LUSTRUM Accelerated Partner Therapy (APT) Chlamydia Trial

Key information regarding data security and information governance arrangements

Contents

1 TRIAL

1.1 Data Protection & Confidentiality – trial data

All trial data will be collected via the RELAY data collection tool to be developed by EpiGenesys, our web-based data collection tool designers, based within Sheffield Clinical Trials Unit. EpiGenesys will be responsible for ensuring that all personal identifiers from patient data are stripped using an automated function and that only a fully anonymised database is provided to the research team for analysis. Data collection procedures will adhere to national standards for information governance, data security, server security and web-based data collection tool protection (see details below). Mr Martyn Steers, Barts Health, Deputy Information Governance Manager attends relevant RELAY data collection tool development meetings and advises on all relevant design and implementation decisions.

EpiGenesys will adhere to the requirements of the Department of Health for all commercial third parties processing personal identifiable data on behalf of NHS organisations and they will complete the Information Governance Toolkit. This will be achieved in the following ways:

1. The database will be commissioned in accordance with current NHS standards for data storage and transfer, under the supervision of NHS Information Officers in relevant NHS trusts. Data will be stored on secure servers with strict access controls; only appropriate clinical staff will have access to personal identifiable data.
2. Collecting the minimum number of data items for appropriate clinical care and justifying the intended use of each data item stored or transferred.
3. The TMG will oversee the commissioning and specification of the RELAY data collection tool to be used for data transfer. The TMG will include a CNWL/Barts Health Trust Data protection lead and at least one member with experience of successfully commissioning electronic health records and a good understanding of relevant legislation and web security issues.
4. Confidentiality: only essential personal information will be obtained for the purpose of the study. All information will be obtained with strict adherence to the Caldicott principles of confidentiality, as outlined in the Caldicott report 1997, and referred for permission to the relevant NHS Data Protection Officer and Caldicott Guardian at every stage.
5. In addition, we will make sure that all staff involved in the trial receive training on the use of the RELAY data collection tool. Finally, the RELAY data collection tool will feature integral security levels which include restricted access controls so that sensitive information can be seen only by the appropriate clinical staff.
6. No information will be collected or stored on the RELAY data collection tool and all data captured through it will be transmitted, processed and stored on the server.

All investigators and trial site staff will comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. The research team (other than research health advisers who are conducting a clinical and research outcome interview with index participants and partners) will only have access to anonymised patient data.

All information relating to participants will be kept confidential and managed in accordance with the Data Protection Act 1998, The Caldicott Report & Caldicott Principles 1997, NHS Confidentiality Code of Practice 2003, The Freedom of Information Act 2000, The UK Policy Framework for Health and Social Care Research, and the conditions of Research Ethics Committee Approval. The Information Governance Toolkit will be applied to the RELAY data collection tool and the appropriate standards met. Any personal identifiable data, both transferred and stored, will be encrypted in line with NHS Information Governance 'Guidelines on use of encryption to protect personal identifiable and sensitive information' 2008. Short message service (SMS) and email use will adhere to the 2010 NHS Information Governance Information Risk Management guidance.

NHS.net will be used for email communications between research health advisers, study clinics and pharmacies. A record of these emails will be kept as part of the patient's electronic health record. The transfer of patient identifiable data via these media will be minimised. Patient electronic health records will be stored on a secure server provided by Google cloud (NB this is not the publicly available cloud). The Google Cloud Platform is a suite of cloud computing services that are provided by Google and hosted in their data centres around the world (see Appendix F, page 68 for more details about the Google Cloud Platform and data security). EpiGenesys uses a variety of services that are available on Google Cloud Platform, including: virtual servers; load balancing; source code hosting, and storage. Google maintains an extensive list of all of the compliance certifications (see Appendix F) and have released a White paper outlining how data are encrypted throughout the Google Cloud Platform (web-link in Appendix F). Specifically, web traffic from end users is encrypted between their computer and the Google Front End load balancer. All traffic between the load balancer and the virtual machine hosting is also encrypted. Internal traffic between Google services may not necessarily be encrypted, but they are authenticated - they are only encrypted if the data is travelling outside of the same physical data centre. For data protection compliance all of EpiGenesys' services are currently hosted within the europe-west2 region which is based in the London area. The physical location of Google premises is protected by a host of high level security measures including 24 hour surveillance and armed security guards.

