

## Review

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# Early-life origins of disparities in chronic diseases among Indigenous youth: pathways to recovering health disparities from intergenerational trauma

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## Abstract

Indigenous women and children experience some of the most profound health disparities globally. These disparities are grounded in historical and contemporary trauma secondary to colonial atrocities perpetuated by settler society. The health disparities that exist for chronic diseases may have their origins in early-life exposures that Indigenous women and children face. Mechanistically, there is evidence that these adverse exposures epigenetically modify genes associated with cardiometabolic disease risk. Interventions designed to support a resilient pregnancy and first 1000 days of life should abrogate disparities in early-life socioeconomic status. Breastfeeding, prenatal care and early child education are key targets for governments and health care providers to start addressing current health disparities in cardiometabolic diseases among Indigenous youth. Programmes grounded in cultural safety and co-developed with communities have successfully reduced health disparities. More works of this kind are needed to reduce inequities in cardiometabolic diseases among Indigenous women and children worldwide.

## Why study the developmental origins of chronic diseases in youth?

Chronic non-communicable diseases (e.g. diabetes, obesity and cardiovascular disease) are the leading causes of death, disability and health care expenditures worldwide.<sup>1</sup> When considered in relation to mortality and disability adjusted life years, the burden of chronic non-communicable diseases eclipses that of infectious diseases.<sup>2</sup> Alarming, rates of chronic diseases are rapidly increasing among youth and young adults with substantial effects on the quality of life, productivity and lifelong health care costs.<sup>3–6</sup> There is growing evidence that this rapid increase is related to population-wide changes in early-life exposures (i.e. maternal gestational obesity/diabetes or exposure to environmental toxins) that contribute to the increased disease burden.

The landmark Dutch Famine<sup>7</sup> and British birth cohort studies<sup>8</sup> provided the first evidence that an altered fetal environment can programme an individual's risk for chronic disease. These data provided the foundation for the developmental origins of disease theory,<sup>9–12</sup> which posits that early-life events biologically programme an individual's risk for chronic disease (reviewed in Barker,<sup>12</sup> Symonds *et al.*<sup>13</sup> and McMillen and Robinson<sup>14</sup>). Studies using animal models with controlled pre- and postnatal conditions replicated these epidemiological observations demonstrating that maternal exposures (i.e. obesity/diabetes, smoking and medication use during pregnancy) programme susceptibility for chronic diseases in offspring.<sup>13–15</sup> Importantly, interventions delivered during the first few years of life can reduce disease risk (i.e. breastfeeding<sup>16,17</sup>/early childhood education<sup>18,19</sup>) demonstrating that the early postnatal period is a key window of opportunity for reducing lifetime chronic disease risk. Critically, these interventions result in substantial, lifelong health, neurodevelopmental and social benefits that reduce inequities associated with exposure to adverse early-life environments (i.e. poverty, diabetes, etc.).

Indigenous youth in Canada and elsewhere face some of the most profound inequities in chronic diseases.<sup>20,21</sup> These inequities directly result from historical and contemporary trauma that Indigenous families face.<sup>22</sup> The effects of this trauma are evident early in the life of Indigenous children. For example, in Manitoba, Indigenous children are more likely to live in poverty, suffer from food insecurity, attend underfunded schools, and women are less likely to

