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ORIGINAL RESEARCH

Implications of Risk Factors for Alzheimer's Disease in Canada's Indigenous Population

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ABSTRACT

Background

Indigenous peoples in Canada have higher prevalence of modifiable risk factors for Alzheimer's disease (AD). The relative importance of these risk factors on AD risk management is poorly understood.

Methods

Relative risks from literature and prevalence of risk factors from Statistics Canada or the First Nations Regional Health Survey were used to determine projected population attributable risk (PAR) associated with modifiable risk factors for AD (low education and vascular risk factors) among on- and off-reserve Indigenous and non-Indigenous people in Canada using the Levin formula.

Results

Physical inactivity had the highest PAR for AD among Indigenous and non-Indigenous peoples in Canada (32.5% [10.1%–51.1%] and 30.5% [9.2%–48.8%] respectively). The PAR for most modifiable risk factors was higher among Indigenous peoples in Canada, particularly among on-reserve groups. The greatest differences in PAR were for low educational attainment and smoking, which were approximately 10% higher among Indigenous peoples in Canada. The combined PAR for AD for all six modifiable risk factors was 79.6% among on-reserve Indigenous, 74.9% among off-reserve Indigenous, and 67.1% among non-Indigenous peoples in Canada. (All differences significant to $p < .001$.)

Conclusions

Modifiable risk factors are responsible for the most AD cases among Indigenous peoples in Canada. Further research is necessary to determine the prevalence of AD and the impact of risk factor modification among Indigenous peoples in Canada.

Key words: Alzheimer's disease, Canada, indigenous, risk factors, population attributable risk

INTRODUCTION

In 2006, 26.6 million people worldwide lived with Alzheimer's disease (AD), a number that is expected to grow as the population ages.[1] AD accounts for most cases of dementia among Canadians aged 65 years and over.[2] To date, there is no cure or disease-modifying treatment for AD. As such, a major focus of research is identifying modifiable risk factors for AD.[3] Many modifiable risk factors for AD are vascular risk factors, including diabetes, hypertension, obesity, smoking, and physical inactivity.[4,5] In addition, research show that low education is strongly associated with increased AD risk.[6,7]

Though the prevalence of AD in the Canadian Indigenous population in Canada has not been well defined, the importance of dementia as a public health concern has recently been recognized.[8] One study found that dementia is more prevalent among First Nations peoples in Alberta compared to non-First Nations people and that dementia was diagnosed at younger ages.[8] The Indigenous population also has a disproportionately high prevalence of most modifiable risk factors. For example, one study found that Indigenous people were two to four times more likely than non-Indigenous people to have diabetes.[9] Prior research also indicates that Indigenous peoples in Canada have higher rates of obesity, physical inactivity, and smoking compared to their non-Indigenous counterparts.[10,11,12] This is especially true for Indigenous (First Nations) peoples who live on-reserve.[13]

Although research has examined vascular risk factors among Indigenous peoples in Canada in the context of cardiovascular disease, there is little research regarding the potential impact of these and other risk factors on AD. The objective of this study was to examine and compare the population attributable risk (PAR) for AD associated with six modifiable

risk factors (diabetes mellitus, midlife hypertension, midlife obesity, physical inactivity, smoking, and low educational attainment) among Indigenous and non-Indigenous peoples in Canada and among on- and off-reserve Indigenous peoples in Canada.

METHODS

For the purpose of this analysis, the Canadian population is segmented into three groups. On-reserve Indigenous peoples in Canada include Indigenous (First Nations) peoples who live in First Nations communities (on-reserve) in Canada. Off-reserve Indigenous peoples in Canada include people who self-identify as First Nations, Inuit, or Metis and live off-reserve in Canada. Finally, non-Indigenous people include any Canadians who live off-reserve and do not identify as First Nations, Inuit, or Metis and, thus, include people of many different ethnicities.

