Canada and the United States, diabetes and PAD prevalence have been rising over the past two decades.<sup>12–14</sup> Therefore, to support limb preservation, it is relevant to closely examine the effect of sex, gender, race and ethnicity on individuals with those comorbidities because of the impact they have on health care disparity.

# Sex and Gender Differences Related to Diabetes and PAD

There is a higher prevalence of diabetes-related foot disease (DRFD) in men than in women, as well as

a higher prevalence of comorbidities and risk factors such as previous history of DFU and revascularization procedures.<sup>15,16</sup> Because there is a higher risk of neuropathy for men, they are at higher risk of DFU recurrence.<sup>17</sup> Women are associated with a higher cardiovascular risk profile.<sup>18</sup> However, there is a higher prevalence of smokers or with a history of smoking, hypercholesterolemia, obesity, ischemic heart disease and cerebrovascular diseases in men that is associated with DRFD.<sup>15</sup> DRFD also affects men at a younger age than women.

Further, a study has demonstrated that the rate of DFU healing is higher for men than for woman (85% vs 63%, p<0.001) and also slower (124 days vs 87 days, p=0.02).<sup>15</sup> While there is no difference in major LEA rate between men and women, the mortality risk is higher for men (25% vs. 16%, p=0.02), as is the risk of recurrence.<sup>15</sup> There is evidence that women are less likely to be screened for DRFD.<sup>16</sup> Despite our universal access to care in Canada, there are disparities in the risk of LEA among patients with diabetes related to socio-economic status and gender. Men living in low-income neighbourhoods are at greatest risk.<sup>19</sup>

PAD is more frequent in high-income countries in woman (3–29% among women aged 45–93 years). However, due to the protective effect of estrogen, women tend to present with PAD 10–20 years later than men. Moreover, women have higher rates of subclinical, asymptomatic and atypical PAD due to the more diffuse involvement of microcirculation and a pro-inflammatory profile. Women are less likely to undergo minor LEA and arterial bypass surgery. Men, however, have been found to experience a greater overall burden of PAD; their arterial tree is more severely involved, with a morphological configuration of characteristics typical of diabetic PAD.<sup>15,16,20–24</sup>

In general, men are less compliant in health habits and follow-up than women are. Men also tend to have lower adoption rates of self-protective habits such as selection of appropriate footwear and regular foot care. Women, however, are less likely to be monitored for foot complications as a regular part of treatment. For these reasons, it is important for clinicians to ensure access to sex/gender-focused care and to support the empowerment of their patients while considering their differences. Targeted education can help with this disparity.<sup>15,25</sup>

Table 1 provides a summary of the primary sex and gender differences in therapeutic approaches to diabetes and PAD.

| Procedures/Drugs  | Sex and Gender Differences   |
|---|--|
| Revascularization   | <ul><li>Men &lt; Women</li><li>Mortality: Men &lt; Women</li></ul>   |
| Amputation  | • Men > Women  |
| • Statins   | <ul><li>Myopathy: Men &lt; Women</li><li>Diabetes risk: Men &lt; Women</li></ul>   |
| Hypoglycemic molecules: thiazolidinediones  | <ul> <li>Exposure: Men &lt; Women</li> <li>Mortality: Men &lt; Women</li> <li>Risk of bone fracture: Men &lt; Women</li> </ul> |
| Angiotensin-converting-enzyme (ACE) inhibitors                                      | <ul> <li>Survival Southern Europe: Men &lt; Women</li> <li>Survival Northern Europe: Men = Women</li> </ul>                    |
| Hypoglycemic molecules:<br>glucagon-like peptide-1 receptor agonists (Glp1-agonist) | <ul> <li>Targeted level of glycated hemoglobin:<br/>Men &gt; Women</li> </ul>  |
| Fibrinolytic therapy  | • Benefit effect: Men < Women  |
| Antithrombotic  | • Use: Men > Women   |
| Antihypertensive  | • Use: Men < Women   |
| Pentoxifylline  | Not known  |
| Cilostazol  | • Not known  |

Table 1: Main sex-gender differences in therapeutic approaches for diabetes and PAD<sup>26,27</sup>



