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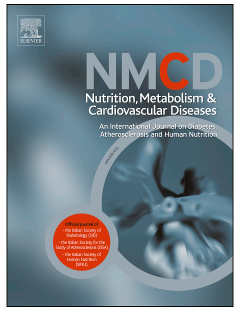

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Carbohydrate restriction in midlife is associated with higher risk of type 2 diabetes among Australian women: a cohort study

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ABSTRACT

Background and Aims: Low-carbohydrate diets (LCDs) are increasingly popular but may be nutritionally inadequate. We aimed to examine if carbohydrate restriction in midlife is associated with risk of developing type 2 diabetes (T2DM), and if this association differs by previous gestational diabetes (GDM) diagnosis.

Methods and Results: Dietary intake was assessed for 9,689 women from the Australian Longitudinal Study on Women's Health in 2001 (aged 50-55) and 2013 (aged 62-67) via validated food frequency questionnaires. Average long-term carbohydrate restriction was assessed using a low-carbohydrate diet score (highest quartile (Q4) indicating lowest proportion of energy from carbohydrates). Incidence of T2DM between 2001 and 2016 was self-reported at 3-yearly surveys. Log-binomial regression was used to estimate relative risks (RR) and 95% CIs. During 15 years of follow-up, 959 women (9.9%) developed T2DM. Carbohydrate restriction was associated with T2DM after adjustment for sociodemographic factors, history of GDM diagnosis and physical activity (Q4 vs Q1: RR 1.27 [95% CI 1.10, 1.48]), and this was attenuated when additionally adjusted for BMI (1.10 [0.95, 1.27]). Carbohydrate restriction was associated with lower consumption of fruit, cereals and high-fibre bread, and lower intakes of these food groups were associated with higher T2DM risk. Associations did not differ by history of GDM (P for interaction >0.15).

Conclusion: Carbohydrate restriction was associated with higher T2DM incidence in middle-aged women, regardless of GDM history. Health professionals should advise women to avoid LCDs that are low in fruit and grains, and to consume a diet in line with current dietary recommendations.

Keywords: carbohydrates; cohort study; gestational diabetes; nutrition; type 2 diabetes

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become an epidemic and is a major public health challenge worldwide (1). A large body of evidence shows that T2DM is largely preventable through lifestyle modifications, with nutrition playing a vital role (2, 3). International diabetes prevention guidelines highlight that limiting energy intake may lower T2DM risk for those at high risk, with the importance of diet quality, such as consuming a Mediterranean-style diet, also recognised (4, 5).

Over the past few decades, low-carbohydrate diets (LCDs) have been amongst the most popular, as they promise weight loss without calorie counting and do not require avoiding many palatable foods (6). These LCDs may however be nutritionally inadequate due to lower intake of core foods rich in dietary fibre such as whole grains and fruit, and higher intake of animal fat, protein and saturated fatty acids, which may in turn increase T2DM risk (7). Limited observational research to date has shown an association between LCDs and higher T2DM risk in the general population (8-10), and among women with a history of gestational diabetes mellitus (GDM) (11).

Women with a history of GDM, an increasingly common pregnancy complication (12), have an approximate seven-fold increased risk of developing T2DM later in life (13, 14). During pregnancy, women with GDM are advised to restrict their carbohydrate intake as part of medical nutrition therapy to optimise glucose control and support healthy foetal growth and development (15, 16). After pregnancy, dietary recommendations are similar to those for the general population, however, women with GDM within the previous 10 years have been shown to have poorer diet quality and lower adherence to dietary recommendations compared with women without a history of GDM (17, 18).

As women with prior GDM are at increased risk of developing T2DM and have poorer diet quality, the influence of carbohydrate restriction on T2DM may differ in this high-risk group compared with the general population. Previous studies have not formally compared whether the association between LCDs and T2DM differs between women with and without GDM within one study population. This evidence is essential to inform dietary recommendations for the long-term prevention of T2DM in women, based on their history of GDM.

The present study therefore aimed to investigate the association between carbohydrate restriction and T2DM risk among middle-aged women, and whether this association differs according to history of GDM. This study also examined the association between consumption of carbohydrate-rich food groups and incident T2DM, to help understand how carbohydrate restriction may influence T2DM risk.

METHODS

Study population

The Australian Longitudinal Study on Women's Health is an ongoing nationally representative survey of Australian women. In 1996, three cohorts of women were established; the young cohort (born 1973-78), the middle-aged cohort (born 1946-51) and the older cohort (born 1921-26). At the first survey in 1996, the women in these cohorts were aged 18-23, 45-50 and 70-75 years, respectively. Random sampling was conducted using the national Medicare health insurance database, which includes all Australian citizens and permanent residents. Women from rural and remote areas were intentionally oversampled to allow for statistical comparison of health differences by women's area of residence. Informed consent was obtained, and the study methods were approved by the ethics committees of the Universities of Newcastle (H0760795) and Queensland (2004000224). Further information on recruitment and response rates have been published previously (19, 20), and are available online at https://www.alswh.org.au/.

The current study includes women from the 1946-51 cohort. After the first survey, women were resurveyed in 1998 (Survey 2) and every three years thereafter until 2016 (Surveys 3-8). The first survey was completed by 13,714 women. The respective response rates for subsequent surveys were n = 12,338 (90%, 1998), n = 11,226 (82%, 2001), n = 10,905 (80%, 2004), n = 10,638 (78%, 2007), n = 10,011 (73%, 2010), n = 9151 (67%, 2013) and n = 8,622 (63%, 2016) (21). In 2001, dietary intake was measured for the first time, therefore this survey has been used as baseline for the present study. Of the women who completed the 2001 survey, we excluded 575 women who reported type 1 diabetes mellitus (T1DM) or T2DM prior to 2001, 403 who reported extreme energy intakes (top and bottom 2.5%), and 559 who had missing dietary data. The final sample for analysis included 9,689 women (**Figure 1**).

