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REPORT ON RETURN-ON-INVESTMENT MODELS

Executive Summary

Despite significant advances in the biobanking field over the last decade, significant issues and limitations remain that are restricting the impact of translational research. The major issues include the need to increase the quality and standardization of biospecimens collected, to enhance accrual capacity in terms of scale and disease representation, and above all, to maintain public trust in these activities. Underlying these issues is the need to ensure sustainability of biobanks. In a first phase we investigated the funding streams of biobanks in Europe, results showed the limited scale, the fragmentation of streams as well as the non-systematic resources dedicated to biobanking.

It has been the expectations that biobanks should be able to conform to business plans of other research technology platforms and that sustainability could be achieved by cost recovery strategies for biological resources retrieval and processing. Thus in a second phase we investigated the real costs of samples and in Europe, which led us to develop a calculation tool for harmonizing the cost access to biological samples. Furthermore, our results show that that financial sustainability of biobanks is unlikely to be achieved solely with a cost-recovery policy.

Since the long-term sustainability of biobanks is a key issue in biomedical and translational research that has not been resolved yet, we examined return-on-investment models for biobanks in more details. Investigations for closely related deliverables 4.2 and 4.3 of the ADOPT BBMRI project, highlighted the fact that it is rare for biobanks to secure long-term funding. We found that most biobanks rely on short-term institutional

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ADOPT BBMRI-ERIC gateway for health

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1. Approaches (Methods)

1.1. Return of investment models

Despite substantial support from public funding bodies for biobanks and the development of multinational research infrastructures, concerns remain about their long-term financial sustainability. We therefore reviewed the current state of the sustainability of health-related biobanks and the means whereby they can achieve sustainability for the long term.

We collected data through a literature review (June-July 2016) and a questionnaire part of the Pan-European Biobanking and BioMolecular Resources Infrastructure (BBMRI) preparatory phase sent to 23 centers in France and 22 centers in the Netherlands.

We identified several streams that may contribute to the funding of biobanks: (i) cost recovery strategies related to sample handling and access, (ii) commercialization of research results or derived products, (iii) funding from private for-profit entities such as biotech companies or pharmaceutical corporations, (iv) funding through governmental institutions and agencies.

2. Results and discussion

2.1 Cost recovery strategies related to sample handling and access

Most of the biobanks analyzed in our review asked users to cover sample handling and shipping, however it is self-evident that long-term financial sustainability requires more than just covering these marginal costs. One main reason is that fees charged by biobanks do not cover the real marginal costs for handling samples, let alone the average costs needed to maintain supply. While only an aliquot or section of a sample may be requested by a user, the probability of that same sample being requested again in the same financial period is probably very low. Therefore, total cost recovery cannot reliably allow for such repeat requests and would require recovery of all annual costs of accrual, processing, storage, handling, transaction and depreciation. The fact that the real total costs of accruing, processing and managing samples is high means that if a biobank seeks to implement a policy to recoup all those costs by charging users, it is highly unlikely to be successful and user resistance is likely (see also deliverable D4.2).

One cost-reduction strategy for biobanks is to avoid redundancy by sharing samples and associated data, and to reduce health care costs, especially in the context of personalized medicine. Biomarkers are currently used to predict survival of patients, assess drug safety and evaluate the immediate consequence on biological processes, identify patients who are more likely to benefit from a treatment, predict outcome given the response to therapy, and monitor disease progression or therapeutic efficacy. By reducing administration of treatments that do not provide benefit to patients, personalized medicine is likely to contribute to the reduction of health care costs. Implementation of

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these biomarkers in the clinic however relies on the prior use of a large number of biological samples and associated clinical data from biobanks during their discovery and validation phases. An appropriate quality of samples is a major requirement to achieve this aim. It has been reported that about 30% of non-reproducible results are related to an inappropriate quality of samples and products, which is responsible for approximately 9 billion € ($8 billion) per year of unnecessary expenditure in the USA alone. A funded national/international strategy aiming to deliver robust diagnosis and reproducible results by the use of an appropriate quality of samples, would prove more economically efficient than a cost recovery strategy aiming to sustain a biobank.

2.2 Commercialization of research results or derived products

The question about whether publicly funded biobanks should claim any ownership of intellectual property rights (IPRs) that are developed by third parties as a result of their access to biobank data and samples has been a topic of debate in recent years. Aside from the legal and theoretical aspects of this question, claiming IPRs requires that the biobank is not only a supplier of biological resources but participates in downstream research and development activity. In addition, despite their ability to generate returns, patents do not necessarily generate predictable revenues, with both the precise moment and amount of returns difficult to anticipate. As a consequence, it may be challenging to rely on them as a source of stable income that supports the long-term sustainability of a biobank.

2.3 Funding from private entities

Funding from private for-profit entities has raised several ethical and societal issues. Several studies and surveys have demonstrated that public trust diminished markedly if industry had funded research projects in public institutes. Reasons cited by individuals included fear over samples or data being used in ways they find morally problematic; loss of control over samples/genetic data and parties they are shared with; limited access to health benefits derived from private or proprietary research and the extent to which this research was being done for the public good. Therefore, the involvement of commercial entities in public biobanking activities may affect patients' willingness to take part and consent to research and the degree of public trust, as well as create conflicts of interest that then negatively affect the financial sustainability of biobanks.

2.4 Funding from governmental institutions and agencies

Biobanking is currently not capable of covering costs through charges at the point of use and therefore needs to be subsidized with governmental and institutional funds. The broad case rests on the widely accepted rationale for government funding of biomedical research and need not be repeated here. If the majority of use comes from the public sector then the practical issue lies in identifying the most

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effective means of allocating the resource, firstly to biobanking as a whole and secondly to users of biobanks.

