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Infectious diseases in Indigenous populations in North America: learning from the past to create a more equitable future

Naomi R Lee, Alexandra King, Deionna Vigil, Dustin Mullaney, Priscilla R Sanderson, Taiwo Ametepee, Laura L Hammitt

The COVID-19 pandemic, although a profound reminder of endured injustices by and the disparate impact of infectious diseases on Indigenous populations, has also served as an example of Indigenous strength and the ability to thrive anew. Many infectious diseases share common risk factors that are directly tied to the ongoing effects of colonisation. We provide historical context and case studies that illustrate both challenges and successes related to infectious disease mitigation in Indigenous populations in the USA and Canada. Infectious disease disparities, driven by persistent inequities in socioeconomic determinants of health, underscore the urgent need for action. We call on governments, public health leaders, industry representatives, and researchers to reject harmful research practices and to adopt a framework for achieving sustainable improvements in the health of Indigenous people that is both adequately resourced and grounded in respect for tribal sovereignty and Indigenous knowledge.

Lancet Infect Dis 2023

Published Online
May 3, 2023
https://doi.org/10.1016/S1473-3099(23)00190-1

Department of Chemistry and Biochemistry (N R Lee PhD), **Department of Biology** (D Mullaney BS), **and Department of Health Sciences, College of Health and Human Services** (Prof P R Sanderson PhD), **Northern Arizona University, Flagstaff, AZ, USA; College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada** (A King MD, T Ametepee MBBS); **Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA** (D Vigil BS, L L Hammitt MD)

Correspondence to:
Laura Hammitt, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21231, USA
lhammitt@jhu.edu

For more on the **First Nations Health and Social Secretariat of Manitoba's COVID-19 data** see https://www.fnhssm.com/covid-19

Introduction

Infectious diseases have disproportionately affected Indigenous peoples since the beginning of colonisation. The COVID-19 pandemic has underscored the persistence of health inequities for Indigenous peoples globally.[1] The increased risk of death from COVID-19 among Native Americans—estimated at 2·1-times higher than White Americans[2]—has largely been attributed to increased comorbidity burden; however, a recent analysis found that Native Americans were more likely to die in hospital than adults of all other races, regardless of comorbidity burden.[3] Indigenous (ie, First Nations, Métis, and Inuit) people in Canada had similar experiences at every point in the COVID-19 care cascade. The Canadian Government reports COVID-19 data only on First Nations living on reserve and does not account for those First Nations people living in urban communities. However, the First Nations Health and Social Secretariat of Manitoba reports COVID-19 data in that province: First Nations account for 27% of total COVID-19 cases and 18% of total COVID-19-related deaths, despite comprising just 10% of the provincial population. Tragically, Native American people had the steepest decline in life expectancy of any racial or ethnic group in the USA, from age 71·8 years to 65·2 years, between 2019 and 2021; the life expectancy gap between the US non-Hispanic White population and the Native American population in 2021 was 11·2 years.[4] There is no recent report on life expectancy changes concerning Indigenous people in Canada; however, the life expectancy gap between Indigenous and non-Indigenous populations has been wide. In 2011, the life expectancy gap relative to the non-Indigenous population was 11·4 years and 11·2 years for Inuit men and women, respectively, and 8·9 years and 9·6 years for First Nations men and women, respectively.[5]

In this Personal View, we discuss the persistent, elevated burden of infectious diseases among Indigenous populations in the USA and Canada. Although better interventions and more equitable use of available interventions are needed, we must also recognise and strive to address the root causes of infectious disease disparities for Indigenous populations. Many of these infectious diseases share common risk factors that are directly tied to colonisation and long-standing inequities in socioeconomic determinants of health, such as poverty, poor access to health care and education, and discrimination in the delivery of health-care services. In our discussion, health equity—the idea that everyone has the opportunity to be as healthy as possible—is the goal. Our underlying premise is that reclaiming and promoting Indigenous ways of knowing (ie, what is considered knowledge and how this knowledge is produced and transmitted in the community), doing, and being is foundational to the work of reclaiming health.

References were identified through searches of PubMed, EBSCO, Clarivate, Google Scholar, Web of Science, and the website of the US Centers for Disease Control and Prevention (CDC) in February, 2022, and searches of the websites of the Public Health Agency of Canada, Indigenous Services Canada, and Canadian Institute for Health Information between Dec 10 and 11, 2022, with the following key words: "Indigenous", "American Indian", "Native American", "First Nations", "Disparity", "Risk Factors", and "Infectious Diseases". In the EBSCO and Clarivate databases, a broad search was conducted with the following arrangement of search terms: dispari* AND Native OR Indigenous OR tribal OR Indian OR First Nations OR Metis OR Inuit AND infection OR infectious. To find additional disease specific literature, a narrower search was conducted in each database with different combinations of the terms and by adding additional terms (eg, RSV). Literature was included if it contained either up-to-date epidemiological information, or discussion of risk factors or community-based intervention strategies. Literature published in

English until Dec 31, 2022, was included in the search and review. Literature that was not specific to Indigenous peoples, but incorporated Indigenous data in the results and discussions, was included. Information published on the CDC and Public Health Agency Canada websites in the form of reports and infographics was also included in the summary table. Although we present only a fraction of the many publications on infectious diseases in Indigenous populations, we highlight the common determinants that influence a wide range of health outcomes and provide a framework for culturally appropriate ways to understand and address infectious diseases in Indigenous populations, privileging Indigenous voices wherever possible.

In the scientific and grey literature, it is common to see publications on Indigenous health or research involving Indigenous people written by non-Indigenous researchers. Sometimes, these researchers have worked with Indigenous communities for years and are trusted allies; however, sometimes they have little to no relationship with the Indigenous peoples they write about and do not have the cultural understanding to contextualise their findings. In writing this Personal View, authorship was intentional, and our positionality is defined at the end of the manuscript.