Dietary assessment

Participants' usual diets were assessed in 2001 (aged 50-55) and 2013 (aged 62-67) via the Dietary Questionnaire for Epidemiological Studies version 2 (DQES v2) food frequency questionnaire (FFQ), which has previously been validated against seven-day food records (22, 23). The energy-adjusted Pearson correlation coefficients for the DQES v2 were 0.70 for carbohydrate, 0.68 for fat and 0.32 for protein (22). Dietary intakes for most nutrients were calculated from FFQ data using Australian food composition data from NUTTAB95 (24). Individual food item glycaemic load (GL) values were obtained from the 2002 International table of glycaemic index (GI) and GL values (25). Dietary GL was calculated by summing the product of carbohydrate intake from each food, by the GI value for the food, while dietary

GI was obtained by dividing the dietary GL by the total carbohydrate intake (25). Alcohol was not included in GI calculations (25).

Between the 2001 and 2013 FFQ's, energy intake decreased by approximately 100 kcal, and the contribution of carbohydrate to total energy fell from 45 to 42% energy (**Supplemental Table 1**). Intakes of total sugar and refined carbohydrate foods such as fruit juice and white bread decreased, whereas intake of total fibre and fibre-rich foods such as fruit and vegetables increased over time. To reflect long-term habitual dietary intake, we averaged food and nutrient intakes over the 2001 and 2013 surveys, or only used the 2001 survey when women did not complete the 2013 survey (n = 2,168; 22%).

The low-carbohydrate diet score

A LCD score was calculated based on participants' proportion of energy from carbohydrate, protein and fat, a method which has been used in previous studies (8, 11, 26). Participants' dietary percentage of energy from carbohydrate, protein and fat were divided into 11 quantiles. From the lowest to highest intake (% energy), the 11 quantiles for carbohydrate were allocated scores from 10 to 0, and from 0 to 10 for protein and fat. The overall LCD score was calculated from the sum of the carbohydrate, protein and fat scores. The LCD score range is 0-30, with a higher LCD score indicating a relatively lower carbohydrate, and higher fat and protein diet.

Food groups

Food groups were created using FFQ data and grouped into 'carbohydrate rich' food groups (including white bread, high fibre bread, cereal, pasta and rice, fruit juice, fruit, vegetables, and discretionary foods) and 'other' food groups related to diabetes risk (including dairy, red and processed meat, and fish) (**Supplemental Table 2**). All serving sizes for food groups were based on the Australian Dietary Guidelines 2013 (27). The consumption in serves or grams per day for white bread and added sugar were very low (median of zero), therefore these variables were dichotomised as consumer (for intakes above zero) versus non-consumer.

Type 2 diabetes assessment

Self-reported T2DM data were obtained at each survey. At the first survey in 1996, women were asked “Have you ever been diagnosed with or treated for diabetes (high blood sugar)?”. At the 1998 and 2001 surveys, women were asked “Since the previous survey, have you been diagnosed with or treated for insulin dependent diabetes?” and “Since the previous survey, have you been diagnosed with or treated for non-insulin dependent diabetes?”. From the 2004 survey onwards, women were asked “Since the previous survey, have you been diagnosed with or treated for diabetes?”. Based on data up to 2001, women with pre-existing diabetes were excluded. Incident T2DM was based on data from 2004 onwards. The self-reported T2DM data was validated against hospital discharge data in a subset of the cohort (women living in New South Wales, Australia), using ICD-10-AM diagnosis codes E10, E11, E13 and E14. Results showed substantial agreement between self-reported diagnosis and hospital records (k = 0.75) (28).

Covariates

Data on covariates including sociodemographic factors, physical activity and BMI were collected at every survey, while GDM history data was assessed in 2007 and 2010. Women were classified as having a history of GDM if they responded “yes” to the question “Have you ever had gestational diabetes (diabetes during pregnancy)?” at either survey. BMI was calculated based on self-reported weight and height (kg/m^2), and classifications of underweight and normal weight were combined, as <2% of women in the sample were underweight. A variable was created to adjust for the number of follow-up surveys women completed, as the likelihood of a woman reporting diabetes increased with the number of surveys completed.

Statistical analyses

Demographic, lifestyle and health characteristics of women were described according to quartiles of the LCD score. Differences between groups were compared using chi-square tests (binary or categorical variables), ANOVA (normally distributed continuous variables) or Kruskal Wallis tests (non-normally distributed continuous variables). All descriptive analyses were weighted by area of residence to account for the intentional oversampling of women from rural and remote areas.

Log-binomial regression analysis with generalised estimating equations (GEE), which accounts for correlations in repeated surveys contributed by a single woman (29) was used to estimate relative risks (RR) and 95% confidence intervals (CI) for associations of quartiles (Q) of the LCD score and carbohydrate-rich food consumption with new onset of T2DM reported from 2004 (aged 53-58) to 2016 (aged 65-70). Covariates were identified from known T2DM risk factors based on the literature and were included in the analysis if they were significantly related to the LCD-score and T2DM in multivariable analysis. Consecutive multivariable models were built, with model 1 adjusted for age, country of birth, total energy intake, highest educational qualification, employment status and years of follow-up, and model 2 additionally adjusted for history of GDM and physical activity. For associations between carbohydrate-rich food groups and T2DM risk we included a third model including all carbohydrate-rich food groups and known diet-related diabetes risk factors including dairy, red and processed meat, and fish. For both the LCD score and carbohydrate-rich food groups, the final model (model 4) was additionally adjusted for BMI as this may be an intermediate in the relationship between diet and T2DM. Country of birth, total energy intake, history of GDM, highest educational qualification and number of follow-up years were fixed over time, and updated time-varying covariates (reported at surveys from 2001 to 2013) were used for age, employment status, physical activity and BMI. Covariates that were considered but not included in the analysis as they were not related to the LCD score and/or T2DM risk were area of residence, number of children, menopause status, smoking status, alcohol consumption, depressive symptoms and history of heart disease.

Multiple imputation by chained equations (MICE) was used to handle missing covariate data (n = 1,938 had missing data on one or multiple covariates) (30). Information on age, country of birth and number of follow-up surveys was available for all women. For all other variables, complete data were available for over 80% of the women. We therefore generated 20 imputed datasets using observed baseline and follow-up data on all potential covariates, dietary intake and T2DM, and reported combined RRs and 95% CIs that appropriately account for the variance within and between imputed datasets (30).

