

NOVA University of Newcastle Research Online

nova.newcastle.edu.au

Quatela, Angelica; Callister, Robin; Patterson, Amanda J.; McEvoy, Mark; MacDonald-Wicks, Lesley K.. 'The protective effect of muesli consumption on diabetes risk: results from 12 years of follow-up in the Australian Longitudinal Study on Women's Health'. Published in Nutrition Research Vol. 51, Issue March 2018, p. 12-20 (2018)

Available from: http://dx.doi.org/10.1016/j.nutres.2017.12.007

© 2018. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <u>http://creativecommons.org/licenses/by-nc-nd/4.0/</u>

Accessed from: http://hdl.handle.net/1959.13/1401593

Accepted Manuscript

The protective effect of muesli consumption on diabetes risk: Results from 12 years of follow-up in the Australian Longitudinal Study on Women's Health



Angelica Quatela, Robin Callister, Amanda J Patterson, Mark McEvoy, Lesley K MacDonald-Wicks

 PII:
 S0271-5317(17)30293-2

 DOI:
 https://doi.org/10.1016/j.nutres.2017.12.007

 Reference:
 NTR 7837

 To appear in:
 7 April 2017

Revised date:14 December 2017Accepted date:18 December 2017

Please cite this article as: Angelica Quatela, Robin Callister, Amanda J Patterson, Mark McEvoy, Lesley K MacDonald-Wicks , The protective effect of muesli consumption on diabetes risk: Results from 12 years of follow-up in the Australian Longitudinal Study on Women's Health. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Ntr(2017), https://doi.org/10.1016/j.nutres.2017.12.007

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The protective effect of muesli consumption on diabetes risk: Results from 12 years of follow-up in the Australian Longitudinal Study on Women's Health

Angelica Quatela¹; Robin Callister^{2,3,5}; Amanda J Patterson^{1,3,5}, Mark McEvoy^{4,5}; Lesley K MacDonald-Wicks^{1,3,5*}.

1 Discipline of Nutrition and Dietetics, School of Health Sciences, The University of Newcastle, Callaghan, NSW 2308, Australia

2 School of Biomedical Sciences and Pharmacy, The University of Newcastle, Callaghan, NSW 2308, Australia

3 Priority Research Centre for Physical Activity and Nutrition; The University of Newcastle, Callaghan, NSW 2308, Australia

4 Centre for Clinical Epidemiology & Biostatistics, School of Medicine and Public Health, The University of Newcastle, Callaghan, NSW 2308, Australia

5 Hunter Medical Research Institute, New Lambton, NSW 2305, Australia

* Correspondence: lesley.wicks@newcastle.edu.au; Tel. +612 49216646

Abstract

Diabetes affects 9.8% of Australian women. Breakfast cereal consumption is potentially protective against diabetes. This study investigated the effects of breakfast cereal consumption on the 12-year risk of developing diabetes among mid-aged participants of the Australian Longitudinal Study of Women's Health (ALSWH). It was hypothesized that any breakfast cereal and higher-fiber breakfast cereals would be protective against the risk of developing diabetes. Data from Survey 3 (S3) to Survey 7 (S7) inclusive, from the 1946-51 ALSWH cohort were analyzed. Dietary data were obtained at S3 and the outcome was incident diabetes between S4-S7. Women were excluded if: they reported existing diabetes or impaired glucose tolerance at S3; dietary data were incomplete; or daily energy intake was <4,500 or >20,000kJ. Logistic regression with discrete time survival analyses investigated the association between breakfast cereal intake and incident diabetes. Models were adjusted for income, BMI, smoking, physical activity, education, and dietary intakes and included a measure of time. There were 637 incident cases of diabetes. Breakfast cereal intake per se was not associated with incident diabetes (OR: 1.00; p=0.98). Muesli consumption on its own (OR: 0.74; p=0.00) or as a part of oats-based cereal (OR: 0.84; p=0.047) was significantly associated with a decrease in the odds of developing diabetes. No other breakfast cereals were significantly associated with diabetes risk. Among mid-aged Australian women, muesli consumption was associated with a reduction in diabetes risk. This effect may be due to a particular profile of muesli eaters, but the relationship warrants further investigation.

Keywords: Breakfast; Edible Grain; Diabetes Mellitus; risk; Longitudinal Studies.

Abbreviations

ALSWH: Australian Longitudinal Study of Women's Health.

BMI: Body Mass Index

DQES-FFQv2: Dietary Questionnaire for Epidemiology Studies Version 2 ().

MBS: Medicare Benefits Schedule

MET: Metabolic Equivalent Task

NHMRC: National Health and Medical Research Council guidelines

PBS: Pharmaceutical Benefits Scheme

RMR: Resting Metabolic Rate

WHO: World Health Organization

1. Introduction

Diabetes mellitus is a major public health concern which affected 9.8% of Australian women in 2012 [1]. Worldwide, 8.5% of adults had diabetes in 2014 [2]. Diabetes has a significant impact on quality of life as it is the main cause of renal failure, lower limb amputation and blindness, and a major contributor to cardiovascular disease [2]. One and a half million deaths were due to diabetes in 2012 worldwide [2]. The World Health Organization (WHO) [2] estimated that the cost of diabetes is US\$827 million per year worldwide [3, 4].

Breakfast cereal can be defined as a grain-based food product usually made from oats, rice, wheat or corn, which may be minimally processed, such as drying and rolling the grain (eg. rolled oats), or cooked and flaked or puffed [5]. Several grain varieties may be combined, and fruit and/or nuts added. It is often consumed with milk or yogurt, or in a dry state. Breakfast cereal is often eaten at breakfast, but it can also be consumed as a snack or at other meals during the day.

It has been hypothesized that whole grain breakfast cereals might reduce the risk of diabetes because of their high fiber content and high nutrient density (phytochemicals, vitamins and minerals). The fiber content of wholegrain cereal products is hypothesized to improve the glycemic response to breakfast, and through this mitigate the development of Type 2 diabetes [6, 7]. Concomitantly, refined grains may increase the risk of developing diabetes due to low fiber content and subsequent high glycemic index (GI) or glycemic load [7].

