

Diabetes

Diet rich in whole grain foods may lower risk of diabetes

Higher consumption of total whole grain foods, such as oatmeal, dark bread, brown rice or whole grain cereals can reduce the risk of developing type 2 diabetes, a meta-analysis has shown.

Data were extracted from the Health Professionals Follow-Up Study (HPFS) and the Nurses' Health Study.

The HPFS was set up in 1986 when 51,529 male American healthcare professionals aged 40-75 years began completing questionnaires about their medical history and lifestyle.

The Nurses' Health Study commenced in 1976 and recruited 121,700 female nurses in the US aged 30-55 years. It was followed by the Nurses' Health Study II in 1989 which included 116,340 female nurses aged 25-42 years.

All three studies sent detailed questionnaires to participants every two years and follow-up has continued long term. Cumulative response rates in the three cohorts was > 90%.

The baseline for this study was taken as 1984 (the study assessment of diet had a major revision at this point) for the Nurses' Health Study, 1991 for the Nurses' Health Study II and 1986 for the HPFS.

The endpoint was the development of type 2 diabetes. Diagnoses were self-reported and 97% of self-reported cases were confirmed by medical records. Average follow-up was 24 years. In 4,618,796 person-years of follow-up, 18,629 new cases of type 2 diabetes were identified.

Consumption of whole grain foods was calculated as a long-term average based on the questionnaires returned

about diet. Patients who suffered a new chronic diagnosis that might be associated with a dietary change were excluded from further follow-up. Total whole grain intake was categorised into five equal groups based on the number of servings of whole grain foods. The five categories were the median values for daily servings: 0.1, 0.4, 0.7, 1.1 and 1.9.

There were noticeable differences between the groups at baseline; although BMI was similar, exercise levels were greater in the higher intake groups, and rates of smoking and chronic ill health were lower.

After adjustment for BMI and other lifestyle and dietary risk factors, higher whole grain consumption was consistently associated with a lower risk of type 2 diabetes. Participants in the highest category for whole grain consumption had a 29% (95% CI: 26-33%) lower rate of diabetes compared with those in the lowest category. Hazard ratio (HR) 0.71 (95% CI: 0.67-0.74; $P < 0.001$ for trend). Similar protection was found with dietary supplements of bran and wheat germ.

The relationship between intake of whole grain foods and reduction in diabetes risk was non linear, showing a plateau effect at > 2 servings a day beyond which further increase showed no further benefit. Maximum effect occurred at only 0.5 servings a day of breakfast cereal or dark bread.

This study has the limitation of being drawn from groups of predominantly white American healthcare professionals and may not be applicable to other populations.

Whole grains are known to contain fibre, antioxidants and phytochemicals which increase insulin sensitivity and basal metabolic rate and decrease cholesterol levels and inflammation.

The findings demonstrate that a healthy intake of whole grain foods reduces the risk of type 2 diabetes but it would be a mistake to view this in isolation. Whole grain food intake is a component of overall lifestyle change needed to reduce the population risk of type 2 diabetes, of which the most important factors are a reduction in overall food intake and increase in exercise.

DR MATTHEW LOCKYER

Hu Y, Ding M, Sampson L et al. Intake of whole grain foods and risk of type 2 diabetes: results from three prospective cohort studies. *BMJ* 2020;370:m2206

Respiratory disease

Is air pollution associated with onset of asthma in childhood?

A nationwide case-control study from Denmark has shown that parental asthma and smoking in pregnancy are risk factors for onset of asthma and persistent wheezing in children. The findings also suggest that exposure to ambient small particles < 2.5 μm ($\text{PM}_{2.5}$) may be a potential risk factor.

Children born between 1997 and 2014 were identified from a Danish national registry and followed up for onset of asthma and persistent wheezing from the age of 12 months to 15 years.

Overall, 122,842 children were identified as having asthma and persistent wheezing based on records of an asthma diagnosis or the provision of two or more asthma inhalers.

The majority of cases (83%) occurred in children aged under 3 years (average age 1.9 years). Each child with asthma was matched, by age and sex, with 25 controls who did not have an asthma diagnosis.

Data on parental asthma, maternal smoking patterns, parental education and socioeconomic status were also extracted from the relevant national databases.

Levels of pollutants were determined from models developed by the Danish air pollution modelling system and related to the children's home addresses.