Effect modification was evaluated to identify potential differences in the association between the LCD score and carbohydrate-rich food groups and T2DM risk among women with and without a history of GDM. Cross-product terms were included in the final model and stratified analyses were performed when significant interactions were found. All statistical analyses were conducted using Stata Version 15.0 (31).

RESULTS

At baseline, the 9,689 women included in this study had a mean age of 53 years. There were 959 reported cases of T2DM (9.9%) over 15 years of follow-up. Of women with a history of GDM, 19.7% reported developing T2DM whereas 9.5% of women without a history of GDM reported developing T2DM (P = <0.0001). Baseline characteristics are described in **Table 1** according to LCD score quartiles. Women who restricted carbohydrate intake the most (LCD score Q4) were more likely to be born in Australia compared with overseas, live in a rural or remote location, be employed full time, be less educated, have a history of GDM, have a higher BMI, and lower levels of physical activity (Table 1).

By definition, a higher LCD score was associated with a lower proportion of energy from carbohydrate (37% vs 50% for Q4 vs Q1) (**Table 2**). Carbohydrate restriction was associated with lower daily intakes of dietary fibre (3.4 g/1,000 kcal), total sugar (28.4 g), fruit (0.6 serves), fruit juice (0.2 serves), cereal (0.7 serves), high-fibre bread (0.2 serves), pasta and rice (0.2 serves) and discretionary foods (0.1 serves), and women were less likely to be added sugar consumers (39% vs 59%). Carbohydrate restriction was also associated with higher dietary intakes of energy, fat (total, saturated, monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA)), protein and vegetables, and women who restricted carbohydrate the most were more likely to be consumers of white bread (Table 2).

Carbohydrate restriction was positively associated with risk of T2DM (**Table 3**). The RR (95% CI) for T2DM was 1.31 (1.13-1.51) for Q4 vs Q1 of LCD score when adjusted for age, country of birth, energy intake, highest educational qualification, employment status and years of follow-up (P for trend = <0.0001). When additionally adjusted for history of GDM and physical activity the RR was 1.27 (1.10-1.48) (P for trend = <0.0001). The RR for Q4 vs Q1 was attenuated to 1.10 (0.95, 1.27) when further adjusted for BMI (P for trend = 0.03) (Table 3).

In the regression analysis of T2DM risk in relation to carbohydrate-rich food group consumption, lower consumption of fruit was associated with higher T2DM risk (RR model 3 Q1 vs Q4: 1.22 [1.01-1.48]), which did not change when adjusted for BMI (**Table 4**). Lower consumption of cereal (RR model 3 Q1 vs Q4: 1.21 [1.01, 1.44]) and high-fibre bread (RR model 3 Q4 vs Q1: 1.15 [1.01, 1.33]) were also associated with T2DM risk, however these associations were attenuated when adjusted for BMI (Table 4). Women who were consumers of white bread and added sugar were also more likely to develop T2DM than non-consumers (RR model 3: 1.34 [1.22, 1.47] and 1.10 [1.01, 1.23], respectively) (Table 4).

No effect modification by GDM history was found based on P-values for interaction (all >0.15). This was confirmed in stratified analyses. For example, the magnitude of the RRs for T2DM were 1.27 (1.05-1.49) for Q4 vs Q1 of the LCD score for women without a history of GDM (n = 9,331), and 1.30 (0.52, 2.21) for women with previous GDM (n = 358) (model 2) (data not shown).

DISCUSSION

This prospective cohort study found a positive association between carbohydrate restriction and incidence of T2DM among middle-aged Australian women, which did not differ according to whether women had a history of GDM. When compared to women who restricted carbohydrate the least (50% of energy from carbohydrates), those who restricted the most (37% of energy from carbohydrates) had a 27% higher risk of developing T2DM after adjusting for sociodemographic factors, history of GDM diagnosis and physical activity. The relationship between carbohydrate restriction and T2DM risk appeared to be partially explained by BMI, which attenuated the association when adjusted for.

Our study's findings align with those from previous studies which have examined carbohydrate restriction in relation with T2DM risk. Results from the cross-sectional 2002 China National Nutrition and Health Survey (10) and the prospective Health Professionals Follow-Up Study (9) have shown that highest compared with lowest carbohydrate restriction, based on the LCD score, was associated with an 86% and 31% higher risk of T2DM, respectively, after adjustment for sociodemographic factors, lifestyle and BMI. Based on data from the Nurses' Health Study, high compared with low LCD scores were associated with a higher risk of T2DM after adjustment for sociodemographic and lifestyle factors among the full study population including women with and without prior GDM (RR 1.40, 95% CI 1.21, 1.61) (8), and among women with a GDM history only (RR 2.13, 95% CI 1.65, 2.76) (11). The association was fully attenuated after adjustment for BMI among the overall study population (RR 0.90, 95% CI 0.78, 1.04) (8), but to a lesser extent among women with prior GDM (RR 1.36, 95% CI 1.04, 1.78) (11). These findings from the Nurses' Health Study suggest that carbohydrate restriction may be particularly harmful for women with a GDM history, however, a formal comparison of differences in the association between the LCD score and T2DM risk by GDM history is not possible as the study by Halton et al (8) included women with and without prior GDM and did not test for effect modification. Collectively, findings from our and previous studies are in the same direction, and demonstrate higher T2DM risk among women with a LCD. It remains unclear whether this is mediated through the influence of a LCD on BMI, with inconsistent findings across studies (8-11). These differences may be explained by variations in the macronutrient composition of the LCDs examined in each study. For example, BMI fully explained the association between LCD and T2DM risk in the study by Halton et al (8), which examined a more extreme low-carbohydrate and high-fat diet (top vs bottom LCD score decile) compared with our study (top vs bottom LCD score quartile). This more extreme LCD diet may have had a larger influence on subsequent BMI, and therefore led to full attenuation of the association between LCD and T2DM.