Data Extraction

Prevalence of Risk Factors

The prevalence of six risk factors (diabetes mellitus, midlife hypertension, midlife obesity, physical inactivity, smoking, and low educational attainment) was determined for the three populations of interest. Although depression was included in a prior publication regarding the population attributable risk of AD,[14] depression was not included here since data regarding the prevalence of depression was not available through the Statistics Canada data sources used for these analyses. In addition, factors that elevate the risk for other types of dementia (for example, alcoholism) but are not among the primary risk factors for AD were also not included.

Data for on-reserve Indigenous peoples in Canada were extracted from the 2008–2010 First Nations Regional Health Survey: National Report on Adults, Youth and Children Living in First Nations Communities, which includes a sampling of 21,757 people from 216 First Nations communities.[15] Data for off-reserve Indigenous peoples (First Nations, Inuit, and Metis) and those who identify as non-Indigenous were extracted from the 2010 Statistics Canada Community Health Survey for people aged 45 years and older (CANSIM Table 105-0512 for off-reserve Indigenous peoples and CANSIM Table 105-0501 for non-Indigenous people). Data on the prevalence of low educational attainment (less than high school diploma) among off-reserve groups was extracted from the 2006 Canadian Census estimates. The prevalence of each risk factor among off-reserve Indigenous peoples in Canada was calculated by weighting the prevalence for First Nations, Metis, and Inuit by their respective population (Off-reserve Indigenous Prevalence = [(Population First Nations × Prevalence First Nations) + (Population Inuit × Prevalence Inuit) + (Population Metis × Prevalence Metis)] / Total Off-reserve Indigenous Population). Similarly, the prevalence estimates for the total Indigenous population were calculated by weighting on- and off-reserve prevalence according to population estimates from the 2011 Canadian Census National Household Survey (Total Indigenous Prevalence = [(Population On-reserve × Prevalence On-reserve) + (Population Off-reserve × Prevalence Off-reserve)] / Total Indigenous Population). Presence of risk factors was self-reported in all data sources.

Relative Risks

A literature review was conducted to determine the relative risk associated with each of the risk factors. Since no updated meta-analyses were published, relative risks were extracted from a prior publication by Barnes and Yaffe.[14] Most relative risks used in the meta-analyses were adjusted for confounding factors, most often including age and education. Since there is no research to indicate that the relative risks associated with modifiable risk factors for AD are different in Indigenous versus non-Indigenous populations, we used the same relative risks for both groups.

Analysis

The PAR is defined as the number of cases of a disease in a population that can be attributed to a specific exposure. For the purpose of this paper, the PAR was the projected portion of cases of AD attributed to one or all six modifiable risk factors of interest. To calculate the PAR for each risk factor, we used the Levin formula,[16] as done previously:[14]

$$\text{PAR} = \frac{P_{RF} \times (RR-1)}{1+P_{RF} \times (RR-1)}$$

where P_{RF} refers to the prevalence of the risk factor and RR refers to the adjusted relative risk for AD associated with that risk factor. A combined PAR was calculated to determine the maximum combined effect of all risk factors:

$$\text{Combined PAR} = 1 - (1 - PAR_1) \times (1 - PAR_2) \times (1 - PAR_3) \ldots$$

The disadvantage of this equation is that it treats each risk factor as independent of the others, which is likely not true. However, it has the advantage of limiting the total sum of PARs to less than 100%. Differences between populations were calculated using the chi-square test.

RESULTS

In both the total Indigenous (on- and off-reserve Indigenous peoples) and non-Indigenous populations in Canada, physical inactivity had the highest PAR for AD. However, the PAR for most risk factors (excluding midlife hypertension) was higher among Indigenous peoples in Canada than among non-Indigenous people. The greatest contrast between groups was for low educational attainment (10.4% difference) and smoking (9.5% difference) (p-for-difference < .001). The

estimated combined PAR for all six risk factors was almost 10% higher among Indigenous peoples in Canada than among non-Indigenous people. For additional detail regarding the prevalence, relative risks, and PAR associated with each risk factor in among the Indigenous and non-Indigenous people in Canadian populations, refer to Table 1.

