Sustainable Biobanking

The Financial Dimension

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Management summary

Supporting researchers in sustainable biobanking

Sustainable Biobanking: The Financial Dimension provides an overview of sustainable biobanking from a business perspective. We chose to focus on the financial dimension as it is considered the most challenging and is currently insufficiently addressed within the Dutch biobanking community. By providing background knowledge, insights, examples, inspiration, and practical advice we aim to support individual biobanks, biobanking professionals, and researchers in their quest for a sustainable academic biobank.

Sustainable Biobanking: The Financial Dimension is part of a BBMRI.nl series on the financial dimension of sustainable biobanking. The series also includes a set of recommendations for sustainable biobanking, a case study analysis on good practices, and a collection of useful business tools, all with the goal to help individual biobanks improve their sustainability.

Sustainability is a balancing act

Sustainability is the capacity of a biobank to remain operative, effective, and competitive over its expected lifetime. Being sustainable involves balancing a biobank's financial, social, and operational dimensions, with the overarching aim to create value. Even though biobanks are often considered a critical resource for translational biomedical research and improved health care, many experience sustainability as a major challenge. And despite increased interest in the topic, including on a policy and funder level, shared solutions or effective strategies for sustainability are still unavailable.

Adopt a business perspective

To improve their sustainability we recommend that biobanks learn from the business world; without losing sight of their not-for-profit identity. Businesses are experts in serving their stakeholders, creating value, and translating this value into resources. To aim for sustained success, biobanks should adopt a clear business model – which describes how their organisation creates, captures, and delivers value for its stakeholders – and adapt their organisation accordingly. This report provides a list of twelve common and uncommon biobanking business models. Each biobank must decide carefully what business models are feasible within their own individual circumstances.

Analyse your stakeholders

The first step in creating a business model is knowing your stakeholders, as satisfaction of your key stakeholders is essential for long-term success. Biobanks should perform a stakeholder analysis to identify, segment, prioritise, and engage their stakeholders according to their motivations, needs, and level of influence. Interaction with your stakeholders, at an early stage, will minimise assumptions and will help discover what they value; allowing the biobank to adjust accordingly.

Know your value

The challenge lies in communicating the right value proposition towards the right stakeholder. A value proposition is an aggregation of benefits a biobank offers in exchange for a certain cost. The benefits often involve solving or preventing a problem or satisfying a need. Luckily, biobanks have many different forms of value to offer. Our Biobank Value Model lists the different types of value a biobank can possess and from which components this value is built.

Funding, revenues, and costs

To be sustainable, a biobank's value has to be translated into resources, mostly consisting of funding and revenues. The biobank and all stakeholders should be aware that a self-sustaining model is almost never achieved and often diversification of funding sources is necessary. However, developing new funding sources takes time and therefore biobanks should start as early as possible.

Commercialisation and public-private partnerships provide an opportunity for additional revenues, opening the door to a number of benefits but also potential issues. To ensure collaborations with private partners are possible a biobank should start a dialogue at an early stage, organise the biobank accordingly, and involve, when possible, an experienced intermediary.

The scarcity of available resources makes cost information essential. Understanding a biobank's costs allows for informed decision-making, the identification of potential cost-saving and efficiency measures, and forward planning. However, many biobanks are not fully aware of their true costs. Our report lists three web-based tools that help biobanks get a grip on their cost structure.

1. Background

1.1. Project context

Sustainable biobanking: The Financial Dimension is a product of Biobanking and BioMolecular resources Research Infrastructure The Netherlands (BBMRI.nl) work package 6: Sustainable and Interactive Biobanking. BBMRI.nl is an initiative of the eight Dutch university medical centres, other Dutch research centres and organisations, as well as the Parelsnoer Institute. In addition, it serves as the Dutch node of the European network of biobanks, united under BBMRI-ERIC.

It is BBMRI.nl's mission to maximize the use of biobanks for health research on the prevention, diagnosis, and treatment of diseases. To achieve its mission, BBMRI.nl provides access to samples, images, and data; tools for capturing, integrating, and analysing data; and support on ethical, legal and societal implications. BBMRI.nl is part of Health-RI, the overarching Dutch research infrastructure on personalized medicine and health.

1.2. A BBMRI.nl series on sustainable biobanking

Sustainable biobanking: The Financial Dimension is part of a BBMRI.nl series on the financial dimension of sustainable biobanking. In this series we provide background knowledge, good practices, business tools, and recommendations, all to help individual biobanks improve their sustainability. The series consists of:

1. Recommendations for Financial Sustainability
2. Sustainable Biobanking: The Financial Dimension
3. Good practices in Sustainable Biobanking: A Case Study Analysis
4. Business Tools for Biobanks

1.3. Definitions

There are many forms of **biobanks** and accompanying definitions. This report adheres to the BBMRI-ERIC definition: *Biobanks are collections, repositories and distribution centres of all types of human biological samples, such as blood, tissues, cells or DNA and/or related data such as associated clinical and research data, as well as biomolecular resources, including model- and microorganisms that might contribute to the understanding of the physiology and diseases of humans* (European Commission 2016). The report concentrates on biobanks containing human samples and data for scientific research. However, the content of this report is also useful for collections consisting exclusively of data (e.g. imaging collections, disease registries) or for non-human sample and data collections.

There are various definitions of **sustainability**, encompassing different criteria. As biobanks are research infrastructures, this report follows the Organisation for Economic Co-operation and Development definition of research infrastructure sustainability: *Sustainability is the capacity of a research infrastructure to remain operative, effective, and competitive over its expected lifetime* (OECD Global Science Forum 2017b).

1.4. Goal: support biobanks in their quest for sustainability

Our goal is to support individual biobanks, biobanking professionals, and researchers in their quest for a sustainable academic biobank. This report serves as a knowledge foundation, providing readers with information, insights, examples, inspiration, and practical advice on sustainable biobanking. The content is based on the currently available scientific and grey literature. For a description of methods see appendix 1.

1.5. Focus on the financial dimension, from a business perspective

Sustainable biobanking consists of an interplay between financial, social, and operational dimensions (Watson, Nussbeck et al. 2014)(see chapter 2). In this report we focus on the financial dimension, from a business perspective, as it is considered the most challenging and is currently insufficiently addressed within the Dutch biobanking community. Furthermore, there have been several recent overview publications by BBMRI.nl and other organisations addressing topics within, predominantly, the social[1] and operational[2] dimensions. We have chosen to adopt a business perspective, as we are convinced this approach will help academic biobanks to look differently towards their biobanking activities and provide an additional edge towards sustainability. However, we do not advocate that academic biobanks become businesses; biobanks should not lose sight of the fact that they are not-for-profit organisations operating in a complex scientific, ethical, and legal environment.

1.6. No one-size-fits-all solutions

Biobanks exist in many forms in terms of organisational setup, scale, focus, and circumstances. This makes classification difficult, if not impossible. Biobanks range from open access, multi-user biobanks to small single-user collections embedded in a research department. For the former, sustainability is a challenge, while for the latter it might be of secondary importance. The differences between biobanks make for a difficult discussion, as every party approaches sustainability from their own perspective. In addition, this variety also means that there are no one-size-fits-all solutions.

Most research on sustainable biobanking focuses on larger biobanks that cater to whole institutions. Smaller department niche collections, where the coordinator is also the main user, are currently overlooked. Still, the knowledge presented in this report and the advocated business and value mind-set can benefit all types of biobanks, large or small. In the end, biobanks should adapt this report's content to fit their own individual situation.

[1] Recent BBMRI.nl publications that focus more on the social aspects of sustainable biobanking are The donor as partner (Boeckhout, Reuzel et al. 2014) and Private individuals as collectors of their own data for biobank research (Eijdems, Boeckhout et al. 2018).

[2] Recent publications that focus more on the operational aspects of sustainable biobanking are ISBER Best Practices: Recommendations for Repositories (ISBER 2018) and NCI Best Practices for Biospecimen Resources (NCI 2016).

2. Sustainable biobanking

2.1. The challenge of sustainability

Biobanks are considered a critical resource for translational biomedical research and better preventive and personalised health care. However, their sustainability is a major challenge. This is of growing concern for individual organisations, policymakers, and funders, as they invest millions of euro's each year into the biobanking field. So far, the increased interest in sustainability has not led to shared solutions or effective strategies for biobanks to become sustainable.

Biobanks experience difficulties in becoming sustainable because they operate in a complex environment, more so than most other research infrastructures. Biobanks act at the interplay of ethical, scientific, and commercial values, balancing both societal and research expectations. In this multidisciplinary environment a biobank's sustainability is constantly challenged by multiple issues, ranging from technical, logistical, legal, and privacy-related issues, to a growing demand for quality, FAIRness[3], transparency, and accountability (Stephens, Dimond 2015, Timmons, Vezyridis 2017, Watson et al. 2014, Wilkinson et al. 2016).

Because of the diversity of the biobanking landscape, each individual biobank will face different challenges, experience different needs, and require different degrees of sustainability; depending on their organisational structure, scale, focus, and planned duration. Sustainability is of particular concern for biobanks that gather samples and data based on an open research question or general research direction, due to their open-ended setup.

Sustainability is all the more challenging because most biobanks operate on a timescale of 10 to 30 years. The collection of samples and data, and the subsequent scientific research, is a time-consuming process. In general, scientific publications already start to accumulate after the first few years. But there remains a considerable lag between a biobank's start and its potential output for the benefit of patients. Due to their timescale, biobanks need to acquire stakeholder[4] commitment and funding over a long time period. Especially funding is considered a major concern (Cadigan, Lassiter et al. 2013, van der Stijl, Scheerder et al. 2018, Rao, Vaught et al. 2019). Particularly the unpredictable and often short-term nature of the available funding makes long-term planning and sustainable exploitation difficult (Gee, Oliver et al. 2015).

