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Trust in Biobank Research

Meaning and Moral Significance

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Abstract

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What role should trust have in biobank research? Is it a scarce resource to be cultivated, or does its moral significance lie elsewhere? How does it relate to the researcher's individual responsibility?

In this thesis I draw four general conclusions. First, trust is still very much present in at least some biobanking settings, notably in Sweden, but possibly also internationally. Second, a morally relevant conception of trust entails that to be trustworthy, researchers must consider the normative expectations that people have of them, and renegotiate expectations that are mistaken. Third, this conception differs from "public trust" assessed through surveys. The main use of the latter is to legitimate policy, not to identify moral duties. Fourth, in spite of ethics review, guidelines and informed consent procedures, ethical issues will always arise during the course of a research project. Researchers can therefore never avoid their individual moral responsibility. Ensuring that one is adequately trusted is one step towards conducting morally acceptable research.

Study I indicates that few Swedes refuse storage of samples in healthcare-associated biobanks and their use in research. Study II suggests that people are somewhat more willing to donate samples than surveys indicate, especially when approached face-to-face by health care personnel. Relationships of trust might thus be important in people's decision-making. Study III investigates trust as a moral concept. The trustee is often in a unique position to determine what the other's trust amounts to. When it is mistaken, the trustee has an obligation to counteract it, compensate for it, or renegotiate the expectations that cannot be met. In Study IV, I critique the feasibility of guaranteeing the trustworthiness of the research apparatus through formal measures such as ethics review and guidelines. Not only are there limitations of such measures to consider. They also risk blinding researchers to ethical issues that are not covered by the rules, fostering moral complacency, and alienating researchers to ethics.

Keywords: Biobank, biobank research, bioethics, biobank ethics, research ethics, trust, trustworthiness, moral responsibility, informed consent, ethics review, ethics guidelines

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To Hannalina and Hilda

I hope that you will
find both trust and
trustworthiness
in your lives.

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I JOHNSSON, L., HANSSON, M. G., ERIKSSON, S. & HELGESSON, G. (2008) Patients' refusal to consent to storage and use of samples in Swedish biobanks: cross sectional study. *BMJ* 337:a345.

II JOHNSSON, L., HELGESSON, G., RAFNAR, T., HALLDORSDOTTIR, I., CHIA, K. S., ERIKSSON, S. & HANSSON, M. G. (2010) Hypothetical and factual willingness to participate in biobank research. *Eur J Hum Genet*, vol. 18, no. 11, pp. 1261-4.

III JOHNSSON, L., HELGESSON, G., HANSSON, M. G. & ERIKSSON, S. (2012) Adequate Trust Avails, Mistaken Trust Matters: On the Moral Responsibility of Doctors as Proxies for Patients' Trust in Biobank Research. *Bioethics*. doi: 10.1111/j.1467-8519.2012.01977.x.

IV JOHNSSON, L., ERIKSSON, S., HELGESSON, G. & HANSSON, M. G. Making researchers moral: Why institutionalised distrust might not work. *Manuscript*.

Contents

Introduction

If this book were a novel, I would not fret about the opening line.

"It all began with a newspaper scoop."

Whatever doubts one might have about the factual accuracy of the series of articles in *Aftonbladet*—one of Sweden's largest tabloids—that hauled the *biobank* phenomenon from the relative safety of laboratory storage rooms into the public eye in 1999, at least it had an impact. Not that many people outside of the biobanking community have necessarily become much acquainted with them (with the notable exception of health care personnel, who tend to associate the term with unwelcome paperwork). But the attention that the scoop stirred up did contribute—at least if the tabloid's own reports on the matter are to be believed—to the enactment of a new law. In its aftermath, with all the legal and ethical inconsistencies and other issues that now need to be discussed and resolved, many bioethicists have secured their employment for many years to come.

The newspaper scoop in question lacked every hint of subtlety. "Scientists perform secret experiments on parts of your body," page one proclaimed in customary huge, bold letters (Trägårdh and Ringman, 1999). Reality, as usual, did not quite live up to the drama. The "body parts" in question were leftover samples from health care, routinely stored in biobanks for many decades with the primary aim of securing quality of care. The ominously ringing "experiments" were, from the scientific point of view at least, quite mundane research projects. And nothing of what was taking place was really "secret"; the practice was simply unknown to the public because to this point, no one had really bothered to ask questions about it.

Several articles highlighted the fact that both storage and research took place without explicit consent from patients. This much, at least, was true. The moral implications were much less obvious. The stance of the reporters was clear: Research on stored samples without explicit consent was, just like research on humans without explicit consent, to be regarded as illegitimate if not illegal. Donors, it was claimed, had in effect lost ownership of their own body or life. Specific attention was given to the PKU Biobank, where dried blood spot samples from newborns have been routinely stored since 1975.[1]

[1] All newborns in Sweden are screened for phenylketonuria, from which the PKU Biobank has derived its name, and a number of other severe metabolic diseases. Blood samples are stored for quality assurance and to facilitate the development of new diagnostics tests.

An elaborate picture was gradually painted of a totalitarian state with secret genetic databases of its citizens and of scientists trying to resurrect the pseudo-science of racial biology.

Perhaps no less can be expected from a tabloid. This time, however, the rhetoric was apparently too much to ignore. Within six months, the Government initiated an inquiry that resulted in the Swedish Biobanks in Medical Care Act (henceforth referred to as the Swedish Biobank Act) in 2002. One of the many rights that the Act granted to sample donors was the right to withdraw consent (actual or presumed) to storage or use of biological samples. As an unintended side-effect, we have gained a tool to evaluate the effects of various scandals and controversies on public attitudes.