When examining the on-reserve and off-reserve Indigenous populations (Table 2), the highest PAR for both groups was again for physical inactivity. Most PARs were higher among on-reserve Indigenous peoples in Canada than among off-reserve Indigenous peoples, with the exceptions being diabetes mellitus (same in the two groups) and midlife hypertension (higher in the off-reserve group). The greatest differences in PARs were in those associated with smoking (7.7%) and low education (7.5%) ($p < .001$). The estimated combined PAR for all six risk factors neared 80% for on-reserve Indigenous peoples in Canada and was approximately 5% lower among off-reserve Indigenous peoples. For additional detail regarding the prevalence, relative risks, and PAR associated with each risk factor in the on- and off-reserve Indigenous peoples in Canada, refer to Table 2.

DISCUSSION

Most modifiable risk factors for AD are more common among Indigenous peoples in Canada than among the non-Indigenous people. As a result, the six risk factors addressed in this study accounted for a higher projected PAR for AD among Indigenous than non-Indigenous groups, with the risk factors responsible for over 75% of AD cases. Optimistically, this suggests that a greater portion of projected AD cases among Indigenous peoples may be preventable.

Most of the difference in the PARs between Indigenous and non-Indigenous peoples in Canada appears to be driven by high prevalence of risk factors among on-reserve Indigenous peoples. In all-cases, the PAR and prevalence of AD risk factors among off-reserve Indigenous peoples fell between the on-reserve and non-Indigenous groups. Consequently, the high risk for AD among Indigenous peoples in Canada is likely driven by a combination of cultural factors and social determinants of health (for example, education, employment, food access, built environment) that differ at least in magnitude between on- and off-reserve groups.

Within both the Indigenous and non-Indigenous populations, physical inactivity had the greatest projected PAR for AD (>30% in both groups). Some barriers to physical activity are likely shared by on-reserve Indigenous, off-reserve Indigenous, and non-Indigenous groups. For example, health conditions, lack of time, and the influence of friends and family are frequently cited barriers to physical activity.[17,18,19,20] The influence of health conditions may be particularly relevant among Indigenous peoples in Canada as almost two-thirds of on-reserve Indigenous peoples in Canada have a chronic health condition.[15] Cultural factors

TABLE 1.
Prevalence, relative risk, and population attributable risk (PAR) associated with modifiable risk factors for Alzheimer's disease in the total Indigenous and non-Indigenous population in Canada

Risk Factor	*Prevalence*	*Relative Risk* (95% CI[a])	*PAR*[b] (95% CI)
		Total Indigenous Population	
Diabetes Mellitus	16.4%	1.39 (1.16–1.66)	6.0% (2.6–9.7)
Midlife Hypertension	27.1%	1.61 (1.16–2.24)	14.2% (4.2-–25.1)
Midlife Obesity	33.7%	1.60 (1.34–1.92)	16.8% (10.3–23.6)
Physical Inactivity	58.8%	1.82 (1.19–2.78)	32.5% (10.1–51.1)
Smoking	40.8%	1.59 (1.15–2.20)	19.4% (5.8–32.9)
Low Education	48.8%	1.59 (1.35–1.86)	22.4% (14.6–29.6)
Combined (maximum)	-	-	76.1%
		Non-Indigenous Population	
Diabetes Mellitus	11.0%	1.39 (1.16–1.66)	4.1% (1.7–6.8)
Midlife Hypertension	31.0%	1.61 (1.16–2.24)	15.9% (4.7–27.8)
Midlife Obesity	19.7%	1.60 (1.34–1.92)	10.6% (6.3–15.3)
Physical Inactivity	53.6%	1.82 (1.19–2.78)	30.5% (9.2–48.8)
Smoking	18.6%	1.59 (1.15–2.20)	9.9% (2.7–18.2)
Low Education	23.1%	1.59 (1.35–1.86)	12.0% (7.5–16.6)
Combined (maximum)	-	-	67.1%

[a] Confidence Interval.
[b] All differences in PAR between populations significant to $p < .001$.