2.2. A framework for sustainable biobanking

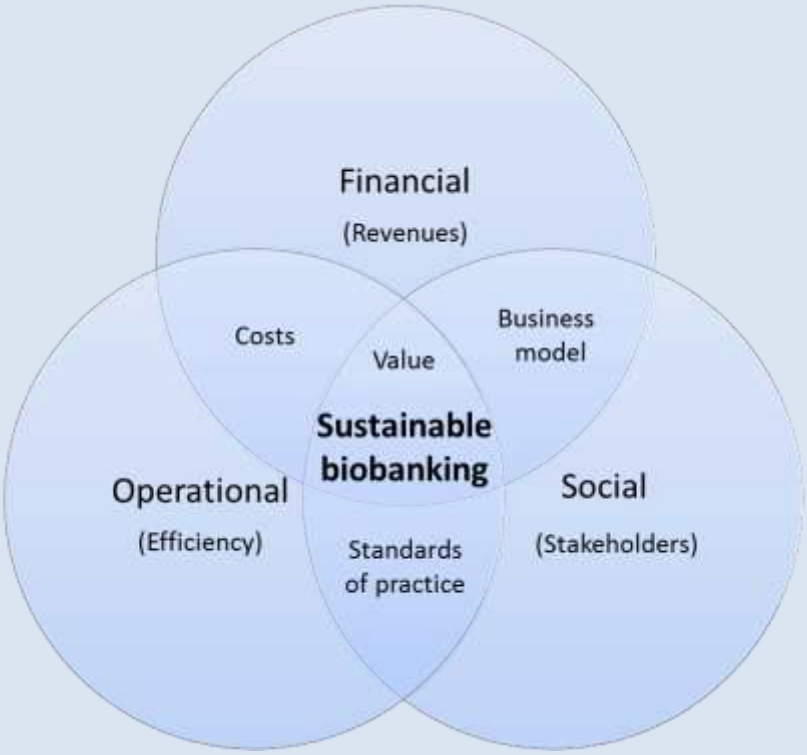
Sustainability is a broad concept and easily misinterpreted by different stakeholders. Being sustainable as a biobank depends on many intertwined aspects and, therefore, sustainability needs to be approached in a holistic manner. Watson et al. were able to define a framework that captures the different aspects of sustainable biobanking; bringing them together in three overlapping dimensions: operational, social, and financial (Watson et al. 2014)(see figure 1). Their framework offers a common understanding, streamlines the discussion, and provides clarity for all parties involved. This increased clarity should lead to more effective actions to improve sustainability.

The three-dimensional framework provides room for everything that influences a biobank's sustainability. Different subjects can be placed within one of the dimensions or at the intersection of multiple dimensions. The three dimensions overlap, and as such each dimension influences the processes and activities in the other dimensions. To become and remain sustainable, biobanks need to continuously balance these three dimensions in the context of their own individual situation.

[3] FAIR stands for Findable, Accessible, Interoperable, and Reusable. For more information see: https://www.dtls.nl/fair-data/fair-principles-explained/ (Wilkinson, Dumontier et al. 2016).

[4] Stakeholders are individuals, groups, or organisations that are affected by or can affect a particular action undertaken by others (Bjugn, Casati 2012).

Figure 1. A framework for sustainable biobanking



The framework for sustainable biobanking consists of the overlapping financial, operational, and social dimensions. Specific issues are located where dimensions overlap. To become sustainable, biobanks need to balance these three dimensions in the context of their own individual situation. Figure adjusted from (Watson et al. 2014).

The operational dimension

The operational dimension involves all aspects related to a biobank's input, internal, or output processes. In other words, it involves the collection, processing, and release of samples and data; the biobanks' organisational and approval structures; access policies; risk and quality management; and standard operating procedures. Optimizing these processes and making them more efficient will contribute to a biobank's sustainability.

The social dimension

The social dimension relates to the interaction and relationship a biobank has with different stakeholders (see 3.2 for an overview of different stakeholder groups). Examples are the contact a biobank has with its funders, donors, and users, the acceptability of biobanking to the general public, and the setting of standards of practice within the biobanking community. The social dimension involves all the ethical, legal, and societal issues that surround biobanking (Tarling, Lasser et al. 2017). Failing in the social dimension can lead to a loss of support by different key stakeholder groups, which is detrimental to the sustainability of an individual biobank and possibly the biobanking field is a whole.

The financial dimension

The financial dimension is concerned with a biobanks' available resources and how these resources are generated and used. Aspects that are part of the financial dimension are a biobank's business model, sources of funding, business plan, and offered products and services. Another financial aspect

is costs, which is influenced by the efficiency of a biobank's operational processes and therefore overlaps with the operational dimension. A biobank's marketing, branding, and customer focus are all financial aspects related to the interaction with different stakeholders, and therefore overlap with the social dimension.

Activities in the financial dimension all work towards creating a stable financial situation, which is necessary for sustainability (Macheiner, Huppertz et al. 2017). Stable is of course a relative term, and in this context it means that biobanks must try to achieve an adequate financial horizon[5] that allows them to focus on long-term investments that support sustainability, rather than on short-term ad-hoc actions (van der Stijl et al. 2018).

Value is at the core of sustainable biobanking

Only by being valuable can a biobank become sustainable. Therefore, the concept of value stands in the centre of the sustainable biobanking framework. All three dimensions are involved in determining a biobank's value. The operational dimension provides the preconditions for high quality and accessible samples and data; necessary to be valuable as a biobank. The social dimension contains the stakeholders that contribute to and receive the biobank's value. And the financial dimension is about converting the available value into resources for the biobank.

The value of biobanks is in their use

A biobank's greatest value lies in improving patient and citizen lives through the advancement of biomedical research and innovation. This all comes down to the utilisation of gathered samples and data. If a biobank just gathers and stores samples and data, which are rarely used for research, the biobank can never live up to its full-potential, provide value for its stakeholders, and become sustainable (Sawyer, Otto et al. 2015). It is therefore "a matter of (…) life and death for a biobank to have customers" (Langhof, Kahrass et al. 2018).

Planning for utilisation requires a client-focused approach: know your target users and their needs; work on the infrastructures, products, and services to address these needs; follow a marketing strategy to advertise within and outside the organisation; and continuously evaluate and adjust (Henderson, Goldring et al. 2017).

Unfortunately, utilisation rates in most biobanks are low. In an international survey, 50 to 70 per cent of biobanks even report 0 to 10 per cent utilisation rates (Simeon-Dubach, Goldring et al. 2018). The utilisation rates of Dutch biobanks are not publicly available. We do know that biobanks such as PALGA and the Netherlands Cancer Institute Biobanking Core Facility frequently issue samples and data. Research on utilisation rates and experiences of Dutch biobanks could form the basis for national policy, guidance documents, and best practices to help individual biobanks increase the use of their samples and data.

[5] The financial horizon, or funding horizon, describes for how far into the future a biobank can sustain itself with its currently available funds and revenues.

3. The financial dimension of sustainable biobanking

Businesses are experts in creating value for their customers, in an efficient way, and translating this value into resources. In working towards financial sustainability biobanks can learn from the business world. By thinking and operating more as a business, without forgetting that academic biobanks are non-profit organisations operating in a complex ethical and legal environment, focus will shift more towards serving stakeholders, increasing use, and creating value. We are convinced that adopting a business perspective will help academic biobanks to look differently towards their biobanking activities and provide an additional edge towards sustainability.

To support biobanks we explore the financial dimension of sustainable biobanking from a business perspective, adopting the general structure of a business model. We will first introduce the business model concept and describe different business models used in the biobanking field (3.1). Second, we discuss the topic of stakeholders in relation to the financial dimension (3.2). Third, we further explore the value proposition and the Biobank Value Model (3.3). Fourth, we describe biobanking revenue and funding sources (3.4) and, to conclude, touch upon biobanking costs (3.5).

3.1. Business models in biobanking

A business model describes how an organisation creates, captures, and delivers value for its customers (Osterwalder, Pigneur 2010). More practical, a business model describes the processes required to run a successful organisation, including the value proposition, the sources of revenue, the intended customer base, the organisation's products and services, and the details of financing (Oxford Dictionaries , Magretta 2002). Choosing a feasible business model and organising your biobank, its personnel, and its activities accordingly will help plan for sustained success. An accessible tool to develop a business model is the Business Model Canvas[6] from Strategyzer. The basis of most business models starts with four key questions (Johnson, Christensen et al. 2008, Johnson 2010, Teece 2010, Mazzarol 2011, Steegers 2016):

1) *Who are your stakeholders?*
   For a business this question would be phrased as: "who are your customers?". For biobanking we are broadening this subject to include all relevant stakeholders, including your users. Divide your stakeholders into groups –called segments or markets– according to their specific attributes and determine which stakeholders are most important for your biobank. See section 3.2 for more information on stakeholders.

2) *What do your stakeholders value?*
   Once relevant stakeholders are identified you need to get to know each segment as best as possible and determine what they value and expect, for example on quality, service, and price. This process will help you to define a value proposition for each stakeholder segment. It is important to minimise assumptions to avoid going in the wrong direction. User feedback surveys can help to continuously sharpen your user understanding.

3) What is your financial structure?
   The financial structure includes the biobank's funding and revenue streams and its cost structure.

4) What are your key resources and key processes?

[6] The Business Model Canvas is developed by Strategyzer and can be downloaded from their website.

This subject relates to the resources and operational processes required to deliver value to your stakeholders. Examples are the facilities, equipment, people, skills, and communication and distribution channels necessary to deliver your products or services.

