Consequences of Colonialism: a microbial perspective to contemporary Indigenous health

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Abstract

Nearly all Indigenous populations today suffer from worse health than their non-Indigenous counterparts, and despite interventions against known factors, this health 'gap' has not improved. The human microbiome—the beneficial, diverse microbial communities that live within the human body—is a crucial component in developing and maintaining normal physiological health. Disrupting this ecosystem has repercussions for microbial functionality, and thus, human health. In this review, we propose that modern-day Indigenous population health may suffer from disrupted microbial ecosystems as a consequence of historical colonialism. Colonialism may have interrupted the established relationships between the environment, traditional lifeways, and microbiomes, altering the Indigenous microbiome with detrimental health consequences.

The development of cheap and fast high-throughput sequencing techniques has illuminated the many roles the human microbiota performs in human health. The term 'microbiota' refers to microorganisms inhabiting a specific environment; these microbes—bacteria, fungi, viruses, and archaea—along with the microbiota's genetic material and environmental products, comprise the 'microbiome' (Marchesi & Ravel, 2015). The human microbiome is essential for vital life functions within the human body; contributing to nutrient absorption and provisions of energy (Brestoff & Artis, 2013; Kau, Ahern, Griffin, Goodman, & Gordon, 2011; Tilg & Kaser, 2011), to processes such as the normal development of the immune system (Gensollen, Iyer, Kasper, & Blumberg, 2016; Mazmanian, Liu, Tzianabos, & Kasper, 2005), as well as providing a barrier against pathogen invasion (Bäumler & Sperandio, 2016; Cameron & Sperandio, 2015; Hooper, Littman, & Macpherson, 2012). Such a high degree of physiological dependence on the microbiome suggests a long co-evolutionary history between human hosts and their microbiota (Zilber-Rosenberg & Rosenberg, 2008). Despite these important findings, the functional capacity of these microbes and how these functions contribute to human health are not well understood, along with the factors that shape and develop these communities and their functions within the body. Existing work has shown that diet (David et al., 2014a; Zimmer et al., 2012), antibiotics (Modi, Collins, & Relman, 2014) , medical treatment (Le Bastard et al., 2018), and disease (Duvallet, Gibbons, Gurry, Irizarry, & Alm, 2017), can impact and modify human microbial communities. Thus, lifestyle and environmental changes altering the original microbe-host co-evolutionary systems are likely to have major impacts on microbial functionality.

As a result, a prominent area of microbiome research focuses on the impact of urban or industrialized lifestyle factors on the microbiome and human health. Several hypotheses (*e.g.* the 'hygiene hypothesis' (Strachan, 1989; Wold, 1998), or the 'old friends hypothesis' (Guarner et al., 2006; Harper & Armelagos, 2013)) have tried to mechanistically explain how

industrialization may have altered the human microbiome. Recent research emphasizes how two critical factors—the post-Industrial diet (*e.g.* low in fiber, high in fat and sugar) and so-called 'Western medicine'—have transformed the human microbial ecosystem into a state of 'dysbiosis': a disruption of the normal and healthy dynamic equilibrium, that is maladapted for human health (Frei, Lauener, Crameri, & O'Mahony, 2012; Kau et al., 2011; Brestoff & Artis, 2013). This post-Industrial diet originated around the 1870s with flour-milling technology pioneering the refined low-fiber grain; a durable staple food commodity (Winson, 2013). Today, wide-spread consumption of fiber-depleted grains is associated with reduced microbial diversity, modified metabolic pathways, and altered bacterial gene expressions (Cordain et al., 2005; Turnbaugh et al., 2009). These microbial changes are likely largely due to the decreased microbial digestion and fermentation of complex plant polysaccharides, which produce the fatty acids (such as butyrate or propionate) hypothesized to be critical immunoregulators (Maslowski & Mackay, 2011; Sonnenburg & Sonnenburg, 2014). Similarly, the pervasive use of antibiotics, starting in the early 20th century, has been shown to disrupt the human microbiome, especially early in life during critical periods of immune system and microbiome development (Larson, 2007; Blaser, 2016). The use of antibiotics diminishes the diversity of gut microbiota, altering the trajectory and maturation of the gut microbiome, and consequently, leads to metabolic perturbation and abnormal immunological development (Cox et al., 2014; Cho et al., 2012; Bokulich et al., 2016). While the long-term microbial repercussions of antibiotic usage are clear in some studies (Jernberg, Löfmark, Edlund, & Jansson, 2007; Jakobsson et al., 2010; Wipperman et al., 2017), there are still numerous confounding factors and unknown variables (*e.g.* the microbial structure prior to disturbance (Raymond et al., 2016)) that can influence the dysbiotic consequences. Further research is needed to fully disentangle and identify significant factors of industrialized lifestyles that alter the microbiome.

Microbial dysbiosis is not exclusive to the lifestyle changes in contemporary industrialized societies and urban environments. Equally dramatic sociocultural changes have occurred throughout human history and over much longer evolutionary time periods. Of these, the changes inflicted globally on Indigenous populations during the colonial period are potentially some of the most drastic and rapid. This review will explore how historical colonialism may have altered Indigenous microbiomes, and subsequently, Indigenous health. First, we discuss the health disparity between Indigenous and non-Indigenous populations and the microbiome-linked diseases that underpin this disparity. Next, we review the co-evolutionary nature of the human microbiome and why disrupting this relationship could have lasting implications for health. Lastly, we explore the potential impacts on Indigenous microbiomes during the colonial period by providing key examples where diet, environment and lifestyle were altered irreversibly. In this article, we attempt to understand microbiome alterations as a unique mechanism that underlies the significant health disparity suffered by Indigenous populations worldwide.

Indigenous population health

Despite global cultural and historical differences, evidence shows that the majority of Indigenous people world-wide have poorer health than their non-Indigenous counterparts (Anderson et al., 2016). However, the assessment of human health is complicated by multiple determinants enmeshed from socioeconomic, environmental, biological, policymaking (including public health services), and personal behaviors (AIHW, 2010; King, Smith, & Gracey, 2009; Woodward & Kawachi, 2000). Measures of health are further complicated by the entanglement of interconnected causal pathways which can attribute or influence health (Leon & Walt, 2000). The concept of 'Indigenous' also convolutes matters; defining Indigenous status, or what constitutes indigeneity, within specific settings can confound

measurements and insights into population health (Kuper, 2005; Stephens, Porter, Nettleton, & Willis, 2006). However, accurately measuring health and monitoring these determinants are critical to the development and sustainability of public health measures to prevent disease and promote health within Indigenous populations (AIHW, 2010, p. 201; Stephens et al., 2006). With an estimated 302 million Indigenous peoples worldwide, it is critical that accurate assessments of global Indigenous health are undertaken, and despite the difficulties, all the various health determinants are explored to improve overall well-being (Hall & Patrinos, 2012).