receive breastfeeding or to have access to public health interventions and primary care services. This structural racism combined with historical and contemporary colonial trauma contributes to high rates of chronic diseases among Indigenous youth in the province, particularly hypertension, obesity and type 2 diabetes. The incidence of chronic diseases with potentially early-life origins like obesity and type 2 diabetes among Manitoban Indigenous youth far exceeds that seen in other provinces in Canada.<sup>23–26</sup> Three critical facts reinforce the notion that these disparities are socially constructed and not due to genetic or lifestyle underpinnings specific to Indigenous peoples and must be acknowledged by Western science. First, these disparities do not exist for non-Indigenous youth in Canada who live in similarly deprived regions or households with similar incomes and are less pronounced among Indigenous peoples that experience less trauma.<sup>27</sup> Second, these disparities did not exist before settlers entered Indigenous territory nor among youth before entering residential schools.<sup>28</sup> Finally, Indigenous nations that experienced less trauma and are currently more culturally connected do not observe the same degree of health inequities.<sup>21,29–31</sup> In select settings across North America, interventions are currently underway to promote Indigenous cultural identity and connectedness as a means of ‘treating’ and reducing health and social inequities<sup>32</sup> as there is growing recognition that connection to culture is an important protective factor for First Nations peoples’ health, particularly in regard to mental health.<sup>33</sup> In fact, in most Indigenous worldviews, the connection between mental, emotional, spiritual and physical wellbeing is clear, and the transmission pathway of embodied suffering from mother to baby is well understood. Western science and the study of epigenesis, on the other hand, is only just beginning to catch up. The purpose of this review is to explore the impact of historical and ongoing trauma on the maternal and early life forces that shape chronic disease risk among Indigenous youth. We will apply both Indigenous and Western worldviews in this review, restrict the discussion to the Canadian context and attempt to provide promising strategies grounded in a ‘decolonizing’ or cultural restoration framework.

### **Colonization and trauma are the main cause of health disparities among Indigenous women and their children**

Obesity and type 2 diabetes are two of the most common chronic diseases in youth in Canada<sup>34–36</sup> and disproportionately affect Indigenous peoples worldwide.<sup>37–43</sup> The inequities in obesity, type 2 diabetes and life expectancy among Indigenous peoples in Canada can be attributed to several unique lifestyle and societal factors.<sup>44</sup> The geopolitical and sociohistorical/colonial experiences of all Indigenous peoples in Canada are paramount to any discussion of health inequities among Indigenous peoples in this country.<sup>45,46</sup> As highlighted in the recent Truth and Reconciliation Commission Report,<sup>47</sup> the legacy of several forms of colonization have impacted the health and wellbeing of Indigenous peoples in Canada.<sup>45,46</sup> Government-led assimilation practices/strategies of Indigenous peoples, including geographic displacement, residential school education and religious suppression are established determinants of disease inequities.<sup>47</sup> The appropriation of traditional land by European settlers and government legislation led to the displacement of many communities away from land that was integral to traditional ways of life. Entire communities were displaced onto lands that forced rapid

transition to a more European lifestyle.<sup>48</sup> Geographic displacement was and is still compounded by the legacy of residential schools, of the Sixties Scoop,<sup>49</sup> and continued assimilation forced upon Indigenous children, youth, their families and communities.<sup>47</sup> The cultural genocide did not stop after the Sixties Scoop; it continues even today through the systematic racist policies that continue to remove Indigenous children from their family, community and traditional lands. Here we argue that the government-sponsored appropriation of land and loss of traditional cultural practices during the early life period, combined with the intergenerational impact of residential schools and the Sixties Scoop policies explain, in large part, the disparities in chronic diseases between Indigenous and non-Indigenous youth in Canada. These include historical and current loss of the connection of Indigenous peoples to traditional lands that are universally considered critical for wellness among Indigenous peoples in Canada.

### **Potential mechanisms for early-life programming of chronic disease risk in youth**

Although epidemiological studies strongly suggest that the risk for premature chronic disease has origins in early life, the biological mechanisms by which fetal and early-life exposures influence physiology and health of children and youth are complex and remain unclear.<sup>50–53</sup> Two traditionally proposed mechanisms involve: (1) permanent structural changes to key organs (i.e. destruction of fetal pancreatic beta cells increasing diabetes risk) and (2) accelerated cellular ageing (i.e. oxidative stress-induced shortening of telomeres leading to cellular senescence and premature age-related pathologies; reviewed in Martin-Gronert and Ozanne<sup>51</sup>). More recently, altered epigenetic regulation of gene expression<sup>50–53</sup> following exposure to prenatal and/or early-life environmental stressors is believed to play a causal role in the link between early-life exposure and lifelong chronic disease risk.

