

Comment on “Lifetime risk of progression from prediabetes to type 2 diabetes: a prospective cohort study” by Ligthart et al

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The prevalence of type 2 diabetes mellitus (T2DM) is increasing globally, and the prevalence of those who are at risk of T2DM (often termed 'pre-diabetes') is even higher. There is good evidence that intensive lifestyle prevention programmes can prevent or delay the onset of T2DM in those at high risk. The efficacy of these interventions has however been lower in real world settings,¹ and there are also concerns regarding the uptake of structured education programmes outside of trial settings.² Communication of risk to individuals at risk of T2DM is therefore an important issue. There has been great interest in patients being involved in decision making, and a number of studies have explored patient preferences for presentation and framing of risk information.³ These have shown that lifetime risk estimates are preferred over 10 or 20 year risk estimates, and absolute risk estimates are preferred over relative risks.³ There is therefore now a move from using 10-20% risk thresholds towards using lifetime risk, which measures the cumulative risk of developing a disease during the remainder of an individual's life.⁴

In a linked article published today, Ligthart and colleagues use data from the prospective Rotterdam Study based in the Netherlands (N=10,050; up to 14.7 years follow-up) to alert us to the high burden of absolute lifetime risk at population level of developing pre-diabetes or progressing from pre-diabetes to diabetes and then onto insulin therapy.⁵ The analyses are quite interesting, with lifetime risks from the age of 45 years old of 48.7% for pre-diabetes, 31.3% for diabetes, 9.1% for usage of insulin, and 74.0% for progressing from pre-diabetes to diabetes. Furthermore the quantification of risk with increasing body mass index suggests that individuals with severe obesity live 10 fewer years without any glucose impairment than normal weight individuals. The choice of graphical formats to convey risk to patients has also previously been explored, and the stated preference for bar charts³ is in line with some, but not all, of the graphs presented in the linked paper. This paper re-emphasises the substantial detrimental burden that those with or at high risk of T2DM have on our healthcare systems with an estimated one in three adults developing T2DM at some point in their life. To build on this work, more research needs to be done in the development of lifetime risk tables and risk communication of these tables to individuals; an area which is still in its infancy.

We welcome this paper's attempt to accurately describe progression rates to T2DM as this is important for clearly identifying people who are at high risk, and for effective planning, interventions, and monitoring.⁶ Nevertheless, progression rates from pre-diabetes to diabetes vary enormously depending on the criteria used for diagnosis.⁶ Ligthart and colleagues identified people who are at high risk or who have screen-detected T2DM predominantly using serial fasting glucose measurements.⁵ There is an increasing move towards use of HbA1c for diagnosis of T2DM and those at risk of T2DM in view of its convenience.⁷ Glucose and HbA1c appear to detect differing T2DM and at risk populations,⁸ and progression rates may differ depending on the method used to diagnose pre-diabetes and T2DM,⁶ thus the lifetime risk observed in practice might differ substantially from that estimated in the linked paper.

It is also notable that the population studied by Ligthart and colleagues were predominantly of white ethnicity (97%).⁵ Therefore, the lifetime risks provided will not be applicable to other ethnic groups, who often have higher progression rates,⁹ and consequently could be expected to have an even higher lifetime risk of T2DM than the one in three risk calculated in the current study. The approach in this study of communicating risk of developing T2DM by

body mass index would also be useful for different ethnicities due to different ethnic cut-points for defining obesity.¹⁰ Finally, another interesting finding from Ligthart and colleagues was that they determined the lifetime risk of insulin use; however, this is very much dependant on clinical practice and there are huge variations when insulin is initiated and there are often long delays in insulin initiation, especially with new classes of glucose lowering therapies being introduced.¹¹

Overall, this study highlights the lifetime risks of developing different states of hyperglycaemia, and adds further evidence on potential novel methods for communicating risk so that efficacious prevention strategies can be implemented.

References

1. Dunkley AJ, Bodicoat DH, Greaves CJ, et al. Diabetes prevention in the real world: effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes and of the impact of adherence to guideline recommendations: a systematic review and meta-analysis. *Diabetes care* 2014; **37**(4): 922-33.
2. Salmela SM, Vahasarja KA, Villberg JJ, et al. Perceiving need for lifestyle counseling: findings from Finnish individuals at high risk of type 2 diabetes. *Diabetes care* 2012; **35**(2): 239-41.
3. Fortin JM, Hirota LK, Bond BE, O'Connor AM, Col NF. Identifying patient preferences for communicating risk estimates: a descriptive pilot study. *BMC medical informatics and decision making* 2001; **1**: 2.
4. Board J. Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart* 2014; **100 Suppl 2**: ii1-ii67.
5. Ligthart SvH, T.T.W.; Leening, M.J.G.; Kavousi, M.; Hofman, A.; Stricker, B.H.C.; van Hoek, M.; Sijbrands, E.J.G.; Franco, O.H.; Dehghan, A. Lifetime risk of progression from prediabetes to type 2 diabetes: a prospective cohort study. *Lancet Diabetes and Endocrinology* 2015.
6. Morris DH, Khunti K, Achana F, et al. Progression rates from HbA1c 6.0-6.4% and other prediabetes definitions to type 2 diabetes: a meta-analysis. *Diabetologia* 2013; **56**(7): 1489-93.
7. WHO. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. Geneva; 2011.
8. Mostafa SA, Davies MJ, Srinivasan BT, Carey ME, Webb D, Khunti K. Should glycated haemoglobin (HbA1c) be used to detect people with type 2 diabetes mellitus and impaired glucose regulation? *Postgraduate medical journal* 2010; **86**(1021): 656-62.
9. Oldroyd J, Banerjee M, Heald A, Cruickshank K. Diabetes and ethnic minorities. *Postgraduate medical journal* 2005; **81**(958): 486-90.
10. Bodicoat DH, Gray LJ, Henson J, et al. Body mass index and waist circumference cut-points in multi-ethnic populations from the UK and India: the ADDITION-Leicester, Jaipur heart watch and New Delhi cross-sectional studies. *PloS one* 2014; **9**(3): e90813.
11. Khunti K, Wolden ML, Thorsted BL, Andersen M, Davies MJ. Clinical inertia in people with type 2 diabetes: a retrospective cohort study of more than 80,000 people. *Diabetes care* 2013; **36**(11): 3411-7.