

P³G Meeting Luxembourg September 2009

Session Summaries, Related Discussions and International Working Group Meeting Reports

- A. Session Summaries for Day 1 Challenges in life Course Projects Integration across the Life course Using Population-base Biobank and Cohort Studies
 - Sub-topic 1** Epidemiological and Public Health Challenges: Including pregnancy/newborns children and minors in population-based studies
 - Sub-topic 2** Epidemiological and Public Health Challenges: Including pregnancy/newborns children and minors in population-based studies
 - Sub-topic 3** Ethical and Public Health Challenges: Elderly participants in population-based studies
 - Sub-topic 4** Epidemiological and Public Health Challenges: Elderly participants in population-based studies
 - B. Topic 5 Summary: Evidenced-based Standards for Pre-analytical Processes
 - C. International Working Group Meeting Reports
-

A. Session Summaries

Regarding Subtopic 1, there was an animated exchange on the involvement of children in research with discussion about the paper "Children and Population Banks" (Gurwitz, Fortier, Lunshof and Knoppers, Science Vol. 325, August 2009). Agreement that children are not just 'small adults' and that they need special protections but this should not be a basis for excluding them from research. We did not come to any firm conclusions but accepted that this needs further discussion.

Sub-topics 3 and 4 were merged in response to comments from participants in sub-topics 1 and 2. The focus of discussion moved toward ethical issues. A representative from the European Commission asked if studies had ever been conducted (in Canada or Europe) on the concept that free access to information serves the public good as opposed to a necessary protection of individual rights when it comes to rare diseases.

Patricia Kosseim of Genome Canada noted that the concept of the circle of care has not yet been extended to include research saying there is a blurring of the line between research and care, and the increasing demand for evidence-based medicine may shift the balance on this issue.

Jane Kaye commented that governance systems around research are not as robust as those around care and that there is a need for these systems to engage participants and patients, and for the development of sustainable partnerships. She noted that ethics committees are struggling with the application of ethical principles that had been established in an old context vs. the newer context that includes global data-sharing, etc.



It was suggested that the issue also needs to be addressed at a systems level, i.e., working through the social contract of equitable access to health for all, and having sustainable publicly-funded health care systems would require recognition that it could be in the public interest to access data without going back to individuals. It was also noted that one consent form at the beginning of a study does not reflect autonomy or dignity; IT mechanisms need to be included in governance arrangements. Patricia Kosseim and Rex Chisholm both emphasized that autonomy should give people the right to participate.

The current focus on protection of privacy resulted in a lack of investigation of vulnerable populations. It was noted that at the time of drafting the Declaration of Helsinki, the main concern was potential for physical harm. The principles of the Declaration have since been applied to potential informational harm, which had not been a consideration at that time. This declaration is still a major reference for ELSI committees and needs to be addressed. Generally speaking, there is a lack of a formal lay-out of responsibilities in these committees, but obligations of REBs are established legally in Alberta and Ontario.

Questions of incentives to research participants came up and were discussed.

B. Topic 5 Summary: Evidenced-based Standards for Pre-analytical Processes

Recent developments in technologies for genotyping and screening of biomarkers will inevitably have an effect on biobanks to establish efficient sample handling and standardized distribution processes.

Presentations were made on new methods for genome sequencing and storage of nucleic acids such as DNA and RNA in ambient temperature. The data looks promising and it is obvious that these new technologies will impact on biobank infrastructure development.

The cost for complete genome sequencing that was more than \$10,000 USD per sample last year now costs less than \$5,000 USD and we anticipate a continued drop in costs and a dramatic increase in capacity. One advantage with these new genotyping methods is that the required amount of DNA has decreased and for some methods it will be enough to send just a few cells that can be amplified. This enables biobanks to replace the protocol from relatively large volumes of 10 ml blood and extract from less than 1ml. By using lower blood volume, the extraction can easily be scaled up with a through-put capacity of 500 up to 1000 samples per day. This will not only lower costs for DNA extraction but will also have a significant impact on storage costs.

New technologies/methods will be highly dependent on cost and sample quality in order to be successful and accepted by the end users. Other critical issues will be whether a method for DNA/RNA extraction can be scaled up with high efficiency, reproducibility and ensure the long term sample integrity after repeated reconstitution, as well as be compatible for high throughput downstream applications.



C. International Working Group Meeting Summaries

IWG1 – Social, Environmental and Biochemical Investigations

(Gunnel Tybring, Karolinska Institutet Biobank)

The discussion was focused on definitions about DNA quality and trying to get a consensus view among the participants about best practices for QC tests. It is also obvious that with the numerous different sample types there is a need to distinguish between tissue biobanks and liquid biobanks and provide sample specific recommendations.

