Item 14b. Why the trial ended or was stopped

Examples—“At the time of the interim analysis, the total follow-up included an estimated 63% of the total number of patient-years that would have been collected at the end of the study, leading to a threshold value of 0.0095, as deter‑ mined by the Lan-DeMets alpha-spending function method … At the interim analysis, the RR was 0.37 in the intervention group, as compared with the control group, with a p value of 0.00073, below the threshold value. The Data and Safety Monitoring Board advised the investigators to interrupt the trial and offer circumcision to the control group, who were then asked to come to the investigation centre, where MC (medical circumcision) was advised and proposed … Because the study was interrupted, some participants did not have a full follow-up on that date, and their visits that were not yet completed are described as “planned” in this article.”

“In January 2000, problems with vaccine supply necessitated the temporary nationwide replacement of the whole cell component of the combined DPT/Hib vaccine with acellular pertussis vaccine. As this vaccine has a different local reactogenicity profile, we decided to stop the trial early.”

Explanation—Arguably, trialists who arbitrarily conduct unplanned interim analyses after very few events accrue using no statistical guidelines run a high risk of “catching” the data at a random extreme, which likely represents a large overestimate of treatment benefit. Readers will likely draw weaker inferences from a trial that was truncated in a data-driven manner versus one that reports its findings after reaching a goal independent of results. Thus, RCTs should indicate why the trial came to an end (see box 5). The report should also disclose factors extrinsic to the trial that affected the decision to stop the trial, and who made the decision to stop the trial, including reporting the role the funding agency played in the deliberations and in the decision to stop the trial. A systematic review of 143 RCTs stopped earlier than planned for benefit found that these trials reported stop‑ ping after accruing a median of 66 events, estimated a median relative risk of 0.47 and a strong relation between the number of events accrued and the size of the effect, with smaller trials with fewer events yielding the largest treatment effects (odds ratio 31, 95% confidence interval 12 to 82). While an increasing number of trials published in high impact medical journals report stopping early, only 0.1% of trials reported stopping early for benefit, which contrasts with estimates arising from simulation studies and surveys of data safety and monitoring committees.206 Thus, many trials accruing few participants and reporting large treatment effects may have been stopped earlier than planned but failed to report this action.