We observed in our study that women who restricted carbohydrate the most were more likely to consume an unbalanced diet, including a lower intake of fibre, fruit, cereals, high-fibre bread, pasta and rice, and were more likely to consume higher daily energy, fats, protein and white bread. Our analysis of food groups showed that women who consumed less fruit, cereal and high-fibre bread, and consumers of white bread had a greater risk of developing T2DM, which may explain why carbohydrate restriction was associated with a higher risk of developing T2DM in our cohort.

We also observed a slight change in dietary intake between the 2001 and 2013 surveys, including lower proportion of energy from carbohydrates, lower intakes of fruit juice and white bread, and higher intakes of fruit and vegetables. This positive change in dietary intake over time has been reported previously by Kusnadi et al. based on data from two Australian national health surveys (1995 and 2012) (32), and may be explained by effective public health campaigns during this time. The most recent Australian Dietary Guidelines (2013) recommend a macronutrient distribution of 45-65% of energy from carbohydrates, 15-25% from protein and 20-35% from fat (27), which is in line with the bottom LCD score quartile in our study (50%, 19% and 31%, respectively) and was associated with the lowest risk of T2DM.

Strengths of this study include its large, nationally-representative sample of women (21), the assessment of data on diet and covariates at multiple time points and the inclusion of long-term habitual dietary intake based on validated FFQ data (22). Further strengths include the long duration of follow-up, the extensive assessment and adjustment for potential confounding factors, and the use of validated self-reported T2DM data (28). Another key strength is the analysis of food group consumption and T2DM risk to help explain why a LCD may be related to T2DM risk. Despite these strengths, several limitations present in our study should be acknowledged. First, a degree of measurement error is likely present within the dietary intake data, as is the case with all FFQ data, as well as the self-reported weight and height data used to estimate BMI. We also relied on self-reported GDM data which has not been validated and may therefore be misclassified. While the self-reported T2DM data used in this study has been validated, in Australia 30% of diabetes cases are estimated to be undiagnosed due to lack of widespread screening (33), and these women would therefore have been misclassified. Lastly, the overall cohort study was not designed to examine subgroups of women by GDM history, and the stratified analyses on the association between dietary intake and T2DM risk in women with a GDM history was based on a small sample of women (n = 358). The magnitude of the associations between the LCD score and carbohydrate-rich food groups and T2DM risk did not differ by GDM history, suggesting there was no effect modification. Further large cohort studies are needed to confirm these findings.

Conclusion

This study has found that long-term carbohydrate restriction may increase the risk of T2DM among middle-aged women, regardless of their history of GDM. While the difference in incidence of T2DM was relatively small between women in the highest compared to the lowest quartile of carbohydrate restriction (2.7% higher), given that there are over 100,000 new cases of diabetes diagnosed in Australia each year (34) this would translate to a clinically relevant difference at the population level. Our analysis of carbohydrate-rich food group consumption and T2DM risk demonstrated that a lower intake of fruit and grain products may explain the association between carbohydrate restriction and T2DM risk. Health professionals should therefore advise women to avoid LCDs which are low in fruit and grains, and to consume a diet in line with current dietary recommendations.

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Data availability: Data are available from the Australian Longitudinal Study on Women's Health (contact ALSWH Data and Analytic Services at www.alswh.org.au/) for researchers who meet the criteria for access to confidential data.

Authors' contributions: ED and DS conceptualised the idea and designed the research. JR and DS performed the statistical analysis, drafted the manuscript and had primary responsibility for the final content of the manuscript. All authors contributed to interpretation of the results, provided important intellectual content, and approved the final manuscript.

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FIGURE LEGENDS

Figure 1. Flow diagram of participants included in the analysis on carbohydrate restriction and type 2 diabetes in the Australian Longitudinal Study on Women's Health cohort of women born in 1946-51.

TABLES

Table 1. Baseline characteristics of the study population according to low-carbohydrate diet score quartiles, N = 9,689

	Quartiles of the low carbohydrate diet score				
	Quartile 1 (least carbohydrate restriction)	Quartile 2	Quartile 3	Quartile 4 (most carbohydrate restriction)	P-value[a]
	n = 2,433	n = 2,748	n = 2,144	n = 2,364	
Age (years), mean (SD)	53 (1.5)	53 (1.4)	52 (1.4)	52 (1.4)	0.0001
Country of birth, %					<0.0001
Australia	67.4	71.7	77.0	75.9	
Europe or other English-speaking country[b]	26.6	24.9	20.3	20.6	
Asia	6.0	3.4	2.7	3.5	
Area of residence, %					<0.0001
Urban	73.1	70.3	69.7	66.8	
Rural or remote	26.9	29.7	30.3	33.2	
History of gestational diabetes, %	3.5	3.6	3.6	4.1	0.04
Highest educational qualification, %					0.004
No formal	14.9	14.1	13.6	13.5	
(High) school certificate	43.8	44.7	49.8	49.9	
Trade/diploma	21.3	22.2	20.2	19.6	

	Quartiles of the low carbohydrate diet score				
	Quartile 1 (least carbohydrate restriction)	Quartile 2	Quartile 3	Quartile 4 (most carbohydrate restriction)	P-value[a]
(Higher) university degree	20.0	19.1	16.4	17.1	
Employment status, %					0.001
Unemployed	23.0	20.8	22.2	19.3	
Part-time employed	35.2	37.1	26.3	35.4	
Full-time employed	41.8	42.1	41.5	45.3	
Physical activity, %					<0.0001
Low/sedentary (<600 MET min/week)	52.0	51.6	55.0	59.2	
Moderate (600 to <1,200 MET min/week)	22.8	22.6	21.2	17.7	
High (≥1,200 MET min/week)	25.2	25.9	23.8	23.0	
Body mass index, %					<0.0001
Normal weight (<25 kg/m^2)	52.0	48.1	46.1	41.2	
Overweight (25 to <30 kg/m^2)	32.4	31.3	31.8	33.5	
Obese (≥30 kg/m^2)	15.7	20.6	22.1	25.3	

