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Changes in body mass index and incidence of diabetes: A longitudinal study of Alberta's Tomorrow Project Cohort

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ABSTRACT

Although obesity is a known risk factor for diabetes, the impact of body mass index (BMI) changes over time, especially BMI reduction, on diabetes development is less than clear. The objective of this study is to characterize the association between BMI changes over time and incidence of diabetes in a cohort of adults in Alberta.

From 2000 to 2008, Alberta's Tomorrow Project (ATP) enrolled participants aged 35–69 to a population-based prospective cohort study. BMI was calculated from self-reported height and weight; change in BMI (Δ BMI) was calculated as the difference between baseline and follow-up measurements. Diabetes cases were identified using the Canadian National Diabetes Surveillance System algorithm applied to linked administrative data (2000–2015). Multivariable Cox regression was used to examine the association between Δ BMI and incidence of diabetes.

In a subset of the ATP cohort ($n = 19,164$), 1168 incident cases of diabetes were identified during 198,853 person-years of follow-up. Overall, BMI increase was associated with increased risk and BMI reduction was associated with reduced risk of diabetes. Particularly, compared to minimal BMI change ($\pm 5\%$), moderate (5%–10%) reduction in BMI was associated with 34% (95% CI: 12%–51%) reduction in risk of diabetes in participants with obesity; whereas 10% or greater increase in BMI was associated with an increased risk of diabetes of 64% or more in participants with overweight and obesity; in participants with normal and underweight, BMI changes was not apparently associated with risk of diabetes.

Public health programs promoting weight loss, even at a moderate extent, would reduce risk of diabetes.

1. Introduction

Body mass index (BMI) is a measurement of the degree of obesity. As a known risk factor of diabetes, high BMI ($> 30 \text{ kg/m}^2$) is associated with 3–10 times greater risk of developing diabetes compared to low BMI ($< 25 \text{ kg/m}^2$) (Chan et al., 1994; Colditz et al., 1990; de Mutsert et al., 2014; Nagaya et al., 2005; Perry et al., 1995; Wannamethee et al., 2005). In addition to BMI measured at a single time point, the role of BMI changes over time in diabetes development has become a focus for both etiological study and intervention programs. The BMI increase (i.e. weight gain) over time has been consistently shown as a risk factor of diabetes in many longitudinal studies (Colditz et al., 1995; Ford et al., 1997; Oguma et al., 2005); however, the impact of BMI reduction (i.e. weight loss) over time on diabetes is less than clear.

A number of controlled intervention studies, including Diabetes Prevention Program (DPP) in the U.S. (Knowler et al., 2002), European

Diabetes Prevention Study (Penn et al., 2013), Finnish Diabetes Prevention Study (Lindstrom et al., 2003), a controlled trial in Japan (Kosaka et al., 2005) and a couple of smaller regional intervention studies in the U.S. (Long et al., 1994; Wing et al., 1998), have shown that modest weight loss (7–10%) achieved through intensive lifestyle intervention resulted in substantial reduction ($> 40\%$) in incidence of diabetes among high-risk groups, including individuals with obesity (Knowler et al., 2002; Long et al., 1994; Penn et al., 2013), family history of diabetes (Wing et al., 1998) and impaired glucose tolerance (IGT) (Kosaka et al., 2005; Lindstrom et al., 2003; Long et al., 1994). However, these evidences for high-risk populations may not be completely applicable in general populations.

Observational studies of general populations have demonstrated inconsistent results. Several observational studies echoed the beneficial effect of weight loss observed in controlled intervention studies in overweight and obese subjects (Resnick et al., 2000; Wannamethee and

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Shaper, 1999; Wannamethee et al., 2005). Studies of health professionals, including the Nurses' Health Study (Colditz et al., 1995) and Health Professionals Follow-up Study (Koh-Banerjee et al., 2004) in the U.S., suggested that weight loss may also be beneficial among low-risk individuals. Nevertheless, more observational studies, including longitudinal investigations of company employees in Japan (Kaneto et al., 2013), university alumni in the U.S. (Oguma et al., 2005) and population-based participants in Framingham Study (Higgins et al., 1993) and in Iowa Women's Health Study (French et al., 1997), have shown inclusive (Kaneto et al., 2013; Oguma et al., 2005) and even contradictory results (French et al., 1997; Higgins et al., 1993).

In this study, we used data from Alberta's Tomorrow Project (ATP), a large population-based cohort study in Alberta, Canada, to further elucidate the impact of BMI changes over time, especially BMI reduction, on risk of diabetes in general populations. Compared to controlled intervention studies, this study provides locally relevant and applicable findings to support public health programs aiming to reduce diabetes incidence in general populations.

2. Methods

2.1. Study population

Alberta's Tomorrow Project (ATP) is a population-based prospective cohort study of cancer and chronic diseases in Canada (Ye et al., 2017). From 2000 to 2008, the telephone random digit dialing (RDD) method was used to randomly recruit adult participants aged 35–69 years living in Alberta with no history of cancer, other than non-melanoma skin cancer at the time of enrollment (Ye et al., 2017). Fig. 1 shows the flow chart of inclusion and exclusion of participants for this study. The study population was thus 19,164 diabetes-free participants with BMI measurement available at the baseline and at least one follow-up measurement.

This study was approved by the Health Research Ethics Board of the University of Alberta (study ID Pro00058561).

