Epidemiology of Diabetes in Pregnancy among Indigenous Women: Insights into the Global Indigenous and Métis Specific Contexts

By

Britt Alexandra Voaklander

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Abstract

Diabetes in pregnancy has been found to be more prevalent among Indigenous women in many countries. It is not clear whether Indigenous women with similar colonial histories have a greater prevalence of both pre-existing diabetes mellitus (pre-existing DM) and gestational diabetes mellitus (GDM) compared to non-Indigenous women. This thesis includes a systematic review of the literature that examined the prevalence of both pre-existing DM and GDM among Indigenous women in Australia, Canada, New Zealand, and the USA. The systematic review identified that Indigenous women living in countries with similar histories of colonialism have a higher prevalence of pre-existing DM (pooled odds ratios (OR) by country ranging from 1.81 (95% confidence interval [CI]:1.53, 2.13) to 3.20 (95%CI: 2.04, 5.03) and GDM (pooled ORs by country ranging from 1.41 (95%CI: 1.22, 1.63) to 2.04 (95%CI: 1.46, 2.84) compared to non-Indigenous women. This thesis also includes a retrospective cohort study of all singleton births in Alberta from 2006-2016 that evaluated the prevalence of pre-existing DM, GDM, and maternal and neonatal outcomes among Métis women compared to non-Métis women in Alberta. Results from the retrospective cohort study demonstrate that Métis women have an increased risk for both pre-existing DM (adjusted OR [aOR]:1.74, 95%CI: 1.18, 2.58) and GDM (aOR:1.30, 95%CI: 1.08, 1.55) after accounting for important clinical and sociodemographic factors, including material and social deprivation. Births to Métis women with GDM have increased odds of having a baby that is large for gestational age (aOR: 1.48, 95%CI: 1.00, 2.19). Results of both studies suggest that risk for diabetes in pregnancy among Indigenous women is substantial and may be due to structural determinants of health. Implications of study results for clinicians and public health are discussed, and future research directions are suggested.

Preface

The work presented in thesis is original work by Britt Voaklander. The overall aim of this thesis is to enhance our understanding of the prevalence, maternal and neonatal outcomes of diabetes in pregnancy among Indigenous women compared to non-Indigenous women. Ethics approval for this research was granted by the University of Alberta Human Research Ethics board (Pro00085391).

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1.1.2 Diabetes in Pregnancy

Diabetes in pregnancy is commonly defined as either pre-existing diabetes (mainly type 1 and type 2 diabetes diagnosed before pregnancy) or Gestational Diabetes Mellitus (hyperglycemia arising during pregnancy).[1] In 2017, approximately 21.3 (16.2%) million births worldwide were impacted by hyperglycemia in pregnancy.[2] Gestational diabetes mellitus (GDM) was responsible for 86.4% of the hyperglycemia in pregnancy; pre-existing diabetes mellitus (pre-existing DM) accounted for 6.2% of cases.[2] While the remaining 7.4% of diabetes in pregnancy is due to other types of diabetes diagnosed at the beginning of pregnancy.[2] Increasing weight and obesity during childbearing years is associated with the increased prevalence of GDM.[1,3] Advanced maternal age is also associated with an increased risk for developing pre-existing DM during pregnancy.[4,5]

1.1.3 Pre-existing Diabetes Mellitus in Pregnancy

Pre-existing DM is predominantly characterized by type 2 diabetes with a smaller proportion of women having type 1 diabetes diagnosed before pregnancy or overt diabetes diagnosed at the beginning of pregnancy.[1] Type 1 diabetes develops due to the destruction of pancreas beta cells that results in insulin deficiency causing hyperglycemia, weight loss and ketoacidosis.[6] The primary treatment for type 1 diabetes is insulin administration. Type 1 diabetic women should continue with glucose monitoring and insulin treatment during pregnancy.[1,6]

Type 2 diabetes most often occurs after the age of 35 and is characterized by the development of insulin resistance or the pancreas' inability to produce enough insulin.[6] The first-line treatment for type 2 diabetes includes diet, exercise, and oral antihyperglycemic medications (i.e. metformin).[6,7] Insulin can also be used as a treatment for type 2 diabetes to improve glycemic control.[6] If metformin or glyburide were taken during conception, then they can also be taken during pregnancy and insulin can be added to improve glycemic control.[1] Screening for overt diabetes in the first trimester should be done for pregnant women that have risk factors for diabete.[1] Risk factors for early screening include being over 40 years of age, having a previous GDM diagnosis, belonging to a high risk population (African, Indigenous, Hispanic, Asian, less socioeconomically advantaged), having an immediate family member with type 2 diabetes, having vascular risk factors (i.e., obesity, smoking), having a previous medical condition associated with type 2 diabetes (i.e., pancreatitis, human immunodeficiency virus), use of drugs associated with type 2 diabetes (i.e., glucocorticoid steroids, antipsychotics), and organ damage related to type 2 diabetes (i.e., retinopathy).[8] Early screening can be done using a hemoglobin A1C test or fasting plasma glucose (FPG).[1] If values of hemoglobin A1C are ≥6.5% or the FPG is ≥7.0 mmol/L then a diagnosis of diabetes is made.[1]

The prevalence of pre-existing DM during pregnancy is approximately 1.8% and has increased over time.[9] Pre-existing DM has been associated with greater rates of preeclampsia, caesarean section, preterm birth, increased birth weight, congenital abnormalities, and perinatal mortality.[10-12] There is also evidence that the offspring of women with pre-existing DM during pregnancy have an increased risk of developing type 2 diabetes.[13,14] Children of mothers with type 2 diabetes during pregnancy also have been found to have an increased likelihood of hospitalization for neurological/developmental disorders, asthma, and infections.[15]

1.1.4 Gestational Diabetes Mellitus

GDM is classified as glucose intolerance that arises during pregnancy above the expected range of normal glucose values that naturally occur in pregnancy.[1,16] During pregnancy without GDM, insulin resistance begins in the first trimester and continues to increase and is at its highest in the third trimester.[16] The diagnostic criteria for GDM remains contentious; however, Diabetes Canada recommends that all pregnant women are screened at 24-28 weeks gestation with a 50 g non-fasting oral glucose challenge test.[1] If 1-hour plasma glucose is ≥11.1 mmol/L, then a GDM diagnosis is made; however, if values are ≥7.8 mmol/L, then a 75 g fasting oral glucose tolerance test is ordered.[1] A FPG of ≥ 5.3mmol/L, or a 1-hour plasma glucose of ≥10.6mmol/L or a 2-hour plasma glucose ≥9.0 mmol/L are indicative of GDM diagnosis.[6] The primary treatment of GDM is diet and exercise counselling; insulin or metformin treatment is added if glycemic control cannot be maintained.[1]

GDM is associated with poor adverse maternal and perinatal outcomes including preeclampsia, caesarean section, macrosomia, large for gestational age, preterm birth, and neonatal intensive care unit admission.[17,18] The treatment of GDM during pregnancy can reduce the risk for perinatal adverse outcomes.[19] Both mothers with GDM and their offspring have an increased risk of developing type 2 diabetes later in life.[13,14,20]

1.1.5 Indigenous Peoples

The World Health Organization defines Indigenous peoples as "communities that live within or are attached to geographical distinct traditional habitats or ancestral territories, and who identify themselves as being part of a distinct cultural group, descendent from groups present in the area before modern states were created and current borders defined."[21] Indigenous peoples

from many countries have been identified as a vulnerable population for poorer health outcomes compared to non-Indigenous peoples within the same country.[22] Even Indigenous peoples with roots in industrialized nations including Indigenous peoples in Australia, Maori (New Zealand), First Nations, Inuit and Métis (Canada), as well as Native American and Alaska Natives (United States of America [USA]) suffer from important health inequalities compared to non-Indigenous people.[22]

1.1.6 Canadian Indigenous Peoples

First Nations, Inuit and Métis are three distinct Indigenous peoples within Canada that are recognized in section 35(2) of the Constitution Act of 1982.[23] First Nation, Inuit and Métis people each have their own unique culture, history and relationship with Canada.[24] Health resources allocation has not been the same for all Indigenous peoples in Canada; First Nations and Inuit people that have either Indian Status or who are recognized by an Inuit Land Claim have access to non-insured health benefits (i.e., dentistry and prescriptions) funded through the First Nations Inuit Health Branch of the Federal Government.[25] However, Indigenous peoples such as the Métis who do not have Status or are not recognized under an Inuit Land Claim do not have access to additional health resources funded by federal programs.[25]

1.1.7 Métis

Métis people's beginnings come from marriages between European (primarily French and Scottish) fur traders and First Nations peoples, who over time combined features of both cultures and created new cultural elements to form their own culture that is separate from both.[26] Elements of this new culture included a unique language (Michif), ways of dressing, political

structure, fiddle music, dance, and land ownership.[26] The Métis homeland stretches from Ontario to parts of British Columbia, covers the southern part of the Northwest Territories and dips into Montana and North Dakota in the United States of America.[27] Métis scrip (land or money), which recognizes the Métis' Aboriginal title, was implemented by the federal government with the intention to open land for settlement in the West.[28,29] However, the Métis did not receive their land due to an overly complex scrip delivery system, excessive delays in land allocation, and speculators conspiring with government officials.[28,30,31]

Contemporary Métis are defined by the Métis National Council as someone that self-identifies, is separate from other Indigenous groups, has ancestry of a historical Métis community, and is accepted by the modern Métis Nation.[32] The Métis National Council is made up of the provincial Métis Nations of British Columbia, Alberta, Saskatchewan, Manitoba, and Ontario that are within the Métis homeland.[33] Métis Nations today are "historically rooted, persistent, continuing to practice Métis culture, politics and obligations of kinship."[34]

The number of self-identified Métis people in Canada is 587,545.[32] In Alberta, there are 114,375 self-identified Métis, constituting the second largest Métis population in Canada after Ontario.[35] The purpose of the Métis governing bodies is to pursue the advancements of Métis self-determination and governance in Canada.[33] The Métis Nation of Alberta (MNA) has six different regions within the province; each with their own democratically elected president and vice-president, who along with the provincial president and vice-president make up the MNA provincial council.[36] In addition to the MNA, there are eight Métis settlements in Alberta that are governed separately by the Métis Settlements General Council.[37] The Métis settlements have their own criteria for who is eligible to live on the settlements that is separate from the Métis

National Council definition of Métis.[32,37] Those who are settlement members can also be MNA citizens, but they are not required to be.

Although Métis people make up a large proportion (35%) of the Indigenous population in Canada, Métis are still largely underrepresented in health research.[35,38] Historically, there have been barriers to conducting health research with Métis Nations. These include the lack of health infrastructure specific to Métis people, lack of human resources, reliance on volunteers, political instability of Métis Nations/communities, and the lack of reliable or linkable Métis registries.[39]

1.1.8 Diabetes in Pregnancy among Indigenous Women

Diabetes in pregnancy has been found to be more prevalent among Indigenous women in many countries, and they report a greater number of adverse perinatal outcomes compared to non-Indigenous women with diabetes during pregnancy.[40-42] These adverse perinatal outcomes include a greater number of preterm births, caesarean sections, congenital anomalies, birth injuries and stillbirths.[40-42] There is great variation in the prevalence estimates of diabetes in pregnancy among Indigenous women from a variety of jurisdictions.[43] Colonialism (i.e., systematic disruption to the lives of Indigenous peoples resulting in culture loss, displaced communities and continued discrimination by the in power settler state) and the social determinants of health (the conditions in which people live and grow) have been identified as key determinants to Indigenous peoples' health and wellbeing.[44,45] Synthesizing the literature on the prevalence of pre-existing DM and GDM among Indigenous women compared to non-Indigenous women in countries that have similar experiences of colonialism (Australia, Canada, New Zealand and the USA) could provide important information about the burden of diabetes in pregnancy among Indigenous women.

In Canada, the small amount of research on diabetes among Métis people has focused on the burden of type 1 and type 2 diabetes among non-pregnant Métis people.[46,47] Previous research has demonstrated that the prevalence of type 1 and type 2 diabetes is greater among Métis in Manitoba (12.0%) and Ontario (11.2%), compared to their non-Métis population (8.9%, 9.0%).[46,47] Métis people with diabetes have also been found to have a greater number of adverse events including a greater number of limb amputations, compared to the non-Métis population.[47] Diabetes during pregnancy among the Métis, both pre-existing DM and GDM has not been systematically evaluated in Canada. To address this knowledge gap, a population-based cohort study assessing the burden and outcomes of pre-existing DM and GDM among Métis women is needed.

The overarching purpose of this thesis is to increase our understanding of the prevalence, maternal and neonatal outcomes of both pre-existing DM and GDM among Indigenous women compared to non-Indigenous women. This will be done by conducting two different studies. A systematic review on the evidence of the prevalence of pre-existing DM and GDM among Indigenous women compared to non-Indigenous women in Australia, Canada, New Zealand and the USA will provide insight into the role of colonialism on the burden of diabetes in pregnancy among Indigenous women. Additionally, there are no studies in Canada evaluating the burden of diabetes in pregnancy among Métis women compared to non-Métis women. The results of a population-based cohort study of Métis and non-Métis births in Alberta will provide knowledge on the prevalence and maternal and neonatal health outcomes of both pre-existing DM and GDM. The information from this study can be used by the MNA, policy makers, and clinicians who are involved in the design and delivery of health services to Métis women.

1.2 Research Objectives

1. To assess the prevalence of pre-existing DM and GDM among Indigenous pregnant women in Australia, Canada, New Zealand, and the USA.
2. To evaluate and describe the epidemiology and maternal and neonatal outcomes of pre-existing DM and GDM in pregnancy among Métis women compared to non-Métis women in Alberta.

1.3 Organization of Thesis

This thesis follows a paper-based thesis format, containing two different manuscripts. Chapter 1 provides background information on diabetes in pregnancy, Indigenous peoples, and gaps in current knowledge. The second chapter is a systematic review summarizing the scientific evidence on the prevalence of diabetes in pregnancy among Indigenous women compared to non-Indigenous women in Australia, Canada, New Zealand, and the USA. Chapter 3 is a retrospective cohort study assessing the burden of diabetes in pregnancy among Métis women compared to non-Métis women in Alberta. Lastly, Chapter 4 provides a general discussion of study results, their implications for clinicians and policy makers, knowledge translation, as well a future research inquiry.

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CHAPTER 2: THE PREVALENCE OF DIABETES IN PREGNANCY AMONG INDIGENOUS WOMEN: A SYSTEMATIC REVIEW AND META-ANALYSIS

2.1 Background

Diabetes in pregnancy, both pre-existing diabetes (pre-existing DM) and gestational diabetes mellitus (GDM), are associated with adverse pregnancy outcomes.[1-3] These include poor maternal outcomes (caesarean section, preeclampsia, postpartum hemorrhage, and gestational hypertension), and perinatal outcomes (preterm birth, large for gestational age, congenital anomaly, stillbirths, birth injury, neonatal death, and neonatal intensive unit admission).[3-5] GDM is associated with an increased risk of type 2 diabetes in the mother; in the child, there is also an increased risk of developing diabetes and early-onset type 2 diabetes.[6-9]

The risk of having diabetes during pregnancy varies across populations with low-risk groups having a prevalence of approximately 2% to 5%.[10] One population at high risk for having diabetes in pregnancy are Indigenous women.[11,12] A previous systematic review on the prevalence and impact of diabetes in pregnancy among Indigenous women from multiple countries found that the prevalence of diabetes in pregnancy was not the same for all Indigenous peoples; 65% of the included studies had prevalence estimates greater among Indigenous women compared to non-Indigenous women.[13] However, this review did not consider pre-existing DM and GDM separately, nor focus on Indigenous women from countries that have had similar experiences of colonialism.

Colonialism has been identified as a critical determinant of Indigenous peoples' health.[14] Effects of colonialism include systematized discrimination, poverty, racism, and a rapid transition to a western lifestyle. Indigenous women in Australia, Canada, New Zealand, and the

USA have similar experiences of colonialism and evidence for early screening and interventions for pre-existing DM and GDM have been compared among Indigenous women from these countries in previous systematic reviews.[12,15] The purpose of this review is to assess whether the prevalence of pre-existing DM and GDM among Indigenous women relative to non-Indigenous women is comparable across Indigenous groups in Australia (Aboriginal and Torres Strait Islander), Canada (First Nations, Inuit, and Métis), New Zealand (Maori) and the USA (Native American and Alaska Natives) that have similar colonial experiences. To the best of our knowledge, this is the first systematic review to systematically identify and collate studies describing the prevalence of pre-existing DM and GDM among Indigenous women compared to non-Indigenous women in these countries.

2.2 Methods

A protocol for this review was registered in PROSPERO*:* International Prospective Register of Systematic Reviews (#CRD42018095971). This study follows the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines for the reporting of systematic reviews.[16]

2.2.1 Literature Search

Comprehensive literature searches were conducted by an information specialist in June 2019 in the following databases: OVID Medline, OVID EMBASE, OVID Global Health, EBSCO CINAHL, SCOPUS, Proquest Dissertations and Theses Global, PROSPERO, and Wiley Cochrane Library. Controlled vocabulary (e.g., MeSH terms) and keywords for Indigenous peoples, diabetes in pregnancy, and included countries (Australia, Canada, New Zealand, and the

USA) were used in the searches.[17] Grey literature searches were executed in BASE (Bielefeld Academic Search Engine) and Google Scholar. Lastly, reference lists of relevant articles were manually searched. No limits on publication type, language of publication, and year of publication were applied. Detailed search strategies are available in Appendix 1.

2.2.2 Study Inclusion

Studies were included if they were epidemiological observational studies that compared the prevalence of either pre-existing DM or GDM among Indigenous women in Australia, Canada, New Zealand, or the USA relative to pre-existing DM or GDM prevalence estimates in a group of non-Indigenous women. Studies were excluded if they were not primary research or were letters to the editor, case report or case-series studies, if they only provided a combined estimate of diabetes in pregnancy grouping pre-existing DM and GDM together, study participants were not Indigenous women, there was no non-Indigenous comparison group, or the study included Indigenous women from countries other than Australia, Canada, New Zealand, and the USA.

Two independent reviewers screened all titles and abstracts. Studies identified as potentially relevant underwent a full-text independent review in duplicate. Disagreements on inclusion were resolved through discussion and if consensus could not be reached, a third reviewer was involved in the eligibility decisions.

2.2.3 Risk of Bias Assessment

Two independent reviewers assessed the risk of bias (RoB) of all included studies; disagreements were resolved by discussion until a consensus was reached. Cohort studies were

assessed using the Newcastle – Ottawa Quality Assessment Scale for Cohort studies (NOS).[18] The NOS assesses three main categories of bias affecting selection of study cohorts, comparability of cohorts, and outcome assessment. Studies were classified as low RoB if they scored 3-4 stars in selection, 1-2 stars in comparability, and 2-3 stars in outcome assessment; unclear RoB was defined as 2-3 stars in selection, 1-2 stars in comparability, and 1-2 stars in outcome assessment; and high RoB was defined as 0 stars in any of the sections.[18] Studies with a cross-sectional design were assessed using a 9-items scale developed by Hoy et al. to assess RoB of prevalence studies in the domains of sample selection, non-response bias, data collection, measurement reliability and validity.[19] A score of 0-3 in any of the categories was classified as a low RoB, 4-6 as unclear RoB and 7-9 as high RoB.[19]

2.2.4 Data Extraction and Meta-Analysis

Information about study design, setting, Indigenous and comparison groups, data sources for exposure and outcomes definition, study sample size, screening guidelines and diagnostic criteria for pre-existing DM and GDM, and data to calculate pre-existing DM and GDM prevalence estimates was extracted from included studies. A standardized data collection form was used to extract all data and data was verified by a second reviewer for accuracy.

A meta-analysis of crude prevalence odds ratios (POR) in a Mantel-Haenszel random-effects model was used to combine data from individual studies comparing the prevalence of pre-existing DM and GDM between Indigenous and non-Indigenous groups. Pooled unadjusted POR with 95% confidence intervals (CI) are the summary statistic. Statistical heterogeneity across the studies was tested using the I^2 statistic and categorized as low (I^2 less than 25%), moderate (I^2 between 26% and 74%), and high (I^2 greater than 75%).[20] Results are reported separately for

each Indigenous group. Subgroups analyses were planned by study design, screening guidelines, diagnostic criteria, and risk of bias.[21] A narrative synthesis of results was conducted to describe the study populations and explore both clinical and methodological heterogeneity across the studies. The analysis was conducted using Review Manager (version 5.3).[2]

2.3 Results

2.3.1 Search Results

Electronic database searches identified 1,294 titles and abstracts. Searching of grey literature and review of relevant reference lists resulted in 53 additional titles and abstracts. After removal of duplicates, there were 808 titles and abstracts screened, which resulted in 174 possible potential articles to be included. After review of the full texts, 42 unique studies were included in the review. More details about the study selection process is available in Figure 1.