Historical context

For the Indigenous Peoples of North America, historical trauma, the roots of government distrust, and centuries of catastrophic losses due to infectious diseases all stem from systematic European colonisation beginning in 1492.[6,7] The steady arrival of colonisers over the coming centuries precipitated waves of infectious disease epidemics among the Indigenous Peoples of North America. Atrocities such as the distribution of smallpox-infected blankets by colonisers[8] (ie, biological warfare), medical experimentation, and forced sterilisation are well documented and contribute to ongoing mistrust, intergenerational trauma, and historical trauma. For example, a First Nations community in Alberta, Canada, believes that the high cancer morbidity and mortality in their community are linked to the polio vaccine experimentation that members were subjected to as children without consent—illustrating how a historic distrust of colonial governments can breed mis-information in the present day.[9] Although provincial governments in Canada repealed the Sexual Sterilization Act in the early 1970s, coerced sterilisation of Indigenous women continued in various parts of the country, with cases reported as recently as December, 2018.[10] Harm was also perpetuated by the disruption of Indigenous people's connection with the land and natural environment, which is fundamental to Indigenous identity and wellness. Governmental agencies in both the USA and Canada have documented the trauma resulting from policies such as the Indian Removal Act in the USA and the Indian Act in Canada.[6,11] This history has been well described;[6] key events pertaining to infectious diseases among the Indigenous Peoples of North America are highlighted in figure 1.

Colonialism in North America and its capitalist economic system continue to play a large role in the way infectious diseases emerge, are managed, and claim the lives of Indigenous peoples and other oppressed communities.[12,13] A summary of infectious diseases that affect Indigenous populations in the USA and Canada is presented in the table. Although each infectious disease has specific risk factors for both contracting the disease and disease progression, there are common factors that contribute to high rates of morbidity and mortality among Indigenous peoples. Inequities in socioeconomic determinants of health, including high rates of poverty, inadequate access to healthy food and running water, overcrowded federal housing, poor indoor air quality, and underfunded health-care delivery systems, contribute to high rates of infectious diseases, especially on tribal reservations.[101] The high prevalence of underlying chronic health conditions in Indigenous populations, including diabetes, heart disease, and lung disease, is driven by these same social determinants and exacerbates infectious disease disparities. Structural oppression and coloniality of power, with the resulting loss of language and culture, environmental deprivation, racism, and disconnection from the land, are at the root of these health inequities and are prime contributors to poor health outcomes in Indigenous communities.[101]

Challenges and successes in reducing the burden of infectious diseases in Indigenous communities

> "Humankind has not woven the web of life. We are but one thread within it. Whatever we do to the web, we do to ourselves. All things are bound together. All things connect."
>
> *Chief Seattle (Suquamish, Duwamish), 1854*

Although Indigenous peoples have some of the highest rates of certain infectious diseases, Indigenous nations and tribes have been successful in their disease prevention and mitigation efforts. In the early 1980s, high rates of diarrhoea and dehydration were documented in the White Mountain Apache population in the southwest USA. Studies in that community demonstrating successful treatment with oral rehydration solution and early refeeding informed both US and global policy, and the contributions of the White Mountain Apache Tribe to these policies were officially recognised in 1995.[102] A focus on the wellness of the collective community has undoubtedly contributed to the ability of Indigenous nations to adapt to and survive dramatic change; this mentality is credited with spurring COVID-19 vaccine uptake during the pandemic.[103,104]

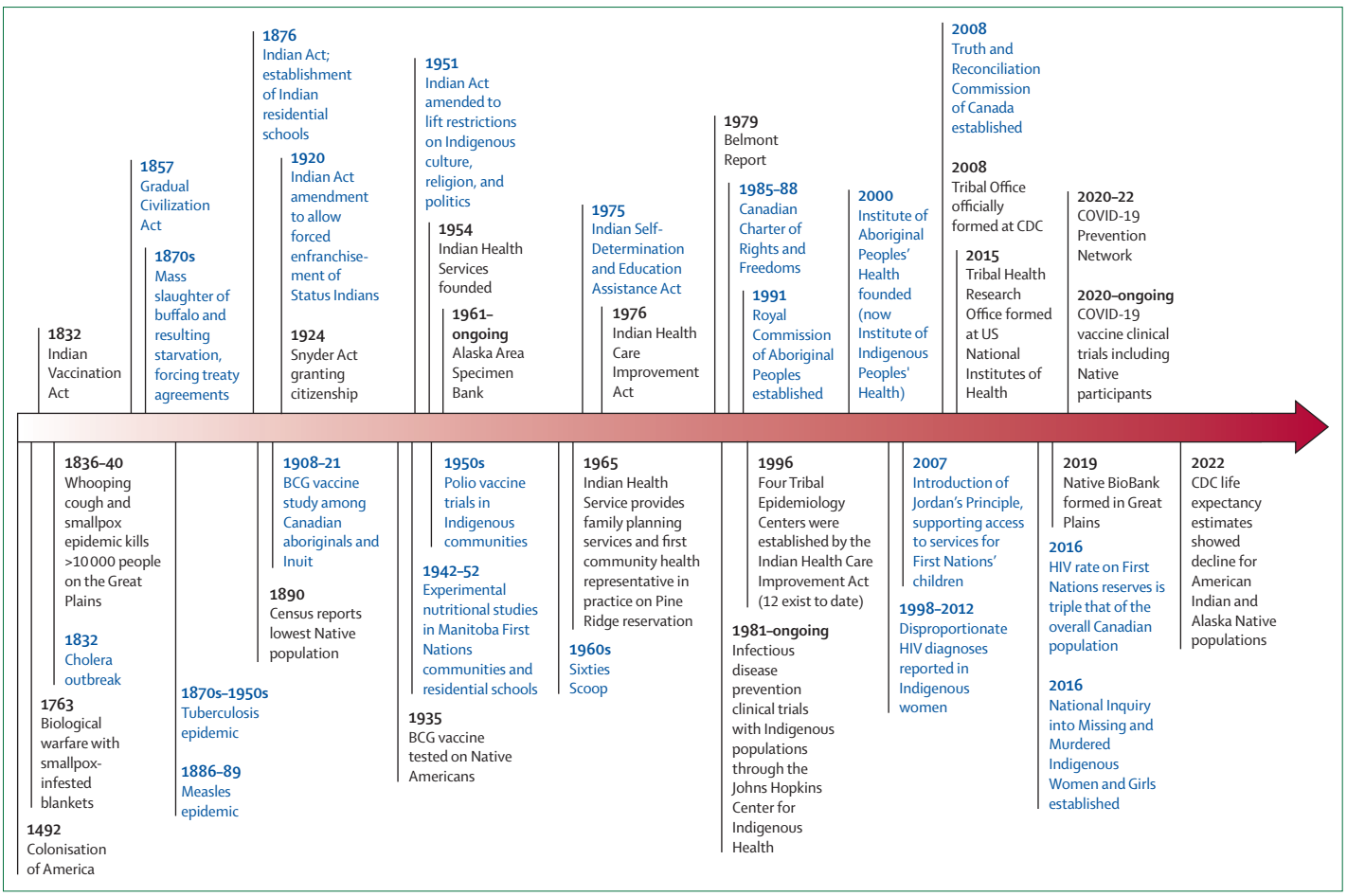

Figure 1: **Infectious disease milestones in government history in relation to Indigenous populations across Canada (blue) and the USA (black)**
CDC=Centers for Disease Control and Prevention.