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#### Race and Ethnicity Differences Related to Diabetes and PAD

In Canada, the prevalence and incidence of diabetes are greater in certain population groups such as First Nations, Métis and Inuit, along with those of African, Caribbean, East Asian, Southeast Asian, South Asian, and Latin descent.<sup>28–31</sup> These groups also experience higher rates of major LEA than the non-Indigenous population (OR = 1.85, 95% CI: 1.04-3.31). The effects of rurality may be closely intertwined with ethnicity, resulting is disparate outcomes.<sup>32,33</sup> However, another systematic review found no significant differences between any racial/ ethnic group.<sup>34</sup> These divergent results may demonstrate the essential relationship that social determinants of health play as important cofactors for those population disparities.<sup>32,34–36</sup>

In addition, in the United States, African American patients are less likely to have undergone a revascularization attempt before an LEA when compared with other patient populations. Following revascularization, the two-year LEA-free survival rate is lower for African American populations (68% vs 75%, p < 0.001).<sup>37–39</sup> Non-white populations are associated with increased primary LEA, decreased revascularization, decreased in-hospital mortality and increased length of stay.<sup>39</sup> A recent study demonstrated that access to funded health-care resources related to limb preservation decreased lower extremity amputations among underserved racial and ethnic minority adults with DFUs in the U.S.<sup>40</sup>

#### First Nations, Métis and Inuit Populations

In Canada's First Nations, Métis and Inuit populations, health disparities may be driven in part by poor access to health care, barriers to clear communication, cultural differences and discrimination.<sup>41,42</sup> LEA frequency is three to five times higher in this population than in the general population. Similarly, the mortality rate following an LEA is 15% higher in First Nations populations than in non-First Nations populations (adjusted HR: 1.15, 95% CI: 1.05–1.26), and median survival is 3.5 years for First Nations versus 4.1 years for the general population. PAD is more prevalent in First Nations populations, but revascularization rates are comparable.<sup>43,44</sup>

# Addressing Disparities in Limb Preservation

It is critical to provide low-cost services to those living in low-income households. Preventing complications with early intervention leads to better health outcomes. Telemedicine and telehealth services that use mobile screening and management can be used effectively to support remote and rural communities and lower transportation costs for patients and organizations.<sup>45–47</sup> Providing better education, screening, investigations and treatment access to those communities particularly impacted by diabetes and PAD, patient-centred care, the use of evidence-based practices and a team approach to limb preservation among all stakeholders and socio-cultural contexts can all improve outcomes.<sup>48,49</sup>

#### **Cultural Security in Care**

Patients' interactions and engagement with diabetes care are influenced by personal and collective historical experiences with health-care providers and contemporary exposures to culturally unsafe health care. Minimizing or eliminating barriers to patient-provider interactions, health services and health systems is critical.<sup>42,51,52</sup>

#### **PROGRESS+PLUS Framework for** Equitable Limb Preservation

PROGRESS+PLUS is a framework of considerations that can be applied to clinical practice, organizational policy and research.<sup>50</sup> The elements of PROGRESS+PLUS are:

- Place of residence
- Race, ethnicity, culture and language
- Occupation
- Gender and sex
- Religion
- Education
- Socioeconomic status
- Social capital

The PLUS extends the original framework to include personal characteristics associated with discrimination (e.g., disability, age), features of relationships (e.g., children of smoking parents) and time-dependent relationships (e.g., release from incarceration).

#### **Taking Action**

To improve population health and overall quality of care in the field of limb preservation, the clinical and research communities must take actions to reduce bias by being more inclusive in care settings and clinical trials. Addressing the lack of access, lack of understanding, lack of trust and lack of a common language in practice, education and research can help to reduce gender and racial gaps.

#### Summary

Health equality, disparity and equity are unique and important concepts that impact how limb preservation is approached. A person's ability to access limb preservation services is impacted by who they are and where they live and we, as clinicians, administrators and policy makers, have the responsibility to support care in all communities. By acknowledging barriers to health care, more effective and equitable health-care systems can be developed and better outcomes achieved.

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