MET, total metabolic equivalent; SD, standard deviation

[a] P-values from chi-square test, ANOVA or Kruskal Wallis test

[b] The category ‘Europe or other English-speaking country’ includes women born in a European country, and a small proportion (<1%) of women born in an English-speaking country other than Australia or Asia, such as the USA

Table 2. Daily dietary intake according to low-carbohydrate diet score quartiles, N = 9,689

	Quartiles of the low carbohydrate diet score				
	Quartile 1 (least carbohydrate restriction)	Quartile 2	Quartile 3	Quartile 4 (most carbohydrate restriction)	P-value[a]
	n = 2,433	n = 2,748	n = 2,144	n = 2,364	
Low carbohydrate score, mean (SD)	5.9 (2.5)	12.5 (1.7)	18.0 (1.4)	24.6 (2.8)	<0.0001
Total energy intake (kcal), mean (SD)	1,501 (423)	1,521 (422)	1,556 (439)	1,547 (478)	0.0001
Total fat intake (energy %), mean (SD)	31.4 (4.1)	34.8 (3.9)	37.8 (3.3)	40.7 (3.2)	<0.0001
Saturated fat intake (energy %), mean (SD)	12.2 (2.6)	13.8 (2.6)	15.2 (2.7)	16.4 (2.6)	<0.0001
Monounsaturated fat intake (energy %), mean (SD)	10.9 (1.6)	12.3 (1.5)	13.5 (1.3)	14.9 (1.5)	<0.0001
Polyunsaturated fat intake (energy %), mean (SD)	5.3 (1.7)	5.5 (1.6)	5.8 (1.7)	5.9 (1.7)	<0.0001
Protein intake (energy %), mean (SD)	18.7 (2.3)	20.3 (2.7)	20.9 (2.6)	23.0 (2.6)	<0.0001
Carbohydrate intake (energy %), mean (SD)	50.1 (3.2)	45.1 (1.6)	41.5 (1.2)	36.5 (3.4)	<0.0001
Fibre intake (grams per 1,000 kcal), mean (SD)	14.8 (3.4)	13.5 (2.9)	12.5 (2.5)	11.4 (2.4)	<0.0001
Glycaemic index, mean (SD)	51.1 (3.6)	50.6 (3.5)	50.7 (3.6)	50.1 (3.7)	<0.0001
Glycaemic load, median (IQR)	93.5 (76.1-113.9)	84.8 (69.2-102.8)	79.9 (64.8-97.0)	69.0 (55.7-84.2)	0.0001
Total sugar intake (grams), median (IQR)	88.4 (74.0-107.6)	79.0 (65.2-95.6)	71.6 (57.6-87.1)	60.0 (47.2-74.7)	0.0001

	Quartiles of the low carbohydrate diet score				
	Quartile 1 (least carbohydrate restriction)	Quartile 2	Quartile 3	Quartile 4 (most carbohydrate restriction)	P-value[a]
Added sugar consumer, %[b]	59.2	51.1	46.0	38.7	<0.0001
Fruit (serves), mean (SD)	1.9 (0.9)	1.6 (0.8)	1.5 (0.8)	1.3 (0.8)	<0.0001
Fruit juice (serves), median (IQR)	0.33 (0.04-0.90)	0.24 (0.04-0.71)	0.17 (0.04-0.62)	0.14 (0.03-0.52)	0.0001
Vegetables (serves), mean (SD)	2.0 (0.9)	2.1 (0.8)	2.1 (0.9)	2.2 (0.9)	0.002
Cereal (serves), median (IQR)	1.3 (0.7-2.0)	1.2 (0.6-1.8)	0.9 (0.4-1.5)	0.6 (0.1-1.1)	0.0001
White bread consumer, %	33.3	33.7	37.8	38.2	<0.0001
High fibre bread (serves), mean (SD)	1.3 (0.9)	1.3 (0.9)	1.2 (0.9)	1.1 (0.8)	<0.0001
Pasta and rice (serves), median (IQR)	0.6 (0.3-0.9)	0.5 (0.3-0.8)	0.5 (0.3-0.8)	0.4 (0.3-0.7)	0.0001
Discretionary foods (serves), median (IQR)[c]	1.5 (1.0-2.4)	1.5 (1.0-2.4)	1.6 (1.0-2.5)	1.4 (0.9-2.1)	0.0001

IQR, interquartile range; SD, standard deviation

[a] P-values from chi-square test, ANOVA or Kruskal Wallis test

[b] Participants were categorised as an added sugar consumer if they reported consumption of at least 1 teaspoon of sugar per day as part of the FFQ

[c] Discretionary foods are, as per the Australian Dietary Guidelines 2013, foods and drinks not necessary to provide the nutrients the body needs, and are high in saturated fats, sugars, salt and/or alcohol. FFQ items included in this food group are: ice cream, biscuits, chocolate, jam, meat pie, pizza, hamburger, cake, flavoured milk, crisps and crackers (Supplemental Table 2)

Table 3. Relative risks and 95% confidence intervals for associations between low-carbohydrate diet score and risk of developing type 2 diabetes, N = 9,689

	Quartiles of the low-carbohydrate diet score				
	Quartile 1 (least carbohydrate restriction)	Quartile 2	Quartile 3	Quartile 4 (most carbohydrate restriction)	P-value for trend
N	2,433	2,748	2,144	2,364	
T2DM cases, %	8.9	8.9	10.5	11.6	
LCD score, mean (SD)	5.9 (2.5)	12.5 (1.7)	18.0 (1.4)	24.6 (2.8)	
Model 1[a]	Reference	1.03 (0.88, 1.19)	1.20 (1.01, 1.43)	1.31 (1.13, 1.51)	<0.0001
Model 2[b]	Reference	1.02 (0.88, 1.18)	1.18 (0.99, 1.39)	1.27 (1.10, 1.48)	<0.0001
Model 3[c]	Reference	0.95 (0.81, 1.10)	1.06 (0.89, 1.26)	1.10 (0.95, 1.27)	0.03

LCD, low carbohydrate diet; SD, standard deviation; T2DM, type 2 diabetes mellitus

