Use of biobanks in register-based research

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What is a biobank?

- A collection of samples that will be stored for more than two months.

- Can be collected within the healthcare system or for research purposes.

- All samples collected for research purposes are regarded as biobank samples.

- Includes all kind of samples collected from human (including foetuses).

- Samples should be possible to link to an individual (if anonymous they are not comprised by the biobank law).
Different samples in biobanks

- Blood – Serum, plasma, buffy coat, clotted blood
- Extracted DNA
- Fresh frozen tissue
- PAP smears/Liquid Based Cytology
- Formalin Fixed Paraffin Embedded tissue
Examples of biobanks

*Healthcare/Clinical*
- Microbiology
- Pathology
- Cytology

*Research*
- For a specific disease
- For a specific exposure etc.
What is stored in a healthcare biobank?

• Samples collected within the healthcare system
  Pathology
  Microbiology
  Cytology
• Are often population-based
• Minimal amount of data connected to the sample identifier, gender, date of birth, date of sampling
• Consent from donors
Why store samples within health-care?

• Diagnostic needs to compare new samples with pervious samples from the same person.
  - Response to treatment in cancer
  - New tumour in patient with previous cancer?
  - Serological diagnosis of infectious diseases: present or past infection?

• Enables request for additional diagnostic analyses.

• Choice of treatment.
  - Cancer treatment may depend on availability of original tumour.
  - Antiviral treatment may depend on virus kinetics of serial samples.
Why store samples within health-care…

• If doubt about accuracy repeat analysis should be possible.  
  - Legal safety for both patient and laboratory.

• Quality control.

• Clinical development.  
  - New diagnostic tests should perform as well as old ones.

• Infectious disease protection.  
  - Location of source of dangerous epidemics: serial samples, comparison of stored samples from different parts of the country.

• Education.
Why *not* biobanking?

- Risk for violation of personal integrity
  (formal 3rd party code-keeping, secure databases)
- Costly, logistic difficult, too much time for follow-up
  (ensure access and quality of existing biobanks with long
  follow-up instead of starting from scratch)
- Accessory information inadequate
  (assess information, obtain information by registry linkages)
- Unreliable case ascertainment
  (don’t do biobanking in countries without comprehensive health
  registries)
Using health care samples for research

• Research was not the main reason when the samples were stored.
• Already existing biobanks open new possibilities for register-based research.

• Unique personal identification number (PIN) allow nationwide tracking of individuals.
  - Multigeneration registry
  - Population registry
  - Cancer registry
  - Patient registry
  - Medical Birth registry
  - Censuses
• The official website for the National Biobank council.
• Website with information about Swedish biobanks.
• Divided into six different regional centres.

• Swedish Biobank Register (SBR)
  A common register for the Swedish county councils with all samples collected within the Swedish healthcare.
Region Skånes biobank – A recourse for life
• Region Skånes Biobank is located at Medicon Village in Lund since March 1st 2012.

• New premises and new equipment facilitates efficiency and security of the activities within Region Skånes biobank.

• Today about 6,6 million biobank samples are stored within Region Skånes biobank.
Follow the sample from donor to biobank

Let's start at clinical chemistry

Documentation is important for tractability of the samples
The samples are frozen at -80³C at clinical chemistry…

… and packed on dry ice for transport to the biobank

The temperature is monitored during transport
The biobank unpack the samples and sort them...
...in temperature monitored freezers
Research Biobanks

• Samples collected and stored with the purpose to perform research.
• Donors often invited based on selection for a specific disease or research purpose.
• A lot of information connected to the samples (questionnaires, measurements)
• Have informed consent from all donors.
• Disadvantages:
  Often low attendance rate
  Small biobanks
Problems with biobanking

- Establishment cost is substantial
- Exact study not known in advance.
  - Collection of accessory information difficult.
  - Optimisation of sample handling and storage is difficult.
- Ethical and legal issues are complex…
Why do we use biobank samples for research?

• Large sample collections within reasonable time
• Virtually complete follow-up of the individuals (register linkages)
• Reliability (avoiding selection bias and reverse causality)
• Efficiency
• Previous exposures
• A biological sample will not lie to you on purpose…
What to think about when using biobank samples in research

• What would I like to analyse?
• How have the samples been collected?
• How have the samples been treated?
• A limited rescore.....
How to get access to the samples?