2.3.2 Characteristics of Included Studies

There were 18 unique studies conducted in Australia,[23-40] eight in Canada,[8,41-46,63] one in New Zealand,[47] and 15 in the USA[27,48-61] (Table 1). Among the included studies, 38 used a retrospective cohort study design, one was a prospective cohort study[24] and three were cross-sectional studies.[41,48,49] All included studies reported the prevalence of GDM (n=42) and 13 studies reported the prevalence of pre-existing DM.[8,23,25-29,42,43,50,51,62,63]

The Indigenous populations in the Australian studies were identified either as Indigenous women [23-26,31,33-39,62] or Aboriginal women and Torres Strait Islanders.[28,29,32] The Indigenous groups included in the Canadian studies were First Nations women[8,42-46,63] or Indigenous women encompassing First Nations, Métis and Inuit.[41] The Indigenous group included in the New

Zealand study were Maori women.[47] Studies conducted in the USA included either Native American[27,48,51-55,58,60] or Native American and Alaska Native women.[49,50,56,57,59,61] Studies from Australia mainly used a comparison group of non-Indigenous women, except those that also included Australasian,[24,32,40] European,[24,32] Caucasian,[25,35,39] African,[40] Asian subgroups,[24,25,32,35,39,40] Pacific Islanders[24,32] and women from the Americas[32] in separate groups. Comparison groups in the Canadian studies were described as either non-First Nations women,[8,42-45] non-Indigenous women,[41,63] Caucasian women, South Asian women and Chinese women.[46] The comparison groups in the study from New Zealand were Pacific Islander women and European women.[47] Comparison groups in studies conducted in the USA were either non-Native Americans,[52] Caucasian,[27,48-51,53-61] African American,[27,48-51,53-55,57-61] Hispanic,[27,49-51,53-55,57,59-61] or Asian/Pacific Islander women.[27,49-51,53-55,57,59,60]

Ascertainment of the exposure (Indigenous ancestry) was defined by self-report in studies from Australia, New Zealand, and the USA. In Canadian studies, Indigenous ancestry was determined by self-report,[8,41,44] place of residence,[43,45,63] language spoken[63] and by using the health care insurance Indian status identifier.[42,46,63] For outcome assessment, Australian studies used national perinatal data sources,[28,30] state/region data,[23,25,26,29,31-33,38,39,62] or clinic/hospital data.[24,34-37,40] USA studies used national data sources,[50,57,59,61] state-level data,[27,48,49,51-55,58] and hospital data.[60] In Canada, studies used databases at the provincial,[8,42-44,46,63] regional,[45] and hospital level.[41]

2.3.3 Risk of Bias of Included Studies

The majority of included studies had unclear or low RoB (75% of studies) (Figure 2). There were 16 studies assessed as low RoB,[8,25,27,32-35,40,42,46,51,54,58-60,63] 15 studies were assessed

as unclear RoB,[26,30,31,39,41,44,45,48-50,52,53,55-57] and 11 studies resulted in a high RoB.[23,24,28,29,36-38,43,47,61,62] Cohort studies performed best on categories 'representativeness of the exposed cohorts, 'selection of the non-exposed cohorts,' 'assessment of the outcome,' 'length of follow up,' and 'adequacy of follow up.'[18] Categories where cohort studies did not perform well were 'ascertainment of exposure,' 'demonstration that the outcome of interest was not present prior to the study,' and 'comparability of cohorts.'[18] All cross-sectional studies resulted in an 'unclear' RoB. Categories where cross-sectional studies did not perform well were if the 'study instrument showed validity or reliability,' if the 'same mode of data collection was used for all study participants' and if the 'study population was a close representation of the national population.'[19]

2.3.4 Association between Pre-existing DM and Indigeneity

The pooled POR of pre-existing DM among Indigenous women in Australia compared to non-Indigenous women was 3.20 (95% CI: 2.04, 5.03), and heterogeneity across studies was high I^2=98% (P<0.00001)(Figure 2.3). The POR of individual Australian studies ranged from 1.40 (95% CI: .28,1.52) to 4.25 (95% CI: 3.45, 5.25). Among Canadian studies, the pooled POR estimate comparing First Nations women to non-First Nations women was 2.66 (95%CI: 1.92, 3.67), but the heterogeneity was also high (I^2=98%, p<0.00001)(Figure 2.4). The POR for individual Canadian studies ranged from 1.71 (95% CI: 1.51, 1.93) to 3.65 (95% CI: 3.35, 3.99). Studies conducted in the USA comparing Native American/Alaska Native women to non-Indigenous women resulted in a pooled POR of 1.81 (95% CI: 1.53, 2.13) and the heterogeneity across the studies was moderate (I^2=48%, P=0.15)(Figure 2.5). The USA individual POR ranged from 1.59 (95% CI: 1.28, 1.97) to 2.58 (95% CI: 1.66, 4.00). We did not identify studies estimating the prevalence of pre-existing DM among Maori pregnant women in New Zealand.

Overall, 13 studies that reported crude PORs indicated that the odds of having pre-existing DM were greater among Indigenous pregnant women compared to their non-Indigenous counterparts, with POR values ranging from 1.40 (95% CI: 1.28, 1.52) to 4.25 (95% CI: 3.45, 5.25) (Table 2).[8,23,25-28,42,43,45,50,51,62] The pooled estimates for the Australian and Canadian meta-analysis should be interpreted with caution due to the high heterogeneity across studies. However, the direction and magnitude of the individual study POR also indicate an association between Indigeneity and pre-existing DM.

2.3.5 Association between GDM and Indigeneity

Combined estimates from Australian studies comparing GDM prevalence between Indigenous women and non-Indigenous women resulted in a pooled POR of 1.41 (95% CI: 1.22, 1.63) with high heterogeneity (I^2=97%, p<0.00001)(Figure 2.3). The POR for GDM in individual Australian studies ranged from 0.44 (95% CI: 0.14, 1.39) to 6.67 (95% CI: 5.11, 8.72). The pooled POR among Canadian studies comparing First Nations women to non-First Nations women was 2.04 (95% CI: 1.46, 2.84), with high heterogeneity across studies (I^2=100%, p<0.00001)(Figure 2.4). Individual POR for the Canadian studies ranged from 1.05 (95% CI: 0.97, 1.13) to 5.47 (95% CI: 3.89, 7.70). Combining studies conducted in the USA comparing GDM among Native American/Alaska Native women to non-Indigenous women yielded a pooled POR of 1.49 (95% CI: 1.32, 1.67) with high heterogeneity (I^2=97%, p<0.00001) (Figure 2.5). The individual study POR ranged from 0.96 (95% CI: 0.82, 1.12) to 2.98 (95% CI: 2.61, 3.41).

Overall, most of the studies (n=24) reported a crude POR indicating that the odds of GDM in pregnancy were higher among Indigenous women compared to non-Indigenous women,

with POR ranging from 1.10 (95% CI: 1.04, 1.16) to 6.67 (95% CI: 5.11, 8.72) (Table 2).[8,23,25,26,28,30,31,38,39,42-45,50-54,56,57,59,61-63] Twelve studies found that the odds of having GDM in pregnancy were not different between Indigenous and non-Indigenous women, with POR ranging from 0.44 (95% CI: 0.14, 1.39) to 2.54 (95% CI: 0.53, 12.24).[24,27,33-37,40,46,55,58,60] Two studies found that the odds of having GDM in pregnancy were lower among Indigenous women, POR 0.59 (95 % CI: 0.48, 0.72) and 0.91 (95% CI: 0.88, 0.94) respectively.[29,32] Interpretation of the pooled POR for studies conducted in Australia, Canada, and the USA should be interpreted with caution due to the high heterogeneity among studies. The magnitude and direction of the study-level POR suggest an association between Indigeneity and GDM that is not as consistent as pre-existing DM and Indigeneity.

Heterogeneity was explored using subgroup analysis. Screening guidelines for studies that reported universal screening versus risk factor-based screening were considered separately. Studies that reported different diagnostic criteria were assessed as subgroups. RoB categories of low, unclear, and high were pooled separately. Limitation of the comparison groups to Caucasian women (low risk) was also assessed. However, none of subgroups assessed meaningfully reduced heterogeneity.

2.4 Discussion

This systematic review provided a comprehensive assessment of the prevalence of diabetes in pregnancy among Indigenous women in Australia, Canada, New Zealand, and the USA. The review found great variations in the prevalence estimates of pre-existing DM and GDM among Indigenous women from Australia, Canada, New Zealand and the USA.

Predominantly, the odds of having pre-existing DM/GDM in pregnancy are greater in Indigenous women compared to their non-Indigenous counterparts.

The crude POR estimates in individual studies showed that pre-existing DM and GDM seem to be strongly associated with Indigenous ancestry of pregnant women, but the magnitude of the association varies across studies and diabetes type. The magnitude of the association between Indigeneity and pre-existing DM is consistently stronger than the association between Indigeneity and GDM. Findings from this review are similar to those of other reviews conducted in this field of research.[11,13] A previous systematic review assessing the prevalence of GDM among Indigenous women in Australia found substantial heterogeneity in prevalence estimates across the studies.[11]

This review provides a systematic comparison of pre-existing DM and GDM among Indigenous women compared to non-Indigenous women from countries with similar histories of colonialism. Indigenous peoples' experience of colonialism is an active agent contributing to loss of identity, language, culture, the rapid transition to a western lifestyle, as well as ongoing oppression and discrimination.[64-66] Increased exposure to the social determinants of health (e.g., income, education, employment) among Indigenous peoples is also a product of colonialism.[14] Social inequalities and colonialism have been recognized as important contributors for developing diabetes among Indigenous peoples and also for barriers to managing diabetes (i.e., physical activity, balanced meals, blood sugar monitoring and insulin injections).[67,68] Alternatively, the high prevalence of diabetes among Indigenous peoples has been proposed to be due to genetic susceptibility, but research has yet to find a strong causative gene.[69]

Clinical care and public health interventions designed for Indigenous pregnant women to prevent and reduce the impact of diabetes in pregnancy should be led by Indigenous women and

grounded in Indigenous culture and traditional practices. Care for Indigenous women also needs to be equitable to ensure that social inequalities are not preventing them from achieving the same health status as non-Indigenous women. Clinicians should be aware that Indigenous women are more likely to have pre-existing DM and GDM in pregnancy and adjust their practice accordingly when treating Indigenous women.

Future research should focus on both the prevention of diabetes in pregnancy and adapting clinical care so that it becomes more meaningful and impactful for Indigenous women. Research on innovative solutions to improve social inequalities should be done in partnership with Indigenous communities. Evaluations of adapted care for Indigenous women should focus on improving outcomes and decreasing the impact of pre-existing DM and GDM. Continued surveillance is necessary but future studies should clearly report the screening and diagnostic criteria that are used so that study interpretation can be improved.

2.4.1 Strengths and Limitations

The strengths of this systematic review include a rigorous methodological approach following a pre-defined protocol that was registered prior to the beginning of the study. Comprehensive database searching using validated search terms,[17] grey literature searching, and searching relevant reference lists reduced selection bias by decreasing the chance of missing potentially relevant studies. The risk of bias assessment and data extraction were done in duplicate to minimize assessor bias.

There are several limitations in this systematic review. Included studies were from a wide range of time periods, over which pre-existing DM and GDM screening guidelines and diagnostic criteria changed. Reporting of pre-existing DM and GDM screening criteria,

diagnostic criteria, and characteristics of comparison groups were limited and prevented meaningful subgroup analyses. Other reasons for high heterogeneity between studies could be due to underlying differences in study participants.

To the best of our knowledge there are no studies conducted in New Zealand that assessed the prevalence of pre-existing DM among Indigenous women compared to non-Indigenous women. In Canada, there were no estimates available for the prevalence of pre-existing DM and GDM among Métis or Inuit women compared to non-Métis or non-Inuit women. Generalizability of results to other Indigenous peoples should be made with caution until studies providing these comparisons are produced, so that pan-Indigenous interpretations are avoided.

2.5 Conclusion

Indigenous women in Australia, Canada, New Zealand and the USA have an increased vulnerability to having pre-existing DM and GDM in pregnancy. Diabetes in pregnancy results in poor birth and delivery outcomes with serious long-term impact on the health of the mother and child. System-wide and structural interventions to address the increased prevalence of pre-existing DM and GDM among Indigenous women should be considered in Australia, Canada, New Zealand and the USA.

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Table 2.1. Characteristics of Included Studies

Study	Study Design	Population	Screening/diagnostic Criteria	Prevalence Estimates and Adjusted OR with 95% CI
Bower, 1992, Australia	Retrospective Cohort	N=111,019 *Aboriginal Women in Western Australia (n=5,481) *Non-Aboriginal Women in Western Australia (n=105,538)	Pre-existing DM: not stated GDM: not stated	GDM Aboriginal – 1.3% (73/5,481) GDM Non-Aboriginal – 0.2% (213/105,538 Pre-existing DM Aboriginal – 0.5% (25/5,481) Pre-Existing DM Non-Indigenous – 0.11% (116/105,538)
Chamberlain, 2014, Australia	Retrospective Cohort	N=3,555,575 *Indigenous Women in Australia (n=121,736) *Non-Indigenous Women in Australia (n=3,433,839)	GDM: not stated	GDM Indigenous – 5.0% (6,121/121,736) GDM Non-Indigenous – 4.2% (142,689/3,433,839)
Porter, 2011, Australia	Retrospective Cohort	N=81,617 *Aboriginal Women in Western Australia (n=4,966) *Non-Aboriginal Women in Western Australia (n=76,651)	Pre-existing DM: not stated GDM: not stated	GDM Aboriginal – 8.4% (418/4,966) GDM – Non-Aboriginal – 6.4% (4,915/76,651) Pre-existing DM Aboriginal – 2.3% (113/4,966) Pre-existing DM Aboriginal– 0.7% (541/76,651)
AIHW, 2010, Australia	Retrospective Cohort	N=832,693 *Aboriginal and Torres Strait Islanders (n=30,518) *Non-Aboriginal Australians (n=802,175)	Pre-existing DM: if type 1 or type 2 diabetes diagnosed before pregnancy or with a 75g OGTT, if fasting glucose ≥7.0 mmol/L or if 2 h glucose ≥11.1 mmol/L then Pre-existing DM. GDM: screening at 26-30wks with a 50 g GCT, if 1h glucose ≥ 7.8mmol/L, then a 75g OGTT, if fasting glucose is ≥5.5mmol, or	GDM Aboriginal/Torres Strait Islanders – 5.1% (1,562/30,518) GDM – Non-Aboriginal – 4.7% (37,539/802,175) Pre-existing DM Aboriginal/Torres Strait Islanders – 1.5% (443/30,518) Pre-existing DM Non-Aboriginal – 0.6% (4,501/802,175)

			1 h glucose is ≥10.00 mmol/L, or 2 h glucose ≥8.0 mmol/L then GDM.	
Thrift, 2014, Australia	Retrospective Cohort	N=265,848 *Aboriginal Women in Queensland (n=13,582) *Non-Aboriginal women in Queensland (n=241,270)	GDM: not stated.	GDM Aboriginal 6.5% (883/13,582) GDM Non-Aboriginal – 5.5% (13,270/241,270)
Abouzeid, 2015, Australia	Retrospective Cohort	N=269,682 *Aboriginal Women in Victoria (n=1,555) *Non-Aboriginal Women in Victoria by race/ethnicity (n=268,127)	GDM: Screening recommended at 26-28wks with 50g GCT, if 1h glucose ≥7.8mmol/L, or a 75g GCT with 1h glucose 8.0 mmol/L, then a 75g OGTT if fasting glucose ≥5.5mmol/L, or 2h glucose of ≥8.0mmol/L then GDM.	GDM Aboriginal – 2.6% (41/1,555) GDM non-Aboriginal– 4.4% (11,708/268,127) Adjusted GDM OR: 1.11 (0.81, 1.52)
Ishak, 2003, Australia	Retrospective Cohort	N=230,011 *Aboriginal Women in South Australia (n=4,843) *Non-Aboriginal Women in South Australia (n=225,168)	Pre-existing DM: not stated GDM: a 75g OGTT if fasting glucose ≥5.5mmol/L, or 2h glucose of ≥8.0mmol/L then GDM. (ADIPS) or WHO a 75g results of 2h glucose ≥11.0 mmol/L then GDM, if between 7.8mmol/L and 11.0 mmol/L then glucose GDM.	GDM Aboriginal– 4.3% (208/4,843) GDM Non-Aboriginal – 2.4% (5,472/225,168) Pre-existing DM Aboriginal – 1.8% (86/4,843) Pre-existing DM Non-Aboriginal – 0.7% (743/225,168) Adjusted GDM OR: 1.83 (1.81, 1.84) Adjusted Pre-existing DM OR: 5.54 (5.40, 5.69)
Stone, 2002, Australia	Retrospective Cohort	N=60,400 Aboriginal Women in Victoria (n=438) *Non-Aboriginal Women in Victoria (n=59,962)	GDM: not stated	GDM Aboriginal- 4.3% (19/438) GDM Non-Aboriginal – 3.6% (2,159/59,962) Adjusted GDM OR – 2.5 (1.54, 4.06)
Simmons, 2005, Australia	Retrospective Cohort	N=99 *Aboriginal Women from 4	GDM: Screening recommended at 26-28wks with 50g GCT, if	GDM Aboriginal – 10.7% (3/24)

		rural hospitals in Victoria (n=24) *Non-Aboriginal Women from the same hospitals (n=75)	1h glucose ≥7.8mmol/L, or a 75g GCT with 1h glucose 8.0 mmol/L, then a 75g OGTT if fasting glucose ≥5.5mmol/L, or 2h glucose of ≥8.0mmol/L then GDM.	GDM Non-Aboriginal – 4.5% (4/75)
Yue, 1996, Australia	Retrospective Cohort	N=3,814 *Aboriginal Women in antenatal clinic NSW (n=89) *Non-Aboriginal Women in antenatal clinic NSW by race/ethnicity (n=3,718)	GDM: universal screening at 24-28 weeks with 50g GCT, if screened positive then then a 75g OGTT, fasting glucose ≥5.5mmol/L, or 2h glucose of ≥8.0mmol/L then GDM.	GDM Aboriginal – 10.1% (9/89) GDM Non-Aboriginal – 6.2% (232/3,718)
DeCosta, 1996, Australia	Retrospective Cohort	N=9,179 *Aboriginal Women (n=180) *Non-Aboriginal Women (8,999)	GDM: not stated.	GDM Aboriginal 1.6% (3/180) GDM Non-Aboriginal – 3.7% (332/8,999)
Moses, 1994, Australia	Prospective Cohort	N=1,829 *Aboriginal Women (n=12) *Non-Aboriginal Women by race/ethnicity (n=1,702)	GDM: testing at the start of the third trimester, patients had to either 1) 75g OGTT, if fasting glucose≥5.5mmol/L or 2 h glucose ≥8.8mmol/L then GDM. 2) take home 75g GTT and if 2 h glucose ≥8.8mmol/L then GDM.	GDM Aboriginal – 0% (0/12) GDM Non-Aboriginal– 7.3% (125/1,702)
Powell, 1999, Australia	Retrospective Cohort	N=285 *Rural Aboriginal Women (n=132) *Non-Aboriginal Women rural (n=137)	GDM: not stated.	GDM Aboriginal– 1.5% (2/132) GDM Non-Aboriginal – 2.2% (3/137
NSW, 1996-2017*, Australia *missing 2011	Retrospective Cohort	N=1,900,947 *Aboriginal women in New South Wales (n=58,158)	Pre-existing DM: not stated GDM: not stated	GDM Aboriginal – 5.3% (3,093/58,158) GDM Non-Aboriginal – 5.8% (107,342/1,842,789) Pre-existing DM Aboriginal – 1.0% (563/58,158)

		*Non-Aboriginal women in New South Wales (n=1,842,789)		Pre-existing DM Non-Aboriginal – 0.7% (12,817/1,842,789)
Sharpe, 2005, Australia	Retrospective Cohort	N=282,260 *Aboriginal women south Australia (n=7,542) *non-Aboriginal Women south Australia by race/ethnicity (n=274,008)	Pre-existing DM: not stated. GDM: not stated	GDM Aboriginal – 2.4% (334/7,542) GDM Non-Aboriginal – 5.6% (6,370/274,008) Pre-existing DM Aboriginal – 1.3% (98/7,542) Pre-existing DM Non-Aboriginal – 0.3% (848/274,008)
Teh, 2011, Australia	Retrospective Cohort	N=2,880 *Urban Aboriginal Women (n=21) *Urban Non-Aboriginal Women Urban (n=2,852)	GDM: screening at 26-28 wks with a 75g GCT, if 1h glucose was ≥8.0 mmol/L then had a 75g OGTT. If fasting glucose ≥5.5 mmol/L or 2h glucose ≥8.8mmol/L then GDM.	GDM Aboriginal – 4.8% (1/21) GDM Non-Aboriginal – 8.8% (250/2,852) Adjusted GDM OR: 1.1 (0.1, 9.3)
Zhang, 2010, Australia	Retrospective Cohort	N=42,440 *Aboriginal Women in the Northern Territory (n=18,614) *Non-aboriginal women in the Northern Territory (n=23,826)	GDM: not stated	GDM Aboriginal – 6.3% (1,173/18,614) GDM Non-Aboriginal – 4.2% (994/23,826)
Markey, 1996, Australia	Retrospective Cohort	N=14,138 *Aboriginal women in the Northern Territory (n=4,937) *Non-Aboriginal women in the Northern Territory (n=9,201)	GDM: not stated.	GDM Aboriginal – 6.3% (311/4,937) GDM Non-Aboriginal 4.02% (370/9,201)
Aljohani, 2008, Canada	Retrospective Cohort	n=324,605 *First Nations Women in Manitoba (n= 39,820)	GDM: <1992 no GDM guidelines >1994 screening recommended at 24th wk with a 50g GTT, if 1 hr glucose ≥7.8 mmol/L, then 100 g OGTT	GDM First Nations – 6.9% (2,764/39,820) GDM non-First Nations - 2.4% (6,708/284,785) Adjusted GDM OR: 2.20 (2.00, 2.42)

		*Non-First Nations in Manitoba (n= 284,785)	>1998: screening at 24th-28th week, with a 50g GTT. 1h glucose ≥ 10.2mmol/L then GDM, if ≥7.8 mmol/L <=10.2mmol/L then they undergo a 75g OGTT. If ≥2 abnormal values, either fasting plasma glucose ≥5.8 mmol/L, or 1h glucose ≥10.6mmol/L, or 2 h glucose ≥9.2 mmol/L, or 3h glucose≥ 8.1 mmol/l then GDM.	
Dyck, 2002, Canada	Cross Sectional	N=1,612 *Indigenous (First Nations and Métis) Saskatchewan (n=252) *Non-indigenous Women in Saskatchewan (n=1,360)	GDM: Women had to meet one of the three criteria: 1) 2 or more abnormal values on 100g OGTT or 2) the result of a 1hr 50g GCT is ≥7.8mmol/L and has a physician diagnosis. 3) if they needed treatment with insulin or diet for high blood glucose levels during pregnancy.	GDM Indigenous – 11.5% (29/252) GDM Non-Indigenous – 3.5% (48/1,360)
Liu, 2012, Canada	Retrospective Cohort	N=487,368 *On Reserve First Nations women in Ontario (n=2,465) *Non-First Nations Women in Ontario (n=484,903)	Pre-existing DM: not stated. GDM: not stated.	GDM First Nations – 6.5% (166/2,465) GDM Non-First Nations – 4.2% (20,365/484,903) Pre-existing DM First Nations – 3.9% (96/2,465) Pre-existing DM Non-First Nations – 1.8% (8,728/484,903)
Oster, 2014, Canada	Retrospective Cohort	N=427,058 *First Nations Women in Alberta (n=28, 306) *Non-First Nations Women in Alberta(n=398,752)	Pre-existing DM: diagnoses made based on patient history, review of patient's chart, and medication record. (combined type 1 and type 2), as well as if a	GDM First Nations – 4.3% (1,217/28,306) GDM non-First Nations – 3.8% (15,153/398,752) Pre-existing DM First Nations – 1.0% (283/28,306)

