SIGNET Trial – Report for CTAG Heart October 2023

Introduction

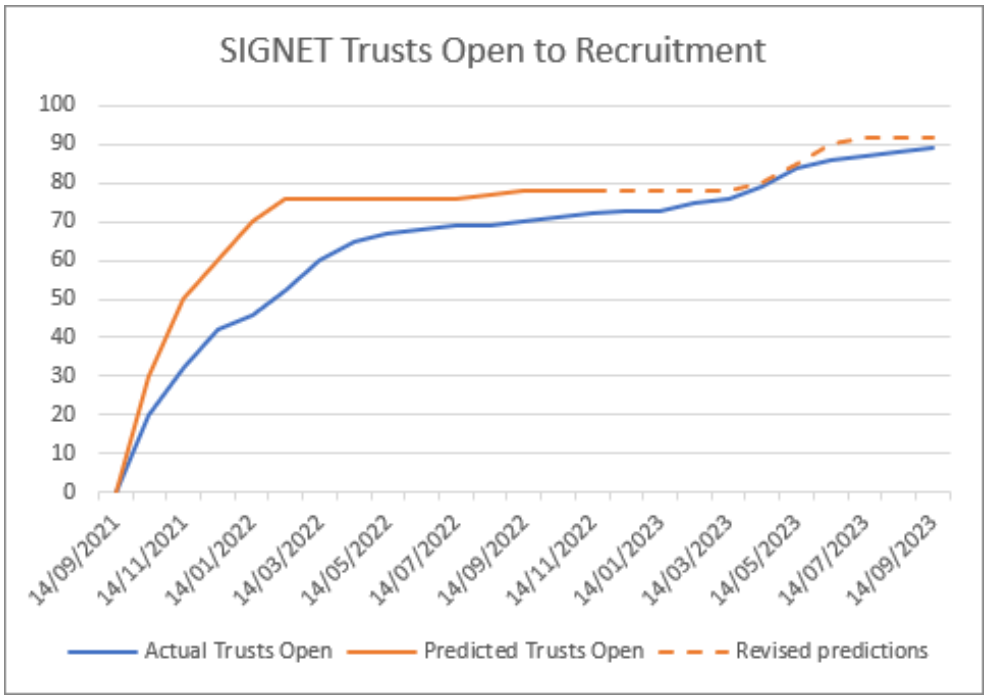
SIGNET is an NIHR funded prospective randomised study investigating a single dose of simvastatin given to adult brain stem dead donors. It followed a small-scale study done in Helsinki where the cardiac recipients of organs from donors who received the simvastatin had less cardiac injury as measured by Troponin and less early rejection. In the same study there was a reduction in ALT at one week in liver recipients and a halving of average PGD grade in lung recipients. The Finnish study showed no disadvantage to any of the recipient groups from donors who received the simvastatin.

Donor families are approached consent for research by the attending SNODs, after obtaining consent for donation. The randomisation, which can only be done after brain death is declared, is done by the SNODs, an expansion to their normal role. The randomisation is stratified only for previous statin treatment (found in about 15% of donors).

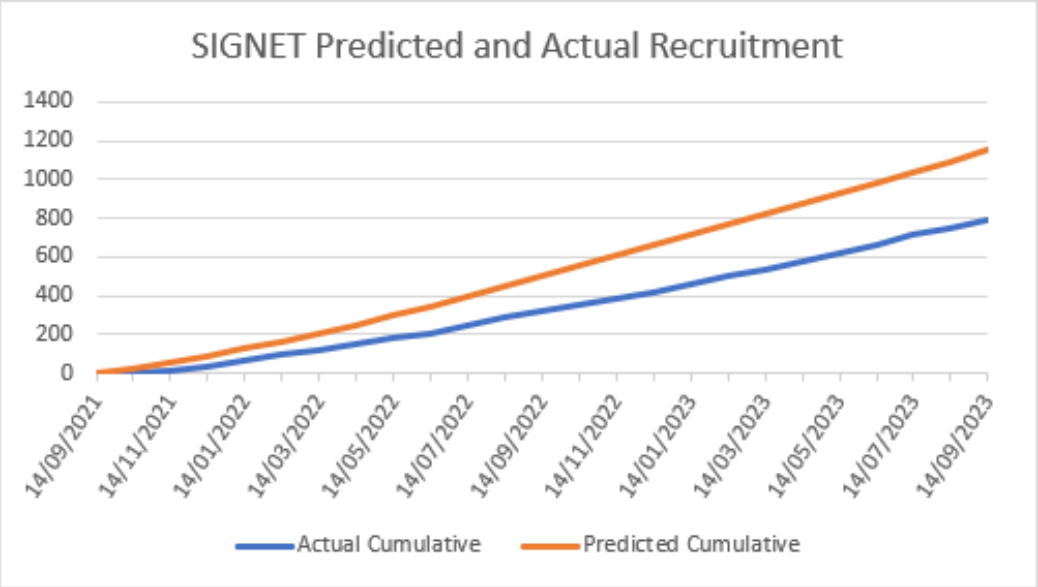
Primary end-points are early dysfunction or early death in cardiac recipients, with secondary endpoints the early outcomes in all the other groups. This information is taken from the UK Transplant Registry. Driven by power calculations for the primary outcome, the trial will randomise 2600 donors at major (level 1, level 2 and selected level 3) donor hospitals over 4 years. We believe it to be the largest donor intervention study anywhere in the world.

Activity

Randomisation began in September 2021, so we are just on two years into the study. There was some delay in recruiting donor hospitals in the post-covid era. Earlier this year we used some money saved on site visits to add some centres to the study



The delay in opening centres lead to randomisations below predicted. The relative reduction in Brain-Dead donor numbers, which continues, has lead to a continuing small shortfall



However, performance remains better than many clinical studies open in the challenging environment of the past few years. As of October 10, the numbers were:

Number of Trusts/Boards Open 89
Eligible Donors 1098
Donors Consented 837
Donors Recruited 825

The consent rate remains gratifyingly high, a tribute to the work of the specialist nurses. Some donors consented and randomised did not in the end donate, or went down a DCD pathway, hence the difference between the two final numbers.

<u>Conclusions</u>
Whilst donor hospitals as not blinded, the retrieval and implant teams are not aware whether the organs come from donors in the treatment or control groups, and this has not, as far as we are aware, been an issue. Similarly, we have not heard of any concerns of the recipients being informed but not consented. There have been so SAE's of any consequence in the donors.

We are grateful to all the transplant centres for their acceptance of this trial in the infrastructure of transplant activity but would like to hear of any issues. This study has shown that the transplant infrastructure in the UK is well, almost uniquely, suited to this big study, and we hope to build on this in the future. We would like to hear of any potential studies suggested by the group.

John Dark, Co-Chief Investigator Dan Harvey, Co-Chief Investigator