2.2. BMI measurement

Weight and height were self-reported by participants at baseline and follow-up 2004 and 2008 and were corrected using sex-specific correction factors for self-reporting anthropometrics (Connor Gorber et al., 2008). Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of participant's height in meters. Participants were grouped into “under or normal weight” (BMI < 24.9 kg/m²), “overweight” (BMI: 25–29.9 kg/m²) and “obese” (BMI: 30 + kg/m²) groups as Health Canada's Guideline for Body Weight Classification (Lemieux et al., 2004). Absolute changes in BMI (Δ BMI) were calculated by subtracting the baseline BMI from the BMI measured at follow-ups. Relative changes in BMI, which make comparison easier between participants with different baseline BMI, were quantified as the percentage of changes from baseline. The magnitude of Δ BMI was further classified into “minimal” (\pm 5%), “moderate” (\pm 5–10%) and “large” ($>$ \pm 10%).

2.3. Diabetes case definition

Diabetes diagnosis and medication information was obtained from Alberta Health (AH) administrative healthcare datasets (2000–2015). Diabetes cases were identified using the Canadian National Diabetes Surveillance System (NDSS) algorithm as described (PHAC, 2009). An additional algorithm was developed to identify all potentially prevalent cases, i.e. self-report of diabetes at enrollment, plus any of the following conditions: i) one hospitalization with ICD code for diabetes, ii) one physician claim with ICD code for diabetes, or iii) one diabetes medication with Anatomical Therapeutic Chemical Classification (ATC) code for insulin (A10A) or glucose-lowering drugs (A10B). The index date of

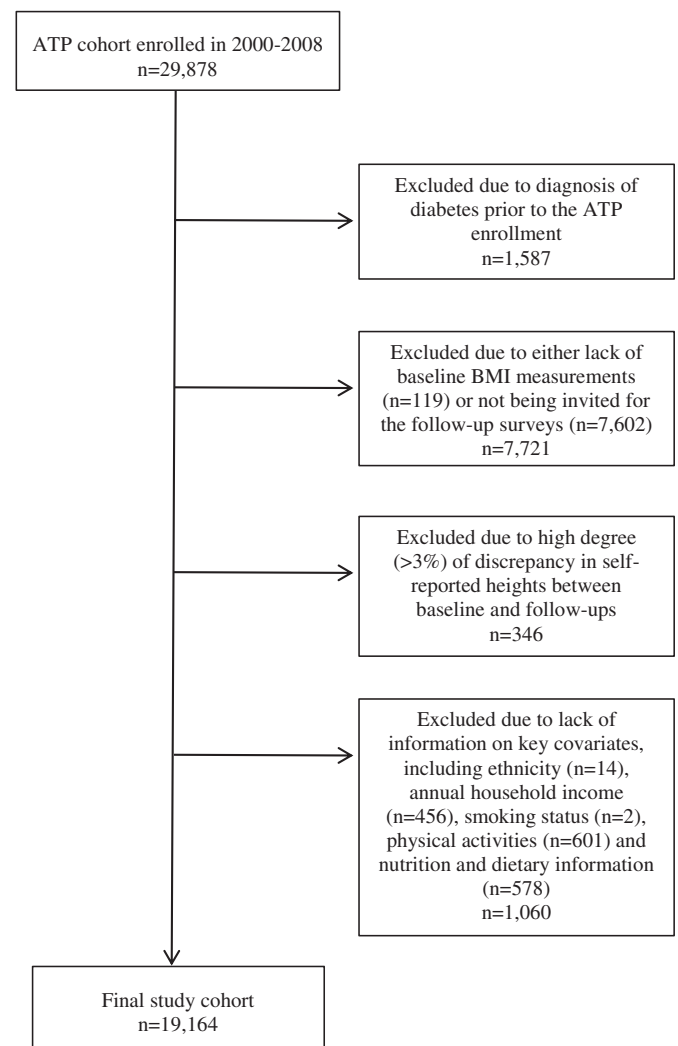


Fig. 1. Flow chart for the inclusion and exclusion of Alberta's Tomorrow Project (ATP) cohort (2000–2008).

diabetes was determined by the earliest date of healthcare records that contribute to the case definition. Cases were identified as “incident” only if the index date was $>$ 6 months after enrollment to ensure true incident cases were identified in a prospective cohort. Incidence rate (IR) of diabetes was defined as number of incident cases per 1000 person-years (PY).

2.4. Other covariates

Based on diabetes risk factors identified in the literature (Wild and Byrne, 2006), participants were further categorized by the following variables at baseline: whether or not (yes/no) they were physically active during leisure time (defined as \geq 210 min of moderate- to vigorous-intensity recreational physical activities per week in the past year) (Whelan et al., 2017); tertiles (high, medium, low) of Healthy Eating Index 2005 Canada (HEI-2005-Canada) (Garriguet, 2009); the Elixhauser comorbidity index [0, 1, \geq 2, as 2 or more comorbidities represent multimorbidity in patients (Ibrahim et al., 2016)], which was calculated using administrative data of a list of disorders, including AIDS, alcohol abuse, anemia, arthritis, cardiovascular diseases, COPD, coagulopathy, depression, diabetes, drug abuse, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, cancers, neurological disorders, paralysis, peripheral vascular disease, psychoses, pulmonary circulation disorder, renal failure, and peptic ulcer disease (Elixhauser et al., 1998; Quan et al., 2005); location of residence (rural/

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