So far, biobanks have not found a uniform business model that results in sustainability. And it is unlikely that such a uniform model will be found anytime soon due to the diversity within the biobanking field (Chalmers, Nicol et al. 2016). Further diversification and innovation of business models might actually be expected as the usual funding streams become ever more competitive; forcing biobanks to look for alternative approaches (Catchpoole 2017). Mixing complementary business models is a feasible strategy. When doing so take into account that each business model requires a specific approach and expertise; and that mixing requires additional time and sound management to prevent a loss of focus.

Here we provide a list of currently used and potential future biobanking business models[7]. Due to regional or national circumstances, it is likely that other business models and variations exist in addition to those listed here. Furthermore, there can be considerable overlap between the different business models. Readers should take into account that this list is drawn up from a business perspective and serves as inspiration. Each biobank must decide carefully what business model is feasible, based on their own position, target stakeholders, available resources, intended impact, and the national and international legal frameworks.

1) Project-based model

This business model focuses on obtaining project-based funding grants from funding agencies, foundations, and research institutes. As a result, a biobank's financial sustainability depends on the available grant budget and the funding application success rate. This model can be successful, especially when starting a biobank. However, it is also risky, because a failed application can lead to financial problems. A risk mitigation strategy would be to apply for multiple grants with different running times. Biobanks that employ a project-based model often also receive some form of structural support from their department or the hosting institute.

Biobanks that use this model often originate from research groups at universities or hospitals. The biobank's manager, often a leading researcher, is used to such project-based funding from their own research projects (Warth, Perren 2014). As most Dutch biobanks originate from UMCs and universities we assume that many Dutch biobanks have adopted the project-based model as their principal business model.

2) Donations-based model

The donations-based model focuses on private and public donors as sources of finance (Warth, Perren 2014). Financial sustainability therefore depends on the availability of willing donors. Effective marketing is essential to reach and persuade prospective donors. Effective marketing involves working with marketing professionals, developing marketing material, and voicing a clear message to the right target audiences. Individual donors can be reached directly, or indirectly through partnerships with for example (patient) foundations. Biobanks that follow this business model often originate from or are directly backed by patient organisations. An example is the ALS (amyotrophic lateral sclerosis) biobank and database within the UMC Utrecht, which only exists due to funding from the Dutch ALS Foundation (ALS Centrum Nederland March 2018). The Dutch Brain Bank partly uses a donation-based

[7] Readers should be aware that there is no consensus on the terminology used to denominate biobank business models. We have used existing terms when available, and otherwise attempted to use terms that reflect, in the author's views, the main message of the business model. Within one model there can already be considerable practical and temporal variation, complicating the naming.

model, attempting to raise both additional funds and brain tissues through specific marketing (e.g. marketing on partner websites)(Rademaker, Huitinga 2018).

3) Contract research model

The contract research model (renaming of the price-based model as described by (Warth, Perren 2014)) focuses on establishing contracts with research institutes, pharmaceutical industry, and biotechnology companies. Biobanks that adopt this model depend for their revenues on the price and volume of ordered samples, data, and services attached to these contracts. However, as the market is hard to predict it is difficult to match sample and data supply with company demand. Because the contracts are often short-term, the long-term financial situation is uncertain.

Biobanks that use this business model must be able to respond fast to company requests and work with quality controlled samples according to protocols and standards from the pharmaceutical industry. What further complicates matters is that it is not always ethically acceptable or legally possible to commercialise human biological samples. Currently, Dutch law does not prohibit the commercial use of donated or 'further use' samples (Geesink, Steegers 2009). New legislation likely does not prohibit it either, as long as donors provide informed consent on commercial use. An example of a biobank that uses this contract research model is the U.S.-based company Asterand Bioscience[8] (Brown, Kelly et al. 2017). It is currently unclear if any Dutch biobanks, or international academic biobanks, use this model as their primary business model.

Biobank-based BBMRI-ERIC Expert Centres

BBMRI-ERIC Expert Centres are non-profit organisations that represent a novel public-private partnership model. They function as intermediaries between the public and private sectors performing the analysis of biological samples under internationally standardized conditions to generate primary data. Expert Centres form a pre-competitive environment, providing access to easily sharable analysis data and high-quality sample information for commercial product development. In addition, they concentrate medical, scientific, and technological expertise related to samples and data. Their experience in public-private transnational research provides Expert Centres with the experience to navigate ethical and regulatory issues. CBmed (Austria), ATMA-EC (Italy), and CNAG-CRG (Spain) are the current BBMRI-ERIC Expert Centres (van Ommen, Tornwall et al. 2015).

4) Strategic partnership model

Within this model the biobank focuses on establishing longstanding strategic research and development partnerships with a company (Lehtimaki, Helen et al. 2017). In order to establish these partnerships a biobank has to adopt an organisational model that is compatible with business collaborations. This is often outside the public institutional framework to allow for lower levels of bureaucracy and higher levels of flexibility. A major challenge is to match a biobank's public health care goals with these increasing commercial activities.

Strategic partnerships can come in many forms. One example is provided by IMIDomics, a Vall d'Hebron Institute of Research spin-off company active in the field of immune-mediated inflammatory diseases (IMIDs), and the academic IMID-Biobank. The company creates value by combining the academic IMID-Biobank with its clinical expertise, high-throughput genomic and genetic analysis, and intellectual property. IMIDomics provides

[8] Since the publication by Brown et al. Asterand Bioscience has been acquired by BioIVT, formerly known as BioreclamationIVT. BioIVT includes a UK-based office.

pharmaceutical and biotech companies access to the biobank and the accompanying database for the identification of new targets and biomarkers, the development of companion diagnostics, and the stratification of patient population for clinical trials. In return, IMIDomics receives project funding and potential royalties from products resulting from the collaboration. The nature of the partnership with the academic IMID-Biobank is unclear.

Another example is the UKCTOCS Longitudinal Women's Cohort (UKLWC), a population cohort containing samples from over 200,000 women. The cohort is hosted by University College London and was created as part of the United Kingdom Collaborative Trial of Ovarian Cancer Screening. The donated samples and data are available for use in secondary studies, both academic and commercial. UKLWC has a strategic partnership with the company Abcodia, providing them with exclusive commercial access to the UKLWC biobank for studies involving the early detection and screening of cancer. There are no restrictions on academic research, except for research on ovarian cancer where Abcodia has exclusive first option to take a license to commercialise any intellectual property developed during such research.

In another example, the Finnish Auria Biobank aims to cover at least half of its annual expenses via commercial collaborations (Lehtimaki et al. 2017). These revenues should come from selling biobank services (see business model 7: service-based model) and building strategic partnerships in medical research and development that benefit all parties involved. From the biobank's point of view these commercial collaborations help to sustain the biobank's infrastructure for academic biomedical research and the development of better health care. However, academic biobanks should be careful not to lose sight of their non-profit principles.

5) Cost recovery model

The cost recovery business model aims to recover the labour and equipment costs made during the biobanking process by charging users of samples and data for the incurred costs. This model requires a biobank to calculate its true and full costs to be able to set a transparent price per sample (chapter 4.5 lists three cost calculation tools biobanks can use). One of the challenges of this model is that the majority of academic users and funders are not able or willing to cover the costs of samples and data. As a result most biobanks have adopted a cost recovery model where they charge different fees to different user groups. Internal and external researchers often pay a partial subsidised cost price, while commercial users pay the full cost recovery fee.

Academic users often underestimate the true cost of biobanking and can react negatively to a full or even subsidised cost recovery fee, creating a barrier for the utilisation of samples and data. In communities where free access to research infrastructures is typical, significant cultural change may be required when implementing a cost-recovery model (Ecological Society of America 2010). In contrast, commercial users have a better understanding of the true cost of biobanking and can be willing to pay a higher than full recovery fee.

A 2017 survey among 21 Dutch biobanks shows that only 0,24% of their overall income was generated through cost recovery (Doucet, Yuille et al. 2017)(see figure 4 in chapter 3.4). It is unclear what the reasons are for this lack of cost recovery and if other, non-surveyed, Dutch biobanks are more successful. Results from international surveys and case studies show that cost-recovery rarely leads to a self-sustaining model (Gee, Georghiou et al. 2013, Albert, Bartlett et al. 2014, Clement, Yuille et al. 2014, Odeh, Miranda et al. 2015). It appears more realistic to strive for 5 to 25 per cent cost recovery (Albert et al. 2014). As such, this business model should always be mixed with other approaches.

6) Core facility model

Biobanks using this business model act as centralised core facility within a hosting research institution and are structurally funded by the hosting institution. Such biobanks cater to other biobanks and collections within the hosting institution by providing, for example, handling, storage, and distribution services. Such a centralised biobanking structure provides scale-related cost-savings and bundles biobanking expertise. The main strength of this business model is the long-term sustainability it can provide, allowing the biobank to plan ahead. However, a structural support model can be inflexible due to fixed multiyear budgets. Such fixed budgets prevent a biobank to grow its operations when faced with increased biobanking activity (e.g. gathering and sending samples) (OECD Global Science Forum 2017a). In addition, a loss of hosting institution support, for example due to a political or strategic shift, can lead to financial problems (van der Stijl et al. 2018). The biobank needs to justify its value to the Board of Directors of the hosting institute to maintain structural support. This can be challenging as members of the board are not direct users, making it difficult for them to evaluate the value of the biobank. Consequently, the biobank has to actively engage the Board of Directors and clarify its added value to the institute, for example through periodic cost-benefit analysis and impact measures (OECD Global Science Forum 2017a).