			OGTT was done in the first trimester and there was a positive result GDM: Screening 24-28 wks, 50 g oral GCT, ≥10.3mmol/L then GDM, if ≥7.8mmol, <10.2mmol/l then 75g OGTT. 2 values of either FBG ≥5.3 mmol/L, 1h glucose >10.3mmol/L, 2h glucose ≥8.9mmol/L then GDM.	Pre-existing DM Non-First Nations – 0.6% (2,393/39,875) Adjusted OR for GDM: 1.47 (1.38, 1.57) Adjusted OR for Pre-existing DM: 1.73 (1.52, 1.96)
Rodrigues, 1999, Canada	Retrospective cohort	N=8,120 *On reserve Cree First Nations Women in Quebec (n=402) *Non-First Nations Women in Montreal (n=7,718)	GDM: screening at 24-30wks with a 50g GTT, if the 1h glucose ≥7.8 mmol/L then patient had a 100g OGTT. If 2 values of either fasting glucose ≥5.8mmol/L, 1h glucose 10.6 mmol/L, 2h glucose ≥9.2mmol/L or 3h glucose ≥8.1mmol/L then GDM.	GDM First Nations – 11.4% (46/402) GDM Non-First Nations – 2.3% (178/7,718)
Shen, 2015, Canada	Retrospective Cohort	N=410,877 *First Nations Women Manitoba (n=71,033) *Non-First Nations Women Manitoba (n=339,844)	Pre-existing DM: not stated. GDM: not stated.	GDM First Nations – 6.6% (4,564/71,033) GDM Non-First Nations – 2.2% (7,342/339,844) Pre-existing DM First Nations – 3.6% (2,561/71,033) Pre-existing DM Non-First Nations – 1.1% (3,580/339,844)
Yeung, 2015, Canada	Retrospective Cohort	N=248,525 *First Nations Women in Alberta (n=14,967) *Chinese, South Asian, and Caucasian Women (n=233,558)	GDM: not stated	GDM First Nations – 5.0% (748/14,967) GDM Non-First Nations – 5.2% (11,169/233,558) Adjusted GDM OR: 1.8 (1.6, 2.0)
Chen, 2019, Canada	Retrospective Cohort	N=234, 850	Pre-existing DM: not stated	GDM First Nations – 10.7% (1,829/17,090)

		*First Nations women in Quebec (n=17,090) *Non-Indigenous women in Quebec (n=217,760)	GDM: universal screening 24-28wks gestation with a 50g GCT, if blood glucose ≥ 7.8mmol/L then a 75g OGTT is done, if 2 values are fasting ≥ 5.3 mmol/L or 1hr ≥ 10.0 mmol/L or 2hr ≥ 8.6mmol/L the GDM	GDM Non-First Nations – 4.8% (10,453/217,760) Pre-existing DM First Nations – 3.9% (667/17,090) Pre-existing DM Non-First Nations – 2,395/217,760)
Yapa, 2000, New Zealand	Retrospective Cohort	N=2,473 *Maori women South Auckland (n=613) *European, pacific islanders and other women (n=1,860)	GDM: screening at 24-28wks with 50g GCT, if 1h glucose is ≥7.8mmol/L then 75g OGTT. GDM if fasting glucose ≥5.5mmol/L or 2h glucose ≥9.0mmol/L.	GDM Maori – 5.7% (35/613) GDM Non-Maori - 4.9% (92/1,860)
Anderson, 2016, USA	Retrospective Cohort	N=5,193,386 *American Indian and Alaska Native women (n=44,570) *Non-Indigenous women (n=5,148,816)	Pre-existing DM: not stated GDM: not stated	GDM American Indian/Alaska natives – 4.3% (1,932/44,570) GDM Non- American Indian/Alaska natives – 3.8% (195,504/5,148,816) Pre-existing DM American Indian/Alaska Natives – 1.1% (499/44,570) Pre-existing DM Non-American Indian/Alaska natives – 0.6% (32,191/5,148,816)
Ralls, 2007, USA	Retrospective Cohort	N=228,680 *Native American women in Utah (n=2,567) *Non-Native American women in Utah (n=226,113)	GDM: not stated	GDM Native American – 5.6% (149/2,657) GDM Non-Native American – 2.3% (5,201/226,113) Adjusted GDM OR: 2.1
Cabacungan, 2012, USA	Retrospective Cohort	N=197,253 *Native American women in Wisconsin (n=2,216) *Non-Indigenous women in	GDM: not stated	GDM Native American– 6.8%(151/2,216) GDM Non-Native American – 4.2% (8,176/195,037) Adjusted GDM OR: 2.27 (1.90, 2.70)

		Wisconsin (n=195,037)		
Dennis, 2019, USA	Retrospective Cohort	N=2,730,146 *American Indian and Alaska Native Women (n=23,926) *Non-Indigenous women excluding those that were not born in the USA. (n=2,706,220)	GDM: not stated	GDM American Indian/Alaska Native-6.5% (1,563/23,926) GDM non-Indigenous-4.0% (109,575/2,706,220)
Fridman, 2014, USA	Retrospective Cohort	N=1,551,017 *Native American women in California (n=6,787) *Non-indigenous women in California by ethnicity/race (n=1,544,230)	Pre-existing DM: not stated GDM: not stated	GDM Native American – 5.3%(357/6,787) GDM non-Native American – 4.9%(75,769/1,544,230) Pre-existing DM Native American – 1.2%(82/6,787) Pre-existing DM non-Indigenous – 0.7%(11,807/1,544,230) Adjusted GDM OR: 1.02 (1.01, 1.03) Adjusted Pre-existing DM OR: 1.0 (1.015, 1.009)
Hunsberger, 2010, USA	Cross Sectional	N=3,767 *American Indian and Alaska Natives in Oklahoma (n=493) *Non-native American and Alaska Natives (n=3,274)	GDM: not stated	GDM American Indian/ Alaska Natives – 7.9% (39/493) GDM Non-American Indian/Alaska Native – 9.7% (318/3,274) Adjusted GDM OR: 1.17 (0.71, 1.95)
Kim, 2012, USA	Retrospective Cohort	N=641,697 *American Indian women in Florida (n=1,211) *Non-Indigenous women in Florida (n=640,486)	GDM: not stated	GDM Native American – 6.5% (79/1,211) GDM Non-Native American – 4.6% (30,376/640,486)
Kim, 2013, USA	Retrospective Cohort	N=1,228,265 *American Indian women in California (n=4,134)	GDM: not stated	GDM American Indian – 7.6% (316/4,134) GDM Non-American Indian – 7.8% (96,045/1,224,131)

		*Non-Indigenous women in California (n=1,224,131)		
Pearson, 2016, USA	Retrospective Cohort	N=544,743 *American Indian and Alaska Natives in California (n=35,792) *White women in California (n=508,951)	GDM: not stated.	GDM American/Alaska Natives – 5.6% (2,004/35,792) GDM Non – Native American/Alaska Natives – 4.4% (22,597/508,951) Adjusted GDM OR: 1.34 (1.28, 1.41)
Singh, 2018, USA	Retrospective Cohort	N=7,480,879 *American Indian and Alaska Natives (n=14,497) *Non-American Indian/Alaska Natives women in USA (n=7,466,382)	GDM: not stated	GDM American Indian/Alaska natives – 10.0% (1,420/14,497) GDM non-American Indian/Alaska Natives – 6.3% (470,049/7,466,382)
Hegwood, 2015, USA	Cross Sectional	N=21,143 *Native Americans in Oklahoma (n=2,451) *White and black women in Oklahoma (n=18,692)	GDM: not stated	GDM Native American – 8.8% (215/2,449) GDM White and Black women – 7.0% (1,304/18,692)
Williams, 1999, USA	Retrospective Cohort	N=41,839 *Native American Women in Washington (n=7,456) *Non-Indigenous women in Washington (34,383)	GDM: not stated	GDM Native American – 2.7% (201/7,456) GDM Non-Native American – 2.8% (962/34,383)
Caughey, 2010, USA	Retrospective Cohort	N=139,853 *Native American women in Northern California (n= 800) *Non-Indigenous women in Northern California (n=139,053)	GDM: not stated	GDM Native American – 5.6%(45/800) GDM – Non-Native American – 6.8% (6,133/139,053) Adjusted GDM OR: 1.31 (0.85, 2.01)

Chu, 2009, USA	Retrospective Cohort	N=3,108,877 *American Indian and Alaska Native women (n=14,617) *Non-American Indian/Alaska Native women (3,094,260)	GDM: not stated	GDM American Indian/Alaska Native – 5.1% (750/14,617) GDM Non-American Indian/Alaska Native – 3.9% (119,473/3,094,260)
Moum, 2004, USA	Retrospective Cohort	N=22,746 *American Indian women in Montana and North Dakota (n=2,664) *White women in Montana and North Dakota (n=20,082)	Pre-existing DM: not stated GDM: not stated.	GDM American Indian – 3.9% (103/2,644) GDM Non-American Indian –2.8%(562/20,082) Pre-existing DM American – 1.0% (27/2,664) Pre-existing DM non-American Indian – 0.4%(80/20,082)

CI=confidence interval; DM = diabetes mellitus; GDM=gestational diabetes mellitus; GCT=glucose challenge test (non-fasting), OGTT= oral glucose challenge test (fasting). OR=odds ratio; PRAMS=pregnancy risk assessment monitoring system; USA = United States of America

Table 2.2 Direction of Prevalence Odds Ratios among Indigenous women compared to Non-Indigenous women.

	Pre-Existing DM	GDM
Number of studies that have POR greater among Indigenous women	13	24
Number of studies that have POR of no difference between Indigenous and non-Indigenous women	0	12
Number of studies that have POR lower among Indigenous women	0	2

DM = diabetes mellitus; GDM = gestational diabetes; POR: prevalence odds ratios

Figure 2.1 PRISMA Study Flow

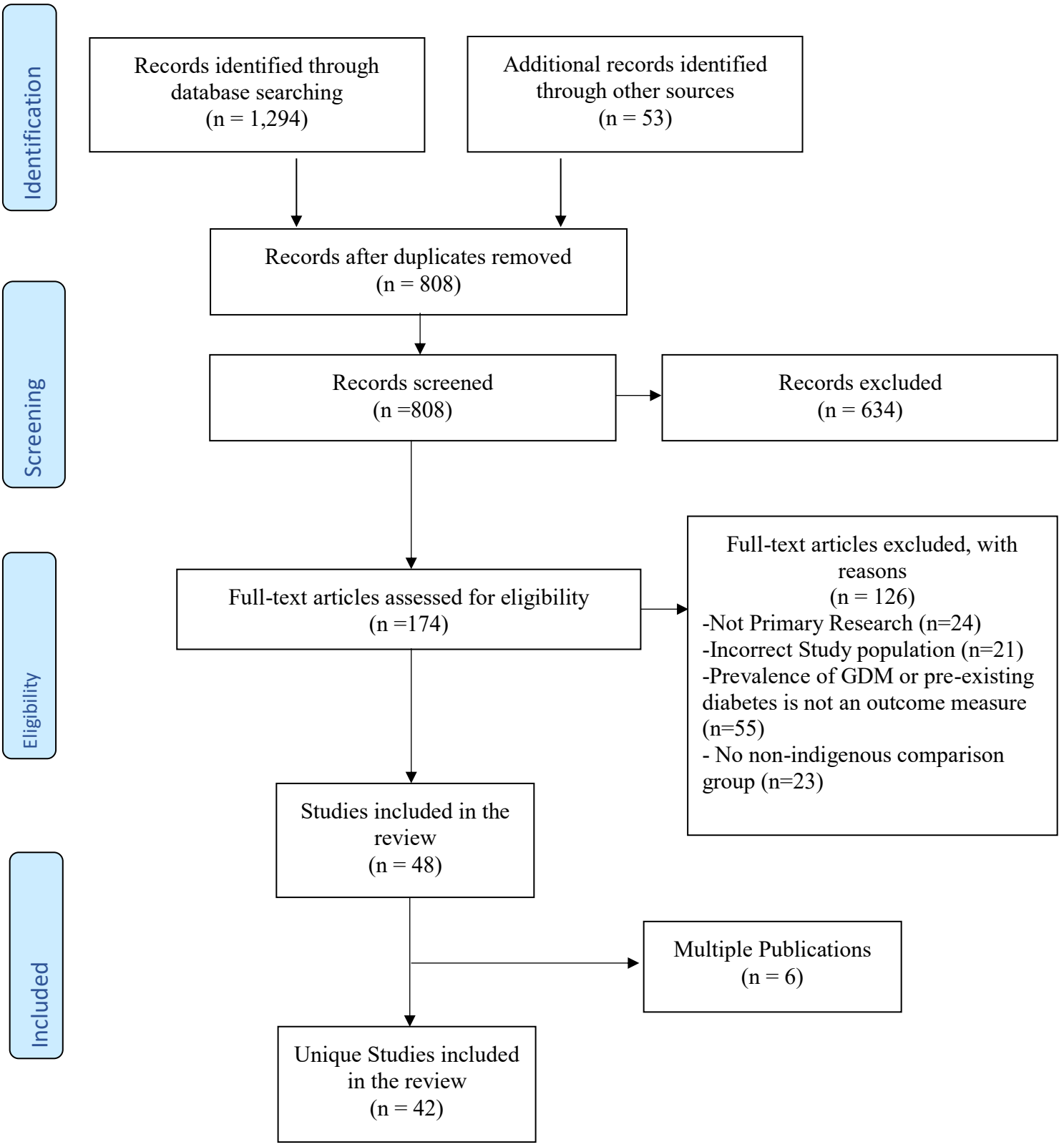


Figure 2.2 Risk of Bias

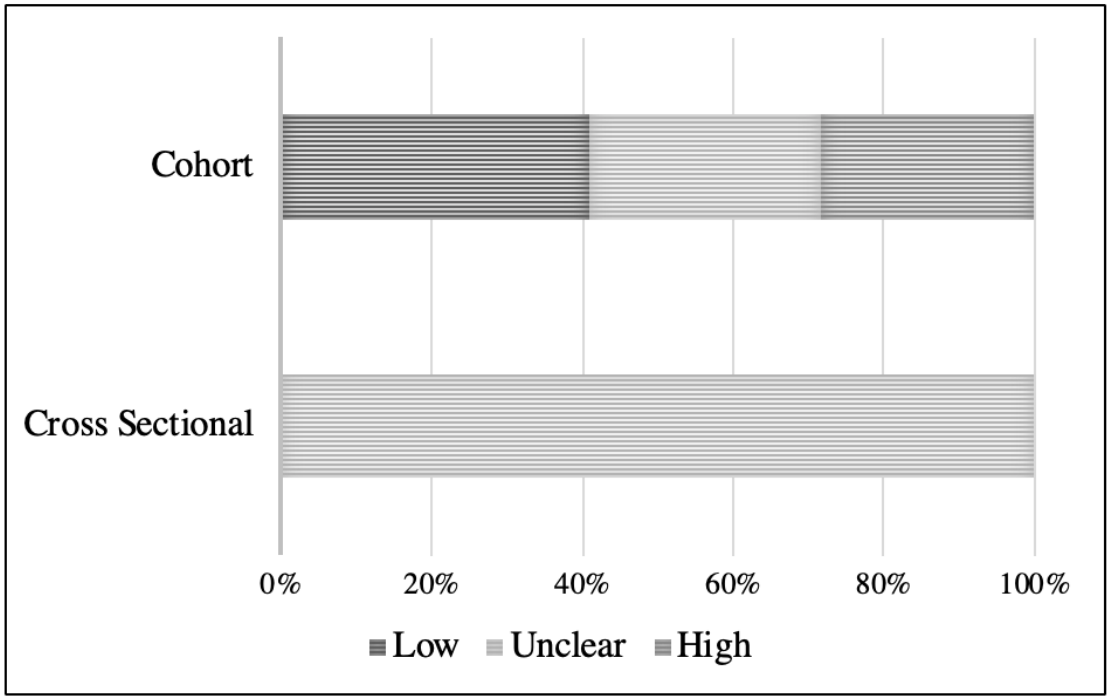
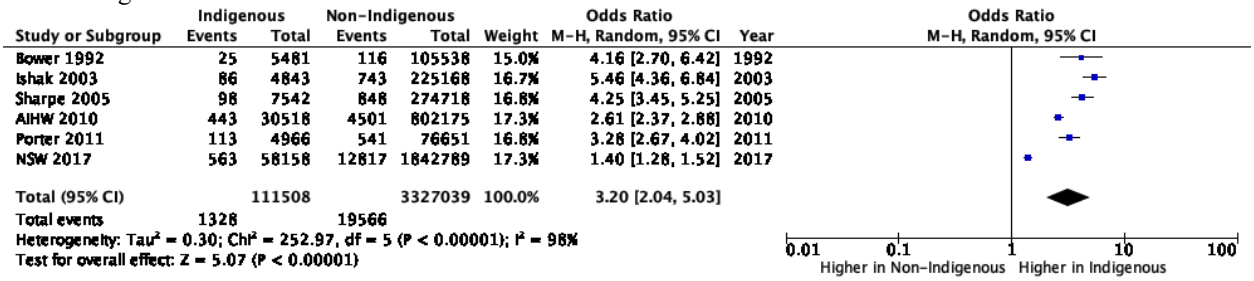


Figure 2.3 Prevalence Estimates of Pre-existing DM/GDM among Aboriginal/Torres Strait Islander Women Compared to Non-Indigenous Women (Australia Studies)

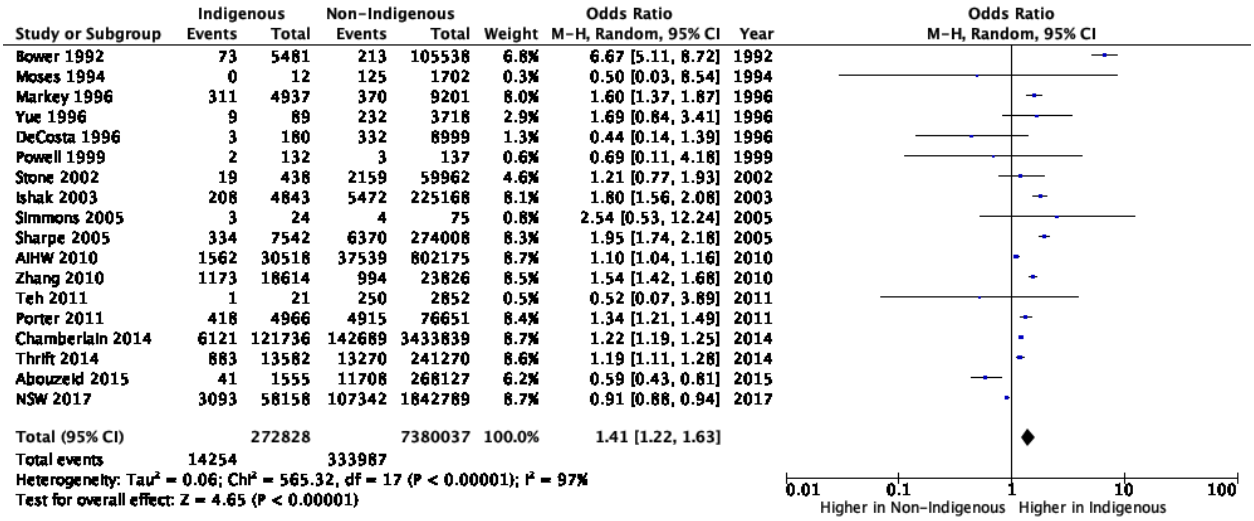
Pre-existing DM



Study or Subgroup	Indigenous Events	Indigenous Total	Non-Indigenous Events	Non-Indigenous Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bower 1992	25	5481	116	105538	15.0%	4.16 [2.70, 6.42]	1992
Ishak 2003	86	4843	743	225168	16.7%	5.46 [4.36, 6.84]	2003
Sharpe 2005	98	7542	848	274718	16.8%	4.25 [3.45, 5.25]	2005
AIHW 2010	443	30518	4501	802175	17.3%	2.61 [2.37, 2.88]	2010
Porter 2011	113	4966	541	76651	16.8%	3.28 [2.67, 4.02]	2011
NSW 2017	563	58158	12817	1842789	17.3%	1.40 [1.28, 1.52]	2017
Total (95% CI)		111508		3327039	100.0%	3.20 [2.04, 5.03]	
Total events	1328		19566				

Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 252.97$, df = 5 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: $Z = 5.07$ ($P < 0.00001$)