The PKU Biobank in particular has come to act as a public thermometer of sorts. In October 2004, Swedish newspapers reported a sudden burst of withdrawals of consent, with 445 people having requested destruction of their samples over the past year (TT, 2004). This was quite unprecedented, a twenty-six-fold increase from the 17 (yes, seventeen) withdrawals the year before. The reason for this sudden interest in stored blood spots was sought in the media attention that followed the exceptional use of this biobank in solving the murder of the Swedish Minister of Foreign Affairs, Anna Lindh, in 2003 (Kettis-Lindblad et al., 2006). The withdrawal rate increased further until 2006 and then seemed to stabilise at 1000 people a year. The year of 2008 proved an exception, with a temporary doubling of withdrawals. Again, the burst was preceded by a public controversy. This time, a new law was about to be passed which enabled the National Defence Radio Establishment (FRA) to tap all cross-border Internet and phone communication. Many people saw this as a step toward a "big brother"-like state; indeed, the bill was passed with a slim majority, and only after the proposal had been revised to allow better protection of individual rights. The fact that this matter is entirely unrelated to research—or to the PKU Biobank for that matter—speaks volumes about people's fears. It also suggests that Swedes in general worry more about Orwellian tendencies than about mad scientists.

Obscure as it may be, biobank research is rapidly gaining ground, not least thanks to recent technological advances. It also raises ethical questions. It has been argued, for instance, that one of the most fundamental safeguards in medical research—informed consent—is not a practicable alternative in biobank research. Alternative implementations may have to be considered, which in turn raises questions on how the interests of various stakeholders ought to be balanced. Theoretical frameworks that were useful in other contexts may not transfer well into this one. Some of the questions that have re-emerged are conceptual: What does "autonomy" mean in this context? Does autonomy relate to informed consent the way we used to think it did? Others are normative: How do we strike a reasonable balance between privacy and research efficiency? What kinds of research are worthwhile? How should research be regulated? Under what conditions can we allow

donated material to be commercialised? Some empirical questions may be just as important: What are people most concerned about? What do they think of various regulative policies? The list is virtually endless and continues to grow alongside biobank research itself.

Traditionally, biobanks used in medical research have been of one of two kinds: clinical biobanks where leftover samples from health care are stored and possibly used in research, or dedicated research biobanks built up during the course of a study. However, in the last decade, a number of large-scale population-based biobanks are being established worldwide, such as the UK Biobank, the Icelandic Health Sector Database with its associated genetic and genealogical databases, HUNT in Norway, the Estonian Genome Project, and LifeGene in Sweden. As researchers have increasingly come to collaborate between institutions and across national borders, the ethical implications of disseminating sensitive data need to be reassessed. Involvement of commercial interests in publicly funded research is another source of concern to many people, even though it may significantly speed up the development of new methods of treatment.

"Issues", "concerns", "problems"—these are the very sustenance of bioethics. Major scandals have often concerned harm and wrong done to research participants, but there are others of note. Reports of scientific misconduct, for instance, serve as a constant reminder of the brittleness of researchers' integrity. Certain kinds of research are controversial not because of any risks they pose to individuals, but because of how they might affect society as a whole. Unsurprisingly, bioethicists are sometimes accused of complicity in the growing bulk of regulations and guidelines that researchers feel obstruct important research goals. Three of my main normative contributions relate to this observation in different ways.

First, bioethics is in some ways *reactive*. In the face of problems, one looks for solutions. As often as not, these come in the form of new regulations, standards or guidelines. The pattern becomes most obvious in conjunction with a public scandal. A predominantly reactive bioethics, if left unchecked, can severely limit researchers' opportunities for taking responsibility for their work and thus for the trustworthiness of the system (Study IV).

Second, the tension between individual rights and public good is no longer a strictly two-sided issue. After many years of subsistence in the shadow of the ideal of the enlightened, self-governing citizen, *trust* has enjoyed somewhat of a renaissance in bioethics, although with a significant drift in its meaning and usage. Today, some authors argue for stricter regulation or more demanding formal procedures because they believe that public trust is at stake and would be thus secured. Public trust, then, is seen as a matter of governance—sensitive to public consultation, for sure, but governance nonetheless. In contrast, I will argue that trust is best understood

in, and best maintained through, interpersonal relationships (Studies I and II).

Third, the moral relevance of trust is often misconceived. Trust, it is claimed, must be cultivated to ensure continued support for biobank research and better health care in the future. But in chasing trust, are we making the system more trustworthy, or less? I will argue that trust implies certain moral obligations, and that determining what those are is not always straightforward (Study III). Easy or not, it is in pursuit of those duties, rather than in the pursuit of trust itself, that the proper use of trust becomes manifest.

Elephants and agendas—Personal reflections

In the article where he exposed 22 cases of unethical research in 1966, Henry Beecher observed that "[a] far more dependable safeguard than consent is the presence of a truly *responsible* investigator" (1966, p. 368). He later admitted that virtue ethics alone is insufficient to protect patients against exploitation (Baker, 1998, p. 324). I suspect that if Beecher's original claim were reiterated today, gut responses would fall broadly into two categories: "No way!" and "Yeah, sue them if they try anything!" And that is a shame. In this thesis, I construe individual responsibility as something other than legal liability. I will argue that while it should not be our only safeguard, it must not be forgotten. But first, I must digress.

It is widely believed that researchers should not have personal agendas. The historical ideal of "disinterested inquiry"—pursuing the truth for the sake of truth—has lately found company in "the good of all" or "the betterment of humanity", though these upstarts are occasionally frowned upon. Even commercial interests are grudgingly tolerated, for the good of all of us if nothing else. But *personal* agendas remain highly suspect. Ironically, after all evil that has been done in the name of ideology, or religion, or national security, we still worry most about individual idiosyncrasies. And so we regulate, and centralise, and bureaucratise.