Legacy planning

What happens to the gathered samples and data when a biobank is unable to continue? Whether it be due to a loss of funding or other circumstances. In its business plan, a biobank should describe the legacy plan for the long-term stewardship of its collection. Especially considering the time and resources that go into building a biobank, the unpredictable funding environment, and the ethical obligation the biobank has towards the participants (Rao et al. 2019). Such a legacy plan details what happens to the collection when a biobank is terminated for any reason. It could involve the destruction of, part of, the collection or its transfer to a third party under certain conditions. The legacy plan should be consistent with current regulations, the informed consent, and any other prior agreements and institutional policies (ISBER 2018, NCI 2016).

7) Service-based model

In the service-based business model a biobank focuses on providing biobank-related services to third parties via short or long-term contracts. Third parties can be internal and external researchers and departments, or private entities. The services provide revenue for the biobank, and provide an outsourcing, and thus cost-saving, option for other parties. There are similarities between this model and the core facility business model, as the latter model is also service-oriented. The difference is that in the service-based model the biobank is not designated as the hosting institutes' core facility and does not receive related structural support.

In addition to providing samples and data, biobanks can provide many different services. Examples are research project design, stratification of patient populations for clinical trials, knowledge on what can and cannot be done with the available samples and data, bioinformatics and data management expertise, training programmes, and additional sample and data analyses. Services can also be more basic, such as leasing part of the sample and data storage capacity or providing emergency back-up capacity for individual departments. Some biobanks, such as Lifelines in the north of the Netherlands, can take the whole biobanking process out of the hands of researchers. Their expertise and infrastructure allows them to manage the collection, handling, storage, and issuance of samples and data for prospective clients. In that way, to create a sample or data collection, you do not even have to do any biobanking yourself.

Contract services are often short-term, unpredictable, and require a relatively high transaction cost (i.e. spend time and money to chase money) (OECD Global Science Forum 2017a). As a result, the service-based model is likely unsustainable as a primary business model for academic biobanks. It can, however, be a good side model to provide additional revenue.

8) Collection on demand model

The U.S.-based commercial biobank Conversant Bio and the academic Women and Infants Health Specimen Consortium biobank completely turned around their business model. They used to collect samples upfront and then wait for researchers to order them. However, they found out that this approach— "if you build it they will come"—was not sustainable. Most of their samples were just collecting freezer dust. Now they collect samples only after a researcher has made a specific request. Their business model focuses on prospective, just-in-time collections that match with active research projects. It allows the biobank to collect, process, and store samples and data exactly the way researchers need them for their projects. And it ensures that samples and data already have a prospective user before they are gathered (Kirkwood 2015).

9) Membership model

In this business model a group of researchers, departments, or organisations become supporting members of the biobank in exchange for a periodic fee. Membership provides certain benefits, such as premium access or the free or discounted use of samples, data, or services (unlimited or up to a certain usage threshold). Advantages of a membership model are the predictable and stable revenue stream and the creation of a community around the biobank. A problem could be that the biobank's revenues scale with additional members, not with the costs of collecting, managing, and using samples and data. In addition, it can be difficult, time consuming, and costly to create and maintain a member community, especially one large enough to cover all costs (OECD Global Science Forum 2017a). A biobank that uses this business model needs to be responsive to the needs of its members and show its value to ensure continued support. The TRAILS biobank uses a variation of this business model, allowing researchers to buy themselves into the biobank in exchange for the use of samples and data.

10) Two-sided business model

The U.S.-based company 23andMe uses a two-sided business model where the company functions as intermediary between two different markets: 1) the general public and 2) public or private research organisations. 23andMe receives revenue from selling genetic sequencing kits directly to consumers. The company then uses any consented genetic information from these consumers to build a genetic database with disease specific communities. Subsequently, based on this genetic database, 23andMe offers research and drug discovery services to public and private researchers in return for service, outcome, or licensing fees (Stoekle, Mamzer-Bruneel et al. 2016).

11) Direct to consumer business model[9]

A direct to consumer business model is used by several non-research biobanks. An example are commercial biobanks that store stem cells or umbilical cord blood from individual citizens. If those individuals get sick in the future, their own stored stem cells might be used as treatment, depending on the disease. The added benefit of such commercial storage-schemes versus their costs is disputed, as the risk of stem cell-associated diseases is low and

[9] Disclaimer: This business model is, to the best of our knowledge, not used by research biobanks. The model serves as inspiration and biobanks should consider carefully if the model would be feasible in some form.

stem cell-based treatments are currently limited. This might however improve in the future, as new stem cell-based treatments become available.

It might be possible to adjust this business model for a research biobank by dividing the stored stem cells or cord blood samples in an aliquot used for research and an aliquot used for the potential future treatment of the donating individual. In the Netherlands this would mean that the resulting biobank would, in addition to its research activities, be classified as a medical tissue bank ('weefselinstelling'), which requires ministerial approval and adherence to strict guidelines and protocols because of its health care-related activities.

12) Freemium model[8]

The Freemium business model is used extensively in the software, web services, and game industry. Freemium is a blending of the words "free" and "premium". Customers have free access to a time or feature-limited product or service, often resulting in a quick customer growth. These customers are then offered a premium-priced full version or additional value adding services. A well-known example is LinkedIn, where creating and using a profile is free, but upgrading to a premium account with additional features requires payment.

It is unclear if variants of the Freemium model are currently used by biobanks. This model is of course harder to implement for a biobank than for a software company. Still, a biobank can provide free access to certain products or services, and hereby increase usage, awareness, and customer contact. When users know how to find the biobank and know what the biobank has to offer, they will be more likely to come back for more. An optional model could be to give users free access to a number of standard or raw datasets or samples to run pilots, taking into account legal, consent, and privacy requirements. Users would then need to pay for additional datasets or samples, data curation services, additional sample analysis, facility access, and value-adding services. The costs related to providing free access would ideally be calculated into the price of the paid products and services.

Sample and data broker companies

Sample broker companies act as intermediaries between biobanks and public or private researchers. Through marketplaces, networks, and online platforms they try to connect supply with demand. The survival of these commercial brokers is indicative of a more mature biobanking market. Broker companies benefit from the gap between academic biobanks, which can have trouble putting their samples to use, and pharmaceutical companies, who have trouble finding the right samples.

Companies focused on data-brokerage are appearing as well. The amount of data connected to biobank samples is growing fast. And as linkage between different data sources becomes more commonplace the potential for research is skyrocketing. The difficulty is in managing these large datasets and finding the right information. Pharmaceutical companies are also interested in these datasets, for example to stratify patients and find the right patient for the right clinical trial (Lehtimaki et al. 2017).

For biobanks, collaborating with sample and data broker companies can result in increased sample and data usage, brand awareness, networking, and potential for public-private partnerships. However, realising effective collaboration between an academic biobanks and a broker company is not simple due to the different perspectives, interests, and processes of academia and commercial companies. When collaborating with broker companies, biobanks need to take into account legal and ethical issues, intellectual property, privacy, security, ownership, and informed consent. To navigate these issues and come to fair agreements that benefit both parties, biobanks should collaborate with their hosting institute's technology transfer office and other supporting departments.

3.2. Stakeholders

The interaction and relationship with stakeholders is part of the social dimension of sustainable biobanking. However, there as a large overlap with the financial dimension as stakeholders play a vital role in a biobank's business model (see 3.1).

The key to success for any commercial or non-profit organisation is the satisfaction of its key stakeholders (Bourne 2009, Bryson 2011, Bjugn, Casati 2012). The same holds true for biobanks. Biobanks exist not in isolation, but within an extensive ecosystem of stakeholders. Different stakeholders are involved in running the biobank, collecting and using the samples and data, and providing support, funds, and revenues. Figure 2 lists the most common biobanking stakeholders.

Figure 2: Biobanking stakeholders

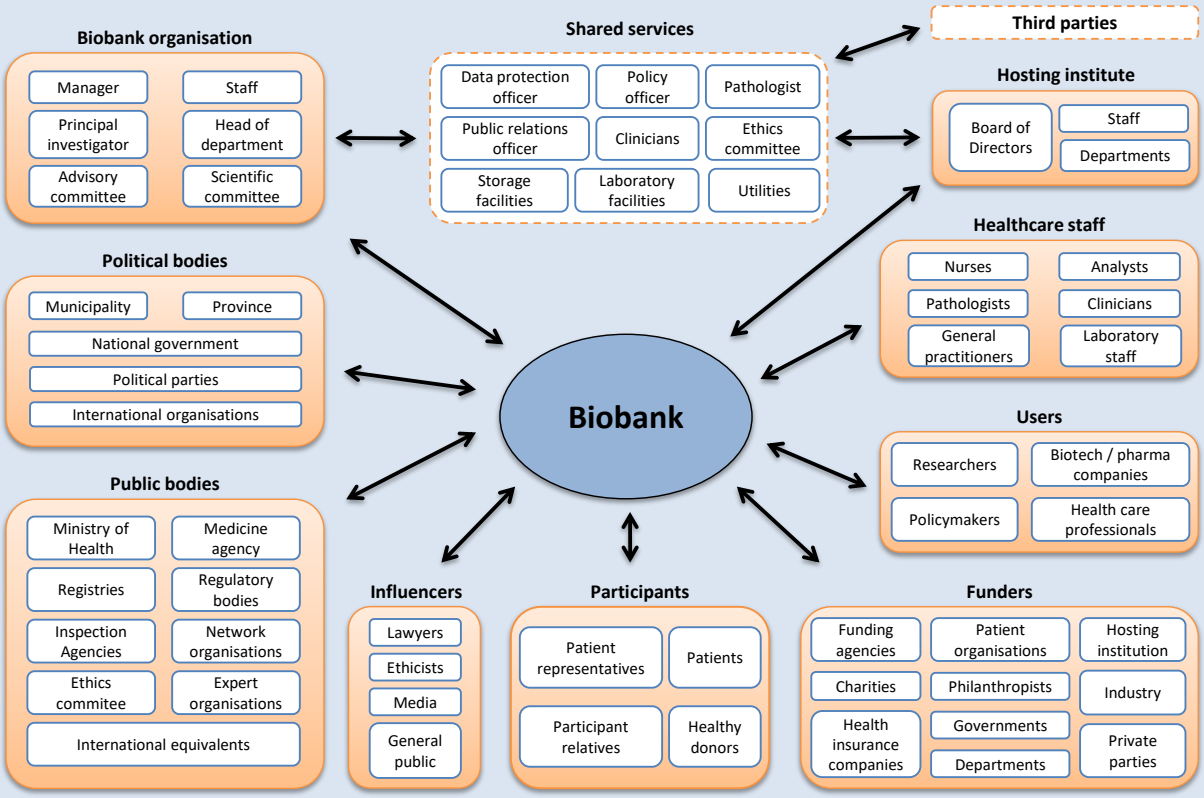


Figure 2 lists the potential stakeholders for an academic biobank. Some stakeholders will be more important for sustainability than others. Depending on the biobank's setup the "shared services" will be integrated in the biobank itself, provided by the hosting institute, or oursourced to a third party. The figure is based on work by (Bjugn, Casati 2012).