The web-based data collection tool used will be designed to securely collect the data from the online survey and a robust ethical hacking methodology will be used to test and validate the RELAY data collection tool and if necessary, preventative and corrective measures will be taken to mitigate the risk of cyber-attack.

Sites will keep their site-specific research data on site for a minimum of three years before sending it to be archived, this will allow time for the retrieval of any site research data should the research be selected for auditing. After the LUSTRUM study has ended, research data will be stored for 25 years and will be organised by the sponsor. Access may be granted only by formal request to the sponsor's office and is only available to members of the research team. Clinical records will be stored by the individual clinical sites according to current NHS practice.

1.2 Consent

Consent for participation in the trial

As this is a pragmatic cluster randomised trial, we will seek consent for trial participation from lead clinicians at participating clinics (cluster-level) and will not seek individual informed consent from index patients. We carefully considered ethical issues raised by this approach and took advice from colleagues with expertise in biomedical ethics and the views of our LUSTRUM PPI Group before arriving at this decision. Following Weijer et al. (35), we believe that APT is a complex, "low-risk" healthcare delivery intervention. APT is being offered *in addition* to standard PN and operationalised as a supplement to usual care, thus index patients have the choice of taking up APT or not.

It is widely accepted that individual consent may not be essential in such trials (36), in which the situation is analogous to the introduction of changed processes in routine services (37) and individual level consent is thought to have contributed to low recruitment numbers in a previous study of APT (18). Richard Ashcroft (collaborator, Professor of Biomedical Ethics, Queen Mary, University of London) supports the chosen approach (clinic-level consent) and advised that as the trial is evaluating a service-level innovation, the target of the intervention is the clinic rather than the individual patient. He advised that it is appropriate to use a cluster randomised design *and* that individual consent is required only for the method of PN rather than to randomisation per se.

1.3 Indemnity

The study will provide indemnity through a NHS insurance scheme should liability arise as a result of the study management, design or conduct. The NHS indemnity does not offer no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance, of NHS Research Ethics Service review and specific guidance, to pay compensation for non-negligent harm.

1.4 Safe Prescribing

Accelerated Partner Therapy (APT) involves remote prescribing of antibiotics to treat chlamydia to sex partners based on a telephone consultation. In preliminary APT feasibility studies, the Medicines and Health Regulatory Agency confirmed that this prescribing model is in accordance with appropriate prescribing legislation. APT conforms to the "remote prescribing" guidance offered by the General Medical Council. The prescribing of empirical treatment for sex partners of patients with chlamydia, without waiting for the results of diagnostic tests, is standard clinical practice therefore APT is no different in this respect.

1.5 Withdrawal Criteria

Clinic withdrawal

Clinics (or clinical services) are able to withdraw from the trial at any point. Should a clinic withdraw before randomisation then we shall seek a replacement clinic, but not otherwise. In the unlikely event of a clinic withdrawing, over-recruitment in other trial clinics will be permitted to compensate patient numbers and thereby partially compensate the loss of power.

Index patients withdrawal

Patients may choose:

1. not to comply with any or all aspects of APT
2. to request that they are not contacted for follow-up or posted a self-sampling kit
3. not to respond to follow-up phone calls
4. not to return follow-up self-sampling kits at 12-16 weeks
5. not to participate in follow-up semi-structured telephone interviews.

