



## Original article

# Potato consumption and risk of type 2 diabetes: A dose–response meta-analysis of cohort studies



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## SUMMARY

**Background & aims:** High potato intake has been suggested as a risk factor for the development of type 2 diabetes. We aimed to investigate the association between potato consumption and risk of type 2 diabetes.

**Methods:** A systematic review was conducted on PubMed and Embase from the database commencement until September 2017 (updated by June 2018) following the MOOSE guidelines. The random effect model dose–response meta-analysis method of Greenland and Longnecker was used to estimate the maximally adjusted log hazard ratio (HR) for a unit (serving per day) increment of potato consumption. A restricted cubic spline model with three knots was used to evaluate the potential non-linear relationship. **Results:** A total of 3544 citations were retrieved from the databases, of which six prospective cohort studies including 4545230 person-year of follow-up and 17,758 diabetes cases met the inclusion criteria. The pooled dose–response HR per an increment of 1 serving/day of total potato consumption was 1.20 (95% CI 1.13 to 1.27,  $P < 0.001$ ,  $I^2 = 27.1\%$ ,  $P$  for heterogeneity = 0.23) both in men and women. The larger risk were observed for 2 serving/day (HR 1.44, 95% CI 1.28 to 1.63) and 3 serving/day (HR 1.74, 95% CI 1.45 to 2.09). We found significant evidence of a non-linear association between total potato consumption and risk of type 2 diabetes ( $X^2 = 17.5$ ,  $P$  for linearity  $< 0.001$ ).

**Conclusion:** Long-term high consumption of potato (each serving a day increase) may be strongly associated with increased risk of diabetes. These findings suggest that diet–health policy may be of importance in the prevention of diabetes.

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## 1. Introduction

Potato is the most consumed staple food after rice and wheat [1] with a global mean per capita intake of 33 kg/year and a notable higher mean intake in the US of 54 kg/year [2]. Recently, potatoes consumption has been the topic of much scientific research regarding their effect on chronic diseases [1,3]. This is due to their

frequency and wide range of consumption globally, but also due to the fact that they are a rich source of minerals while they have a low fat and sodium content. Besides, potatoes have a high glycemic index (GI) and glycemic load (GL) and are a source of starch. This may contribute to a detrimental effect on health and some prospective studies have shown a positive association between dietary GL with higher risk of developing diabetes [4,5]. Although compelling evidence is available linking metabolic and cardiovascular disease risk factors to diabetes, our understanding of the association between some staple foods such as potatoes and risk of type 2 diabetes remains limited.

Dietary factors play an important role in developing of type 2 diabetes [6]. In the United State dietary guidelines, potatoes are

Abbreviations: GI, glycemic index; GL, glycemic load; FFQ, food frequency questionnaires.

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included in the vegetable food groups and similar to other vegetables encourage to be consumed [7]. Although the beneficial association between dietary vegetable intake and chronic disease were shown, there was some debates for dietary recommendation intake of potatoes, because some studies demonstrate adverse relation between high potato intake and chronic disease include diabetes and hypertension [8–10]. Higher potato intake indicated that increase fasting blood glucose and insulin resistance, and may increase the risk of diabetes [11]. We therefore undertook a dose–response meta-analysis of prospective cohort studies to reliably determine and combine the available evidence in the association between potato consumption (per serving/day) and risk of type 2 diabetes.

## 2. Methods

### 2.1. Search strategy

A systematic review was conducted on Medline/PubMed and Elsevier/Embase for relevant studies from the database commencement until September 2017 (updated by June 2018) without time or language restrictions and following the MOOSE guidelines [12]. A complementary search was carried out on leading diabetes and nutritional journals and all reference lists of identified papers, reviews, meta-analyses, letters, and other relevant documents, with terms related to potatoes as well as those for diabetes as key words. Search terms included Mesh term related to potato consumption and diabetes disease. Two qualified investigators separately screened titles and abstracts for eligible studies. In addition, the reference lists from the retrieved article were scrutinized for additional relevant studies. We set an email alert in databases and journals in order to get notification for any new published paper. Also, in the case of inadequate information in the paper, communication was made via electronic mail. The same investigators checked these articles in full text base on the eligibility criteria. Any disagreements in the review were resolved by a consensus or adjudication of principle investigator. EndNote X8 software was employed for citation management.

