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Response to letter to editor “Only ITT analysis provides information about the actual effects of a health policy”

Assessment of health policy effects of health checks requires a broader perspective than the ITT

Lars Bruun Larsen¹, Trine Thilsing¹, Jens Sondergaard¹, Anne-Louise Bjerregaard²

¹ Department of Public Health, Research Unit of General Practice, University of Southern Denmark, J.B. Winsløws Vej 9A DK-5000 Odense
² Department of Public Health, Institute of General Medical Practice, Aarhus University, Bartholins Allé 2, DK-8000 Aarhus C

Lars Bruun Larsen (corresponding author) lblarsen@health.sdu.dk +45-65503058
Trine Thilsing tthilsing@health.sdu.dk
Jens Sondergaard jsonsoendergaard@health.sdu.dk
Anne-Louise Bjerregaard albj@ph.au.dk

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We thank Bender and colleagues for their reply and will briefly provide some comments. With its firm focus on internal validity a RCT is first and foremost used to estimate intervention effects. Why else use such a firm design? In our reply to the original letter we merely argued that under the assumption of non-compliance bias, that is first, incomplete participation, and second, differences between actual participants and non-participants, then a CACE analysis will provide a less biased estimate of the intervention effects (not the population effects) than an ITT and a per-protocol analysis (1). In a CACE analysis the intervention effect is estimated by comparing the mortality rate among actual participants and the would-have-been participants in the control group had they received the intervention. As such, a CACE actually intends to eliminate the bias seen between participants and non-participants by applying the counterfactual condition to causal inference in RCTs with incomplete participation. Therefore, we do not agree with Bender and colleagues when they state that "the analyses performed by the authors are heavily biased – close to useless."(2). Contrary, an estimate of
the intervention effect derived from a CACE analysis may be a valuable and less-biased supplement to estimates derived from ITT and per-protocol analyses.

In their original letter Bender and colleagues conclude that “In the future, we encourage researchers to be cautious when basing conclusions on results from effect analyses restricted to participants, as these results most likely will overestimate effects of general health checks.” (3). Since population level effects from RCTs may well differ from real world implementation, we add that researchers and policy makers should be cautious to base conclusions solely on ITT analyses derived from RCTs with an obvious non-compliance bias. Assessment of population level effects of health checks may require studies that: 1) capture the clinical complexity of health checks, 2) show effects on those who actually may benefit from health checks, and not merely assess the effects on the general population whatever their risk and former health care usage, and 3) allow for changes to the intervention during implementation, in order to embrace contextual influences and new evidence. This is not an easy task, and one that will require a broader analytical perspective than that of the RCT combined with an ITT.

Hard statements on the population level effects of general health checks from RCTs may be convincing to policy makers, but not fruitful to the scientific debate. We like to push a more nuanced debate informed by results from RCTs, observational studies, qualitative studies and studies of contextual factors, and use new designs and research methodologies to evaluate health checks, and not just rely on the ITT. The first step is to come to some kind of agreement in the research community to move forward scientifically and to point to the direction. In our understanding this will be more fruitful in a push for a more evidence–based use of health checks.

Finally, we support the statement of Bender and colleagues that health checks may well be effective at an individual level. We furthermore suggest that the next step is to move from “What is the effect of health checks?” to “How do we translate the intervention effects from RCTs to the clinical setting and to a real world population-level setting in such a way that both the intervention and population level effects may be assessed while scaling up?”. 


HIGHLIGHTS

- A CACE analysis may provide a less biased estimate of the long-term intervention effects than an ITT or per-protocol analysis.
- Suggest a move from a question of “What is the effect of health checks?” to “How do we translate the intervention effects from RCTs to the clinical setting and to a real world population-level?”