Appendix A – Technical details for calculations

It was necessary to reproduce sample size calculations for each of the two case studies in order to construct the power and precision plots. These plots were produced based on the sample size parameters reported in the original publications. Sometimes approximations have been made (detailed below) and sometimes some simplifications have been made (again detailed below). These approximation and simplifications are not expected to have any impact on the over-arching conclusions presented in this paper. The power and precision curves have been constructed using methodology presented elsewhere [13].

Technical details case study 1

The primary outcome was screening uptake which was around 53%. The trial was powered for a test of interaction (across 5 deprivation groups) and it was reported that under individual randomisation the sample size needed per arm was 13,500 for 90% power at 5% significance (reported in trial protocol available on trial website[i]). We approximate this power calculation by assuming a study designed to detect a standardised effect size of 0.04 (which requires 13,500 per arm for 90% power and 5% significance under individual randomisation). The ICC used in the sample size calculation, estimated from the national routinely collected dataset, was 0.0002.

Technical details for case study 2

The trial had a non-inferiority design, powered on a composite of serious patient complications which had an estimated baseline rate of 9.94%; with an absolute non-inferiority margin of 1.25%, equating to an upper bound of 11.19%; and an adjusted alpha value of 0.04 to allow for an interim analysis. It was estimated that to achieve 80% power a cluster size of 950 was required across 90 clusters. To replicate this non-inferiority calculation we double the alpha value (i.e. 0.04*2) and retain a 2 sided test.

A value for the ICC is not provided in the paper, but back calculations suggest it is in the region of 0.004 (Appendix A). Under individual randomisation, to detect a difference in two proportions from 0.094 and 0.1119 at 80% power and 8% significance a total sample size of 16,254 is needed. The sample size estimated under cluster randomisation was reported to be 85,500 (=950 (cluster size)*90 (number clusters)). This means the design effect (DE) was 5.26 (=number needed under cluster randomisation / number needed under individual randomisation). Back calculation from the conventional formula for the DE=1+(cluster size -1)*ICC gives an ICC of 0.00448.

[i] : https://www.ucl.ac.uk/dahr/pdf/study_documents/ASCEND_Protocol