There will be no replacement of index patients after withdrawal. In the event that the patient does not wish to be contacted for follow-up, the research health adviser will note the withdrawal so no further follow-up attempts will occur. They will also ask the index patient and record whether the withdrawal relates to an adverse event or any other any reason.

1.6 Adverse Events

We will collect reports of adverse events relating to either the intervention or participation in the trial, which shall be reviewed by the TSC. The TSC could recommend the trial be stopped if members are sufficiently concerned about these events. The trial will not be stopped early due to demonstration of efficacy, harm or futility in the primary outcome.

1.7 Storage and Analysis of Samples

This is a trial of a health service intervention and there are only two types of biological sample which will be collected and processed:

Sex partner self-sampling kits for Chlamydia and Gonorrhoea and HIV and syphilis

Clinics which routinely offer self-sampling kits as part of clinical practice have a laboratory which handles these samples routinely and is licensed to do so for this trial; sex partners will return their self-sampling kits to the relevant laboratory (the partner packs contain an addressed, postage paid envelope in which to return the samples safely).

On arrival at the laboratory, samples will be handled and tested according to routine practice and as per the licensing conditions. For clinics who do not routinely offer self-sampling kits, this service will be provided by The Doctors Laboratory who are licensed to store and analyse these samples for this trial.

Index patient self-sampling kits for chlamydia re-testing 12-16 weeks post treatment
Index patients will return their self-sampling kits to the study laboratory (TDL) (the index patient packs contain an addressed, postage paid envelope in which to return the samples safely). On arrival at the laboratory, samples will be handled and tested according to routine practice and as per the licensing conditions.

1.8 Storage and Mailing of Sex Partner Antibiotic Treatment

The antibiotics to be used in sex partner APT packs will be provided by the clinic responsible for their care (who conducted the phone sexual health consultation) and will be the same antibiotics as would usually be prescribed and dispensed by the clinic as part of routine management of Chlamydia. No new antibiotics will be introduced to the clinic. All antibiotics used in the APT pack will be stored according to local clinic protocols for the storage of medication. Antibiotics are supplied as trial packs and will be added to the APT pack either for posting or to be given to patients to give to their sex partner(s). The label on the antibiotics specifies duration of use in line with routine practice and the healthcare professional/health adviser will write the sex partners' name on the packaging. All posted antibiotics will conform to safe storage and transport guidance, under the supervision of Ms Dena Godward (acting) Chief Pharmacist and Carol Greening (acting) Head of Outpatients at Barts Health NHS Trust.

1.9 Risk of Sex Partners' Wider Sexual Health Needs not being addressed

APT differs from standard Partner Notification (PN) in that the sex partners are tested and treated for chlamydia at home, without needing to attend a clinic. There is therefore a risk that they will miss out on the wider sexual healthcare they would otherwise have received at a clinic, including testing for other Sexually Transmitted Infection (STIs). To address this, the partner's urine sample/vulvo-vaginal swab will be tested for gonorrhoea at the same time as chlamydia (routine practice in clinics). In our previous exploratory trial of APT, the testing and treatment pack included an invitation to sex partners to attend the sexual health clinic for HIV testing, but uptake was very poor [1]. Since that exploratory study, advances in diagnostic testing and a shift to self-managed care within sexual health services has meant that several sexual health clinics and National Chlamydia Screening Programme services routinely offer postal self-sampling HIV kits along with STI self-sampling. We will therefore provide a HIV self-sampling kit (finger-prick test) and syphilis self-sampling kit in the APT testing and treatment pack. The pack will also include condoms and an information leaflet about chlamydia detailing causes, transmission and prevention, signs, and symptoms, testing and diagnosis, treatment and complications, and information about how to access further.