The findings of a recent study conducted by Pastorino et al [8] found a significant increase in the risk of developing diabetes for 43 year old women who consumed a diet higher in fat, higher in GI and lower in fiber (p<0.01 adjusted for confounding factors). This suggests a protective effect for a low fat, low GI and high fiber diet in the development of diabetes for women of this age; however, similar analyses were not significant for men. The Pastorino et al study [8] investigated these characteristics for the diet generally, but the results suggest that the effect of varying glycemic load, fiber and fat content of breakfast cereals warrants investigation in the development of diabetes.

A study by Xu et al [9] reported that in the NIH-AARP Diet and Health Study a highly significant reduction in mortality from diabetes was found for breakfast cereal consumers compared with non-consumers in 367,442 subjects in the U.S.A. (p<0.05, quartile four (highest) OR 0.70, CI: 0.47,1.03) [9]. These promising findings in a U.S. population support the need to investigate these relationships further in other populations.

In 2014 a systematic review [10] conducted by Williams concluded there was limited evidence (grade B of the Australian National Health and Medical Research Council guidelines (NHMRC) [11-13]) supporting the protective effect of regular whole grain and high fiber breakfast cereal consumption regarding the development of diabetes [10]. These findings were supported by a recent systematic review that reported a significant association between high whole grain ready to eat cereal consumption and reduced risk of Type 2 diabetes risk [14]. Furthermore, the systematic review conducted by Williams found only weak evidence (grade D) to indicate that regular breakfast cereal consumption per se may reduce the risk of developing diabetes [10].

It is clear that further research to investigate the effect of breakfast cereal consumption on the risk of developing diabetes is warranted. It was hypothesized that consumption of any breakfast cereal and consumption of higher-fiber breakfast cereals would be protective against the risk of developing diabetes. This hypothesis was investigated by undertaking a longitudinal analysis assessing the effect of consuming any breakfast cereal, higher-fiber breakfast cereal and different types of breakfast cereal on the risk of developing diabetes in a large representative cohort of mid-aged Australian women over a 12-year period.

2. Methods and materials

The ALSWH is a longitudinal study of women in Australia (n=58,000) collected from four age cohorts (14,247 women aged 18-23 y, 13,714 women aged 45-50 y and 12,432 women aged 70-75 y in 1996, and 17,015 women aged 18-23 y in 2013). Data were prospectively gathered from 1996 to 2013. More details regarding the ALSWH are described elsewhere [15].

For the purpose of these analyses, data were obtained from the mid-aged (women aged 45-50 y in S1 in 1996) cohort. Surveys were conducted every 2-3 years since 1996. Dietary data obtained from a food frequency questionnaire [16, 17] at S3 were used to identify participants who consumed breakfast cereal from a list of options. Diabetes incidence data were obtained at S4 (2004) to S7 (2013), up to 12 years after S3 (2001).

2.1 Participants

Data from a representative sample of Australian women born between 1946-51 who formed the mid-aged cohort of the ALSWH [18] were used. These women were randomly sampled from the database of the national health insurance scheme, Medicare, which included all Australian permanent residents and citizens. The women from rural and remote areas were sampled at double the rate of women in urban areas [15]. Ethics approval for the ALSWH was provided from the Human Research Ethics Committees of the University of Newcastle and the University of Queensland [15]. Permission for access to these data for the purpose of these analyses was provided on the 19th of January 2015.

2.2 Predictor variables

The predictor variable was breakfast cereal consumption reported at S3. Dietary data were obtained from a validated food frequency questionnaire: the Dietary Questionnaire for Epidemiological Studies Version 2 (DQES-FFQv2). The DQES-FFQv2 was developed by the Cancer Council Victoria [16-18]. The dietary data were analyzed using the Australian NUTTAB 95 database [19]. The DQES-FFQv2 has been validated amongst childbearing age women who completed the DQES-FFQv2 and a 7-day weighed food diary; the comparison between these two dietary methods confirmed that the DQES-FFQv2 is a valid tool to assess dietary intake in adult women [17].

The DQES-FFQv2 asked the following question: 'Over the last 12 months, on average, how often did you eat the following foods?' The following breakfast cereal options were listed: 1)

All-Bran; 2) Sultana Bran, Fiber Plus, Branflakes; 3) Weet Bix, Vita Brits, Weeties; 4) Cornflakes, Nutrigrain, Special K; 5) muesli; 6) porridge. Sultana bran, Fiber Plus and Branflakes are predominantly flaked wheat products that are high in insoluble fiber and may contain dried fruit. All-bran is a predominantly wheat cereal with a very high total fiber content. Weet Bix, Vita Brits and Weeties are wheat-based products in the form of biscuits. Cornflakes, Nutrigrain and Special K are breakfast cereals low in fibre. Muesli is a rolledoats based cereal, which may or may not be toasted. It usually contains dried fruit and/or nuts and seeds. Porridge is a cooked cereal from rolled oats. It may be whole rolled oats or it may consist of oats that are finely chopped and fast cooked. The frequency of consumption options allowed categorization into a dichotomous variable where 'yes' referred to any consumption higher than 'never' and 'no' referred to no consumption ('never').

The 'any breakfast cereal' variable was a dichotomous variable assigned 'yes' when at least one of the six breakfast cereal categories was consumed and 'no' when no breakfast cereal from these categories was consumed (all six breakfast cereal variables were equal to 'never')[5]. The oats-based cereal category was a dichotomous variable assigned 'yes' when muesli or porridge or both were consumed and 'no' when neither of these breakfast cereals were consumed (both these breakfast cereals were equal to 'never'). The wheat cereal category was 'yes' if any or a multiple of Sultana Bran, Fiber Plus, Branflakes, All-Bran, Weetbix, Vitabrits and Weeties were consumed, and 'no' if none of these cereals were consumed (i.e., all these breakfast cereals were equal to 'never'). The 'higher fiber' (or whole grain) breakfast cereal was a dichotomous variable assigned 'yes' when at least one of the five breakfast cereal groups (muesli, porridge, All-Bran, Sultana Bran group, Weet Bix group) was consumed.