[a] adjusted for age, country of birth, energy intake, highest educational qualification, employment status and years of follow-up

[b] additionally adjusted for history of gestational diabetes and physical activity

[c] additionally adjusted for body mass index

Table 4. Relative risks and 95% confidence intervals for associations between carbohydrate-rich food groups and risk of developing type 2 diabetes, N = 9,689

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
Fruit					
N	2,436	2,415	2,418	2,420	
T2DM cases, %	11.2	9.8	9.8	8.9	
Intake (serves/day), mean (SD)	0.62 (0.17)	1.18 (0.17)	1.77 (0.18)	2.74 (0.60)	
Model 1[a]	1.32 (1.11, 1.58)	1.15 (0.96, 1.37)	1.13 (0.91, 1.40)	Reference	0.005
Model 2[b]	1.26 (1.06, 1.51)	1.07 (0.89, 1.29)	1.10 (0.89, 1.37)	Reference	0.01
Model 3[c]	1.22 (1.01, 1.48)	1.02 (0.86, 1.23)	1.09 (0.87, 1.36)	Reference	0.03
Model 4[d]	1.22 (1.01, 1.48)	1.06 (0.88, 1.26)	1.10 (0.88, 1.36)	Reference	0.03
Fruit juice					
N	2,423	2,422	2,422	2,422	
T2DM cases, %	9.8	9.8	9.9	10.0	
Intake (serves/day), mean (SD)	0.01 (0.01)	0.10 (0.05)	0.43 (0.14)	1.30 (0.7)	
Model 1[a]	0.97 (0.83, 1.15)	0.96 (0.80, 1.15)	0.99 (0.85, 1.16)	Reference	0.36
Model 2[b]	0.96 (0.82, 1.13)	0.95 (0.79, 1.14)	0.99 (0.85, 1.15)	Reference	0.31

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
Model 3[c]	0.94 (0.80, 1.10)	0.92 (0.77, 1.09)	0.96 (0.82, 1.12)	Reference	0.25
Model 4[d]	0.94 (0.80, 1.10)	0.90 (0.75, 1.07)	0.95 (0.82, 1.11)	Reference	0.28
Vegetables					
N	2,423	2,423	2,421	2,422	
T2DM cases, %	10.2	10.0	9.8	9.7	
Intake (serves/day), mean (SD)	1.11 (0.31)	1.75 (0.14)	2.26 (1.17)	3.28 (0.67)	
Model 1[a]	1.05 (0.86, 1.28)	1.02 (0.82, 1.27)	1.01 (0.86, 1.17)	Reference	0.84
Model 2[b]	1.04 (0.85, 1.28)	1.03 (0.83, 1.28)	1.01 (0.87, 1.18)	Reference	0.91
Model 3[c]	1.03 (0.84, 1.28)	1.02 (0.83, 1.26)	1.01 (0.86, 1.18)	Reference	0.95
Model 4[d]	1.03 (0.84, 1.26)	1.02 (0.82, 1.26)	1.01 (0.87, 1.19)	Reference	0.96
Cereal					
N	2,423	2,422	2,423	2,421	
T2DM cases, %	11.3	10.3	9.5	8.7	
Intake (serves/day), median (IQR)	0.09 (0.02-0.22)	0.70 (0.56-0.86)	1.30 (1.14-1.47)	2.21 (1.91, 2.79)	

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
Model 1[a]	1.30 (1.07, 1.57)	1.23 (1.03, 1.48)	1.11 (0.93, 1.32)	Reference	0.004
Model 2[b]	1.26 (1.05, 1.51)	1.19 (0.99, 1.43)	1.09 (0.91, 1.30)	Reference	0.01
Model 3[c]	1.21 (1.01, 1.44)	1.12 (0.94, 1.34)	1.07 (0.84, 1.27)	Reference	0.02
Model 4[d]	1.09 (0.91, 1.31)	1.05 (0.87, 1.26)	1.01 (0.84, 1.20)	Reference	0.63
High fibre bread					
N	2,533	2,566	2,830	1,760	
T2DM cases, %	10.2	9.9	9.7	9.1	
Intake (serves/day), mean (SD)	0.17 (0.20)	0.92 (0.17)	1.59 (0.18)	2.60 (0.48)	
Model 1[a]	1.17 (1.03, 1.36)	1.14 (0.98, 1.33)	1.12 (0.98, 1.29)	Reference	0.04
Model 2[b]	1.16 (1.03, 1.35)	1.14 (0.99, 1.33)	1.11 (0.97, 1.27)	Reference	0.04
Model 3[c]	1.15 (1.01, 1.33)	1.08 (0.93, 1.26)	0.97 (0.82, 1.15)	Reference	0.05
Model 4[d]	1.12 (0.97, 1.30)	1.09 (0.93, 1.28)	0.99 (0.83, 1.19)	Reference	0.08
Pasta and rice					
N	2,423	2,422	2,422	2,422	
T2DM cases, %	10.0	9.9	9.9	9.8	

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
Intake (serves/day), median (IQR)	0.18 (0.11-0.23)	0.38 (0.33-0.43)	0.61 (0.54-0.70)	1.10 (0.93-1.44)	
Model 1[a]	1.12 (0.94, 1.33)	1.11 (0.92, 1.33)	1.11 (0.88, 1.40)	Reference	0.07
Model 2[b]	1.10 (0.92, 1.31)	1.09 (0.90, 1.31)	1.12 (0.89, 1.41)	Reference	0.32
Model 3[c]	1.07 (0.88, 1.28)	1.09 (0.90, 1.31)	1.12 (0.89, 1.41)	Reference	0.38
Model 4[d]	1.05 (0.87, 1.26)	1.08 (0.89, 1.31)	1.10 (0.88, 1.37)	Reference	0.38
Discretionary foods					
N	2,423	2,422	2,422	2,422	
T2DM cases, %	9.5	9.7	9.9	10.2	
Intake (serves/day), median (IQR)	0.66 (0.48-0.81)	1.23 (1.10-1.36)	1.85 (1.67-2.06)	3.07 (2.62-3.86)	
Model 1[a]	0.93 (0.75, 1.16)	0.95 (0.76, 1.17)	0.97 (0.81, 1.17)	Reference	0.32
Model 2[b]	0.98 (0.78, 1.21)	0.97 (0.79, 1.20)	0.98 (0.81, 1.19)	Reference	0.97
Model 3[c]	0.99 (0.79, 1.23)	0.97 (0.79, 1.19)	0.97 (0.80, 1.18)	Reference	0.98
Model 4[d]	1.02 (0.81, 1.28)	1.00 (0.82, 1.23)	0.99 (0.82, 1.20)	Reference	0.96