1.10 Risk of Under Treatment of Sex Partners with Complicated C. trachomatis (Chlamydia) Infection

During the telephone consultation with the HA/HCP, sex partners will be questioned about symptoms potentially indicative of complicated chlamydial infection. Such contacts will be strongly advised to attend a sexual health service or primary care setting for full assessment. APT would not identify asymptomatic complicated infection in sex partners, whereas if these partners attended a clinic via standard PN, they may be identified during physical examination, for example, by the presence of tubal tenderness, which might prompt prescription of a longer course of antibiotics. However, asymptomatic complicated infections are thought to be rare, and such physical signs in the absence of symptoms are not sensitive or specific indicators of pelvic infection, therefore, we do not believe that APT would compromise medical care.

1.11 Risks to Patient of Offering Treatment to Partner

In routine clinical practice, all patients diagnosed with STIs, including chlamydia, are instructed to inform their sexual partners that they have been in contact with an STI and the need to attend clinic for testing and treatment. We do not anticipate APT exposing patients to more risk of personal safety (such as partner violence) than standard PN. No violent episodes were reported by any of the 1783 participants in an American randomised controlled trial of patient −delivered partner treatment [2] nor in our earlier APT studies.

1.12 Anonymity of published results

Analysis of trial outcomes is at a clinic level therefore it will not be possible to identify any results for individual patients, and data for clinics will be aggregated such that results for individual clinics will not be identifiable in any publications.

Publications may include quotes from patients and clinic staff participating in the process evaluation qualitative research. All research outputs, including reports, presentations and publications of results will be written in a way that prevents the identification of individual participants. For dissemination purposes, unique identifiers and/or pseudonyms and broad terms, such as ‘sexual health adviser, Glasgow’, ‘index patient, London’ might be used following a qualitative data extract/quote. Furthermore, demographic data and attributions such as gender, age and location will only be presented in a collective way in order to maintain participants’ anonymity.

1.13 Monitoring, audit & inspection

The trial will be subject to monitoring, auditing and inspection by the sponsor or the sponsor’s delegated representatives, and the relevant authorities responsible for each of the sites where the research will take place. The purpose of the monitoring is to ensure that the study is conducted in accordance with the authorised study protocol, the principles of GCP and all applicable regulations.

The sponsor and regulators will require access to the study site for these inspections which will be supervised by the site investigator(s). The inspection activities apply to the following, and associated, areas in order to:

6. review the trial master/site file (hard and soft copies);
7. review the study participant consent forms;
8. review research documents as approved by applicable regulatory body and those referenced in protocol;
9. review participant facing, current and superseded versions;
10. review the storage facilities/spaces for research documentation (paper and electronic);
11. review site delegation of duties log;
12. review trial amendment log.

Data monitoring will also be undertaken by the DMC as detailed in section Roles and Responsibilities of Trial Management Committees/Groups & Individuals. The group is comprised of individuals with all the relevant skills & experience required for such roles and the trial is a low risk health service intervention. The TMG will include the CNWL/Barts Health NHS Trust data information officer.
The central responsibilities of this TMG will be to make recommendations to the CI and sponsor on further conduct of the trial, based on results of the monitoring procedures described below. Such recommendations could include modifying its protocol. Any such modifications should not violate the concepts behind the original study protocol.

If changes in the study conduct are recommended by the TMG, sufficient information will be provided to allow the sponsor and the CI to decide whether and how to implement them. The implementation of any TMG recommendation is the responsibility of the CI and sponsor who are also free to neglect (in whole or in part) any recommendations of this TMG. The sponsor and the CI bear the final responsibility for the conduct of the exploratory study. This responsibility cannot be transferred to the TMG.

The TMG will review accumulating data in an un-blinded fashion in order to monitor and audit the study conduct. Two months following the beginning of patient recruitment, the data manager will collate and clean all data as necessary, and the study statistician will perform interim analyses. The study statistician will apply the statistical methods specified in the protocol to analyse study outcome measures and provide the DMC with data and analysis for checking.

