To the Editor:

We thank Drs. Armoiry and Connock for their thoughtful comments and questions regarding our report on the cost-effectiveness of transcatheter edge-to-edge mitral valve repair (TEER) for patients with heart failure and severe secondary mitral regurgitation (MR) from the perspective of the UK National Health Service (1). They raise two important questions regarding our analysis: the first regarding alternative approaches to life expectancy projection and the second regarding the disparity between the results of the MITRA-FR and COAPT trials.

The reason why we did not incorporate 3-year follow-up data from the COAPT trial in our projections is straightforward. As described in our paper, after completion of 2-year follow-up, patients randomized to the control group (guideline-directed medical therapy alone) were permitted to cross over to the MitraClip procedure if they continued to meet the trial's original inclusion criteria; a substantial proportion of surviving patients in the control group did so (2). Consequently, the data beyond 2 years no longer represent a valid comparison of MitraClip + GDMT vs. GDMT alone. Moreover, the suggestion that using 3-year data (which are only available for the MitraClip group) rather than 2-year data would "considerably influence estimated survival gains" is unfounded. The observed 3-year mortality in the MitraClip group was 42.8%, which is well within the uncertainty limits of our base case projection (38%), and nearly identical to the rate in our "worst case" scenario (40%). Given the lack of meaningful empirical 3-year mortality data for the control group, we continue to believe that our approach of using complete 2-year mortality data from the trial population coupled with several alternative long-term projections covering a range of effect estimates is both reasonable and justified.

We agree that there are many unanswered questions as to why the treatment effect observed in COAPT differed so dramatically from that seen in MITRA-FR (3,4). Given the marked disparity in the results of the two trials, it seems unlikely that the explanation is purely play of chance. Differences between the trials in disease severity, the balance between ventricular dysfunction and the severity of MR, background medical therapy, or technical aspects of the procedure, alone or in combination, seem more likely to account for the disparate results. For example, MITRA-FR (but not COAPT) enrolled a substantial proportion of patients with only moderate MR according to US American Society of Echocardiography criteria and others with extreme left ventricular dilatation-- subgroups of patients who may not benefit from TEER. Ongoing work to pool the two trial databases may yield useful insights into why the results of these trials differed. Furthermore, at least one further substantial randomized trial (RESHAPE-HF2) should report in the next few years that will provide further evidence on how best to select patients for TEER (5). Nonetheless, given the robustness of the COAPT outcomes, our analysis from this trial provides valid insights into the cost-effectiveness of TEER in appropriately selected patients.

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Competing Interests Statement

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