

## RESPONSE TO REVIEWER

Reviewer Name: Paul Vermeersch  
Review Date: 2018-02-02 09:06  
Comments To Authors: important topic , nicely written nice overview of current status on PFO closure , pro and con's are discussed and the remaining uncertainties are mentioned this meta analysis adds information small remarks : any argument for differences in the sort of device used? amplatzer more problems or less? etc  
Classification: Grade B (Very good)  
Language Evaluation: Grade A: priority publishing  
Conclusion: Accept  
Comments To Authors(File):

REPLY:

Dear Editor in Chief,

We would like to thank you and the reviewer for taking the time to review the manuscript. We would like to thank the reviewer for his very nice comments. Our responses are

### 1. Any argument for differences in the sort of device used?

Regarding the differences in sort of device used, we couldn't find any specific pattern. REDUCE was sponsored by Gore and associates and the trial used GORE Helex/Cardioform whereas CLOSE was sponsored by French Health Ministry and they used a variety of devices. RESPECT and PC used only Amplatzer whereas CLOSURE I used STARFLEX which is not being used anymore.

### 2. Amplatzer more problems or less?

Regarding complication rates, we should admit that we did not have enough power to calculate the difference in rates of adverse events between the various closure devices. We have now added a statement in our limitations (highlighted) explaining the same, thanks to the reviewer for pointing this out. Atrial fibrillation was mostly observed in the immediate post-procedural period and this could be related to the type of device used but we cannot prove or refute the hypothesis. Older trials namely the RESPECT and PC, which used only Amplatzer did not show significant atrial fibrillation events in the device group but CLOSE (variety of closure devices) and REDUCE (GORE) did show significant increase in atrial fibrillation. Again, we cannot conclude that atrial fibrillation events are low with Amplatzer as CLOSE also had Amplatzer use but still had an overall higher incidence of atrial fibrillation. Further trials are essential to address this question.