Management & prevention of type 2 diabetes

DIABETES CARE

Metabolic markers better predict onset of type 2 diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 To identify people at increased risk for type 2 diabetes, a subcohort of 2500 people from the EPIC (European Prospective Investigation into Cancer and Nutrition)-Potsdam study (n=27 548) were assessed at baseline and followed-up by questionnaire.

2 The study aim was to determine whether metabolic biomarkers and single nucleotide polymorphisms (SNPs) significantly improve the prediction of type 2 diabetes beyond age, anthropometry and lifestyle risk factors.

3 In total, 801 incident cases of type 2 diabetes were identified in the subcohort during the 7-year follow-up; 579 qualified for analyses.

4 Different prediction models were evaluated by comparing the receiver-operating characteristics (ROC) area under the curve (AUC) and integrated discrimination improvement.

5 The ROC-AUC significantly increased when HbA_{1c} and plasma glucose were incorporated into a model with the German Diabetes Risk Score (from 0.8464 to 0.8862).

6 Case-control discrimination by important lifestyle risk factors (e.g. physical activity, smoking, alcohol and diet) was significantly improved by glucose, HbA_{1c}, HDL-cholesterol, triglycerides and liver enzymes; 20 SNPs did not further improve prediction.

7 Plasma glucose and, in particular, HbA_{1c} were concluded to improve the prediction of incident type 2 diabetes beyond age, anthropometry and lifestyle characteristics.

Schulze MB, Weikert C, Pischon T et al (2009) Use of multiple metabolic and genetic markers to improve the prediction of type 2 diabetes: the EPIC-Potsdam Study. *Diabetes Care* **32**: 2116–19

Comparing differing tests to predict type 2 diabetes: Simple scores plus HbA_{1c} may be best

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This short report from Germany (Schulze et al, 2009; summarised alongside) reveals several interesting aspects relevant to the prediction (and thus also screening) of type 2 diabetes.

First, simple, non-laboratory-based or lifestyle factors on their own (i.e. even before blood tests are taken) can give good prediction of future diabetes risk. Indeed, it is increasingly clear from this and several similar reports (Hippisley-Cox et al, 2009; Kahn et al, 2009) in a range of diverse populations that good prediction of diabetes using a common set of parameters (such as age, ethnicity, BMI, history of smoking, blood pressure and family history of diabetes) is possible. Indeed, the predictive ability for diabetes from such measures is easily on a par with the ability of established risk factors to predict incident cardiovascular events.

Second, the report also highlights the potential of HbA_{1c} to improve prediction of diabetes beyond simple risk scores, with tantalising evidence to show that it may do so better than fasting glucose. This latter point makes biological sense as postprandial excursions predate major changes in fasting glucose in individuals destined to develop diabetes. In other words, the use of a measure that captures some element of postprandial glucose excursions is clinically important if we are to move to widespread diabetes screening, and HbA_{1c} captures this information.

Third, further improvements in diabetes prediction, albeit modest, can be captured by other simple blood tests such as lipids and liver function tests. However, the extent of such improvement is unlikely to be clinically beneficial or cost-effective unless such tests are to be measured anyway as part of combined vascular/diabetes screening, and programmes to incorporate these measures into a diabetes risk score that combine both non-laboratory and laboratory-based tests can be easily developed and implemented. While such programmes are possible, they may be too complex for widespread implementation.

Finally, and perhaps the headline from the present article, genetic markers do not improve on the prediction of diabetes beyond simple risk scores and a glycaemia measure. For those who have been following this area, this finding should not be surprising given at least three prior studies in different populations have come up with near identical conclusions (Lyssenko et al, 2008; Meigs et al, 2008; Talmud et al, 2010). Of course, this does not mean genetics have no role in future diabetes research; uncovering genes may help to identify better causal pathways, identify new targets to lower glucose and improve drug targeting. However, it is clear that genes will not be needed to predict diabetes when we have much simpler, cheaper and effective options.

Perhaps the key next question in considering a potential widespread move towards systematic diabetes screening is whether HbA_{1c} is ratified for diagnosis of diabetes. Personally I think this will occur despite some limitations for HbA_{1c}, but its simplicity and its ability to be measured in non-fasting samples is a big advantage over current methods. If this change is approved, this in turn may pave towards simple and pragmatic processes to integrate HbA_{1c} into a two-stage diabetes screening programme, with a first stage involving some form of risk score.

This article highlights the excellent prediction of diabetes afforded by combining simple risk score with HbA_{1c}. Future work should be undertaken to quickly translate such evidence into clinical practice.