### 2.2. Study selection and quality assessment

All retrieved articles were screened based on titles and abstract, using the following general exclusion criteria: 1) irrelevant and non-original papers; 2) *in vitro*, cell line and animal studies; 3) case reports and case series reports. This was followed by a full text review on remaining articles. In the next step, a full text review was conducted on the selected papers, excluding cross-sectional or case–control studies, studies on patients with diabetes or cardiovascular disease at baseline, studies with follow-up < 1 year or sample size < 100 and studies on patient groups or pregnant women. Studies were included in the final statistical analysis if they meet the following criteria: cohort or clinical trial (control arm) studies, objective diagnostic procedure for diagnosis of valid diabetes cases, valid measurement of white potato consumption, and the authors reported adjusted measure of association (hazard ratio, rate ratio, risk ratio) with 95% confidence intervals. Our interested exposure was white potato consumption and studies of other potatoes type (such as sweet and purple potato) were excluded. In cases where the same study data were reported in multiple papers, only the paper with the more number of diabetes cases were included. The flowchart showing the selection procedure is provided in Fig. 1. Five methodological components which might bias the association between potato consumption and risk of diabetes including study design, follow-up duration, adjustment for well-

known confounders, sample size, and number of diabetes cases were used for quality assessment purposes [13].

### 2.3. Data extraction

Data extraction procedure was performed using a standard data extraction form independently by two investigators (JD and FT). The following information was extracted from each study: first author name, years of publication, sex, age, name of study, study location, duration of follow-up, exposure assessment tool, outcome definition, number of observed incident cases, sample size, type of potatoes (bakes, mashed or boiled, French fries), case ascertainment, potato consumption categories, covariates adjusted for in the multivariable analysis and relative risks with 95% CI for all categories of potatoes consumption. When several models estimate were available, we considered the maximally adjusted model. Any reported HRs stratified by sex were considered as two separate paper in statistical analysis.

