Author’s response to reviews

Title: Understanding factors associated with the translation of cardiovascular research: a multinational case study approach

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Author’s response to reviews: see over
Dear Professor Sales

Understanding factors associated with the translation of cardiovascular research: a multinational case study approach

Thank you for the email of 16 Sept in relation to the above paper. We are grateful to the reviewers and editors for the comments, which have led us to strengthen the paper in several ways.

We believe several responses are appropriate to the main comment from the editors, based on Reviewer 1’s observations about what the manuscript adds to the conclusions already published in the original reports from RAND Europe. First, we had of course been completely open about the existing reports in our initial correspondence, and we agree with Dr Pearson that the paper provides useful signposts to the original reports. Indeed, we believe it is important that the findings of studies such as this are disseminated as widely as possible.

But second, we have now also undertaken some further analysis with the aim of enhancing the contribution that the study could make to the field of implementation science. We have supplemented the findings of our original study through applying a parallel approach to a detailed analysis of a single case. So again we started with the impact achieved, and on this occasion thoroughly examined the text of the selected full case study in order to identify the complexities that were involved in the translation of even a single body of research into policy and practice. We wanted to uncover the diversity of theories and conceptual discussions that could contribute to an understanding of the complexities of how various features of just one original research project interact and influence the degree of translation achieved. This new material is described in appropriate places of all the sections of the paper (usually towards the end) and especially in the new Table 4.

We hope that this satisfactorily addresses the concerns raised in your email about how the article differs from the previous published reports, and we believe our further analysis has added to the contribution made by the paper. Furthermore, based on a comment from Reviewer 2, we have, as explained below, re-analysed the data used to prepare Table 3, using an alternative approach, and while the conclusions remain the same, the precise numbers have changed slightly and this is, therefore, now a somewhat different table from the one in the original reports. Finally, Table 2 did not appear in the original RAND reports - it displays data that were presented in the original reports, but as a Figure with no specific numbers stated.
RESPONSE TO REVIEWER 1:

Minor Essential revisions:

2. The authors state that the final choice was by random choice, though they do not make clear exactly how this was done, nor how many PIs were approached and how many responded (probably a biased sample). We are not told whether the relatively small sample was balanced across all stratifying categories.

3. They stratified and scored the payback from the studies in 4 categories. The current manuscript does not make clear how many grants were categorised as “large” or “small” (page 7) or what this equates to financially: the summary analysis does not include an estimate of payback according to grant size, which seems at least as relevant as the other ways to stratify the data.

Response: We have responded to these 2 points together by making the following amendments to the Selecting a stratified sample for case studies, section of the Methods (with as far as possible the additional material here shown in bold). The addition also has End Note a linked to it. Together these give more details about how the selection was made with the number of PIs approached and how many responded, and the balance across the stratifying categories, including the number that were categorised as large or small:

‘For each country we populated a selection matrix using the three key characteristics (types of research, size of grant, and initial estimate of impact). This gave us eight cells for each country and we randomly selected a case from each cell.

The Canadian team were able to conduct an additional four cases, divided between the various categories. As explained below, one additional case study was undertaken in the UK leaving the final total of 29 cases as being 12 Canadian, nine British and eight Australian. Of the original 28 researchers selected at random from the various cells, 22 agreed to participate, but three of the 22 were not completed. a Finding suitable replacements contributed to an eventual slight imbalance in the set of cases: five of the eight Australian cases were selected from the high impact group, and three from the low impact group. For the UK there were four selected from the high impact and five from the low impact. In Canada there were six in each group. Overall, the balance between basic (15 case studies) and clinical (14) was maintained, as was that between cases initially estimated to have high impact (15) and low impact (14), and between large size (15) and small (14). Nevertheless, in the basic, small, low impact group we ended up with just two studies instead of the intended three, and both of these were
from the UK as an additional case was required in this cell because there was no case study from Australia or Canada [22].’

’a In one of the three cases it transpired that the grant did not meet our inclusion criteria, in another study insufficient evidence was available to allow full completion, and in the third the researcher had moved to Japan. [22].’

We have also added End Note b which links to the end of the Identifying factors that might explain variations in impact sub-heading in the Methods section and explains how there was variation between the grant sizes in different countries, and why for that and other reasons we decided not include comparisons between large and small grants. (This End Note also explains why we did not include country comparison):

’ b We eventually decided not to attempt any analysis based on grant size as the range of sizes turned out to be relatively small, differed between countries and was not always correctly reported in funders’ records [22]. Similarly, we do not include any country comparisons because of concerns that any differences between scores for countries might have been a reflection of the fact that each country had its own specific team to conduct the cases, and despite our attempts to ensure consistency in the conduct of the cases, some differences might have emerged.’