An agenda that cannot quite be concealed but is not questioned outright becomes an elephant in the room. It makes us suspicious of the researcher's supposed impartiality. But elephants are not necessarily sinister. In systems where doctors double as torturers, those who refuse to take part are the ones thought to have "personal" agendas. They often face sanctions as a result (Riquelme, 1998). In bioethics, elephants are more commonly seen than in other fields because the act of uttering normative statements *is* to point at them: "*This* is what I think!" Nevertheless, since elephants can be dangerous, they should not be allowed to run rampant.

Readers of this thesis will no doubt become familiar with my elephant. It is not about personal gain; it is personal only in the sense that I have strongly felt ideas that I need to develop and propose. My journey begins with doubt.

Sceptics to ethics as a science are sometimes heard claiming that it is just a matter of voicing opinions. Ethicists, on the other hand, like to think that reasonable justification for their moral convictions can be found in moral principles. Their elephants stand, as it were, on feet made of principles.

Perhaps due to my disconcerting doubt of this image, a series of entries on the Ethics Blog (Segerdahl, 2012a, Segerdahl, 2012b) resonated with me. What if, Pär Segerdahl asks, our moral convictions are not derived from the principles that justify them? Do we not often look for evidence to support beliefs that we already have? If our grand principles turn out to be nothing but projections, is not the scientific status of the whole bioethical enterprise thrown into doubt? To my great relief, Pär argued, rather convincingly, that while convictions are not derived from principles, neither is the reverse the case. Rather, convictions and principles are simply different parts in systems of thought. Occasionally, alien thoughts encroach on our thinking; when they are insistent enough, we reach a tipping point—upon which we find that our earlier convictions and principles must be abandoned, and new ones embraced. But we do not abandon ethics as such. It is not its principles that make ethics a science, but the activity of approaching problems through systematic reasoning. That is how I will carry out my "agenda" in this thesis.

Time has come to stare up the elephant's trunk, as it were—the thing that bioethicists like to call moral intuition. Mine is a strong one; no matter how I wiggle, its grip of me remains firm. I state it thus: *Moral judgment must never be reduced to rule-following.* This particular intuition was the reason that Kant struck a note with me, though I am far from a hard-boiled Kantian. It also runs like a drone note throughout my account of trust. I do not mean to say that morality must reject rules; only that once rules are prescribed by an authority, principled thinking risks being forgotten.

Such displacement of ethics would be catastrophic. This conviction is fundamental to my thesis. I will present arguments to support it, certainly; but abandoning it was never really an alternative for me. Maybe that makes me biased; but in that case, so are those who argue for stricter control because they firmly believe researchers to be untrustworthy. I hope that my particular bias will make for an interesting read.

Biobanks in modern medicine

Though the term "biobank" is a rather recent invention, what it refers to is not. According to a commonly accepted definition, biobanks are systematic collections of human biological material and associated data (Cambon-Thomsen, 2004, p. 866). Pathologists recognised their usefulness in exploring the cellular basis of disease already in the 19th century (Lindberg, 2003, p. 21). In modern health care, biobanks are all but indispensable. To successfully combat recurring cancer, for instance, one may need to compare new samples to those taken at disease onset, which would not be possible unless samples were routinely stored (Hansson, 2007).

Biobanks may also benefit health care indirectly by facilitating research into new methods for diagnosis and treatment. So-called "clinical" biobanks—collections established primarily to allow safe and efficient diagnosis and treatment of those patients from whom the samples were taken—have proven useful in certain kinds of research projects. The Swedish PKU Biobank, for instance, has been used in epidemiological research, and "Pap smears" (cytological samples from the cervix of the uterus) have been used to prove a relationship between Human Papilloma Virus (HPV) infection and cervical cancer (Wallin et al., 1999).

Other kinds of biobanks include those associated with cohort studies and population-based biobanks. Cohort studies are, as the name indicates, research projects carried out on large numbers of people. They are usually designed to investigate the relationship between various genetic, environmental as well as life style-associated risk factors, and a few specific outcomes (for instance, morbidity and mortality in cardiovascular disease). Health and lifestyle data are collected along with samples at the onset of the study and sometimes also continuously during its course, typically for one or several decades. Once a study has been completed, accumulated samples and data can be used for other research purposes. Population-based biobanks, in contrast, are not research projects *per se* but rather infrastructures expressly designed to support any number of studies. Both designs allow prospective studies through which researchers can draw conclusions about causal relationships between risk factors and disease.

Current challenges and promises

The current trend in biobanking is to collect *more data*—both genetic (including data from whole-genome sequencing) and phenotypic (diagnoses, risk factors, physical and metabolic parameters)—in *larger datasets* (Harris et al., 2012, p. 1105). Larger collections of samples and data allow researchers to investigate multifactorial diseases—many of which are common ones—where the contribution of any single factor is too small to be studied prospectively using smaller datasets (Hansson et al., 2006, Kaiser, 2002). Technologies for extracting and processing data from biological material are becoming ever more powerful (European Commission, 2012, p. 8). At the extreme end, researchers "mine" the data for correlations without *a priori* hypotheses (Gulcher and Stefánsson, 2000, p. 1827). In theory, there is no upper limit to the amount of data that can be stored even in a limited physical space, and high-speed internet connections make transfer of information between researchers fast and cheap compared to handling physical samples. In practice, biobank researchers constantly struggle with an ever increasing need for digital storage space and computing capacity.

In the case of rare diseases, obtaining enough samples remains a major hurdle. Collaboration between biobanks, even across state borders, is necessary to maximise resource utilisation and promote synergy (Harris et al., 2012, p. 1110, Steinsbekk and Solberg, 2011, pp. 240–241). The European Commission envisions a pan-European infrastructure linking biobanks from different countries. This would allow researchers to access samples and data on a much grander scale than is the case today. For this to be possible, harmonisation of guidelines, standard operating practices and exchange formats is key. The BioBanking and Molecular Resource Infrastructure (BBMRI.eu) is one of several such networking initiatives (European Commission, 2012, pp. 19–20).

