Review of: "Communicating polygenic and non-genetic risk for atherosclerotic cardiovascular disease - An observational follow-up study"

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With interest I have been reading this study. I have long contemplated on how to go about polygenic risk scores (PRS) for cardiovascular disease (CVD). To answer this question one first needs to decide on where to use it for. If you want to improve individual risk precision, adding the PRS to the traditional risk factors seems reasonable and has been shown to better predict future CVD. On the other hand, from a societal point of view, this seems an costly undertaking and might not be necessary when trying to prevent CVD in the future. Concerning costs in health care it might be cheaper to create a fishing net approach, in which one roughly identifies the high risk individuals (> 10% risk), by screening disease (diabetes, hypertension, inflammatory disease ect) and family history together with cheap risk factor measurements and in addition add a coronary calcium score (CACs) to identify whom is actually still LOW risk. In other words, you do not need the *precision* when your treatment is particularly safe, you just do not want to treat to many individuals falsely, leading to incremental costs. On the other hand, positively predicting by adding the PRS or using the negative predictive value of the CACs, entirely depends on the additional costs that comes along with it.

This is a nice and well executed large cohort study, with a solid methodology and statistical analysis. The study shows that a risk evaluation tool was able to motivate individuals with a high CVD risk to healthier behaviour leading to a decline in risk factors (either due to the initiation of treatments, or because individuals stopped smoking or lost weight). I am not really sure what the authors intended when conducting this study. In my opinion either you would like to know whether adding the PRS to the risk factor profile would lead to even healthier behaviour or did the authors simply wanted to show the simplicity in the functioning of their risk evaluation tool. If the fist is what the authors intended, I would have expected a randomized controlled trial, randomising to either only information on conventional risk factors versus a more elaborated approach also including the PRS results. The outcome blood lipids, plasma glucose and blood pressure, as well as health behavioural actions could then be scored between both groups, leading to a conclusion of whether the addition of PRS indeed leads to significantly better health behaviour. In my opinion this is the key information you would want to know, before spending more money on risk prediction.