**Discretionary revisions:**
4. The authors draw considerable attention to the variation in impact between basic and clinical research projects. However, this reviewer finds nothing surprising about the conclusions. Research forms a continuum from discovery to development and application. While it is correct to emphasize that the lag period across this spectrum is often 15-20 years, not all discovery research will ever lead to development, and not all development will be successfully translated into health benefit. This is probably inevitable, but without support of discovery research there will be nothing to develop and translate. The conclusion (page 17) that funders should [preferentially] encourage and support basic research that has a clinical motivation is therefore misguided.

**Response:** We have addressed the wording referred to in the reviewer’s final sentence, and amended the end of the penultimate paragraph of the Policy Implications section of the Discussion to read:

‘Perhaps along similar lines, the findings about basic research with a clinical motivation being associated with high impact, at least in the time period over which this study was conducted, are findings that funders should consider in relation to their portfolios of research
and the timescales over which they hope to make an impact. This also correlates with a previous study of research on diabetes [23].’

And we also amended the penultimate sentence of the Conclusion to read:
‘They should also, where relevant, consider the finding that basic research proposals which have a clear clinical motivation seem, at least in a 15-20 year timescale, more likely to make a wider impact.’

5. “Strategic thinking” is defined as showing evidence that the researchers had “thought through the pathways” to translation. Exactly what evidence is not clear. By this definition strategic thinking was associated with higher non-academic impact. This reviewer suspects that “strategic thinking” is not a true variable in this spectrum of projects, whatever evidence is adduced. All those carrying out cardiovascular research understand that it may provide knowledge relevant to human health. Simply encouraging provision of statements of potential pathways to impact will neither alter individual researchers’ approaches to their projects nor hasten translation. Funders need to use other mechanisms to maximise the potential for research to be translated from discovery through to clinical application, for example by better educating basic scientists in the steps needed to translate their research and providing resources to facilitate this.

Response: We have added an additional sentence (the one highlighted in bold) to the Results to provide a fuller explanation of how we identified strategic thinking:

Strategic thinking by clinical researchers is associated with high wider impact:

‘We defined strategic thinking by clinicians as having occurred when there was evidence in the case study that the research team had thought through the pathways by which research could potentially be translated into practice. This was identified through the analysis of the text in relevant sections of the case studies, such as those where we reported on researchers answers to questions about why they had applied for the research, and what gaps it might fill.’

We also drew on the point made by the reviewer to make a helpful addition to the relevant comments in the Discussion, and also in the Conclusion:

‘Funders should also consider what mechanisms they might be able to use to assist researchers to consider ways to maximise the potential for research to be translated.’

‘They should encourage researchers to engage potential research users in the research process and do what they can to assist researchers consider pathways towards impact.’
RESPONSE TO REVIEWER 2:

Major Compulsory Revisions:
1) The authors stratified case studies according to factors which included Country of research (UK, Canada, Australia) and Grant size (large or small). It is not clear whether either of these factors influenced research payback and they should comment on this.

Response: This point partially overlaps with the first two points from Reviewer 1, and we have attempted to combine our response to both reviewers in the amendments which are set out in detail in the relevant response to Reviewer 1 (although the part of that response that addresses the country issue is really only relevant to the point made here by Reviewer 2).

Minor Essential Revisions:
2) A Spearman rank correlation is used to generate the data in Table 3, using an n of 261. This includes 9 ratings of each project. I am not sure whether this approach is valid. Would it have been more appropriate to use an n of 29 with the median values for each project to calculate the r values? The authors should briefly discuss this.

Response:
In response to this comment we re-ran the analysis, and then replaced old Table 3 with a new version based on an n of 29, using the median values for each project. We have also added the following comment as End Note c to the current explanation of the approach used in Table 3:

*c We checked two statistical approaches: our initial approach of using all 261 ratings, as described in the report [22]; and a possible alternative of using the 29 median values to calculate the r values. In Table 3 we present the findings from using the latter approach. We found that in terms of the conclusion we draw - i.e. the grouping of the categories - the method used for the test does not affect the conclusion. Using all the 261 ratings ensures we don’t lose data, but probably over estimates the n because they are not fully independent observations; but using the medians may overestimate the magnitude of the correlation because it excludes the outlying observations.*