New insights into interactions between genes and environment in disease development have given rise to significant optimism that diagnostics and treatment for many diseases could, in the future, be tailored to the needs of particular patients. This vision is commonly referred to as *personalised medicine* (European Commission, 2012, p. 17). The enthusiasm surrounding biobank research in general and personalised medicine in particular has sometimes been accused of bordering on hype (Kaiser, 2002, Sutrop, 2007, p. 196, Racine et al., 2006, Hofmann, 2009, p. 127, Dickenson, 2012). Though many biobank research projects have successfully generated new knowledge, it is not self-evident that such research is always the best or most cost-efficient way of improving people's health. Several different concerns have been expressed in this regard (Kaiser, 2002, Khoury et al., 2007, Dickenson, 2012). First, the major causes of many common chronic diseases are already known to be diet and lifestyle factors. In the case of adult-onset diabetes for instance, genetic tests may add little that cannot already be

learned from family history, and do not necessarily provide any additional incentive for behavioural change. Second, genotypes which are strongly associated with disease may nevertheless have low penetrance—that is, people with the disease often have the gene, but most people with the gene do not have the disease—which makes genetic testing cost-inefficient and potentially stigmatises people for no or little gain. Third, where access to health care is unequally distributed, focusing on high-tech solutions risks increasing the divide between social groups. Fourth, in order to tailor therapy to particular genotypes, one needs to replace a small set of relatively "broad" drugs (such as chemotherapy in cancer treatment) with a much larger set of "narrow" ones; pharmaceutical companies will thus be able to create new niche markets to increase their revenue and, by implication, health care costs.

Nevertheless, if conducted wisely, biobank research has the potential to produce knowledge that can be used to direct both individual-level and population-level interventions. Better insight into gene-environment interactions could allow clinicians to target screening tests to patients at risk without burdening others with information that lacks validity. In other cases, subpopulations with a high prevalence of high-risk alleles could receive interventions without individual patients ever being tested . The validity and effectiveness of genetic tests is itself an area of research which could be approached through "human genome epidemiology", that is, the application of epidemiological methods to population-level gene variation (Khoury et al., 2007, pp. 313–314).

Traditionally, there has been a divide between health care and medical research in that the former concerns itself with the individual patient's health, while the latter aims to create generalisable knowledge (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979). The difficulties inherent in translating data gained from samples taken from a person into knowledge that can be directly applied to that person's care is one reason for upholding this distinction. It has been argued, for instance, that findings should not be returned from research projects to participants on the individual level (Forsberg et al., 2009, p. 1548, Solberg and Steinsbekk, 2012). Some biobanks—notably, the CuraRata biobank at Leiden University in the Netherlands—challenge this tradition by embedding the biobank in a health care setting. Not only are samples taken for both diagnostic and research purposes, but results from patients suffering from similar conditions are integrated and used to adjust the treatment strategy (European Commission, 2012, pp. 56–57). While theoretically appealing, it remains to be seen if such projects can carry the weight of their promises.

Ethical issues and concerns

The practice of extracting information from biological samples can itself be a source of worry. Genetic data in particular is sometimes awarded special status compared to other kinds of information about persons—a position commonly referred to as *genetic exceptionalism* (Manson and O'Neill, 2007, pp. 131–133). Sometimes this is because DNA is seen as the essence of a person, alternatively as the blueprint that reveals "everything" about him or her. Some people describe it as sacred: "I consider that absolutely sacrosanct, that's ME, really the inner me they're looking at." (Levitt and Weldon, 2005, p. 314) These are variations on a single theme sometimes referred to as *genetic essentialism*. Especially with the advent of whole-genome sequencing, it is becoming more widespread and insistent (Steinsbekk and Solberg, 2011, p. 239).

An alternative justification of genetic exceptionalism points to the sheer amount of information that can be extracted from biological samples as well as its "sensitive" nature. While the former claim is incontestably true, the latter is problematic. Let us first note that without further qualification, it is clearly mistaken. Granted, *some* genetic data is, to the extent it can be interpreted correctly, information about the health and constitution of individuals, and thus potentially sensitive. Other times however, the reverse is the case: We commonly regard someone's religious and political beliefs as more sensitive than, say, eye colour, though the latter but not the former is a genetically determined property. Much of the data gathered by researchers to study disease mechanisms cannot be meaningfully described as information about the individual at all despite being genetic in nature (Manson and O'Neill, 2007, pp. 136–137). Although many facts are both genetic and sensitive, the sensitivity of facts does not appear to depend on their being genetic. Some genetic facts might be sensitive because they refer to properties that can be inherited. Then again, so are many social and lifestyle factors, although through non-genetic mechanisms of inheritance.

What is crucial, one could argue, is rather to what uses the data in question is or can be put. In this regard, genetic exceptionalism may be a self-fulfilling prophecy. Even when its clinical significance is uncertain or questionable, genetic information may be stigmatising. For instance, a middle-school pupil in California was recently forced to transfer to a different school due to carrying the gene for cystic fibrosis. Though he did not have the disease (most carriers do not), it was feared that he would develop it and thus come to pose a risk to another pupil, who did have the disease, through bacterial cross-contamination (Flam, 2012). The stigma was caused by hyping the gene, proving, in a sense, genetic exceptionalism right. Similarly, genetic data is potentially interesting to insurance companies or potential employers (Helgesson et al., 2007, Ashburn et al., 2000, p. 3378, Levitt and Weldon, 2005, pp. 316–317). When the Icelandic Health Sector

Database (HSD) was conceptualised by the biotech company deCODE in the late 1990s, its founder expressed interest in selling information to the insurance industry (Rose, 2001)—though, one may presume, in an anonymised form.

