

## Financial Sustainability of Biobanks: From Theory to Practice

**Moderator:** Martin Yuille<sup>1</sup>

**Participants:** Irwin Feller,<sup>2</sup> Luke Georghiou,<sup>3</sup> Philippe Laredo,<sup>3,4</sup> and Eric W. Welch<sup>5</sup>

### Moderator's Introduction

I WOULD LIKE TO THANK EVERYONE for their participation in this international roundtable and to thank *Biopreservation and Biobanking* for its support.

This roundtable is an experiment. Hitherto, scientists have only discussed the question of economic sustainability of biobanking with each other and perhaps with our funders, but, here, perhaps for the first time, a group of economists is speaking with and to scientists. Can their expertise help us, scientists, to find a long-lasting solution to the problem of sustainability in biobanking?

Let us first locate biobanking. It takes place in the research cycle. This is often considered to comprise three stages: (1) frame your testable hypothesis; (2) test your hypothesis; and (3) modify your hypothesis for further testing.

Biobanking sits in the second stage of this cycle. It is responsible for four steps that enable the hypothesis to be tested. In these steps, resources—human samples—are accrued, processed, stored, and retrieved. This resource management is an active research topic in its own right and so biobanking is primarily a research activity—not a service activity.

Resource management is less complex in other areas of science. An astronomer only needs access to the sky at night. A particle physicist at the Large Hadron Collider only needs access to a bottle of compressed hydrogen, but biobankers make samples accessible after a series of complex operations for all the types of resources that they manage: bacteria, fungi, seeds, plants, animal models, viable tissue, and, of course, human blood, urine, other liquids, and tissue.

Health research biobanks exist either within research organizations or within private companies, but their sustainability is discussed as a problem just for research organizations. By chance or by design, biobanking has been made the subject of an experiment in funding. This ongoing transnational experiment is to test the hypothesis that biobanking can be undertaken at no overt direct cost to research funders. The idea of zero cost—of something for nothing—holds a certain attraction.

If this cost recovery hypothesis is true, then biobanking would be sustainable financially even if the consequence is that new transaction costs are introduced and that a scientific price would be paid (e.g., risks to quality and to scientific innovation in biobanking). If the hypothesis is false, then a bigger scientific price would be paid. This latter possibility has led some funders to exclude highly prestigious biobanks from the experiment—UK Biobank, for example.

So, the questions to which biobankers need answers are as follows:

- Does this cost recovery model make any sense?
- If not, why not?
- Has it been successfully or unsuccessfully adopted in any other area of research infrastructure?
- How important is timing of the introduction of aspects of the market economy to the success of the transition from research to innovation?
- What are the intellectual underpinnings to the zero-cost policy and in what ways are these underpinnings sound or unsound?
- What studies would economists perform to test the success or failure of the policy?
- What measures would they advocate for cost-effective sustainable biobanking?

Maybe we can start to answer some of these questions today.

**Dr. Martin Yuille:** I obtained research funding some 15 years ago for one of the first biobanks and certainly the first biobank network. Within a few years, the funders decided to insist that this work should recover its own costs. This had never happened to me in previous decades of research funding. Why?

**Dr. Philippe Laredo:** As a preamble, we should frame the idea of a biobank and the funding universe surrounding the biobank. It is important to specify that with the term biobank, we mean the collection, storage, enrichment, and

<sup>1</sup>Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom.

<sup>2</sup>Department of Economics, Pennsylvania State College of the Liberal Arts, University Park, Pennsylvania.

<sup>3</sup>Manchester Business School, The University of Manchester, Manchester, United Kingdom.

<sup>4</sup>Institut Francilien, Recherche, Innovation et Société, Université Paris-Est, Paris, France.

<sup>5</sup>Center for Science, Technology and Environmental Policy Studies, School of Public Affairs, Arizona State University, Phoenix, Arizona.

distribution of human biological samples. To parse that out, the samples have three main elements: first, they come with a rich dataset about their origin and with standard characterization; second, one of the rules of distribution is return of complementary information coming from the analyses made by users, or the notion of enrichment; and third, samples are a finite resource—meaning many possible aliquots for distribution.

