Author reply: Which risk engines are best to assess CVD risk in diabetes?

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We thank Chamnan and colleagues for their interest in our News and Views article (Diabetes: Which risk engines should be used to assess patients with diabetes? *Nat. Rev. Endocrinol.* 5, 302–303; 2009),¹ but believe that they have potentially misinterpreted the content of our paper in their correspondence (Which risk engines are best to assess CVD risk in diabetes? *Nat. Rev. Endocrinol.* 6, doi:10.1038/nrendo.2009.100-c1) and on more careful rereading would find that we are both in broad agreement. For points of further clarification we respond as follows. Our article referred to a cross sectional study by Price *et al.* in a trial population of men which suggested that using the UK Prospective Diabetes Study (UKPDS) risk engine, 2% more patients would be considered eligible for statin treatment versus the Framingham risk engine.² We highlighted that the relevance of this was unclear as that study was unable to compare observed versus predicted risk and hence was uninformative for discrimination and calibration and also net clinical reclassification. To this end, we have cited the helpful work of Simmons and Griffin who have previously described that both the UKPDS and the Framingham risk engine overestimate risk by 8% to 12%, respectively, in the EPIC Norfolk study.³

We respectfully disagree with Chamnan *et al.* that the prediction of short-term risk is more useful than accurate estimation of long-term risk given that the treatments offered are life-long and as clinicians we are duty bound to assess risk and benefits from any intervention. Hence lifetime risk is being considered more relevant to long-term

decisions with respect to individuals with chronic disease, with the caveat that there remain methodological uncertainties on how to assess lifetime risk.

Single studies do not preclude the potential benefit of adding any biomarker to risk prediction models,⁴ particularly as it is well recognized that individual studies have much less power than prospective pooling projects which are 10–20 fold larger. Subgroups such as women or younger individuals have fewer events and are likely to require much larger numbers of incident cases before one can confirm or refute the clinical utility of any given risk score or any given biomarker. This is likely to require access to individual data rather than summary data to allow for harmonizing of endpoint definitions and consistent adjustment for confounders. For instance, the large ERFC (Emerging Risk Factors Collaboration) dataset enabled the demonstration of the etiological relevance of lipoprotein(a) to coronary heart disease and stroke, albeit a modest effect, and by its size provided reliable information in important subgroups.⁵ That noted, we entirely agree and recognize that the benchmark for any new biomarker to add any useful information beyond established risk scores is indeed high, as we recently concluded.⁶

Regardless, perhaps the crucial issue is that given the global shift towards treating all individuals beyond a certain age threshold with type 2 diabetes mellitus with statins, perhaps we should identify clinicians who would act on risk factor information or simply treat everyone. We would suggest that among patients with diabetes mellitus who are at higher life

time risk one does not need to assess how information on risk scores translates into uptake of good clinical practice, but rather the strategies which optimize risk factor control and promote healthy lifestyles after the diagnosis of diabetes mellitus require further assessment.

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Competing interests

K. K. Ray declares an association with the following company: Novartis. N. Sattar declares associations with the following companies: GlaxoSmithKline, Merck, MSD and Novo Nordisk.

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