Stakeholder analysis

A thorough stakeholder analysis is essential to identify those stakeholders that are required for the long-term future of a biobank (Bjugn, Casati 2012). The analysis should result in the identification, segmentation, and prioritisation of stakeholders, followed by an appropriate engagement strategy per stakeholder or stakeholder group, taking into account their motivations, needs, interests, and level of influence. The results should be used for shaping the biobank's business model and its value proposition (see section 3.1 and 3.3). The University of Nottingham performed a detailed breakdown of four stakeholder groups (i.e. the biobank itself, academic users, industry users, and the "general public") that can be useful as a starting point for individual biobanks (University of Nottingham).

Time and economic restraints may force a biobank to skip the stakeholder analysis. However, this could lower a biobank's sustainability on the long run as important stakeholders and their concerns might remain unaddressed. Any organisation can perform a stakeholder analysis, as neither sophisticated equipment nor deep theoretical knowledge is required. What is required is a will to face possible negative future factors and risks, to engage with people who might have different views, and to change objectives and strategies if deemed necessary to reach overall goals. The discussion accompanying the analysis will in itself already provide new insights and a shared understanding (Bjugn, Casati 2012). For more information on how to perform a stakeholder and power-interest analysis see the BBMRI.nl report *Business Tools for Biobanks*.

3.3. Value

To become sustainable, biobanks need to create and show value for their key stakeholders. Value is however a broad and subjective concept; it comes in many forms and its meaning depends on perspective. What one stakeholder finds valuable, another might find less so. A biobank offers many different forms of value and the challenge is to clearly communicate the right value to the right stakeholder, and convert this value into support or resources for the biobank.

Value proposition

"A good business model will provide considerable value to the targeted customers (Teece 2010)". Value, or the value proposition, is central to any business model. It is the reason why stakeholders turn to one specific organisation over another (Strategyzer). The value proposition is an aggregation of benefits a biobank offers to each of its stakeholder groups, in exchange for a certain cost. Translated into a formula it would be:

Value proposition = Benefits – Costs (Barnes, Blake et al. 2009a)

The benefits often involve solving or preventing a problem or satisfying a need. The benefits for a stakeholder can be quantitative (e.g. price, speed of service, cost reduction) or qualitative (e.g. customer experience, risk reduction, status, customisation). A common approach to develop a value proposition is to (Barnes, Blake et al. 2009b):

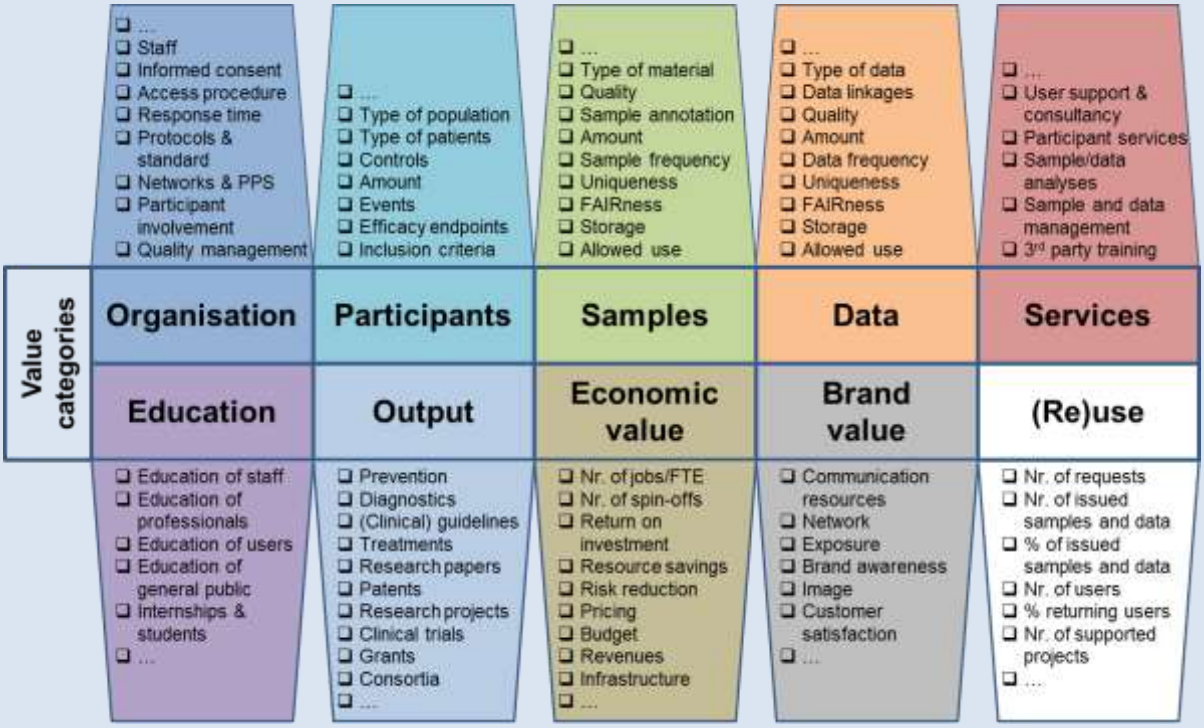
1) Identify the stakeholder or stakeholder group;
2) Understand what the stakeholder or stakeholder group values (what are their problems? What are their needs?); survey the stakeholder group. What question will you answer for them?
3) Define the product or service;
4) Identify the benefits of the product or service to the stakeholder, including its cost;
5) Identify the benefits of the product or service over what currently exists, including competition; and
6) Provide proof to substantiate the claims.

To direct users of sample and data, the benefits of a biobank, and thus its value, are clear. For stakeholders that are indirect users it is more difficult to appreciate a biobank's benefits, judge its value, and determine the price they are willing to pay for its upkeep. Engaging these stakeholders, especially if they are funders, is essential for sustainability. To keep them on board, a biobank requires a clear value proposition and provide proof to support its value claims, for example by tracking performance indicators[10] and performing cost-benefit and impact analyses (OECD Global Science Forum 2017a). It should be noted however, that judging the full value of biobanks from a balance sheet of performance metrics is just as challenging as assessing the long-term value and

[10] There are multiple publications on performance indicators for biobanks, such as (V. Hofman, Ilie et al. 2013, Mabile, Dalgleish et al. 2013, Watson et al. 2014, Brown et al. 2017)

impact of basic research programs (Watson et al. 2014). So in addition to providing metrics, biobanks should also emphasize the more indirect value they provide, such as the generation of knowledge, the education of users, and the discovery of clinical innovations (Catchpoole 2017).

Figure 3. The Biobank Value Model



The Biobank Value Model consists of ten categories that together contribute to the overall value of a biobank. In turn, each category contains multiple parameters that determine the value of that specific category.

Biobank value model

For many stakeholders, biobanking professionals included, it can be unclear what value a biobank represents and from which aspects this value is built. A biobank consists of many intertwined parts that need to be in tune to deliver value. Of course, at its core, a biobank's value consists of its samples and the associated data. And when these are of high quality, their potential value often only grows over time. Still, a biobank can have data and samples of the highest quality, but if access is slow and poorly organised their scientific and societal impact will be restricted, lowering the overall value of the biobank.

To make biobanks aware of the different types of value they possess and how their biobank's overall value is built, a Biobank Value Model was developed during a BBMRI.nl workshop (van der Stijl et al. 2018), supplemented with insights from the Europe Biobank Week 2018 and the report's authors (see figure 3). The current Biobank Value Model consists of ten categories that together build the overall value of a biobank. In turn, each category contains multiple parameters that contribute to the value of that specific category. Keep in mind that some categories or parameters are more valuable than others, depending on perspective. Biobanks can use this model to get more insights on how their value is built and to identify blind spots or points of improvement. Being aware of one's own value will help to articulate a clear value proposition towards each stakeholder.

3.4. Funding and revenues

The purpose of any business model is to convert the created value into resources for the organisation. Gathering resources, which largely consist of funding and revenues, is central to the financial dimension of sustainable biobanking. A biobank needs to collect sufficient resources to cover both its start-up and its operational costs. Often, hosting institutes or research grants provide start-up resources for a certain amount of time (e.g. 3-5 years). During this time the biobank's organisation and collection are established. After this initiation period, biobanks need to make the transition to sustainable operations. However, this changeover remains difficult to achieve (Warth, Perren 2014). There are limited public grants directly aimed at supporting a research infrastructure's operational activities, making funding for biobanks highly competitive. As new funding sources take time to develop, biobanks should start early, preferably after operations have been established and several years before the existing funding sources dry out. In many cases the hosting institute is addressed to (continue to) contribute or biobanks depend on intermittent project-based research funds (Meijer, Mattson et al. 2010).