These three elements warrant a number of considerations, such as providers making the content free. We can deduce that they do this because they expect it will generate added value for all researchers, bringing in the notion of a public research good, and in particular for themselves, as it seems they are also the first users of the biobank. Second, there are strong ethical rules to consider, in particular dealing with the privacy of individuals from whom the samples come. In addition, the resource is finite, so one can expect that any access to samples will depend on the potential scientific benefits of their use, driving in most cases conditional access, as in many large research infrastructures.

If I look at other more classical databases—without samples or material to store and move—whenever there is a possibility of emergence of a market, there are attempts, with start-ups and the like, to help its formalization and capture. The dynamics are that most such markets concentrate around a few actors and that later entry costs become higher. Another illustration is that the more concentrated the original resource, the more likely such a development.

Biobanks, it could be said, exist because of the network of providers. We can anticipate that providers deliver information and samples because they are interested in getting the returns from the amalgamated knowledge, but they expect this return free of charge or at the marginal cost of distribution. This means that any market will at best be made of those nonparticipating entities. Are they numerous enough?

In your question, the central funders of a biobank make a wrong initial assumption: if they wish the biobank to become self-sustainable, they should not fund the biobank itself, but give incentives to providers/users to invest in the creation and maintenance of the biobank. To put it another way, the biobanks are a public good and funders support the cost of the central infrastructure, then providers bear the costs of providing content and of marginal costs of the use.

I was struck in the reports of Biobanking and BioMolecular Resources Research Infrastructure (BBMRI), in that whatever banks they considered, the management and the biobank expertise represented between 60% and 80% of the costs. Then, I looked whether they took into account the people who take the samples in, I did not find that dimension in the costing. Why it is important for me is because I am unable to say what the difference is between the providers and the users, necessarily. How should you organize a system where the provider gives something for free and then when he wants a service out of it, pays for it?

**Dr. Yuille:** I can tell you my experience. We ran the UK DNA Banking Network, which was funded by the Medical Research Council (MRC) and which was put onto a cost recovery policy by the MRC. The way in which that network worked was that a dozen principal investigators (PIs) around the country were funded to collect patients in different diseases and they then sent the samples to us for processing, storage, and distribution.

The primary people to whom we distributed were the collectors themselves. So, collection A from PI A was distributed primarily to PI A. He or she—sometimes with new collaborators—was the main user of the samples. So, in this case, the provider and the user are essentially the same person.

**Dr. Eric W. Welch:** Yes, but I think one thing we could think about is that these interactions occur over time. It is not simply a repository; it is an active medium. It is an active place where materials and data are exchanged and used over time.

Within those biobanks, lots of things are added and knowledge is gained. Data are returned after the research in many cases to sit alongside the materials. People can see that at very different levels, and so the value of the bank increases.

The reason why an individual would want to buy back is because the group and the community have actually contributed to that bank in ways that increase the value of what had been placed in it originally. If it is done well, it essentially provides interest in the material that was deposited.

**Dr. Luke Georghiou:** The difficulty is it cannot be done perfectly. It can be done well, but it cannot be done perfectly, and there still remains a massive advantage in terms of knowledge of what the value of a collection is, which is acquired by the provider in the first place. He or she, the collector, understands the collection and the data behind the collection and the metadata and so forth far better than anyone just because it is not possible to capture all the experience that the collector has had in the process of collection in the database. You cannot capture all of that at the moment.

Until you can, it will not be possible for an investigator to understand what the collection is wholly about without the help of the collector. So, users and collectors cannot be fully independent of each other at this point.

**Dr. Laredo:** A further question on biobanks' financial models: Are prices usually different for different types of users?

**Dr. Georghiou:** Yes that is true.

**Dr. Laredo:** So, you could very well think that a provider would have a marginal cost of delivery as a pricing method. Another public user would have a certain cost that covers the maintenance, but not the initial equipment, and then the private sector person would have a cost that would cover a depreciation of the initial investment or something like that.

I am asking this because if you compare it with what happens in other infrastructures, the basic principle that you see is that you do not recover the costs of the initial investment. So, if you have an initial cost, you could introduce the depreciation part into your costing afterward.

**Dr. Georghiou:** I do not know if this will be true for the United States, but in the United Kingdom and for all of Europe, it would actually be illegal to provide a service to industry less than cost price.

**Dr. Yuille:** Luke, you are saying that legally there is a requirement to include for industrial uses the depreciation cost?