Vaccine research in partnership with Indigenous communities has proven the efficacy of numerous products that are recommended for routine use (eg, the *Haemophilus influenzae* type b vaccine, pneumococcal conjugate vaccine, and rotavirus vaccine),[105–109] and vaccines have been powerful tools for the reduction of infectious diseases in Indigenous populations.[46,64,95,110,111] Although distrust of health care and health-care abandonment have resulted in reduced vaccine uptake in some Indigenous populations, community-informed, community-led initiatives to improve vaccine uptake can improve vaccine impact.[104,112,113] However, even the best vaccines cannot accomplish health equity for Indigenous peoples. Investment in improving the structural, economic, educational, and social determinants of Indigenous health, along with investment in local research and public health capacity are essential, but have been lagging. The continued exclusion of Indigenous participation from health policy design and implementation, and the absence of sovereignty over Indigenous health data management, while relying on deficit-based and suboptimal health statistics for intervention design, perpetuate these health inequities.[114] Concerted effort is needed to understand the root causes of adverse health outcomes and to support Indigenous communities to develop community-centric health-care interventions that operationalise self-determination and are based in each community's specific model of health. We discuss different approaches to reducing the burden of select infectious diseases and highlight successes and lessons for future work.

Helicobacter pylori

H pylori is a Gram-negative bacterium that colonises the gastric mucosal epithelium in individuals of all ages. Established risk factors for *H pylori* transmission and infection include environmental factors (eg, crowded housing and contaminated water), cigarette smoking, and consumption of preserved or smoked meat or fish.[89] Most people infected with *H pylori* are asymptomatic; however, chronic infection is strongly associated with an increased risk of gastric cancer. Indigenous populations in the USA and Canada have a higher prevalence of *H pylori* infection than non-Indigenous members of

	Summary of infectious disease	Risk factors
Respiratory viral diseases		
COVID-19[2,14–18]		
USA	Native Americans are more than twice as likely to be hospitalised or die from COVID-19 than White, non-Hispanic Americans	Underlying medical conditions and adverse social determinants of health
Canada	Indigenous people in Canada have higher rates of infection and more severe disease than non-Indigenous Canadians—eg, in January, 2021, First Nations people, who account for 10% of the population in Manitoba, represented nearly 70% of COVID-19 cases; cumulatively, they account for 27% of all cases as of December, 2022	Underlying medical conditions and adverse social determinants of health
Influenza[19–21]		
USA	Native Americans have higher rates of influenza-associated hospitalisation than the US White population	Underlying medical conditions and adverse social determinants of health
Canada	First Nations People are at least 4–5-times more likely to be hospitalised from influenza and pneumonia than the general Canadian population	Underlying medical conditions and adverse social determinants of health
Influenza H1N1[22–28]		
USA	Native Americans had higher rates of influenza-like illness compared with non-Hispanic White people during the H1N1 pandemic	Underlying medical conditions, geographical isolation or on-reserve residence, and adverse social determinants of health
Canada	Indigenous people in Canada have rates of hospitalisation nearly 3 times the rate of the general Canadian population, and were 6·5-times more likely to be admitted to an intensive care unit with pandemic H1N1; the odds of hospitalisation were twice as high for First Nations people living on reserve than people living off reserve	Underlying medical conditions, geographical isolation or on-reserve residence, and adverse social determinants of health
RSV[29–35]		
USA	Rates of RSV-associated hospitalisation among Native American children are 2–10-times higher than that of the general US population; the highest rates of disease are reported in Alaska Native, Navajo, and White Mountain Apache children	Underlying medical conditions, lower levels of breastfeeding, household crowding, insufficient access to piped water, smoke exposure, and poverty
Canada	Baffin (Qikiqtani) Region, Nunavut, has the highest known rates of RSV bronchiolitis requiring hospitalisation in the first year of life—484 hospitalisations per 1000 infants compared with 27 hospitalisations per 1000 infants in temperate Canada and the USA	Underlying medical conditions, lower levels of breastfeeding, household crowding, insufficient access to piped water, smoke exposure, and poverty
ALRI[36–40]		
USA	Indigenous people are at increased risk of ALRI, with children being most at risk for severe ARLI; lower respiratory tract infection morbidity and mortality for Native Americans is nearly twice that of the general US population; vaccines against select pathogens responsible for causing ARLI have decreased morbidity and mortality; however, rates remain high and have increased in the past 30 years compared with the general US population	Underlying medical conditions, tobacco use, crowded housing and indoor air pollution, insufficient access to piped water, poverty, poor access to health care, and living in rural areas
Canada	Rates of lower respiratory tract infection hospitalisations, including bronchiolitis and pneumonia, are high in Inuit infants in Nunavut (235 hospitalisations per 1000 infants) and First Nations infants in the Sioux Lookout First Nations Health Authority region of northwestern Ontario (44 hospitalisations per 1000 infants) compared with 25 hospitalisations per 1000 infants in the general population	Underlying medical conditions, tobacco use, crowded housing and indoor air pollution, insufficient access to piped water, poverty, poor access to health care, and living in rural areas
Bacterial disease		
MRSA[41–45]		
USA	The prevalence of invasive MRSA in the Navajo Nation and White Mountain Apache Tribal lands is higher than the general US population	Household crowding, insufficient access to piped water, and underlying medical conditions
Canada	MRSA is increasingly being reported in First Nations communities in northern Manitoba, Saskatchewan, and Nunavut; in northern Saskatchewan, the annual rate increased from 8·2 cases in 2001 to 142·6 cases per 10 000 people in 2008, with rates as high as 482 cases per 10 000 people in a First Nation community	Household crowding, insufficient access to piped water, and underlying medical conditions
IPD[46–52]		
USA	Highly efficacious pneumococcal conjugate vaccines have resulted in substantial reductions in vaccine serotype IPD, but disparities persist, largely because of disease caused by serotypes not covered by existing vaccines; prevalence of IPD is approximately 3–5-times higher in children and adults living in the Navajo Nation than in the general US population, and approximately 4–5-times higher among Alaska Native individuals than among non-Alaska Native individuals	Underlying medical conditions,[53] household crowding, indoor air pollution, and insufficient access to running water have been associated with pneumococcal carriage
Canada	Despite vaccine use, Indigenous people are disproportionately affected by IPD; 29% of patients hospitalised for IPD at the Thunder Bay Regional Health Services, northwestern Ontario, between 2006 and 2015 identified as Indigenous, despite making up 19% of the population	Underlying medical conditions,[53] household crowding, indoor air pollution, and insufficient access to running water have been associated with pneumococcal carriage
Tuberculosis[54–59]		
USA	Programmes for case finding and treatment of latent tuberculosis infection have achieved substantial reductions in the burden of tuberculosis in Indigenous populations, but disparities persist; prevalence is approximately 8-times higher in US Native American individuals than in non-Hispanic White people	Concurrent HIV infection, tobacco smoking, indoor air pollution, and underlying medical conditions such as diabetes, kidney disease, and alcoholism
Canada	Tuberculosis prevalence is approximately 4-times higher in Indigenous people than in the overall population of Canada; the rate of tuberculosis in Inuit Nunangat is over 300-times higher than in the Canadian-born, non-Indigenous population, whereas the rate of tuberculosis in First Nations living on reserve is over 40-times higher than in the non-Indigenous population	Concurrent HIV infection, tobacco smoking, indoor air pollution, and underlying medical conditions such as diabetes, kidney disease, and alcoholism

