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The Importance Of Biobanking To Support HPV-based Research

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Why biobank?

Given recent developments in cervical disease prevention and screening, cervical biobanks represent extremely valuable resource(s) to 1) support evaluation on the effectiveness of existing primary and secondary prevention strategies;[1] 2) offer opportunities to evaluate new applied technologies; 3) support "proof of concept" basic research. Notably, in a survey of key opinion leaders on priorities for HPV research and development in 2018, optimal biobanking was considered 6th out of 46 research "topics".[2] However, for biobanked material to be of optimal use, it must be annotated with longitudinal clinical information with the veracity of information checked regularly. If not, one of the fundamental attributes of the biobank (to ask research questions that require longitudinal data without having to wait), is lost.[3] Consequently, the set-up and maintenance of biobanks clearly requires sustained efforts with respect to physical infrastructures and, crucially, data-linkage.

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In the present work, we will use two examples of Cervical/HPV biobanks (The Scottish HPV Archive[4] and the Swedish Cervical Cytology Biobank (SCCB)[5,6]) to illustrate some of the successes and challenges therein.

Working examples of biobanks to support HPV research: structure and content

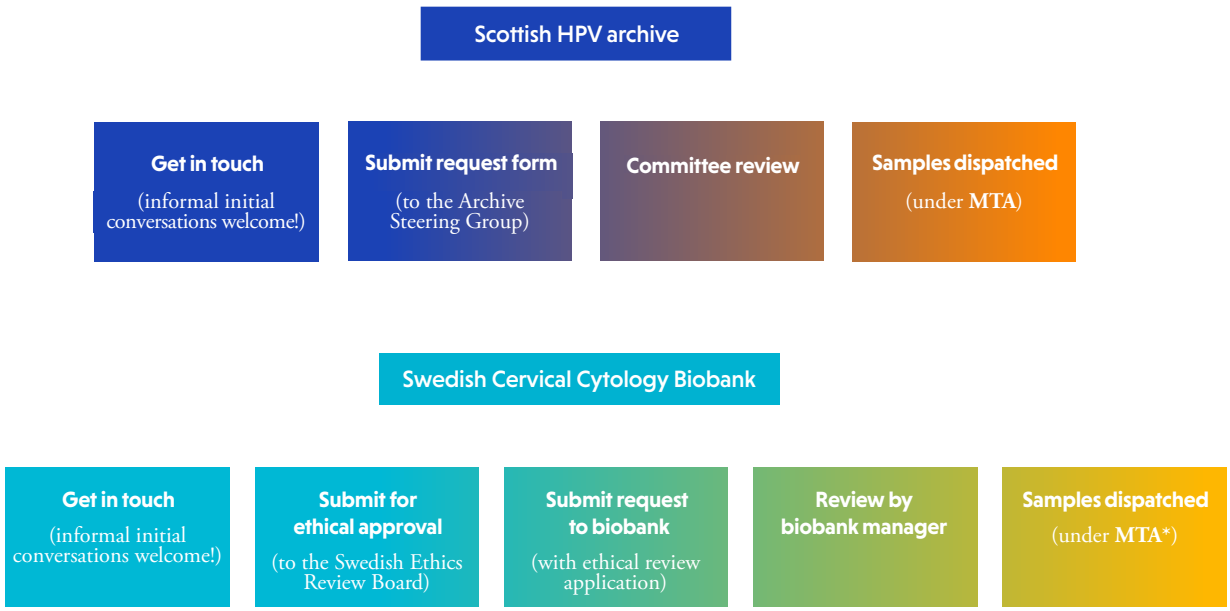
The nature and volume of stored biospecimens will depend on a number of factors including automation, capacity, what is routinely available and research priorities. For example, the Scottish HPV Archive is a "collection of collections" with samples derived from research, immunisation surveillance and screening contexts (~45,000 samples). It contains a variety of biospecimens (including non-cervical samples) and holds multiple aliquots at -25˚C and -80˚C. In Sweden, the SCCB biobank currently contains >700,000 unique residual samples from women attending for the cervical screening programme, stored prospectively in highly concentrated aliquots, all at -25˚C.

The overarching nature of research that biobanks support

The Scottish HPV Archive has governance in place to support HPV-associated research whereas the samples stored in the SCCB are associated with

Figure 1

Process to request samples from biobanks



*MTA=Material Transfer Agreement

permissions that allow HPV- and non-HPV-based research. Figure 1 shows the application process for potential users. Additionally, Figure 2 shows the type of projects that have been facilitated by the Scottish HPV Archive organised as themes. So far, the most common type of research has related to developing new technologies (i.e biomarkers to triage for cervical precancers).

