Biobanks and Biorepositories for Stratified Medicine April 2015

Summary report on a focused workshop held in partnership with University of Leeds,

Introduction

Biological samples collected from patients during their treatment, or as part of clinical research, are stored, along with the accompanying patient data, in national biobanks and biorepositories to provide a very valuable, cost effective research tool to study disease progression. New technologies have allowed scientists to use these samples and data to determine definite molecular and genetic differences within a disease category. Clinical scientists then use diagnostic tools to stratify (group) patients according to the subcategory of their disease to go on to determine which drug will most likely have a positive therapeutic effect for that group of patients. Patients can then be offered a more "precise" drug treatment that is "personalised" to their condition; so they receive the most appropriate drug at the start of their treatment, optimised at the correct dose and compatible with their other medications. This is described as stratified, personalised or precision medicine; as opposed to symptoms based medicine, where patients are prescribed their treatment based on the signs or symptoms of disease.

However, providing the necessary infrastructure, legal and regulatory frameworks to make effective use of the samples and associated data stored in biobanks and biorepositories is a challenge that requires significant resources and funding.

The UK Pharmacogenetics and Stratified Medicine Network, in partnership with the University of Leeds, invited a group of leading academic scientists, research funders, industry, regulators, patient groups and representatives from UK tissue banks, to discuss the issues, and offer solutions to developing effective biobank and biorepositories in terms of:-

- Patient and public involvement in donating their samples and data to bio-banks
- Consent and ethics around collecting and storing patient samples and data
- Quality of patient data, including electronic health-data records linked to bio-banks
- UK biobank standards, including phenotyping, collecting/storing of samples and data

Summary of group findings

Gaining patient and public support for biobanks

The public recognise the need for research to improve the treatment of diseases and are willing to give financially to registered medical charities carrying out research. However, public understanding of the requirements for human tissue for research is not as well established so must be improved to help make tissue donation as "normal" an activity as regular blood donation. Most research organisations involved in clinical research have dedicated patient representatives or have developed patient public involvement (PPI) groups. However, often these groups are mostly comprised of people that are already well educated and there are concerns about the low level of representation from ethnic minorities and those who had not undergone higher education. Encouraging all patients to join these groups to learn about the research being conducted into their condition will help gain more widespread donations of biological samples and associated data to biobanks for research purposes.

Patient advocate groups partnering with academic researchers / healthcare professionals to provide an understanding of why and how research is conducted helps relieve patient anxieties around participating in academic studies / clinical trials and encourage patients to donate their samples and data for research. For example, raising awareness through patient advocate groups has been particularly successful in gaining support for obtaining samples for oncology studies.

Patients donate their samples to biobanks for altruistic reasons to move research forward without any thought for immediate gain for themselves. Therefore, it is important to make the patient feel their contribution is valued by providing patients with opportunities to discuss their condition with researchers, and the healthcare professionals collecting their samples, so the patient is recognised as "a person with individual needs" rather than as just "another patient". Providing updates on the outcomes of the research will also make patients feel valued and encourage continued donation of their samples and data.

Patients and the public in general want information on how their samples and data will be used so more transparency around the aims of research projects will earn patient respect and trust for the research being carried out. Healthcare professionals in the clinic might be

hesitant to ask patients for samples by assuming patients do not want to be burdened with being asked to participate in research initiatives at a time when they are facing a devastating diagnosis, such as cancer. However, patient representatives felt there should be less of a protective approach to patients and that patients are able cope with being asked to be involved; and indeed should be given the opportunity to donate their tissue to research to benefit others suffering from the same conditions. The NHS has launched an "OK to ask" campaign, which encourages healthcare professionals to discuss research opportunities with patients.

Healthcare professionals must be provided with the appropriate training and communication skills so they are confident to approach patients for research samples after they have received bad news and may be feeling very emotional. This is especially true when being over sensitive towards relatives after a patient has passed away may result in the loss of very valuable post mortem samples. To avoid this loss of samples potential donors should be encouraged to involve family members in discussions around donating post mortem tissue so their wishes are known prior to their death. However, there also has to be some realism on the part of donors that in some cases their tissue may not be suitable for research, or there is no possibility of actually being able to physically collect their samples.

Patients genuinely donate their samples to biobanks to move research forward and make a difference in preventing others from suffering with their condition. Researchers, including those from commercial organisations, must also adopt this altruistic nature of donation and collaborate more by passing on research findings from donated tissue so that research moves forward rather than being duplicated unnecessarily.

Obtaining patient consent

Patients must have the opportunity to be part of the decision making process on the use of their samples and data and their informed consent is required before any research may commence. Information to obtain patient consent should be designed to maximise public trust in research and at times may need to be in excess of legal requirements. The information must be delivered in a format that is easily understood so that patients are not overburdened with complex information. The patients must understand the type of

research being carried out on their samples, and how the data associated with the sample will be stored and then used in the research.