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
	Consumer	Non-consumer			
White bread					
N	3,451	6,238			
T2DM cases, %	12.2	8.7			
Intake (serves/day), median (IQR)	1.13 (0.75-1.50)	-			
Model 1[a]	1.48 (1.28, 1.72)	Reference			<0.0001
Model 2[b]	1.37 (1.24, 1.52)	Reference			0.005
Model 3[c]	1.34 (1.22, 1.47)	Reference			0.01
Model 4[d]	1.37 (1.22, 1.53)	Reference			0.005
Added sugar					
N	4,745	4,944			
T2DM cases, %	10.6	9.3			
Intake (serves/day), median (IQR)	12.50 (6.25-12.50)	-			
Model 1[a]	1.13 (1.05, 1.27)	Reference			0.03

	Quartiles of carbohydrate-rich food groups				
	Quartile 1 (lowest consumption)	Quartile 2	Quartile 3	Quartile 4 (highest consumption)	P-value[e]
Model 2[b]	1.11 (1.02, 1.24)	Reference			0.04
Model 3[c]	1.10 (1.01, 1.23)	Reference			0.04
Model 4[d]	1.09 (0.97, 1.22)	Reference			0.08

IQR, interquartile range; LCD, low carbohydrate diet; SD, standard deviation; T2DM, type 2 diabetes mellitus

[a] adjusted for age, country of birth, energy intake, highest educational qualification, employment status and years of follow-up

[b] additionally adjusted for history of gestational diabetes and physical activity

[c] additionally adjusted for all other carbohydrate-rich food groups, dairy, red and processed meat and fish

[d] additionally adjusted for body mass index

[e] P value for trend was calculated for all food groups analysed as quartile

SUPPLEMENTAL TABLES

Supplemental Table 1. Comparison of daily dietary intake in 2001 and 2013

	2001 Survey 3 Age 50-55 years N = 7,521[a]	2013 Survey 7 Age 62-67 years N = 7,521[a]	P-value[b]	Average[c] N = 9,689
Energy intake (kcal)	1,570 (470)	1,476 (531)	<0.0001	1,530 (441)
Low carbohydrate diet score	14.8 (7.0)	15.0 (7.4)	0.03	15.0 (7.2)
Total fat (energy %)	35.1 (6.0)	37.1 (5.3)	<0.0001	36.1 (5.0)
Saturated fat (energy %)	13.9 (3.5)	14.8 (3.2)	<0.0001	14.3 (3.1)
Monounsaturated fat (energy %)	12.4 (2.4)	13.1 (2.3)	<0.0001	12.8 (2.1)
Polyunsaturated fat (energy %)	5.6 (2.0)	5.6 (1.8)	0.98	5.6 (1.7)
Protein (energy %)	20.5 (3.2)	21.0 (3.3)	<0.0001	20.7 (3.0)
Carbohydrates (energy %)	44.6 (6.4)	42.1 (6.1)	<0.0001	43.5 (5.6)
Dietary fibre (grams/1,000 kcal)	13.0 (3.6)	13.6 (3.3)	<0.0001	13.1 (3.1)
Glycaemic index	51.9 (4.2)	49.4 (4.3)	<0.0001	50.6 (3.6)
Glycaemic load, median (IQR)	86.2 (68.1-108.5)	73.1 (56.1-93.4)	<0.0001	81.5 (65.5-100.9)
Total sugar (g), median (IQR)	76.5 (58.6-97.5)	71.7 (55.2-91.2)	<0.0001	75.2 (59.2-92.7)
Added sugar consumer, n (%)	3,125 (41.6)	2,772 (36.9)	<0.0001	4,745 (49.0)
Fruit (serves)	1.58 (0.97)	1.64 (0.93)	<0.0001	1.60 (0.85)
Fruit juice (serves), median (IQR)	0.26 (0.06-0.75)	0.15 (0.01-0.62)	<0.0001	0.21 (0.04-0.69)
Vegetables (serves)	2.09 (0.98)	2.17 (0.95)	<0.0001	2.10 (0.88)
Cereal (serves), median (IQR)	0.89 (0.16-1.64)	1.09 (0.31-1.92)	<0.0001	1.00 (0.40-1.65)
White bread consumer, n (%)	2,225 (29.6)	1,114 (14.8)	<0.0001	3,451 (35.6)

High fibre bread (serves)	1.31 (1.09)	1.15 (0.88)	<0.0001	1.22 (0.88)
Pasta and rice (serves), median (IQR)	0.54 (0.29-0.93)	0.35 (0.18-0.62)	<0.0001	0.48 (0.28-0.79)
Discretionary foods (serves), median (IQR)	1.47 (0.87-2.35)	1.46 (0.85-2.33)	0.006	1.46 (0.86, 2.35)

IQR, interquartile range

Values are mean (SD) unless otherwise stated

[a] Dietary intake in 2001 and 2013 is based on data from women who completed both surveys

