Case 1 Overlap of research and clinical practice

A pharmacogenomics research team is conducting studies looking at the genetics underlying immunologically driven adverse drug reactions in gastroenterology. In one of their studies they have identified genetic variants associated with an increased risk of thiopurine induced pancreatitis. This risk is estimated at 10% if patients/participants have one copy of the risk variant, 18% if patients/participants have 2 copies of the risk variant.

The thiopurine drugs (Azathioprine and Mercaptopurine) are the most commonly used immunosuppressive drugs used to treat patients with inflammatory bowel disease, taken by approximately 30% of patients. More effective (but less durable) alternative therapies are available but they are at least 10 times more expensive.

In the Research Ethics protocol for these studies the team was asked by the NHS Research Ethics Committee to include:

> *Individual data will not be made available to participants or their doctors unless the results could potentially impact on the individual's clinical care. Results would then be shared with the participant and their GP/consultant. This decision would be made by the Chief and Principal Investigators.*

The team is unsure about whether, based on this finding, they should/are obliged to inform patients/participants to avoid this drug. On one hand, they feel that the results might potentially improve treatment and quality of life for some patients/participants. On the other they feel it might be premature to share this information; although they have published this finding, the results have not been replicated by other groups and the clinical utility and cost-effectiveness has not been explored. This dilemma is intensified by the fact that the research team is also involved in the clinical management of patients/participants.

Case 2 Change of technology

Genetic research projects, like other types of studies, often last for several years. Genetic technology and analytical methods are evolving very quickly and it is not unusual for research teams to exploit these novel technologies as they emerge during the course of the project. For example a project conceived in 2010 may have originally planned to use Genome Wide Association (GWA) technology, genotyping 300,000 SNPs (single nucleotide polymorphisms) in affected individuals and controls. Since the start of the project the costs of sequencing have fallen dramatically and the investigators decide to utilise exome sequencing – a more comprehensive technique that provides additional information on rare, as well as common, variants identified by GWA. Exome sequencing generates a vast amount of incidental genetic information some of which might be clinically actionable (for example factor V leiden variants associated with an increased risk of venous thrombosis or BRCA1 variants associated with breast cancer).

Often research teams do not update participants/patients about changes of technology used in a study. Should research participants be updated? If so, how? Should participants/patients be updated in relation to *any* change of technology, or in specific circumstances e.g., when the change may have ‘significant’ implications as in the example above?

Case 3 Freedom of Information request

A patient is recruited to a research project which aims to develop a genetic risk score for predicting the likelihood of developing type II diabetes. The project includes healthy and affected patients. The research staff are blinded. They consent the patients, take a blood sample and a fat biopsy.

The Principle Investigator, who is not a clinician, receives a Freedom of Information (FOI) request from a recruited patient, a health conscious anxious young man with a family history of Type II diabetes. The patient demands all their data and wants to know if they are going to develop diabetes.

This would mean unblinding the study. The PI discusses the request with a consultant in the team and it is decided that the consultant would send the genotype risk score to the participant.