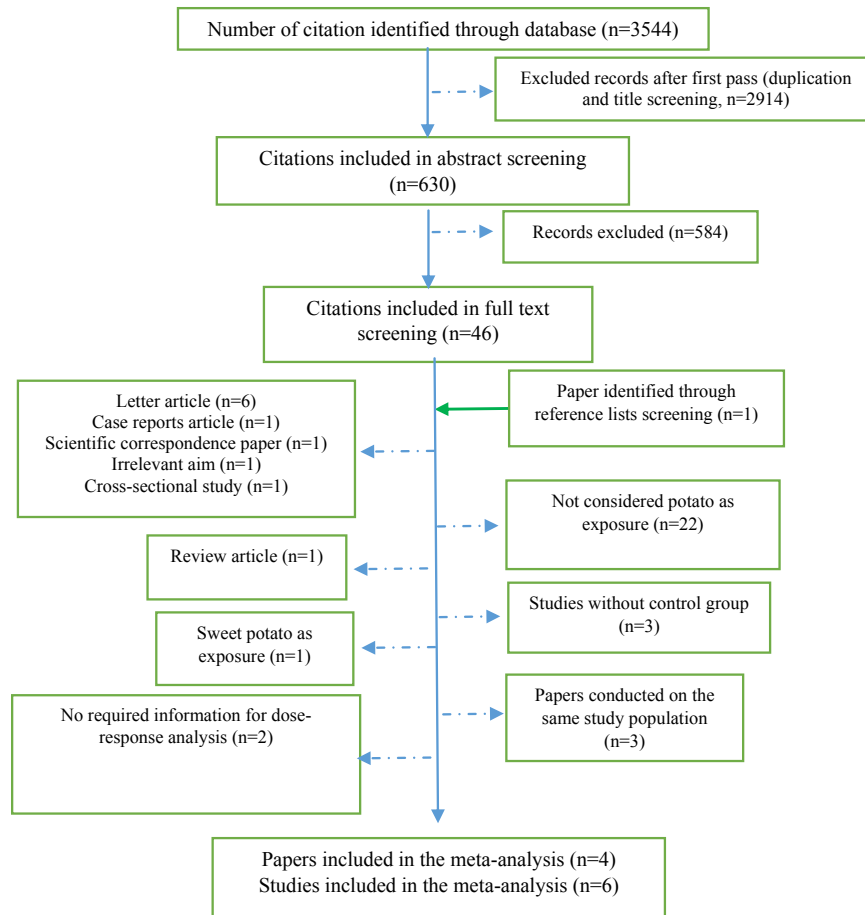
### 2.4. Statistical analysis

In the present study, HR and correspondent 95% CI were considered as the effect size (all the included papers reported HR as main measure of association). The random model dose–response meta-analysis method of Greenland and Longnecke [14] was used to estimate the maximally adjusted log HR for a unit (serving per day) increment of potato consumption. According to the method, the following information extracted for statistical analysis: the amount of potato consumption per each categories (dose), number of type 2 diabetes cases and equivalent person years, and HR and 95% CI. The median of each potatoes consumption categories was assigned to the corresponding HR (as corresponding dose). For studies reporting open boundaries, the best estimates were made based on the descriptive information contained in the paper. A restricted cubic spline model with three knots at the 25th, 50th, and 75th percentiles of potatoes intake was used to evaluate the potential non-linear relationship (different knots at different place had no effect on the result), with generalized least square regression based on the correlation within each category of HRs. *P*-value for non-linearity was calculated using Wald's statistics, testing the null hypothesis of regression coefficient equal to zero for second spline [15]. The Cochran's Q test and  $I^2$  statistic were conducted to determine the presence of heterogeneity among studies. All statistical analyses were performed using R version 3.4.1 [16].

## 3. Results

### 3.1. Literature search

The process of systematic-review exhibited in Fig. 1. First, we retrieved 3544 citations from which duplicate citations and studies that did not meet the inclusion criteria were excluded ( $n = 2914$ ). Next, 630 papers included in the abstract screening. In the second step, 46 papers selected for full text screening (see follow-chart for detailed description) (Fig. 1). Among 46 selected full-text papers, four papers included for statistical analysis. In addition, one paper retrieved from manual searching of references lists [4]. Causes of inclusion and exclusion of studies are showed in supplementary Table S1. Finally, four papers (contain data from six prospective cohort studies) included for statistical analysis [4,17–19]. Four papers [19–22] were reported the association between potatoes and risk of type 2 diabetes using data from the same source (Nurses' Health Study). We selected the paper reported by Muraki et al. [19], because of they had more number of type 2 diabetes incident cases with updated follow-up information [19].



**Fig. 1.** Selection of studies for inclusion in a meta-analysis of potato consumption and risk of type 2 diabetes.

### 3.2. Characteristics of included studies

A total of four papers were retrieved of which six prospective cohort studies totaling 17,758 type 2 diabetes cases and 273144 participants met the inclusion criteria, and thus, were included in the meta-analysis. The detailed characteristics of each study is presented in Table 1. All of the included studies, however, had been published as full manuscripts, had prospective cohort design (full cohort studies) and enjoyed a high quality methodology with multivariate statistical analyses. Validated semi-quantitative food frequency questionnaires (FFQ) were used to measure potatoes consumption in all studies. Two studies were from Finland (FMCHES) and Australia and the other four studies were from US (WHS, NHS, NHSII, HPES). All of studies included participants higher than mean age 34 years old. Three studies evaluated women only [17,19], two studies include both men and women [4,18] and the remaining one study include men only. All the papers excluded participants with history of diabetes at baseline.