Allocation of public resources within biomedical research is not a true market and hence any perceived underfunding of biobanking lies in the failures of the funding system to allocate resources effectively rather than in the costing system. This failure is most likely to reside in the structure of project-based funding systems in which biobanking is always a subsidiary input to a proposal. There have been several arguments in the field of research equipment showing how in the absence of complementary institutional funding, generic infrastructure (defined as that not justified by a single project) can be the victim of "hollowing-out".

Assuming the need for subsidy, there are several possibilities for its delivery. One would be to create a quasi-market by encouraging grant-holders to budget properly for acquisition of samples and for a fee-based system to be put in place. There are several arguments against this, including the likely high transaction costs and the difficulty of effecting a transition to this model when multiple funders operate in a system. At the other end of the spectrum is complete subsidy – a consortium of public funders meeting all costs and allocating services by means of a peer review process. This is analogous for example to the allocation of beam time at a synchrotron. The issues here would include selection of which biobanks should benefit from subsidy, the nature of contract to be awarded to the biobank and how efficient the allocation process would be for small-to-medium-sized biobanks. The analogous physical science infrastructures operate at large scale, indeed that is their raison d'être.

Ensuring a balance between supply and demand could also be a challenge. On the one hand, samples if seen as a 'free good', may be over-used while on the other hand biobanks may find it difficult to predict what capacity and capabilities they should have to meet demand. There is also a risk that inefficient structures would persist without an incentive to consolidate and scale-up. Greater efficiency due to consolidation and scaling-up cannot only reduce unit costs but may also accelerate the development of biobanking from its beginnings in research to its applications in improved health care. These considerations underlie the UK's NIHR National Biosample Centre initiative which will test whether this particular approach is sufficiently flexible to deal with the fast-changing and fragmented landscape of health research and public involvement.

A mixed model would appear to be the best compromise but departing from the present situation by ensuring that core costs are fully covered by relevant funders. Commercial rates (i.e. full costs plus a contribution toward sustaining the infrastructure) could and should be applied to commercial users and indeed would violate EU State Aid provisions if they were not.

Provision of existing subsidies can markedly vary, depending on issues faced by funding bodies and the difficulty in securing highly competitive research grants. Cuts in research programs budgets or reorganization of health care systems following economic policies and crises can additionally endanger the sustainability of biobanks. In this respect, science generally has been experiencing a shift from

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Mertonian functionalism to agency-based frameworks that focus on performative processes. This has occurred during a phase when political ideologies shifted from social corporate liberalism to neoliberalism. In other words, it was argued that the biobanking community must accept market-driven priorities such as profit, patents/licenses, sustainability and the favoring of translational research aiming at bringing products and therapies quickly to market.

Biobanks can however hardly fit this scheme since they do not generate profits. They will therefore not become sustainable without public support or self-sustaining without acquiring new roles. One such new role is their becoming embedded in health care systems that use longitudinal samples from individuals as part of their personal care. The BBMRI-ERIC Work Plan has identified this role, recognizing biobanking as not only supporting basic biomedical research but also acting as a service infrastructure. This opens up new potential lines of support but also brings into the frame the particular means of costing, pricing and charging within different healthcare systems. It might be particularly problematic in systems where a patient moves between providers (whether by choice or by virtue of re-location) and where those providers do not have common access arrangements to historical samples and associated data. Similar arrangements to those being contemplated for health data need to be considered in these circumstances to ensure portability and compatibility while preserving privacy and respecting consent. Another new approach to biobanking sustainability has arisen in the context of establishing a global approach to the problem of anti-microbial resistance (AMR). Here a global funding mechanism has been proposed. The research required to tackle AMR requires global biobanking with global standards and this infrastructure will be required as long as AMR remains a health problem for humans and animals.

Health care cost reductions will therefore only be attained if biobanks are supported by long term investment and commitment from public and governmental funding sources, as well as support from industrial users.

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3. Impact

The above studies clearly describe the funding streams of biobanks in Europe and provide a solid analysis of several retun of investment models. It shoul be disseminated aand discussed in a meeting regrouping actors from the field, economists and representatives of appropriate ministries and EU commission services. It should lead to an analysis of the socio-economic impact of the infrastructure which includes among other cost reduction, avoidance of redundancy and an increase in the reliability of diagnosis and biomedical research.

4. Dissemination of project results

4.1 Peer-reviewed scientific publications

- Clément B, Yuille M, Zatloukal K, Wichmann HE, Anton G, Parodi B, Kozera L, Bréchot C, Hofman P, Dagher G, EU-US Expert Group on cost recovery in biobanks. Public biobanks: calculation and recovery of costs (2014). Science Translational Medicine, 6(261):261fs45
  DOI: 10.1126/scitranslmed.3010444

- Doucet M, Yuille M, Georghiou L, Dagher G. Biobank sustainability: current status and future prospects (2017). Journal of Biorepository Science for Applied Medicine, 5:1-7.
  DOI: https://doi.org/10.2147/BSAM.S100899 (open access)

4.2 An online calculator to harmonize cost access

To facilitate the dissemination of the endeavor to harmonize cost access, an online calculator was built to estimate the real costs of tumors and help harmonizing costs for accessing samples. This was done in close collaboration with the FP7 funded project BBMRI-LPC.
https://epi.helmholtz-muenchen.de/tools/calc/

4.3 Lectures

Results were disseminated by lectures given at several meetings in Europe and China.

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