Defining the term Indigenous is the first step in assessing Indigenous health. The term 'Indigenous' is typically used with recourse to the first recorded inhabitants in a nation or area at the time of European contact, especially where there is a clear distinction between the native population and the colonial settlers (for example, Australia, New Zealand, Canada, and the United States) (Anderson et al., 2006; Montenegro & Stephens, 2006; Stephens et al., 2006). In other parts of the world, this distinction is less clear when the colonial history and Indigenous status is obscured by ethnic or intra-population domination, serial conquests, or imperialism (Ohenjo et al., 2006; Stephens et al., 2006). For example, over 100,000 years of colonial history in South Africa convoluted with the apartheid, civil wars, intra-population domination, and ethnic genocide, have formed a very complex platform for identifying indigeneity (Ohenjo et al., 2006). Therefore, self-identification is commonly the most prominent means for inclusion within Indigenous definitions, followed by community acceptance: most governments now include these definitions in national censuses (Stephens et al., 2006). As the nature of population health data often relies on systematic analysis of government census data, the discussion and accuracy of global Indigenous population health is affected by the use and nature of accepted Indigenous status (Stephens et al., 2006).

With the use of large-scale census data, Anderson *et al.* was able to conduct one of the first global Indigenous population health studies (2016). However, social and health information was only available from 23 of the total 90 countries, representing only half of the total estimated global Indigenous populations (Anderson et al., 2016; Gill et al., 2006). Despite this limited and incomplete data set, common themes in Indigenous health still emerged; lower life expectancies, higher infant, child, and maternal mortality rates, greater infectious and chronic disease loads, increased levels of malnutrition, and escalating poor mental health, substance abuse, and structural violence were all higher in Indigenous populations in comparison to their non-Indigenous counterparts, (Anderson et al., 2016; Gracey & King, 2009; King et al., 2009; Valeggia & Snodgrass, 2015).

Of all the troubling themes in Indigenous health, the higher rates of infectious disease than their non-Indigenous counterparts is most notable (Butler et al., 2001; Carville et al., 2007; Gracey & King, 2009; Montenegro & Stephens, 2006; Ohenjo et al., 2006). While numerous socioeconomic, geographic, and health-related factors influence the intensity, severity, and frequency of infection, Indigenous populations are discernibly more vulnerable to infectious diseases than non-Indigenous people (Butler et al., 2001; Gracey & King, 2009). The impact of colonization and accompanying introduction of novel pathogens to new continents is well known; so-called 'virgin soil' epidemics decimated multiple native populations who had no immune defence to these unfamiliar pathogens (Crosby, 1976; Kunitz, 1996). However, the risks of such epidemics continues today with both the vulnerability of Indigenous populations to infection and the repercussions of globalization on isolated Indigenous tribes, bringing them into proximity with unfamiliar infections (Hurtado et al., 2005; Valeggia & Snodgrass, 2015).

While chronic diseases are largely burdensome within industrialized societies, these diseases appear to have a greater debilitating effect on health and mortality of Indigenous

populations (Gracey & King, 2009; King et al., 2009; Marmot, Friel, Bell, Houweling, & Taylor, 2008). For example, the prevalence of diabetes is three to five times higher in Aboriginal Australians and Torres Strait Islander populations relative to Australia's non-Indigenous population (Australian Bureau of Statistics, 2013). In Canadian Aboriginals, while diabetes prevalence in an age-standardized population was similar to non-Aboriginals, diabetes prevalence in Aboriginal children was far greater than their non-Aboriginal counterparts (*e.g.* 20-fold higher in Aboriginal children in Manitoba, Canada) (Amed et al., 2010; Public Health Agency of Canada, 2011). Notable chronic diseases within Indigenous populations, especially cardiovascular disease and diabetes, are often attributed to the impacts of urbanization and industrialization, which have emerged more recently for the majority of Indigenous populations compared to their non-Indigenous counterparts (Gracey, 2014; Gracey & King, 2009; Popkin, 1999). Today, chronic health problems and risks associated with urbanization are being especially felt even within remote and rural Indigenous communities, usually concomitant with the loss of ancestral land, depletion or dispossession of traditional resources, or the overall the abandonment of traditional lifestyles, which impacts dietary composition, physical activity, and psycho-emotional health (Kirmayer, Brass, & Tait, 2000; Kirmayer, Dandeneau, Marshall, Phillips, & Williamson, 2011; Kuhnlein, Receveur, Soueida, & Egeland, 2004; Snodgrass, 2013; Valeggia & Snodgrass, 2015). Chronic diseases are a worldwide health problem in which preventable risk factors are heightened by environmental and social change; it is an epidemic that is only worsening, for which Indigenous populations are disproportionately suffering (Anderson et al., 2016; Gracey & King, 2009; Strong, Mathers, Leeder, & Beaglehole, 2005).

The limited public health data available on Indigenous health largely precludes our understanding of the underlying causes of the gap between Indigenous and non-Indigenous populations. Many of these disparities are entrenched within social inequalities; poor health is

aggravated by low socioeconomic standing and social marginalization (Evans & Kantrowitz, 2002; Frohlich & Potvin, 2008; Woodward & Kawachi, 2000). Yet, despite efforts of government programs engaged in closing the health gap and providing strategies and programs administering clinical services and health education, the Indigenous health disparity has shown little improvement, and in some cases, worsened (Marmot et al., 2008; Mitrou et al., 2014). Strikingly, some studies even suggest that the health of Indigenous populations is worse than that of other populations of similar socioeconomic standing (Valeggia & Snodgrass, 2015; Williams, Mohammed, Leavell, & Collins, 2010). Therefore, while socioeconomics is a vital component in the discussion of population health, the limited progress in bridging the socioeconomic gap to improve Indigenous health disparities calls for an exploration of all potential contributors to health and disease.

The human microbiome

The number of microbes hosted by a human body rivals the number of human cells of that individual and the microbial genomic capabilities outnumber the human genome 100:1 (Sender, Fuchs, & Milo, 2016; The Human Microbiome Jumpstart Reference Strains Consortium, 2010; Yang, Xie, Li, & Wei, 2009). Human-associated microbes are predominantly bacteria (estimates between 88-99%) (Qin et al., 2010; Xie et al., 2010; Zhernakova et al., 2016); therefore, microbiome research typically focuses on the bacterial communities that constitute the microbiome. Human-associated microbes are often described as beneficial or 'commensal'; *i.e.* a biological relationship between humans and the microorganisms for which their interactions are typically either benign (of neither detriment nor benefit) or symbiotic (with mutual benefit) (Blaser & Falkow, 2009; Brucker & Bordenstein, 2012). Until the development of molecular tools, research was limited to the minority of bacteria taxa that could be grown within a laboratory (*i.e.* cultured). Now with

culture-independent and high-throughput DNA sequencing technology, the study of microorganisms has moved past single isolates into community-based analyses, which serve as the foundation of the human microbiome research.