(Table continues on next page)

those countries.[89,90] Similarly, Indigenous populations have a disproportionately high prevalence of gastric cancer, especially in Alaska.[91] The pattern of gastric cancer in First Nations in Canada is similar to that in the Alaska Native population, with cancer occurring at higher rates in younger Indigenous people and women than those in the non-Indigenous population.[115]

Data about successful approaches to *H pylori* eradication are scarce among Indigenous communities. Although several studies have documented successful initial eradication following treatment, reinfection is common.[89,92] One study that followed individuals after successful *H pylori* treatment found that 22% of Alaska Native people in rural areas were reinfected by 2 years post treatment and more than 35% of people were reinfected by 12 years post treatment (unpublished),[116] a rate much higher than those reported in other populations in developed countries.[92,116] These studies demonstrate the limitations of a purely microbiological approach and underscore the need for more comprehensive, community-engaged strategies for the eradication of *H pylori*.

In the southwest USA, a team of investigators from the University of Arizona College of Public Health, the

	Summary of infectious disease	Risk factors
(Continued from previous page)		
Sexually transmitted infections[53,60,61]		
Chlamydia[53,60,61]		
USA	In 2019, the rate of chlamydia among Native Americans was the second highest among all racial and ethnic subgroups and was 3·6-times greater than the rate among White Americans	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Canada	Indigenous youth are diagnosed with chlamydia at a rate 7-times higher than the diagnosis rate among non-Indigenous youth	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Gonorrhea[62]		
USA	In 2019, the rate of gonorrhoea infections among Native Americans was the second highest among all racial and ethnic subgroups and was 4·8-times greater than the rate among White Americans	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Canada	In 2015, the Northwest Territories (815·9 cases per 100 000 people), Nunavut (837·6 cases per 100 000 people), and Yukon (302·2 cases per 100 000 people) had the highest gonorrhoea rates in Canada compared with the general population (55·4 cases per 100 000 people)	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Syphilis[63]		
USA	As of 2019, the rate of syphilis infection among Native Americans is more than triple the rate among White Americans; of the 12 Indian Health Service regions, four had higher case rates of syphilis than for all other races and ethnicities	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Canada	Within the first 6 months of 2022, there was a 928% increase in syphilis cases from 2019 in northern Saskatchewan on-reserve communities	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
HPV[64–68]		
USA	Native American women have elevated rates of both HPV infection (estimated) and cervical cancer. High-risk (cancer-causing) types of HPV not covered by the current vaccine are prevalent in Native American communities; within the Great Plains Indian Health Service, nearly 35% of Native American women were positive for at least one type of HPV and 22% of women from the Hopi community were positive for at least one type of HPV	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Canada	Indigenous communities across Canada have higher rates of HPV infection than the non-Indigenous population; in the Northwest Territories, HPV prevalence was approximately 50% higher among Indigenous women than non-Indigenous women; Indigenous women have a 2–20-times greater risk of being diagnosed with cervical cancer	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
HIV[58,69–71]		
USA	Prevalence of HIV and AIDS among Native Americans is lower than that of the general US population, but Indigenous people with HIV and AIDS have higher rates of hospitalisation and increased mortality compared with White Americans with HIV and AIDS	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions
Canada	Indigenous people in Canada are disproportionately affected by HIV, particularly in the prairie provinces such as Saskatchewan, where Indigenous people account for 65–80% of HIV infections despite making up only 16% of the provincial population; between 1998 and 2012, nearly half (47·3%) of all positive HIV test reports among Indigenous people were for women, compared with 20·1% of reports for people of other ethnicities	Poverty, health-care access, physical and sexual victimisation, insufficient sexual health education, and loss of traditional coming-of-age teachings, inadequate treatment, and care interruptions

(Table continues on next page)