Hippisley-Cox J, Coupland C, Robson J et al (2009) Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ* **338**: b880

Kahn HS, Cheng YJ, Thompson TJ et al (2009) Two risk-scoring systems for predicting incident diabetes mellitus in US adults age 45 to 64 years. *Ann Intern Med* **150**: 741–51

Lyssenko V, Jonsson A, Almgren P et al (2008) Clinical risk factors, DNA variants, and the development of type 2 diabetes. *N Engl J Med* **359**: 2220–32

Meigs JB, Shrader P, Sullivan LM et al (2008) Genotype score in addition to common risk factors for prediction of type 2 diabetes. *N Engl J Med* **359**: 2208–19

Talmud PJ, Hingorani AD, Cooper JA et al (2010) Utility of genetic and non-genetic risk factors in prediction of type 2 diabetes: Whitehall II prospective cohort study. *BMJ* **340**: b4838

"People with a higher total, white and oily fish intake (one or more portions a week) had a decreased risk of diabetes; a higher total fish intake decreased the risk of diabetes by 25%."

CLINICAL ENDOCRINOLOGY

Smoking is an independent risk factor for diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 A total of 10 038 people were assessed at baseline and at 4 years to determine the link between smoking and the incidence of type 2 diabetes; the results of 4041 men were included in the study.

2 Ex-smokers and heavy smokers (≥20 cigarettes/day) had the highest incidence of diabetes (12.5% and 11.1%, respectively) compared with never smokers (7.9%); current smokers had an incidence of 10.7%.

3 Of the men with impaired glucose tolerance at baseline, heavy smokers had a 2.9-fold increased incidence of diabetes than never smokers.

4 After adjustments were made for confounding variables, current and heavy smokers had more than a two-fold increased risk of type 2 diabetes at 4 years compared with men who had never smoked, and showed higher relative risk compared with ex-smokers.

5 The risk of new-onset diabetes was highest in men with low beta-cell function and high insulin resistance both in smokers and never smokers.

6 After adjustment of confounding factors, smoking was found to be an independent risk factor for type 2 diabetes and showed synergistic interaction with the status of low insulin secretion and high insulin resistance for developing diabetes.

7 The authors concluded that smoking cessation plays an important role in diabetes prevention.

Cho NH, Chan JCN, Jang HC et al (2009) Cigarette smoking is an independent risk factor for type 2 diabetes: a four-year community-based prospective study. *Clinical Endocrinol* **71**: 679–85

DIABETES CARE

Dietary fibre reduces risk of type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Although studies have shown that dietary fibre may reduce the risk of type 2 diabetes, the role of hepatic and inflammatory markers remains unclear.

2 This prospective study examined the dietary intake and blood measurements of 3428 men aged 60–79 years; there were 162 incident cases of type 2 diabetes over the mean follow-up of 7 years.

3 Low dietary fibre intake (≤20 g/day) was associated with an increased risk of diabetes (relative risk –1.47).

4 The data suggest that a high fibre intake may lessen diabetes risk in part by reducing inflammation and in part by reducing liver fat accumulation, both pathways known to be linked to development of diabetes.

Wannamethee SG, Whincup PH, Thomas MC, Sattar N (2009) Associations between dietary fibre and inflammation, hepatic function and risk of type 2 diabetes in older men. *Diabetes Care* **32**: 1823–5

DIABETES CARE

Metformin reduces risk of cancer in type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 Metformin is used in type 2 diabetes to reduce blood glucose levels by activating AMP-activated protein kinase (AMPK); however, AMPK can also suppress tumour formation and inhibit cell growth.

2 This study examined whether people with type 2 diabetes controlled by metformin therapy had a reduced risk of cancer.

3 The study comprised people with type 2 diabetes who were on metformin therapy (n=4085) and matched comparators not taking metformin (n=4085) who were followed-up for a maximum of 10 years; the primary outcome was diagnosis of cancer.

4 Cancer was diagnosed in 297 people in the metformin group (7.3%) with a median time to cancer of 3.5 years, compared with in 474 comparators (11.6%) with a median time to cancer of 2.6 years (P<0.001).

5 The authors concluded that further studies are required to determine whether metformin is protective in a group that has a high cancer risk.

Libby G, Donnelly LA, Donnan PT et al (2009) New users of metformin are at low risk of incident cancer. *Diabetes Care* **32**: 1620–5

DIABETES CARE

Eating white and oily fish reduces diabetes risk

Readability	✓✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 This study assessed the habitual intake of white, oily and fried fish and shellfish in 21 984 men and women (aged 40–79 years) to determine any link between fish consumption and developing type 2 diabetes.

2 Fish and shellfish intake were determined by questionnaire, with a mean follow-up of 10.2 years; during the study 725 people developed type 2 diabetes.

3 People with a higher total, white and oily fish intake (one or more portions a week) had a decreased risk of diabetes; a higher total fish intake decreased the risk of diabetes by 25%.

4 Eating shellfish once or more a week was found to increase the risk of diabetes by 36%.

Patel PS, Sharp SJ, Luben RN et al (2009) Association between type of dietary fish and seafood intake and the risk of incident type 2 diabetes. *Diabetes Care* **32**: 1857–63