Implementing a research project on the development of diabetes

THE EXETER Research Alliance for Diabetes (EXTRA study) is a new research project recently implemented at the Royal Devon and Exeter Hospital. This project aims to investigate the genetic and environmental influences on the development of diabetes and its associated complications. The project will combine clinical, laboratory and genetic information to improve on the current understanding of diabetes. The EXTRA study is a resource from which novel aspects of research in diabetes will be identified and developed in the Exeter locality.

This article describes the process of instigating the study from an initial research idea through to the implementation of the project (Fig 1).

The research idea

The first stage of any research is the conception of an idea worthy of study. The need for this study was highlighted by people with diabetes, at patient forums, through Diabetes UK. They felt that it was important to investigate who developed diabetes complications.

Diabetes is a major cause of morbidity and mortality. About 1.3 million people in England are known to have diabetes, with projections that by the year 2010 the number of people with diabetes in the UK will reach 3 million (Department of Health, 2002). Diabetes has been estimated to account for 10 per cent of spending within the NHS and with the rising prevalence of the disease, this is likely to increase. Therefore, understanding how to prevent complications of diabetes is a major health priority.

Both genetic susceptibility and environmental factors are involved in the development of complications such as retinopathy, nephropathy, myocardial infarction and stroke (Roper, 2001). For all diabetes-related complications genetic susceptibility is shown by a familial tendency. However, other factors such as the control of diabetes, blood pressure and cholesterol are critically important in defining who is likely to develop complications. These specific risk factors in turn have their own genetic and environmental determinants.

Considerable work has been done on the molecular genetic basis of type 2 diabetes, but to date the major genes causing the common forms of type 2 diabetes have not been identified (Gloyn and McCarthy, 2001). A total genome scan, in which Exeter has been a major contributor, has identified the chromosomal regions where the genes that confer susceptibility lie (Wiltshire, 2001). It is expected that this will result in identification of genes within the next 3–5 years. Once these genes are identified there will be a need to understand how the genetic susceptibility is manifested in individuals within a geographically defined area. This will give a clearer indication of the role of genes in diabetes across a wide range of people, rather than just in those families who were targeted because of a family history of diabetes.

Type 1 diabetes is an autoimmune disease where the body destroys its beta cells leading to absolute insulin deficiency. What triggers this process is still unknown. There are also environmental influences on the development of diabetes as well as a genetic cause. The EXTRA study will examine the genetic/environmental influences in a large community cohort and expand on the nature–nurture debate associated with diabetes and its onset.

Funding

The NHS South and West Region funded the EXTRA project as part of an initiative to support trusts involved with the new Peninsula Medical School (PMS). The Royal Devon and Exeter research and development directorate also supported the study financially. Other funding opportunities can be identified through the research and development support unit (RDSU) in your area.

Naming the project

After brainstorming, the project was named the Exeter Research Alliance for Diabetes or EXTRA. This title was felt to be innovative, punchy and easy for patients and professionals to remember. It summarises the focus of the project, which is to provide a diabetes research resource for all professionals in the Exeter and District NHS boundary.

For individuals with diabetes, the shortened title indicated that being involved in this study was additional to their usual diabetes care and would not affect it in any way. The EXTRA study is a collaboration between patients and professionals, and the study title was designed to reflect this.

Steering committee

The EXTRA project formed a team of individuals to act as a steering committee. This seven-person committee is involved in the running of the study and includes both professionals and lay people, including a patient with diabetes. The committee receives an update on a six-monthly basis. It will convene at least annually and at any time when there are specific questions about the use of the resource. Much of this can be done electronically but if there are any areas of concern then the committee will meet to discuss them in detail.

The EXTRA protocol

All research proposals need a protocol. This is the scientific background to the prospective project and it needs to be submitted for scientific review before an application is made to an ethics committee. It need not be an onerous
task and the support of colleagues is invaluable. In the planning of the EXTRA study, preparing the protocol was a joint effort between the professor of molecular genetics, doctors and nurses.

All areas of the study have been devised using the Department of Health’s Research Governance Framework (2001). This framework helps to ensure that health and social care research is undertaken to high ethical and scientific standards by setting out standards and the responsibilities of professionals involved in research.

Consent

Consent for the EXTRA project is divided into three main areas and volunteers may choose to abstain from one or more of the sections:

- To be included in the retrospective and prospective collection of clinical and biochemical data for use in research;
- The taking of a blood sample for DNA that will be stored and used for genetic analysis relating solely to diabetes and diabetes-related disorders;
- Permission to be contacted with details of future research and for these details to be stored on a database for this purpose.

Patients are specifically asked if they consent to being given details of further studies. Unless there is express permission, they will not be contacted again from this period of data collection. Names of subjects who have given their consent are available to any researcher involved in recruiting patients with diabetes or control subjects in the Exeter district. However, it can be recorded at any time if the volunteer decides that he or she does not wish to be contacted for future research.

Scientific review by the trust

The research and development directorate in the trust needs to be informed about every study that includes hospital patients, staff or premises. A trust notification form (TNF) was designed and it needs to be completed before a study begins. Our medical director uses the information gathered to decide whether it is appropriate for the work to take place in the trust. This is based on the resources that will be required for the research to take place in the trust and the expected scientific quality. Included with the TNF is a data protection questionnaire that is reviewed prior to trust approval.

Ethics approval

The ethical committee must give its approval for the research before it is commenced. In this case it was necessary to apply to the local research and ethics committee (LREC) as the study is focused on a specific geographical area limited by North and East Devon NHS boundaries.