	Summary of infectious disease	Risk factors
(Continued from previous page)		
Gastrointestinal and hepatic infection		
HCV[71-81]		
USA	Native Americans have the highest incidence rate of acute HCV infection and the highest HCV-related mortality rate of any ethnic group in the USA; between 2002 and 2014, Native Americans had the largest increase in rates of liver and intrahepatic bile duct cancer of any ethnic group	Poverty, poor access to health care, and injection drug use
Canada	Despite declining national rates, the newly diagnosed HCV rate was 3-times higher in First Nations living on reserve than the overall Canadian population in 2016; anti-HCV positive prevalence for Indigenous people is 7% compared with 1% in the general population	Poverty, poor access to health care, and injection drug use
Hepatitis A and B[81-88]		
USA	Hepatitis A, once affecting Native Americans at rates 10-times greater than the national average, is now uncommon due to good uptake of highly effective vaccines; similarly, use of hepatitis B vaccine has resulted in a dramatic decline in disease incidence and eliminated this health disparity in the USA	Hepatitis A: crowded housing, and inadequate or water or sewage systems; hepatitis B: born to a mother with hepatitis B, sexual transmission, and injection drug use
Canada	Although hepatitis A and B diagnosis rates are low in Canada, Indigenous people are still considered at high risk of infection; between 1999 and 2008, the cumulative incidence rate of acute hepatitis B virus infection for Indigenous people was 1·92 cases per 100 000 people compared with 0·78 cases per 100 000 people in non-Indigenous Canadians; Indigenous people were 3·32-times more likely to develop acute HBV infection than non-Indigenous Canadians; the incidence rate of acute HBV in Indigenous women was 4·34-times higher than in non-Indigenous women; the incidence rate was 1·86-times higher in Indigenous men than in non-Indigenous men	Hepatitis A: crowded housing, and inadequate or water or sewage systems; hepatitis B: born to a mother with hepatitis B, sexual transmission, and injection drug use
Helicobacter pylori[89-94]		
USA	Native Americans have a higher prevalence of *H pylori* and higher incidence rates of gastric cancer than non-Hispanic White people	Multifamily or multigenerational living quarters, insufficient access to refrigeration and plumbing, contaminated drinking water sources, high salt and nitrate intake, tobacco smoking, and certain underlying medical conditions
Canada	Despite low prevalence in Canada, studies have shown a high prevalence of *H pylori* in Indigenous communities; the Wasagamack First Nation community in Northern Manitoba reported 95% seropositivity, and peptic ulcer disease hospitalisation rates approximately 2-times that of non-Indigenous populations (394 cases per 100 000 people *vs* 204 cases per 100 000 people)	Multifamily or multigenerational living quarters, insufficient access to refrigeration and plumbing, contaminated drinking water sources, high salt and nitrate intake, tobacco smoking, and certain underlying medical conditions
Rotavirus[95-100]		
USA	Before the availability of rotavirus vaccines, the diarrhoea-associated hospitalisation rate in Native American infants was higher than for US children	Insufficient access to running water, and close contact with a person infected with rotavirus
Canada	Prolonged diarrhoea and malnutrition were a primary cause of morbidity and mortality in Indigenous populations before vaccine availability	Insufficient access to running water, and close contact with a person infected with rotavirus

RSV=respiratory syncytial virus. ALRI=acute lower respiratory infection. MRSA=methicillin-resistant *Staphylococcus aureus*. IPD=invasive pneumococcal disease. HPV=human papillomavirus. HCV=hepatitis C virus.

Table: **Summary of selected infectious diseases affecting Indigenous People of North America**

Arizona Cancer Center, Northern Arizona University, the Navajo Nation's community health representatives, and Winslow Indian Healthcare Center developed the Navajo Healthy Stomach Project to explore the prevalence of *H pylori* in the Navajo Nation using a mixed-methods research approach.[117] The Navajo Healthy Stomach Project initially conducted a series of focus group discussions to establish knowledge and perceptions of *H pylori* and stomach cancer among Navajo adults. This work documented little knowledge of *H pylori* infection, concerns for gastric cancer, and challenges in doctor–patient communications related to a perceived inability of physicians to adequately address stomach-related health issues.[92] The team subsequently conducted a cross-sectional survey in three Navajo communities.[89] Using urea breath tests, the study found that 65% of all participants had an active *H pylori* infection. Use of unregulated water (ie, water from a natural spring, community spigot, windmill, or private well) or untreated water was significantly associated with active infection.[89] Programmes to screen and effectively treat *H pylori* infection from childhood to adulthood are urgently needed. However, as was demonstrated in Alaska, reinfection will be common unless environmental risk factors are addressed. Future planned activities include providing culturally tailored educational materials, including outreach programmes conducted in the local language, improving provider education, and holding discussions with stakeholders on the reduction of environmental risk factors.

The approach taken by the Navajo Healthy Stomach Project exemplifies several best practices for addressing infectious disease disparities in Indigenous populations. Investigators should engage with local tribal leaders and community stakeholders to understand the root causes of infectious diseases, cultural knowledge and practices, and considerations related to treatments or interventions. A community advisory board that includes Elders, youth, community members who have had related health issues, and representatives from local agencies that could

be agents of change (eg, tribal Environmental Protection Agencies, water treatment facilities, and housing programmes), should be convened to guide all phases of work. Of note is the importance of working with a community advisory board or tribal leaders to identify words in the Indigenous language to create a descriptive definition of the infectious disease that can be embraced by community members and used in educational materials.

HIV and hepatitis C virus (HCV)—wise practices include both Western and Indigenous ways

Colonisation was not a single event that happened long ago, but rather, an event that happened in waves, over time, leading to coloniality—a living legacy of interconnected systems that perpetuates settler colonialism.[118] These processes are highly gendered, specifically targeting Indigenous women who held considerable, if not primary, power in many Indigenous nations, which were matriarchal precolonial contact.[119,120] Although Indigenous men fare worse than women across various health determinants, studies have highlighted the role of gendered power differentials experienced by women in the lopsided HIV risks associated with injection drug use.[69] Indigenous women in Canada are over-represented among people diagnosed with HIV; for example, in 2011, the estimated infection rate among people in Canada self-identifying as Indigenous was about 3·5 times higher than among the non-Indigenous population.[121] Indigenous women received nearly half (47%) of all HIV diagnoses among Indigenous people between 1998 and 2012, whereas non-Indigenous women received 20% of HIV diagnoses among non-Indigenous people.[70] In British Columbia, approximately 6% of the population self-identifies as Indigenous, and yet Indigenous people have been consistently over-represented in HIV diagnoses, ranging from 8% to 17% of new HIV diagnoses over the same timeframe. The HIV inequity experienced by Indigenous women was especially pronounced in 2017, when they represented 33% of new HIV diagnoses among women in British Columbia.[121–124] Although women, including Indigenous women, tend to engage with research and health care—especially during their reproductive years—numerous testing events, in addition to clinical care and research, consistently report higher HIV rates in Indigenous women than in Indigenous men and non-Indigenous Canadians. Although there is a comparative over-representation of Indigenous people in HIV diagnoses in Australia, New Zealand, and Canada, the rates of Indigenous young women diagnosed with HIV in Canada were substantially higher.[69] In Saskatchewan, Indigenous people have long been over-represented in HIV diagnoses. As far back as 1985, 50% of HIV diagnoses were in people self-identifying as Indigenous, when the Indigenous population made up approximately 10% of people living in Saskatchewan.[125] By 2008, the disproportionate HIV burden borne by Indigenous people in Saskatchewan had increased to 76%, and from 2010 to 2018, hovered around 70%, whereas the Indigenous population in Saskatchewan increased to just over 16% over the same time period. In 2018, Indigenous women accounted for 87% of all female cases and comprised 49% of all Indigenous cases (an increase from the average of 45% of cases in the period between 2009 and 2018).[126] In 2021, 237 HIV diagnoses—a record number—were reported in Saskatchewan, with injection drug use as the primary risk factor. The increase (nearly 30% over the course of 2020) has been attributed to decreased access to prevention, testing, and care related to COVID-19, but underlying structural problems including insufficient harm reduction and needle or syringe exchange services, which are severely underfunded, are the actual causes.[127] Indigenous identity and gender analyses for HIV diagnoses in Saskatchewan in 2021 were not available at the time this Personal View was written.