The human microbiome is initially established during an infant's post-natal period and is essential for the correct morphological and functional development of their immune system (Gensollen et al., 2016; Mazmanian et al., 2005). The human microbiome continues to develop over the first three years of life and eventually becomes largely partitioned into five major sites across the human body: the oral cavity, respiratory tract, gastrointestinal tract, skin, and vaginal sites. Each of these body sites has specific environmental conditions that form distinct microbial communities. This intrapersonal variation in the microbiome is characteristic of both environmental and physical factors, such as temperature, pH, and available nutrients, that influence which microorganisms can inhabit a particular niche (Costello et al., 2009; Fisher, Mora, & Walczak, 2017; The Human Microbiome Project Consortium, 2012). Despite these diverse site differences, these communities across the human body are interrelated (Costello, Stagaman, Dethlefsen, Bohannan, & Relman, 2012); alterations in a single microbial community can impact other communities across the body. In rheumatoid arthritis patients, Zhang *et al*. (X. Zhang et al., 2015) found that both the oral and gut microbiomes were in an associated state of dysbiosis compared to healthy individuals. The concordance of oral and gut microbiomes was reiterated when these same patients were treated with anti-inflammatory disease-modifying anti-rheumatic drugs; both oral and gut microbiome dysbiosis were partially relieved (X. Zhang et al., 2015). Hence, site-specific microbiomes are not disconnected from one another.

Understanding microbial ecosystems and their functions, networks, and development is fundamental for health research, since the functions of the human microbiome are imperative for human physiological well-being and development. For example, the

microbiome and microbial-derived compounds (nutrients or metabolites) in the gut contribute to the education of the immune system, influence epithelium homeostasis, and guide developmental cell programming (Aidy, Hooiveld, Tremaroli, Bäckhed, & Kleerebezem, 2013; Brestoff & Artis, 2013; Hooper et al., 2012; Kau et al., 2011; Maslowski & Mackay, 2011). The gut microbiome is also vital in the regulation of energy homeostasis, fermentation, metabolism, and nutrient utilization (Brestoff & Artis, 2013; Cheesman & Guillemin, 2007; Sonnenburg & Sonnenburg, 2014; Tremaroli & Bäckhed, 2012) and is crucial to develop the signaling mechanisms required for normal brain development, the hypothalamic-pituitary-adrenal axis programming, central nervous system function and subsequent behavioural functions (*e.g.* stress reactivity) (Cryan & Dinan, 2012; J. A. Foster & McVey Neufeld, 2013; Heijtz et al., 2011). There is surmounting evidence for the role of the microbiome in normal physiological development, yet there is much to be explored regarding the effect of microbiome compositional change or variation.

Intra- and interpersonal variation within the human microbiome is driven by numerous, sometimes linked factors, including host genetics and physiology (Blekhman et al., 2015; Bonder et al., 2016; Mariat et al., 2009; Yatsunenko et al., 2012), and lifestyle factors, such as, physical activity (Clarke et al., 2014), medication (Blaser, 2014; Modi et al., 2014), diet (David et al., 2014a; Zimmer et al., 2012), and interactions with the physical environment (Broussard & Devkota, 2016; David, et al., 2014b). Human genetics and physiological differences shape microbial communities in the human body through abiotic factors (*e.g.* pH, oxygen-levels, or temperature) and biotic components, such as host-to-microbes interactions that control microbial inhabitants; environmental compartmentalization through epithelial barriers; or microbial monitoring through Toll-like receptor proteins (Rakoff-Nahoum, Paglino, Eslami-Varzaneh, Edberg, & Medzhitov, 2004; Slack et al., 2009; The Human Microbiome Project Consortium, 2012). These host factors have matured

through selection pressures on the host genome for a beneficial (or neutral) microbiome (K. R. Foster, Schluter, Coyte, & Rakoff-Nahoum, 2017; Ley, Peterson, & Gordon, 2006a) and are most commonly immune-related functions (Zhernakova et al., 2016; Blekhman et al., 2015; Bonder et al., 2016). However, the contribution of human genetics in microbial heritability (*i.e.* the variation of microbial composition attributable to human genetics) is only estimated between 1.9% to 8.1%, suggesting that lifestyle and environmental factors largely drive intra- and interpersonal variations (Rothschild et al., 2018). For example, diet has been shown to be a major driving force in microbiome diversity (Falony et al., 2016). Dietary research has typically concentrated on variations in macronutrient consumption; high-fat and high-sugar versus low-fat and high-fiber diets embody the main differences between industrialized societies and traditional hunter-gatherer ones (Schnorr et al., 2014; Rampelli et al., 2015; Obregon-Tito et al., 2015). Yet, these diet-induced changes of the microbiome have shown a range of plasticity, from repetitive reversible dysbiosis (Davenport et al., 2014; David, et al., 2014a; Turnbaugh, Backhed, Fulton, & Gordon, 2008) to unrecoverable microbial species extinctions and permanent transitions (Sonnenburg et al., 2016a). These irresolute results point to a hysteresis of the gut microbiome, wherein the state of complex microbial system is dependent upon historical exposures, not just the current circumstances (Carmody et al., 2015; Griffin et al., 2017). Other factors, such as sociality, may play smaller roles in guiding microbiome diversity, but are no less important (Lax et al., 2014). For example, household sharing contributes to microbial similarities between family members (Rothschild et al., 2018; Song et al., 2013), with shared environments driving analogous microbial compositions and functionality (Korpela et al., 2018; Rothschild et al., 2018; Chu et al., 2017).

Collective studies on the factors that shape the composition and structure of the microbiome community highlight how population level differences in microbiota can arise;

genetic factors, alongside lifestyle and environmental exposures, both early and later in life, each play key roles (Dehingia et al., 2015; Strickland, Lauber, Fierer, & Bradford, 2009). As there is little evidence of a core microbiome across individuals – as yet, no single taxon has been found universally shared across all humans – this, therefore, limits the current theoretical framework in understanding how compositional differences impact the microbial functions in different human populations (Shade & Handelsman, 2012). Thus, the significance of external factors on the microbiome composition and structure must be explored to fully understand how changes in microbial function may subsequently impact human physiology and health (McFall-Ngai et al., 2013), especially within unique human populations.