Providing the appropriate level of information to gain patient consent is challenging and must be designed to reassure patients. Patients working alongside healthcare professionals and researchers will ensure the information contained in the leaflet is relevant, meaningful and in a patient friendly language. Trying to protect and promote patient choice of how their samples are used by providing very detailed information about the research being carried out may actually have a negative effect as patients feel less inclined to read too much information and may feel overwhelmed. However, it is not sufficient to only give patients a minimal amount of information on the use of their samples and data. Investigating patient's main concerns around the use of their samples and data, and then targeting information to these concerns, may result in gaining the right balance on the level of information to provide.

Consent obtained for a research project at the time of collection of the sample may not be transferable to later applications for access to the samples stored in biobanks for additional research projects. It is almost impossible to predict all the potential uses of samples and data so having a robust procedural infrastructure governing access to samples and data stored in biobanks for future research may help reassure patients they have control of the ongoing use of their samples and data. As patients have willingly donated their samples to biobanks the consent process could be viewed as an opportunity for patients to provide permission for their samples and data to be used for all research and 'opt-out' of controlling the use of their data and samples; rather than continually having to 'opt-in' and give their consent to each individual research project. However, automatically allowing use of their samples of data for research does not mean that consent should be in any way presumed or that a formal consent process is no longer required for the new research project.

Providing different levels of consent is an important part of maintaining a level of public trust in research and once again patient advocates have an important part to play in supporting the development of the whole consent process. Tiered consent, where patients 'opt-out' of their samples being used in certain circumstances was considered as almost impossible to manage as it was too difficult to operate. Dynamic consent (where a

personalised, digital communication interface connects researchers and participant) places participants at the heart of decision making process; enables individuals to tailor and manage their own consent preferences; improves transparency in the process; and develops public trust. This type of consent system also benefits the researcher by streamlining recruitment and enabling more efficient re-contacting of participants.

Unsolicited findings

During analysis of patient data information about an unconnected condition which the patient has no knowledge of may be inadvertently uncovered. Any consideration of these unsolicited findings must recognise that the results will have arisen in a research arena and outside the clinical environment. In most cases these findings would not be communicated to the patient as they would be unlikely to influence patient care. If the results were to be communicated a clearly defined pathway must be in place for the results to be validated within the clinical environment prior to contacting the patient.

It should be remembered these unsolicited findings may have a knock on effect on the whole family. Patients should be made aware of the psychological issues that could arise from such findings, and have the opportunity to discuss the potential impact of the finding with their families, before donating their samples for research. Furthermore, it is important that the consent process should allow patients to make the choice of not wanting to be informed about unsolicited findings before any research is carried out.

Whilst patients may not want to be informed about unsolicited findings in some cases there is an ethical responsibility to offer a patient treatment once a condition is revealed. For example, patients donating their samples to the 100,00 genome project could ‘opt out’ of being informed about incidental findings, but if a serious disease on a predetermined list was discovered their opting out would be waivered and they would be offered treatment for the disease discovered to meet good medical practice standards.

Protection of samples and data

Patients are comfortable about donating their biological samples and do not have concerns about how their tissue or samples are stored; but they are concerned about the security of the storage, and potential unauthorised use, of their personal data. Therefore, patients

should be given information about how personal data arising from their samples might be stored and used to provide them with the confidence to donate their samples. It is important to reassure patients their data is fully anonymised before being released to researchers and that their identity is protected as much as possible at all times.

Patient groups and researchers must work together to make sure robust governance systems are in place to meet the informatics challenges that arise from handling and protecting these large data sets to provide individuals with the confidence that their data is held securely. Furthermore, governance and regulatory hurdles have to be overcome so as researchers have access to patient samples and data within existing biobanks to maximise research rather than collecting a new set of samples.

Setting up a biobank

There are a vast number of collections of all types of biological samples stored in universities and hospital biobanks / biorepositories across the UK, many of which are not suitable for research. Long-term storage of patient samples that are unlikely to ever be used does not meet patient expectations and will be detrimental to gaining patient support for other research projects. It is important to make sure that samples are collected for a definite purpose and that stored samples are always used effectively and not wasted, it is not ethical to just collect and store patient samples for future reference.

It is imperative that essential planning around the standards for collecting samples, and the long term objectives of the biobank / biorepositories resource, is in place before commissioning of a facility begins to ensure it is fit for research purposes. Regulation, legal and ethical compliance, plus a robust governance structure that is supported by patients and the public, must be established prior to the collection of any samples.