Unfortunately, intersectional, Indigenous, and gender data are often not available, making it difficult to secure funding for programmes in Indigenous communities that address HIV and HCV inequities; for example, in 2020, only 36% of new HIV diagnoses included race or ethnicity data.[128] Data concerning HCV are even more scarce, but the data that do exist suggest a similar pattern.[71,72] When such data are reported, indigeneity is erroneously portrayed as a risk factor, failing to underscore the historical and contemporary inequities that are actually responsible for such over-representation. Furthermore, Indigenous women are over-represented in the behaviours and circumstances considered high risk for HIV and HCV infections, including injection drug use, incarceration, and sex work, but attempts at linking these circumstances to coloniality are very rarely made.[71] The misclassification of Indigenous as a separate risk factor was discussed by Fayed and colleagues[73] as simultaneously at-risking and asterisking Indigenous women while ignoring the high-risk circumstances and activities of Indigenous over-representation, thereby minimising Indigenous leadership and voices in solutions. Many in the Indigenous HIV space see the need for structural changes to both programme and research funding so that distinctions-based, locally-led initiatives can be sustainably resourced.

Indigenous women with living and lived experience of HIV or HCV are our mothers, daughters, sisters, aunties, and grandmothers. Many have come through poverty, often chronic and profound, as well as other poor socioeconomic circumstances. Most Indigenous women carry intergenerational trauma, including from residential schools, day schools and the Sixties Scoop (a period extending from the late 1950s to the early 1980s during which policies in Canada enabled child welfare authorities to take or scoop up Indigenous children from their families for placement in non-Indigenous foster homes

or adoptive families), and have themselves experienced family or intimate partner violence, sometimes fuelled by alcohol or drug use. These women faced and continue to face multiple, intersecting forms of oppression, and are portrayed as victims, marginalised, and vulnerable. Although these labels might apply, Indigenous women are also survivors, strong, and resilient. Many have transformed themselves and their lives, recognising that Western medicine is (in the case of HIV anti-retroviral therapy) or could be (in the case of an HCV cure) necessary, but rarely sufficient. They have returned to their culture—to First Nations, Métis, and Inuit ways of knowing, being, and doing—and healed. Many Indigenous women now work in outreach, navigation, and mentorship, supporting other Indigenous women on their own healing and wellness journeys. Some women have become researchers, shaping research priorities, ethics, and the mobilisation of results into policy and programming. Such Indigenous-led initiatives include the DRUM & SASH, a culturally grounded, community-led project in which shared-care models for First Nations and Métis are being developed and evaluated; the CheckUp Project, an Inuit-specific project focused on sexually transmitted and blood-borne infection prevention among Inuit youth through social-media and land-based intervention; Peers4Wellness, an Indigenous women-focused project emphasising Indigenous ways of supportive HIV and HCV care by exploring the applicability of peer navigation as a promising practice within Indigenous contexts; FOXY, an expressive arts platform for young women and gender-diverse youth across northern Canada to convey knowledge, opinions, and questions about sexual health with a strong focus on empowered decision making; and SMASH, a programme parallel to FOXY, which educates young men on positive masculinity and encourages realistic discussions about sexual health and relationships, and straightforward strategies for communication, consent, and respecting boundaries. Under the guidance of Indigenous women across several innovative programmes, our understanding of Indigenous approaches to harm reduction has been broadened to include decolonisation and the application of harm reduction to Indigenous culture and ceremony. Indigenous women are helping to redefine health care for Indigenous women so that it can become truly culturally safe and responsive.

For more on the **DRUM & SASH project** see https://www.drumandsash.ca

For more on the **CheckUp Project** see https://www.facebook.com/CheckUpProject

For more on the **Peers4Wellness project** see https://indigenouswellness.ca/projects/peers4wellness

For more on the **FOXY platform** see https://arcticfoxy.com

For more on the **SMASH programme** see https://arcticsmash.ca

Respiratory syncytial virus (RSV)—a multipronged approach

Indigenous infants have among the highest rates of hospitalisation for acute lower respiratory tract infections in the world, and RSV is a leading cause.[129,130] Studies in partnership with the Navajo Nation and White Mountain Apache Tribe demonstrated that the high rate of infant RSV hospitalisation was not attributable to low maternal anti-RSV antibody titres, low transplacental antibody transfer rates, or ineffective RSV-neutralising antibodies. Known risk factors for RSV disease include prematurity, lower levels of breastfeeding, household crowding, insufficient access to piped water, woodstove use, and poverty, many of which are more prevalent in Indigenous communities.[36,131,132]

There are two broad approaches to RSV prevention: risk factor reduction and biomedical interventions. Work in both the USA and Canada suggest that reductions in respiratory disease might be possible through home remediation and household environmental education, while underscoring the need for extensive community engagement to understand perceptions and priorities and to ensure optimal roll-out of proposed interventions.[133,134] A team led by the Alaska Native Tribal Health Consortium evaluated the feasibility of environmental assessment and remediation in the homes of children with known lung disease. Following assessment of indoor air quality and the provision of educational materials, local housing authorities completed low-cost modifications relating to ventilation, mould or moisture mitigation, and heating sources. The researchers found that improving household ventilation, replacing woodstoves, and providing in-home education resulted in decreased self-reported respiratory symptoms, clinic visits for respiratory illness, and school absenteeism.[135]

Biomedical interventions are a crucial complement to risk factor reduction, and the combination of these two approaches is likely to result in the most substantial and sustainable reductions in RSV disease burden. Currently, palivizumab, a monoclonal antibody against RSV, is the only licensed RSV-prevention product in the USA and Canada, and its use is generally restricted to a small subset of infants at the highest risk of severe RSV. Several studies have documented the effectiveness of palivizumab, including in Alaska Native infants.[136] However, a recent study in Canada found no evidence that administration of palivizumab reduced RSV hospitalisations in healthy, full-term Inuit infants.[137] The suboptimal coverage with recommended palivizumab doses during the three RSV seasons suggested feasibility challenges in this setting. Furthermore, the study team documented concerns with programme implementation, including insufficient consultation with the Inuit population at all points.[138] This work underscores the importance of community engagement in all phases of work.

