Theme: Design; Pilot & feasibility studies

Title: Estimating recruitment rates in pilot trials: how many sites do I need? (12/25 words)

Authors: D Wilson, S Cowtan, C Vyner, D Cairns

Introduction: Successful recruitment is key to the feasibility of clinical trials. Recruitment rates are often estimated prior to trials in small pilot studies, where these estimates are used in pre-specified decision rules (known as progression criteria) to help decide if the main trial should go ahead. For these decisions to be reliable, the pilot trial must be large enough to produce sufficiently precise recruitment rate estimates. For multi-centre trials with some variability in the site recruitment rates, precision will be driven not only by the number of participants in the pilot but also by the number of recruiting sites. There is, however, a lack of guidance as to how the number of sites in a pilot study should be determined.

Methods: We conducted a simulation study to examine the relationship between the precision of recruitment rate estimates and the numbers of participants and recruiting sites in pilot trials, varying the heterogeneity in site recruitment rates and the number of sites which will be recruiting for the main trial. We used a hierarchical model to estimate overall recruitment rates from the simulated pilot data to allow inter-site variability to be captured. We then developed a method for the power analysis of pilot trials estimating recruitment rates, implemented this in the R package “fahb”, and used it to help determine appropriate numbers of participants and recruiting sites for an illustrative example.

Results: Our simulation study demonstrates that the precision of recruitment rate estimates is strongly driven by the number of recruiting sites, with a comparably weak dependence on the number of participants. Our power analysis of the example illustrates how appropriate numbers of pilot sites and participants can be determined, and how historical recruitment data can be leveraged to gain precision.

Discussion: We have found that the number of sites in a pilot trial is a crucial determinant of its ability to produce precise estimates of recruitment rates and thereby make reliable progression decisions. By recognising variability in site recruitment rates in a formal power analysis when designing pilot trials we can ensure they have enough sites and participants, and reduce the risk of launching subsequent trials which fail to recruit to target.

(361/400 words)