2 PROCESS EVALUATION

2.1 Consent for participation in semi-structured interviews and focus groups

Individual informed consent will be sought for participation in the semi-structured interviews and focus groups for the process evaluation, as described in section **Error! Reference source not found.**. C onsent for telephone interview will be verbal, and will be audio-recorded at the start of the interview. Written consent will be obtained for face-to-face data collection (focus groups and face-to-face interviews).

2.2 Security of process evaluation data

Data protection measures will be applied to ensure the confidentiality and anonymity of all participants in the study and GCP guidelines will be followed to handle all information in confidence. Semi–structured interviews and focus groups with participants will be audio recorded and stored on audio-recorders before being transferred to the research teams' (GCU and/or UCL researchers only) restricted access network drives that are regularly backed up by GCU/UCL information systems departments. Downloaded recordings will be labelled with a unique identifier. Following data transfer, all recordings will be deleted immediately from the audio-recorders. Transcribers will sign a confidentiality agreement with regards to the audio recordings and the research data they will receive.

All recordings will be destroyed at the end of the study, provided that the research team has received all full transcripts from transcribers. All interview and focus group transcripts will be anonymised by removing any identifiable information (including names, places and other personally identifiable information). Anonymised interview and focus group transcripts will be held securely at GCU and/or UCL premises in researchers' password-protected computers and/or locked filing cabinets in areas accessible only by named individuals. Verbal consent forms and all other monitoring documents with participants' details will be held securely on password protected university computers at GCU and/or UCL premises as these institutions are the lead research institution and the lead for the process evaluation research. Researchers at both institutions will need access to these files throughout the duration of the trial and for the remainder of the programme. Anonymised transcripts and all relevant forms and documents (including verbal consent forms) will be retained for five years following the end of the LUSTRUM Programme of Research.

Unique identifiers and/or pseudonyms will be assigned to each participant to support data management and maintain confidentiality. To ensure compliance with the Data Protection Act 1998, where pseudonyms are used alongside a codebook, the latter will be stored separately from the data in a password-protected file and will be accessible only to named members of the GCU and/or UCL research team. All research outputs, including reports, presentations and publications of results will be written in a way that prevents the identification of individual participants. For dissemination purposes, unique identifiers and/or pseudonyms and broad terms, such as 'sexual health adviser, Glasgow', 'index patient, London' might be used following a qualitative data extract/quote.

Furthermore, demographic data and attributions such as gender, age and location will only be presented in a collective way in order to maintain participants' anonymity.

In the case of focus groups with HA/HCPs participants will be asked to treat any information revealed within the group in confidence. Inevitably, other people in the discussion group will hear what other participants will say but researchers will ask all group members to respect the confidentiality of what is said in the group.

In rare circumstances, a participant in this study may disclose information that gives cause for concern about their or someone else's immediate safety. If a patient or sex partner discloses something during the consultation or follow-up phone calls that gives the HA/HCP and or research health adviser cause for concern, the situation will be managed as follows:

1. Disclosure during index patient or partner's APT consultation: the clinic health adviser will manage according to routine clinic procedures
2. Disclosure during the research health adviser follow up calls and or during the in-depth interviews (process evaluation) the research HA will inform the CI immediately. She will convene an emergency meeting with the research team and Site Principal Investigator to discuss the individual's safety and wellbeing. If appropriate, the research team may then follow legal guidelines for breaking confidentiality outlined in Good Medical Practice guidance manuals.

If a patient or sex partner discloses something during the in-depth interviews (process evaluation) that gives the researchers cause for concern the research team will uphold their duty of care to the participant and contact the Chief Investigator as soon as possible, who will convene an emergency meeting with the research team and Site Principal Investigator to discuss the individual's safety and wellbeing.

If appropriate, the research team may then follow legal guidelines for breaking confidentiality outlined in Good Medical Practice guidance manuals. All patients and participants will be made aware that their participation is confidential, however, in the event that they disclose information which leads the HA/HCP and/or the research team believes to be at risk of harm, the HA/HCP or research team may need to share that information.