GDM

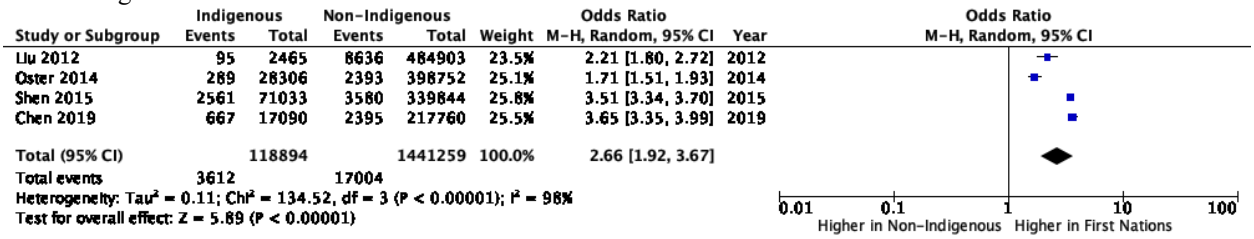


Study or Subgroup	Indigenous Events	Indigenous Total	Non-Indigenous Events	Non-Indigenous Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Bower 1992	73	5481	213	105538	6.8%	6.67 [5.11, 8.72]	1992
Moses 1994	0	12	125	1702	0.3%	0.50 [0.03, 8.54]	1994
Markey 1996	311	4937	370	9201	8.0%	1.60 [1.37, 1.87]	1996
Yue 1996	9	89	232	3718	2.9%	1.69 [0.84, 3.41]	1996
DeCosta 1996	3	180	332	8999	1.3%	0.44 [0.14, 1.39]	1996
Powell 1999	2	132	3	137	0.6%	0.69 [0.11, 4.18]	1999
Stone 2002	19	438	2159	59962	4.6%	1.21 [0.77, 1.93]	2002
Ishak 2003	208	4843	5472	225168	8.1%	1.80 [1.56, 2.08]	2003
Simmons 2005	3	24	4	75	0.8%	2.54 [0.53, 12.24]	2005
Sharpe 2005	334	7542	6370	274008	8.3%	1.95 [1.74, 2.18]	2005
AIHW 2010	1562	30518	37539	802175	8.7%	1.10 [1.04, 1.16]	2010
Zhang 2010	1173	18614	994	23826	8.5%	1.54 [1.42, 1.68]	2010
Teh 2011	1	21	250	2852	0.5%	0.52 [0.07, 3.89]	2011
Porter 2011	418	4966	4915	76651	8.4%	1.34 [1.21, 1.49]	2011
Chamberlain 2014	6121	121736	142689	3433839	8.7%	1.22 [1.19, 1.25]	2014
Thrift 2014	883	13582	13270	241270	8.6%	1.19 [1.11, 1.28]	2014
Abouzeid 2015	41	1555	11708	268127	6.2%	0.59 [0.43, 0.81]	2015
NSW 2017	3093	58158	107342	1842789	8.7%	0.91 [0.88, 0.94]	2017
Total (95% CI)		272828		7380037	100.0%	1.41 [1.22, 1.63]	
Total events	14254		333987				

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 565.32$, df = 17 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: $Z = 4.65$ ($P < 0.00001$)

Figure 2.4 Prevalence Estimates of Pre-existing DM/GDM in First Nations Women Compared to Non-Indigenous Women (Canada Studies)

Pre-existing DM



GDM

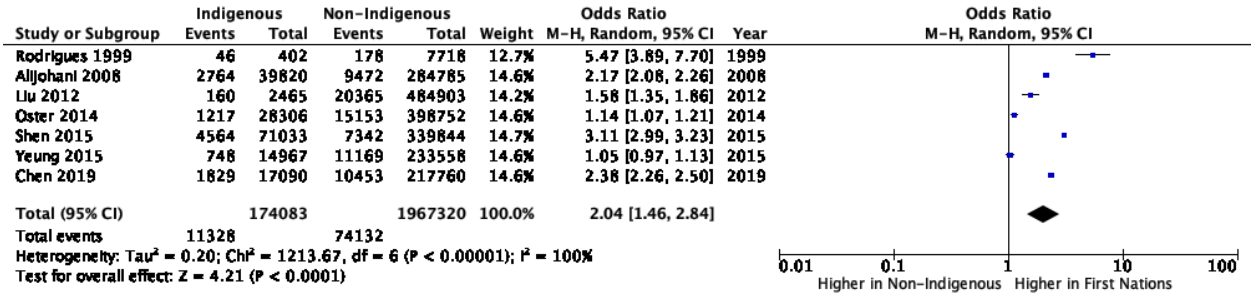
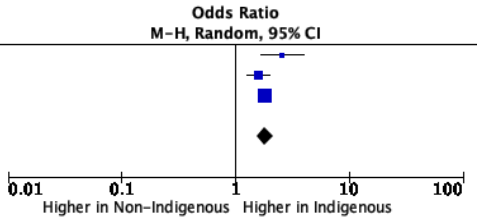


Figure 2.5 Prevalence Estimates of Pre-existing DM/GDM in Native America/Alaska Native Women Compared to Non-Indigenous Women (USA studies)

Pre-existing DM

Study or Subgroup	Indigenous Events	Indigenous Total	Non-Indigenous Events	Non-Indigenous Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Moum 2004	27	2644	80	20082	12.0%	2.58 [1.66, 4.00]	2004
Fridman 2014	82	6787	11807	1544230	31.3%	1.59 [1.28, 1.97]	2014
Anderson 2016	499	44570	32191	5148816	56.7%	1.80 [1.65, 1.97]	2016
Total (95% CI)		54001		6713128	100.0%	1.81 [1.53, 2.13]	
Total events	608		44078				

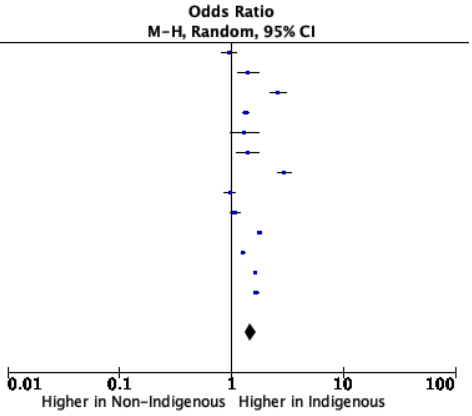
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.85$, $df = 2$ ($P = 0.15$); $I^2 = 48\%$
Test for overall effect: $Z = 6.94$ ($P < 0.00001$)



GDM

Study or Subgroup	Indigenous Events	Indigenous Total	Non-Indigenous Events	Non-Indigenous Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Williams 1999	201	7456	963	34383	7.5%	0.96 [0.82, 1.12]	1999
Moum 2004	103	2644	562	20082	6.7%	1.41 [1.14, 1.74]	2004
Ralls 2007	149	2567	5201	226113	7.4%	2.62 [2.21, 3.10]	2007
Chu 2009	750	14617	119473	3094260	8.4%	1.35 [1.25, 1.45]	2009
Caughey 2010	45	800	6079	139053	5.5%	1.30 [0.96, 1.76]	2010
Kim 2012	79	1211	30376	640486	6.5%	1.40 [1.12, 1.76]	2012
Cabacungan 2012	253	2216	8173	197258	7.8%	2.98 [2.61, 3.41]	2012
Kim 2013	316	4134	96045	1224131	8.0%	0.97 [0.87, 1.09]	2013
Fridman 2014	357	6787	75769	1544230	8.1%	1.08 [0.97, 1.20]	2014
Anderson 2016	1932	44570	127485	5148816	8.5%	1.78 [1.70, 1.87]	2016
Pearson 2016	2004	35792	22597	508951	8.5%	1.28 [1.22, 1.34]	2016
Singh 2018	7520	75404	470079	7466382	8.6%	1.65 [1.61, 1.69]	2018
Dennis 2019	1563	23926	109575	2706220	8.5%	1.66 [1.57, 1.74]	2019
Total (95% CI)		222124		22950365	100.0%	1.49 [1.32, 1.67]	
Total events	15272		1072377				

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 426.16$, $df = 12$ ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: $Z = 6.58$ ($P < 0.00001$)



CHAPTER 3: THE BURDEN OF DIABETES IN PREGNANCY AMONG MÉTIS WOMEN: A RETROSPECTIVE COHORT STUDY

3.1 Background

Métis people are distinct Indigenous peoples in Canada whose beginnings can be traced back to unions between European fur traders (mainly French and Scottish) and First Nations women, and who over time developed their own unique culture, language and identity.[1] Métis are one of the three recognized Aboriginal peoples in the Canadian Constitution Act, 1982,[2] and in Alberta there are approximately 114,000 self-identified Métis people.[3] The Métis Nation of Alberta (MNA) is the representative body for Métis in Alberta and defines a Métis person as someone that self-identifies as Métis, is separate from other Indigenous peoples, has ancestry of a historic Métis community, and is accepted by the modern Métis Nation.[4] The Métis Nation of Alberta Information Registry contains approximately 42,000 registered Métis citizens.

Diabetes in pregnancy, both pre-existing diabetes (pre-existing DM) and gestational diabetes mellitus (GDM), are serious pregnancy conditions associated with adverse maternal and perinatal outcomes. These adverse maternal and perinatal outcomes include preeclampsia, caesarean sections, preterm birth, macrosomia, stillbirth, and birth injuries.[5] GDM is associated with future development of type 2 diabetes in the mother and the child.[6-9] Previous research assessing diabetes in pregnancy among Indigenous women in Canada has focused on First Nations or Indigenous women (combining First Nations, Métis and Inuit).[10-14] These studies have predominantly found that First Nations and Indigenous women overall have a greater prevalence of both pre-existing DM and GDM and an increased number of adverse outcomes compared to non-Indigenous women with diabetic pregnancies.[11,12,15] These adverse outcomes include

stillbirths, perinatal deaths, preterm births, increased birth weight, and shoulder dystocia.[11,12,15] Métis women, however, were not evaluated separately in this research and due to their unique history, culture, and contemporary experience in Canada, they should be.

Limited health research available for Métis has focused on type 2 diabetes. Findings indicate that they have a greater prevalence of type 2 diabetes than non-Métis and a greater number of adverse outcomes of diabetes (i.e., limb amputations).[16,17] However, in Canada, there have not been any studies assessing diabetes in pregnancy among Métis women compared to non-Métis. The purpose of this study is to address the knowledge gap about the burden of both pre-existing DM and GDM among pregnant Métis women. Specifically, the purpose is to evaluate the prevalence of pre-existing DM and GDM and associated obstetric and neonatal health outcomes of Métis women compared to non-Métis women in Alberta.

3.2 Methods

3.2.1 Study Design

A population-based retrospective cohort study of all births in Alberta from 2006-2016 was conducted. Reporting of the study follows the RECORD (Reporting of Studies using Observational Routinely Collected Health Data) guidelines for observational epidemiological studies.[18] Ethics approval was received from the Human Research Ethics Board at the University of Alberta (#Pro00085391).

3.2.2 Data Sources

The *Alberta Perinatal Health Program* (APHP) is a validated clinical perinatal database that records information for all births in a hospital and delivered by registered midwives in the

province of Alberta.[19-21] The database contains information collected on the delivery record, including information on pre-pregnancy characteristics, issues during the current pregnancy and the delivery.[20,21] The *Discharge Abstract Database* (DAD) captures information on all acute hospital admissions in Alberta, including maternal and perinatal admissions. International Classification of Disease 10th revision (Canadian Version) is used to report diagnoses made in the hospital.[22] The *Pampalon Material and Social Deprivation Index* (PMDI) database uses information collected from the 2006 Canadian census to create small area-level measures of material and social deprivation.[23] A principal components analysis is used to create two independent variables that represent groups of correlated variables from the Canadian census. The variable material deprivation is representative of the highly correlated variables education, employment, and income.[23] The variable social deprivation is representative of the following correlated variables: number of single-family homes; the number of people widowed, single or divorced, and the proportion of people that live alone within a dissemination area.[23] Material deprivation and social deprivation are both divided into five quantiles that range from the most privileged (Q1) to the most deprived (Q5).[23] The PMDI also contains information on area of residency, where urban and rural communities are characterized by their population density, distance from municipal or metropolitan centres and services, local infrastructure, movement patterns of those living in the area, and types of work.[24] The mothers' postal code at the time of delivery was used to assign area of residency.

The *Métis Nation of Alberta Information Registry* (MNAIR)is a dataset maintained by the MNA, that includes demographic information of all MNA citizens. The MNAIR is an objectively verifiable identification registry of Métis people in Alberta. The *Pharmaceutical Information Network* (PIN) contains information on drug dispensing from outpatient pharmacies.

This includes drug dispensing event information (time, pick up date), drug identification number, anatomical therapy code, and dosage information.[22] Not included in the PIN dataset are prescriptions that are unfilled, the diagnostic reason for the prescription, and drugs dispensed in the hospital.[22] *Alberta Health Care Insurance Plan* (AHCIP) is a database that captures demographic information of people living in Alberta who are covered by the universal health care system. It contains information on the migration of people into the province, personal identifiers (date of birth, gender, address), activity of coverage, and if coverage was cancelled.[22]

3.2.3 Study Population

All singleton births in Alberta from 2006 to 2016 were identified in the APHP.

3.2.4 Identification of the Métis and non-Métis Cohorts

Identification of births to citizens of the MNA and the first level of their dependents were identified by probabilistic linkage between the MNAIR (names, date of birth) and the AHCIP.[25] Deterministic data linkage using scrambled unique lifetime identifiers was used to link the APHP, AHCIP, DAD, PMDI and PIN databases.[26] Births in the APHP, in which a Métis identifier (yes/no) was not available were excluded from the study. All non-Métis births, including births to First Nations and Métis who are not citizens of the MNA were included as the non-Métis comparison group. An Information Sharing Agreement between the MNA and Alberta Health facilitated this data linkage, and a research agreement between Dr. Ospina and the MNA facilitated data sharing with the research team.

3.2.5 Study Outcomes and Covariates

The primary study outcomes were the prevalence of pre-existing DM and GDM. Pre-existing DM was defined as those that had reported "diabetes controlled by diet," "insulin use" and/or "retinopathy documented" on their antenatal risk assessment. GDM was defined as those women that had "Gestational Diabetes documented" as an issue in their current pregnancy. This information is captured on the delivery record and inputted into the APHP. The APHP has previously been used as the gold standard method for identifying GDM during pregnancy in Alberta.[21]

In addition, two main obstetric outcomes (pregnancy-induced hypertension and Caesarean section) and two main neonatal outcomes (preterm birth and large for gestational age) were evaluated for both pre-existing DM and GDM comparing Métis and non-Métis births. Women were classified as having pregnancy-induced hypertension if "gestational hypertension" was identified as a problem in the current pregnancy but were not classified as having pre-existing hypertension. Size for gestational was calculated using Canadian sex-specific reference small for gestational age <10th percentile and large for gestational age >90th percentile[27] and preterm was defined as a birth before 37 weeks' gestation.

Secondary study obstetric and neonatal outcomes were also evaluated by diabetes type. The maternal outcomes were preeclampsia (pregnancy-induced hypertension and proteinuria), obstetric hemorrhage (intrapartum; ICD-10: O67-O679 and postpartum; ICD-10: O72-O724)), induction of labor, and maternal death at delivery. Secondary neonatal outcomes evaluated were congenital anomalies, birth injuries (ICD-10: P10-P159), admission to the neonatal intensive care unit, small for gestational age, induced preterm, spontaneous preterm, birth weight, stillbirth and neonatal death (death within 28 days of birth).

The study covariates included maternal age at the index birth, pre-pregnancy weight (<45kg or >91kg), insulin prescriptions (insulin prescription dispensed within four months prior to delivery date), antenatal risk assessment score (classified as low <3, moderate 3-6 and high >6 based on the antepartum risk score which is calculated based on pre-pregnancy characteristics, past-obstetrical history, problems in current pregnancy and other risk factors captured on part one of the delivery record), substance use during pregnancy (alcohol and drug use), pre-existing hypertension and material deprivation, social deprivation, area of residency (urban/rural). The maternal postal code at the time of delivery was used to assign area of residency, and the dissemination area which is linked to the census variables used to calculate material and social deprivation for that dissemination area. Material and social deprivation are both categorical variables each with five quintiles that range from the least deprived (Q1) to the most deprived (Q5).[23] All study covariates were identified from the APHP, except for insulin use during pregnancy which was identified in the PIN (Anatomical Therapeutic Chemical code: 'A10A').

3.2.6 Statistical Analyses

Study covariates and outcomes were described using frequencies and proportions for categorical data and means with standard deviations (SD) for continuous variables. Comparisons of Métis and non-Métis births study covariates were made using either t-tests for continuous variables or chi2 test/Fishers exact test for the categorical variables. Crude period prevalence estimates were calculated for the whole study period and annually for proportion of births complicated by pre-existing DM and GDM among the Métis and non-Métis cohort (i.e. the number of Métis births with GDM/number of Métis births). Age standardization was done using the direct standardization method using a reference population of all births in Canada by age

group in 2006.[28] A multivariable analysis adjusting for theoretically important study covariates comparing outcomes among Métis and non-Métis births was done.[29-33] Covariates assessed for their potential confounding effects include maternal age, smoking, parity, pre-pregnancy weight, pre-pregnancy hypertension, material deprivation, social deprivation, and insulin prescriptions and area of residency (urban or rural).

Multilevel logistic mixed models with random effects were used to adjust for multiple singleton births to the same mother during the ten-year study period. Multiple births per woman (level-1) were nested within mothers (level-2). Model fit was assessed using the likelihood ratio test that compares the multilevel model with single level logistic model.[34] Intraclass Correlation Coefficients (ICC) were calculated to quantify the variance in the outcome variable that was explained by differences in the level-2 variable.[34] Adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were calculated comparing study outcomes among Métis and non-Métis births after adjusting for theoretically important study covariates. Analysis was done using SAS software v. 9.4 (SAS Institute., Cary, NC, USA) and STATA Statistical Software (Release 15. College Station, TX: StataCorp LLC).

3.3 Results

3.3.1 Characteristics of the Study Population

There were 497,400 singleton births in Alberta during the study period (2006-2016). After merging datasets, there were 483,300 (97%) singleton births in which a Métis identifier (yes/no) could be assigned. The final study population included 7,977 Métis births and 475,323 non-Métis births. Of these births there were 3,512 (0.7%) births in which diabetes status during

pregnancy could not be determined and they were removed from the analysis. Further details on the data linkage are available in Figure 1.

3.3.2 Characteristics of Métis and non-Métis Births

Table 3.1 presents characteristics of the study cohorts by diabetes type. Métis women with pre-existing DM were significantly younger at delivery (mean age of 30 years; SD:5.4) compared to non-Métis women with pre-existing DM (mean age of 32years; SD:5.4). A greater proportion (41%) of Métis women had a pre-pregnancy weight greater than 91kg compared to non-Métis women (23%). More Métis women with pre-existing DM smoked during pregnancy (29%), live in rural areas (33%) and belonged to the most deprived quintile of material deprivation (33%) compared to non-Métis women with pre-existing DM (15%, 23% and 24%, respectively). There were no significant differences between Métis and non-Métis with pre-existing DM for the proportion of pre-existing hypertension, substance use, and social deprivation. More Métis pregnant women with pre-existing DM were categorized as having a high-risk pregnancy (>6 on their antepartum risk score), compared to non-Métis women (53% and 41%).

Similar characteristics were seen in births by women with GDM. The mean age at delivery of Métis women who had GDM was 31years (SD: 5.7) while the mean age of non-Métis women was 32 years (SD:5.1). A greater proportion of Métis women with GDM smoked during pregnancy (32%), had a pre-pregnancy weight greater than 91kg, and lived in rural areas (33%) compared to non-Métis women with GDM (17%, 11%, and 15% respectively). A higher proportion of Métis women with GDM were on insulin (37%) compared to non-Métis women (26%). A smaller proportion of Métis women with GDM were in the least deprived material

social deprivation quintile (7.3% and 19%). More Métis women with GDM were in the most deprived material deprivation quintile than non-Métis woman (29% and 23%). A greater proportion of Métis women with GDM and pre-existing DM during pregnancy also were classified as high-risk pregnancies compared to non-Métis women.

3.3.3 Pre-existing DM and Pregnancy Outcomes among the Métis

The crude prevalence of pre-existing DM for the whole study period (2006-2016) among Métis births was 1.4% compared to non-Métis births is 1.2%. When pre-existing DM prevalence estimates were age-standardized, the prevalence among Métis births was 1.8%, and 1.1% among non-Métis births. The prevalence of pre-existing DM increased for both groups over the study period, but the increase was greater among Métis women (0.8% to 2.1%) than non-Métis women (1.0% to 1.5%) (Figure 2).

Métis women had 74% increased odds of having pre-existing DM in pregnancy after adjusting for important study covariates and births clusters (aOR: 1.74 95%CI: 1.18, 2.58). There were no differences in the main obstetric (pregnancy-induced hypertension and caesarean sections) and neonatal outcomes (preterm birth and large for gestational age) between Métis and non-Métis after adjusting for important study covariates and birth clusters (Figure 3.2). Among the secondary outcomes, the only difference found between Métis and non-Métis births with pre-existing DM was an increased likelihood of having preeclampsia during pregnancy among Métis women (Métis: 9.8% and non-Métis: 3.4%, aOR: 3.5 95%CI: 1.60, 7.7) (Table 3.4). No differences were found between Métis and Non-Métis births for induction of labour, obstetric hemorrhage, congenital anomalies, babies small for gestational age, birth weight, inducted

preterm, spontaneous preterm, NICU admissions, birth injuries, stillbirths, maternal and neonatal deaths.

3.3.4 GDM and Pregnancy Outcomes among the Métis

The crude prevalence of GDM among Métis births over the study period (2006-2016) was lower than the prevalence of GDM among non-Métis births (4.9% and 5.4% respectively). After age standardization, this difference was reversed, with the age-standardized prevalence of GDM among Métis births of 6.3% compared to 5.3% among non-Métis births. GDM prevalence increased during the study period for both Métis (2.7 to 5.7%) and non-Métis births (3.8 to 6.5%) (Figure 3). Among Métis births, there was a 30% increased odds of having GDM during pregnancy compared to non-Métis births after adjusting for maternal covariates and birth clusters. Métis women with GDM also had 48% increased odds of having a baby that was large for gestational age (Métis: 23% and non-Métis: 14%, aOR: 1.48 95%CI:1.00, 2.19). There were no differences between the two birth cohorts for pregnancy-induced hypertension, the number of caesarean sections, and preterm birth.

Further differences between Métis and non-Métis births complicated by GDM were identified in the secondary outcomes. Métis women with GDM in pregnancy had reduced odds of having an obstetric hemorrhage (Métis: 6% and Non-Métis 10% aOR: 0.53 95% CI: 0.33, 0.85) and having a baby small for gestational age (Métis: 6% and Non-Métis: 9% aOR: 0.45 95% CI: 0.26, 0.80) compared to non-Métis women with GDM. Births to Métis women with GDM had increased odds of resulting in congenital anomaly (Métis: 2.9% and Non-Métis: 0.9%, aOR: 3.46 95%CI: 1.68, 7.12). Birth weights to Métis women with GDM pregnancy were on average 157 g (β: 156.5 95% CI: 93.7, 219.4) heavier than births to non-Métis women with GDM. No

differences were found between Métis and non-Métis GDM complicated births for preeclampsia, maternal death, induction of labour, induced preterm, spontaneous preterm, NICU admissions, still birth, neonatal death and birth injuries.

