**Interpretation of an underpowered study with pre-specified minimum clinical important difference?**

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*To the editor:*

In the DECISION randomized clinical trial, Dr. Lomivorotov and colleagues reported that intraoperative administration of dexamethasone compared with placebo did not reduce major complication and mortality among infants undergoing cardiac surgery.1 However, we are concerned about the conduct and interpretation of this study.

First, the trial was planned to detect a 15% benefit in the primary composite endpoint. This target effect size (assumed between group difference) was reported as minimally clinically important difference (MCID), which implied that current sample size would the largest number expected. However, the authors emphasized that the study may have been underpowered. On the contrary, DECISION study is already overpowered (>80%) and the actual enrolled number of patients (n=394) is further increasing from planned sample size (n=384) with 25% increasing than the minimal sample size required (reported as 306) during study design. Moreover, if we used the event-driven method to estimate the sample size, we found that the minimum required number of events were around 143with the target relative risk (RR) of 0.625, where the RR was estimated through the expected control rate and MCID ((40%-15%)/40%=0.625).2 Obviously, this is smaller than the actual number of 165 (74 from dexamethasone and 91 from placebo). Taken together, we believe that the negative findings of DECISION trial may not be simply attributed to underpower to detect the clinical important difference. If the authors would share more potential reasons regarding the attenuated observed effect size compared with the target effect size, it will help the readers interpret the results more appropriately.

Second, in the protocol, open-label steroids could be administered only after randomization code break. However, we noticed that an unexpected high and uneven rate of open-label steroids use occurred during the study (15.4% in the dexamethasone group and 22.0% in the placebo group). This may imply an equal or higher rate of randomization code break in this study. Therefore, we believed that providing the reasons of breaking randomization code will be very informative to the readers. Meanwhile, a further analysis could be provided to assess the impact on the primary outcome collection and analysis result, particularly for those without primary outcome identified before code breaking.

**Reference**

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