There is no “one size fits all” for setting up a biobank and there must be communication, training and education for all stakeholders on the value of the facility during the conception phase. This includes funders of the biobank, those collecting the samples, maintaining and managing the resource as well as the patients donating the samples.

Samples are often difficult to obtain from patients so it is wise to consider if there is an alternative source of material more readily available; for example, by-products of surgery,

transplantation, blood transfusion, or tissues / organs / cells / blood found to be unsuitable for therapeutic use could be diverted to research. However, appropriate regulatory steps, and ethical permission to use this material would need to be put in place to permit this alternative use of biological material.

Biobank standards

A lack of quality standards at the time of collecting patient's samples may cause the samples to be rejected by researchers. The samples may be rejected on such grounds as inappropriate methods of collecting, processing, preserving, storing of the samples; or insufficient patient data accompanying the sample.

Biobanks have a responsibility to ensure that their samples are of appropriate quality and have adequate documentation for researchers to assess whether they are fit for their particular research purpose. In addition to ensuring the integrity of the sample, biobanks also have a responsibility for tracking and tracing samples, attributing them to patients and to appropriate patient consent. The biobank must ensure the samples and data are suitably anonymised prior to release to researchers so they cannot be traced back to an individual patient.

Standards between biobanks differ greatly so a quality management system for all biobanks to comply to would be helpful, especially for smaller biobanks who may struggle with putting in their own governance. Putting these standards in place to improve the service provided across the UK may ultimately help foster patient co-operation to donate their samples, and encourage patients to trust researchers and allow them access to their data.

Often research studies are carried out on data sources from multiple biobanks so data collected in the same format across all biobanks would greatly enhance the ability for researchers to compare and contrast results from small studies and then pool the data to increase the number of patients within a study. This is especially important when comparing results obtained from patients with rare variants of a disease.

Data Quality

Often essential information, such as deep phenotyping information, may be omitted from patient records, or the data collected may be presented in an inappropriate format. Therefore a training programme is required to raise awareness of the importance of the quality of patient data for research to provide healthcare staff (at all levels from senior consultants to nurses) with the skills they need to collect / handle data to the appropriate levels of quality assurance and control. Linking electronic patient record data with patient trial data to improve the annotation of bio-specimens would be beneficial but not without challenges.

Any patient data collected needs to be appropriate and related to the intended research use of the samples. Data may then have to undergo "cleaning and validation" before it is available for research purposes. A set of standardization or guidance procedures would support correct collection and preparation of data for research studies. An accreditation system may be a logical progression to improving standards across the field, but how this will be funded and whether the additional burden will provide value for money is unclear and must be decided by the customer and regulators.

Financial considerations

Patients receive no financial reward for donating their samples and data, but in some cases these samples and data may have a commercial application and bring in significant financial gains for the pharma company. For example, the sample may be important to industry to identify a target for developing a novel drug; or using patient data to target a drug to a specific group of patients may significantly improve the overall efficacy of the drug and so help licence the drug. Patients must be must be made aware of potential profit being made from the study and provide their consent before they enter the study.

Funding of biobanks

Grouping patients into the genetic or molecular subcategories of their disease to offer them a stratified medicine approach to their treatment relies heavily on the use of patient samples and data collected in biobanks. The running costs of collecting/storage of the samples and data for the initial research must be considered against the cost benefit of

using the research results to ultimately provide patients with an improvement in their drug treatment. The NHS budget is continually being stretched so the question arises should resources be diverted from the NHS budget to maintain biobanks for a specific population of patients or should they be funded and maintained as part of a national research infrastructure strategy?

Currently many biobanks are set up for a specific research project and there is no national register of the numerous biobanks across the UK resulting in sample collections being easily duplicated. Biomedical researchers need to work with research councils, charities, corporate and government funding bodies, to help overcome institutional barriers and obtain the funding to construct a sustainable biobanking infrastructure for the whole of the UK.

Often research grants will cover the collection of samples but not the ongoing costs of maintaining the facility. Provision for the considerable ongoing costs of housing a biobank must be considered before sample collection begins. Cost recovery structures to cover collection and maintenance costs of the storage of samples, plus technical support to manage and maintain the facility, have been put in place by many biobanks but these are still in their infancy. For the biobank facility to be sustainable and self-funding access charges aimed at recovering the cost of both establishing the facility and covering the hidden costs of running biobanks must be considered, but recovering these costs are seen by many as being unrealistic.

To save costs there should be an obligation to return samples to the biobank, and share research findings, so valuable samples are not used to duplicate results. However, the quality of the samples may have been compromised and no longer be sufficient to be returned to the bio-bank for use in other research projects. Aliquoting patient samples into small amounts at the time of collection and providing researcher with an aliquot may alleviate this risk and help maximise the use of samples in the biobank.