3.4 Discussion

To the best of our knowledge this is the first population-based study in Canada examining the prevalence, maternal and neonatal outcomes of diabetes in pregnancy among Métis women compared to non-Métis women. Study results indicated that Métis women had an increased prevalence and likelihood of having pre-existing DM during pregnancy compared to non-Métis women. The association between being Métis and pre-existing DM remained after accounting for maternal age, area of residence, and material and social deprivation. Important to note is that although Métis women had an increased likelihood of having pre-existing DM in pregnancy there were no differences between Métis and non-Métis births for the primary obstetric and neonatal outcomes. Among the secondary outcomes, the study identified that Métis with pre-existing DM had increased odds of having preeclampsia during pregnancy compared to non-Métis women.

The crude prevalence of GDM was not greater among Métis women compared to non-Métis women. After adjusting for important sociodemographic and clinical covariates (maternal age, pre-existing hypertension, area of residency, material and social deprivation), Métis women had an increased likelihood for developing GDM. This study identified that more Métis women with GDM were on insulin during pregnancy, suggesting a greater severity of GDM cases among Métis women in which blood glucose could not be controlled by diet and exercise alone. This result is in line with the study finding that Métis women with GDM also had an increased risk of

having a baby large for gestational age, which results from elevated blood glucose during pregnancy.[5] The association between GDM and large for gestational age among Métis women remained after accounting for insulin use during pregnancy. This is particularly concerning due to the relationship between high birth weight and the development of type 2 diabetes and obesity later in life.[35] The reasons for poor glucose control during pregnancy could be due to many complex reasons including emotional distress triggering negative eating patterns, a troubled home, economic and social pressures.[36] Although, Métis women with GDM have increased odds of having a large for gestational age baby they did not have an increased risk for have an obstetric hemorrhage or birth injury both of which have previously been found to be associated with babies born large for gestational age.[37]

Among the secondary outcomes, this study found that Métis women with GDM during pregnancy had increased odds of having a baby experiencing a congenital anomaly. The elevated risk among births to Métis women with GDM could be due to a greater proportion of Métis women with GDM that have a pre-pregnancy weight >91kg or it could be due to elevated blood sugars during pregnancy, both of which have been associated with an increased risk for congenital anomalies in pregnancies complicated by GDM.[38,39] Due to the small number of events among GDM complicated Métis births adjustments were not made to further understand this association.

Métis women with pre-existing DM also have increased odds of having preeclampsia during pregnancy compared to non-Métis women. Pre-existing DM is an established risk factor for preeclampsia and has previously been found to have 3.7-fold increased risk for developing preeclampsia compared to women without pre-existing DM.[40] In addition to pre-existing DM, maternal obesity has been identified as a risk factor for preeclampsia.[40] A greater proportion of

Métis women with pre-existing DM have a pre-pregnancy weight > 91kg, which could be a contributor to the increased risk that Métis women with pre-existing DM have for preeclampsia. Due to the small number of Métis women with pre-existing DM who develop preeclampsia further adjustments were not made. Future analysis is needed to fully understand this relationship.

It has been well established in the literature that First Nations women in Canada have an elevated prevalence of diabetes in pregnancy.[12,13,15,41] Genetic studies have not been able to provide an easy answer for the cause of this elevated risk of diabetes among Indigenous peoples, and this elevated prevalence of diabetes in pregnancy is not exclusive to Canadian Indigenous peoples.[42,43] Similar, elevated prevalence of pre-existing DM and GDM have also been found in Aboriginal and Torres Strait islanders (Australia) and Native Americans and Alaska Natives(United States of America), countries that have similar colonial histories and social inequalities.[44,45]

The results of this study imply that there is an unmeasured residual risk among Métis women for pre-existing DM and GDM during pregnancy. Pre-existing DM and GDM have a complicated genesis involving a combination of genetic, lifestyle, and environmental factors (social determinants of health).[33,46] The social determinants of health (i.e., employment, education, housing) play an important role in the development of diabetes in pregnancy.[47] In addition to the social determinants of health, Métis and other Indigenous peoples in Canada are survivors of colonialism which has been identified as a fundamental determinant to Indigenous people's health worldwide.[48,49] Colonialism has caused large disruptions to Indigenous peoples lives over many generations including a rapid transition to a Western lifestyle, systemic discrimination, racism, institutionalization, and loss of culture.[50] This has had profound impacts

on the mental, spiritual and physical wellbeing of Indigenous peoples[50] and could be an important contributing factor to the residual risk that Métis women have for diabetes in pregnancy at younger ages and with greater risk profiles.

Clinicians engaging with Métis women who have diabetes in pregnancy should be aware of the historical context in which Métis health inequalities stem from so that they can provide informed and attentive care for Métis women during pregnancy. Particular attention should be focused on monitoring blood sugars during pregnancy among Métis women with GDM to modify the risk of having a baby large for gestational age. Programs and services to support Métis women who have pregnancies complicated with diabetes, should be co-created and delivered in partnership with the MNA, so that Métis culture and specific needs are meaningfully incorporated.

3.4.1 Study Strengths and Limitations

One of the primary study strengths of this research is the use of the MNAIR to identify citizens of the Métis Nation within existing administrative health data in Alberta. Métis identity in Canada continues to be a contentious topic, and by using this database, the Métis cohort in this study have verified connections to historic and contemporary Métis communities.[51] In addition, this study used a validated clinical database that has built in verification steps to ensure accuracy in the definition of study outcomes as well as regularly updated administrative health databases.[19,22]

In addition to our study strengths, there are also several study limitations that should be considered when interpreting the results. Births from other Indigenous women in Alberta including First Nations, and Métis that are not citizens of the MNA were included within the

non-Métis comparison group. This misclassification bias would likely be a bias towards the null (no effect). Probabilistic data linkage was used to identify Métis births and it is possible that some people were assigned the wrong Métis identifier. The generalizability of the study results is limited to citizens of the MNA and may not be applicable to Métis that self-identify but are not citizens of the Métis Nation.

The APHP classifications of diabetes during pregnancy do not discriminate between type 1 and type 2 diabetes. It is therefore unclear the proportion of pre-existing DM during pregnancy that is made up of type 1 and type 2 diabetes, and if obstetric and neonatal outcomes were different based on the pre-existing DM subtype. Finally, material and social deprivation were area-level measures based on dissemination area.[23] Misclassification of individual births to a material and social deprivation quintile that does not accurately reflect individual material and social circumstance might have occurred. It is likely that this misclassification bias would equally affect both Métis and non-Métis births.

3.5 Conclusion

This study has identified that births to Métis women have an increased risk for having both pre-existing DM and GDM during pregnancy compared to births of non-Métis women after accounting for important study covariates. Births to Métis with GDM complicated pregnancies also have an increased risk of having a baby large for gestational age. Increased risk for pre-existing DM and GDM among Métis women could largely be due to social inequalities that stem from Métis people's complex history in Canada. Further research is needed to understand the mechanistic pathway's between social inequalities and increased risk for pre-existing DM and GDM among Métis women.

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Table 3.1 Characteristics of Births to Métis and Non-Métis Women with pre-existing DM and GDM

	Pre-existing DM		GDM	
	Métis (n=112)	Non-Métis (n=5,509)	Métis (n=384)	Non-Métis (n=25,285)
Maternal age	30.09 (5.4)	32.12 (5.4)*	30.85 (5.7)	32.26(5.1)*
Pre-pregnancy weight>91kg	46 (41.1%)	1,274 (23.1%)*	125 (32.55%)	4,258 (16.8)*
Smoking During pregnancy	32 (28.6%)	824 (15.0)*	122 (31.8)	2,861 (11.3)*
Pre-pregnancy Hypertension	14 (12.5)	395 (7.2)	8 (2.1)	302 (1.2)
Substance Use	5 (4.5)	130 (2.4)	10 (2.6)	389 (1.5)
Rural	36 (32.7)	1,238 (22.6)*	107 (27.6)	3,622 (14.5)*
Insulin Use	58 (51.8)	2,616 (47.5)	133 (36.6)	6,497 (25.7)*
Multiparous (2-4 births)	20 (17.9)	1359 (24.8)	122 (29.2)	6,218 (24.7)*
High Risk Pregnancy	59 (52.7)	2,273 (41.3)*	73 (19.0)	3,641 (14.4)*
Material Deprivation				
Least Deprived	10 (9.4)	912 (17.6)*	27 (7.3)	4,522 (18.8)*
2	12 (11.3)	996 (19.2)*	71 (19.1)	4,610 (19.1)
3	24 (22.6)	991 (19.1)	87 (23.5)	4,694 (19.5)*
4	25 (23.6)	1,057 (20.4)	77 (20.8)	4,829 (20.1)
Most Deprived	35 (33.0)	1,225 (23.6)*	109 (29.4)	5,431 (22.6)*
Social Deprivation				
Least Deprived	15 (14.2)	658 (12.7)	47 (12.7)	3,127 (13.0)
2	14 (13.2)	1,025 (19.8)	46 (12.4)	5,328 (22.1)*
3	23 (21.7)	1,211 (23.4)	90 (24.3)	5,393 (22.4)
4	29 (27.4)	1,193 (23.0)	113 (30.5)	5,219 (21.7)*
Most Deprived	25 (23.6)	1,094 (21.1)	75 (20.2)	5,019 (20.8)

Data presented are numbers with percentages (%) or mean with standard deviations.
*Statistically significant difference ($p<0.05$) between Métis and non-Métis cohorts

Table 3.2 The Prevalence and Primary Outcomes of Pre-existing DM among Métis and Non-Métis Births

	Métis	**Non-Métis**	**Adjusted OR‡**	**Adjusted OR †**
Pre-existing DM Age standardized †	112 (1.42%) 6,227 (1.8%)	5,509 (1.17%) 4,111 (1.1%)	1.25 (0.88, 1.78)	**1.74 (1.18, 2.58)***
Pregnancy induced hypertension	16 (14.3)	556 (10.1)	1.66 (0.81, 3.39)	1.45 (0.71, 2.96)
Caesarean section	59 (52.7)	2,630 (47.7)	3.27 (0.20, 55.0)	3.53 (0.48, 26.13)
Preterm birth	30 (26.8)	1,098 (19.8)	1.72 (0.92, 3.21)	1.30 (0.68, 2.51)
Large for Gestational Age	35 (31.3)	1,481 (26.9)	1.54 (0.76, 3.12)	0.99 (0.50, 1.96)

† Standardized to the number of births in Canada by age group in 2006.

* Statistically significant difference ($p<0.05$)

‡Adjusted for multiple births to the same mother over the ten-year study period

†Adjusted for maternal age, material and social deprivation, area of residency, pre-existing hypertension, pre-pregnancy weight, insulin use, parity, smoking and multiple births to the same mother over the ten-year study period.

Table 3.3 The Prevalence and Primary Outcomes of GDM among Métis and Non-Métis Births

	Métis	**Non-Métis**	**Adjusted OR‡**	**Adjusted OR†**
GDM Prevalence Age Standardized†	384 (4.86%) 22,294 (6.3%)	25,285 (5.36%) 18,889 (5.3%)	**0.83 (0.70. 0.99)**	**1.30 (1.08, 1.55)***
Pregnancy Induced Hypertension	44 (11.5)	2,391 (9.5)	1.40 (0.86, 2.28)	1.50 (0.91, 2.48)
Caesarean section	140 (36.5)	9,734 (38.5)	0.92 (0.74, 1.13)	0.82 (0.34, 1.96)
Preterm birth	38 (9.9)	2,754 (10.9)	0.85 (0.54, 1.13)	0.82 (0.52, 1.30)
Large for Gestational Age	88 (22.9)	3,606 (14.3)	**2.51 (1.68, 3.75)***	**1.48 (1.00, 2.19)***

† Standardized to the number of births in Canada by age group in 2006.

* Statistically significant different ($p<0.05$)

‡ Adjusted for multiple births to the same mother over the ten-year study period

† Adjusted for maternal age, material and social deprivation, area of residency, pre-existing hypertension, pre-pregnancy weight, insulin use, parity, smoking and multiple births to the same mother over the ten-year study period.

Table 3.4 Secondary Obstetric and Neonatal Outcomes of Pre-existing DM and GDM Among Métis and Non-Métis births

	Pre-existing DM			GDM		
	Métis	Non-Métis	OR or Beta Coefficient (95% CI)†	Métis	Non-Métis	OR or Beta Coefficient (95% CI) †
Preeclampsia (superimposed)	11 (9.8)	189 (3.4)	**3.51 (1.60, 7.69)***	10 (2.6)	216 (1.6)	1.24 (0.60, 2.58)
Maternal Death	0 (0)	1 (0.0)		0 (0)	6 (0.2)	
Induction of Labour	51 (62.2)	2,321 (57.5)	1.26 (0.69, 2.32)	190 (62.3)	11,332 (56.6)	1.35 (0.98, 1.87)
Obstetric Hemorrhage	10 (8.9)	567 (10.3)	0.81 (0.37, 1.78)	23 (6.0)	2,578(10.2)	**0.53 (0.33, 0.85)***
Congenital Anomaly	1 (0.9)	122 (2.2)	0.40 (0.06, 2.87)	11 (2.9)	216 (0.9)	**3.46 (1.68, 7.12)***
Small for Gestational Age	10 (8.9)	374 (6.8)	1.50 (0.57, 3.99)	20 (5.6)	2,297 (9.1)	**0.45 (0.26, 0.80)***
Birth Weight	3342.2 (731.1)	3363.8 (842.5)	-4.39 (-147.76, 138.97)	3,463.3 (576.4)	3308.9 (594.5)	**156.5 (93.70, 219.42)***
Induced Preterm Birth	10 (7.0)	359 (7.0)	1.55 (0.68, 3.54)	17 (4.5)	922 (3.8)	1.22 (0.68, 2.17)
Spontaneous Preterm Birth	13 (12.4)	375 (7.3)	2.00 (0.97, 4.15)	13 (3.5)	1,131 (4.6)	0.71 (0.36, 1.40)
NICU Admission	19 (18.6)	1,079 (20.6)	0.87 (0.38, 1.97)	37 (10.2)	3,243 (13.3)	0.69 (0.46, 1.04)
Birth Injury	2 (1.8)	179 (3.3)	0.54 (0.13, 2.25)	8 (2.1)	845 (3.36)	0.61 (0.29, 1.26)
Stillbirth	3 (2.7)	80 (1.5)	1.87 (0.58, 6.01)	4 (1.0)	105 (0.4)	2.52 (0.93, 6.89)
Neonatal Death	1 (0.6)	1 (0.1)	1.54 (0.21, 11.39)	2 (0.5)	43 (0.2)	3.07 (0.74, 12.73)

*Statistically significant ($p<0.05$)

†Adjusted for multiple births to the same mother over the ten-year study period.

Figure 3.1. Data Merging Flow Diagram

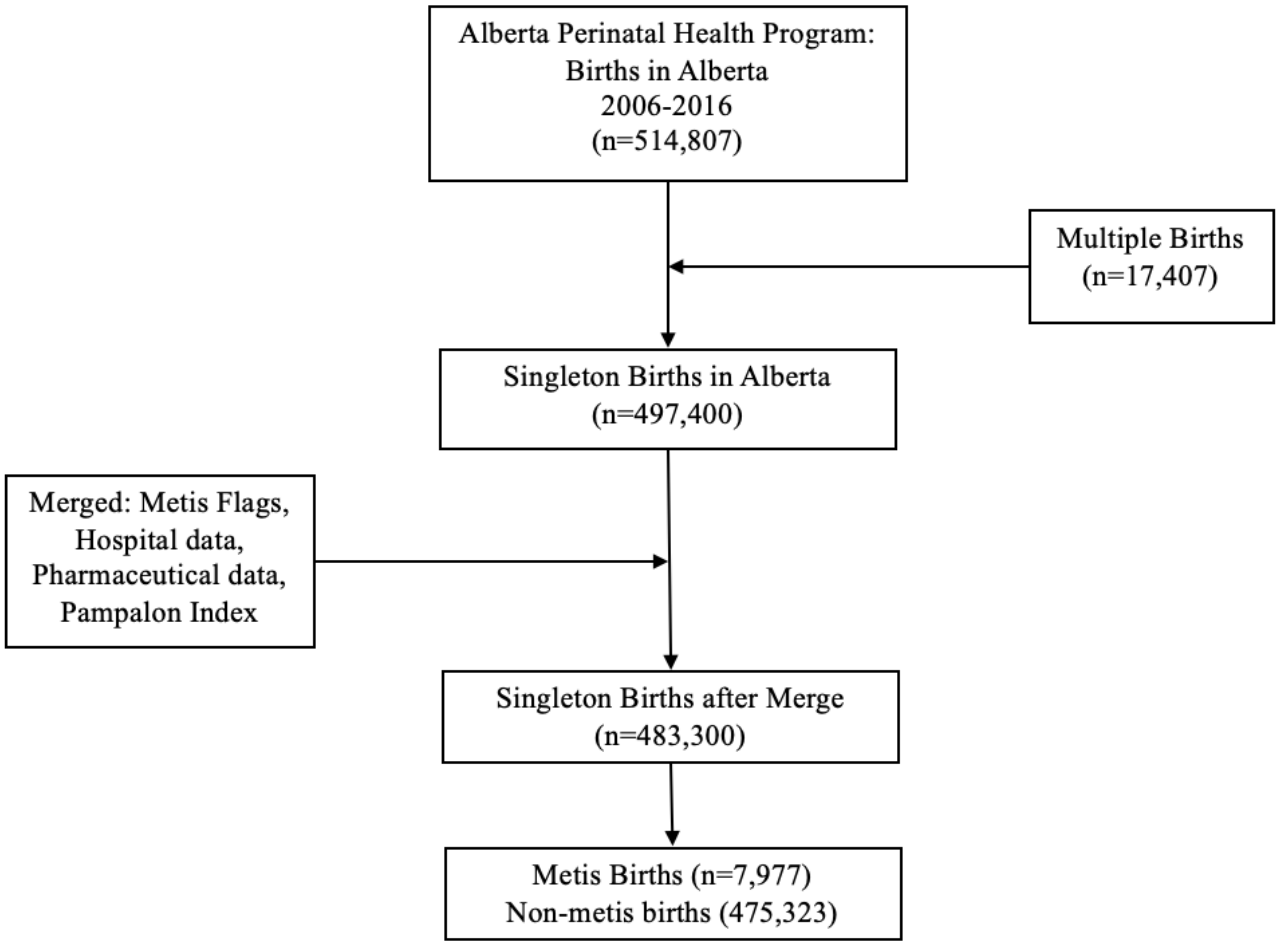


Figure 3.2 Prevalence of Pre-existing DM by Study Year

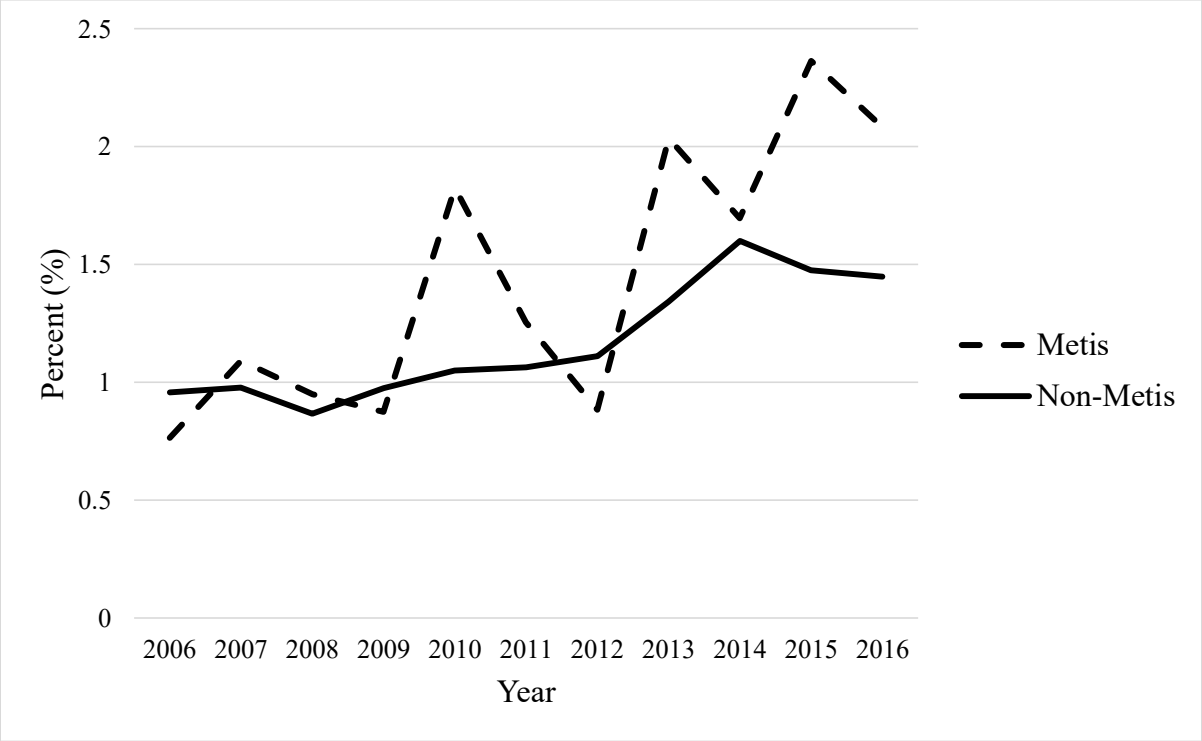
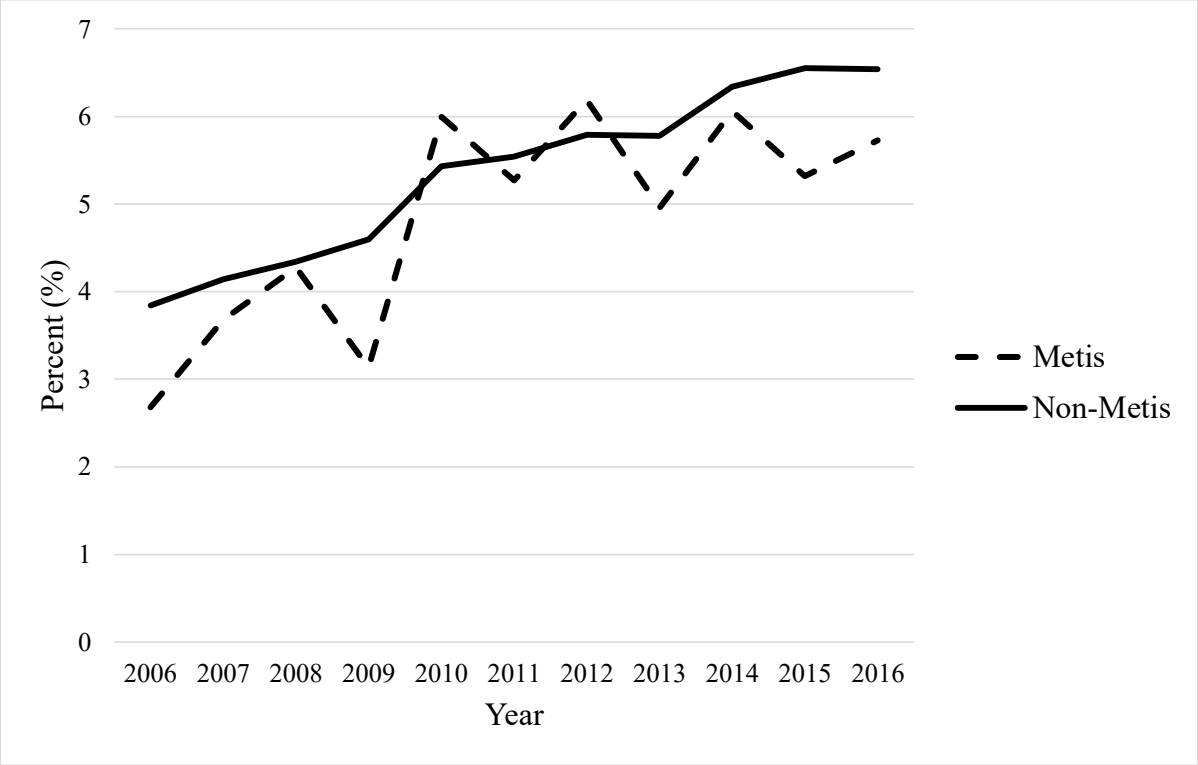


Figure 3.3 Prevalence of GDM by Study Year



CHAPTER 4: DISCUSSION, CLINICAL IMPLICATIONS, FUTURE RESEARCH DIRECTIONS, AND KNOWLEDGE TRANSLATION

4.1 Overview of Study Results

The overarching purpose of this thesis was to enhance our understanding about the prevalence and maternal and perinatal outcomes of diabetes in pregnancy among Indigenous women compared to non-Indigenous women. This was done through two different studies, the first was a systematic review examining the prevalence of pre-existing DM and GDM among Indigenous women compared to their non-Indigenous counterparts in countries that have similar colonial histories. The second study was a retrospective cohort study conducted to address the knowledge gap about the epidemiology of diabetes in pregnancy among Métis women in Alberta. This observational study evaluated the prevalence, maternal and neonatal outcomes of both pre-existing DM and GDM among Métis and non-Métis women. The following will be a discussion of the results of both studies.