The epigenome is a complex layer of regulatory information superimposed on the genome and includes nucleosome occupancy, positioning, composition, modification and dynamics, as well as DNA methylation that influence the expression of genes.<sup>54–56</sup> Owing to phenotypic plasticity in early life, epigenetic mechanisms are very significant in the maternal-placenta–fetal transmission of disease phenotypes.<sup>57</sup> Epigenetic modification of DNA contributes to the transmission of risk from mother to child during gestation and contributes to the offspring’s susceptibility to chronic diseases.<sup>58–61</sup> Moreover, epigenetic programming can be influenced by how the offspring are nursed, by infection or allergen exposure or even by how the gut is colonized by bacteria.<sup>62</sup> Epigenetic programming of gene expression may also have an intergenerational effect and as a result may perpetuate chronic disease risk in the next generation.<sup>63</sup>

Perhaps the earliest series of epigenetic studies that could support the fact that colonial atrocities have rendered Indigenous youth at greater risk of chronic disease stem from the work of Michael Meaney and colleagues from McGill University.<sup>64</sup> In brief, they demonstrated in rodents that creating stressful environments that increased the stress response early in life epigenetically modified the glucocorticoid receptor gene.<sup>65</sup> The epigenetic shift altered gene expression for glucocorticoid genes that further altered the offspring’s stress response. Importantly, these epigenetic shifts were buffered by higher maternal care and support.<sup>65,66</sup> Data from this animal model provide insight into the

mechanistic underpinnings for the importance of maternal roles (and potentially communal roles) in buffering the lasting effects of trauma on offspring. These concepts have long been recognized and promoted within Indigenous communities in Canada but have been lost in some communities due to colonization and the impact of Western medicine on birthing practices (i.e. removal/evacuation of women from communities to give birth), the child welfare system and the shunning of traditional birthing/family practices by the church and state.

Elders have long warned that the impact of the cultural genocide First Nations peoples experienced would last generations.<sup>67,68</sup> The Truth and Reconciliation Commission of Canada has called on health care providers and scientists to recognize that there is a direct link between these atrocities and current health inequities among Indigenous peoples.<sup>22</sup> From a Western standpoint, changes in specific epigenetic markers have been documented in survivors of residential schools, secondary to the starvation imposed on children attending the schools.<sup>69</sup> These epigenetic effects are believed to underpin not only the stress response, but may also increase risk for cardiometabolic diseases in adulthood. What remains unclear, but is worth examining, is whether maternal factors such as breastfeeding, returning birth to communities and/or restoring traditional early-life cultural practices can buffer and eventually erase adverse epigenetic changes from intergenerational trauma and begin the path towards health equity for Indigenous peoples.<sup>70</sup>

### Early-life interventions elicit significant lifelong health and social benefits

The effectiveness of lifestyle interventions to prevent chronic disease in adults is mixed. However, growing experimental evidence demonstrates that interventions delivered during the prenatal or early postnatal years yield lasting benefits into adulthood.<sup>71–74</sup> Improving conditions for physical, nutritional and social health during the early years of life decrease the incidence of non-communicable chronic diseases, encourage healthy lifestyle in adults and reduce health care expenditures. More importantly, interventions delivered early in life seem to confer lifelong protection from several chronic conditions. Accordingly, expert health panels like the World Health Organization and The World Bank build on a conceptual framework for early childhood development outcomes with a focus on health, nutrition and early learning,<sup>75–77</sup> particularly: (1) breastfeeding promotion; (2) access to and provision of prenatal care and (3) formal early learning. An extensive series was published early in 2017 reviewing each of these areas as well as challenges associated with scaling this evidence into programmes offered globally. Here we will provide brief summaries of the three main areas with relevant work conducted in Manitoba, Canada.