Sources of funding and revenue

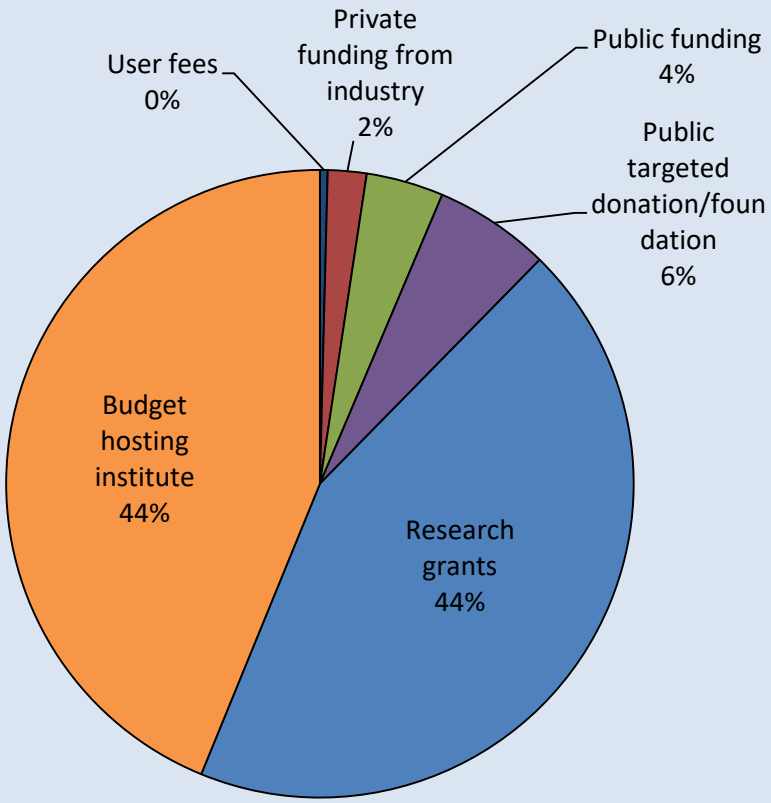
Biobanks are increasingly challenged to turn to additional sources of finance (Gee et al. 2015, Doucet et al. 2017). The fact that there are commercial biobanks indicates that it is possible for a biobank to efficiently translate its value into revenue. However, most academic biobanks have trouble generating sufficient revenues to fund their operations. And as a result, a self-sustaining model is almost never achieved (Vaught, Rogers et al. 2011). Ideally, biobanks would have multiple sources of funding and revenue, some of which scale with increased use and costs. The sources currently used by academic biobanks are:

- Commercialisation of research results, products, and services (e.g. intellectual property royalties, consultancy fees, assay and tool development, sample analysis)
- Donations from (patient) foundations or individuals
- Institution budget
- Private funding (e.g. pharmaceutical companies)
- Public funding (e.g. national government, research grants)
- User fees for samples, data, and services

Strategies when facing funding shortages

Almost inevitably biobanks will face some form of funding shortages during their lifetime. There are different strategies for managing short-term budgetary issues, among them are: deferring acquisitions of new capital equipment, reducing the scale of operations, and reducing staff. A recent international survey from Rao et al. showed that the first two options were the most common, with none of the respondents opting for a reduction in staff. This is most likely because the training and experience of biobank staff represents a significant human resource investment that is not easily replaced. In addition, a reduction in staff is often greatly disruptive to effective operations, much more so in the complex field of biobanking than in other business areas (Rao et al. 2019).

Figure 4. Distribution of overall income of 21 Dutch biobanks per financial category



The income distribution of 21 Dutch biobanks, according to supplementary data from (Doucet et al. 2017), see appendix 2.

The Dutch situation

In the Netherlands, biobanks rely heavily on institutional funding and research grants (see figure 4). The only publicly available data about the financial arrangements of Dutch biobanks comes from a publication of Doucet et al., which surveyed 21 Dutch biobanks on their income distribution per financial category (Doucet et al. 2017)(see appendix 2 for financial arrangements per surveyed Dutch biobank). This data shows that the surveyed Dutch biobanks receive most of their funds from research grants (44%) and institutional budgets (44%), and that they appear to have difficulty in generating revenues from other sources. It is even plausible that the reported contribution from institutional budget is underestimated as the, often significant, in-kind and indirect institutional contributions are hard to map and likely overlooked. These results appear in contrast to a US-biased international survey, which showed that 18% of funding came from internal start-up funds, 26% from government/non-profit grants, and 31% from recovered user fees[11] (Odeh et al. 2015).

Generalising these results to all individual Dutch biobanks is not possible, as there are always exceptions. For example, the Doucet et al. survey showed that TRIONL, a longitudinal asthma follow-up cohort, and the Netherlands Cohort Study received 30 to 50 per cent of their funds from targeted donations or foundations. Furthermore, the MDL biobank and the Amsterdam Cohort Studies

[11] The survey from Doucet et al. and the international survey from Odeh et al. are difficult to compare as the survey questions are not known –and can thus be substantially different–, the calculation method is not retraceable, and the funding categories are different or partly overlap. However, the difference in reported cost recovery is clear between the Dutch and the international situation.

received 30 and 50 per cent public funding, respectively (Doucet et al. 2017). A quick internet search suggests that several other Dutch biobanks receive at least part of their funding from individual donations, (patient) foundations, public sources, or private partners (see table 1). Based on the currently available data we can assume that most funding for the Dutch biobanking landscape comes from research grants and institutional budgets, but that for individual biobanks other sources of finance can play a substantial or even major role.

Table 1. Publicly listed partnerships of Dutch biobanks per financial category

Biobank	Financial category [A]
ALS Biobank and database	(patient) foundations
De Maastricht Studie	(patient) foundations, public funding, private funding
Dutch Brain Bank	(patient) foundations, individual donations, public funding
Generation R	(patient) foundations, public funding, private funding
Hecovan Biobank	(patient) foundations
Prospectief Landelijk CRC cohort	(patient) foundations, private funding
TRAILS	Research grants, (patient) foundations, public funding

[A] The partnerships or sponsors listed on a biobank's website were placed in one of the financial categories. It is possible that the listed biobanks also receive funding from other sources not listed on their website (e.g. national and international research grants, user fees).

Commercialisation of biobanks

'Commercialisation of biobanks' is a broad concept. It can refer to the direct transfer of data and samples to private for-profit entities or refer to the commercial use of research results or products derived from those samples and data. In addition, it can refer to publicly funded biobanks partnering with or receiving funding from private entities, so called public-private partnerships (see below) (Caulfield, Burningham et al. 2014).

Commercialisation brings a number of potential benefits for biobanks. For example, commercialisation can help biobanks to achieve their overarching societal goal, which is the improvement of prevention, diagnosis and/or treatment of disease. To accomplish this goal, products will eventually need to be brought to the market. And here the involvement of commercial entities seems crucial and inevitable as they have the funds, expertise, and experience to bring new medical innovations from bench to bedside. Another potential benefit is that private entities can function as users, investors, and partners, providing a source of income for the biobank; improving its financial sustainability. However, commercialisation also brings with it a number of issues, such as the potential adverse impact on public trust and donor participation, consent challenges, privacy issues, oversight challenges, ownership issues, and concerns regarding the control of samples and data following bankruptcy (Caulfield et al. 2014).

International literature contains numerous articles on the ethical and public concerns related to commercialisation and the potential approaches to handle these concerns (Critchley, Nicol et al. 2015, Spector-Bagdady, De Vries et al. 2018, Gibson, Axler et al. 2017). For example, qualitative research shows that independent governance and transparency with regards to commercial involvement can overcome people's prejudice against commercialisation (Nicol, Critchley et al. 2016). In addition, patients are often positive towards commercialisation when explained that private partners are necessary to bring a clinical solution to the market. Be careful that the subject of commercialisation should be treated differently for each country, due to differences in culture, tradition, and public attitude towards commercialisation (Evers, Forsberg et al. 2012).

Public-private partnerships

Public–private partnerships (PPPs) can take many forms, from bilateral agreements between one academic and one industrial partner to large multi-stakeholder and multinational consortia including many actors from the public and private sectors. Their typical aim is to generate benefits for both

sides, for example by providing access to the other parties' resources or expertise, joint scale advantages, outsourcing part of the work, and increasing the efficiency of product development. PPPs are often geared towards joint discovery, precompetitive research, or biomarker development; with shared data gathering, software development, the creation of protocols, training, and joint research programmes as other options (Hamalainen, Tornwall et al. 2019).

However, the goals of public and private partners are not automatically aligned. In general, academic parties aim for publications, while private partners market products and services for profits. Timely negotiations are necessary to find common ground and align interests. Collaborations can fail due to misunderstandings, wrong perceptions, or a lack of clear communication. Understanding the differences between the academic and private research environment is key for collaborative success (Hamalainen et al. 2019).