[b] P-values from chi-square test, t-test or Mann-Whitney test

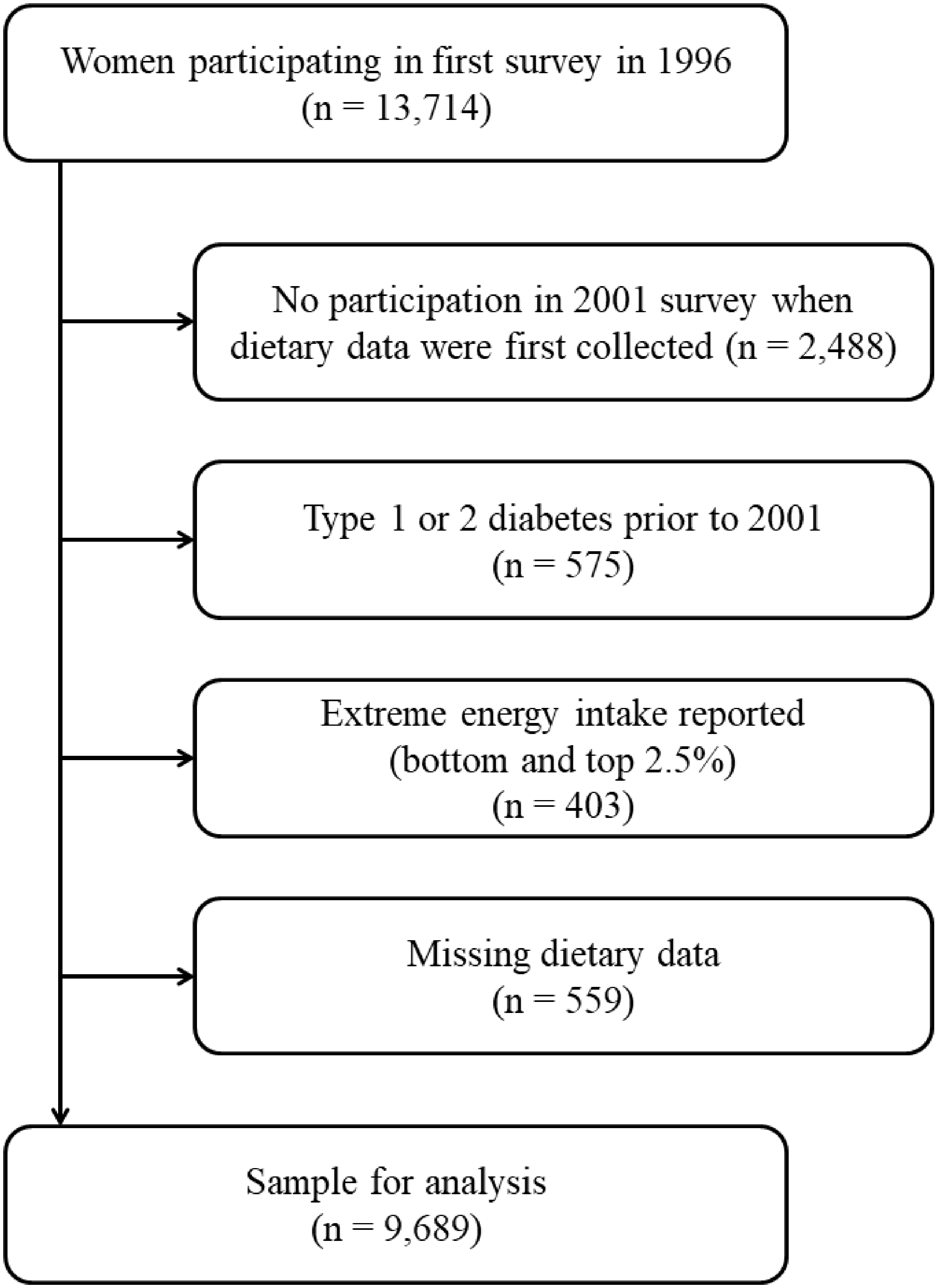
[c] Average nutrient and food intake was based on dietary data collected in 2001 and 2013, or in 2001 when women did not complete the 2013 survey (n = 2,168; 22%). For food groups reported as percentage consumers the average intake reflects consumption at one or both survey time points

Supplemental Table 2. Food items and serving sizes for carbohydrate-rich food groups and other diabetes-related food groups used in analysis

Food group	Serving size[a]	Food items included
Carbohydrate-rich food groups		
White bread	40g	White bread
High fibre bread	40g	High-fibre white bread, wholemeal bread, multi-grain bread, rye bread
Cereal	30g	All-bran, bran flakes, cornflakes, muesli, Weet-Bix
	120g	Porridge
Pasta and rice	100g	Pasta and rice
Fruit juice	125g	Fruit juice
Fruit	150g	oranges, apples, pears, bananas, melon, pineapple, strawberries, apricots, peaches, mangoes, tinned fruit
	45g	Avocado
Vegetables	75g	Bean sprouts, beetroot, broccoli, cabbage, carrot, cauliflower, capsicum, cucumber, celery, garlic, green beans, mushrooms, onion, peas, pumpkin, spinach, tomatoes, zucchini, potatoes
Discretionary foods	75g	Ice cream
	25g	Sweet biscuits and chocolate
	60g	Jam, meat pies, pizza, hamburgers
	40g	Cakes
	200g	Flavoured milk drink
	30g	Crisps
	35g	Crackers
Other food groups		
Dairy	250g	Full cream milk, reduced fat milk, skim milk and soy milk
	200g	Yoghurt
	120g	Ricotta or cottage cheese
	40g	Hard cheese, firm cheese, soft cheese and low-fat cheese
Red and processed meat	65g	Beef, veal, lamb, pork

	80g	Bacon
	60g	Ham, salami, sausages
Fish	100g	Fish (steamed/grilled/baked/tinned)

[a] Serving sizes according to the Australian Dietary Guidelines 2013


Women participating in first survey in 1996 (n = 13,714)
No participation in 2001 survey when dietary data were first collected (n = 2,488)
Type 1 or 2 diabetes prior to 2001 (n = 575)
Extreme energy intake reported (bottom and top 2.5%) (n = 403)
Missing dietary data (n = 559)
Sample for analysis (n = 9,689)

HIGHLIGHTS

- Of 9,689 mid-aged Australian women, 10% developed type 2 diabetes over 15 years
- Carbohydrate restriction was associated with a 27% higher risk of type 2 diabetes
- This association was attenuated after adjustment for BMI
- The association was comparable for women with and without prior gestational diabetes
- Women should be advised to avoid carbohydrate restricted diets low in fruit and grains