Dysbiosis, or alteration of the microbiome in a negative capacity to support disease, has already been linked to nearly all chronic diseases, such as cardiovascular health (Ettinger, MacDonald, Reid, & Burton, 2014), cancer (Ou et al., 2013; Sears & Garrett, 2014), respiratory diseases (Fujimura et al., 2014; Riedler et al., 2001; Ruokolainen et al., 2015), obesity (Ley, Turnbaugh, Klein, & Gordon, 2006b; Tilg & Kaser, 2011; Turnbaugh et al., 2008), and diabetes (Qin et al., 2012), as well as mental illness, for example schizophrenia (Liu et al., 2014) and depression (J. A. Foster & McVey Neufeld, 2013), immunity disorders (Kau et al., 2011; Mathis & Benoist, 2011; Nikoopour & Singh, 2014; X. Zhang et al., 2015) and the rise in allergies and asthma prevalence (Armelagos & Barnes, 1999; Haahtela et al., 2013). However, these findings have been largely conducted in populations of European origin, which have all undergone similar sociocultural changes over time. These findings bias the predictive accuracy of microbiome related diseases in non-European populations (Lewis, Obregón-Tito, Tito, Foster, & Spicer, 2012). Alterations to microbiomes in other populations may lead to different diseases or manifestation of disease in separate human populations. For example, some ethnic populations have greater risk factors for disease than others, even

accounting for socioeconomic status (Ward et al., 2004); while this can sometimes be attributed to genetic disease, the concomitant contributions of the microbiome remain unexplored.

Co-evolution of humans and the microbiome

Several features of the human microbiome imply that humans and their microbes are co-evolved and have co-adapted; these microbes are (1) specifically conserved within human hosts, (2) persistent through generations of familial inheritance, and (3) defined by environmental exposures and lifestyle factors (Blaser & Falkow, 2009; Zilber-Rosenberg & Rosenberg, 2008). This co-evolutionary relationship is mutually dependent; humans cannot live without their microbiome any more than human-established microbes can survive without a human host. Indeed, the human microbiome is so crucially beneficial to physiological health that the microbiome and human genome may be considered a "human supraorganism" (Turnbaugh et al., 2007). Through the analysis of three predominant gut taxa and their evolutionary relationships, Moeller *et al.* (2016a) traced the evolutionary diversification from modern ape species and modern humans and found these specific bacterial species were maintained throughout hominid evolution (microbial divergence dated to 15 million years ago from gorilla-hominid split), suggesting that this symbiotic association that has persisted over evolutionary time. While the composition and structure of the microbiome have developed in response to external environmental factors, it is also importantly influenced by its evolutionary history: the past chronicle of events that have shaped and constructed its present structure.

Human evolutionary history indicates that groups of human populations diverged and remained isolated from one another for thousands of years, imprinting geographical signatures on the human and mitochondrial genomes (Rosenberg et al., 2002). Human

populations in the Americas, Australia, and the Pacific Islands remained isolated by oceans (Bonatto & Salzano, 1997; Duggan et al., 2014; Tobler et al., 2017). Likewise, populations throughout Europe, Asia, and Africa, while not geographically disconnected, inhabited distinct territories for tens of thousands of years (Barbujani & Sokal, 1990; Melton, Clifford, Martinson, Batzer, & Stoneking, 1998; Tishkoff et al., 2007). Thus, the microbiomes associated with each isolated human population have genomes that are divergent from any other population (*e.g. Helicobacter pylori* (Falush et al., 2003; Wirth, Meyer, & Achtman, 2005)). Research into contemporary populations' microbial differences have shown that these different geographical and sociocultural populations maintain distinct microbial community configurations and diverse functional potential (Rampelli et al., 2015; Yatsunenko et al., 2012). For example, an Indigenous ethnic group of hunter-gatherers, the Hadza, living in north-central Tanzania have a microbiome that is compositionally unique from both urban/industrialized individuals and other hunter-gatherer groups (Dehingia et al., 2015). The Hadza microbiome has distinguishable and unique metabolic functions that are adapted to the consumption of complex polysaccharides (Rampelli et al., 2015), including the unusual presence of *Treponema* bacterium in healthy Hadza gut. The gut *Treponema* strains provide a beneficial metabolic role in carbohydrate digestion, challenging the common perception of *Treponema* as solely a pathogenic microorganism (Obregon-Tito et al., 2015). Human adaptation to a unique physical and cultural environment over evolutionary time suggests that the microbiome similarly adapts to that environment and is therefore likely shaped by the available dietary resources, established human customs and behaviors, and the physical climate and environment.

Understanding the potential health consequences arising from changes in dissimilar Indigenous microbiomes requires an understanding of how these different microbiomes had previously adapted throughout their evolutionary life history, and how severely these co-

evolutionary processes between the microbiome and host were disrupted. The majority of Indigenous populations globally have experienced extreme and rapid lifestyle changes throughout their recent evolutionary history, when many of their non-Indigenous counterparts did not. These recent changes were constituted through historical colonialism – one of the most influential sociocultural transitions throughout human history.

Colonialism and the impacts upon the human microbiome

Colonialism, within this article, is defined as a form of intergroup domination (*i.e.* between culturally heterogeneous societies) where a substantial number of settlers permanently migrated to a colony from a colonizing power (Horvath, 1972). There were differing motives for long-term or permanent changes during colonialism (*e.g.* exploration, the conquest of nations, or riches) that often determined the subsequent interactions with Indigenous populations and their land, hence the nature of the colonial transitions manifested in a variety of different ways. There are numerous shared processes that occurred cross-culturally; colonialism transformed native populations' dietary lifeways (*i.e.* the cultural behaviors or customs surrounding diet, including particular foods consumed), adjusted their social networks and behaviors, and impacted their physiological health. These changes occurred rapidly, prompting drastic adaptations within a single individual's lifetime, and collectively demanded both humans and their microbes to adapt (Whittaker, 1972; Zilber-Rosenberg & Rosenberg, 2008). We will explore three overarching transformative changes that colonialists often enforced upon Indigenous populations, directly or indirectly, which have been documented in current research to significantly impact the human microbiome. Specifically, through colonialism, Indigenous populations experienced (1) pronounced changes to their established dietary lifeways, (2) rapid adjustments in behaviors, rituals, and social dynamics, and ultimately, (3) were introduced to novel, destructive agents of infectious disease. While it

can be challenging to discuss these interconnected factors exclusively, the following examples of combined historical documentation and recent corroborating microbial research support our hypothesis: Indigenous populations underwent alterations to their microbiomes because of the lasting lifeway changes during the colonial period.