The recently published P³G-supported observational study on the estimation of DNA concentration in 13 laboratories (ref: BMC Research Notes 2009, 2:2089), clearly indicates the need for further standardization in QC measurements. But it was also stated that recommended methods should be based on better knowledge about major sources of variation between labs. A second observational study lead by Dr Martin Yuille, head of the UK DNA Biobank Network that includes more than 100 labs will start shortly.

The general opinion was that picogreen in combination with 260/280 UV ratio was the most accurate methods for DNA quantification and DNA purity, respectively. These two methods are good enough for samples collected and with good control and processed in labs with a quality system in place.

Alternative methods that can be useful for evaluating DNA quality with respect to DNA integrity in combination with the above mentioned methods are agarose gel and electrophoreses. Long PCR is also worth mentioning for its sensitivity to detect oxidation and hydrolysis which reflect suboptimal sample handling.

One idea raised was the use of mitochondrial DNA. Since the sequence is highly repetitive, the method provides a simple and cheap surrogate for quality measurement using very low amounts of DNA.

Conclusion: The IWG 1 group will continue its effort to document the usefulness of DNA extracted from different sample types and also coordinate this with the work done so far within ISBER.

IWG2 – Information Curation and Information Technology

(Samuli Ripatti, V LifeGene)

Target 1: How to Support the Development of Emerging Biobanks

1. Identify the principal needs of the biobanks and/or the questions that are frequently asked by the investigators/funders?
 - data collection & management
 - data sharing
 - privacy and access control management



Obtaining basic guidelines and information on IT tools and solutions which are currently available to emerging biobanks would be useful. This could be provided as “frequently asked questions” page.

2. Identify tools that could be developed or actions that should taken to support them

Not so much “which tools are out there”, rather what are the most urgent issues about the tools that have to be addressed. For instance: overall integrity, i.e., compatibility and interoperability between different solutions.

Optimization of operational and funding mode that would allow for sustainable and reliable service based on open source software (e.g., OBIBA) has to be taken into consideration alongside with the above mentioned question. For instance, Paul White’s system is currently hosting 60 studies by customizing the underlying open source package and providing infrastructure for those data centres which would have had to develop their own in-house solution otherwise.

Gen2Phen database is operating on the same infrastructural principles

The same idea is behind caBIG infrastructure.

Tools for data harmonization at the moment of sample collection are essential.

3. Development of which sorts of tools and/or actions should be given the highest priority?

There was an overall feeling that additional effort should be made to enhance the exchange about software and services available to support the IT infrastructural needs of emerging biobanks. This could be started as an FAQ and extended into a discussion forum, perhaps together with Gen2Phen. It was agreed that a draft for a P³G Core on a biobank IT knowledge centre would be drafted. As part of the Core activity, Philippe Laflamme volunteered to assemble the initial content and a prototype based on their experience in OBIBA (e.g., wiki page, forum, etc), so that IWG2 could revise and decide how to sustain this exchange and communication over the longer term.

Target 2: Support the Realization of New Science and New Scientific Discoveries Based on Biobanks

1. What are the current challenges and opportunities in bringing biobanks together to promote pooled, scientific analysis of data and generating new scientific discoveries?

IT services and infrastructures for the support of data collection and fundamental research have distinctive differences in how their performance is assessed. The former has to be reliable, sustainable and facilitate maximal data consistency and minimal redundancy during the collection process. The latter is expected to be flexible towards the various data access needs of a researcher. Perhaps P³G should focus on bringing the data collection services to the production level of performance in order to serve the operational needs of biobanks rather than diversified needs of basic researchers.

2. Please identify REAL examples of pooling projects that would be of interest to scientists and funders alike, and which could be considered as potential submissions for competitive grant applications?

A project bringing together individual level high-density genomic data (genotyping or sequencing) from various data centres in Europe would be a useful and novel IT case study.



IWG3 – Ethics, Governance and Public Engagement

(Alistair Kent, Genetic Interest Group)

Building and Operating an Ethically Robust Biobank - Issues and Suggestions from the P³G Working Group on Ethics, Governance and Public Engagement

[An expanded version of this report will be published later this year]

“FAQs” (in no particular order)

1. How can biobanks secure funding to maximise their potential for delivery of tangible health gains?

Future funding can be supported by present experience but, in the foreseeable economic climate for public sector resources, biobanks will need to be innovative in demonstrating scientific and clinical gain in cost effective ways.

2. Personalised genomics - will it deliver?

The expectations around a personalised healthcare agenda (PHC) are enormous. Biobanks will have an important role to play in either validating or rebutting the claims of some of the Direct to Consumer companies, but have an opportunity to provide a trustworthy source of valid, independent advice to consumers and patients about the validity of the test batteries on offer. Independence from commercial pressures ought to provide a buffer for public trust and confidence, and we endorse citizen acceptance of high quality biomedical research translated into practical medical advice in a timely and effective way.