2.3 Outcome variable

The outcome variable was diabetes incidence from S4-S7. Women with pre-existing diabetes (S1-3) or impaired glucose tolerance (IGT) (S3) were excluded from the analyses. These outcomes were determined from the following questions: 'Have you ever been told by a doctor that you have', which was followed by a list of diseases including diabetes in S1 or insulin dependent diabetes and non-insulin dependent diabetes in S2. In the subsequent surveys (S3-S7) the question was: 'In the past three years have you been diagnosed or treated for' where the list of options included IGT, insulin dependent diabetes and non-insulin dependent diabetes and non-insulin dependent diabetes (high blood sugar) in S3; or diabetes (high blood sugar) in S4 to S7. Diabetes and IGT variables were dichotomous variables (yes/no development of diabetes and/or IGT). Lowe et al [20] compared 388 mid-aged women suffering from diabetes in one or more of these surveys (S1-4) with the Medicare (MBS) and Pharmaceutical Benefits Scheme (PBS) databases for the years 2002-2005 [20]. This study demonstrated self-reported diabetes to be a reliable assessment of diabetes incidence in this cohort [20].

2.4 Identification and measurement of confounding factors

Marital status, income, body mass index (BMI), smoking, physical activity, education, area of residence, sedentary behavior, dietary intakes (fiber and daily energy) were considered as potential confounders. The potential confounding variables were obtained from S3 apart from education level which was collected at S1.

Income was considered in terms of the ability to manage on current income rather than consideration of the actual monetary income level. The ability to manage on current income was categorized as: easy (it is not too bad or it is easy) or difficult (it is impossible; it is difficult all the time; it is difficult some of the time). BMI was calculated based on selfreported height and weight. Burton et al [21] validated the self-reported height, weight and BMI in 159 women from the mid-aged cohort and found substantial agreement between the measured and self-reported height, weight and BMI [21]. BMI was provided as a continuous variable, however for the purpose of this analysis, this variable was categorized as: BMI <30 and BMI \geq 30 kgm⁻². Smoking status was categorized as: never-smokers, ex-smokers, or smokers.

Physical activity was determined using items from Active Australia's 1999 National Physical Activity Survey [22]. Physical activity level was estimated in Metabolic Equivalent Task (MET) minutes. MET refers to a unit of resting metabolic rate (RMR) and is typically considered to be $3.5\text{mL O}_2/\text{kg/minute}$ [23]. MET minutes were calculated using different coefficients for each intensity of physical activity as follows: 3.0* X minutes of walking, 4.0*X minutes of moderate intensity activities, and 7.5* X minutes of vigorous intensity activities; activity was then summed to provide total MET minutes per week [23, 24]. Physical activity was categorized as: Nil/sedentary for <40, low for 40 to <600, moderate for 600 to <1200, and high for \ge 1200 MET minutes per week [24].

Education was determined at Survey 1 and was categorized as the following three options: no formal qualifications; Intermediate Certificate (or equivalent) or Higher School or Leaving Certificate (or equivalent) or Trade/apprenticeship (eg. Hairdresser, Chef) or

10

Certificate/diploma (eg. Child Care, Technician); University degree or University Higher degree (eg. Grad Dip, Masters, PhD).

The dietary factors, daily energy intake (kJ/d) and daily fiber intake (g/d) intake), were derived from the DQES-FFQv2 using the NUTTAB 95 database [19] as described above.

2.5 Statistical analyses

The characteristics of the women who did or did not report consuming breakfast cereal were compared using two sample t tests for proportions, two sample independent t tests (for parametric distributions), or Wilcoxon Rank Sum Tests (for non-parametric distributions).

Multiple logistic regression models were used to investigate the association between breakfast cereal intake category (coded as yes/no consumption) at S3 and the risk of developing diabetes between S4 to S7. Associations between breakfast cereal consumption and subsequent incidence of diabetes were determined using unadjusted and adjusted (for confounding factors) logistic regression with discrete time survival analysis models. Women were excluded if: DQES-FFQv2 at S3 was not completed; they reported existing diabetes at S1-3 or impaired glucose tolerance at S3; or if daily energy intake at S3 was \leq 4,500 or \geq 20,000 kJ/d [25, 26].

The following method was used to identify potentially confounding factors for the longitudinal analyses. A variable was considered a potential confounder when the p value of the regression analysis for the potentially confounding variable with both the predictor and outcome variables was ≤ 0.2 [5]. Variables that met these criteria were included in multivariate analyses. In order to account for the consumption of breakfast cereals in addition to the category being investigated, the 'other breakfast cereal consumption' variable (coded as 'yes' or 'no') was created and adjusted for in the analysis.

Four statistical models were produced. The first (unadjusted, univariate) had only the breakfast cereal variable of interest and a discrete measure of time (survey wave). The second model included non-dietary confounding factors (income, BMI, smoking status, physical activity and education). The third model included the dietary confounding factors (daily energy intake, fiber intake, and consumption of other breakfast cereal). The fourth fully adjusted model included all confounding factors (dietary and non-dietary). Separate analyses were undertaken to examine associations with consumption of any breakfast cereals; for each of the six categories of cereals listed in the survey; for any of the wheat-based cereals; for any of the oats-based cereals and for any of the higher fiber (whole grain) breakfast cereals. The Hosmer–Lemeshow goodness-of-fit test was used to determine how well the logistic regression models fit the data. All analyses were completed using STATA version 13.

