Study Title: HPS2-THRIVE trial legacy study: long-term follow-up of participants using electronic health records

Short title: HPS2-THRIVE Trial Legacy Study

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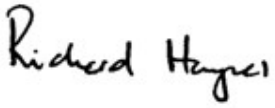

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1 SYNOPSIS

Study Title	HPS2-THRIVE trial legacy study: long-term follow-up of participants with electronic health records	
Internal ref. no. / short title	HPS2-THRIVE Trial Legacy Study	
Study Design	Extended follow up of randomised controlled trials using electronic health records and other routinely collected data.	
Study Participants	UK participants in HPS2-THRIVE trial	
Planned Sample Size	HPS2-THRIVE UK = 8,035	
Planned period of research	Planned analyses based on at least 20 years' follow-up from trial initiation (2007) with continued data linkage to allow for future analyses.	
	Objectives	**Outcome Measures**
1	To determine whether participants randomly allocated to treatments leading to lower levels of LDL cholesterol during the scheduled treatment period have a lower risk of dementia	Dementia measured in trial records, hospital episode, death and other health records up to data linkage date
2	To determine whether participants randomly allocated to treatments leading to lower levels of LDL cholesterol during the scheduled treatment period have a lower long-term risk of major vascular and other diseases	Vascular diseases measured in trial records, hospital episode, death and other health records up to data linkage date
3	To measure the association between baseline and in-trial vascular risk measures with future dementia	Dementia measured in trial records, hospital episode, death and other health records up to data linkage date
4	To measure the association between baseline genetic and blood biomarkers and the occurrence of later disease	Vascular diseases, dementia, neurological disease and other outcomes

2 ABBREVIATIONS

ASCEND	A Study of Cardiovascular Events iN Diabetes
ASCOT	The Anglo-Scandinavian Cardiovascular Outcomes Trial
CAG	Confidentiality Advisory Group
CTSU	Clinical Trial Service Unit
EHR	Electronic health record
ELISA	Enzyme-Linked Immunosorbent Assay
FDA	US Food and Drug Administration
HES	Hospital Episode Statistics
HDL	High-density lipoprotein
HR	Hazard ratio
HPS	MRC/BHF Heart Protection Study
HRA	Health Research Authority
ICF	Informed Consent Form
K-M	Kaplan Meier
MI	myocardial infarction
MRC	Medical Research Council
NDPH	Nuffield Department of Population Health, University of Oxford
NIH	National Institutes of Health
PPIE	Patient and Public Involvement and Engagement
PPV	Positive Predictive Value
REC	Research Ethics Committee
RR	Risk ratio
SEARCH	Study of the Effectiveness of Additional Reduction in Cholesterol and Homocysteine
THRIVE	Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE)
UKPDS	United Kingdom Prospective Diabetes Study

3 BACKGROUND AND RATIONALE

3.1 HPS2-THRIVE

HPS2-THRIVE was a randomised, international multi-centre trial of 2g of extended-release niacin and 40 mg of laropiprant or a matching placebo daily in 25,673 participants with a history of vascular disease that ran in 245 sites in six countries (89 UK clinical centres).[1] This study showed that participants allocated to niacin–laropiprant did not have a lower risk of major vascular events than those allocated to placebo, but the niacin/laropiprant did increase the risk of serious adverse events, particularly diabetes diagnosis and control, bleeding and infection.[2]

Assignment to niacin–laropiprant, as compared with assignment to placebo, was not associated with a significant reduction in the incidence of major vascular events (1696 participants with events [13.2%] and 1758 participants with events [13.7%], respectively; RR, 0.96; 95% CI, 0.90-1.03; P=0.29) with no effect on fatal or nonfatal stroke (198 vs 199, RR 1.00, 95%CI: 0.88-1.13, p=0.56). Assignment to treatment with niacin–laropiprant was associated with an average reduction in the LDL cholesterol level of 0.25 mmol/L (as measured in the central laboratory), an average increase in the HDL cholesterol level of 0.16 mmol/L, and an average reduction in the triglyceride level of 0.37 mmol/L, as compared with assignment to placebo.