Post-contact modifications to dietary lifeways

European colonists reduced Indigenous access to resources required for diverse subsistence farming, indirectly or directly eliminated traditional dietary sources, and often demanded tributes for missionaries and government administrators, which impacted both socioeconomic status and the food available for consumption (Earle, 2010; Klaus & Tam, 2010; Larsen, 1994; Nunn & Qian, 2010). Frequently, native agriculture was also fully replaced by European crops to maintain a traditional European diet or for exportation or trade (Franke, 1987). Novel additions to dietary lifeways were more often an indirect consequence of global trade networks created by the dominant colonizing power (*i.e.* the importation of European food stuffs, such as wheat, wine, olive oil, and livestock (Earle, 2010). In South America, ethnohistoric evidence suggest colonists emphasized the proliferation of specific crops for trade, giving priority to foods, such as tomatoes or cacao, for exportation back to Europe (Nunn & Qian, 2010). Food was also a tool used in 'civilizing' Indigenous populations; eating European foods was thought to make them more like the colonizers (Earle, 2010).

The impact of diet upon the gut microbiome is one of the better studied areas in contemporary microbiome research, as alterations to diet have the greatest potential for therapeutic self-regulation of microbiome-associated conditions (Brown, DeCoffe, Molcan, & Gibson, 2012; Cotillard et al., 2013; Ercolini et al., 2015). More specifically, one of the largest areas of dietary research relates to the consumption of microbiota-accessible carbohydrates (MACs), defined as carbohydrates for which the human host is unable to

digest and absorb nutrients without the prior metabolism by members of their gut microbiome (Sonnenburg & Sonnenburg, 2014). MAC intake has been linked to greater microbial diversity, broader carbohydrate metabolic capabilities (Rampelli et al., 2015), short chain fatty acid production (Campbell, Fahey, & Wolf, 1997), and increased clinical markers for health (Sonnenburg & Sonnenburg, 2014). Research looking at 'humanized' gut microbiome in mouse models (*i.e.* a previously germ-free mouse colonized by human fecal microbes) showed that a low-MAC diet induces microbial extinction, successively reducing the microbial diversity of the gut over multiple generations (Sonnenburg et al., 2016b). Although this loss could be recovered if a high-MAC diet was re-introduced within a single generation, the damage was irreversible and microbial diversity never returned to its original state after several generations (Sonnenburg et al., 2016b). While the underlying mechanisms of the link between microbial diversity and health are still unknown, increased species diversity within a community is thought to develop greater ecosystem stability, promote sharing of resources, and lower host invasibility, thus supporting greater metabolic and colonic health (Cardinale, Palmer, & Collins, 2002; Cotillard et al., 2013; Gonzalez et al., 2011; Tilman, 2004).

A population in the small town of Mórrope, Peru, provides a definitive example of dietary change and a case study to examine the impact of colonialism on Indigenous Andean foodways (Klaus & Tam, 2010). Anthropologists, Klaus and Tam (2010), used both regional ethnohistoric evidence and skeletal remains from both late pre-contact and post-contact periods to examine changes in diet and health. After the Spanish colonization, the people of Mórrope became increasingly reliant on starchy carbohydrate consumption, as evident by increased prevalence of dental caries and tooth loss (due to poor oral health) and heightened accumulation of calculus (symptomatic of greater plaque progression, which can extend to additional oral problems) (Hillson, 1996; Klaus & Tam, 2010). It was suggested that the elevated consumption of starchy carbohydrates would have helped buffer against

malnutrition from restricted access to traditional food sources, after being resettled in a resource-poor area due to European exploitation of arable land for cash crops (Franke, 1987; Klaus & Tam, 2010). However, a carbohydrate-based diet not only stimulates oral disease, but also leads to growth retardation and impaired skeletal development from nutrient deficiency (Larsen, 1995). The metabolic stress within the Mórrope post-contact population was great enough to leave skeletal lesions, such as cribra orbitalia and porotic hyperostosis (*i.e.* localized areas of spongy porous bone tissue caused by anemia) (Klaus & Tam, 2010).

From Sonnenburg *et al.* (2016b), it could be inferred that the people of Mórrope would have experienced microbial extinctions over several generations caused by a reliance on starchy carbohydrates and limited access to complex carbohydrates (*i.e.* a low MAC diet). Ancient DNA research in ancient European populations also suggests that the switch to starchy carbohydrates had marked impacts on composition of the microbiome (Adler et al., 2013; Weyrich et al., 2017). However, carbohydrates are not the sole cause of alterations in microbial ecosystems. Many additional dietary modifications have been shown to induce changes in the gut microbiome composition and function, such as the switch from a plant-based diets and to that of animals (David et al., 2014a; Zimmer et al., 2012), seasonal dietary variation (Davenport et al., 2014; J. Zhang et al., 2014), and consumption of fermented products (Veiga et al., 2014). Probable unexplored consequences include individuals consuming a novel introduced dietary source for which they have little to no evolutionary experience, or inversely, consequent adaptation to the indefinite removal of a dietary food source.

Colonialism's influence on social structures and behaviors

Historically, the enforcement of 'European ways' on native populations represents one of the most direct cases of sociocultural change established through colonial settlers and governing

authorities, most commonly in the form of missionisation (Earle, 2010; Larsen, 1994; Van Buren, 2009). 'Missionisation' is the process of Christian proselytism and its corresponding acculturation programs instituted at formal bases, known as 'missions' (Van Buren, 2009). The consequences of missionisation varied regionally; however, it almost always resulted in significant and cumulative changes to native lifeways. For example, the historical colony 'New Spain' enforced Indigenous acculturation through the *reducción* (Van Buren, 2009). As part of this process, the Indigenous population were forced from their villages and homes and were bound to reside within mission centers (Larsen, 1994). The spatial organization of the mission imposed close living conditions on diverse multi-ethnic populations, with no organizational attention to linguistic barriers or tribal animosities, which fractured families and impeded traditional courtship customs and practices (Panich & Schneider, 2015; Van Buren, 2009). Even in the absence of aggressive missionisation, exposure to European customs and behaviors prompted far-reaching cultural adaptations.