**Dr. Georghiou:** Full cost, I believe. The relevant regulations come from state aid that says that you should not provide subsidies to firms, particularly for large ones. Therefore, you should not provide services of any kind at less than cost.

**Dr. Laredo:** My thought is, after 15 years, if there is no major market for biocollections or biobanks, nobody has found a way of marketing it. I choose 15 years because it is a period since 2000 during which we may see whether, with all our start-up ecology and all our new things, there would be firms that could become real businesses. So, it is an open question to my colleagues in the United States. They might know better the chance that this might happen in the United States rather than in Europe.

**Dr. Irwin Feller:** Conceptually, in response to Philippe's question about the U.S. setting, a possible approach to establishing a biobank would be to approach venture capitalists for start-up funds for infrastructure and early operations and, assuming some evidence of commercial viability, to then float an Initial Public Offering (IPO) for expanded operations and long-term sustainability. This answer, though, flies in the face of current realities. In the United States, public sector suppliers, such as the National Institutes of Health-sponsored Human Genetics Cell Repository, already exist. As best I can determine, this repository already fulfills many of the same functions as a biobank. Operated by an independent, nonprofit biomedical research center, the repository receives, stores, and certifies cells, making them available to users, mainly for research purposes, at a nominal fee.

Thus, while one can always project the potential for additional privately sponsored biobanks, the absence of such activity suggests that investors do not see a viable market, at least at this point.

Reading the background report, *Biobanking Finances: A Socio-Economic Analysis and Review*, I also was struck by its account that a number of the organizations listed under the generic heading of biobanks were (to varying degrees) engaged in what I would term technology development: pharmaceutical firms, for example. This pattern points to a more general proposition: the more advanced or developed a field of research, the greater the potential for commercialization; conversely, the lesser the justification (on grounds of market failure propositions) for a public sector's role.

This has been indicated by U.S. experiences in agricultural and health-related research, as the internal dynamics of research discoveries in a field make its commercial feasibility increasingly apparent—the greater involvement of the private sector, with a corresponding push upon the public sector to direct its research to ever more upstream (basic) questions. There are neither clear nor fixed boundaries here. Rather, there are often gray areas of overlapping capabilities of relative interests and roles of the two sectors, with no well-defined algorithm to determine what is public and what is private. Answers to the questions of what and how much the public sector does and the terms of its relationships with the private sector tend to be contingent upon prevailing philosophies and/or political influences.

However, you also have private sector models where you have agriculture germplasm banks that are privately funded operations and they have specific kinds of collections that are in high demand, such as microbial collections.

In the United States, you have a lot of experimentation with this, and public funders are asking for the biobanks to figure out ways of sustaining what they do because it is an important kind of infrastructure. It is perceived to be an important infrastructure for science, and yet there is still a question of what mechanism do you develop to help sustain them? Right now, through a lot of experimentation, you can see different models going on simultaneously.

**Dr. Welch:** I would agree with that. In my experience in gene banks and genomic consortia, what is happening now is a huge amount of experimentation with these kinds of organizations. There are some that are clearly funded by public funds and that have been in place for 10 or 20 years. There are others that are moving off public funding and are considering charging user fees.

As part of these changes, there is an increasing effort to provide a range of services that would be of value to potential users. For example, some organizations offer technical, informational, or analytical services that help potential users understand, navigate, and better use material stored in biobanks. Many have substantial data storage facilities that are continuously updated, while others have sophisticated material collection and documentation systems that improve access and availability.

Private sector models also exist where you have agriculture germplasm banks that are for-profit businesses with special collections that are in high demand, such as microbial collections and seed collections.

In the United States, you have a lot of experimentation with this, and public funders are asking for the biobanks to figure out ways of sustaining themselves. Biobanks are recognized to be an important infrastructure for science, and yet there is still a question: given limited public funding, what mechanism do you develop to help sustain them? Right now, through a lot of experimentation, you can see different models going on simultaneously.

**Dr. Yuille:** As we discuss the models, we need to bring in the idea of ethics. For instance, we were obliged to sell DNA from patients by the microgram or nanogram. To avoid the criticism that we were selling human body parts, we presented this as selling access to samples. Is there any economic distinction? What is the role of ethics in creating a market?

**Dr. Welch:** The question of ethics has both human ethics and access divide dimensions. Both are economically relevant and have research consequences.