3.2 CHOLESTEROL LEVELS AND DEMENTIA

Cholesterol levels are of particular interest because a genetic risk factor for Alzheimer's disease is the ε4 allele of the ApoE gene. This allele codes for the E4 isoform of a lipid chaperone which is found in intermediate density lipoprotein and chylomicrons. It binds to receptors in low-density lipoprotein and other lipid transport species, and is involved in the neuronal transport of cholesterol. People with an ε4 allele have higher levels of total cholesterol (about 0.25-0.5 mmol/L higher) and triglycerides than those without, and therefore higher blood LDL cholesterol is one potential mechanism for the effect of the ε4 allele.[3] In the brain, the role of ApoE is less certain, but it is clearly a strong risk marker for dementia.

In observational studies, higher midlife total cholesterol is associated with later life cognitive impairment or dementia[4–6] though the magnitude of this effect, the associations with lipid sub-fractions, or the extent to which this is mediated by confounding by other vascular risk factors is unclear. Two meta-analyses that mixed observational studies with randomized trials suggested statins reduce the risk of dementia by about a third (OR 0.70: 95% CI: 0.59-0.83),[7,8] although there was no evidence of reduction in cognitive impairment at the end of the scheduled treatment period in the large randomised trials.[9]

Nor did either of the randomised trials that measured short term (<5 years) cognitive performance as a pre-specified outcome show any reduction in the rate of deterioration of cognitive abilities or end of trial cognitive ability with pravastatin[10] or simvastatin.[11] There does not seem to be any effect of statins on the rate of deterioration of dementia once it has developed, although the trials have all been small (<1000).[12,13] A recent Mendelian randomisation

study of 3,904 patients with late onset Alzheimer's disease, and 6,664 controls did not show any change in risk of dementia in those with higher predicted lifetime levels of LDL, HDL or triglyceride lipid fractions, though the genetic risk score only explained a small proportion of the variance of lipid levels, and so the study may have been underpowered.[14]

In 2012, the FDA added a warning to the statin product label stating that some patients may experience "ill-defined memory loss" and "confusion." This warning followed rare post-marketing reports of cognitive impairment (e.g., memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. The American Heart Association/American Stroke Association clinical guidelines recommend:

"in people at risk for vascular cognitive impairment, treatment of hypercholesterolemia may be reasonable (Class IIb; Level of Evidence B)."[15]

Therefore, there is ongoing uncertainty about the long-term effects of LDL-cholesterol lowering with statins or other agents on the risk of dementia.

3.3 VASCULAR RISK AND DEMENTIA

Dementia is a condition that develops over a long period before manifesting in a clinical diagnosis. In the short-term (up to 10 years) lower cardiovascular risk factor levels have often been associated with an increased risk of dementia, which may be because of reverse causal effects of the incipient dementia leading to lower levels. However, raised mid-life levels of cardiovascular risk factors (such as LDL-cholesterol) have been found to be associated with increased risk of dementia 15-20 years later. There is little data, however, on whether raised levels of cardiovascular risk factors at older ages are associated with an increased risk of dementia 15-20 years later. Continued follow-up for dementia in studies in older people initiated many years ago is therefore extremely valuable for investigating such effects now (rather than having to wait much longer for more recent studies like UK Biobank to acquire long follow-up). Our series of large-scale cardiovascular trials from the Heart Protection Study[11] (HPS) through to the recently completed ASCEND[16] trial have recruited over 60,000 UK participants at high vascular disease risk and with a mean age of about 62 at recruitment.

Dementia is a leading cause of death in the UK and it is likely that over a third of these populations will develop dementia at some point. Hence, many people in these older studies may by now have developed dementia. Therefore, these studies now constitute a uniquely rich resource for study of the relationships of vascular risk factors to dementia incidence many years later. Separately, HES data in HPS and ASCEND studies is being acquired but larger numbers are needed. This study will look at the association of vascular risk factors measured at baseline with dementia incidence at various times into the future, with longer delays between measurement of risk factors at recruitment and incidence of dementia being particularly valuable.