Biobanks that want to collaborate with private parties should start a conversation with their desired partners as early as possible to find common ground and discuss obstacles and requirements. Public-private projects are always tailor-made and involving an intermediary that has experience from both sides can make all the difference. Foremost, biobanks have to arrange their informed consent accordingly. When initiating a public-private partnership always draft clear contracts describing the responsibilities of each partner. In addition, provide transparency on the public-private partnership towards the biobank's participants, emphasising the benefits and the built-in ethical and privacy safeguards. Examples of such safeguards are keeping "ownership" at the biobank, signing material transfer agreements, and working within a secure data workspace. Before attempting to collaborate with private parties, biobanks should reflect on how they handle the main bottlenecks as experienced by industry (P. Hofman, Brechot et al. 2014):

- Complex and slow administrative and regulatory processes (i.e. long turnaround time after a sample or data request by industry)
- Unclear pricing structures and user conditions
- Lack of business experience on the biobank's side
- Biobank collections often not fit for purpose due to stringent industry quality requirements
- Unacceptable requirements on intellectual property rights, scientific collaboration, and co-authorship

Biobanks that want to collaborate with private parties should focus on becoming attractive partners. Private parties often look for (P. Hofman et al. 2014, Zatloukal 2018):

- Fast and transparent access to traceable, well-documented, and well-characterised samples connected to clinical data
- Quality and reproducibility according to industry standards
- Clear agreements on intellectual property rights
- Access to expertise
- An R&D partner in a specific disease area

At the moment clear and practical Dutch guidelines on commercialisation and public-private partnerships are missing. Such guidelines would streamline the conversation between academic biobanks and private parties by indicating what is and is not possible in the context of Dutch legal, ethical, and societal constraints. For hands-on support Dutch biobank's should contact their local technology transfer office. They can also make use of the European CORBEL Helpdesk, a complementary service which focuses on multi-party and multi-country public-private partnerships.

Examples of public-private partnerships

U-BIOPRED
U-BIOPRED, which stands for Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes, was a public-private partnership between 20 academic institutions, 11 pharmaceutical companies, 6 patient organisations and 4 small and medium enterprises. The project was initiated in 2008 as part of the European Innovative Medicines Initiative. The partnership's goals were to better understand severe asthma phenotypes through the, at the time, ambitious integration of clinical and multi-'omics approaches. A 2018 paper by John H. Riley et al. describes the value of such collaborative projects for industry (Riley, Erpenbeck et al. 2018).

Finngen
Finngen is a large international public-private partnership involving all nine Finnish academic biobanks, their hosting institutes, hospitals, and nine big pharmaceutical companies (Abbvie, Astra Zeneca, Biogen, Celgene, Genentech, GSK, Merck, Pfizer and Sanofi). The project will gather genomic information of 500,000 biobank participants and combine this with digital health care data from national health registries. The aim is to identify genotype-phenotype correlations in the Finnish population and hereby enrich drug discovery programmes. The project is funded for €59M by Business Finland, the Finnish funding agency for research and technology development, and the partnering pharmaceutical companies.

Lifelines Living Lab Newborn
Living Lab Newborn is a public-private partnership between the biobank Lifelines, University Medical Center Groningen, Philips and the Life Cooperative; a group of 20+ Dutch small and medium sized life science enterprises. Within Living Lab Newborn participants of the Lifelines NEXT cohort –a cohort containing 1500 mothers and their baby's aiming to investigate the link between preconception, early life and healthy ageing– form a community for testing health related devices. Examples are smart tooth brushes, health watches, baby monitors, and diaper sensors. The project is funded by European and regional subsidies.

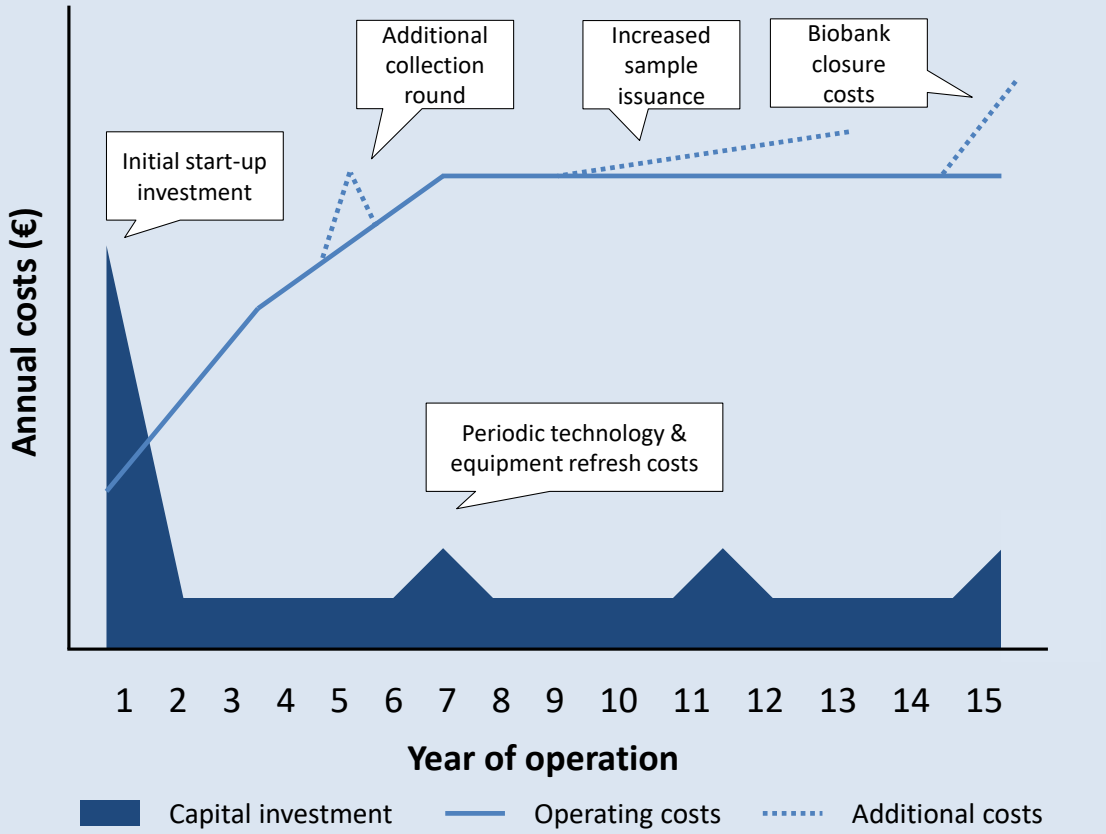
3.5. Costs

Costs exist at the interplay of the operational and financial dimension and are an essential part of sustainable biobanking (Odeh et al. 2015). "Even a modest biobank represents a significant funding commitment (Graham, Molster et al. 2014)". What is often overlooked is that the resources needed for the successful design of a biobank are already around ten per cent of the final implementation costs (OECD Global Science Forum 2017b). Understanding the total cost of biobanking is important to identify potential cost-saving and efficiency measures. In addition, knowledge on costs in relation to received benefits provides actionable insights for resource allocation and stakeholder management.

Personnel is a biobank's main expense

There is limited published data on the costs involved in starting, operating, and maintaining a biobank. The data that is available tends to be highly variable and specific to the type of biobank (Odeh et al. 2015). In the end, each individual biobanks' cost build-up is complex and depends on the biobanks' setup, size, services, and adopted workflow. Overall, a biobank's initial starting investment is high and consists for a large part of capital investments in buildings, space, and equipment (Vaught et al. 2011, Parry-Jones 2014)(see figure 5). During operational years these costs decrease, with the exception of periodic equipment renewal costs and expansions.

Figure 5. General biobank cost distribution



A generalised cost distribution for the duration of a biobank. The cost distribution differs between biobanks, depending on the biobank's setup. During its operational years a biobank can encounter additional costs, for example due to the collection of additional samples, increased issuance of samples and data, or closure of the biobank. Figure adjusted from (Vaught et al. 2011)

As a biobank matures, operating costs associated with sample and data collection, processing, storage, and distribution start to rise significantly. Operating costs can be divided over the following six categories[12]:

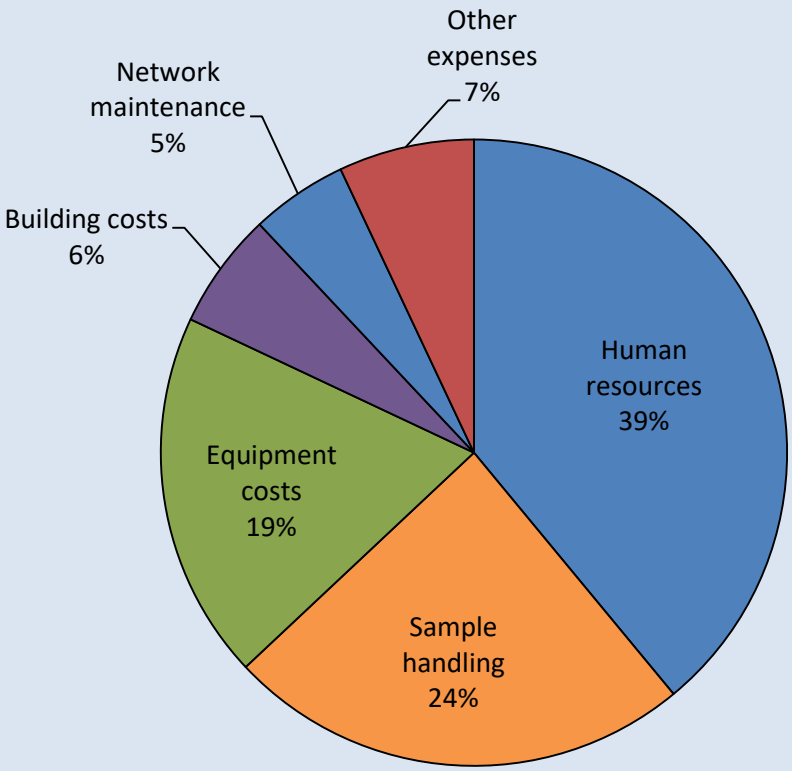
1. Human resources (e.g. salary, benefits, training for personnel; including researchers, technicians, quality managers, administrative staff)
2. Sample handling and data management (e.g. laboratory supplies; consumables; collection, processing, storage, and distribution of samples and data; project management)
3. Building costs (e.g. rent and loans for facilities)
4. Infrastructure and equipment costs (e.g. IT infrastructure, storage facilities, data repositories, monitoring equipment, depreciation allowance, maintenance contracts)
5. Network maintenance (networking with clients, other biobanks, and relevant organisations)
6. Other expenses (e.g. branding & marketing, office supplies, transport)

[12] We chose these six categories as there is data available from 23 Dutch biobanks according to this cost format (Doucet et al. 2017). Additional categories can be added depending on the individual biobank. Some authors subdivide categories to a more detailed level or include additional categories such as business development, research programmes, marketing costs, or quality and safety (Ciaburri, Napolitano et al. 2017, ISBER 2018).