4.2 Systematic Review Results

The systematic review evaluated observational evidence about the prevalence of GDM and/or pre-existing DM among Indigenous women compared to non-Indigenous women in Australia, Canada, New Zealand and the USA. A total of 42 studies were included, 18 studies from Australia, eight from Canada, one from New Zealand, and 15 from the USA. The majority of studies used a retrospective cohort study design. All of the included studies assessed the prevalence of GDM, and 13 studies assessed the prevalence of pre-existing DM. The risk of bias among included studies ranged from low to high risk of bias, indicating wide variation in the methodological quality of this body of evidence.

4.2.1 Prevalence and Meta-Analysis

A meta-analysis of 39 (39 for GDM, 13 for pre-existing DM) included studies was conducted based on country and diabetes type (pre-existing DM or GDM). Overall, the meta-analyses for the prevalence of pre-existing DM among Indigenous women compared to non-Indigenous women in Australia, Canada, and the USA found that pre-existing DM and GDM were more frequent among Indigenous women in Australia, Canada and the USA. Similarly, the pooled prevalence odds ratios for the comparison of GDM between Indigenous women and non-Indigenous women indicated that GDM prevalence was greater among Indigenous women. The relationship between Indigeneity and GDM was less consistent then Indigeneity and pre-existing DM due to a greater diversity in individual study prevalence estimates.

The diverse group of Indigenous women included in these studies have had similar experiences of colonialism which includes institutionalization (residential/mission schools, incarceration), a rapid transition to a Western lifestyle, loss of culture, and systemic racism/discrimination.[1] Colonialism has had profound impacts on the health and wellbeing of Indigenous peoples.[1] One way that it has done this is through increasing Indigenous women's exposure to the social determinants of health (i.e. income, employment, education).[2,3] However, the social determinants of health alone may not completely explain this disproportionate burden of diabetes in pregnancy.[4]

Interacting with the social determinants of health, is also historical trauma and the continuing legacy of that trauma that impacts the psychosocial wellbeing of Indigenous women.[4] One potential pathway in which the psychosocial stress could be embodied is through the dysregulation of cortisol that is associated with insulin resistance, fat gain around the abdomen, and endothelial dysfunction which then could lead to diabetes.[5] The increased psychosocial

stress that Indigenous women experience could also be associated with a decreased ability for self-care and maintaining a healthy lifestyle before and during pregnancy.[6] The complicated history of colonialism, the contemporary exposure to the social determinants of health, the impact of these factors on psychosocial stress and healthy behaviours are likely all contributors to the increased prevalence of diabetes in pregnancy among Indigenous women. Therefore, interventions to improve the health of Indigenous women before and during pregnancy should have a wider focus on historical traumas and structural inequalities that Indigenous women experience within their countries and communities.[7]

4.2.2 Clinical and Public Health Implications of the Systematic Review

The message of this systematic review to clinical practice, is that clinicians must be aware that the increased prevalence of diabetes during pregnancy among Indigenous women may not be due to an inherent risk or individual poor lifestyle choices. Rather the root of increased prevalence of diabetes in pregnancy among Indigenous women could be related to a complex history and social inequalities creating an environment preventing Indigenous women from achieving the same health status of non-Indigenous women.[1,8]

Diabetes during pregnancy has long-term impacts on the health of both the mother and child. Pregnant women with GDM have an increased risk for developing type 2 diabetes later in life, and the children of a mother who had diabetes during pregnancy also have increased risk for developing obesity and type 2 diabetes later in life.[9-12] Therefore, the increased prevalence of diabetes during pregnancy among Indigenous women has impacts on the diabetes burden among Indigenous peoples for future generations to come. Within Australia, Canada, New Zealand and the USA, the increased burden of diabetes in pregnancy could also be an indication that prenatal

education and clinical care is not meeting the needs of Indigenous women. Due to the great diversity between Indigenous women, culturally safe care that incorporates traditional indigenous maternal practices should be integrated at the community level with prenatal education and clinical care.

4.3 Results from the Retrospective Cohort Study

The purpose of this study was to assess the prevalence, maternal and neonatal outcomes of pre-existing DM and GDM complicated pregnancies among Métis women who are citizens of the MNA compared to a non-Métis cohort. Included in this study were 483,300 singleton births over a ten-year study period; 7,977 of births to Métis women and 475,323 births to non-Métis women. Métis women with diabetes during pregnancy were younger, a greater number lived in rural areas, a larger proportion smoked during pregnancy, and a greater number were classified as high-risk pregnancies compared to non-Métis women with diabetes during pregnancy. In addition, more Métis women were assigned to the most deprived material deprivation quintile compared to non-Métis. This study identified important differences in the characteristics of Métis pregnancies with diabetes compared to non-Métis pregnancies with diabetes.

4.3.1 Métis and pre-existing DM

Métis women had increased odds of having pre-existing DM during pregnancy compared to non-Métis births after adjusting for important study covariates and cluster of births. However, there were no differences between Métis and non-Métis for the main obstetric (pregnancy induced hypertension and caesarean section) and neonatal outcomes (preterm birth and babies born large for gestational age) evaluated. Métis women with pre-existing DM had increased odds

of having preeclampsia during pregnancy compared to non-Métis women after adjusting for birth clusters.

There has been a limited number of studies conducted in Canada on the prevalence, maternal and neonatal health outcomes of pre-existing DM among Indigenous women, primarily focusing on First Nations women.[12-15] First Nations women in Canada have also been identified as having an elevated prevalence of pre-existing DM compared to non-First Nations women.[12-15] Other research among pre-existing DM among First Nations women has identified that births to First Nations women that have pre-existing DM also have an increased risk of perinatal death.[15] However, this association was not found among Métis women with pre-existing DM.

4.3.2 Métis and GDM

The multivariable analysis showed that Métis women had increased odds of having GDM during pregnancy compared to non-Métis women, after adjusting for study covariates and multiple births per mother. Métis women with GDM have increased odds of having a baby that is born large for gestational age and having a baby that has a congenital anomaly. However, Métis women with GDM have reduced odds of having an obstetric hemorrhage and for having a baby that is small for gestational age.

Previous research conducted in Canada found that First Nations women with GDM in pregnancy had a greater number of preterm births, stillbirths, shoulder dystocia and babies born with a high birth weight compared to non-First Nations women.[13,14] There are some similarities in the risk for adverse outcomes of GDM-complicated pregnancies (high birth weights and congenital anomalies) between Métis and First Nations women; however, our study identified that Métis women with GDM do not have an elevated risk for preterm birth, stillbirths and

shoulder dystocia. Differing outcomes of GDM identified among First Nations women and Métis demonstrates that Métis do not have the same GDM risk profile.

4.3.3 Clinical and Public Health Implications

Métis women have an elevated risk of pre-existing DM and GDM during pregnancy and are younger, a greater number lived in rural areas, and more belonged to the most deprived material deprivation quintiles than non-Métis with pre-existing DM and GDM during pregnancy. Important for clinicians to know is that Métis women with GDM may have increased need for insulin prescriptions to manage blood sugars during pregnancy, or they may need more education and support to manage their GDM with diet and exercise. The increased risk for Métis women with GDM for having a baby that is large for gestational age, indicates that Métis women need close monitoring of blood sugars levels during pregnancy.

There are also important public health implications of this research. Previous research has demonstrated that diabetes during pregnancy impacts the mother and offspring later in life.[9-12] The intergenerational effects could have an important impact on the health of future generations of citizens of the MNA in Alberta. Pre-existing DM and GDM disease profiles found among Métis are different than what have been previously found among First Nations women in Canada. Therefore, information about risk and prenatal care needs should be specifically tailored to target Métis women within a culturally relevant context.

4.4 Future Research Directions

4.4.1 Measuring Colonialism and the Causal Pie

It is beyond the scope of the research presented in this thesis to make causal inferences about the role of colonialism on the risk for diabetes in pregnancy among Indigenous women. Future research should delve deeper into the mechanism of how colonialism works to create structural inequalities for Indigenous women before and during pregnancy. A useful theory for potentially understanding the complex role and pathway that colonialism has on the health of Indigenous peoples is the *Ecosocial theory.*[16] This theory provides a way of conceptualizing how people embody historical, political, and social structures in which they live, how these accumulate over the life course, and variations in community and individual level responses to them.[16] Using this theoretical framework to guide the creation of a tool to quantify difference components of colonialism (i.e. residential schools, change to Western lifestyle change, loss of language), how they exist in social and political structures could increase our knowledge about the direct relationship that colonialism has on Indigenous women's health before and during pregnancy. This would hopefully enhance our understanding of how colonialism interacts with other disease causes and to what extent it makes up the causal pie for pre-existing DM and GDM among Indigenous women.[17]

4.4.2 Longitudinal Follow-up of both Métis Mothers and Children

Research in this thesis is limited to the pregnancy period and shortly after and we do not know the long-term health outcomes of the Métis children exposed to diabetes in utero and long-term risk for future type 2 diabetes among Métis women with GDM. Therefore, an important follow up study would be to conduct a longitudinal evaluation of Métis women with diabetes and their children. This could be similar to research that was conducted in Manitoba among a cohort of First Nations women to quantify the risk for future type 2 diabetes in the mother and the

child.[11,12] Although this association has previously been evaluated in other populations, it is not clear how great the risk magnitude would be among Métis women in Alberta.

4.4.3 Qualitative Research among Métis about the Management of Diabetes in Pregnancy

To further understand diabetes in pregnancy among Métis women, a qualitative study should be conducted to explore Métis women's experience with clinical care during the perinatal period. The purpose of this study would be to identify ways in which Métis women with pre-existing DM and GDM during pregnancy would want to be supported through the identification of pregnancy and/or diabetes in pregnancy to the postpartum period. Specific questions could be: "What has been your experience managing your blood sugars during pregnancy?"; "What kind of support allowed you to have a healthy pregnancy?". Results of this research could be used to inform culturally safe prenatal care for Métis women who have pre-existing DM or GDM.

4.5 Knowledge Translation

Epidemiological research on the health of Indigenous peoples in many cases has served the purpose of re-stigmatizing an already stigmatized population because researchers fail to put study results into the complicated historical and contemporary context in which Indigenous peoples live in Canada.[18,19] Putting study results into the context that Indigenous peoples live allows for an exploration of the social inequalities that perpetuate adverse health outcomes among Indigenous peoples, preventing an oversimplification of a deficit identified by epidemiological research.[18]

Epidemiology does not often incorporate Indigenous ways of knowing directly into their methods, but epidemiological research, when conducted in partnership with Indigenous

governments/communities can be an important tool to understand health inequalities of Indigenous peoples.[20] The results of this type of research can be used "in order to help procure the recognition and resources needed to protect and promote indigenous health."[20]

The MNA has been an active research partner engaged throughout conducting the retrospective cohort study examining diabetes in pregnancy among Métis women. The purpose of this partnership is so that research questions, results and interpretations are co-created with the MNA. Therefore, this research is both responsive to the needs of the MNA, but also inclusive in the research process so that research results are useful to the MNA.[18] Through this partnership the MNA now has evidence to inform their strategic planning and to use to advocate on behalf of their citizens for future health resources. A report and research snapshots will be co-created with the MNA to use and to share with their Métis citizens.

4.5.1 Key Outcomes of Research for Knowledge Translation

- Diverse Indigenous women, with similar experiences of colonialism have a greater prevalence of both pre-existing DM and GDM compared to non-Indigenous women in the same country.
- Métis women have 1.74 times increased risk of having pre-existing DM (aOR:1.74 95%CI: 1.18, 2.58) and 30% increased risk for developing GDM (1.30 95%CI: 1.08, 1.55) during pregnancy compared to non-Métis women in Alberta.
- Among Métis women with GDM, there was an increased risk of having a baby born large for gestational age (aOR: 1.48 95%CI: 1.00, 2.19), and for having a baby with a congenital anomaly compared to non-Métis women (aOR: 3.46 95%CI: 1.68, 7.12).

- Métis women with pre-existing DM have three and half times greater odds of having preeclampsia during pregnancy (aOR: 3.51, 95% CI: 1.60, 7.69).
- Increased risk for pre-existing DM and GDM could be a result of the complex history and context that Métis women live in, that have created social inequalities preventing Métis women from achieving the same health status as non-Métis women.
- Further research is needed to understand the context and pathways of social inequalities that increase Métis women's risk for diabetes during pregnancy and to identify culturally safe ways to support Métis women with pre-existing DM and GDM before, during and after pregnancy.

4.6 References

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APPENDICES

Appendix 1: MEDLINE Search Terms

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid
MEDLINE(R) <1946 to Present>
Search Strategy:
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1 (exp Nunavut/ or Nunavut.mp. or Eastern Arctic.mp. or Alert Bay.mp. or Alexandra Fiord.mp. or Amadjuak.mp. or Aquiatulavik Point.mp. or Arctic Bay.mp. or Arviat.mp. or Baffin Island.mp. or Baker Lake.mp. or Bathurst Inlet.mp. or Belcher Islands.mp. or Bylot Island.mp. or Cambridge Bay.mp. or Iqaluktuttiaq.mp. or Cape Dorset.mp. or Cape Dyer.mp. or Cape Smith.mp. or Charlton Depot.mp. or Chesterfield Inlet.mp. or Clyde River.mp. or Coral Harbour.mp. or Craig Harbour.mp. or Dundas Harbor.mp. or Ellesmere Island.mp. or Ennadai.mp. or Eskimo Point.mp. or Fort Conger.mp. or Fort Hope.mp. or Fort Ross.mp. or Gjoa Haven.mp. or Grise Fiord.mp. or Hall Beach.mp. or Hazen Camp.mp. or Igloolik.mp. or Ikaluit.mp. or Iqaluit.mp. or Isachsen.mp. or Kekerten.mp. or Kimmirut.mp. or King William Island.mp. or Kipisa.mp. or Kitikmeot o r Kivalliq.mp. or Kivitoo.mp. or Kugaaruk.mp. or Kugluktuk.mp. or Maguse River.mp. or Nanasivik.mp. or Nottingham Island.mp. or Nuwata.mp. or Padlei.mp. or Padloping Island.mp. or Pangnirtung.mp. or Perry Island.mp. or Pond Inlet.mp. or Port Burwell.mp. or Qoloqtaaluk.mp. or Qikiqtarjuaq.mp. or Rankin Inlet.mp. or Read Island.mp. or Repulse Bay.mp. or Resolute Bay.mp. or Resolution Island.mp. or Sanikiluak.mp. or Taloyoak.mp. or Tanquary Camp.mp. or Tavani.mp. or Thom Bay.mp. or Umingmaktok.mp. or Victoria Island.mp. or Wager Bay.mp. or Whale Cove.mp. or Eastern Arctic.mp. or ((L upin or Polaris or Eureka or Fullerton) and Canad*).mp.) not (exp behavior, animal/ or exp ecosystems/ or exp endangered species/ or (sediment* or mantle or basalt* or cretaceous* or fossil* or paleo* or geolog* or stratigraph* or glaci* or refugia* or moraine* or pliocene or gravity or methylmercury or hydrolog* or hydrogeol* or volcan* or mesospher* or inferomet* or habitat* or animal behavior* or endangered species).mp.) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word,
rare disease supplementary concept word, unique identifier, synonyms] (609)

2 ((Carcross or (Tagish not meteorite*) or Champagne First Nation or Aishihik or Ehdiitat or Nacho Nyak Dun or Gwichya or Little Salmon or Carmacks or Nihtat or Selkirk First Nation or Ta'an Kwach'an or Tetlitn or Tr'ondek Hwech'in or White River First Nation or Vuntut or Yellowknives or (Hare adj2 (man or men or woman or women or child* or youth* or adult* or people* or person or persons or tribe or tribal or band or bands)) or Tanana or Tanana or Tutchone* or Denesuline or Tahltan or MacKenzie Valley or Old Crow or "Upper Liard" or "Eagle Plains" or "Keno City" or Carcross or Teslin or "Fort Selkirk" or Carmacks or Haines Junction or Dawson City).mp. or ((Canad*.mp. or exp Canada/) and (Beaver Creek or Pelly or Destruction Bay or Watson Lake).mp.) or ((exp Indians, North American/ or exp Health Services, Indigenous/ or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/ or Indigenous*.mp. or Aboriginal*.mp. or Amerindian*.mp. or Autochtone*.mp. or Métis.mp. or First Nation.mp. or First Nations.mp. or exp Inuit/ or Inuit*.mp. or Chipewyan.mp. or Kaska.mp. or Kaskas.mp. or Tlingit.mp. or Dene.mp. or

Gwich'in.mp. or Gwichin.mp. or Gwitchin.mp. or Kutchin*.mp. or Sahtu.mp. or Tlicho.mp. or Tli Cho.mp. or (traditional adj1 (medicine* or heal* or food* or health*)).mp. or Urban Indian*.mp. or "on reserve".mp. or "off reserve*or country food*".mp. or shaman*.mp. or medicine m?n.mp. or medicine wom?n.mp. or treaty.mp. or treaties.mp. or ((native* or Indian or Indians) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands)).mp.) and (exp Yukon Territory/ or Yukon*.mp. or ((Beaufort Sea or Whitehorse) and Canad*).mp.))) not ((exp Alaska/ or Alaska*.mp.) not ((exp Alaska/ or Alaska*.mp.) and (exp Yukon/ or Yukon*.mp.))) not (Yukon-Kuskok* or lepus or geology* or stratigraphi* or subduction* or volcan* or Holocene or pleistocene).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (115)