TABLE 2.
Prevalence, relative risk, and population attributable risk (PAR) associated with modifiable risk factors for Alzheimer's disease in the on-reserve and off-reserve Indigenous Canadian population.

Risk Factor	*Prevalence*	*Relative Risk* (95% CI[a])	*PAR*[b] (95% CI)
		On-reserve Indigenous Population	
Diabetes Mellitus	16.0%	1.39 (1.16–1.66)	5.9% (2.5–9.7)
Midlife Hypertension	21.8%	1.61 (1.16–2.24)	11.7% (3.4–21.3)
Midlife Obesity	40.2%	1.60 (1.34–1.92)	19.4% (12.0–27.0)
Physical Inactivity	62.5%	1.82 (1.19–2.78)	33.9% (10.6–57.2)
Smoking	57.0%	1.59 (1.15–2.20)	25.2% (7.9–40.6)
Low Education	65.9%	1.59 (1.35–1.86)	28.0% (18.7–36.2)
Combined (maximum)	-	-	79.6%
		Off-reserve Indigenous Population	
Diabetes Mellitus	16.0%	1.39 (1.16–1.66)	6.0% (2.6–9.8)
Midlife Hypertension	29.0%	1.61 (1.16–2.24)	14.9% (4.4–26.2)
Midlife Obesity	32.0%	1.60 (1.34–1.92)	16.0% (9.7–22.6)
Physical Inactivity	58.0%	1.82 (1.19–2.78)	32.1% (9.9–50.7)
Smoking	36.0%	1.59 (1.15–2.20)	17.5% (5.1–30.1)
Low Education	44.0%	1.59 (1.35–1.86)	20.5% (13.3–27.3)
Combined (maximum)	-	-	74.9%

[a]Confidence Interval.
[b]All differences in PAR between populations significant to $p < .001$ with the exception of diabetes mellitus.

may also influence physical activity among Indigenous groups. For example, Canadian Indigenous youth reported a preference for traditional Indigenous forms of physical activity.[21] Developing culturally acceptable physical activity programs in coordination with the local community may be critical to increasing physical activity among Indigenous peoples in Canada. Poor access to facilities is another barrier to physical activity that may be particularly pertinent to Indigenous people living on-reserve.[22,23,24,25] In a study of the Six Nations Reserve (Brant County, Ontario), participants reported poor walkability and difficulty accessing walking and cycling facilities.[26] This suggests that the built environment may be a key social determinant of physical activity among the Indigenous peoples in Canada, which could be altered by developing and maintaining community centres, roads, sidewalks, and trails.

Low educational attainment had the second highest projected PAR for AD among Indigenous peoples in Canada and also accounted for the biggest discrepancy in the PAR between Indigenous and non-Indigenous groups (>10%). This is in line with prior research that indicates that the portion of off-reserve Indigenous peoples in Canada who do not complete high school is twice that of non-Indigenous people.[27] The rate of low education is an additional 20% higher among on-reserve versus off-reserve Indigenous peoples in this study (66% versus 44%). Differences in education between Indigenous and non-Indigenous groups are likely influenced by colonialism and forced assimilation of Aboriginal peoples in Canada.[28,29] The history of imposed education through the residential school system contributes to the high rates of dropout among Indigenous peoples in the present day.[30] Furthermore, the trauma of the residential school system continues to affect Aboriginal peoples' psychological health and wellbeing, taking the form of increased stress such as post-traumatic stress disorder.[31] Research has shown low rates of education then contribute to high rates of unemployment and low socioeconomic status among Indigenous peoples in Canada,[32] which in turn drive other AD risk factors such as smoking and obesity.[15,33]

To date, there has been limited research on strategies to improve education and literacy among Indigenous youth.[34] Research indicates Indigenous youth are less likely to attend school if they consider the teaching style unacceptable or are unable to relate to the content.[35,36] Successful strategies to increase educational attainment may require inclusion of cultural practices and values and delivery in local languages.[36] Such culturally appropriate strategies may drive student interest and attendance and,[35] thus, increase educational attainment and reduce AD risk.