Challenges in biobanking

1. Regulatory/governance

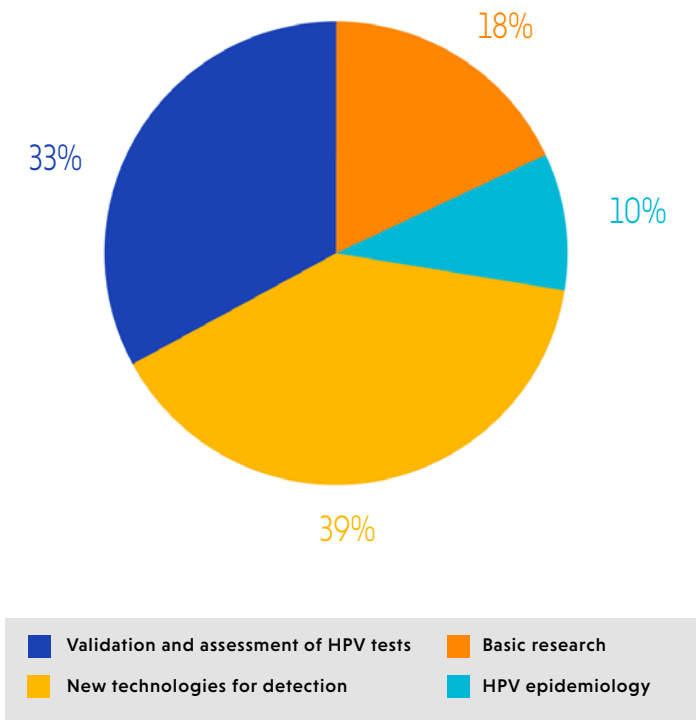
Clearly, governance considerations determine the type of research samples that can be used. Biobanks must be reactive to shifting and sometimes complex legislation, which together with differing interpretation of guidelines by the different authorities can create tensions and delays. Ljøsne et al[7] articulated elegantly the key legal, ethical, socio-political and financial challenges faced by biobanks (Table 1). While legislation will differ between countries, one advantage of developing international biobank networks is to create core principles to support both physical and regulatory aspects of biobanking, which may be used to inform discussions at a national level.

2. Sustainability and profile

Sustainability of a biobank is paramount. Public research funding for establishment can be helpful - the Scottish HPV Archive received core

Figure 2

Nature of requests for sample access received in the last 9 years at the Scottish HPV Archive



funding for 5 years through a government-funded grant and the SCCB obtained core-funding through the Swedish hub of The Biobanking and Molecular Resource Infrastructure (BBMRI.se). However, biobanks must endeavour to reduce costs and become self-sustainable. Strategies to achieve this include establishment of lean processes and tendered supplies to ensure cost-efficiency – this helps ensure biobanks can operate at a 100% cost-recovery when fully operational.

Moreover, raising profile is essential to interest potential users. Dissemination of positive outputs accomplished through biobank use not only increases awareness among researchers but can be used to engage the public. The request for specific feedback from biobank users helps inform these messages.

3. Technical (samples and information)

Maximising biospecimen quality is a key issue and optimising storage conditions to support this is clearly important. Capture of high quality nucleic acid (NA), particularly mRNA, can be challenging when starting with samples taken a priori for morphological assessment rather than molecular biology. Performing quality assessments that quantify stability of cells and derivatives (including NA) can allow expectations to be

Table 1

Examples of challenges and strategies for the biobank community. Adapted from Ljøsne et al.[7]

CHALLENGES	POTENTIAL SOLUTIONS
Legal challenges	
• Lack of appropriate biobank regulations • Varying interpretation of national regulations by national institutions • Varying requirements from oversight/governance bodies and fast-changing guidance	• Robust and reciprocal cooperation with national authorities for the development of appropriate biobank regulation • Development of biobank networks
Ethical challenges	
• Varying design, scope and interpretation of consent • Privacy and data protection	• Comprehensive consultation of expert and stakeholders groups to support the development of ethical, legal and socio-political guidelines • Development of IT-based solutions for privacy and data protection and for secured data sharing
Socio-political challenges	
• Lack of knowledge surrounding biobank research among general public and lack of public debate surrounding biobank research • Different views on how biobank resources should be used	• Procedures to share outcomes raised from biobank research • Organisation of public forums and meetings
Financial and educational challenges	
• Insufficient funding/incomplete sustainability plans • Lack of expertise among researchers and members of ethics committees regarding biobank research • Lack of tradition and incentive to encourage sharing of stored biobank resources	• Development of cost-recovery systems • Development of training courses for staff • Development of incentive tools
Technical challenges	
• Optimisation of biospecimen quality • Access to relevant samples from willing partners • Maintenance of a robust inventory system	• Share guidelines and standards for quality assessment procedures • Profile raising and engagement events

managed around what is achievable. For example, at the Scottish HPV Archive, longitudinal monitoring of DNA, RNA and protein is performed. Besides technical constraints, ensuring that the information associated with samples is accurate and complies with regulatory requirements is fundamental. Both internal and external audit(s) to support this should be performed. Checking that the biobank files can be linked is an essential quality criterion and this information needs to be ready at the time of initial discussions with researchers to determine study feasibility.

Given the natural history of cervical cancer which takes decades, biobanks, through having samples associated with longitudinal data, can provide answers in a timely and efficient way

Conclusion

Cervical biobanks represent a key resource for researchers. Given the natural history of cervical cancer which takes decades, biobanks, through having samples associated with longitudinal data, can provide answers in a timely and efficient way. International collaborations that lead to best practice for "dry" and "wet" aspects of biobanking will refine processes and also help raise profile with the public, regulatory and scientific community. Furthermore, continued engagement with the international HPV community through publications such as HPV World, provides opportunity for welcome feedback.

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