#### Breastfeeding

Breastfeeding was traditionally the main source of nutrients, immune factors and calories in the first year of life. As alternative forms of infant feeding have become more common, science has extensively studied the differences in child health outcomes associated with breastfeeding.<sup>16</sup> Extensive literature exists demonstrating the benefits of breastfeeding on infant weight status.<sup>17,78</sup> Data from our group and others found that initiation of breastfeeding alone confers protection against type 2 diabetes in both mothers and their offspring.<sup>79–82</sup> Importantly, this protection appears to be dose-dependent with the intensity (exclusiveness) and duration of

breastfeeding for both mothers<sup>81</sup> and offspring.<sup>83</sup> Unfortunately, while breastfeeding initiation rates are relatively high, the duration and exclusivity of breastfeeding is suboptimal<sup>16</sup> and costs are extensive. A recent economic analysis in the United States revealed that if rates of exclusive breastfeeding in the first 6 months of life increased to 90% of families, a country could save \$13 billion in health-related expenditures annually and save close to 1000 lives.<sup>84</sup> Similar data are needed in Canada; however, this reinforces the potential economic health care savings associated with early-life behavioural interventions.

Similar to other modifiable lifestyle behaviours, the impacts of colonization and cultural genocide have led to profound disparities in breastfeeding practices among Indigenous women. In a recent study by our group, we found that only 56% of First Nations mothers, compared with 83% of non-First Nations mothers, initiated breastfeeding in the hospital following birth.<sup>79</sup> Similar disparities exist among Indigenous women in Australia.<sup>85</sup> These disparities are grounded in historical and contemporary injustices: interventions focused exclusively on education are unjust and prove ineffective in populations affected by structural racism. Interventions to support breastfeeding among Indigenous women should be grounded in factors that support them to breastfeed, including cultural traditions, community and family support, and addressing socioeconomic challenges.<sup>86</sup> Interventions with particular success relied on Elder and/or peer support, media/community campaigns to address stigma and home-visiting programs.<sup>87,88</sup> There is a significant research gap in community-driven participatory models of breastfeeding promotion among Indigenous women. Increasing the number of community-driven interventions that promote breastfeeding in a culturally safe and grounded way may reduce inequities in breastfeeding rates among Indigenous women in Canada.

#### Access to and provision of prenatal care

Improvements in prenatal care contributed significantly to the reduction in maternal and infant mortality in high-income countries over the last century.<sup>89</sup> Prenatal care is considered a universal right in Canada and is provided within the public health system.<sup>90</sup> National societies of obstetrics and gynaecology recommend women attend prenatal visits with increasing frequency throughout pregnancy to screen for pregnancy-related health risks, receive information on healthy pregnancy and track fetal growth and development. Despite universal access to prenatal care in Canada, significant disparities in prenatal care exist worldwide,<sup>89,91,92</sup> particularly among Indigenous women and women living in low-income households. A recent systematic review identified several social factors associated with not accessing prenatal care. We have compared these factors with those identified in a Manitoba-based case-control study of women living in an underserved urban area (Table 1). Similar to disparities in health outcomes, the disparities in access to prenatal care that Indigenous women experience are grounded in historical and contemporary trauma that created and maintain adverse social conditions. Similar to breastfeeding disparities, interventions aimed at improving access to care, particularly for Indigenous women, must be culturally grounded in traditional knowledge and practices and on decolonizing and/or social justice frameworks.

Several models of prenatal care support exist worldwide.<sup>92–94</sup> Prenatal care is associated with better health outcomes in mothers

**Table 1.** Published barriers to prenatal care

Systematic review	Manitoba case-control study <sup>82</sup>
Young maternal age	Low household income
Low maternal education	Importance was unclear
Nonmarital status	Relied on friends/family
Ethnic minority	Dissatisfied with care
Unplanned pregnancy	Depressed/stressed
High parity	Family/partner problems
Late recognition of pregnancy	Concern for child apprehension