Smoking is another risk factor with a substantially higher (almost 10%) PAR for AD among Indigenous peoples in Canada. This confirms prior research indicating higher tobacco use in Indigenous populations, particularly among those living on-reserve.[10,37] Low income and unemployment are important social determinants of smoking among Indigenous peoples.[38,39] As a result, factors limiting

education and employment opportunities may also drive smoking rates. However, Indigenous status is also associated with higher rates of smoking independent of socioeconomic status.[40] Although some suggest lack of taxation for tobacco among Indigenous peoples in Canada may contribute to high smoking rates, there is no evidence that increasing taxation reduces smoking.[41] One small study suggested that a culturally sensitive smoking-prevention program may be effective among Indigenous youth.[42]

The PAR for AD associated with diabetes and obesity were also higher in the Indigenous population in Canada. High rates of each of these factors have been previously reported in Indigenous peoples in Canada.[9,10,11,12] Since off-reserve Indigenous peoples in Canada have lower rates than on-reserve Indigenous peoples, there may be both general Indigenous factors and reserve-related factors contributing. Increasing rates of physical inactivity and poor diet are understood to contribute to obesity and diabetes among Canadians in general, as well as psychosocial factors.[43,44] Indigenous peoples in Canada are more likely to be physically inactive, due to a combination of factors discussed above. Environmental factors related to living on-reserve or in remote locations may also increase obesity rates due to poor access to healthy foods.[22] Colonialism may be another factor that influences diet. Forced relocation of Indigenous people reduced hunting and gathering practices and increased Indigenous reliance on less nutritious store-bought foods.[45] Access to affordable, healthy food, either through stores or traditional hunting and gathering, would likely improve diets and reduce obesity, diabetes, and, thus, AD rates.

The PAR associated with midlife hypertension was slightly higher among non-Indigenous people than among Indigenous peoples. Since high blood pressure was self-reported, it is unclear whether blood pressure controlled by treatment was reported as high blood pressure or not. One study found higher rates of treated hypertension among Indigenous peoples in Canada, though there was no difference in the current systolic blood pressure,[10] in line with our results.

An important factor that may influence the prevalence of all AD risk factors among the Indigenous population in Canada is poor relationship with health-care providers. The devaluation of Indigenous knowledge and traditions fostered by colonization as well as historically imposed colonial institutions contribute to high rates of withdrawal of Indigenous people from Canadian institutions including the medical system.[30] Indeed, medical institutions are considered a powerful symbol of colonialism.[46] Studies indicate that Indigenous people in Canada feel that medical personnel do not relate to them and dismiss their concerns.[47,48] In addition, poor communication and relationships with physicians were evident.[48] Poor relationships may influence risk-factor diagnosis, treatment, and self-management and, thus, influence AD risk. The relationship of Indigenous people with Canadian health providers may be enhanced if patients are involved in decision making and experience respect for their culture and identify.[47]

Of note, remnant trauma from the residential school system may affect risk for AD through more than education. The trauma continues to affect Aboriginal peoples' psychological health and wellbeing, taking the form of increased stress such as post-traumatic stress disorder.[31] This may affect AD risk both directly, through increased stress and associated inflammation over the life course,[49] and indirectly, by influencing behaviour. People who have experienced post-traumatic stress disorder are less likely to be physically active and are more likely to have poor diet, which is likely to influence AD risk.[50]

Chronic-disease self-management strategies may be an important approach to managing the burden and implication of all risk factors among Indigenous peoples in Canada. In particular, self-management strategies that involve communities in chronic-disease management and consider Indigenous-specific socio-ecological factors may be most effective.[46] For example, the Aboriginal Diabetes Wellness Program which was implemented in Alberta (Canada) includes culturally sensitive programming using a holistic approach to health management and offers programming in local native languages.[46] Such strategies could also be effective for other risk factors, particularly vascular risk factors that increase an individual's risk not only for AD but also for cardiovascular disease. However, it is important to note that devaluation of Indigenous knowledge imparted by colonialism creates self-doubt and makes self-management and behaviour change more difficult.[29]