3.4 LEGACY EFFECTS OF LDL-CHOLESTEROL LOWERING

There may be important post-trial 'legacy' effects after a period of treatment with LDL-cholesterol lowering agents. LDL cholesterol lowering with a statin might have important effects on the future clinical course of atherosclerosis. Twenty year follow up of the WOSCOPS study demonstrated a reduction in all-cause mortality (HR 0.87; 95% CI: 0.69-0.90), mainly attributable to cardiovascular deaths in the pravastatin arm. There were reductions in hospitalisations for myocardial infarction (24%) and heart failure (35%), although not due to non-cardiovascular causes.[17] In the ASCOT trial long-term follow-up (median 15 years), there were fewer deaths in participants allocated to atorvastatin than in control (HR 0.85; 95% CI: 0.72–0.99).[18]

Based on these findings, a follow-up study is proposed that will determine how long the "legacy effect" after LDL-cholesterol lowering lasts, and to understand better the effects of early LDL cholesterol lowering in patients with a history of vascular disease on important long-term clinical outcomes. In HPS2-THRIVE, whether there are any legacy effects on the other serious adverse outcomes that were increased by niacin during the trial will be assessed i.e. diabetes onset and control, major bleeds and infections.

3.5 GENETIC AND BIOMARKER ANALYSIS OF THE HPS2-THRIVE COHORT

In order to improve our understanding of vascular disease and its treatments, genomic and other relevant blood-based analytic studies of cardiovascular diseases, its risk factors and potential sequelae (e.g. cognitive function), and of patient response to therapy may be undertaken. For example, through the use of genome-wide association studies to identify new genetic determinants, Mendelian randomization to explore potentially causal relationships, genetic risk scores to examine potential interactions and genetic correlations, and other genomic and blood-based studies (e.g. DNA methylation) to examine wider features of the genome and their relevance to the prevention of and treatment for vascular disease. As such, the HPS2-THRIVE data provides a unique opportunity to address and answer questions that other smaller, less well phenotyped studies cannot.

Genotyping/sequencing and generation of other measures within the above remit may be undertaken at specialist laboratories under strict contractual agreements (e.g. REGENERON, USA; McGill University, Canada; Leicester, UK). All data will be returned to Oxford for statistical analyses.

4 STUDY DESIGN

4.1 EXTENDED FOLLOW UP OF A RANDOMISED CONTROLLED TRIAL USING ELECTRONIC HEALTH RECORDS AND WITHIN TRIAL DATA

Record level data is requested from Data Custodians such as NHS England, Public Health Scotland, Digital Health & Care Wales (or appropriate equivalent registries) after all necessary approvals have been granted with repeat requests on an ad-hoc basis. The data requested will include, but

will not be limited to, Hospital Episode Statistics (HES), mental health data, cancer, and mortality data and their equivalents in devolved administrations.

5 STUDY OBJECTIVES

1. To determine whether participants randomly allocated to treatments leading to lower levels of LDL cholesterol have a lower risk of dementia
2. To determine whether participants randomly allocated to treatments leading to lower levels of LDL cholesterol have other long-term health effects
3. To measure the association between baseline and in-trial vascular risk measures with future dementia
4. To determine the association between DNA and plasma markers with dementia and other long-term health effects, particularly lipid fractions and ApoE alleles

6 STUDY POPULATION

All participants in HPS2-THRIVE where linkage is possible to resources held by NHS Data Custodians in England, Scotland, and Wales.

7 INTERVENTION

No interventions are planned as part of this study.

8 OUTCOME ASCERTAINMENT

The following outcomes will be measured in linked electronic health record data: dementia, stroke, all major cardiovascular disorders, other vascular disease complications, myopathies, heart failure, cancer, renal impairment, other health and care outcomes, and death. UK participants will be linked with the following datasets:

1. NHS England: Hospital episode statistics (HES) (Admitted Patient Care), Mental Health datasets, Cancer Registrations, and Civil Registrations of Death
2. PHS (Public Health Scotland): Scottish Morbidity Record (SMR) Inpatients (SMR01), Cancers (SMR06) and NRS death statistics.
3. Digital Health and Care Wales (DHCW): Patient Episode Database Wales; Admitted Patient Care, and Outpatients.
4. Existing data within HPS2-THRIVE systems and records.