3. How can clinicians cope with this new knowledge?

There are two issues (at least) to be addressed in this question. The first is the potential benefit for public health programmes through the development of initiatives to introduce screening programmes and preventative health promotion measures. These will require a parallel development of robust cost and clinical effectiveness tools and an investment in training and continuing professional development in order to ensure that community - facing medical and health professionals have the skills and knowledge to implement worthwhile measures, and that they are backed up by investment in infrastructure to allow this to happen in a timely and effective way.

The second issue is at the level of the individual clinical interaction between the doctor and patient. Interpretation of new knowledge resulting from biobank-driven research and development will call for the creation of novel structures to support clinicians that will allow them to consult databases, clinical networks and other resources in order to relate biological knowledge about risk and opportunity to the patient in front of them in a sensible and practical way. Progress on both of these will call for the development of translation mechanisms to support the timely transfer of validated new knowledge from the academic into the clinical practice setting. Systematic collection and dissemination of local good practice would help secure the spread of possibilities through the clinical and patient communities quickly and effectively.

4. How can we safeguard individuals when we cannot predict what the future may bring?

Given that the purpose of undertaking population or disease based genomic studies through the creation and operation of biobanks, the threat of misuse of data is perhaps less significant than the possibility of a failure to use data in either public health programmes or in individual clinical encounters. It would be interesting to conduct a systematic information gathering exercise to establish the extent to which new knowledge arising from biobank based research has already influenced medical policy and practice in different jurisdictions. If we are using what we know effectively this is likely to provide a boost to sustainability and a protection against abuse.

5. Are there practical measures we can take now to promote sustainability and uptake?

There are a number of tools which may facilitate tracking the impact of biobanks and help to promote interoperability in the exchange of data and/or samples. Biobanks all operate in the legal and ethical context of the state and the institutions which set them up. Nevertheless, they share commonalities across jurisdictions that could and should be made public in a standardised format that would allow potential collaborators to identify one another and move to agreeing a work programme quickly and easily.

Cross-sectoral boundaries also need to be examined to clarify those elements of (for example) public/private partnerships which pose real barriers to progress, and those which might be matters of perception rather than legislation.

It is also possible to learn from experience and expertise in other sectors. Electronic health records, banking and forensics all offer examples (both positive and negative) of ways in which systems have struggled to balance the potential gains to be had from data sharing with the protection of legitimate interest of individuals and groups under the law.

6. Can we all speak the same language?

The P³G Lexicon has made a valuable start in defining terminology and creating a common vocabulary, but it is a work in progress that needs and will benefit from constant scrutiny and updating. Accurate communication requires more than just a consistent use of words, but also a shared understanding of the assumptions and cultures behind the words. For example, when the Hap Map project asked communities how they wished to define themselves this was regarded as an expression of good practice and respect by some, and as a demonstration of a lack of expertise by others.

Perhaps there is a role for P³G to develop a systematic communication strategy that will allow for the exploration of these issues and the development of a shared understanding and common purpose.

7. Are all biobanks the same?

Clearly, not; circumstances alter cases and the limits and possibilities for research and development will be influenced by legal and cultural constraints and also by the original purpose for which the tissue and sample collection were established. Thus, the issues relating to disease-specific and population biobanks are different, and



the special measures that need to be put in place and enforced for the protection of vulnerable populations need to be articulated and enforced.

Conclusion

Re-inventing the wheel (and not always coming up with a circular object rotating around an axle) is a constant temptation. The role of P³G as a response and as a route to the dissemination of good and interesting practice can and should promote effective use of hard won knowledge and expertise. However this is a dynamic process and will require continued investment in development and evaluation of models developed in the constitutional biobank members of the P³G Consortium. This will add value to the scientific and technical component of the Consortium, and help contribute to sustainable investment in public sector biobanks worldwide with the consequent opportunity to address unmet medical needs inaccessible by other means.

IWG4 – Epidemiology and Biostatistics

(Julian Little, University of Ottawa)

We briefly reviewed progress of calibration core (for the benefit of those who could not be present for topic 6). In the light of the discussion of the Steering Group the previous day, it was noted that there was now an opportunity for smaller studies with intensive phenotyping to participate in P³G and these could be especially relevant to calibration. As a possible example, Karine Sargsyan (meduni-adjgraz.at) spoke about the Graz baby study on determinants of body composition).

The group discussed the Obesity DataSHaPER and reiterated the need for specific workshop that would cover methodological issues and specific projects. Paul Burton mentioned that this could be linked with a meeting of the Wellcome Trust Obesity initiative which he chairs. We also noted the involvement of the European Multiple Morbidity project (led from Groningen).

Parminder brought up that disability in the elderly is a big issue in international comparisons. As there is also longstanding interest in DataSHaPER concepts for newborn and physical/biological/social environment, thinking to future, we have to think of ways of keeping workload of group working with Isabel reasonable. Important to work with revitalization of HuGENet network of networks.