Cultural alterations in behavior or customs are the most erratic and variable of any post-contact colonial change, and therefore, impacts of any Indigenous sociocultural behavioural alteration should be explored within the local background and history of the Indigenous-colonist relationships. However, this makes the exploration of microbial alterations difficult; accordingly, this article will focus on how the transmission of microbes may have been impacted by sociocultural changes. As the human microbiome is inherited by social transmission, then matures throughout growth and development by the surrounding environment (especially through contact between household members), differences in kinship structures and social networks will impact the vertical transmission of microorganisms between individuals (Moeller et al., 2016b; Tung et al., 2015; Yatsunenko et al., 2012). Microbiome research has shown, despite direct maternal microbial exposure at birth, fathers also share as many microbial similarities with their children as does the mother (Yatsunenko

et al., 2012). While not yet explored in humans, social interactions and relationships within a community of baboons imprinted explicit patterns of exchange within their microbiome, highlighting the importance of social interactions in structuring and composition of the microbiomes (Tung et al., 2015). This research suggests that the differences in cultural behavior and social networks impact microbial dispersal and transmission routes in defining microbiome structure and community development (Martínez et al., 2015). Whether the colonialists goal was to exterminate, assimilate, or remain in relative equilibrium with the Indigenous population (neither extermination or assimilation), changes certainly occurred to Indigenous kinship structures, social networks, and cultural lifestyle alterations (Horvath, 1972).

The breakdown of the historic Hawaiian Kapu system is a good example of microbial change through sociocultural restructuring. The Kapu system dictated native Hawaiian daily life through religious rules and regulations, governing social stratification, the interactions between social classes, and gender roles and relationships (Else, 2004). However, the acceptance of the European cash economy led to the breakdown of traditional subsistence farming, directly impacting and eroding the relationships between social classes (Else, 2004; Friedman, 1985). The deterioration of the Kapu system lead to greater enduring cultural changes; such as economic distributions of food encouraging the immigration of foreigner laborers; or the adoption of the colonial religion, as a result of missionaries and subsequent establishment of missions; or the creation of a mercantile economy, inducing the revaluation of sex for commerce (Buck, 2010; Else, 2004).

As social networks influence microbial transfer between individuals, changes within social networks can introduce new microbes from foreign exposures, or restrict contact with native microbes (*i.e.* the missions adjusting the social dynamics and accessible contact between individuals, which altered the transmission of microbes between the members of

Indigenous community and simultaneously introduced European microorganisms). Sociocultural behavior adaptations can potentially introduce new sources and recipients of foreign microbes, but changes to cultural customs or behaviors can equally restrict or assist access to microbes from certain individuals or groups. The breakdown of the Kapu and the introduction of the cash economy changed cultural ideals regarding divisions of labor, emphasizing the European values of females within the domestic spheres and males within the public spheres, which created differential group access to unique microbial sources (Van Buren, 2009). The gendered roles in food preparation and consumption within Hadza society contributed microbial differences between males and females, thus it is likely that historical gendered-based microbial differences could be detected, perhaps playing a role in health (Schnorr et al., 2014). On a larger scale, it is likely that the Kapu microbiome would have integrated some level of commensal microorganisms from a European-adapted microbiome, through increased interactions with Europeans. Furthermore, contact between individuals within the society itself would have changed (*e.g.* differences in caretaking and caregiving, socially acceptable sexual liberties, interactions through occupation), which could impact microbial inheritance of the next generation.

Introduction of infectious disease

Unquestionably, the most devastating effect of colonialism was the introduction of novel pathogens. Globally, native populations were decimated by epidemics of infectious diseases introduced by colonialists; some of the hardest hit areas lost up to 90 percent of their population (Cook, 1998; Kunitz, 1996; Zubrow, 1990). In the Americas, no specific case study can be reliably ascertained because the speed by which the pathogenic agents spread and obliterated the native population outran European ethnohistorical records, leaving only indirect archaeological evidence, such as specific demographic patterns in mortuary samples

(Hutchinson & Mitchem, 2001; Milner, 1980). Despite inadequate information, it is presumed that the native population had no "immunological memory" of the introduced diseases from the "Old World" and that the malignance of these pathogens was due to the separate evolutionary histories between the continents (Crosby, 1976; Ramenofsky, Wilbur, & Stone, 2003). The evident introduction of novel pathogenic microorganisms simultaneously proposes the introduction of non-pathogenic microorganisms; supporting evidence of changes to the microbiome and immune profiles of Indigenous populations.

Research has implicated the microbiome in the development and education of the immune system in infancy, but the microbiome also plays a role in pathogen resistance through 'bacterial interference' or 'colonialization resistance' (Brook, 1999). Bacterial inference refers to antagonistic and competitive relationships between bacterial species, in which bacteria have developed mechanisms to interfere with the capability of other bacteria to colonize and survive alongside them (Buffie et al., 2015; Falagas, Rafailidis, & Makris, 2008). There are a number of mechanisms of bacterial interference; principally nutrient rivalry or host-cell binding site competition, where the endemic human microbes out-numbered and out-competed invading microorganisms (Reid, Howard, & Gan, 2001) Another aspect of bacterial interference is the capacity of endemic microbes to produce antagonistic compounds, such as bacteriocins, (*i.e.* toxic proteins produced by bacteria that inhibit the growth of, or even kill, other bacteria, without causing harm to themselves) or simple molecules, like hydrogen peroxide or lactic acid, in order to change the microenvironment to deter invader establishment (Brook, 1999). Some research has shown that dysbiotic perturbations to the microbiome can weaken the effects of colonization resistance, leaving the host susceptible to pathogen invasion (Bäumler & Sperandio, 2016; Brown et al., 2012). The impact is cumulative; the establishment of a pathogen can exacerbate dysbiosis and disrupt microbial functionality, negatively influencing host

physiology, immunity, and susceptibility to infectious disease (Kau et al., 2011; Lu et al., 2013). Pathogens can also induce apparent competition, utilizing host immune response to preferentially displace or alter the host microbiome for its own benefit in such that the dysbiotic microbiota act as a pathogenic community (Hajishengallis, Darveau, & Curtis, 2012; Sears & Pardoll, 2011).

Infectious disease would have directly altered the microbiome, but the consequential human depopulation would have also altered human population structures, both genetically and socially, further impacting microbial transmission to surviving generations. While there is little agreement on the timing of depopulation, the size of pre-colonial native populations, or the overall mortality rates, there is a shared consensus on the indirect impacts of disease on the native population; high mortality and morbidity would have disturbed subsistence activities and the labor force, reduced political influence, and forced social reorganization (Cook, 1998; Dobyns, 1966; Milner, 1980; Snow & Lanphear, 1988; Zubrow, 1990). Survivors of one community decimated by disease often resettled among different communities, contributing to the spread of disease and influencing horizontal microbial transmission amongst different communities (Warrick, 2003). It is hard to predict the variety of indirect repercussions depopulation had on Indigenous life, let alone the subsequent impact upon their microbiomes. A case in point, albeit with very little available archaeological evidence, is the suggestion that depopulation of South America resulted in the loss of domesticated crop diversity (Clement, 1999). The reduction in labor force would have reduced the number of horticulturalists to maintain widespread minor crops, and a loss in dietary diversity would have induced a loss in microbial diversity, potentially instigating dysbiosis, and thus, further increasing pathogen susceptibility (Clement, 1999; Ley et al., 2006a). Under colonialism, native populations likely encountered novel pathogens at an alarming rate, while simultaneously enduring the impacts of dietary change and/or

malnutrition, socioeconomic restricting, and both psychological and biological stress. All of which are factors that have been described in contemporary research as instigators of microbial dysbiosis (Bailey et al., 2011; Brown et al., 2012; David et al., 2014a; De Palma, Collins, Bercik, & Verdu, 2014).