Events occurring in-trial will be defined as in the original trial procedures. Definitions are:

Stroke

Stroke will be defined as an acute symptomatic episode of focal or global neurological dysfunction caused by brain, spinal or retinal vascular injury as a result of infarction or haemorrhage.

Stroke Data sources

EHR/death records

ICD codes will be used to define stroke of different types when recorded in the primary or secondary position (approx. to 94% (95% CIs 88% to 98%) PPV, pers. comm. Kristiina Rannikmae). Date of diagnosis will be recorded. Note: no laterality is likely to be available in these records.

Within trial assessment of stroke

Dementia

Dementia is defined as a chronic or persistent disorder of the mental processes caused by brain disease or injury and marked by memory disorders, behavioural and psychological symptoms with impaired reasoning. For the purposes of analysis, all cause dementia will be used. In secondary analysis, should there be sufficient data, vascular dementia will be looked at, Alzheimer's dementia and other dementias and a broader outcome including all outcomes indicative of cognitive impairment.

Dementia Data sources:

EHR/death records.

Mental health records

Within trial measurement of dementia

Myocardial infarction:

HES Admitted Patient Care definition of MI

MI Data sources:

EHR/death records

Within trial measurement of myocardial infarction

In addition, other codes will be examined indicating major vascular and other diseases, including (not limited to):

- Admissions and deaths due to heart failure
- Surgery on large arteries: aorta, carotid, brachial, femoral, iliac etc.
- Acute coronary syndromes
- Cardiac revascularisation procedures by interventional cardiologists or cardiac surgeons
- Cardiac valve surgery
- Renal replacement therapy
- All mortality

9 DISSENT

Participants who have already opted out from having their data stored by NHS England (or other NHS Data Custodian) will be excluded. In addition, participants who have read the privacy notice and have decided that they do not wish their data to be used in this study will be able to opt out. The privacy notice is available on the trial website (https://www.ctsu.ox.ac.uk/research/hps2-thrive - originally https://www.thrivestudy.org which redirects to the current site), and is a

supplement to the NDPH Privacy notice (https://www.ndph.ox.ac.uk/about/data-privacy-notice-1/ndph-privacy-policy-for-research-participants)

10 GENETIC AND PROTEIN BIOMARKER ANALYSES

During HPS2-THRIVE study, participants provided blood and urine samples for long-term storage and subsequent analyses. HPS2-THRIVE has an extensively phenotyped database, and active follow-up during the scheduled treatment period (in particular, for mortality, major vascular events, cancer and other major morbidity).

Genetic, proteomic and metabolomic analyses can provide additional valuable scientific insight into treatment response, the risks and causes of cardiovascular event and other related chronic diseases and potential sequela (e.g. cognitive function) especially when linked to traditional biomarker and extensive phenotypic data and to long-term prospective follow-up information. As such, the HPS2-THRIVE data provides a unique opportunity to address and answer questions that other smaller, less well phenotyped studies cannot.

In order to improve understanding of vascular disease and its treatments, genomic and other relevant blood and urine-based analytic studies may be undertaken in stored buffy coat plasma, and urine to ascertain between markers of cardiovascular disease, as well as its risk factors and consequences, and of patient response to therapy.