3. Results

A total of 11,226 women completed S3 of whom 10,629 completed the DQES (5.3% did not complete the DQES-FFQv2); 536 (4.8%) women were excluded because they reported existing diabetes at S1/S2/S3 and 60 (0.5%) women were excluded because they reported

12

existing IGT at S3 (baseline); 1611(14.4%) women were excluded because their daily energy intake at S3 was either \leq 4500 kJ or \geq 20,000 kJ/day. A total of 8422 (75%) women were included in the analyses (Figure 1).

3.1 Participant characteristics

The characteristics are presented for all participants, and for those who consumed any breakfast cereal, no cereal, and each individual breakfast cereal category (Tables 1 and 2). For the overall population, age was 52.5 (1.5) y (median (inter quartile range)). Most women (82.0%) were either married or in a defacto relationship. A large proportion of the study population (61.8%) found that managing on their income was either easy or not too bad. Forty two percent were healthy weight, 30.4% were overweight and 21.5% were obese. The majority of the participants (61.7%) were never smokers. Fifty percent of the population was sedentary or engaging in low levels of activity. The majority of the study population (68.8%) had a school qualification (Intermediate Certificate (or equivalent) or Higher School or Leaving Certificate (or equivalent) or Trade/apprenticeship (eg. Hairdresser, Chef) or Certificate/diploma (eg. Child Care, Technician)). The median and interquartile range for dietary factors were: energy intake from diet 6699 (2482) kJ/d, energy intake from alcohol 121.3 (435.2) kJ/d, and fiber intake 20.0 (9.2) g/d. When compared to the Nutrient Reference Values for Australians and New Zealanders, median alcohol intake provided 1.7% of energy ingested, which met the Australian recommendation of <5% [27]. Median fiber intake (20.0 g/d) was lower than the Australian recommendation of 28 g/d [27].

Breakfast cereal consumers differed significantly from those who did not eat any breakfast cereal on a number of characteristics (Table 1). Those who did not eat cereal were more

likely to be smokers, sedentary or less engaged in moderate levels of physical activity, and had lower education qualifications. Furthermore, those who did not eat breakfast cereal consumed lower daily energy from diet but more energy from alcohol and had lower fiber intakes than cereal consumers.

3.2 Breakfast cereal consumption and the risk of developing Diabetes

During 12 years of follow-up, 637 (7.6%) incident cases of diabetes mellitus were reported. Table 3 presents the logistic regression models with survival analyses for all breakfast cereal categories both unadjusted and adjusted for confounding factors. Consumption of 'any' breakfast cereal (one or more cereal categories) was not significantly associated with the risk of developing diabetes (OR: 1.00; p=0.98). Muesli was the only individual breakfast cereal found to be significantly associated with a reduction in the risk of diabetes (OR: 0.74, p=0.00). None of the other individual breakfast cereal categories were associated with a reduction in the risk of diabetes (Table 2). Oats-based cereal (either porridge or muesli or both) consumption was significantly associated with a reduction in the risk of developing diabetes (OR: 0.84; p=0.047). Wheat-based cereal (one or more of Sultana Bran, Fiber Plus, Branflakes; All-Bran; Weet bix, Vita Brits, Weeties) consumption was not significantly associated with risk of developing diabetes (OR: 1.16; p=0.14). Higher fiber breakfast cereal (one or more of five breakfast cereal categories excluding Cornflakes, Nutrigrain and Special K) was not significantly associated with risk of developing diabetes (OR:0.82; p=0.12).

4. Discussion

This study investigated the role of consuming breakfast cereal on the risk of developing diabetes in a large cohort of mid-aged Australian women. The majority of the breakfast cereal categories had no protective effect on developing diabetes over 12 years. Only muesli, consumed either by itself or as part of the oats-based cereal category, was protective against the development of diabetes. Also, consumption of higher fiber (whole grain) cereals did not provide protection from diabetes in these women. Therefore, our analysis did not support the hypothesized protective effect of consuming any breakfast cereal or higher-fiber cereals on diabetes risk.

Williams [10] conducted a systematic review that investigated a number of research questions pertinent to this study. Although Williams [10] found only limited evidence supporting the beneficial effect of regular breakfast cereal consumption on diabetes, our study found no significant relationship between breakfast cereal intake per se and risk. Xu et al [9] reported a highly significant reduction in mortality from diabetes for breakfast cereal consumers compared with non-consumers in a large cohort in the US. The odds ratio (0.70) of benefit was similar to the one obtained with muesli (0.75) in our study investigating diabetes incidence. In our cohort, although there was not a significant relationship between 'any' breakfast cereal intake and diabetes incidence, breakfast cereal eaters had significantly healthier lifestyle characteristics compared with non-consumers, specifically regarding smoking status, physical activity and dietary intake, which are all factors believed to be protective against the risk of developing diabetes.

The protective effect of oats-based breakfast cereal (muesli and porridge) in our study did not extend to porridge when analyzed individually. It is possible that this association of oatsbased cereal with diabetes is being driven by muesli consumption, and that something other than the oats in muesli is protective against diabetes, or that there is something particular about muesli eaters that we have not been able to adjust for. Also, porridge consumption in Australia is very seasonally based and is mostly consumed in the winter months. Therefore, porridge intake may not be sufficiently consistent to exert a protective effect against diabetes. Another option is that porridge intake may have not been assessed to its full potential due to the season when the dietary data were gathered.

Williams [10] did not report on cohort studies that investigated muesli or oats-based cereal and diabetes, but did review short-term interventions in diabetic or normal populations investigating the effect of oats-based cereal, muesli or other types of breakfast cereals on glucose and insulin metabolism. In the majority of the studies conducted in diabetic populations, consumption of oats-based cereals or barley resulted in better glycemic control [28-32]. This suggests that the better glycemic control may be a possible mechanism of action for the protective effect of muesli or oats-based breakfast cereals on diabetes. However, this potential mechanism of action does not help to explain the differences we have observed in this study between muesli and porridge consumption.