### 3.3. Dose–response analysis

Four papers contain six cohort studies were included in the dose–response meta-analysis of total potato consumption and risk of type 2 diabetes. Figure 2 shows linear and non-linear fitted random-effects dose–response plot for association between total potato consumption (per serving/day) and risk of type 2 diabetes both in men and women. The pooled dose–response HR per an increment of 1 serving/day of total potato consumption was 1.20

(95% CI 1.13 to 1.127,  $P < 0.001$ ,  $I^2 = 27.1\%$ ,  $P$  for heterogeneity = 0.23). The larger risk were observed for 2 serving/day (HR 1.44, 95% CI 1.28 to 1.63) and 3 serving/day (HR 1.74, 95% CI 1.45 to 2.09) (reference group was 0 serving/day). Using Wald' test, we found significant evidence of a non-linear association between total potato consumption and risk of type 2 diabetes ( $X^2 = 17.5$ ,  $P$  for linearity  $< 0.001$ ). No publication bias were found using Egger's regression test (coefficient = -0.12,  $P = 0.90$ ). Besides, we evaluated this association for three studies conducted on women population. The summary HR of diabetes for an increment of potato consumption was 1.18 (95% CI 1.03 to 1.13,  $p = 0.01$ ,  $I^2 = 56.9\%$ ,  $P$  for heterogeneity = 0.009) according to studies on women only. Furthermore, combined HR of type 2 diabetes was 1.39 (95% CI 1.07 to 1.81) for 2 serving/day and 1.65 (95% CI 1.11 to 2.45) for 3 serving/day increase. The test for checking linearity showed significant non-linear association in women ( $p$  for linearity = 0.02).

## 4. Discussion

### 4.1. Important findings

In the present dose–response meta-analysis of six cohort studies, higher consumption of potato was positively associated with risk of type 2 diabetes. Furthermore, we found that each serving/day increases in potato consumption was associated significantly with 20% (CI 13%–27%) increased risk of type 2 diabetes. Although, the statistical test suggested a non-linear relationship ( $P < 0.001$ ), but dose–response plot exhibited near linear

**Table 1**  
Characteristics of studies included in the dose–response meta-analysis of association between potato consumption and type 2 diabetes.

First author	Year	Sex	Country	Study period	Age	Study name	No of diabetes	Sample size	Potato consumption Categories (Serving/day)	HR	95% CI	Adjusted factors
Liu	2004	Female	US	10 years	>45	Women's Health Study	1614	38,018	Q1: 0.13 Q2: 0.28 Q3: 0.43 Q4: 0.56 Q5: 0.93	Ref 1.03 0.97 0.96 1.02	Ref (0.87 (0.79 (0.81 (0.86 (1.22)	Age, smoking, energy intake, alcohol use, BMI, exercise, history of hypertension, history of high cholesterol, and family history of diabetes
Montonen	2005	Both	Finland	6 years	40 to 69	Finnish Mobile Clinic Health Examination Survey	383	4304	Q1: 0.74 Q2: 1.14 Q3: 2.4 Q4: 2.7	Ref 1.09 1.27 1.42	Ref (0.82 (0.94 (1.02 (1.98)	Age, sex, BMI, energy intake, smoking, family history of diabetes, and geographic area
Muraki	2015	Female	US	26 years	40 to 65	Nurse Health Study	7436	70,773	Q1: 0.11 Q2: 0.14 Q3: 0.42 Q4: 0.78 Q5: 1.2	Ref 1.08 1.15 1.22 1.27	Ref (0.93 (1.00 (1.05 (1.04 (1.56)	Age, ethnicity, smoking, alcohol, multivitamin use, physical activity, family history of diabetes, menopausal status and postmenopausal hormone use, premenopausal, postmenopausal, oral contraceptive use, energy intake, BMI
Muraki	2015	Female	US	20 years	25 to 42	Nurse Health Study II	4621	87,739	Q1: 0.11 Q2: 0.14 Q3: 0.42 Q4: 0.78 Q5: 1.2	Ref 0.95 0.99 1.09 1.38	Ref (0.78 (0.82 (0.90 (1.31 (1.76)	Age, ethnicity, smoking, alcohol, multivitamin use, physical activity, family history of diabetes, menopausal status and postmenopausal hormone use, premenopausal, postmenopausal, oral contraceptive use, energy intake, BMI
Muraki	2015	Male	US	24 years	40 to 75	Health Professionals Follow-Up Study	3305	40,669	Q1: 0.11 Q2: 0.14 Q3: 0.42 Q4: 0.78 Q5: 1.2	Ref 0.94 1.03 1.09 1.38	Ref (0.76 (0.85 (0.89 (1.32 (1.78)	Age, ethnicity, smoking, alcohol, multivitamin use, physical activity, family history of diabetes, menopausal status and postmenopausal hormone use, premenopausal, postmenopausal, oral contraceptive use, energy intake, BMI
Hodgo	2004	Both	Australia	4 years	40 to 69	Melbourne Collaborative Cohort Study	365	31,641	Q1: 0.22 Q2: 0.42 Q3: 0.74 Q4: 1.1	Ref 0.84 0.82 0.98	Ref (0.63 (0.60 (0.70 (1.37)	Age, sex, country of birth, physical activity, educational, weight change, energy intake, BMI, WHR