Setting up the EXTRA project involved detailed factual and ethical consideration of the information to be gathered. At all times the submission process should encourage researchers to consider areas involved in their research to ensure that beneficence, non-maleficence, justice, fidelity, veracity and confidentiality are accounted for (International Council of Nurses, 1996). These six ethical principles help to ensure that patients are guarded from harm when being recruited into research projects and reflect the role of a nurse according to the Code of Professional Conduct (NMC, 2002).

Anonymity for volunteers

Samples of DNA will be stored under a study identification number only. They are under the care of the Royal Devon and Exeter NHS Trust with ultimate responsibility resting with the professor for molecular genetics who is the principal investigator of the study. DNA is stored in line with Medical Research Council guidelines (MRC, 2001) on the handling of human tissues to ensure that it is impossible for laboratory personnel to trace the names of the people from whom the samples were taken.

There is no time limit on the duration for which the DNA may be stored. DNA is considered a critical resource the use of which should not be limited by time, because it is assumed that there will be continuing advances in understanding the genetics of diabetes and its complications in future. This collection of DNA will also represent a unique resource for assessing the impact of diabetes in a community cohort.

Data protection

The DNA database is maintained in accordance with the trust’s data regulations and the Data Protection Act (1998). The act, which has eight principles of ‘good information handling’, sets rules for processing personal information and applies to some paper records as well as those held on computer. All appropriate measures are taken to ensure that the collection of details is secure and

REFERENCES


For related articles on this subject and links to relevant websites see www.nursingtimes.net
only used by authorised professionals. The clinical database is kept separate from any genetic information.

However, for the purposes of conducting the DNA analysis limited information from the clinical database, such as type of diabetes, presence of specific complications and rate of development of complications, is provided. This is updated on a three-monthly basis but apart from this updating process there is no transfer of information between the two databases, which are held on separate computers.

Study participants
Based on the Research Governance Framework (DoH, 2001), the aim is that all patients with diabetes in the Exeter region will be approached. The only exception will be if the patient is unable to understand the consent form. We also invited partners, spouses and/or friends to take part as controls if they had no history of diabetes among their first degree relatives.

An estimated 8,000 people are to be recruited from the Exeter region. This is expected to comprise 5,000 patients with diabetes and 3,000 controls based on the assumption of an uptake of 70 per cent in people with diabetes and 50 per cent in the control group.

Minimal details of each participant’s diabetes will be taken and recorded, including age of diagnosis and treatment. In addition anthropometric measurements such as height, weight, waist and hip measurements will be recorded. A blood sample is also to be taken in order to convert white cells to DNA. A sample of serum will be stored for future analysis.

Volunteers can choose separately whether to: have blood samples taken, have clinical details collected; and be informed of future research studies. Individuals are able to withdraw at any point during the study with no future clinical or medical implications. However, it is necessary to be able to trace a volunteer to his or her blood sample, in order to remove it, if he or she did wish to withdraw. The blood samples will be coded in such a way that the research nurse can trace the donor. If the participant gives his or her permission to be recruited for future research, his or her contact details will be stored on a separate database for this purpose.

Benefits for volunteers
People who volunteer to participate in research rarely expect to gain something financially or medically from taking part. In genetic studies such as this, it is important to highlight to volunteers that they are unlikely to benefit directly from taking part and that their blood samples and information are in effect gifts to the trust. No participant (patients with diabetes and controls) will receive the results of any individual genetic test, which means there can be no impact on insurance premiums.

Samples from control subjects will also undergo routine biochemical analysis. If a result is abnormal the participant will be informed. The biochemical tests to be performed on control samples are:

- Urea and electrolytes;
- Total cholesterol screen;
- Glucose;
- Glycated haemoglobin (HbA1c).

It will be possible to update patients’ clinical information by using medical notes. This information will ultimately be integrated with the DNA database that evolves from the collection. Future generations should benefit from the study by the development of new treatments and increased medical knowledge.

Progress to date
Participant recruitment has been achieved by local GP practices posting questionnaires to all their adult patients with diabetes on our behalf. Included with this questionnaire is a prepaid return envelope to the research nurse. Individuals who have returned the questionnaire are then contacted by telephone to invite them to take part. Patients are seen either at the Royal Devon and Exeter Hospital, their local hospital or their GP practice.

Negotiations are being held with the retinal screening service and GP practices to gain access to patients during their screening appointment. A poster presentation and local radio station appeal for volunteers on World Diabetes Day (14 November 2002), during the trust’s research open day, also attracted participants.

The EXTRA project is in its infancy and minor problems, which were not foreseen in the planning stages have become apparent. These involve minimal changes to data collection sheets to make them more user-friendly. The most efficient and cost-effective way of approaching individuals for recruitment is being considered, bearing in mind that the participant always takes priority.

The next step is to secure funding in order to apply to the Office for National Statistics (ONS). The ONS will allow volunteers who give their consent to be tracked through their journey in the NHS to their eventual death. This ‘tagging’ is expected to generate yet more research areas in diabetes.

Conclusion
Developing the EXTRA study has been a huge but exciting challenge. It has taken time, patience and skills in collaboration, negotiation and innovation. I have consistently gained from the support of colleagues and their advice has been invaluable. This new project is developing a large community-based research resource in diabetes, its complications and genetic causes. Although the EXTRA project’s full impact has yet to be realised and assessed, it will undoubtedly provide improvements in medical and scientific understanding, and in the treatment of diabetes.

The channels used in setting up this diabetes study are available for all nurses. Research and development support units (RDSUs) exist in many trusts and are there for all staff to utilise. Nurses I have spoken to often feel their ideas are not worth pursuing and do not contact their RDSU. This lack of conviction means they are missing out on sound advice, which could enable their research question or idea to become an investigation.