The trials summarized in the systematic review by Williams [10] were predominantly shortterm studies and in populations diagnosed with diabetes. Long-term intervention studies and longitudinal analyses in prospective cohorts (like the analysis in this paper and the one

conducted by Xu et al [9]) are needed in other populations to further investigate the effects of muesli, porridge and other breakfast cereals on diabetes risk to develop more robust evidence.

Two systematic reviews [14, 33] reported evidence supporting an association between regular or frequent whole grain or higher fiber breakfast cereal consumption and lower risk of diabetes from two prospective studies: the Physicians Health study [29] and the Nurses Health study [34]. Specifically, Kochar et al [35] found that breakfast cereal consumption was associated with a significantly decreased risk of diabetes over a mean of 19.1 years follow up among 21,152 US males physicians (fully adjusted models: ≤1 serving/week 0.83 (0.79 to 0.93); 2-6 servings/week 0.76 (0.67 to 0.86), \geq 7 servings/week 0.69 (0.60 to 0.79); p for linear trend <0.0001). This association was stronger for whole grain consumption (fully adjusted models: ≤ 1 serving/week 0.75 (0.64 to 0.88); 2-6 servings/week 0.76 (0.66 to 0.87); \geq 7 servings/week 0.60 (0.50 to 0.71); p<0.001) compared to refined grains (fully adjusted models: ≤ 1 serving/week 0.88 (0.70 to 1.1); 2-6 servings/week 0.69 (0.53 to 0.90); ≥ 7 servings/week 0.95 (0.73 to 1.3); p for linear trend= 0.05). The findings from the analyses of the Nurses Health study [34] also reported a significant protective effect of whole grain breakfast cereal on diabetes risk over 10 years among 75,521 women (fully adjusted models: ≤1 serving/week 0.81 (0.71, 0.93); 2 to 4 servings/week 0.70 (0.60, 0.81); 5-6 servings/week 0.71 (0.62, 0.82); ≤1 serving/day 0.66 (0.55, 0.80), p trend <0.0001) [34]. However, Williams' review reported on another prospective study (Whitehall Study II), which found conflicting results [36]. This study analyzed 7,339 participants aged 39-63 y for 12 years and found no significant association between medium or higher fiber breakfast cereal consumption and diabetes risk. These conflicting results suggest the need for more studies to be conducted on this topic to further explore the effects of whole grain and higher fiber cereal on diabetes risk. One possible explanation for the difference between these studies is cultural

differences in the foods eaten, that are an alternative to cereal consumption and their association with diabetes risk.

In our study, 'any higher-fiber cereal intake' was significant in unadjusted analyses or models adjusted for other dietary factors but not significant when adjusted for other lifestyle or demographic factors, such as smoking status, physical activity level, education and income. This suggests that the consumption of whole grain or higher-fiber cereals is associated with other positive lifestyle and demographic characteristics aligned with good health

Our study has a number of strengths, the first of which is the large representative sample of women used in the analysis. Furthermore, the longitudinal analysis of prospectively collected data, reducing potential bias, is a major strength of the study. The long period of follow-up (12 years) is a strength of this analysis in relation to other studies looking at breakfast cereal consumption. Additional strengths include the robust statistical approach used and the utilization of a validated FFQ.

In terms of limitations, our study relies completely on self-reported data. However, two validation studies, one validating the DQES-FFQv2 [15, 17] and the other diabetes incidence [20], suggest that the reported data are adequately accurate. The DQESv2 FFQ does not allow completers to specify when the breakfast cereal was consumed or how it was prepared. Also, rice-based breakfast cereals are not captured by the DQESv2, so we cannot comment on the role of these on diabetes risk. Whether diabetes incidence was Type 1 or Type 2 diabetes was not able to be determined, as the majority of the surveys did not provide this detail, however,

considering the age group investigated, most will have developed Type 2 diabetes. This paper followed a rigorous methodology to establish the confounding factors to adjust for in this analysis. Though, it is possible that some unknown factors not collected in the surveys may have acted as confounders and they could have not been adjusted for. We acknowledge that the DQESv2 FFQ includes a limited list of breakfast cereal options, and the bluntness of this tool is likely to have influenced our ability to examine some aspects of breakfast cereal consumption. While the breakfast cereal categories do cover most common cereal types from the perspective of nutrition professionals, it is possible that if the women from the ALSWH cohort did not see their particular breakfast cereal listed in the FFQ, then they might have chosen none. The listed brand names within the FFQ are designed to be examples of the types of cereals that would fit in these categories (eg. Sultana Bran, Fiber Plus, Branflakes are examples of high fiber wheat-based cereals of which there are many other brand names in Australia). However, there is no specific direction on how to complete the breakfast cereal questions in the DQESv2 FFQ or that these examples should be used to enable people to categorize their cereal choices.

Finally, consumption of muesli by itself or as part of an oats-based cereal category in the eating pattern of Australian women was found to be protective against the development of diabetes. This effect may be due to a particular profile of muesli eaters, but these relationships warrant further investigation.

Acknowledgment

The research on which this paper is based was conducted as part of the Australian Longitudinal Study on Women's Health, the University of Newcastle and the University of Queensland. We are grateful to the Australian Government Department of Health for funding and to the women who provided the survey data. The authors thank Professor Graham Giles of the Cancer Epidemiology Centre of Cancer Council Victoria, for permission to use the Dietary Questionnaire for Epidemiological Studies (Version 2), Melbourne: Cancer Council Victoria, 1996. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Human Research Ethics Committee of the University of Newcastle and University of Queensland. Written informed consent was obtained from all subjects. This work was supported by the Australian Government Research Training Program (RTP) Scholarship. All authors (AQ; RC; AP; MM; LMW) have made substantial contributions to all of the following: conception and design of the study, analysis and interpretation of data, drafting the paper, critically revising the paper for important intellectual content and final approval of the version to be submitted. There are no conflicts of interest to declare.