Access to the inputs to science—biomaterials for research in the form of human and animal tissues, plant and microbial germplasm, and DNA and genetic data—is a determinant of research collaboration and outputs.

There are at least two important perspectives on access to biological materials: macroinstitutional and microindividual. The first concerns how to make the inputs to science available for uptake and use to enable research that advances medicine and other fields. The structure and functioning of the system for accessing materials, as well as the quality, cost, and institutionalization of the services provided, constitute this macrolevel.

To parse that out, structure includes the number, specialization, and heterogeneity of biobanks. Functioning

concerns the linkage among the biobank nodes, communication and coordination, or fragmentation. In medicine, we know that biobanks are of varying sizes and while they are increasingly networked across the world, there is a certain degree of structural and functional fragmentation.

In agriculture, the structure looks different as there are many large gene banks that are global in scope, while global policies aim to coordinate global access to germplasm.

Macro-level factors—structure, function, and management—have a lot to do with access and accessibility. These factors tie in with the approaches in place to manage rights, ownership, ethical considerations, and compensation or recognition for access related to biomaterials. This includes balancing rights and ethics with the availability of the material for various different purposes—from knowledge creation to commercialization.

Micro-level considerations frame the second perspective on access, which concerns how individuals and organizations obtain material. This perspective is about how a scientist knows what is available and how to obtain what she or he wants. It also concerns the rules associated with material use and exchange, data associated with the material, obligations associated with managing the material during and after research, and obligations for contributing data and findings to the biobank.

Integration of the two levels, macroinstitutional and microindividual, creates a role for governance. Governance and management are costly for either the provider or the user. For the provider, effective management of materials, data, rights, and responsibilities is expensive. For the user, access is costly when researchers spend a lot of time to find material, there are delays in the provision of material, there are significant uncertainties about the material itself, and the constraints on use are complex. The context of access leads us to note that access to biological material represents a service rather than a good for sale.

Currently, there is significant fragmentation and heterogeneity in biobanking. In health, fragmentation exists because of the number of biobanks, lack of access standards, differences in materials management, and in the quality of information and data associated with the materials.

Because it is difficult to move toward standardization of access, the burden falls on the scientist. Some scientists are better positioned and have more capacity than others to navigate the access system; those with more experience, more funding, greater reputation, and better institutional connections will have more access than those who do not. Scientists with greater access will likely benefit in terms of collaboration, outputs, and reputation. The concern is that a poorly governed and managed system that does not reduce uncertainty, complexity, and fragmentation can create or exacerbate an access divide.

**Dr. Laredo:** When you discuss access, at the same time, you discuss the ethical aspects of it, which are the rights of the providers in a way or the right of the samples mediated by the providers.

**Dr. Welch:** Yes. Often human ethical rights affect access to samples, but more broadly, there could be a range of constraints and limitations associated with materials in biobanks. There is increased intellectual property associated with materials that are in banks—researchers have made

changes to materials and those are also in the banks. There are national ownership rights associated with biological materials in many countries.

This is certainly the case in agriculture and for other non-medical sciences, where national ownership or different kinds of sovereign rights are present. Additionally, constraints and limitations may be related to biosafety and biosecurity.

In health, ethical rights of donors and permissions to use samples are often the focus of discussion, but I think there is an increasingly complex set of rights, rules, and responsibilities associated with biological materials, and the services required to manage these are increasingly costly.

**Dr. Laredo:** Luke, is it for that reason that the people in the BETA Group in Strasbourg proposed a copyleft solution? The idea is exactly what Eric was saying—that people have property rights in the knowledge they add—and the solution that BETA mentioned is that they use something like a general license. They leave the copyrights to the biobank. So, you leave to another operator the management of the rights in a global way.

**Dr. Yuille:** Well, I do not know if that is really an issue for us because we have distributed several hundred thousand aliquots to different groups all over the world, and we have not had any issues arising in relation to intellectual property rights; nothing at all.

I think that makes sense because all that you are doing when you receive one of these samples is analyzing it to observe its components at a molecular level and to describe those components. It is simply an observation that you are making. You are not in any way transforming the material that you receive, except to enable the observation.

**Dr. Laredo:** Of the hundreds of thousands that you distributed, how many people give you back information that enriched the understanding of the sample?