and children and data from recent systematic reviews suggest that group-based prenatal care confers even greater health benefits than individual care.<sup>93,95</sup> Group-based therapy can provide the additional benefit of creating social support networks and information-sharing at a lower cost, making it attractive as a public health intervention among groups suffering from inequities in care. Midwifery is another emerging model of prenatal care that may help reduce gaps in care and support women during the prenatal period.<sup>96,97</sup> A systematic review that included six cluster randomized trials ( $n = 138,549$ ) and seven quasi-experimental studies ( $n = 72,225$ ) indicated that interventions with traditional birth attendants, including midwives, was associated with a 24% reduction in perinatal death, 21% reduction in neonatal death and a trend towards lower maternal mortality.<sup>97</sup> These effects seem to be greatest among women and children living in low resources environments.<sup>98,99</sup> A recent intervention in Winnipeg, the largest city in Manitoba, was guided by the results from a case-control study of barriers and facilitators to prenatal care.<sup>91,100</sup> Co-developed between practitioners, mostly Indigenous women from a low-income neighbourhood in the inner city of Winnipeg, and researchers, the intervention was perceived by participants as reducing inequities in prenatal care. The study was strengthened by creating positive relationships with health care providers, flexible schedule and support with transportation and care. This is an attractive model to consider for reducing inequities in prenatal care among Indigenous in Canada and scale-up models need to be tested.

### Early-life interventions

It is posited that interventions delivered in the first few years life confer lifelong social and health benefits.<sup>101,102</sup> Supporting early-life brain development, optimal nutrition and mastery are core goals for a resilient first 1000 days of life.<sup>75,103</sup> Unfortunately, although several interventions have targeted women living in low- and middle-income countries, some of these efforts engaged Indigenous community in an effort to address inequities in health among Indigenous women and children.

The Abecedarian study is one of the most widely cited early-life interventions with longitudinal follow-up into adulthood. It provides an excellent example of the lifelong benefits of early-life interventions.<sup>18,71</sup> Children from low-income families who received full-time, high-quality educational intervention in a childcare setting from infancy through age 5 were twice as likely to graduate from college, displayed higher cognitive function from age 5 to 21 years and were 20–50% less likely to develop hypertension and the metabolic syndrome at 30 years of age.<sup>18</sup> This model of intensive early child care has influenced several provincial child care policies in Canada;

however, it has remained targeted to non-Indigenous children. Models of intensive early-life education and care, grounded in Indigenous cultural teachings need to be developed and tested with Indigenous community stakeholders to determine if similar effects are achievable in Canada.

### Examples inform future efforts to reduce inequities in indigenous maternal-child health outcomes

The United Nations Declaration on the Rights of Indigenous Peoples state that Indigenous peoples have the right 'to maintain and have access to their traditional medicines and health practices, including the conservation of their vital medicinal plants, animals and minerals'. The Declaration also calls for the 'right to access, without any discrimination, all social and health services'. We would like to highlight specific models of co-developed culturally safe care that could be used to guide future interventions. These examples have relied on ethical reciprocal university-community partnerships grounded in justice or equity. They also recognize the importance of co-creating interventions or policies guided by the voice and priorities of community.

#### Strengthening families maternal-child health

In some First Nations communities, there are programmes and services that are geared towards pre- and postnatal women, such as the Strengthening Families Maternal Child Health (SF-MCH) home-visiting program, which is being delivered in 16 of 63 First Nations communities in Manitoba. The SF-MCH programme provides intensive home visiting to prenatal women and families with children from 0 to 6 years of age, with a focus on prenatal health, preparing for birth, attachment and bonding, breastfeeding, screening for postpartum depression and early childhood screening/development. The programme uses a strength-based approach and the accredited Growing Great Kids Curriculum<sup>TM</sup><sup>104</sup> that has been culturally adapted to each individual community. Two successive evaluations have demonstrated that the programme has been effective in developing strong parental skills, increased breastfeeding rates, supporting positive relationships within the family, improved family functioning and improved access to health services among the participants.<sup>105,106</sup> The programme has been recognized as a best practice by the Health Council of Canada,<sup>107</sup> particularly around the joint partnership model with First Nation leadership.