3 ((Ahtahkakoop or Asimakaniseekan or Amisk Lake First Nation* or Assiniboine First Nation* or Beardy or Big River First Nation* or Birch Portage or Bittern Lake or Budd's Point or Mamawetan or Carry the Kettle or Canoe Lake or Carrot River or Chicken First Nation* or Kelsey Trail Health or Sunrise Health or Prince Albert Parkland Health or Day Star or Dipper Rapids or Eagles Lake First Nation* or Elak Dase or English River First Nation* or Prairie North Health or Fishing Lake First Nation* or Flying Dust First Nation* or Fond du Lac or Four Portages or Fox Point First Nation* or Athabasca Health Authority or Gordon First Nation* or Grandmother's Bay or Hatchet Lake or Hay First Nation* or Ils a la Crosse or James Smith First Nation* or Joseph Bighead or Kawacatoose or Kahkewistahaw or Key First Nation* or Kinistin or Kinookimaw or Kitsakie or Knee Lake First Nation* or La Loche First Nation* or La Plonge or Lac La Hache or Lac La Ronge or Little Black Bear or Little Bone First Nation or Little Hills First Nation* or Little Pine First Nation* or Little Red River or Lucky Man or Makaoo or Makaw or Meadow Lake First Nation* or Ministikwan or Minoahchak or Mirond Lake or Mistawasis or Montreal Lake First Nation* or Moosomin First Nation* or Morin Lake or Mosquito-Grizzley Bear's or Muscowpetung or Muskeg Lake First Nation* or Muskeg River First Nation* or Muskoday or Muskowekwan or Nekaneet or New Thunderchild or Cypress Health or Ocean Man or Ochapowace or Okanese or Okemasis or Old Fort First Nation* or One Arrow or Onion Lake or Opawakoscikan or (Pasqua not wheat) or Peepeekisis or Pelican Lake First Nation* or Pelican Narrows First Nation* or Peter Ballantyne or Peter Pond First Nation* or Pheasant Rump or Piapot or Potato River or Poundmaker First Nation* or Primeau Lake First Nation* or Red Earth First Nation* or Red Pheasant or Sakimay or Seekaskootch or Shesheep or Standing Buffalo or Starblanket or Tumor Lake or Wahpeton or Wapachewanak or Wa-Pii or Moos-Toosis or Waterhen or Willow Bunch or Witchekan or Wood Mountain or Yellowquill or Yellow Quill or (northern Saskatchewan not (uranium or selenium))).mp. or ((exp Indians, North American/ or exp Health Services, Indigenous/ or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/ or (Indigenous* or Aboriginal* or Amerindian* or Autochtone* or First Nation or First Nations or Métis or Michif or Urban Indian* or "on reserve" or "off reserve*" or country food* or residential school* or shaman* or medicine m?n or medicine wom?n or Buffalo River or Island Lake or Lean Man or Pine Bluff or Salteaux or Saulteaux or Sandy Narrows or Shoal Lake or Southend or Stanley or Sturgeon or Sucker River or Sweetgrass or White Bear or White Cap or Woody Lake or Cree or Dene or Chipewyan or Dakota or Algonquian).mp. or (traditional adj1 (medicine* or heal* or food* or health*)).mp. or ((native* or Indian or Indians) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands or reserve or reserves or

treaty)).mp.) and (exp Saskatchewan/ or (Saskatchewan* or Sask or Regina or Estevan or Moose Jaw
or Saskatoon or Lloydminster or Swift Current).mp.))) not (exp Medicine, Chinese Traditional/ or populus.mp. or India.mp. or Wisconsin.mp. or exp Plant Extracts/ or poplar.mp. or rats.mp. or veterinary.mp. or ve.fs.) (322)
4 (Abenaki or Abenakis or Abitibiwinni or Akwesasne* or Atikamek* or "Barriere Lake" or Betsiamite* or Cacouna or Chisasibi or Coucoucache or "Eagle Village" or Eastmain or Essipit* or Ekuanitshit* or Gespeg or Gesgapegiag* or Huron-Wendat or "Huronne Wendat" or Essipit or Inuk or Kahnawake or Kahnawa?ke or Kanesatake or Kawawachikamach* or Kebaowek or Kipawa or Kitcisakik or Kitigan Zibi or "Lac Romanie" or "Lac John" or "Lac Simon" or Listuguj* or "Long Point First" or Maliotenam or Maliseet or Malecite* or Mamit Innuat or Mamuitun or Manawan or Mashteuiatsh or Matimekush* or Matimekosh* or Mawiomi or Migmaw or Mig Maw or Mi?gmawei or Mingan or Mistissini* or Montagnais or Naskapi* or Natashquan* or Nemiscau or Nemaska* or Obedjiwan or Odanak or Opitciwa* or dopitciwa* or Ouje?Bougoumou or Pakuashipi* or Pessamit* or Pikogan or "Rapid Lake" or Schefferville or Sept-Iles or Takuaikan or "Uashat Mak" or "Mani-Utenam" or Temiscaming or Timiskaming or Ungava or Uashat or "Unamen Shipu" or Waban-Aki or Waskaganish or Waswanipi or Wemindji or Wemotaci or Wendat* or Wendake or Whapmagoostui or Wolinak or Kitcisakik or "Pakua Shipu" or "Pakua Shipi" or Winneway).mp. or ((exp Indians, North American/ or exp Inuits/ or exp Health Services, Indigenous/ or exp Shamanism/ or exp Medicine, Traditional/ or exp Ethnopharmacology/ or American Native Continental Ancestry Group/ or (Peuple adj (autochtones or indidgenes or premier or racing or natif*)) or "Premiere Nation" or "First Nation" or "First Nations" or Métis or Cree or Algonquin* or Algonquian* or Anishinabe* or Anishinaabeg* or autochthon* or Inuit* or Innu or Innus or Innue or Micmac or Mic?Mac or Mi?gmaq or Mi?kmaq or Mowhawk or (urban adj3 (Indian* or Native* or Aboriginal*)) or (Native adj3 (american or man or men or women or woman or boy* or girl* or children or people* or indian* or Nation or tribe* or tribal or band or bands or groups or communit* or population* or health)) or indigenous* or Aboriginal* or autochone* or treaty or on-reserve or offreserve or country food* or Shaman* or (traditional adj (medicine or heal*)) or residential school*).mp. and (exp Quebec/ or (montreal or "trois rivieres" or quebec* or "james bay" or "baie james" or Laval or Gatineau or Longueuil or Sherbrooke or Saguenay or Doncaster or Levis or Terrebonne or Mascouche or l?Estrie* or Lanaudiere or l?Outaouais* or Capitale-Nationale or Chaudiere-Appalaches or Cote-Nord or Gaspe* or Mauricie or Monteregie or Laurentides or Bas-Saint-Laurent or Saint-Laurent or Nunavik).mp. or (QC or

quebec).in.)) (1404)
5 ((Aamjiwnaang or Pikwakanagan or (Animbiigoo adj Zaagi?igan adj Anishinaabek*) or Wauzhushk Onigum or Naongashiing or Anishnabekwe or Anishnawbe* or "ARMSTRONG SETTLEMENT" or Aroland or ASSABASKA or "Atikameksheng Anishnawbek" or Attawapiskat or "Aundeck-Omni-Kaning" or Batchewana or "Bearfoot Onondaga" or "Biinjitiwabik Zaaging" or Bimose or "Bingwi Neyaashi" or Bkejwanong or "chapleau cree" or dokis or Eabametoong or "Fox Lake Cree" or (moravian adj2 thames) or Ginoogaming or "Kasabonika Lake" or Kashechewan or KABAPIKOTAWANGAG or Keewaytinook or Kee?Way?Win or "Kiashke Zaaging" or Kitchenuhmaykoosib or Konadaha Seneca or Koocheching or Magnetawan or Matachewan or Mattagami or "MacDowell Lake" or M?Chigeeng or Mishkeegogamang or Missanabie or Mitaanjigaming or Stanjikoming or

Mocreebec or (Mohawks adj (Akwesasne or Gibson)) or "Moose Cree" or Naicatchewenin or Namaygoosisagagun or Naotkamegwanning or Neskantaga or Nibinamik or Nigigoonsiminikaaning or Nipissing or OBADJIWAN or Obashkaandagaang or "Washagamis Bay" or Ochiichagwe Bibigo?ining or Onigaming or Parmachene or Sabaskong or Sagamok or (Oneida Nation adj2 Thames) or Shawanaga or Sheguiandah or Sheshegwaning or Taykwa Tagamou or Temagami or Wabaseemoong or Wabauskang or "Wabigoon Lake" or Wahgoshig or Wahnapitae or "Wahta Mohawks" or Wapekeka or Wasauksing or Wauzhushk Onigum or Wawakepewin or Webequie or Weenusk or Wikwemikong or ((Ardoch or Algonquin or Beausoleil or "big grassy" or "Iskatewizaagegan 39 Independent" or beaverhouse or "brunswick house" or "buffalo point" or caldwell or "cat lake" or Couchiching or "Curve Lake" or "deer lake" or delaware or "duck lake" or "Eagle Lake" or Thames or "Fort William" or "Garden River" or "Grassy Narrows" or Hiawatha or Henvey Inlet or Hornepayne or "Gull Bay" or "King Fisher" or (Lac adj Mille adj Lacs) or (Lac adj Croix) or "Long Lake" or Magnetawan or "Marten Falls" or "Martin Falls" or Mississauga or "New Credit" or "Moose Deer Point" or Munsee?Delaware or "Muskrat Dam" or "North Caribou Lake" or "North Spirit Lake" or Northwest Angle or Sioux Narrows or Pays Plat or Pic Mobert or "Red Rock" or "Sachigo Lake" or "Sandy Lake" or "Savant Lake" or Saugeen or Seine River or Serpent River or "Shoal Lake" or Stony Point or Stoney Point or "Grand River Territory" or "Slate Falls" or Whitefish River or Whitesand or "Whitewater Lake" or "Wunnumin Lake") adj2 first nation*)).mp. or (exp Indians, North American/ or exp Inuits/ or exp Health Services, Indigenous/ or exp Shamanism/ or exp Medicine, Traditional/ or exp Ethnopharmacology/ or American Native Continental Ancestry Group/ or (Peuple adj (autochtones or indidgenes or premier or racing or natif*)).mp. or ("Premiere Nation" or "First Nation" or "First Nations" or Métis or chippewas or Cree or Algonquin* or Algonquian* or Anishinabe* or Anishnabeg or Anishinaabe* or autochthon* or Inuit* or Innu or Innus or Innue or Micmac or Mic?Mac or Mi?gmaq or Mi?kmaq or Mowhawk or Ojibw* or Cayuga).mp. or (urban adj3 (Indian* or Native* or Aboriginal*)).mp. or ((Native not (bacteri* or plant* or species or micro* or biot* or strain or strains or probiotic or zoo* or geno*)) adj3 (american or man or men or women or woman or boy* or girl* or children or people* or indian* or Nation or tribe* or tribal or band or bands or groups or communit* or population* or health)).mp. or ((indigenous* not (bacteri* or plant* or species or micro* or biot* or strain or strains or probiotic or zoo* or geno*)) or Aboriginal* or (autochon* not (bacteri* or plant* or species or micro* or biot* or strain or strains or probiotic or zoo* or geno*)) or treaty or on-reserve or off-reserve or country food* or Shaman* or (traditional adj (medicine or heal*)) or residential school*).mp.)) and (exp Ontario/ or (ontario or toronto or ottawa or sarnia or london or hamilton or windsor or roseneath or "golden lake" or beardmore or "christian island" or "Cedar Point" or morson or "bay of quinte" or "bear island" or "Bearskin Lake" or "whitefish lake" or naughton or "little current" or "Kirkland lake" or "big island" or macdiarmid or "thunder bay" or wallaceburg or chapleau or leamington or "georgina island" or "CAPE CROKER" or "FOX LAKE" or "CHIEF'S POINT" or "Constance Lake" or "Curve Lake" or "deer lake" or "duck lake" or "Eagle Lake" or "ENGLISH RIVER" or Rama or Erie St?Clair or "FACTORY ISLAND" or "Flying Post" or "FORT ALBANY" or "FORT HOPE" or "Fort Severn" or "Fort William" or Wiarton or Southampton or Saugeen or Muncy or Calstock or "Fort Frances" or "FRENCH RIVER" or Thamesville or Monteville or "Eabamet Lake" or Nipigon or "Georgian Bay" or "Long Lac" or "Long Lake" or Grassy Narrows or Keene or Pickerel or Hornepayne or Glebe Farm or "GOULAIS BAY" or Grey? Owen Sound or GROS CAP or "Shoal Lake" or Kashechewan or INDIAN RIVER or "King Fisher Lake" or "Big Trout Lake" or "Sandy Lake"

or "Fort Frances" or "Lac Seul" or "LAKE HELEN" or (LAKE adj WOODS) or Hudson or Britt or Okoki Post or "MANITOU RAPIDS" or gogama or "McDowell Lake" or "Red Lake" or Wawa or "New Osnaburgh" or "Garden River" or "Blind River" or Hagersville or "Port Perry" or "Moose Factory" or Cornwall or Deseronto or Mactier or Muncey or Delvin or Pawitik or "Whitefish Bay" or "Landsdowne House" or "Summer Beaver" or "Weagamow Lake" or "North Spirit Lake" or "Rainy Lake" or "Rainy River" or "Sioux Narrows" or Keewating or Kenora or "Sault Ste Marie" or "Nestor Falls" or "Heron Bay" or Southwold or "Pays Plat" or Mobert or "Pic River" or "Moon River" or Massey or "Sachigo Lake" or "Savant Lake" or Cutler or Nobel or Sheshegwaning or Kejick or Ohsweken or "Slate Falls" or Cochrane or "Lake Tamagami" or Thessalon or Whitedog or "Ear Falls" or Dryden or Matheson or Bala or Capreol or "Angling Lake" or "Parry Sound" or "Sioux Lookout" or Webequie or Peawanuk or "Birch Island" or Armstrong or "Wunnumin Lake" or Silverwater or Walpole Island or WINISK).mp.) (1404)

6 (((((Indigenous* or Aboriginal* or Amerindian* or Autochtone* or First Nation or First Nations or (traditional adj1 (medicine* or heal* or food* or health*)) or Urban Indian* or "on reserve" or "off reserve*" or country food* or shaman* or medicine m?n or medicine wom?n or (native* or Indian or Indians)) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands)) or Montagnais or Maliseet or Naskapi* or Mi'kmaq or Micmac or Mic mac or Migmaw or Mig maw or Beothuk*).mp. or exp Health Services, Indigenous/ or exp Indians, North American/ or Métis.mp. or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/) and (((Wolfville or Middleton or Kentville or Berwick or Inverness or New Waterford or Sackville or Springhill or Halifax or Dartmouth or Truro or New Glasgow or Sydney or Canso or Guysborough or Parrsboro or Pictou or Liverpool or Lunenburg or Amherst) and Canad*).mp. or exp Nova Scotia/ or Nova Scotia*.mp. or Nouvelle Ecosse.mp. or Pictou Landing.mp. or Bear River.mp. or Boat Harbour.mp. or Annapolis Royal.mp. or Antigonish.mp. or Baddeck.mp. or Cheticamp.mp. or Cape Bretan.mp. or Neil's Harbour.mp. or Glace Bay.mp. or Tatmagouche.mp. or Sheet Harbour.mp. or Cambridge Reserve.mp. or Annapolis Valley First Nation.mp. or Chapel Island First Nation.mp. or Cole Harbour.mp. or Eskasoni.mp. or Fisher's Grant.mp. or Franklin Manor.mp. or Paq'tnkek.mp. or (Glooscap adj1 (First Nation or reserve)).mp. or Acadia First Nation.mp. or Gold River Reserve.mp. or Horton Reserve.mp. or Shubenacadie First Nation.mp. or Indian Brook Reserve.mp. or Wagmatcook.mp. or Waycobah.mp. or Millbrook First Nation.mp. or Malagawatch.mp. or Medway River.mp. or Membertou.mp. or Merigomish.mp. or Musquodoboit.mp. or New Ross Reserve.mp. or Pennal Reserve.mp. or Pomquet.mp. or Poonhook.mp. or Sheet Harbour.mp. or St Croix Reserve.mp. or Summerside Reserve.mp. or Sydney Reserve.mp. or Truro Reserve.mp. or We'koqma'q.mp. or Wycocomagh.mp. or Wildcat Reserve.mp. or Yarmouth Reserve.mp.)) not (geology or geologic or stratigraphy* or animal* or cat or cats or kitten or deer or bird* or dog or dogs or feline or canine or bovine or equine or porcine or pig or piglet or swine or rat or rats or horse or horses or mouse or mice).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (36)

7 ((((exp Medicine, Traditional/ not Chinese.mp.) or exp Shamanism/ or exp Indians, North American/ or exp Inuits/ or exp Health Services, Indigenous/ or exp Ethnopharmacology/ or (Inuit* or Eskimo* or Esquimau* or Athapaskan or Gwich'in or Métis or Inuvialuktun or Cree or Aboriginal* or Indigenous* or off-reserve or on-reserve or First Nation or First Nations or Amerindian or (urban adj3 (Indian* or Native* or Aboriginal*)) or ethnomedicine or country

food* or residential school* or shaman* or traditional medicine* or traditional heal* or traditional food* or medicine man or medicine woman or autochtone* or treaty or (Native adj1 (man or men or women or woman or boy* or girl* or adolescent* or youth or youths or person* or adult or people* or Indian* or Nation or tribe* or tribal or band or bands))).mp.) and (exp Northwest Territories/ or Northwest Territories.mp. or NWT.mp. or Yellowknife.mp. or Western Arctic.mp.)) or (Aklavik or Banks Island or Behchoko or Rae Edzo or Colville Lake or De Cho or Deline or Denendeh or Fort Good Hope or Fort Liard or Fort McPherson or Fort McPherson or Fort Providence or Fort Providence or Fort Simpson or Fort Smith or Gameti or Hay River or Inuvik or Jean Marie River or Lutselk'e or Norman Wells or Paulatuk or Sachs Harbour or Trout Lake or Tsiigehtchic or Tuktoyaktuk or Tulita or Tulit'a or Ulukhaktok or Victoria Island or Whati or Wha Ti or Wrigley or (Hare adj2 (man or men or boy or boys or girl or girls or adult* or youth* or adolescent* or Nation or people* or Indians* or tribe* or tribal*)) or Slavey or Chipewyan or Tlicho or Dogrib or Yellowknives or Dene or Sahtu or Inuvaluit* or Inuinnaqtun).mp.) not ((fort smith adj1 ar*).mp. or ((rabbit* or lepus or lemming* or fox or foxes or wolf or wolves or (wrigley adj1 (n or g or forcep*))).mp. or ve.fs.)) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (564)

8 ((exp Inuits/ or exp Indians, North American/ or exp Health Services, Indigenous/ or Medicine, Traditional/ or Shamanism/ or Ethnopharmacology/ or (Inuit* or Eskimo* or Esquimau* or Innu or Inuk or Innus or Métis or Montagnais or Maliseet or Naskapi or Mikmaq or Micmac or Mic mac or Migmaw or Micmaw or Beothuk* or Indigenous* or Aboriginal* or Amerindian* or autochtone* or First Nation or First Nations or Urban Indian* or on reserve* or off reserve* or country food* or medicine man or medicine men or medicine wom$n or shaman* or ethnomedicine* or ethnopharmacology).mp. or (Native adj3 (american* or man or men or women or woman or boy* or girl* or adolescent* or youth or youths or person* or adult or people* or Indian* or Nation or Nations or tribe* or tribal or band or bands)).mp. or (traditional adj1 (medicine* or heal* or food*)).mp.) and (exp "Newfoundland and Labrador"/ or (Newfoundland or Labrador or NFLD or Goose Bay or Sheshiatshiu or Nain or Rigolet or Hopedale or Utshimasset or Davis Inlet or Conne River or Postville or Makkovik or Lake Melville or Nunatsiavut or Urahimassit).mp.)) not (horse or pony or ponies or dog or dogs or puppy or puppies or
canine or retriever*).mp. (162)

9 (exp Indians, North American/ or exp Health Services, Indigenous/ or Métis.mp. or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/ or Indigenous*.mp. or Aboriginal*.mp. or Amerindian*.mp. or Autochtone*.mp. or Métis.mp. or First Nations.mp. or First Nation*.mp. or (traditional adj1 (medicine* or heal* or food* or health*)).mp. or Urban Indian*.mp. or "on reserve".mp. or "off reserve*".mp. or country food*.mp. or residential school*.mp. or shaman*.mp. or medicine m?n.mp. or medicine wom?n.mp. or ((native* or Indian or Indians) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands)).mp. or Montagnais.mp. or Maliseet.mp. or Naskapi*.mp. or Mi'kmaq.mp. or Micmac.mp. or Mic mac.mp. or Migmaw.mp. or Mig maw.mp. or Beothuk*.mp.) and (((Fredrickton or Moncton or New Jersey).mp. and (exp Canada/ or Canad*.mp.)) or exp New Brunswick/ or New Brunswick*.mp. or Nouveau Brunswick.mp. or Big Hole Tract.mp. or Metepenagiag.mp. or Eel Ground First Nation.mp. or Buctouche.mp. or Esgenoopetitj.mp. or Burnt Church.mp. or Devon Reserve.mp. or St Mary's First Nation.mp. or

Eel River Reserve.mp. or Eel River Bar.mp. or Fort Folly Indian Point Reserve.mp. or Indian Island First Nation.mp. or Indian Ranch Reserve.mp. or Kingsclear.mp. or St John River Valley Tribal Council.mp. or Oromocto.mp. or Pabineau.mp. or Pokemouche.mp. or Mawiw.mp. or (Red Bank adj2 Reserve).mp. or Richibucto.mp. or St Basile.mp. or Madawaska.mp. or Soegao.mp. or Tabusintac.mp. or Tobique.mp. or Wolastoqiyik.mp. or Woodstock First Nation.mp.) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word,
rare disease supplementary concept word, unique identifier, synonyms] (18)
10 (Opaskawayak or Little Saskatchewan or Fisher River Cree or Peguis or Sagkeeng or Roseau River or Norway House or Sapotaweyak or Wuskwi Siphik or Skownan or Dauphin River or Pinaymootang or Kinonjeoshtegon or O-Chi-Chak-Ko-Sipi or Tootinaowaziibeeng or Lake Manitoba or Keeseekoowenin or Waywayseecappo or Birdtail Sioux or Canupawakpa or Dakota Tipi or Brokenhead Ojibway or Northlands Nursing Station or Lac Brochet or Sayisi Cree or Tadoule Lake or Brochet orO-Pipon-Na-Piwin or South Indian Lake or Mathias Colomb or Pukatawagan or Tataskweyak or York Landing or Nisichawayasihk or Nelson House or Shamattawa or Bunibonibee or Manto Sipi or God's River or God's Lake or Red Sucker Lake or St Theresa Point or Wasagamack or Pauingassi or Berens River Bloodvein).mp. or ((Sandy Bay or Long Plan or Sioux Valley or Fox Lake or War Lake or Pine Creek or Lake St Martin or Hollow Water or Little Black River or Rolling River or Dakota Plains or Swan Lake or Oxford House or Cross Lake or Split Lake or Barren Lands or Garden Hill or Poplar River or Little Grand Rapids).mp. and (exp Canada/ or Canad*.mp.)) or ((exp Indians, North American/ or exp Health Services, Indigenous/ or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/ or Indigenous*.mp. or Aboriginal*.mp. or Amerindian*.mp. or Autochtone*.mp. or First Nation.mp. or First Nations.mp. or Métis.mp. or (traditional adj1 (medicine* or heal* or food* or health*)).mp. or Urban Indian*.mp. or "on reserve".mp. or "off reserve*".mp. or country food*.mp. or shaman*.mp. or medicine m?n.mp. or medicine wom?n.mp. or ((native* or Indian or Indians) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands)).mp.) and (exp
Manitoba/ or Manitoba*.mp. or Winnipeg.mp. or Brandon.mp. or St Boniface.mp. or Dauphin.mp. or Flin Flon.mp. or Morden.mp. or Portage la Prairie.mp. or Selkirk.mp. or Steinbach.mp. or Thompson.mp. or Winkler.mp.)) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (538)
11 (((Athapaskan.mp. or exp Indians, North American/ or exp Inuits/ or exp Health Services, Indigenous/ or exp Ethnopharmacology/ or Saulteaux.mp. or Wakashan.mp. or Cree.mp. or Aboriginal*.mp. or Indigenous*.mp. or Métis.mp. or off-reserve.mp. or onreserve.mp. or First Nation.mp. or First Nations.mp. or Amerindian.mp. or (urban adj3 (Indian* or Native* or Aboriginal*)).mp. or ethnomedicine.mp. or country food*.mp. or residential school*.mp. or (exp Medicine, Traditional/ not Chinese.mp.) or shaman*.mp. or traditional medicine*.mp. or traditional heal*.mp. or traditional food*.mp. or medicine man.mp. or medicine woman.mp. or autochtone*.mp. or (Native adj1 (man or men or women or woman or boy* or girl* or adolescent* or youth or youths or person* or adult or people* or Indian* or Nation or tribe* or tribal or band or bands)).mp. or exp Shamanism/) and (British Columbia or Columbie Britannique or exp British Columbia/ or Williams Lake or Vernon or White Rock or Salmon Arm or Quesnel or Powell River or Port Moody or Port Hardy or Port Coquitlam or Port