**Dr. Yuille:** One of the requirements of the UK DNA Banking Network was that users should return the new data that they had acquired. That was impossible to implement.

**Dr. Laredo:** Okay, so that question of enrichment is not a real question.

**Dr. Yuille:** I think in more tightly governed contexts, it can be. I know that the NIH runs a very tight ship about data return for at least some of its samples that go out, but that was not the case for the UK DNA Banking Network.

For the UK Biobank project—this is the biggest epidemiological cohort in the world—samples are rarely distributed because the argument goes that we, UK Biobank, must keep control of all the samples, and when we decide that certain types of data will be extracted from all the samples or a subset of samples, we will decide to do that and we will do it in the best possible way at the time, and then we will enable access to those data to all interested parties.

So, they make access to data the critical step, and, in fact, you have to pay a small amount for access to the data at UK Biobank if you get permission to receive that access based on your proposal. So, this is a very different model, and actually I think it is a model that scientists need to pay close

attention to. It is really a very good model for ensuring the quality of data.

**Dr. Welch:** I have a question about that because that has come up in other circumstances. To what extent do you actually need the material to do your research? Can you just get the data or do you really need the material?

This question of the requirements for the research has come up more frequently, that is, what is the trajectory of research? Is it more toward data? Do we need a different model for that?

I would also just add my voice to the importance of data and return the data to the source as management and governance issues for biobanks. That is part of the complexity and part of the reason why the value of the material goes up.

**Dr. Yuille:** These are important questions. I do not know whether you get a certain kind of output from that method of not distributing the material and just providing the data, whether that pushes science in a certain direction.

**Dr. Georghiou:** One effect is that the control of what data are to be collected is in the hands of a small number of scientists; those who are most closely associated with the biobank, and the other effect is that the decision as to whether or not to undertake data collection of a new type or to undertake collection of data from that sample collection is then made directly and explicitly by the funders themselves. So, there is much less of a hands-off approach by the funders to the ways in which the scientists proceed with their experiments. It is much more in the direct control of the funders, which is an issue, and it is has both positive and negative consequences.

**Dr. Feller:** I agree about the importance of the institutional and organizational relationships among the biobanks, their sponsors, and the communities of contributors and users of their services. The governance arrangements set for biobanks will have major influences on collaboration structures, research questions, and trajectories of science.

**Dr. Laredo:** I can make a comparison with something very different; the characterization of nanomaterials. That is an experiment I have been following for a few years.

We have a big research organization in France and they said, "The quality of characterization is a priority, so we are going to build a central service where we are sure that the characterization will be done the right way."

At the beginning, people had no access to the equipment, so they were obliged to go through central service. Then, you could see them fighting to get pieces of equipment and funding from other resources, other funders. Then, in discussions with them, they say, "When we characterize, we see things we were not looking for." Research is all about these surprises.

So, if you give it to technicians who do exactly what you have asked, but do not look at what happens on the side, do not understand, then you lose that chance to really find something new. So, the centralization into a professional body to do the characterization or the analysis is something that will be resisted by the scientific community. There are things you will never learn if you just have the data.

**Dr. Georghiou:** Nor will you learn it (I think) if you outsource it to a private service provider.

**Dr. Laredo:** I agree with you. The question is: is this an intrinsic part of the research process? There are a lot of things you need to undertake yourself as a researcher to find those surprises. You make a hypothesis, and if your hypothesis can be falsified, then you are really learning something very important, but you may not know that if you just delegated the process as a service.

**Dr. Georghiou:** The same could be true in the context of the development of new ways of processing samples. It could well be that by doing that in the context of a research laboratory, you will pick up issues or insights that you would not know about if you had it done outside of a research laboratory context.

**Dr. Laredo:** So, in a way, it is the model of null distribution, I do not think it is the model of the future. It is a model for stabilized businesses. It is a model where knowledge is well established. It is a model for analytical purposes and personalized medicine, maybe where things are completely stabilized, but it is not a model for research.

**Dr. Welch:** I would like to put a fine point on the idea that genomic data may not be the same as biomaterials. There are different kinds of analytical techniques for accessing, integrating, and analyzing data across locations and individuals. Importantly, this type of pooling and production of metadata allows a certain type of access to information that differs from how material is accessed or distributed. The research environment for data and information is not the same in the laboratory as in the clinical environment in which biomaterials are being used. The ways in which materials are exchanged and used differ, often fundamentally, from the ways in which information is exchange and used. Similarly, rights, responsibilities, and even policies associated with access and use of data may differ from those related to materials, and so biobanks increasingly have these two different directions to manage and integrate. They have this dichotomy that will be shaping the future.