Clinical biobanks in Sweden

Before the Swedish Biobank Act was passed in 2002, samples obtained from patients for diagnostics and follow up purposes were routinely stored in biobanks for shorter or longer periods of time. "Routinely" here implies most of the time, effortlessly, and without anyone thinking much of it. The practice was but a small part of the extensive public health care system that had been built during the second half of the 20th century. In this setting, it is not surprising that one did not ask patients what they thought about having tissue stored—tissue that was, after all, no longer of any use to them. It would be misleading to say that consent was presumed; in all likelihood, the practice was regarded unproblematic, and consent was never even considered (Hoeyer, 2008, p. 430). From time to time, samples stored in these health care associated biobanks were used in medical research, again without consent, and again without the practice being considered problematic.

The Swedish Biobank Act

For better or worse, the Biobank Act put an end to this tradition by introducing several requirements and restrictions pertaining to the establishment of biobanks, retrieval and use of samples, anonymisation and coding procedures, and dispersal of samples and data to third parties. Notably, the Act also prohibits storage of samples without prior consent and gives the patient the right to revoke his consent at any time (Sveriges riksdag, 2002).

As noted earlier, the practice of storing samples is a prerequisite for safe health care. When the Biobank Act was enacted, great care was therefore taken to ensure that critical routines would as far as possible remain undisturbed and to avoid bloating the bureaucracy. The Act exempts samples taken for short-term storage—by convention, less than two months—from many of its requirements. The vast majority of samples taken for biochemical analysis fall into this category. Other kinds of samples, notably biopsies, cervical smears and blood samples for serological analysis, are often stored longer, and therefore generally fall under the Act.

Neither the Biobank Act nor the additional directives issued more recently by The National Board of Health and Welfare (Socialstyrelsen, 2008) offer many details on how consent is to be obtained. Interestingly, no

signature from the patient is legally required for the decision to be valid. While health care and research have traditionally been considered separate activities that occasionally engage in a potentially problematic relationship (World Medical Association, 1964), the Act moves in the opposite direction. Implicitly, the practice of oral consent which is seen in health care is allowed into medical research. Quite in line with the general requirement on health care professionals to document all interaction with the patient, consent or refusal must be documented by the caregiver. The patient's medical record is usually used for that purpose.

Organisation and governance

In Sweden, public health care is governed by twenty-one autonomous, politically elected County Councils.[2] As most counties are too small to support all kinds of highly specialised health care, County Councils collaborate over certain shared resources in more loosely-knit organisations known as health care regions, of which there are currently six. Each health care region has at least one university hospital at its disposal. University hospitals provide specialised health care to the population in its own county as well as highly specialised health care to patients from other parts of the region. Counties that lack a university hospital have at least one county hospital that provides specialised health care to its citizens. Until a few years ago, a large number of smaller hospitals (typically several in each county) provided specialised care within fields with high throughput, such as internal medicine; but with few exceptions, the trend has been to centralise such resources as well. Lastly, publically funded health care centres,[3] of which there is one or several in each municipality, provide primary care, which constitutes the bulk of Swedish health care.

In the face of the need for an organisational structure to govern, co-ordinate and oversee the numerous biobanks across the country, collaborating through the same channels was a natural choice. The County Councils thus installed six Regional Biobank Centres (RBCs), one for each health care region. On each of these centres rests the responsibility for maintaining a Regional Biobank Register (RBR) where data on all biobank samples obtained in the region are aggregated and stored together with their consent status. Besides operating RBRs, the role of RBCs is primarily to accumulate and provide knowledge about the operation of biobanks (Nationellt biobanksråd, 2009, p. 9). They collaborate through The National Biobank Council (Nationellt biobanksråd), an independent body appointed

[2] To be precise, they are only twenty; the municipality of Gotland carries out the duties of a county council without formally counting as one.

[3] Since 2010, privately and publicly owned health care centres that live up to certain pre-defined standards compete on equal terms for public funding.

by the Swedish Association of Local Authorities and Regions (SALAR, Sveriges kommuner och landsting).

While RBCs and The National Biobank Council mainly deal with knowledge sharing and strategic issues, operational tasks are generally handled further down the hierarchy. Consent issues, for instance, are delegated to specially appointed "biobank co-ordinators" at the county hospitals. Each biobank co-ordinator is in turn responsible for a number of physically and organisationally distinct biobanks, some owned by the County Council, others by private companies.

When Study I was conducted in 2007, the Biobank Act had only begun to be implemented. Although the basic organisational structure was in place, responsibilities were still partly in flux, not to mention routines. Nation-wide coordination of efforts was rudimentary. For instance, procedures for ensuring that patients' wishes were respected were established by biobank co-ordinators or at individual laboratories, and often involved manually tracking and physically marking individual samples. Patient information documents used in different parts of the country differed slightly in both design and wording. Since then, routines and documents have been harmonised to some extent, not least through the efforts of The National Biobank Council (Nationellt biobanksråd, 2009). In 2012, SALAR and the Swedish Research Council declared their intent to support closer collaboration between health care and medical research with regard to the development of biobanks and biobank registers (Vetenskapsrådet, 2012b). The National Biobank Council joined with BioBanking and Molecular Resource Infrastructure of Sweden (BBMRI.se) in a strategic effort to create a nationwide biobank structure.

The patient's choice

The practical implementation of one of the central requirements introduced by the Biobank Act, the obtainment of consent, is an interesting chapter in the history of Swedish biobanking. As noted above, the Act gave significant leeway in this regard. In the years that followed, national consensus gradually emerged and was later formalised by The National Biobank Council in 2004 (Nationellt biobanksråd, 2009).