Albernie or Pitt Meadows or Penticton or New Westminister or Nanaimo or Kelowna or Kamloops or Fort St John or Fernie or Enderby or Dawson Creek or Coquitlam or Chilliwack or Campbell River or Tumbler Ridge or Skidegate or Sandspit or Queen Charlotte or Port Clements or Kitimat or Hudsons Hope or Haida Gwaii or Fort St James or Fort Nelson or Dease Lake or Pouce Coupe or Chetwynd or Gransile or Atlin or Alexis Creek or Sooke or Cache Creek or Chehalis or Cheslatta or Kingcome Inlet or Kitwanga or Iskut or Kyuqot or Kanaka or Clo-oose or Nicomen or Liard River or Mount Currie or Keremos or Matsqui or Nanaimo or Tahsis or Gitwinkshilkw or Osoyoos or Popkum or Sechelt or Skookumchuk or (Siska not Karol) or Barriere or Spuzzum or Sumas or Saanichton or Tsawwassen or Ucluelet or Quadra or Nemaiah Valley or ((Windermeer or Victoria or Vancouver or Terrace or Soda Creek or Surrey or Prince George or Prince Rupert or Parksville or Nelson or Merritt or Langley or Langford or Kimberley or Greenwood or Grand Forks or Duncan or Cranbrook or Courtenay or Colwood or Burnaby or Bonaparte or Armstrong or Abbotsford or Castlegar or Vanderhoof or Valemount or Stewart or Smithers or McBride or Massett or MacKenzie or Houston or Hazelton or Burns Lake or Fraser Lake or Alkali Lake or Ashcroft or Boston Bar or Spences Bridge or Port Douglas or Chase or Litton or Mill Bay or Lomcolith or D'Arcy or Sidney or Agassiz or Harrison Mills or Invermere or Telegraph Creek or Hope or Boothroyd or Trail) and Canad*))) or (Duneza or Dunne-za or Dakelh or Babine or Wet'suwet'en or Haida or Sto:lo or Staulo or Stahlo or "Fraser River Indians" or Coast Salish or Kaska or Ktunaxa or Kootenay or Kwakwaka'wakw or Gitxsan or Gwich'in or Gwitich'in or Gitksan or Gwitchin or Gwichin or Kutchin or Tsimshian or Musqueam or St'at'imc or In-SHUCK-ch or Lil'wat or Lillooet or Nisga'a or Nuu-chah-nulth or Nootka or Nuxalk or Sekani or Wuikinuxv or Secwepemc or Sinixt or Skwxwu7mesh or (Tagish not meteorite) or Tahitan or Tahltan or Haisla or ((Nicola or Kitimat or Beaver or Okanagan or Sechelth) adj3 (man or men or boy or boys or girl or girls or adult* or youth* or adolescent* or Nation or people* or Indians* or tribe* or tribal* or band* or bands)) or (Carrier adj3 (Nation or Nations or Indians* or tribe* or tribal*))) or (Tsilhqot'in or Cowichan or Chilcotin or Nlaka'pamux or Tlingit or Tsetsaut or Oweekeno or Kwakiutl or Heiltsuk or Bella Bella or Saulteaux or Bella Coola or Shuswap or Squamish or Stl'atl'imx or Stl'atl'imc or Stlatliumh or Slatemuk or Dane-zaa or Tsattine or Tutchone or Tuchone or Akisq'nuk or Esdilagh or Acho Dene Koe or Dene-tha or Adams Lake or Ahousaht or Aitchelitz or Beecher Bay or Blueberry River or Tsleil-Waututh or Burrard or Cacli'p or Canim Lake or Canoe Creek or Dog Creek or Cheam or Chawathil or Aishihi or Chehalis or Chemainus or Cheslatta or Comox or Da'naxda'xw or Ditidaht or Doig River or Dzawada'enuxw or Ehattesaht or Esketemc or Esquimalt or Gitanmaax or Gitanyow or Gitsegukla or Gitwangak or Gitxaala or Glen Vowell or Gwa'sala or Gwawaenuk or Hagwilget or Halalt or Halq'emeylem or Hesquiaht or Homalco or Hupacasath or Hul'quimi'num or "Ka:'yu:'k't'h" or Che'k'tles7et'h or Katzie or Kispiox or Kitselas or Kitsumlamun or Klahoos or Kluskus or Lhoosk'uz or K'omoks or Kwadacha or Kwaw-kwaw-a-pilt or Kwiakah or Kwicksutaineuk or Kwikwentlem or Lakahahmen or Lax-kw'alaams or Leq'a:mel or Lheidli-T'enneh or Lhatko Lyackson or Malahat or Mamalilikulla or Matsqui or Metalakatla or Moricetown or Mowachaht or Muchalaht or Musqueam or Nadleh or Nak'azdli or 'Namgis or Sununeymuxw or Nanoos or Nazko or Nee-Tahi-Buhn or Neskonlith or Nisga'a or Nisgaa or Nooaitch or N'quatqua or Nuxalk or Ostlq'emeylem or Pacheedath or Pauquachin or Penelakut or Qayqayt or Quatsino or Saik'uz or Samahquam or Scowlitz or Semiahmoo or Shackan or Shxwha:y or Shw'ow'hamel or Simpcw or (Siska not Karol) or Skatin or Skawahlook or Skin Tyee or Skowkale or Skuppah or Skwah or Sliammon or Soowahilie or Spallumcheen or Squiala or Stellat'en or Taku River or T'it'qet or Tla-o-qui-aht or Tlatlasikwala or Tl'azt'en or

Tl'etinqox-t'in or Tlowitsis or Toosey or Toquaht or Tsartlip or Tsawataineuk or Tsawout or Tsay Keh Dene or Tseshaht or Tseycum or Tsi Del Del or Ts'kw'aylaxw or Tsleil-Waututh or T'souke or Tzeachten or Uchcklesaht or Ulkatcho or We Wai Kai or Cape Mudge or Wuikinuxv or Xaxli'p or Yaakweakwioose or Yekooche)).mp. not (animals not (humans and animals)).sh. not (isotope* or radiocarbon* or geology* or stratigraph* or Wisconsin or Michigan or Beaver County or (Alaska not (Alaska and (Canada or British Columbia)))).mp. (866)

12 ((Aakom Kiyii or Alexis Cardinal River or Alexis Elk River or Alexis Nakota Sioux or Allison Bay or Assineau River or Atikameg or Athabasca Chipweyan or Beaver First Nation or Beaver Lake Cree or Bearspaw or Beaver Ranch or Bigstone Cree or Bistcho Lake or Blood Tribe or Cadotte Lake or Carajou Settlement or Chateh or Chiniki or Chipewyan Prairie or Cold Lake First Nations or Dene Tha or Desmarais Settlement or Dog Head or Driftpile or East Prairie or Elizabeth Settlement or Enilda or Enoch Cree or Duncans First Nation or Ermineskin or Fort Chipewyan or Frog Lake or Garden Creek or Goodfish Lake or Gregoire Lake or Grouard or Heart Lake or Hobbema or Hokedhe or Horse Lake* or Janvier Health or Jere Ghalil or Jean Dor or John Dor or Kainai or Kainaa or Kapaweno or Kee Tas Kee Now or Kehewin or Ki Tue or Kapaweno or Kikino or Kinuso or Jackfish Point or Little Buffalo or Little Red River Cree or Loon Prairie or Louis Bull or Lubicon Lake Indian Nation or Maggie Willier or Makaoo or Maskwacis or Meander Health or Mikisew or Nakota or Nakoda or Namur Lake or OChiese or Old Fort or Paddle Prairie or Paul Band or Paul First Nation or Peace Point or Peavine Settlement or Peigan or Peerless Lake or Peerless Trout or Piikani or Pikuni or Pikani or Puskiakiwenin or Red Earth Creek or Saddle Lake or Samson Cree or Sarcee or Sawridge Band or Siksika or Siksikawa or Sao-kitapiiksi or Stoney First Nation or Stoney Tribe or St Isadore or Sturgeon Lake Cree or Tasttine or Tallcree or Tall Cree or Thabacha or Thebathi or Tsuu Tina or Tsu Tue or Tsu Kadhe or Unipouheos or Utikoomak or Wabasca or Wesley Band or ((Alexander or Athabasca or Beaver Lake or Blue Quill* or Cold Lake or Duncans or Enoch or Fort McKay or Fort McMurray or Loon River or Paul or Smiths Landing or Sucker Creek or Sunchild or Swan River or Whitefish Lake) adj2 (First Nation* or tribe or Indian*))).mp. or (exp Indians, North American/ or exp Health Services, Indigenous/ or exp Medicine, Traditional/ or exp Shamanism/ or exp Ethnopharmacology/ or Indigenous*.mp. or Aboriginal*.mp. or Amerindian*.mp. or Autochtone*.mp. or First Nation.mp. or First Nations.mp. or Dene.mp. or Blackfoot.mp. or Anishinaable.mp. or Assiniboine.mp. or Métis.mp. or Mischif.mp. or Mitchif.mp. or Metif.mp. or Metchif.mp. or Bois-brule*.mp. or Mixed-blood*.mp. or Half Breed*.mp. or halfbreed*.mp. or (traditional adj1 (medicine* or heal* or food* or health*)).mp. or Urban Indian*.mp. or "on reserve".mp. or "off reserve".mp. or country food*.mp. or shaman*.mp. or medicine m?n.mp. or medicine wom?n.mp. or ((native* or Indian or Indians) adj2 (person or persons or man or woman or men or women or child* or youth or youths or population* or people* or band or bands)).mp.)) and (Beaver Lake or Brownvale or Fort McMurray or Edmonton or Calgary or
Hythe or Slave Lake or Valleyview or Fort Vermilion or Morinville or Glenevis or Lac La Biche or Cold Lake or Rocky Mountain House or Duffield or Brocket or Morley or Whitecourt or Amber River or Big Horn or Buck Lake or Charles Lake or Collin Lake or Cornwall Lake or Cowper Lake or Devils Gate or Eden Valley or Fox Lake or Little Red River or Hay Lake or Lesser Slave Lake or Bonneyville or Loon Lake or Wetaskiwin or Pigeon Lake or Lake Athabasca or Fort McLeod or Barrhead or Stony Plain or Sturgeon Lake or High Prairie or Swampy Lake or Upper Hay River or Wabamun or Trout Lake or Whitefish Lake or Winefred Lake or Nordegg or Boyer River or Calling Lake or Berwyn or Fort Chipewyan or Black

Diamond or Fishing Lake or Gift Lake or Kananaskis or Medicine Hat or Ponoka or Stand Off or StandOff or Alberta).mp. (361)
13 or/1-12 (4949)
14 (exp Australia/ or Queensland.mp. or New South Wales.mp. or NSW.mp. or Northern Territory.mp. or Canberra.mp. or (Sydney not Canada).mp. or ((Melbourne not (England or United Kingdom)) or Adelaide or Tasmania or (Perth not Scotland) or Austral*).mp.) and ((Indigen* or Aborig* or tribe or tribal or tribes or traditional or remote or outback or Blackfella* Aborigin* or Indigenous* or first people* or original people).ti,ab. or Torres Strait Island*.mp. or Ngunnawal.mp. or Murrawarri.mp. or Alyawarre.mp. or Anmatjera.mp. or Arrernte.mp. or Gurindiji.mp. or Kunibidji.mp. or Luritja.mp. or Murrinh Patha.mp. or Pitjantjatjara.mp. or Tiwi.mp. or Waripiri.mp. or Yoingu.mp. or Guugu Yimithirr.mp. or Kalkadoon.mp. or Torres Strait Islander*.mp. or Adnyamathanha.mp. or Adynyamathanha.mp. or Dieri.mp. or Kaurna.mp. or Maralinga Tjarutja.mp. or Ngarrindjeri.mp. or Narungga.mp. or Gunai.mp. or Kurnai.mp. or Kulin.mp. or Yorta Yorta.mp. or angerang.mp. or Kailtheban.mp. or Wollithiga.mp. or Moira.mp. or Ulupna.mp. or Kwat Kwat.mp. or Yalaba Yalaba.mp. or Ngurai illiam wurrung.mp. or Jarrakan.mp. or Noongar.mp. or Nyungar.mp. or Nyoongar.mp. or Pila Iguru.mp.) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (12806)
15 Indians, North American/ or Native American*.mp. or (Native adj2 (Alaska* or Hawaiian*)).mp. or American Indian*.mp. or Abenaki.mp. or Absaroke.mp. or Alaskan Athabascans.mp. or Aleut.mp. or A'aninin.mp. or Anishinaabe.mp. or Aniyunwiya.mp. or (Apache not Apache II).mp. or Arapaho.mp. or Arikara.mp. or Baxoje.mp. or Blackfeet.mp. or Bode'wadmi.mp. or Caddo.mp. or Cayuse.mp. or Chahta.mp. or Cherokee.mp. or Cheyenne.mp. or Chikasha.mp. or Chickasaw.mp. or Chippewa.mp. or Choctaw.mp. or Comanche.mp. or Cree.mp. or Cayuga.mp. or Dakelh.mp. or (Dine' not "Dine 1").mp. or Eskimo*.mp. or Ewiiaapaayp.mp. or Gaigwu.mp. or Gayogohono.mp. or Gros Ventre.mp. or Havasupai.mp. or Hinonooeino.mp. or Haudenonsaunee.mp. or Hidatsa.mp. or Ho-Chunk.mp. or Hopi.mp. or Hualapai.mp. or Houma.mp. or Illiniwek.mp. or Illini.mp. or Iyiniwok.mp. or Ininiwok.mp. or (Iroquois not (homeobox or transcription)).mp. or Kadohadacho.mp. or Kanienkehaka.mp. or Kanonsionni.mp. or Karok.mp. or Kickapoo.mp. or Kiowa.mp. or Kiwigapawa o Klickitat.mp. or Kumeyaay.mp. or Lanape.mp. or Lakota.mp. or Lumbee.mp. or Maidu.mp. or Maklak.mp. or Mamaceqtaw.mp. or Mandan.mp. or Maumee.mp. or Menominee.mp. or Meskwaki.mp. or Miccosukee.mp. or Mikasuki.mp. or Minisink.mp. or Mohawk.mp. or Mohegan.mp. or Mohican.mp. or Mohingan.mp. or Muheconneok.mp. or Munsee.mp. or Muskogee.mp. or Myaamia.mp. or Nakota.mp. or Nanigansek.mp. or Nantego.mp. or Narragansett.mp. or Navajo.mp. or Narragansett.mp. or Nde.mp. or Ndee.mp. or Niukonska.mp. or Numakiki.mp. or Numinu.mp. or Nunt'zi.mp. or Nuutsiu.mp. or Nuxbaaga.mp. or Odawa.mp. or Ojibway.mp. or Ojibwe.mp. or Ohkay Owingeh.mp. or Olekwo'l.mp. or Onandowaga.mp. or Oneida.mp. or Onondaga.mp. or Onundaga'ono.mp. or Onyota'aka.mp. or Osage.mp. or Pahoja.mp. or Panawahpskek.mp. or Passamaquoddy.mp. or Papago.mp. or Pend 'O reilles.mp. or Penobscot.mp. or Peskotomuhkati.mp. or Piaute.mp. or Pima.mp. or Pokanoket.mp. or Pomo.mp. or Ponca.mp. or Potawatomi.mp. or Powhatan.mp. or Po-wo-ge-oweenge.mp. or Pueblo.mp. or Puget Sound Salish.mp. or Quapaw.mp. or Qwulhhwaipum.mp. or Sahnish.mp. or Sauk.mp. or Sekani.mp. or Seminole.mp. or Shawnee.mp. or Shawanwa.mp. or Schitsu'msh.mp. or Shoshonee.mp. or Shuyelpee.mp. or Siksika.mp. or Skarooren.mp. or (Souix not "Souix

Falls").mp. or Ta-o-ta.mp. or Tetawken.mp. or Tete de Boule orTeton.mp. or Thlingchadine.mp. or Tohano O'odham.mp. or Tonkawa.mp. or Tlingit-Haida.mp. or Tohono.mp. or Tsalagi.mp. or Tsitsistas.mp. or Tuf-shum-tia.mp. or Tus-Tah.mp. or Tuscarora.mp. or O'odham.mp. or Ugakhpa.mp. or Umon'hon.mp. or Ute.mp. or Wampanoag.mp. or Wendat.mp. or Wihyot Winnebago.mp. or Who-ge-owenge.mp. or Wyandot.mp. or Yakima.mp. or Yaqui.mp. or Yavapai.mp. or Yurok.mp. or Yuman.mp. or ((Alabama or Illinois or Fox or Carrier or Miami or Omaha or Taos or Colville or Creek or Crow or Dakota or Delaware or Kalispel or Klamath or Stockbridge or Nanticoke or Nde) adj2 (Indian* or medicine man or medicine men or medicine woman or medicine women or Aboriginal* or Amerindian* or Indigenous* or reservation* or tribe or tribes or tribal or shaman or traditional food* or people* or man or woman or child* or youth or boy or boys or girl* or elder or elders or clan or clans)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (29226)

16 maori.mp. (2811)

17 tangata whenua.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (5)

18 (New Zealand and (indigenous or aboriginal or "first people*" or shaman* or tribe or tribes or tribal or clan or clans)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1145)

19 16 or 17 or 18 (3403)

20 exp American Native Continental Ancestry Group/ (20134)

21 13 or 14 or 15 or 19 or 20 (52308)

22 exp Diabetes, Gestational/ (10249)

23 gdm.mp. (5589)

24 ((gestat* or pregnan* or expectant or pre birth or perinatal or trimester) adj2 (diabetes or glucose or DM or
melitus)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (16173)

25 exp Pregnancy in Diabetics/ (12197)

26 exp Diabetes Mellitus/ and (gestat* or pregnan* or expectant or pre birth or perinatal or trimester).mp.
[mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (20517)

27 22 or 23 or 24 or 25 or 26 (30106)

28 21 and 27 (299)

29 remove duplicates from 28 (295)

Appendix 2: Screening of Titles and Abstracts Instructions

Below are the instructions for screening titles and abstracts. During the screening phase the purpose is to remove those studies that are not relevant, but if it is unclear based on the title and abstract include the study for full text review.

Screening Criteria:

- Studies to be included are observational studies assessing the prevalence of pre-existing DM and GDM among Indigenous women in Australia, Canada, New Zealand and the USA compared to non-Indigenous women (limiting too: Canada, Australia, New Zealand and USA).

Types of Studies to be Included:

- Observational epidemiological studies including cohort (retrospective and prospective) and cross sectional. Any type of review, case series and case reports are not to be included.

Exposure:

- Being an Indigenous woman during pregnancy in Australia, Canada, New Zealand and the USA.

Outcomes:

- Prevalence of pre-existing GDM and prevalence of GDM.

Comparison

- Non-indigenous pregnant women comparison group in Australia, Canada, New Zealand and the USA.

Appendix 3: Study Inclusion Form

Study Inclusion and Exclusion (Adapted from Cochrane Data Extraction Template)

Study Characteristics	Eligibility criteria	Eligibility criteria met?		
		Yes	No	Unclear
Type of study	Cohort Study	☐	☐	☐
	Cross Sectional Study	☐	☐	☐
	Other design (specify):	☐	☐	☐
Participants	Indigenous women in either Canada, United States, Australia or New Zealand	☐	☐	☐
Type of comparison	Non-Indigenous women comparison	☐	☐	☐
Types of outcome measures	Prevalence of Gestational Diabetes	☐	☐	☐
	Prevalence of pre-existing diabetes before pregnancy	☐	☐	☐
INCLUDE ☐	EXCLUDE ☐			
Reason for exclusion				

Reference:
1. Cochrane Collaboration. Data Extraction Forms. Available from

https://dplp.cochrane.org/data-extraction-forms. Accessed June 15, 2018.

Appendix 4: Data Extraction Form

Data Extraction form: Prevalence of Diabetes During Pregnancy Among Indigenous women: A systematic review (Adapted from Cochrane Data Extraction Template)

Refworks ID	

Characteristics of included studies

Methods

	Descriptions as stated in report/paper
Aim of study	
Study Funding	
Design	
Start date	
End date	
Duration of participation	

Participants

	Description
Indigenous group	
Comparison Group	
Study Setting	
Methods for Recruitment of Study population	
Withdrawals and exclusions	
Mean Age Age standard Deviation Age range	

Outcome: Pre-existing DM

	Description as stated in report/paper			
Time point pre-existing diabetes is measured				
Pre-existing diabetes definition				
Person measuring/ reporting				
Results	Indigenous women		Non-indigenous women	
	No. with pre-existing diabetes	Total in group	No. with pre-existing diabetes	Total in group

Odds ratio (95% confidence interval)		
No. missing participants		
Reasons missing		

Outcome: Gestational Diabetes

	Description as stated in report/paper			
Time point GDM is measured				
GDM definition				
Person measuring/ reporting				
Results	Indigenous women		Non-indigenous women	
	No. with pre-existing diabetes	Total in group	No. with pre-existing diabetes	Total in group
Odds ratio (95% confidence interval)				
No. missing participants				
Reasons missing				

Sources:

1. Cochrane Collaboration. Data Extraction Forms. Available from

https://dplp.cochrane.org/data-extraction-forms. Accessed June 2015, 2018