References

[1] Australia Diabetets (AusDiab). The australian diabetes, obesity and lifestyle study,

https://www.bakeridi.edu.au/Assets/Files/Baker%20IDI%20Ausdiab%20Report_interactive_FINAL.p df.; (2012) (accessed 21 April 2017)

[2] World Health Organization (WHO). Global Report on Diabetes.,

http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf?ua=1; 2017 (Accessed 14 December 2017)

[3] Seuring T, Archangelidi O, Suhrcke M. The Economic Costs of Type 2 Diabetes: A Global Systematic Review. PharmacoEconomics. 2015;33:811-31.

[4] Collaboration NRF. Worldwide trends in diabetes since 1980: a pooled analysis of 751 populationbased studies with 4.4 million participants. The Lancet. 2016;387:1513-30.

[5] Quatela A, Callister R, Patterson A, McEvoy M, MacDonald-Wicks L. Breakfast Cereal Consumption and Obesity Risk amongst the Mid-Age Cohort of the Australian Longitudinal Study on Women's Health. Healthcare. 2017;5:49.

[6] Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr. 2000;71:921-30.

[7] Aune D, Norat T, Romundstad P, Vatten LJ. Whole grain and refined grain consumption and the risk of type 2 diabetes: a systematic review and dose–response meta-analysis of cohort studies. Eur J Epidemiol. 2013;28:845-58.

[8] Pastorino S, Richards M, Pierce M, Ambrosini GL. A high-fat, high-glycaemic index, low-fibre dietary pattern is prospectively associated with type 2 diabetes in a British birth cohort. Br J Nutr. 2016;115:1632-42.

[9] Xu M, Huang T, Lee AW, Qi L, Cho S. Ready-to-Eat Cereal Consumption with Total and Cause-Specific Mortality: Prospective Analysis of 367,442 Individuals. J Am Coll Nutr. 2016;35:217-23.
[10] Williams PG. The Benefits of Breakfast Cereal Consumption: A Systematic Review of the Evidence Base. Adv Nutr. 2014;5:636S-73S.

[11] Allman-Farinelli M, Byron A, Collins C, Gifford J, Williams PG. Challenges and lessons from systematic literature reviews for the Australian dietary guidelines. Aust J Prim Health. 2014;20 236-40.

[12] Mational Health Medical Research Council (NHMRC). NHMRC additional levels of evidence and grades for recommendations for developers of guidelines,

http://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/stage_2_consultation_levels_and_grades.pd f; 2009 (Accessed 5 june 2017)

[13] NHMRC. How to asses the evidence, https://www.nhmrc.gov.au/guidelines/publications/cp69, 2011 (Accessed 5 june 2017).

[14] Priebe MG, McMonagle JR. Effects of Ready-to-Eat-Cereals on Key Nutritional and Health Outcomes: A Systematic Review. PLoS ONE. 2016;11:e0164931.

[15] Lee C, Dobson AJ, Brown WJ, Bryson L, Byles J, Warner-Smith P, et al. Cohort Profile: The Australian Longitudinal Study on Women's Health. Int J Epidemiol 2005;34:987-91.

[16] Giles G, Ireland P. Dietary Questionnaire for Epidemiological Studies (Version 2),. Melbourne: Cancer Council Victoria 1996

[17] Hodge A, Patterson AJ, Brown WJ, Ireland P, Giles G. The Anti Cancer Council of Victoria FFQ: relative validity of nutrient intakes compared with weighed food records in young to middle-aged women in a study of iron supplementation. ANZJPH. 2000;24:576-83.

[18] ALSWH. Australian Longitudinal Study on Women's Health: Surveys Women's Health Australia, , from http://www.alswh.org.au/for-researchers/surveys. 2017 (Accessed 5 June 2017).

[19] Lewis J, Milligan G, Hunt A. NUTTAB95 Nutrient Data Table for Use in Australia. Canberra 1995.[20] Lowe J, Byles J, Dolja-Gore X, Young A. Does systematically organized care improve outcomes for women with diabetes? J Eval Clin Pract. 2010;16:887-94.

[21] Burton NW, Brown W, Dobson A. Accuracy of body mass index estimated from self-reported height and weight in mid-aged Australian women. ANZJPH. 2010;34:620-3.

[22] Armstrong T, Bauman A, Davies JP. Physical activity patterns of Australian adults: Results of the 1999 National Physical Activity Survey. Canberra: Australian Institute of Health and Welfare; 2000.
[23] Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis jF, et al. Compendium of Physical Activities: classification of energy costs of human physical activities. Med Sci Sports. 1993;25:71-80.

[24] ALSWH. Physical Activity – Survey 2 and later surveys,

http://www.alswh.org.au/images/content/pdf/InfoData/Data_Dictionary_Supplement/DDSSection2 PA_S2andlater.pdf. 2017 (Accessed 5 June 2017).

[25] Meltzer HM, Brantsæter AL, Ydersbond TA, Alexander J, Haugen M. Methodological challenges when monitoring the diet of pregnant women in a large study: experiences from the Norwegian Mother and Child Cohort Study (MoBa). Matern Child Nutr. 2008;4:14-27.

[26] Dodd JM, Cramp C, Sui Z, Yelland LN, Deussen AR, Grivell RM, et al. The effects of antenatal dietary and lifestyle advice for women who are overweight or obese on maternal diet and physical activity: the LIMIT randomised trial. BMC Med. 2014;12:1-19.

[27] NHMRC. Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes. 2005.

[28] Colagiuri S, Miller JJ, Holliday JL, Phelan E. Comparison of Plasma Glucose, Serum Insulin, and C-Peptide Responses to Three Isocaloric Breakfasts in Non-Insulin-Dependent Diabetic Subjects. Diabetes Care. 1986;9:250-4.

[29] Golay A, Koellreutter B, Bloise D, Assal J-P, Würsch P. The effect of muesli or cornflakes at breakfast on carbohydrate metabolism in type 2 diabetic patients. Diabetes Res Clin Pract Suppl. 1992;15:135-41.

[30] Tsihlias EB, Gibbs AL, McBurney MI, Wolever TM. Comparison of high- and low-glycemic-index breakfast cereals with monounsaturated fat in the long-term dietary management of type 2 diabetes. Am J Clin Nutr. 2000;72:439-49.