Genomic and blood- and urine- based analyses may be undertaken as appropriate to address a wide variety of aims in order to generate new biological insights and influence therapeutic developments including:

- Assessing clinical benefit of therapy by strata of genetic risk/polygenic risk scores
- Identifying genetic determinants of treatment efficacy and adverse events as well as wider cardiovascular risk factors and outcomes using hypothesis-free genome-wide association analyses as well as candidate gene approaches with protein and urine based biomarkers
- Determining the causal relevance of risk factors and therapeutic mechanisms for disease as well as the potential effects of treatment using Mendelian randomization analyses and measurement of blood and urine based biomarkers
- Elucidating functional mechanisms relevant to the prevention and treatment of cardiovascular disease by exploring rare variation in coding regions using single-variant and gene-burden tests

10.1 METHODS

Any genome-wide genotyping would be undertaken using the up-to-date genome arrays, which combines genome-wide content, curated clinical research variants, and quality control markers for precision medicine research. Subsequently, genomic assays would be performed, such as exome sequencing, as appropriate.

Genotyping/sequencing and generation of other genomic and biomarker measures within the above remit may be undertaken at specialist laboratories under strict contractual agreements (e.g. REGENERON, USA; McGill University, Canada; Leicester, UK). All data will be returned to Oxford for statistical analyses.

Any protein analyses would be performed using up-to-date proteomic chips and with individual ELISA tests where these will be expected to provide useful information.

Any urine analyses would be performed using standard protein and metabolite analyses.

Only samples where consent for future research and, where applicable, genetic study will be used. All published research findings will be openly accessible to the public, but there will be no feedback of individual findings to the study participants.

11 STATISTICAL ANALYSES

Analyses of randomised interventions will be by "intention to treat" and results will be displayed using Kaplan-Meier survival analyses. Appropriate survival analysis methods (e.g. Log-rank, Cox-regression analysis) will be used to compare the risk ratios for first occurrence post-randomisation of each outcome of interest (e.g. stroke, myocardial infarction, dementia, mortality) between both allocated treatment groups. The association between baseline vascular risk with later dementia will be assessed.

The first planned analyses will be based on at least 20 years' follow-up from trial initiation with further analyses planned at approximately 5 yearly intervals based on on-going linkage to NHS records.

12 CROSS-STUDY META-ANALYSES

NDPH has conducted several similar studies (THRIVE, SEARCH, HPS, and REVEAL) with common aims. Due to the similarities between the studies and the cohorts used, where any one study does not give sufficient power for an analysis, the study team will perform meta-analyses to a common protocol. Where the randomised allocations are similar, the study team will perform study level and individual participant data meta-analyses to look at the effect of variables on major health events such as stroke, myocardial infarction and dementia. This work is possible because NDPH has been conducting trials in similar populations over decades and the study cohorts are similar enough to combine. This means that analysis can be done with larger numbers, resulting in better data and the ability to investigate things that wouldn't be possible with a smaller dataset. This work could include using data about blood results and genetic information. There will also be methodology work conducted. Any such work would be undertaken within the NDPH, University of Oxford.

An example of work planned includes meta-analysis on major vascular events (MVEs) in a secondary prevention population to investigate how much we can rely on data linkage for participants with prior disease. A separate Protocol describes this work.

13 DATA MANAGEMENT

13.1 ACCESS TO DATA

All data will be transferred, handled and processed in agreement with the Data Sharing Agreements or equivalent contracts with each Data Custodian, and these will be specific to THRIVE. All processing will be subject to Fair Processing requirements.

13.2 DATA RECORDING AND RECORD KEEPING (SEE APPENDIX B FOR DATA FLOW)

NHS Data Custodians hold the linkage between trial participant numbers and participant identifiers. This will allow the Data Custodians to create a dataset of trial participant numbers linked to electronic health records. Data will be received back by Oxford in an encrypted format via a secure transfer method as required by each Data Custodian.

On receipt of data at NDPH, the Senior Data Analyst checks that the returned data is of reasonable quality, applying format, dictionary or look-up checks where practical. Pseudonymised data is then moved to the trial database. Identifiers that are only required for linkage will not be included in the trial dataset but will be kept separately. The pseudonymised trial dataset is passed to analysts and statisticians to conduct analysis as appropriate.

The data will be stored at the Nuffield Department of Population Health (NDPH), Richard Doll Building, and the Big Data Institute, Li Ka Shing Centre for Health Information and Discovery within the University of Oxford. Any NDPH researchers involved will have appropriate training in information governance and in handling confidential and participant sensitive data.