Annual operating costs range from €200,000 to €800,000, with an average of around €400,000, according to a recent survey of 22 French and 23 Dutch biobanks (Doucet et al. 2017). This excludes any expenses related to research. Figure 6 shows the distribution of operating costs per category. Human resources account for ~39% of operating costs, followed by sample handling (~24%) and equipment related costs (~19%). This is in line with other sources stating human resources as the largest expense for biobanks (Parry-Jones 2014, Wilson, D'Angelo et al. 2014, Odeh et al. 2015, Brown et al. 2017, Andry, Duffy et al. 2017). In the coming years the costs associated with data infrastructure and FAIR data management are expected to rise considerably as biobanks generate and link with increasingly large data sets (e.g. large-scale 'omics' studies, high-resolution images, electronic health records).

A biobank's specific cost distribution will depend on its business model, as certain models, for example, emphasise business development and stakeholder contacts. Overall, biobanking activities are highly resource-consuming with a significant proportion of fixed costs from human resources, infrastructure, and equipment. Variable costs, for example in consumables and sample processing, vary proportionally to the volume of handled samples (Gonzalez-Sanchez, Lopez-Valeiras et al. 2014).

Figure 6. Distribution of operating costs for academic biobanks.



Source: (Doucet et al. 2017)

Potential cost-saving measures

Taking a critical look at the cost structure, expenses, and workflow associated with your biobank can result in surprising insights and cost savings. Scientific and grey literature contains numerous articles and case studies that state potential cost effectiveness measures. We summarize some of them here below. Keep in mind that each of these measures must be evaluated in the light of a biobank's individual situation.

- Gather consent and enrolment data, but only collect samples after an investigator request has been approved. This avoids making a significant upfront investment in collecting and processing samples that may never be used (Bromley 2014).
- Stop routine product extraction (e.g. DNA, RNA, protein) when these extractions are only partly distributed or used for research (Watson et al. 2014). What do your (future) users require?
- Improve your storage efficiency to decrease maintenance cost and costs per stored sample (Shea, Wagner et al. 2017).
- Automate specific procedures to lower personnel costs. Often only efficient with a high turnover of samples. Calculate beforehand.
- Consider a different supplier of laboratory consumables, equipment, and maintenance.
- Lower your capital start-up investments by making use of existing infrastructure.
- Build according to a modular setup to avoid full costs at the start of biobank operations.
- Streamline your consent procedure to reduce the personnel time per consent, for example by incorporating the procedure in the healthcare system (Ost, Newton et al. 2017).
- Lower human resource costs by outsourcing temporary assignments, employing personnel that can perform multiple functions, or sharing employees with for example the hosting institution.
- Fuse with other biobanks to exploit economies of scale by sharing personnel, procedures, and facilities.
- Collaborate with other biobanks on joint material procurement and software licenses.
- Be critical on which samples to store and which to discard. Maintaining freezers full of unused samples increases your costs. What do your (future) users require?
- Curtail operating costs, for example by shutting down or divesting parts of your operation.

Know your costs

Understanding and assessing your costs is essential to project and plan for the future (Ecological Society of America 2010). The scarcity of available resources and the need to use them efficiently makes cost information essential for any organisation, as it allows informed decision-making aimed at sustainability (Gonzalez-Sanchez et al. 2014). In addition, knowing the costs of biobanking provides transparency towards funders and users on the costs per sample.

Many biobanks are not fully aware of their true costs, partly because many costs are 'hidden', often as a result of complex inter-institutional arrangements and mixed funding streams (Gee et al. 2013). Ambiguity about costs might lead to early termination of the biobank. Biobanks should carry out periodic cost analyses, including accurate budgets and future projections. Identifying which processes and activities are the key cost drivers (e.g. consenting process, sample issuance, collection size, sample types) often provide insights for future projections (Bromley 2014). Estimated costs should be regularly reviewed to examine the actual costs, identify potential cost-effectiveness measures (see text box Y for suggestions), and optimize biobank processes without compromising on quality (ISBER 2018).

Help in calculating your costs

A better understanding of a biobanks' costs supports improved spending practices and more efficient management. Gonzalez-Sanchez and colleagues published a step-by-step implementation of a cost-accounting tool to support strategic decision-making and internal biobank management (Gonzalez-

Sanchez et al. 2014). Various web-based tools exist to support biobanks in calculating costs, determining sample and service fees, and developing financial forecasts:

1) **Biobank Economic Modeling Tool (discontinued)**
   Developed by the United States National Institutes of Health, National Cancer Institute's Biorepositories and Biospecimen Research Branch to support cost recovery and financial planning activities for biobanks. Link: https://bemt.nci.nih.gov/bemt/public/index

2) **BBMRI-LPC (Large Prospective Cohorts) Cost Calculator (free)**
   Developed by the Munich Helmholtz Center for the BBMRI-LPC network. The tool enables biobanks to calculate their biobanking associated costs. It is designed for population based cohorts and biobanking in clinical studies according to a modular, process-oriented design. Link: https://epi.helmholtz-muenchen.de/tools/calc/

3) **Biospecimen User Fee Calculator (membership only)**
   Developed by the University of British Columbia Office of Biobank Education and Research. A comprehensive and easy to use tool that captures annual expenses, resources, and biospecimen accrual and calculates the appropriate user fees. Link: http://biobanking.org/webs/biobankcosting

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5. Appendices

Appendix 1: Literature search strategy

To construct this report we used peer reviewed and non-peer reviewed (grey) literature, information from a recent Dutch workshop on sustainable sample and/or data infrastructures[13], and information from the Europe Biobank Week 2018.

Search Strategy

We gathered recent reports and publications from websites of national and international biobanking cluster organisations (BBMRI.nl, BBMRI-ERIC, BBMRI national nodes, Parelsnoer Institute, Health-RI, Global Biobanking Week, P3G, NCI, OECD, ISBER, ESBB). Furthermore, the journals *Biopreservation and Biobanking* and *Cell and Tissue Banking* were consulted. In addition, we performed literature searches through the Pubmed search engine based on a keyword/timespan strategy (See table A1), complemented with additional searches for "similar articles" in PubMed and using the reference lists of the found articles.

Table A1. Pubmed search strategy

Keyword string		Timespan	Nr. of articles	Time of search
((biobank*[Title/Abstract])	OR	published in the last 5 years	186	24 April 2019
(biorepositor*[Title/Abstract]))	AND			
((sustainabl*[Title/Abstract])	OR			
(econom*[Title/Abstract])	OR			
(business*[Title/Abstract])	OR			
(financial*[Title/Abstract]))				

[13] BBMRI.nl workshop organised on the 20th of April 2018 with 22 participants from Dutch biobanks and data infrastructures. A workshop report is available on the BBMRI.nl website (van der Stijl et al. 2018).

Appendix 2: Financial arrangements per category per biobank

Table A2. Financial arrangements per funding category

Biobank	Institution budget	research grants	public targeted donation/ foundation	Public funding	private funding from industry	User fees	
COPACETIC study		1,00					
Asthma follow-up cohort (longitudinal)	0,10	0,50	0,30		0,10		
Asthma trios (TRIONL)	0,10	0,50	0,30		0,10		
Wheezing Illnesses Study Leidsche Rijn (WHISTLER)	0,20	0,70			0,10		
PIAMA Research Project	0,10	0,70	0,10	0,10			
Netherlands Cancer Institute	0,05	0,95					
MDL: University Medical Center Nijmegen (UMCN)	0,40	0,20		0,30	0,05	0,05	
Amsterdam Cohort Studies (ACS) on HIV infection and aids	0,50			0,50			
Nijmegen Breast Cancer Frozen Tissue Bank	1,00						
AGORA	0,90	0,09	0,01				
Genetic Modifiers of Traumatic Brain Injury Sequelae	1,00						
Brain Imaging Genetics (BIG)	0,90	0,10					
Dutch Dyslexia Program (DDP), genetic component	0,10	0,90					
International Multicenter ADHD Genetics Study, Dutch part: Image NL	0,90	0,10					
Family and Health Study (FHS)	0,50	0,50					
Nijmegen Biomedical Study	1,00						
Netherlands Cohort Study	0,10	0,30	0,50		0,10		
Polygene Study (Integraal Kankercentrum Nederland)	0,10	0,85			0,05		
Netherlands Study of Depression and Anxiety (NESDA)	0,25	0,75					
Netherlands Twin Register (NTR)	0,10	0,90					
International Multicenter persisting ADHD collaboration Dutch part: Impact NL	0,90	0,10					
Sum	9,2	9,14	1,21	0,9	0,5	0,05	21
% of total funding	**43,8**	**43,5**	**5,8**	**4,3**	**2,4**	**0,2**	**100**

To allow calculation, percentages are presented as numbers (1,00 = 100%). Based on supplementary data from (Doucet et al. 2017).