association. The largest observed risk increase was for 3 serving/day (62%, CI 37%–91%).

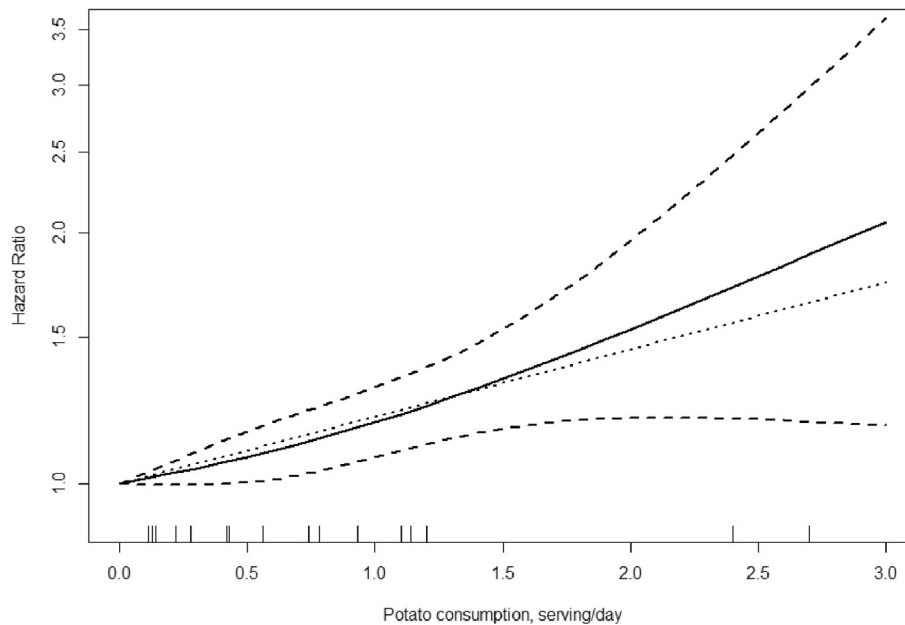
#### 4.2. Literature review

To our knowledge, this meta-analysis is the first to assess dose–response association between potato consumption and risk of type 2 diabetes. Several individual studies of the relationship between potatoes consumption and risk of type 2 diabetes have been published. The majority of cohort studies have found positive association between potato consumption and risk of type 2 diabetes. Our finding is generally in agreement with Muraki et al. [19] findings which reported 7% increase in risk of type 2 diabetes per 2–4 serving/week. In this pooled study, although neither non-linear dose–response association nor non-linear dose–response

plot were performed for more detailed assessment of the association, significant trend was found between potato consumption and risk of type 2 diabetes. This study with a total number of 15,362 incident cases of type 2 diabetes was one of the largest prospective research using individual participant data from three cohort studies in the US.