**Dr. Yuille:** I would say there are some basic observations that can be made and where it is okay to, as it were, outsource to a factory-type environment. That has proved to yield many positive results. There is no need for everything to be done within the environment of a research laboratory. There are some things that can be done outside.

There are some things, of course, in relation to the patients or the subjects that are always done outside. A lot of the measurement of biomarkers directly on patients before there being any biobanking at all, the clinical history of the patient, is based on data that are accrued in pathology laboratories.

**Dr. Yuille:** Moving on, the idea that science is a public good and the observation that markets can fail provided Richard R. Nelson and Kenneth Arrow with the classical 1960s rationale for public funding of research. Why was this? Can you explain these terms? Do you agree with these rationales? Is there more recent research that contradicts or strengthens these rationales? Are there new rationales?

**Dr. Feller:** The Nelson–Arrow market failure remains a foundational building block in accounting for public sector support of basic research. The applicability of the framework to the current status of biobanking and today’s discussion is limited, however. The framework applies primarily to considerations of governmental support for basic science. In the strictest narrowest sense, drawing the public good, market failure boundary lines involves assessment of the extent to which the conditions of nonrivalry and nonexcludability exist. As noted before, these conditions do not hold for the range of activities engaged in by a number of biobanks. Some portions of the activities currently engaged in by biobanks approximate technological development. Rivalry exists in who gets the biobank material, especially in terms of downstream applications. Excluding participants seems to be a rather straightforward matter.

Phrased more positively, one requires a detailed mapping of the activities of specific biobanks, especially documentation of their dominant emphasis on basic research, before employing the Nelson–Arrow framework as a justification for public sector support of biobanks.

More generally, speaking as an economist, I see the emphasis on formal economic frameworks as too constraining to contribute much either to an analytical or to a prescriptive understanding of the complex institutional setting described by other participants on this panel.

Our conversation has made me more appreciative of the complexity of the questions that Martin has posed for us as well as the contrast between the United Kingdom and the United States in their respective financial, organizational, and thus public policy approaches to establishing and sustaining biobanks. My knowledge of existing institutional arrangements is limited, but I am impressed with the ways in which the United States, through the National Institutes of Health (NIH), has addressed many of the concerns evident in Martin’s questions. For example, the NIH repository model that we mentioned provides for public sector funding of a nonprofit organization which receives, certifies, and distributes cells to users, primarily academic researchers, charging them a nominal fee.

My answer to the question, “Can you come up with alternative frameworks?” is yes. One reason why researchers would be motivated to submit samples to a biobank is that by doing so, they contribute to increasing the size of a common good resource pool, thereby contributing to the enrichment of work in their field of interest. Both those who contribute and the larger community of researchers benefit from individual contributions. Obviously, this scenario opens the possibilities of free rider behaviors. A special concern would appear to be opportunistic on the part of one actor who exploits the common good resource, to which one or several have contributed, by tweaking out its commercial applications and then proceeding to establish intellectual property rights.

The extent to which such issues arise and how they are resolved depend on the institutional framework surrounding the establishment of the biobank. To return to my comment above, the central issues surrounding establishment of the biobank appear to relate less to considerations of market failure and more to contract theory—the contractual arrangements that are set up among the funder, the repository, and the community of users.

Allow me to add a further example of the best analytical framework in which to present the case for public funding of biobanks—that of Don Stokes’ Pasteur quadrant. Listening to the discussion, it sometimes sounded to me that it was concentrated in the upper left-hand corner or Bohr quadrant. At other times, it seems to be in Pasteur’s quadrant. It seems to me our repeated references to the complexities surrounding the functions of biobanks and the related issues of public sector/private sector funding in large part derive from the empirical fact that biobanks operate in both quadrants.

Returning to the core question of the justification for public sector funding, to begin with, someone has to pay the capital or infrastructure costs for establishing the biobank. The rationale for public sector support is not market failure *per se*, but rather considerations of economies of scale and economies of scope. They also relate to standardization of criteria governing submission, quality control, access, and use. Most critically, it involves establishing a governance regime. Noting again that I have only limited familiarity with the spectrum of biobank arrangements, I still would propose a funding and governance model similar to the one now operated under NIH auspices in establishing a model for biobanks.