• Ethical approval

• Consent from the samples donors
  Opt in/Opt out

• Apply for samples at the biobank…
Opt-in

• Individual informed consent
• Typically:
  - If the analysis results will be released to the subject.
  - If the analysis is highly sensitive.

• The informed consent process can cause harm (anxiety, loss of anonymity, resource loss).
Opt-out – right to say ”no”

• Typically:
  - Now the most common decision by Ethical Committees for biobank-based studies.

• Public announcement of a scientific study (typically newspaper advertisements + press conferences) with information on how to say ”no” to the study

• Registry over persons saying no to stored samples or research

• Typically, a ”no” is so rare that selection biases can not be a problem: In a series of biobank-based studies of infections and genetic risk factors for cervical cancers, only occasional subjects report that their samples may not be used, despite extensive press coverage.
No consent

• Typically:
  - Studies on quality assurance
  - Obviously harmless study
  - Completely anonymised study
Opt Out rather than Opt in

• If the study is very large, such that it would be impossible to perform the study by opt-in.

• If the samples are very old, such that it would be difficult to track the individuals.

• If the research being done is similar to the reason why the samples were taken.

• If the tracking of the individual (or his relatives if he is deceased) is likely to cause substantial harm.

• If the code will remain unbroken for ever, particularly if the results are not of importance for the health of the individual.

• If the health benefits clearly outweigh the violation of the autonomy principle and the code-keeping is done in a secure fashion.
Ethical guidelines

- Edinburgh version of the Helsinki declaration mandates informed consent also for data and biospecimen research.

- CIOMS (Council for International Organizations of Medical Sciences), Article 4: Informed consent not necessary if minimal risk and important health problem.

- European Convention on Human Rights and Biomedicine §22: New use of biological sample must have "appropriate" consent.
  Comment 137: express consent is not always required for research on stored biological samples, as long as the option to opt out (withdraw) from the study is maintained.

- Swedish Research Council Ethics Committees Guidelines:
  A number of specific instances where informed consent is not required are listed.
Study design

- Cohort studies
- Case control studies
Different perspectives

- Case-Control studies
- Cohort studies

Time

Retrospective design
Prospective design

Right now
Prospective biobank studies

Case

Control

Sample
Sample

Tissue sample

Time

DIAGNOSIS
Biobank-based research steps

• Is the disease inherited?
  - Use Multigeneration registry (or twin registry) to locate subjects and/or genetic data

• Search for cases, controls and accessory information
  - Cancer registries, diagnostic registries: Cases
  - Biobank registries: Samples
  - Health and data registries: Information

• Retrieve and code samples

• Perform biochemical/genetic tests

• Statistical analysis

• Archiving of the samples for future research ("secondary biobank") or return to original biobank depending on agreement with biobank giving out samples.
BBMRI.eu / BBMRI.se / BBMRI Nordic

• National platforms for biobanking working together with Nordic and European platforms.

• Aims to optimising collection, storage and analysis of samples.

• Has created a sample collection register: www.bbmri.se
the Nordic Information for Action eScience Centre (NIASC)

- http://www.nordicehealth.se/
- Nordic collaboration funded by NordForsk.
- Aim to exploit already existing Nordic infrastructure to achieve increased health and to develop eSience tools.

(Nordic Biobank registry; tools for handling next-generation sequence data, producing Nordic standards for identification of incidental findings of genetic risk; generic eSience tools and resources for predictive models and micro-simulation; ICT for data collection, safety and communication)
ISBER Vision
To be the leading international forum for promoting consistent, high quality standards, ethical principles and innovation in biospecimen banking by uniting the global biobanking community.

ISBER Mission
ISBER creates opportunities for sharing ideas internationally and harmonizing approaches to evolving challenges in biobanking and repository operation. ISBER fosters collaborations, creates education and training opportunities, and provides an international showcase for state-of the art research findings and cutting edge technologies, products and services. Together, these activities promote best practices that cut across the broad range of repositories that ISBER serves.

ISBER Best practices for repositories.
Third edition published 2012 in Bioreservation and Biobanking.
TuBaFrost - The European Human Tumour Frozen Tissue Bank

www.tubafrost.org

OECI (Organisation of European Cancer Institutes) TuBaFrost is a virtual network of clinical based biobanks.

The samples stay at the local collector but is available for research. The decision to share or not is however made by the institute where the sample resides, preferably by a biobank committee.