#### 4.3. Biological plausibility

One possible biological mechanism that could justify this association is glycemic load related to potato consumption. The high glycemic load of potato consumption may increase the risk of type 2 diabetes. Potato is a starch rich food with high GL and high GI [23] and it can increase postprandial glucose and insulin levels [20]. It suggested that hyperglycemia chronically overstimulate



**Fig. 2.** Pooled dose–response association between total potato consumption (per serving/day) and risk of type 2 diabetes (solid line). Total potato consumption was modeled using restricted cubic splines in a multivariate random-effects dose–response model. Dashed lines represent the 95% confidence intervals for the spline model. No potato consumption (0 serving/day) considered as the references value.

pancreatic  $\beta$ -cells for insulin secretion, and in long term reduced islet insulin stores, whereas cannot increase the  $\beta$ -cell mass. Consequently, hyperglycemia induced oxidative stress to pancreatic cells may leads to  $\beta$ -cell dysfunction [4], defect in glucose homeostasis, and finally fibrosis of pancreatic cells [5,6]. All the included studies in this meta-analysis conducted on the western community and the prior reports showed that consumption of potatoes is very high in western countries. A great majority of this potato consumption is belong to fried potato [24,25]. It has been demonstrated that consumption of French fries and other fried foods is in association with dietary advanced glycation end products and other degradation products from frizzling oil which may lead to increased risk of insulin resistance and diabetes [26,27]. Another potential justification may be related to adiponectin, a cytokine secreted by adipose tissue, which thought may enhance insulin action, improve glucose metabolism and lipid profile [28]. Studies suggested that low plasma concentrations of adiponectin may be a risk factor for type 2 diabetes [29] and in line with this high consumption of food with high GI level is in relationship with low adiponectin level in plasma [30]. In addition, it have been reported that adiponectin expression in adipose tissue is inversely associated with fasting plasma glucose and insulin in humans [30]. Consequently, it is possible that lower plasma adiponectin after consumption of high GI foods has been mediated through glucose levels, which increased after consumption of high GI foods and consequently induced both hyperglycaemia and hyperinsulinemia. Further biological interpretation of these finding is not possible through a meta-analysis study and it needs further biochemical studies.

#### 4.4. Limitations

The present study is the first dose–response meta-analysis to identify the role of potato consumption in the development of diabetes. Besides, a large number of type 2 diabetes cases, enabling a much greater power of reaching conclusive result between potato consumption and type 2 diabetes risk. However, there were some

limitations in this meta-analysis. First, although we used maximally adjusted HR, but the possible effect of residual confounding and reverse causality is unknown. Second, measuring dietary data are imperfect in current nutritional sciences, as a result measuring of potato intake using self-administered questionnaire in the included studies have some level of misclassification, which most likely results in attenuation of the association to null. Third, the small number of included studies restricted the ability for using subgroup analysis for assessing the reliability of the association in different subgroups. Fourth, we were unable to assess French fries, boiled or mashed potato and Chips, because the reported information in the included paper was not enough for evaluating these associations.

#### 5. Conclusions

Consumption of total potato is in association with higher risk of type 2 diabetes based on studies from developed countries. These findings suggest that diet–health policy may be of importance in the prevention of diabetes. We suggest further large prospective cohort studies for assessing the causal association in different population with different dietary pattern.

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#### Author contributions:

Study concept and design: ZB, MN.

Data extraction: ZB, SJD, FT.



Statistical analysis: MN.

Analysis and interpretation of data: MN, ZB, FT.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Study supervision: MN.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at doi:[10.1016/j.clnesp.2018.06.004](https://doi.org/10.1016/j.clnesp.2018.06.004).

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