The NDPH servers are protected against unauthorised external access by an appropriate strength firewall. Access to patient identifiable information is protected by the appropriate authentication procedures (user IDs and passwords). Authentication is only given to personnel with an approved need, and authorisation, to access the required data. Only personnel involved in the long-term follow-up study for HPS2-THRIVE (processing and analysing data) will have authorised access to this data. The University of Oxford is on the ICO data protection register (registration reference: Z575783X). NDPH also meet the standards of the NHS Data Security & Protection Toolkit (origanisation code: EE133863-MSD-NDOPH-NDPH).

Personal data (including identifiers) will be kept until 2035. After this, anonymised datasets will be kept indefinitely to provide: an audit trail for published findings, ability to respond to regulatory requests for further information and for further analysis.

14 ETHICAL AND REGULATORY CONSIDERATIONS

The protocol, previous informed consent forms, and PPIE and other supporting materials have been submitted to a Research Ethics Committee (REC), and Confidential Advisory Group (CAG) for

approval. REC approval has been granted by the West of Scotland REC 3 (ref: 19/WS/0116) and support is given by the CAG (ref: 19/CAG/0166).

The Chief Investigator (or their delegate) will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

Participants will not be approached for further consent and data sharing agreements will be in place accordingly.

15 FUNDING

Health Data Research UK (HDRUK)
Nuffield Department of Population Health, University of Oxford

16 PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge the source of funding for the study. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

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18 APPENDIX A: PATIENT & PUBLIC INVOLVEMENT & ENGAGEMENT

18.1 PPIE DECEMBER 2023

The most recent PPIE was conducted in December 2023. While there is no longer any contact with the original THRIVE cohort, the PPIE team at the Nuffield Department of Population Health (NDPH), also known as Oxford Population Health, coordinates the work of three Public Advisory Groups (PAGs).

The public contributors were recruited via various methods, such as collaborating with regional and national networks, charities and community groups but also using our communication channels. They come from across the UK with various socioeconomic, ethnic and age backgrounds and were recruited to represent the UK's diverse population and ensure that they bring their unique lived experiences in each study.

At the most recent face-to-face meeting of these groups (on 2nd December 2023), we asked 28 public contributors for their input on the continued use of data for long-term follow-up trials (including THRIVE).

Overwhelmingly participants felt that using data long term after trial participation was a good use of the data. They thought that anyone who had consented to the original trial would likely be willing for their data to continue to be used, and that if it were them (that had been a participant in the trial), they would be happy with this use of data. They also highlighted the importance of communicating information where possible. While the THRIVE team are no longer in direct contact with the trial participants, the study website is used to provide information about the trial, and any results.

18.2 COMMENTS FROM 6 PPI PANELS (2018/2019)

The proposed use of patient identifiable data is to identify participants based on similar methods previously used by the NDPH, University of Oxford group in other large-scale trials. The data to be gained is similar to those required for previous studies, in which more than 230 000 participants were identified (without consent) for recruitment into the study with no significant problems encountered, the ASCOT study in Imperial College, and the ACST-1 study. Six patient and public panels were approached to test the acceptability of follow-up in electronic health records of participants from old randomised controlled trials that were designed before long-term follow up in electronic health records was thought to be routinely feasible. The following panels were consulted:

1. SEARCH and HPS2-THRIVE study participants
2. NIHR Stroke Research Network Panel
3. Clinical Trial Service Unit, University of Oxford
4. University College London PPI group
5. ASCOT participants PPI group

6. OCDEM PPI Group

18.2.1 Study participant feedback

Participants from the SEARCH main trial and also another large study (HPS-THRIVE) were approached to give feedback on the acceptability of this protocol from a participant perspective:

"As a participant I am perfectly happy for my data to be analysed as described and cannot believe others won't be. So I do not think additional consent is required."

"As a participant in both the SEARCH and HPS2-THRIVE trials I have no problem in giving the OK to this new work."