Our study has both strengths and weaknesses. Few studies have examined dementia risk among Indigenous groups, particularly in Canada. As a result, this analysis of the PAR for AD associated with modifiable risk factors gives insight into the impact of modifiable risk factors on AD among Indigenous and non-Indigenous groups. The relative risk of each risk factor came from the most recent systematic reviews and meta-analyses, suggesting accuracy of estimates. Our data regarding prevalence also came from either Statistics Canada data or the First Nations Health survey, which minimizes sampling bias. However, most data were self-reported in 2010. Thus, the data may be influenced by reporting bias, which would be likely to result in under-reporting of risk factors. Furthermore, prevalence rates from 2010 may not be consistent with current prevalence. The Levin equation used to estimate PAR may also have some limitations.[16] In particular, the equation assumes that each risk factor is independent, which is likely not true due to clustering of health behaviours. As such, this may lead to an overestimation in the PAR for all risk factors combined. However, the Levin equation is thought to underestimate the PAR in cases where the adjusted relative risk is less than the crude relative risk, which is the case for the modifiable risk factors discussed here. In addition, Indigenous populations were identified differently based on residence, where on-reserve Indigenous people were identified by place of residence (that is, on-reserve) whereas off-reserve Indigenous people were self-identified. This may lead to some bias in the comparison between groups.

Furthermore, data for the off-reserve Indigenous population include First Nations, Inuit, and Metis peoples. This prevents any differentiation between these Indigenous groups, which may be diverse in not only the prevalence of risk factors for AD but also the contributing factors. Further, there may be additional risk factors that contribute either directly or indirectly to the risk of dementia among Indigenous peoples in Canada, including depression and alcoholism which were not considered here. Depression was not included since it was not in the Canada Community Health Survey, our source of data for non-Indigenous people. Alcoholism was not included because it is chiefly a risk factor for alcohol-related dementia rather than AD. Finally, our analysis uses the same relative risks for the Indigenous and non-Indigenous groups. It is possible that the relationship between each risk factor, AD, and confounding factors may differ between the Indigenous and non-Indigenous groups in Canada due to living context of each population.

CONCLUSION

Our results indicate that modifiable risk factors may account for over 75% of cases of AD among Indigenous peoples in Canada. Reducing the prevalence of physical inactivity and smoking and increasing education may have the greatest impact on the prevalence of AD among Indigenous peoples in Canada. The causes of high rates of risk factors among Indigenous peoples in Canada are likely complex and multifactorial and are likely to include sociocultural factors as well as environmental factors associated with on-reserve living. It is possible that successful strategies to reduce risk factors may need to be culturally sensitive and developed in collaboration with Indigenous peoples in Canada. Further research should determine the prevalence of AD in the Indigenous population in Canada and develop culturally appropriate interventions to reduce risk factors for AD.

Key Points

The Indigenous population in Canada has a disproportionally high prevalence of modifiable risk factors for AD.

Thus, the population attributable risk (PAR) associated with most AD risk factors is higher among Indigenous groups than among non-Indigenous groups, suggesting that a greater portion of AD cases are preventable.

Low educational attainment and physical inactivity carry the greatest PAR for AD among Indigenous peoples in Canada.

The greatest difference in PAR was for low educational attainment and smoking, where the PAR among Indigenous peoples in Canada was approximately 10% higher than among non-Indigenous people.

Strategies to reduce risk factors may include improving access to healthy food and a health-promoting built environment on-reserve but need to take into account the cultures of Indigenous communities.

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CONFLICT OF INTEREST DISCLOSURES

Neither the study nor the researchers were directly funded for this work. The authors declare that no conflicts of interest exist. This paper will be disseminated through the National Collaborating Centre for Aboriginal Health (NCCAH) to ensure Indigenous populations in Canada have access to the study findings and information reported in this article.

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