Essentially, consent is obtained through a two-step opt-out procedure. In the first step of the procedure, the health care professional who is responsible for obtaining consent—usually, the patient's doctor—informs the patient about biobanks and possible uses of biobank samples. The doctor then asks the patient whether he or she objects to having the sample stored for purposes of health care and medical research. Even though recommendations state that written information should be given, preferably using the information sheet authored by the Council itself, this is not always the case in practice. The general availability of information is decent—posters are

usually seen hanging in waiting rooms, and there is a web page for those who wish to investigate the matter further. The posters, just like the patient information sheet, contain brief summaries on potential uses, measures taken to ensure confidentiality, and the rights to refuse and withdraw previous consent. The patient's response is documented in his or her medical record and specified on the laboratory referral form.

In the second step, those patients who refused to have their sample stored or wished to restrict its usage fill in and return a "dissent form" (in Swedish, "Nej-talong") in which their wishes are specified. Dissent forms consist of a single page with a short introductory text, labelled boxes to tick for each of the alternatives ("no" to storage, "no" to research and clinical trials, and "no" to use for purposes of education, quality assurance and development projects within the health care system), and a place for a signature. The same form can be used to declare withdrawal of previously given consent, though in the latter case the patient must return the form by mail to a specified official instead of handing it to her doctor. This solution aims to keep paperwork to a minimum and to prevent crucial samples being accidentally destroyed while granting patients with concerns freedom to refuse.

Interestingly, the patient information sheet—intended to be handed to the patient whenever potential biobank samples are taken—is rather ambiguous on the role of the Council, declaring that "Storing your samples is important because it allows us to […] carry out medical research in order to better prevent and treat diseases" (Nationellt biobanksråd, my translation). The use of first person can be taken to imply that the Council itself is a research institution, or perhaps even *the* research institution, which it is not. Alternatively, the Council positions itself as a guarantor for biobank research in general. Since people are generally (I assume) unfamiliar with the Council, it is reasonable to suspect that many patients will instead think of "us" as referring to the health care system, or the County Council. The impression of an alliance between health care and research, already made strong by the fact that samples are collected in a familiar setting by familiar people and through the familiar practice of oral (as opposed to written) consent, is thus reinforced.

The shaping of biobank ethics

In this chapter I take a historical perspective on biobank ethics. I will suggest a particular way of understanding the relationship between biobank ethics and its "parent" discipline, research ethics, in the light of past events. For simplicity, I will use these terms as though referring to distinct fields, though in reality, they are intertwined. My aim is not to educate the reader in history but to problematise some aspects of biobank ethics. I do so by recounting *critical events* and drawing attention to an emergent *pattern* of interpretation.

Biobank ethics, just like research ethics, carries its own canon of critical events. By this term I refer to anomalies that either bring up new ethical issues or stir up a lot of public attention. This includes public scandals. Research ethics is mainly informed by events in "invasive" research, that is, research involving procedures that potentially cause a change in the human body or mind. Biobank ethics, on the other hand, looks to biobank research and handling of human tissue. It is tempting to conclude that since the *matter* of ethics differs between these two fields, the relationship between them must be one of *form.* One could imagine it to be mediated by, for instance, abstract theories, concepts and principles, learned in one field and then carried over to the other. But critical events are interpreted neither independently of each other nor simply in the light of abstract concepts and principles learned from previous ones. For better or worse, we tend to bring whole patterns of interpretation with us from one context to another. In the biobanking context, informed consent is part of a pattern of which we need to become aware. Otherwise, talk about trust will appear to be nothing but a thinly disguised attempt to revive paternalism.

To learn of critical events, one studies history; to learn *from* them, one studies history through a particular lens. The lens that I suggest is employed by keeping one's eyes out for two interrelated trends in research ethics: *bureaucratisation* and *displacement of responsibility*. The first is external to the researcher in that it pertains to the system in which she is a part. The spirit of the Nuremberg Code was, in essence, an imperative not to harm others or subject them to interventions against their will, and to do research competently and conscientiously. Today, the imperative tells us fill out certain forms and have research participants fill out others; and as through magic, morally acceptable research will ensue. The second trend pertains to actual morals and is thus internal to the researcher. Historically, doing the right thing has been the responsibility of individuals. When there was doubt,

one resorted to ethical reflection. Today, rules and regulations suggest that final responsibility resides with institutions and governmental bodies; all that the individual has to do is to comply with the rules set up by these bodies. This paradigm shift in attribution of morality is reflected in how research ethics is taught today: fill out these fields like this, tick these boxes like that, and use these words rather than those, and you will be fine.

A qualification is in place. Clearly, many examples can be found of harms and wrongs done in the name of research that would have constituted punishable acts if inflicted to others outside of the research context. These are rightly thought of as *legal* issues. Hence, the general tendency to address critical events, even those that are more suitably referred to as ethical issues, through regulation and governance is unsurprising. Nevertheless, it is an important one to have in mind when, later in this thesis, I argue that reliance on formal measures is insufficient to secure the trustworthiness of the research apparatus (Study IV).

Critical events in invasive research

There is no doubting the enormous successes of medical research. The discoveries of penicillin, several vaccines, and safe methods for anaesthetics and surgery are but a few of the breakthroughs that have enabled us to combat some of the most lethal and disabling diseases of the 20th century. Regrettably, history has also provided numerous examples of harm and wrong done in the name of research. The most infamous of them all—the atrocious experiments carried out by Nazi doctors on Jews and other "undesirables" interned in concentration camps during WWII—deserve to be mentioned. However, for two reasons, they are singularly ill-suited to illustrate ethical problems in research. First, what took place was not morally problematic, but evil. If the example is taken to illustrate or justify a set of ethical principles, those are precisely the ones for which we need no particular illustration or justification. Second, though the defendants in the "doctors' trial" were charged with unethical research rather than murder (Rothman, 1998, p. 51), the "research" in question was but a tiny part of the harm and wrong done. To illustrate a principle in *research* ethics, a case must help to clarify how the research should be done differently to make it ethically acceptable. But to even begin trying to amend the Nazi experiments is inconceivable. Some lessons, it appears, we should learn not as researchers, but as humans.