So, in building your case, I would start with detailed accounts of the public good nature of certain dimensions of science, and then move on to justifications relating to the governance of science, and standardization and certification for quality assurance. Recognizing that it is already a crowded field, you are almost trying to establish your market position relative to others out there who, however logical your argument may be, may feel that whatever it is you do begins to chip away at their presence.

**Dr. Yuille:** Biobanking is becoming integrated into healthcare. Indeed, the distinction between research and healthcare is becoming increasingly blurred. For example, clinical trials increasingly need to be conducted as real-world trials (i.e., in the context of normal treatment or prevention) to measure more accurately the effects of a new intervention. What does this mean for the funding of biobanks and similar research infrastructure that has emerged from research?

**Dr. Georghiou:** I think one of the reasons that we in this field started, with the traditional economics of basic research, was almost to provide a reference point from which we could move away. That has some important assumptions about knowledge, indivisibility, nonexcludability, and nonrivalry. Those conditions, to me, only partly apply in the case of biobanking. So, if we hold that, then I can come to the question itself, which was to look at consolidation and sharing and then where would we go beyond those.

Clearly there must be scope. There must be a possibility to get economies of scale and scope in biobanking in the nature of it being a capital-intensive activity. So, we could see that process costs per unit could benefit from scale, and more importantly, still the analytical value from emerging data and sample sets rises under certain conditions.

Economies of scope come from higher value from investment in biomedical research. If you can reuse samples, if there can be secondary uses—that is, if something is done on behalf of researcher A and you give it back to researcher A, but researchers K to Z can also use it—then, obviously, there are much greater returns to the initial investment.

This is closely tied in to the data associated with samples. If this is not also compatible and perhaps continuously updated, the samples themselves are not likely to be useful for future research projects, as far as I understand the science of this.

So indeed, some of the samples, as with the UK Biobank project mentioned earlier, would rise in value through the life of the project if there is continuous updating of those data. So, all of this creates a complex market for biobanking. Going back to cost-free sample collection from the point of view of a biobank could be seen as a free good in the sense that it is paid for out of research grants.

However, even so, unless you are incentivizing those who are doing the collecting to adopt standards and observe the appropriate ethical principles and so on, the sample itself may not have that value in other circumstances.

We discussed it in our team in the context of the economic perspective of fungibility, which means that one good is the same as another in a market. So, a kilogram of gold is always the same as another kilogram of gold. You do not mind if you swap it.

One sample, though, is not the same as another sample. They would have different prices and values. Then, at the time of storage, you do not know the future value of your samples. The standards may become more demanding as new discoveries are made in medical research, which means that older samples will not have been collected to answer your future questions. It is not a bank in the sense that things stay there with constant or value. It could go up. It could go down.

As has been raised earlier, they are also a finite resource with costs just to keep them there as well. All of these things combined indicate that while there are benefits in economies of scale, individual biobanks are not particularly incentivized to try to achieve those economies of scale. We have already heard that they would commit to costs that are unlikely to be recovered.

So, unless the system as a whole can find some means to achieve these benefits, I suspect that we are going to stay very much as we are with what we describe as the fragmented system.

So, to me, the question about consolidation and sharing is as much a question of pathway, as to whether or not there are benefits to having it.

**Dr. Yuille:** I am wondering whether are there other studies that economists in particular could perform to test the success or failure of models of biobanking?

**Dr. Feller:** Two different tests come to mind. One is if you fund an organization, even such as yours, and try to make it self-sustaining, you test whether or not it would work. You essentially frame it with some period of time, and you basically use financial viability as the ultimate test. This is a very simple, but very conventional, notion.

If there is a market for something, do you get a foundation or sponsor, the government, to fund it as a start-up? Then, you basically see if it becomes self-supporting. This is the National Science Foundation (NSF) model in a lot of the centers that they have funded, particularly those with ties to industry. Can this become self-sustaining over time?

In general, almost all those experiments show that these things are not self-sustaining and that basically at the end of

the funding period, they have to dramatically cut back their activities, particularly those that are manifestly public good types of activities, and narrow their focus into those things for which there are markets.

