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Re: The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis

Cust, A.E., Smit A., Newson, A. (2 May 2016)

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Hollands et al provide an important contribution to evidence on the potential impact of DNA-based disease risk information on health behaviours. Based on the findings of their systematic review and meta-analysis, the authors conclude that: "existing evidence does not support expectations that such interventions could play a major role in motivating behaviour change to improve population health (1)." However, we contend that this conclusion is premature. In particular, there has been limited population-based research using risk estimates based on multiple genomic variants, for a broad range of health behaviours, and lack of evaluation of whether the impact may be influenced by the presence of other risk factors. We also agree with other rapid responses (Hay and McBride, Janssens, Burton) that highlight other limitations of the previous studies and the need for more research to more fully assess the potential role of genomics in facilitating behaviour change.

With regards to "population health", few studies in the review were representative of the general population. Most of the studies were based on 'high-risk' groups and some studies were restricted to small population subgroups such as factory workers or university students. A number of differences in characteristics between 'high-risk' groups and the broader average-risk population have been observed, such as base rates of screening and other health habits, and awareness of genetic testing and genetic literacy (2). Such differences could mean that genomic risk information might impact the broader population differently, but to date, few studies examining the impact of DNA-based disease risk

[1] Hollands GJ, French DP, Griffin SJ, et al. The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis. BMJ 2016;352:i1102.

information have been undertaken in populations not defined by a particular characteristic, such as being at higher risk of a particular condition.

Many of the studies in this systematic review communicated disease risk estimates based on single or few genomic variants. Single-gene common variants underestimate the complexity of genomic contributions to common diseases, have little effect on personal risk and are likely to produce risk messages of low motivational potency (2,3). Furthermore, expectations for the role of DNA-based disease risk information in improving population health are arguably based on testing for multiple (as opposed to single or few) genomic variants.3 As technology is advancing, we are finding more genomic variants that contribute to common, complex diseases. In our field of melanoma prevention, common genomic variants have been found in at least 20 genes (4) and they make a strong contribution to melanoma risk prediction (5,6). We recently conducted a pilot randomised controlled trial in which we provided the public with personalised genomic risk as a combined risk estimate based on variants in 21 melanoma genes. Our results showed strong interest, feasibility and acceptability of giving such information to the public, and potential 'clinically important' improvements to prevention behaviours (manuscript submitted). However, a larger, adequately-powered study is required to fully assess the impact of this intervention.

Only one study (Glanz et al, 2013)(7) in this review measured sun-related behaviours as a primary outcome. Despite only 73 people in the study, they found a standardised mean difference of 0.43 (95% CI -0.03 to 0.90, P=0.07), indicating a borderline-significant increase in sun protection for the intervention group compared to the control group. Another finding by Glanz et al, not reported in the review by Hollands et al, was a significant increase in the frequency of skin self-examinations (P=0.002), which is important for secondary prevention of melanoma. Hollands et al argue that "clear justification" is required to conduct additional large scale trials in this field. We submit that these moderate effect sizes represent justification "that efficacy of a clinically important degree is possible" and deserve further investigation in a larger study, and with a broader population since the people in this study had a family history of melanoma. Equally important is a wide-ranging and interdisciplinary discussion as to what a "clear justification" can and should comprise.

In summary, we contend that in order to make firm conclusions about a role for DNA-based disease risk information to improve population health, we need more population-based research using risk estimates based on multiple genomic variants, and evaluation of whether the impact may be influenced by the presence of other risk factors. More research is also needed to assess whether the effect of genomic risk information might differ when used as a strategy for primary prevention (e.g. targeting health behaviours to reduce disease incidence) versus secondary prevention (e.g. targeting screening behaviours to improve early detection) of disease. These investigations should be accompanied by psycho-social and ethical evaluations of the impact of this information, and deliberation over what criteria are appropriate to use as justifications for this kind of data.

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