Recently, the long-acting RSV monoclonal antibody nirsevimab was found to have an efficacy of 75% in protecting healthy late-preterm and term infants from medically attended RSV-associated lower respiratory tract infection.[139] The global multisite phase 3 clinical trial of nirsevimab included Indigenous participants from the southwest USA. Investigators joined the study following both community approval of the trial and preliminary work with health-care providers and community members that established high familiarity with and concern for RSV disease. Obtaining approval for clinical trials in Indigenous communities is often a lengthy

process and requires modification of study materials to accommodate community regulations and preferences. However, without dedicated efforts to ensure that Indigenous and other marginalised populations have opportunities to participate in clinical trials, the erasure of these populations from the scientific literature will continue and decisions on licensure and usage of interventions will be made without knowledge of whether products are safe and efficacious in the populations with the highest burden of disease.[140,141]

The successful roll out of any of RSV-prevention interventions—whether a vaccine or a monoclonal antibody or a better woodstove—will be crucially dependent on engagement with community members, tribal leaders, and health-care providers, the development of culturally informed educational materials, and community-designed, community-led initiatives to increase awareness of RSV and the ways to prevent it.

Charting a way forward for infectious disease prevention in Indigenous communities

> "I'll go and I'll do more."
>
> *Annie Dodge Wauneka (Diné), first Native American recipient of the Presidential Medal of Freedom, awarded for her long crusade for improved health programmes*

Much progress has been made in the past several decades toward reducing the infectious disease burden in Indigenous populations; however, disparities persist and are driven by inequities in underlying socioeconomic determinants of health. Although the US Federal Government has a treaty obligation to provide needed services, it is generally acknowledged that federal spending has been inadequate for the past century. The US Federal Government allocates a smaller amount of funding per capita to the Indian Health Service than to any other federally funded health-care programme.[142,143] The Government's inability to make substantial improvements in socioeconomic conditions on tribal lands has left Indigenous populations in a state of perpetual precarity. In Canada, Indigenous people are subjected to haphazard and inconsistent health care, depending on their place of residence and status (as Indians) because health-care responsibilities are shared between federal and provincial governments. The absence of clarity on the roles and responsibilities of each government has often led to worse, and occasionally fatal, circumstances for Indigenous people in need of care.[144]

We propose a framework for achieving sustainable improvements in the overall health of Indigenous people, including reductions in infectious diseases (figure 2). We must start by acknowledging the enduring effects of colonisation and assimilation tactics, and the existence of structural racism in modern society. To overcome these effects, government and health-care providers should focus on cultural humility (respect for tribal sovereignty, active self-reflection, and the addressing of power imbalances, etc) and community power building. Additionally, health care should recognise the holistic approaches to health reflected in Indigenous wellness models. Although safe and efficacious vaccines have greatly reduced the burden of infectious diseases, fundamental changes to laws and policies are needed for upstream disease prevention and control. Directing resources to Indigenous communities to improve health-care services and address the myriad environmental, household, educational, and economic factors that drive health disparities is crucial. To start, the health-care infrastructure must be strengthened by increasing access to primary (eg, vaccinations) and secondary (eg, disease detection) disease prevention. Community health representatives comprised of paraprofessionals have successfully delivered health-care, health-promotion, and disease-prevention services in rural community-based settings and support for community health representative programmes should be increased.[145] Indigenous nations should be appropriately resourced so that they can exercise sovereignty in co-creating culturally safe health-care systems rooted in Indigenous wellness perspectives and traditional practices, while being supported by Western medical services in a respectful and productive space that promotes complementary worldviews.[146]

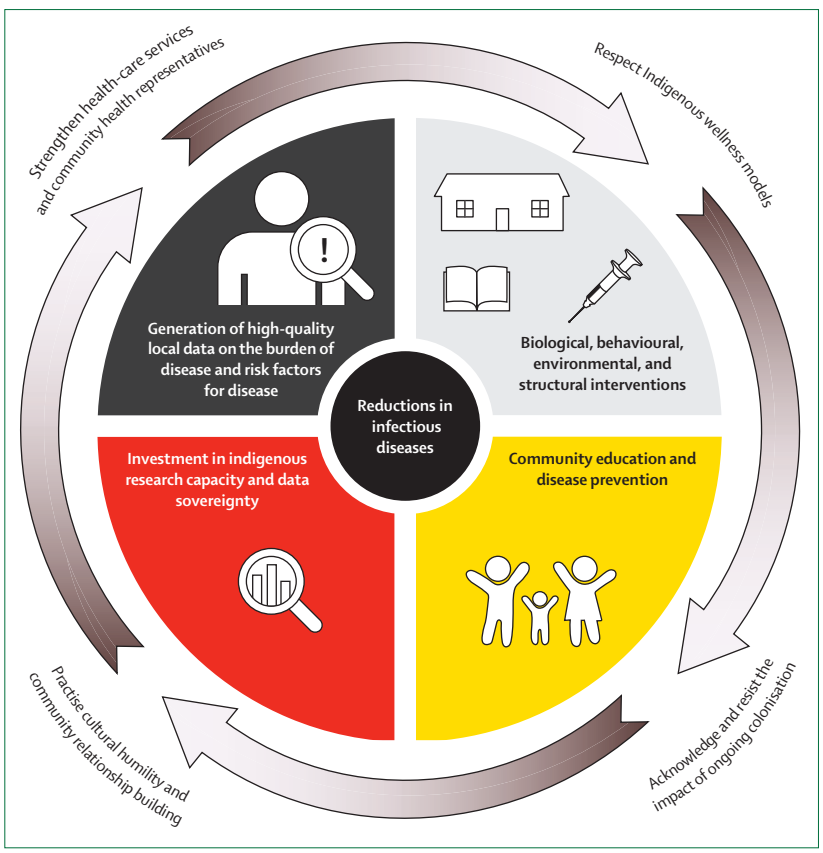

Figure 2: **Framework for attaining sustainable improvements in Indigenous People's health**