It reminds me of my early involvement in the United Kingdom toward the end of the Thatcher administration where I heard the Minister of Finance say that if academic research has value, industry should pay for it and there is no need to have public sector support. It seems to me, I still hear echoes of that in this conversation.

Another test, which I think is a more substantive one, is to consider the competition. For example, in this case, let us say, between the United Kingdom in this field and the United States in this field in terms of scientific output, alternative governance, and funding regimes for supporting biobanking materials. I think that will be the ultimate experiment—which regime produces the largest amount of the highest-quality science as a function of its support of its scientific infrastructure.

**Dr. Yuille:** So, this sounds like a job for economic historians, would you say, rather than economists.

**Dr. Feller:** I would not call them economic historians. It is program evaluation by people who work in science policy or the sociology of science. For example, there are some studies being done now, actually completed, by economists at Massachusetts Institute of Technology (MIT) comparing scientific output from block grants, let us say, on the Gates Awards or block grants against NIH project funding. That is a raging issue in science funding. Yes, it can be done with economics, but with evaluative sociologists as well.

**Dr. Laredo:** We are discussing two very different institutional settings, and the types of problems, in terms of funding models, if we take the initial terms by Irwin, really are set in very different ways. It tells us that the role of local institutional conditions is very important, and I like very much the differentiation that Marianna Epicoco makes when she discusses the dynamics of knowledge production.

She differentiates the field level and the space level. The field level is what happens within the field, the way scientists define the research agenda, the way they define the ethical conditions of the user sample, etc., and most of the scientists, whether they are from the United States, United Kingdom, etc., might share views about that.

However, this is one way of looking at things. The oversight is that everybody is employed and gets resources in a limited space. If you are in the United Kingdom, in France, or in the United States, and in these systems, the way things work and the types of debates about the institutional settings are different.

I use that example when I compare what I do when I am in the United Kingdom with what I do when I am in France where I am in two very similar laboratories in terms of size. In the United Kingdom, we look for grants, and in France, we look for labelization, a proof that we are acceptable and which opens us to the market, while here in the United Kingdom, what opens us to the market is the money we get from the funding agencies.

So, the institutional systems drive two very different sets of questioning. In a way, when Irwin says this is how it works at NIH, it defined a system that seems to be very

different now to the way it works in the United Kingdom. So, the practical conditions for sharing, etc., *de facto* differ between the different spaces.

**Dr. Feller:** I think Philippe has captured it. I am struck by the manifest differences between governance regimes. However, it ties in and shapes a lot of what you were referring to as the cultural issue because we take as given the funding environment and the rules of the game of our particular setting, often our institutional setting where we are employed and our funding sources.

**Dr. Laredo:** If I go one step further, we may share the notion that collections of human biological samples are critical for science. However, we may go about it in a very different way; in the United States, they may say, “I do them. I keep them. I open them, and it is my business,” and the funding agency in the United Kingdom says, “I do not want to fund them. I will not pay the cost.”

Luke has proposed a system whereby in a way the funding agency would create something similar to the NIH with a differentiated pricing, which would help support its maintenance.

**Dr. Feller:** In my view, the most persuasive argument for U.K. support of biobanking rests less on the Nelson–Arrow market failure framework. Rather, it is international scientific competition. The U.K. funding model is likely to put U.K. researchers at a disadvantage in pursuing lines of re-

search that require access and use of biological materials, to the disadvantage of U.K. science (along with the attendant societal and economic benefits that flow from new findings), as well as the reputation and competitive attractiveness of its research institutions.

**Dr. Georghiou:** Yes, I agree.

**Dr. Yuille:** The point that Philippe makes is really important—that the cultural and organizational context in which science is carried out plays a major role in determining in what direction policy goes on biobanking and on the funding of biobanking in those different countries.

Therefore, it may make a lot of sense for us to take this conversation forward, if we can, not just in our countries but also more widely. Thank you all for the great discussion today and I look forward to future work on this important topic.

Address correspondence to:  
*Martin Yuille, PhD*  
*Faculty of Biology*  
*Medicine and Health*  
*The University of Manchester*  
*Stopford Building*  
*Oxford Road*  
*Manchester M13 9PT*  
*United Kingdom*

*E-mail:* martin.yuille@manchester.ac.uk