[31] Tappy L, Gügolz E, Würsch P. Effects of Breakfast Cereals Containing Various Amounts of β -Glucan Fibers on Plasma Glucose and Insulin Responses in NIDDM Subjects. Diabetes Care. 1996;19:831-4.

[32] Rendell M, Vanderhoof J, Venn M, Shehan MA, Arndt E, Rao CS, et al. Effect of a Barley Breakfast Cereal on Blood Glucose and Insulin Response in Normal and Diabetic Patients. Plant Foods Hum Nutr. 2005;60:63-7.

[33] Williams PG. The Benefits of Breakfast Cereal Consumption: A Systematic Review of the Evidence Base. Adv Nutr 2014;5:636S-73S.

[34] Liu S, Manson JE, Stampfer MJ, Hu FB, Giovannucci E, Colditz GA, et al. A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women. Am J Public Health. 2000;90:1409-15.

[35] Kochar J, Djousse L, Gaziano JM. Breakfast cereals and risk of type 2 diabetes in the Physicians' Health Study I. Obesity (Silver Spring, Md). 2007;15:3039-44.

[36] McNaughton SA, Mishra GD, Brunner EJ. Dietary Patterns, Insulin Resistance, and Incidence of Type 2 Diabetes in the Whitehall II Study. Diabetes Care. 2008;31:1343-8.



Figure 1. Flow chart of participant selection

Table 1. Characteristics of participants from the mid-age (2001) cohort of the Australian Longitudinal Study of Women's Health at Survey 3 (n=8422); comparison of participants consuming 'any' cereal or 'no' cereal.

	All	'Any'	'No'	No cereal vs
	participants	cereal	cereal	cereal
				P value
Sample size (n)	8422	91.5% (7702)	8.6% (720)	
		(× .	
*Age (y)	52.5 (1.5)	52.5 (1.5)	52.5 (1.4)	0.7097
Managing income				
¹ Difficult	37.2%	37.0%	40.4%	0.0659
² Easy	61.8%	62.0%	59.2%	0.1280
Education				
No qualification	15.0%	14.7%	17.8%	0.0288
³ School	68.8%	68.8%	69.4%	0.7105
⁴ University	15.5%	15.8%	12.1%	0.0088
Weight status				
⁵ Healthy weight	41.7%	41.5%	44.0%	0.1945
⁵ Overweight	30.4%	30.6%	28.3%	0.2082
⁵ Obese	21.5%	21.7%	19.7%	0.2150
Smoking status				
Never smokers	61.7%	62.7%	50.7%	0.0000
Ex-smokers	24.0%	23.8%	26.3%	0.1475
⁶ Current smoker	13.9%	13.1%	22.6%	0.0000

	All	'Any'	'No'	No cereal vs	
	participants	cereal	cereal	cereal	
				P value	
Physical Activity					
Sedentary	17.2%	17.0%	22.1%	0.0005	
Low PA	33.0%	33.1%	32.1%	0.5760	
Moderate PA	20.9%	21.2%	16.9%	0.0068	
High PA	27.6%	27.6%	27.4%	0.8719	
Diet			5		
*Energy from diet (kJ/d)	6699 (2482)	6737 (2507)	6249 (2178)	0.0000	
*Energy from alcohol (kJ/d)	121 (435)	120 (410)	153 (650)	0.0157	
*Fiber (g/d)	20.0 (9.2)	20.4 (9.3)	16.7 (6.6)	0.0000	

This table summarizes the data from the 8422 women included in the analyses.*Data are presented as median (interquartile range). The rest of the data are presented as mean (SD) or % of participants. ¹Income difficult: Managing income is impossible, difficult all or some of the time

²Income easy: Managing income is not too bad or is easy

³School: Intermediate Certificate (or equivalent) or Higher School or Leaving Certificate (or

equivalent) or Trade/apprenticeship (eg. Hairdresser, Chef) or

Certificate/diploma (eg. Child Care, Technician)

⁴ University: University degree or University Higher degree (eg. Grad Dip, Masters, PhD)

⁵Healthy weight, overweight and obese classifications based on BMI.

⁶Current smoker: was defined as (smoker, an indeterminate amount; smoker, less than 10 per day;

smoker, 10-19 per day and smoker, 20 or more per day)

Table 2. Characteristics of participants from the mid-age (2001) cohort of the Australian Longitudinal Study of Women's Health at Survey 3 (n=8422) by individual breakfast cereal consumption category.

	Muesli	Porridge	All-Bran	Sultana Bran,	Weet Bix, Vita	Cornflakes,
				Fiber Plus,	Brits, Weeties	Nutrigrain &
				Branflakes		Special K
Sample size (n)	36.2% (3,051)	51.1% (4,306)	22.7% (1,910)	31.9% (2,685)	53.2% (4,478)	44.0% (3,707)
*Age (y)	52.5 (1.4)	52.5 (1.5)	52.5 (1.4)	52.4 (1.5)	52.5 (1.5)	52.5 (1.5)
Managing income			NF			
¹ Difficult	32.6%	37.9%	35.4%	37.1%	38.2%	38.9
² Easy	66.6%	861.4%	63.6%	62.0%	60.9%	60.1%
Education						
No qualification	9.1%	14.3%	13.3%	14.5%	15.0%	15.8%
³ School	66.9%	68.9%	69.4%	68.6%	70.2%	70.2%
⁴ University	23.3%	16.0%	16.3%	15.8%	14.1%	13.3%