"I do not see any issue with the approach and procedure being proposed, and agree the process should effectively manage any risk to confidentiality. I am also of the opinion that participants who sign up for trials want their data used for effective on-going research. I would therefore very much support the study."

"However after considering your reasons for using this unique data long-term and the fact that through encryption, privacy will be protected; all overrides my concerns."

18.2.2 NIHR, CTSU and UCL groups

The following questions were asked:

Do you think the research proposed here is of sufficient interest and could have sufficient benefits to warrant linking information from GP and hospital records to participants' trial data?

Yes: 33/35 (94%)

No: 0

Unsure 2/35 (6%)

Do you agree that in the circumstances described here it is not practical to seek individual patient consent and therefore it is reasonable to carry out the research in the way described here?

Yes: 27/36 (75%)

No: 3/36 (8%)

Unsure 6/36 (17%)

Do you agree that concerns around individual participant privacy are extremely low?

Yes: 24/35 (69%)

No: 4/34 (12%)

Unsure 6/34 (18%)

Do you have any other concerns about the project that have not been made sufficiently clear?

Yes: 6/36 (17%)

No: 26/36 (72%)

Unsure 4/36 (11%)

18.2.3 ASCOT trial participants

Question 1

	Yes	No	Don't know
Do you think that this research study is a good idea?	19/19 (100%)	0	0

Question 2: Why do you think it is a good or bad idea?

All respondents thought the project was a good idea. Some representative comments:

"More research in an ageing population can only be a good thing"

"It makes sense to carry out a study on dementia"

"Any research into the causes of dementia is a good thing. It is a progressive disease which affects many people"

"I think there will be long term benefits as a result of this. Benefits would not otherwise be evident"

"If [dementia] could be avoided, it would be excellent. It would save the NHS money, families distress and enable those with the disease to continue contributing to their communities"

"Any potential resource held in medical records should be used to advance research and knowledge"

"All research helps"

"If it helps someone it has to be good"

"I would be happy if the ASCOT data could be of assistance in pursuing knowledge of dementia"

Question 3

	Yes	No	Don't know
Do you have any concerns about such a study being carried out?	0	19/19 (100%)	0