For more on the **First Nations Perspectives on Health and Wellness** see https://www.fnha.ca/wellness/wellness-for-first-nations/first-nations-perspective-on-health-and-wellness

Going forward, reductions in infectious diseases in Indigenous populations require: ensuring that Indigenous communities have access to accurate data that reflect the unique cultures and health needs of their communities; designing and implementing biological, behavioural, environmental, and structural interventions centring on a holistic approach to health care; providing opportunities for Indigenous community members to participate in clinical research in a way that is respectful of tribal sovereignty and Indigenous research ethics; and supporting development and evaluation of community-led and community-informed interventions that incorporate protective cultural knowledge and practices. It is important that health-care providers and researchers engage community stakeholders at all stages of work, from research conceptualisation and grant writing, to designing and evaluating solutions, and disseminating findings.[60,147–149]

We must work together for the collective liberation of Indigenous and all other oppressed peoples. The Haudenosaunee (Iroquois) Seventh Generation philosophy states that in our every deliberation, we must consider the impact of our decisions on the next seven generations. Tribal nations across the USA and Canada follow this philosophy by organising toward liberation and by exercising sovereignty through the management of health-care services, research that benefits tribal citizens, and the training of the next generations of scientists and health-care providers. Non-Indigenous researchers, clinicians, educators, public health professionals, and beyond can support Indigenous nations to strengthen self-determination by understanding and teaching others about their historical and cultural contexts, advocating for funding to address inequities, building respectful relationships with Native nations, listening to and organising alongside Indigenous-led movements toward liberation, and committing to ensuring opportunities for Indigenous participation in clinical trials of potential disease interventions (even when that means that the process takes longer). Culturally relevant, scientifically sound approaches offer a path toward a reduction in infectious diseases and the restoration of wellness for Indigenous peoples.

Positionality

Our personal and professional insights offer a unique Indigenous lens through which to view infectious diseases impacting Indigenous communities across the USA and Canada. The following is a brief summary of who we are, our expertise, and our relationship with Indigenous communities.

NRL is Onödowága or referred to as the Seneca Nation of Indians from western New York state. She is a tenure-track Assistant Professor in the Department of Chemistry and Biochemistry at Northern Arizona University. NRL focuses on vaccine design along with clinical and translational research in Native American populations. As a member of various organisations and research programmes, NRL has served numerous Native American populations across the USA.

AK is a citizen of the Nipissing First Nation in Ontario, Canada. She is the Cameco Chair in Indigenous Health and Wellness at the University of Saskatchewan and has an adjunct appointment in Health Sciences at Simon Fraser University. Her research focuses on HIV/AIDS, and HCV, as well as frequently associated conditions (eg, drug use and incarceration). AK carries out research with First Nations, Métis, and Inuit people, focused on wellness, land-based and culture-based healing, and Indigenous ways of knowing, being, and doing. She is also developing Indigenous research methods.

DV is Tewa from Nanbé Ówîngeh (Nambe Pueblo), New Mexico. She is a Master of Public Health student studying infectious diseases and vaccinology at the University of California, Berkeley. Deionna is mentored by LLH at the Johns Hopkins Center for Indigenous Health with an emphasis on RSV, research ethics, and improving the health and wellbeing of Native Nations.

DM identifies as a White man from Denver, Colorado. He graduated from Northern Arizona University with a Bachelor degree in biology. He was mentored by NRL and focused on developing novel HPV vaccines. Currently, DM is a postbaccalaureate at the National Institute of Neurological Disorders and Stroke. DM plans to pursue a medical career with the goal of serving at-risk communities.

PRS is an enrolled member of the Navajo Nation. Her Diné (Navajo) clans are Ozeíí Tachii'nii (Red-Running-Into-the-Water Clan), born for Kinyaa'aanii (Towering House People), her maternal grandfather's clan is Naakaii Dine'é (Mexican Clan) and paternal grandfather's clan is Bit'ahnii (Leaf Clan). She is a Professor in the Department of Health Sciences, College of Health and Human Services at Northern Arizona University. PRS's research includes southwest Native American knowledge, attitudes, and beliefs regarding cancer screening and prevention, *H pylori* infection and stomach cancer, the evaluation of the Healthy Diné Nation Act, and exploring public health resiliency factors. Through her research and professional networks, PRS has worked with over 30 Indigenous communities in the USA in grant-writing training, conducting community-based participatory research in tribal communities, and training and technical-assistance activities.

TA is a first-generation settler in the Treaty 6 Territory and Homeland of the Metis in Saskatoon, Canada. With roots in Ghana and Nigeria, he completed his bachelor's degree in Medicine and Surgery at the University of Ilorin, Nigeria. Before migrating to Canada, he had over 10 years of clinical practice and health-care management experience. He is currently a second-year Master of Public Health student at the University of Saskatchewan.

He is also under AK's mentorship in Indigenous-health research.

LLH identifies as a White woman who lives in the southwest of the USA. She is an Associate Professor at the Johns Hopkins Bloomberg School of Public Health and the Director of Infectious Disease Programs at the Center for Indigenous Health. Her expertise includes the epidemiology and prevention of infectious diseases in underserved populations. LLH has worked with Indigenous communities in Alaska and the southwest USA for over 15 years. She serves in an advisory capacity to the Diné (Navajo) Nation's Epidemiology Center and COVID-19 Health Command Operations Center.

Contributors

NRL, AK, DV, PRS, and LLH contributed to the conceptualisation and writing of this Personal View. DV, DM, and TA conducted thorough literature searches. All authors were involved in the review and editing of this Personal View. All authors approved the final manuscript.

Declaration of interests

LLH reports research grant funding to her institution from AstraZeneca, Merck, and Pfizer. All other authors declare no competing interests.

Acknowledgments

NRL and PRS are supported by the partnership for Native American Cancer Prevention (NCI grant number U54CA143925, and grant number U54CA143924 [PRS]). NRL was supported by the National Institute of Minority Health and Health Disparities (grant numbers 3U54MD012388–04S5 and 888-15-16-29). The authors gratefully acknowledge Beth Tennessen for assistance with the design of figure 2.

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