Maternal asthma was associated with a higher risk than paternal asthma for asthma in offspring; hazard ratio (HR) 1.72 (95% CI: 1.72-1.77) vs 1.51 (95% CI: 1.48-1.53). Having two parents with asthma was associated with a 2.40-fold (95% CI: 2.34-2.47)

increased risk of asthma and persistent wheezing.

Maternal smoking during pregnancy was associated with an increased risk of asthma, and there was a positive dose-response relation between the number of cigarettes smoked daily and an increased risk of asthma and persistent wheezing.

Higher maternal educational level was associated with a reduced risk of asthma and persistent wheezing; HR 0.58 (95% CI: 0.56-0.59) for those with the highest level of education compared with those with the lowest.

The effect of a range of pollutants was examined but only a positive association between PM_{2.5} and asthma and persistent wheezing was found across all three models used (HR 1.03, 1.04 and 1.05 respectively) and in sensitivity analyses.

The study authors conclude: 'The findings from this study strengthen the evidence that parental asthma, parental education, and maternal smoking during pregnancy are risk factors for onset of asthma and persistent wheezing in children.

'Moreover, we found that children exposed to high levels of PM_{2.5} were more likely to develop asthma and to have persistent wheezing. These findings therefore support emerging evidence that exposure to air pollution might influence the development of asthma.'

'This finding needs to be substantiated in future studies,' they add.

DR PETER SAUL

Holst GJ, Pedersen CB, Thygesen M et al. Air pollution and family related determinants of asthma onset and persistent wheezing in children: nationwide case-control study. *BMJ* 2020;370:m2791

Smoking cessation

Nausea may affect adherence to varenicline

Nausea during the first few weeks of varenicline therapy may reduce adherence, a study from North America has found.

The authors analysed data on 870 adults receiving varenicline in two smoking cessation trials conducted at multiple sites in Canada and the United States. A total of 449 were taking part in the Quit2Live and 421 in the Pharmacogenetics of Nicotine Addiction Treatment (PNAT) trial.

Information on nausea severity was self-reported and adherence to treatment was assessed by measuring plasma or salivary varenicline concentration. Smoking abstinence was confirmed with either cotinine or carbon monoxide testing at a range of study time points.

At week 12, of the 381 participants for whom full data were available in Quit2Live, 108 had stopped smoking and 273 were still smoking. Respective values for PNAT were 144 (of 376) and 232.

Early nausea was indirectly associated with lower cessation rates at multiple time points in Quit2Live; odds ratios (OR) ranging from 0.92 (95% CI: 0.83-0.99) to 0.94 (95% CI: 0.86-0.99). This relationship was associated with reduced varenicline adherence (assessed by plasma varenicline levels).

The relationship between nausea, adherence and cessation was similar in direction but weaker in effect size; ORs ranging from 0.98 (95% CI: 0.90-1.01) to 0.99 (95% CI: 0.95-1.03) in PNAT, where adherence was assessed using salivary varenicline levels.

Varenicline has been shown to be an effective pharmacotherapy in helping smokers achieve long-term

cessation, significantly increasing stop rates compared with placebo.

However up to half of smokers treated with varenicline fail to achieve abstinence,¹ and reduced medication adherence may be one factor contributing to failure to quit.

Previous studies have shown that a third of varenicline-treated smokers were non-adherent by the second treatment week (one week post-dose titration),¹ and non-adherent smokers are significantly less likely to be abstinent at a range of treatment time points. In surveys investigating discontinuation of, and non-adherence with, varenicline the most frequently cited reason was adverse events, the most common being nausea.¹ Nausea in varenicline treated patients is generally mild to moderate, starting in the first 2 weeks of treatment and diminishing over the course of treatment.

The authors say that better management of early nausea during varenicline treatment may improve smoking cessation success rates by increasing varenicline adherence. They suggest extending the varenicline titration period and/or allowing patients to control the rate of titration and using lower dose regimens (0.5 mg twice daily). Explaining to patients that nausea may occur in the early treatment stages, and that the effect lessens over time, and providing antiemetic medication during early treatment may also help improve adherence, they say.

DR JEZ THOMPSON

Peng AR, Swardfager W, Benowitz NL et al. Impact of early nausea on varenicline adherence and smoking cessation. *Addiction* 2020;115:134-44

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¹ Kaur K, Kaushal S, Chopra SC. Varenicline for smoking cessation: a review of the literature. *Curr Ther Res Clin Exp* 2009;70:35-54

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