Conclusion

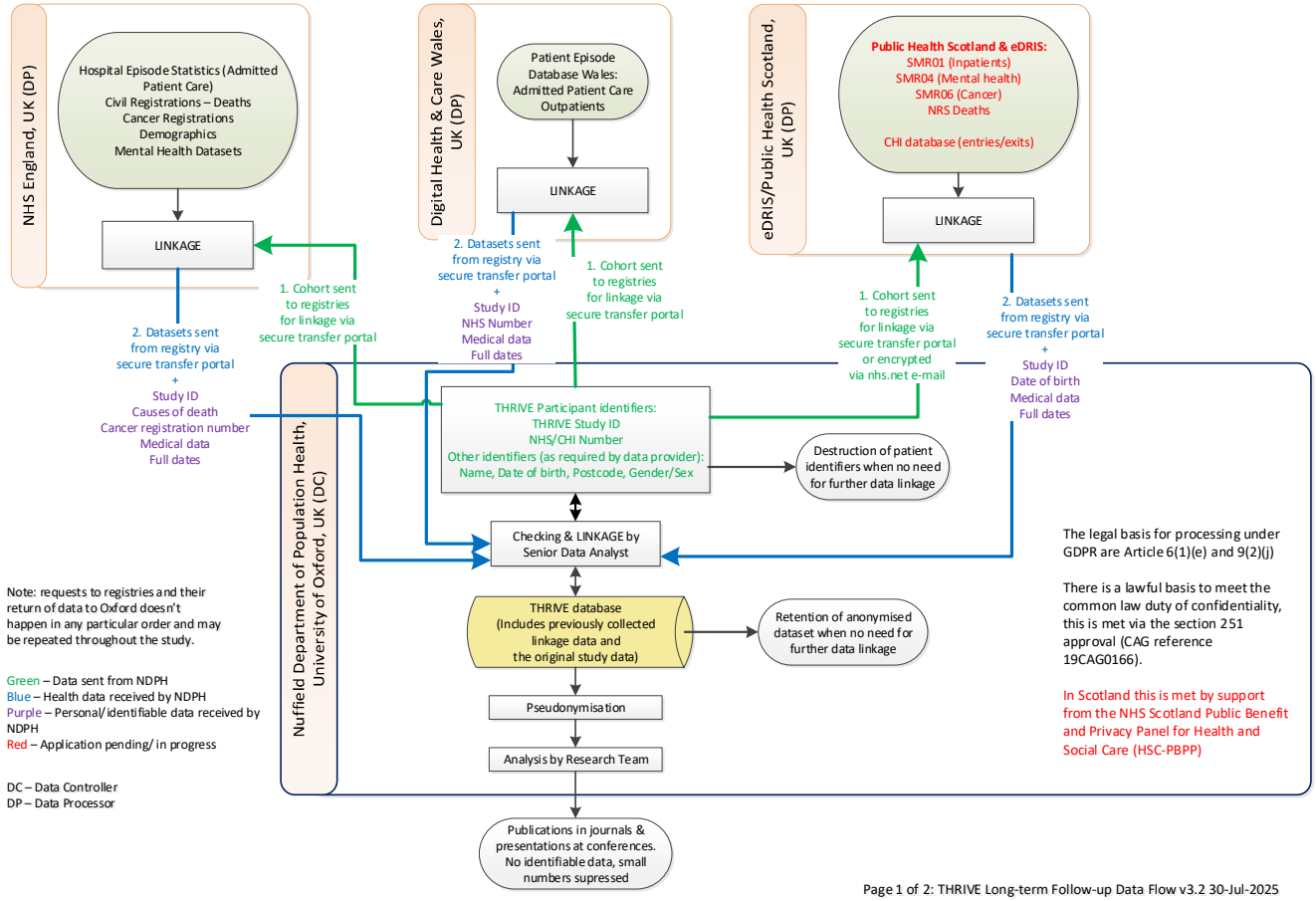
All respondents felt that the research was a good idea, and none had any concerns about the project. No respondent has concerns about the use of medical records for this research question.

18.2.4 OCDEM PPI Group

	1	2	3	4
Do you think this research study is a good idea?	Yes	Yes	Yes	Yes
If YES, please say why	Any study that can reduce the worst effects of diabetes should be supported. Any reduction that can be made in the number of diabetic amputations should be actively promoted	It seems sensible to me to that we study if the risk of complications (for T2D) can be reduced by the use if certain medications and what the benefits might also be.	It is well known that poorly controlled diabetes increases the chnace of heart disease, strokes, kidney failure etc., so any research that can give possible improvements in treatments / medicines has to be a very good thing	If a correlation between long term blood glucose control and dementia, death or other major diseases (e.g. heart attacks, strokes and kidney disease) can be established, then it is potentially worth investing in research to establish the cause(s).
If NO, please say why				
Do you think it is acceptable to look further at the data from participants in UKPDS without asking for consent again?	Yes	Yes	Yes	I don't know

If YES, please say why	**Once one has given permission to take part in a study, it should follow on that continuation studies MUST be included**	Had I signed up for the original study then I would have no objection – so I am carrying that logic forward	Patients have already given you permission to look at their data; exploring that data further is no more intrusive than the first study and will expland knowledge on ho diabetes may lead to dementia or other ocnditions if controlled	It depends on the exact nature of the consent they gave for the UKPDS research. I.e. what did the consent form they signed say? E.g. if the form said that thy would be contacted should further use of their data be a possibility, then it does not seem reasonable to use their data without requesting explicit permission for further use of that data.
If NO, please say why				
Do you have any other comments about this research?	See my initial comments	I would insist that the electronic data interface described is robust and not a laptop on a train …	Given the number of people being diagnosed with diabetes and the huge costs to the NHS any researcg that may lead to improvements in care has to be a good thing. Patients also need to be proactice in their treatment	

19 APPENDIX B: DATA FLOW DIAGRAM



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