Mission Impossible! Retaining old randomised clinical trial data: the ISIS-2 Legacy Database experience

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INTRODUCTION

ISIS-2 (Second International Study of Infarct Survival) was a clinical trial that investigated whether streptokinase (used to dissolve clots in blocked arteries) and aspirin (a blood thinner) helped prevent death in people having a heart attack. The trial found that patients taking streptokinase and/or aspirin were more likely to survive than those taking the placebo. These results transformed clinical practice worldwide and are still relevant today. Initial results were published in 1988, with follow-up results published in 1998, which showed that benefits lasted for at least 10 years.

Participants were recruited in hospitals from 1985-1987 in the UK and 15 other countries. In the UK further information was collected via electronic health records (EHR) from Central Registries e.g. the Office for National Statistics (ONS). EHR data collection continued until 1997.

Oxford researchers want to preserve the original database which produced these important findings and to keep the data for further research using EHR data linkage to investigate the long-term effects of these medications.

METHODS

CHALLENGES

-Original consent no longer valid
-Impractical to contact surviving participants to reconsent
-Database includes identifiable data
-NHS Digital now responsible for data originally provided by ONS
-How to retain data while meeting current legal requirements?

SOLUTIONS

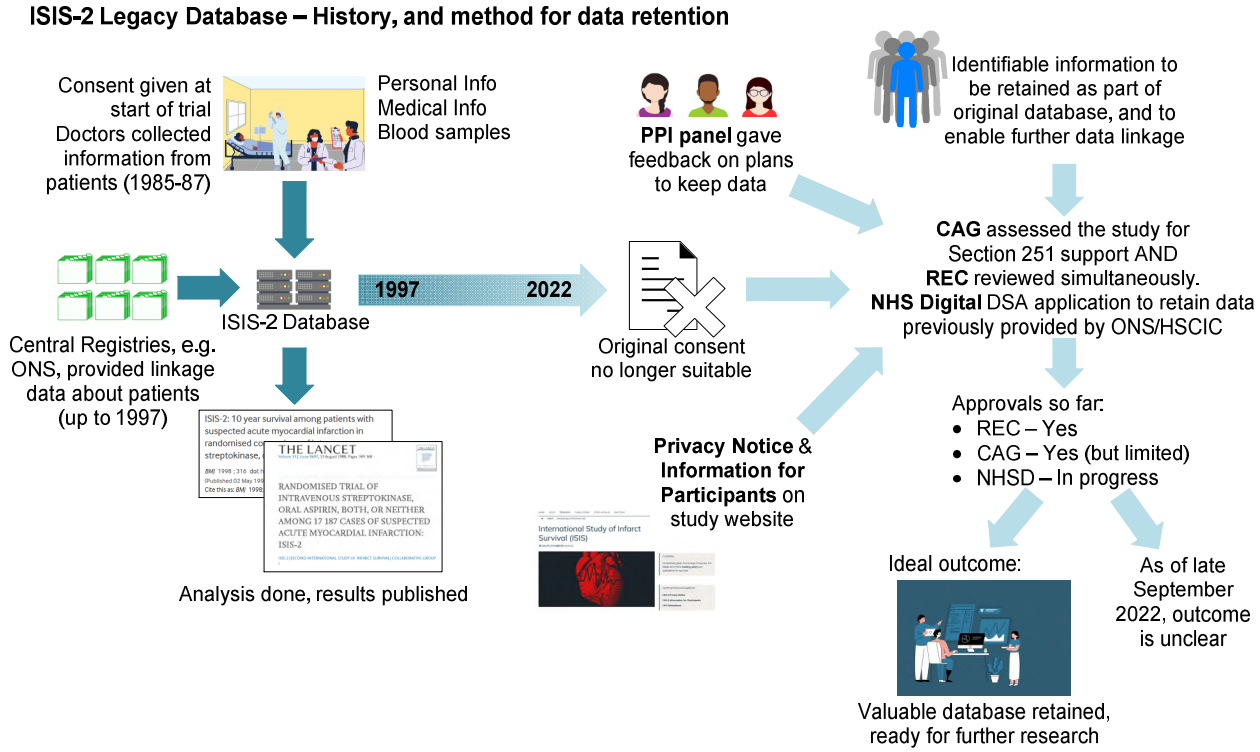
-Consultation with a Patient and Public Involvement (PPI) panel
-Privacy Notice provided on study website
-Application to Confidentiality Advisory Group (CAG) for Section 251 support (to allow data retention without explicit consent)
-Application to a Research Ethics Committee (REC) for a Research Database
-Data Sharing Agreement (DSA) with NHS Digital

DISCUSSION

The PPI panel were strongly in favour of retaining data providing appropriate protections are in place and any future research is done in line with the original protocol.
The REC granted a favourable opinion for 5 years. CAG gave a favourable opinion allowing us to keep patient identifiers, but only for 1 year.

Attempting to retain this old database has proved challenging. Issues encountered include:

-Establishing who's responsible for pre-1997 ONS mortality data
-Different organisations having varying definitions of 'identifiable data'
-Staff and funding needed to do the applications and administration
-Overall length of approvals process (1.5 to 2 years)
-1 year approval from CAG removes the option to pursue linkage to datasets not yet available e.g. General Practice Data for Planning and Research



CONCLUSION

Retaining an old database with patient identifiers can be done and has the potential to be used to undertake long-term follow-up via data linkage to electronic health records, thereby maximising the value of the data and the contribution of the ISIS-2 participants. However, the process is complex, time consuming and requires considerable resources.

This work can be considered proof of concept, although the 1-year limit granted by CAG severely limits our options for continuing research with this dataset. We are challenging this outcome and as of September 2022 discussions with CAG are ongoing.