There are many more examples of harm and wrong done to research subjects throughout history than can be reasonably discussed here. I will look at two of them in detail and briefly mention a few others. Here, they do not serve as precautionary tales, but rather as illustrations of how critical events have shaped bioethics and research ethics into their present form

(Miller and Boulton, 2007). As will become evident, they are sometimes used not only as examples, but more liberally—and questionably—to draw general normative conclusions that can purportedly be transferred into new contexts.

The Willowbrook hepatitis study

Between 1956 and 1971, a study on the natural history of infectious hepatitis was conducted on mentally disabled children at the Willowbrook State School (Beauchamp and Childress, 2001, pp. 428–430, Resnik, 2012). The ultimate aim of the study was to help develop a vaccine. Due to low sanitary standards and overcrowding, the disease—which is transmitted through the faecal-oral route—was endemic at the institution. Over time, between 750 and 800 children, all of which were newly admitted, were included. The study was approved by the New York Department of Health. It was one of the 22 unethical studies that Henry Beecher drew attention to in his famous paper in New England Journal of Medicine (Beecher, 1966, p. 371).

The study was controversial in several respects. First, it involved deliberately infecting the children. The researchers argued that only minor harm was done. As a consequence of the crowded and unsanitary living conditions, the children were likely to contract hepatitis anyway. By isolating the subjects in a separate ward, one could hope to prevent concurrent exposure to other infections, thus reducing their overall risk of complications. The expected outcome of inoculation was a subclinical infection and possibly immunity to the particular virus strain. Critics argued, however, that immunisation was not the aim of the study but rather a fortunate by-product; even after a gamma-globulin inoculation programme had reduced the natural incidence of hepatitis at Willowbrook by 80-85%, the study continued. At the time of inception, the researchers were prepared to use—and possibly harm—some people for the benefit of others.

Second, though parental consent had been sought, critics of the study have argued that the risks were downplayed, as was the fact that the children were deliberately infected. It has also been suggested that the parents were manipulated into consenting. In 1964, parents were informed that no further admissions were possible due to overcrowding. Shortly thereafter, they were told that there were vacancies in the hepatitis unit, and that their children could be admitted on the condition that they were "volunteered" as participants in the study (Beauchamp and Childress, 2001, pp. 428–430). The principal investigator blamed this on administrative errors (Rothman, 1982, p. 6).

The Tuskegee syphilis study

In 1932, the US Public Health Service initiated a study in Tuskegee, Alabama, to investigate the natural history of syphilis (Brandt, 1978). At that time, the perils of untreated syphilis were well known: cardiovascular and central nervous system lesions, and death. Treatment with arsenic compounds was therefore strongly advocated even in latent stages of the disease.

The researchers recruited 400 infected men—exclusively poor African-Americans from rural Alabama—along with 200 healthy controls. Obtaining enough research subjects was not a problem; promised free care for their illness, colloquially referred to as "bad blood", many men were more than willing to participate. The promised treatment was a lie. All interventions, including the "special treatment"—a spinal tap—were for purely diagnostic purposes. When penicillin became widely available in the 1950s, the investigators did not rejoice. Rather, the fact that their subjects were now able to obtain treatment elsewhere was lamented since it could threaten the scientific validity of the study. Consequently, they sent letters to doctors in the vicinity discouraging them from prescribing drugs to study subjects. To sum up, people were lied to, badly used, and withheld widely available treatment for a life-threatening condition.

Interestingly, the lesson ultimately taught to the world was a rather different one. Soon after details of the study found their way into media in 1972, it was ended by the Department of Health, Education and Welfare (HEW). Two reasonable framings of the study were effectively downplayed in HEW's final report. First, the racism that infused the scientific institutions at the time was probably crucial. Academic papers habitually described African-Americans as promiscuous and unintelligent, and the occurrence of syphilis among them was considered "natural" (Brandt, 1978). Second, what began as simply observing a "natural" phenomenon ended with efforts to perpetuate the circumstances of social deprivation that made the study possible in the first place (Rothman, 1982). Instead, the main criticism against the investigators was that they had *failed to obtain informed consent* from their subjects (Brandt, 1978). Thirty years later, this rather surprisingly simplistic conclusion still echoes in academic papers (Caulfield, 2007, p. 216).

Other critical events of note

A few other critical events—not all of which are strictly medical in nature—deserve brief mention to bring out some recurrent themes.

- In 1942–1943, mental patients at Ypsilanti State Hospital, Michigan, were included in a study aiming to help develop an effective vaccine for

influenza. The original plan was to vaccinate them to see whether this protected them against the epidemic. As the anticipated yearly outbreak did not occur, they were instead deliberately infected (Francis et al., 1945).