	Muesli	Porridge	All-Bran	Sultana Bran,	Weet Bix, Vita	Cornflakes,
				Fiber Plus,	Brits, Weeties	Nutrigrain &
				Branflakes	~	Special K
Weight status					<i>P '</i>	
⁵ Healthy weight	47.2%	41.5%	46.0%	40.6%	40.9%	38.3%
⁵ Overweight	29.6%	31.0%	29.8%	31.5%	30.5%	31.3%
⁵ Obese	18.3%	21.5%	18.0%	21.9%	22.4%	23.3%
Smoking status			- NP			
Never smokers	65.8%	64.3%	65.6%	65.1%	63.7%	63.2%
		16				
Ex-smokers	24.3%	23.8%	23.9%	22.2%	23.3%	22.7%
	~					
⁶ Current smoker	9.6%	11.6%	10.2%	12.3%	12.8%	13.8%
Physical Activity						
Sedentary	12.0%	16.1%	13.0%	14.5%	16.2%	17.6%
Low PA	34.1%	33.4%	33.2%	35.9%	34.1%	34.7%

	Muesli	Porridge	All-Bran	Sultana Bran,	Weet Bix, Vita	Cornflakes,
				Fiber Plus,	Brits, Weeties	Nutrigrain &
				Branflakes		Special K
Moderate PA	22.8%	21.3%	22.8%	21.6%	21.8%	20.9%
				CP		
High PA	30.2%	28.3%	30.1%	27.2%	26.9%	25.8%
Diet				N		
*Energy from diet (kJ/d)	6782 (2450)	6859 (2592)	6813 (2528)	6818 (2601)	6857 (2545)	6904 (2644)
*Energy from alcohol	178 (483)	113 (387)	153 (462)	138 (437)	113 (400)	108 (398)
(kJ/d)						
*Fiber (g/d)	21.6 (9.0)	20.9 (9.4)	23.4 (11.3)	21.4 (9.7)	20.6 (9.4)	19.7 (9.2)

This table summarizes the data from the 8422 women included in the analyses.*Data are presented as median (interquartile range). The rest of the data are presented as mean (SD) or % of participants.

¹Income difficult: Managing income is impossible, difficult all or some of the time

²Income easy: Managing income is not too bad or is easy

³School: Intermediate Certificate (or equivalent) or Higher School or Leaving Certificate (or equivalent) or Trade/apprenticeship (eg. Hairdresser, Chef)

or

Certificate/diploma (eg. Child Care, Technician)

⁴ University: University degree or University Higher degree (eg. Grad Dip, Masters, PhD)

⁵Healthy weight, overweight and obese classifications based on BMI.

. 10 per da ⁶Current smoker: was defined as (smoker, an indeterminate amount; smoker, less than 10 per day; smoker, 10-19 per day and smoker, 20 or more per

day)

Table 3. Logistic regression models with descrete time survival analyses of the effect of consuming breakfast cereal at S3 on the risk of

developing diabetes at S4-7 amongst 8422 mid-age women.

Breakfast cereal	Model 1*		Model 2*	, C	Model 3*		Model 4*	
	Odd ratio	Р	Odd ratio (CI)	Р	Odd ratio	Р	Odd ratio	P value
	(CI)	value	1An	value	(CI)	value	(CI)	
Any cereal	0.93 (0.70,	0.60	1.01 (0.74,	0.95	0.96 (0.73,	0.80	1.00 (0.73,	0.98
	1.23)		1.38)		1.28)		1.38)	
Muesli	0.61 (0.51,	0.00	0.74 (0.61,	0.00	0.62 (0.52,	0.00	0.74 (0.61,	0.00
	0.73)		0.90)		0.74)		0.90)	
Porridge	0.89 (0.76,	0.15	0.95	0.55	0.88 (0.75,	0.13	0.93 (0.78,	0.42
P	1.04)		(0.80,1.13)		1.04)		1.11)	
All-Bran	0.93 (0.77,	0.46	1.01 (0.82,	0.91	0.99 (0.81,	0.93	1.01 (0.82,	0.90
	1.13)		1.25)		1.21)		1.26)	

Breakfast cereal	Model 1*		Model 2*		Model 3*		Model 4*	
	Odd ratio	Р	Odd ratio (CI)	Р	Odd ratio	Р	Odd ratio	P value
	(CI)	value		value	(CI)	value	(CI)	
Sultana Bran/ Fiber Plus/	0.99 (0.84,	0.91	1.00 (0.83,	0.98	1.01 (0.86,	0.87	0.99 (0.83,	0.96
Branflakes	1.17)		1.20)	C	1.20)		1.20)	
Weet Bix/ Vita Brits/ Weeties	1.13 (0.96,	0.14	1.13 (0.95,	0.16	1.14 (0.97,	0.11	1.13 (0.95,	0.16
	1.32)		1.34)		1.34)		1.35)	
Cornflakes/ Nutrigrain/ Special	1.25 (1.07,	0.01	1.16 (0.98 ,	0.08	1.23 (1.05,	0.01	1.17 (0.99,	0.07
Κ	1.46)	C	1.38)		1.44)		1.39)	
Oats-based cereal	0.74 (0.63,	0.00	0.86 (0.72;	0.09	0.73 (0.62,	0.00	0.84 (0.70,	0.05**
	0.87)		1.02)		0.86)		1.00)	
Wheat-based	1.12 (0.94,	0.22	1.15 (0.95,	0.17	1.18 (0.98,	0.08	1.16	0.14
cereal	1.33)		1.39)		1.41)		(0.95,1.41)	
Higher fiber (or whole grain)	0.76 (0.61,	0.02	0.85	0.19	0.77 (0.61,	0.02	0.82	0.12
cereal 0	.95)	((0.67,1.08)		0.97)		(0.64,1.05)	

*Model 1 univariate model with predictor variable, outcome and a discrete measure of time (wave)

Model 2 with predictor variable, outcome, a discrete measure of time and adjusted for non dietary counfounding factors (income, education,

BMI, smoking and physical activity)

Model 3 with predictor variable, outcome, a discrete measure of time and adjusted for dietary counfounding factors (daily energy intake, fiber,

and other breakfast cereals consumption)

Justed for d Model 4 with predictor variable, outcome, a discrete measure of time and adjusted for dietary and non dietary counfouding factors.

**p=0.047