Discussion and Conclusion

Colonialism represents one of the greatest and swiftest historical sociocultural adaptations throughout human evolutionary history. Through anthropological and archaeological evidence, it is evident that the process of colonialism was detrimental to the traditional lifestyles and health of the Indigenous populations. Moreover, it is evident that the ensuing rapid lifestyle changes that Indigenous populations endured would have acutely altered their microbiomes. Explorations of the unintentional alterations to the microbiome throughout progressive industrialization have shown that modifications to the composition and structure of the microbiome can be detrimental to human health. However, our fundamental understanding of contemporary microbiome alterations require recognition of the current ascertainment bias; the majority of microbiome studies examine populations of European descent, who live industrialized lifestyles (Lewis et al., 2012; Warinner & Lewis, 2015). The little existing research on different racial/ethnic populations has shown that there are taxonomic, compositional, and functional differences in the microbiomes of different human populations (Anwesh et al., 2016; Martínez et al., 2015; Ozga et al., 2016; Rampelli et al., 2015; Yatsunenko et al., 2012; Zhang et al., 2014). Therefore, it cannot be assumed that the same instigator will equally impact different microbiomes; dysbiosis may take different forms, provoking various disease responses. Researchers have shown that rheumatoid arthritis patients' disease-associated dysbiosis was compositionally similar across all patients, but the 'stabilization' of the microbiome after taking rheumatoid arthritis-drugs of each

patient concluded with compositionally disparate recoveries (Zhang et al., 2015). The impact of alterations to different microbiomes (especially across different populations) has not been explored with regard to the subsequent co-evolutionary histories of populations, and therefore the burden upon health.

The rapid transition into a disadvantageous lifestyle, inflicted upon the Indigenous populations throughout colonialism, would have selected for the best microbiome for survival through the detrimental transition, or rather a microbiome most suitably adapted for the novel lifestyle (Ley et al., 2006a; Wilson, 1997; Zilber-Rosenberg & Rosenberg, 2008). However, the microbial functional repercussions of these alterations may not necessarily be the best adaptations for human physiological health. Recent investigations suggest that genetic predisposition to disease is contingent upon the composition and function of the microbiome (Bonder et al., 2016; Knights et al., 2014). Thus, the dysbiosis of the ecologically-adapted functional microbiome could trigger adverse immunological and metabolic genetic phenotypes with the microbiome (Bonder et al., 2016). Furthermore, human genetics were altered during the colonial period. Ancestry admixture has shown a strong link between population-specific alleles and host genetic factors that mediate immunity and pathogen-resistance (Lindo et al., 2016; Rishishwar et al., 2015); as previously discussed, the greatest genetic influence on the human microbiome stems from immune-related factors. The disruption to the Indigenous microbiome, induced by colonialism, altered the stable co-evolutionary relationship that was pre-determined by genetic background and cultural history.

While the effects of colonialism are still being felt today, especially among Indigenous populations, our current understanding of microbial kinship patterns implies that alterations to the microbiome could be passed onto future generations and may not ever be restored to their original state (Ley et al., 2006a; Sonnenburg et al., 2016b). While the long-term repercussions of microbial change over successive generations are not fully understood,

there are a number of mechanisms that can propagate and participate in transgenerational inheritance of microbiome alterations. Primarily, there is selective maternal transmission of specific bacterial strains to young infants (Korpela et al., 2018; Chu et al., 2017). The origin of some specific species can be traced back to the mother, and they remain consistent and stable during and throughout infant development, implying a selective advantage in familial microbial inheritance and an adaption of some symbiotic bacterial species to have evolved vertical transmission dependence (Duranti et al., 2017; Korpela et al., 2018). However, while caregivers transfer microbes to the infant microbial community throughout their development, recent evidence does suggest that environmental drivers are more critical for the maturation of microbiome composition (Chu et al., 2017). Therefore, shared environments (*e.g.* family household) will promote shared microbes through sociality; transgenerational inheritance occurs within nuclear family units sharing familial microbes (Bokulich et al., 2016). This means that community dysbiosis can also be 'inherited' in a non-traditional sense; if the fetus or neonate are exposed to maternal dysbiosis during this critical developmental window, the infant 'inherits' a dysbiotic microbial state, although not necessarily the same dysbiotic state as their mother (Mulligan & Friedman, 2017; Miyoshi et al., 2017). The dysbiosis experienced by Indigenous populations today may not represent the dysbiosis directly caused by the events of colonization, but instead is the downstream remnant of historical perturbations that define the hysteretic microbiome.

In suggesting the colonial transition was detrimental to contemporary Indigenous health, introduces the paradox of contemporary colonial Europeans, who immigrated to novel lands and experienced changes to their own diets, lifestyles, and contact with novel diseases, but have consistently better health than their Indigenous counterparts. However, the perturbations to the colonial microbiome, and the consequential impact on their health, may be different to their Indigenous counterparts. It is possible that the microbial disruption felt

by colonists was less drastic than what was experienced by Indigenous populations; colonialists were able to maintain some microbial stability through cultural lifestyle (*e.g.* preservation of familiar dietary sources, such as wheat or milk, or sustained familial ties maintaining familial microbes (Earle, 2010; Phillips, 2009)). As long as the colonialists were able to maintain some cultural stability, the largest demarcating factor between Indigenous and non-Indigenous populations during the colonial transition is the fact that Indigenous populations were not able to reestablish precolonial lifestyles and traditions; the environmental factors that underpin the origin of their microbiomes. On the other hand, perhaps the co-evolutionary history between European populations and their microbiomes through ancestral perturbations of the Neolithic Revolution and earlier population transformations provides greater resilience or adaption to change within new environments (Mathieson et al., 2018; Olalde et al., 2018; Adler et al., 2013). Understanding the impacts of disruptive change on both the Indigenous populations and their colonial counterparts will be critical in illuminating microbial ecosystem functions for the improvement of human health.