#### Indigenous doula initiative

Another of these examples is the training and implementation of Indigenous doulas to support women during pregnancy, delivery and postpartum period. Travelling for birth is a typical experience for many First Nations women in Canada from remote and rural communities. Traditionally, Canadian women, particularly First Nations women, gave birth in their home communities, among friends and extended family. Cultural practices established strong community roots for the mother, her infant and the family. The children born in the community developed a clear sense of identity that helped them to become resilient and responsible members of that community. In the 1960s, the government began building local nursing stations staffed by nurses and at least one midwife;<sup>108</sup> however, by the 1970s, the efforts to decrease maternal mortality and morbidity in the general population led to a move towards hospital deliveries for all women. Criteria was established for evacuating mothers with high-risk pregnancies to

tertiary centres, but by the 1980s essentially all deliveries occurred outside of the community.<sup>108</sup> For First Nations women in particular, this led to their being transferred out of their home community weeks before their due date, an event which often resulted in a cascade of negative social consequences.<sup>109,110</sup> Often unaccompanied, women must leave their communities to experience labour and delivery in a distant referral centre where they reside in short-term boarding houses for weeks. This leaves them feeling culturally alienated or isolated over the course of the birthing period. Teenage girls may be particularly vulnerable when left without their mothers/caregivers for weeks at a critical time in their development<sup>110</sup> and may increase the instances of racism and isolation and creates the susceptibility to trafficking.<sup>111</sup>

Although many Indigenous communities are now exploring the possibilities of returning birthing back to communities for women characterized as low risk, there are still unmet needs that diminish the quality of the birthing experiences for women, whether they deliver in the community or in tertiary care centres. To date, discussions of risk have focused exclusively on the medical aspects of pregnancy, ignoring risks associated with dislocating the birthing event from its sociocultural context. In Manitoba, research is underway to explore the potential for trained birth workers to support pregnant and delivering women who travel for birth and in relearning traditional ways of nurturing and caring for pregnant women. In Winnipeg, Indigenous doulas provide support and mentorship for prenatal Indigenous women, during pregnancy, delivery and postpartum through the Manitoba Indigenous Doula Initiative. Indigenous doulas in Manitoba are rooted in cultural teachings, spiritual connections and traditions but do not provide clinical assessment. It is increasingly recognized that a trained birth companion could have large impacts on some of the psychological and social stressors experienced by women, as well as birth and health outcomes especially for women who travel for birth.<sup>112</sup> This programme is working in tandem with the Indigenous leadership on implementing a culturally and community-driven Indigenous doula programme designed for women in First Nations communities where women are required to travel for birth. Expectant mothers will be paired with a local Indigenous doula who has undergone culturally-specific doula training along with mentorship from an Indigenous doula/midwife team in the city. The expectant mothers will receive doula care from pregnancy to postpartum from her 'doula team'. Researchers are measuring a variety of outcomes related to psychological and social stressors and health outcomes using a variety of qualitative, quantitative and clinic evaluation. Some of these prenatal measurements include quality of prenatal care,<sup>113</sup> interpersonal processes of care,<sup>114</sup> stress<sup>115,116</sup> and postpartum depression.<sup>117</sup> This project is determining if health, social and cultural outcomes for mothers and newborns improved with First Nations, culturally-based doulas for women who travel for birth. Underpinning this project is the concept of resilience. Despite years of having traditions of birthing and midwifery replaced by biomedical notions of risk and safety, communities have developed pathways of resiliency. This project supports resiliency and is reflective of the larger response to domination faced by evacuated First Nations communities.

### Inuit midwives

In addition to Doula support, communities are advocating for and piloting the use of local midwives to support returning

birthing back to communities. A Canadian example of this model is the midwifery education programme at the Inuulisivik Health Centre, which trains Inuit midwives within the community-based birthing services programme.<sup>118–120</sup> Interventions such as these (Maternal Child Health Strengthening Families, the Indigenous Doula Initiative and others) grounded in restoring precolonial ways of life are critical as they keep the family together, support the healthy families by restoring traditional parenting roles that were violently taken during the era of residential school, Sixties Scoop and continue today through the child and family services system.

### Conclusions

In conclusion, the health disparities that exist among Indigenous women and children can be linked directly to historical trauma and colonial policies which severed the connection of Indigenous peoples to the land and culture, which is essentially cultural genocide. Interventions grounded in cultural restoration in the first 1000 days of life may be critical to overcoming the lasting effects of this trauma on Indigenous families. Efforts to promote prenatal care, breastfeeding and restoration of traditional birth practices are essential for gradually restoring the health of Indigenous families to the levels once observed before colonization.

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