To be clear, highlighting a microbial role in Indigenous health does not negate the significance of the role of socioeconomics in the Indigenous health disparity. There is evidence that indicates socioeconomic status impacts the composition of the microbiome (Belstrøm et al., 2014; Chong et al., 2015); hence, socioeconomic status may be exacerbating the influence of the microbial evolutionary history on Indigenous health. In proposing an underlying microbial element in Indigenous health disparities, we offer a potential explanation for an additional 'unknown' risk factor that contributes to the discrepancy in health between Indigenous peoples and their non-Indigenous counterparts. Effective reduction of any disease prevalence requires a consideration of all determinants involved (Findley, Williams, Grice, & Bonham, 2016). Factors involved in disease risk—social, behavioural, biological, economic, and environmental—are also involved in the structuring of

the microbiome; thus, a greater understanding of the symbiotic microbiome-human relationship will aid public health efforts within Indigenous communities to improve population health.

In the implementation of such microbial investigations, researchers need to go beyond global health programs, and look towards community engagement and translating microbiome research into something malleable for health care providers or public health policies (O'Doherty, Virani, & Wilcox, 2016; Valeggia & Snodgrass, 2015). Most notably, these inquiries require the inclusion of Indigenous communities, especially in regards to therapeutic benefits (Lewis et al., 2012). Partnerships between researchers and communities can provide opportunities for locals to gain first-hand experience regarding specific factors contributing to illness and disease, to learn preventative techniques in health care, and to understand health-related skills and management (Gracey, 2014). Importantly, allowing community control over both their own health care and research, including sharing experimental data, allows efficient research processes to assist in developing tangible beneficial community outcomes (James et al., 2014; Sankaranarayanan et al., 2015). Research efforts need to be cognizant in ethics of care frameworks, to be aware of the potential challenges in research practices that may do disservice to Indigenous communities, and give attention to the relationship between researchers and Indigenous communities (Held, 2006; Sharp & Foster, 2007; Taylor & Guerin, 2010). While these potential issues may be community-specific, additional challenges can stem from interpretation of these ethical guidelines. For example, difficulties can arise in the ability to disentangle group interests from individual concerns, identifying whom is able to provide community representation, and furthermore, whether this representative is able to present the range of community perspectives (M. W. Foster & Sharp, 2000; Sharp & Foster, 2007). The global health inequalities between the Indigenous populations and their non-Indigenous counterparts

demand greater efforts in tracking the health of Indigenous communities; failure to note the impact of Indigenous identity within microbiome research is not a neutral stance, but risks hiding existing inequities or neglecting communities (Kirmayer & Brass, 2016). Studying the microbiomes of Indigenous peoples involves recognition of specific local, cultural, and historical contexts (Kirmayer & Brass, 2016).

While we propose colonialism as the agent for microbial dysbiosis, it is equally likely for microbial dysbiosis to be an independent variable of the consequential physiological and psychological changes endured by Indigenous peoples throughout colonialism. In other words, was dysbiosis of the microbiome caused by the alterations in diet, introduction of novel microorganisms, and adjustments to cultural lifestyles, or did microbial dysbiosis arise in parallel to the nutritional disease, infectious diseases, and psychological trauma caused by colonialism? Both scenarios are plausible. Furthermore, both scenarios have significant ramifications for Indigenous health. Elucidating the cause of dysbiosis enables diagnosis and treatment of dysbiotic-related pathology, for it is therapeutically important to discern whether remediating dysbiosis will cure disease, or merely provide palliative remedy. In order to delineate between cause and effect, Frank *et al*. (2011) suggest three modes of investigation: observation, experimentation and modelling. Firstly, large-scale surveys of both microbial composition and functionality must be integrated alongside screening human genotypes and their molecular phenotypes, which can provide associations between microbial profiles and genetic predispositions (Frank, Zhu, Sartor, & Li, 2011). Secondly, there needs to be experimental support for the contribution of dysbiosis to disease (*e.g.* double-blind, randomized controlled experiments involving both the normalization of dysbiotic profiles in individuals with disease and inducing dysbiosis in healthy individuals), and lastly, it is necessary to be able to model, experimentally demonstrate, and analyse these relationships computationally and statistically (Frank et al., 2011). Realistically, the determination of

colonialism's impact on modern-day Indigenous health will not be straightforward, as these cause or effect scenarios are not mutually exclusive. Until the cause of dysbiosis can be explained, perhaps insight can be instead gained by studying the historical populations of the past and investigating their microbial changes through colonialism in real time.

We may be able to reconstruct and examine the historic changes in Indigenous microbiota using ancient DNA research; microbial DNA from the past can be extracted from archaeological or paleontological remains and provide a direct assessment of the evolutionary history of ancient microorganisms and microbiomes (De La Fuente, Flores, & Moraga, 2013; Willerslev & Cooper, 2005). Ancient DNA extracted from dental calculus has already been used to ascertain oral microbiomes of ancient populations, providing direct biological evidence of microbiome-related changes linked to alterations in lifeway, diet, and environment (Adler et al., 2013; Warinner et al., 2014; Weyrich et al., 2017). In this case, ancient microbial DNA could be used to reconstruct the ancient oral microbiomes of pre- and post-colonial individuals, allowing researchers to directly analyse alterations to the microbiome community composition, structure, and function throughout the colonial transition. While contemporary research is concentrated on the gut microbiome, the preservation of the ancient oral microbiome in dental calculus (calcified dental plaque) is superior to fossilized feces (source of ancient gut microbiome) in protecting microbial DNA from exogenous DNA, contamination, and the post-mortem environment (Warinner, Rodrigues, et al., 2014; Weyrich, Dobney, & Cooper, 2015). The interconnection of the microbial niches on the human body suggest that if significant changes within the oral microbiome occurred, this would also indicate transformations in the gut community (X. Zhang et al., 2015; Said et al., 2013). By reconstructing the microbial profile of ancient populations, we can detect microorganisms that have evolved exclusively within specific populations and environments, track the introduction of novel microorganisms, and

distinguish those microorganisms that adapted and adjusted to the alternative environment introduced with colonialism. Furthermore, we can identify which microorganisms persisted into subsequent generations, and how they function to assist in modern human health or disease. Since the long-term effects of alterations to the microbiome are presently unknown, it is important to evaluate the capacity for these ancient and historic transitions to impact modern-day human population health, especially where it is detriment. Through the reconstruction of ancestral microbiomes, we can gain a greater comprehension of microbiome and the host interactions, strengthening the foundation of microbiome research to be used in contributing to the improvement of Indigenous health.

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