- From 1944 until the 1980s, government-sanctioned secret experiments on the effects of radiation were conducted in the US on cancer patients, pregnant women and military personnel. They were declassified in 1994, and an official apology issued by the President's office (Resnik, 2012).
- Between 1946 and 1948, the US Government carried out research on venereal diseases on over 5,000 Guatemalan soldiers, prisoners, mental patients, orphans and prostitutes. 1,308 adults were exposed to syphilis, gonorrhoea and chancroid without being told of the fact. The experiments were uncovered in 2010 (Walter, 2012, pp. 148–149).
- From 1947 to 1955, mentally disabled people living at Vipeholm, Lund, Sweden, were included in a study on the causal relationship between diet and the development of caries. A particularly sticky caramel was developed explicitly for this purpose and fed to some of the study subjects. Neither the subjects nor their families were informed about the purpose of the study (Petersson, 1994, pp. 220–261).
- From the early 1950s until 1973, the CIA conducted research on behavioural engineering of humans. The project involved various forms of manipulation, abuse and torture, including administering drugs (such as LSD), isolation and sensory deprivation (Select Committee on Intelligence and Committee on Human Resources, 1977).
- In the 1950s, prisoners at the Ohio State Prison and women at the Sloan-Kettering Cancer Center were injected with live cancer cells in order to study how the human body combats malignancies (Terry, 1957). "Cancer cells" were never mentioned; the patients were told that they were to undergo "tests for immunity" (Baker, 1998, p. 323). The study was repeated in 1963, this time on elderly patients at the Jewish Chronic Disease Hospital in Brooklyn, New York (Mulford, 1967).

These studies, like many others that later have been condemned, have four things in common. First, people were either overtly harmed or subjected to significant risks of harm. Second, with few exceptions, these studies were not the work of individual "mad scientists". Typically, they were sanctioned by the state, university, or some other institution with a legal mandate to approve or reject research proposals. Third, most of them targeted vulnerable groups—prisoners, soldiers, minorities, elderly patients, orphans, or the mentally disabled—conveniently packaged in institutions and usually lacking the capacity or liberty to refuse. Fourth, the wrong done has often been framed in terms of lack of informed consent (Rothman, 1987, Baker, 1998).

Research ethics as a regulatory framework

The events at Tuskegee and Willowbrook as well as many other cases of unethical research led to a public outcry. This was, partly at least, because they coincided with the civil rights movement. Already in 1959, Beecher had published an article similar to the one for he became famous in 1966, but with very little public uptake (Stark, 2012, p. 159). These events led up to the US National Research Act of 1974, by which independent review of research proposals became mandatory (p. 163). Shortly thereafter, the Department of Health, Education and Welfare (HEW) established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was charged "to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles." (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) The result was the now venerable but still influential Belmont Report with its three principles: respect for persons, beneficence, and justice. More recently, they have been expanded to four, with "non-maleficence" explicitly capturing the Hippocratic dictum "do no harm" (Beauchamp and Childress, 2001).

Research ethics has come to evolve along two parallel tracks. First, it is an academic discipline. Here, as in academic research generally, disinterested inquiry remains the ideal. Second, research ethics can be more proactive, stating certain outcomes (better and ethically more justifiable research, for instance) as its aims. This "regulatory" branch of research ethics can be thought of as a framework for an extra-legal regulatory system, much like jurisprudence relates to legal regulation (Hoff, 2003). It rests on four pillars: ethics review, guidelines, informed consent, and regulatory bodies.

Ethics review

There is no unified procedure for ethics review; implementations differ between countries and have changed significantly over time. In the US, independent review of research proposals has been carried out by Institutional Review Boards (IRBs) since 1966. As the name suggests, these have traditionally been located at the research institutions themselves, though private IRBs have become increasingly common in recent years (Stark, 2012, p. 5). In Sweden, the same function is carried out by regionally based Research Ethics Committees (RECs). Since 2003, their constitution and operation is regulated by law. Notably, they are now headed by a judge and required to include at least two lay representatives (Sveriges riksdag,

2003). Once independent bodies, their operation is now directed by the Central Ethical Review Board, which also handles appeals. In its preparatory work (Utbildningsdepartementet, 2003, p. 28), the Government expressed hopes that the new system would better protect research participants, engage the public, cultivate public trust, and lead to more predictable review outcomes. Of course, legislation was also necessary in order to ratify the Council of Europe's Convention on Human Rights and Biomedicine. There has been an analogous development in many other European countries, for instance in the UK (Kerrison and Pollock, 2005).

Though implementations of ethics review differ, they share a common origin and purpose. For most purposes we can therefore think of ethics review as a single activity carried out by a reviewing body.[4] Most importantly, ethics review was not, as one might suppose, invented by bioethicists. Rather, the idea arose from the interplay between two agendas: ensuring future research and preventing litigation.

RECs as we know them today were first seen in the 1960s when IRBs began to be enacted across the US (Stark, 2012). But the story goes back even further, to 1953, when the National Institutes of Health (NIH) opened its research hospital, Clinical Center, in Bethesda, Maryland. Patients who were admitted here were not necessarily ill. Many were "normal volunteers", or "Normals" as they were sometimes called. These patients were admitted precisely because they were in good health—and because they had few other options besides enrolling. Among them were conscientious objectors to the Korean War, poor students, and later, prisoners. The length of their stay, during which virtually all aspects of their lives were meticulously controlled, ranged from a few months to several years. During this time, the Normals were enrolled as participants in one or several research projects, many of which included administration of experimental drugs. There are clear similarities between these experiments and those carried out on religious objectors during WWII (pp. 84–100).

While NIH leaders needed to deflect suspicion from this unusual use of public funding, they felt that ethics codes were too rigid to accommodate the many different kinds of research that they had in mind. They were also sceptical about the feasibility of obtaining informed consent according to some pre-defined criteria. Instead, they invented a new procedure involving "group consideration" as a complementary layer on top of the traditional model of bedside decision-making. It was embodied in the Clinical Research Committee (CRC), a subset of the Clinical Center's Medical Board. Review became mandatory for projects involving unusual risks as well as for all work on Normals. The new policy provided great flexibility as it allowed the institution itself to define proper conduct within its walls. By embracing

[4] I will refer to such bodies collectively as RECs unless I am specifically denoting American IRBs.

consensus and *expert opinion*, the policy also carried significant moral and rhetorical force. It soon proved strong enough to fend off the threat of lawsuits from subjects participating in research within the Clinical Center (pp. 106–108).

Projects funded by NIH through its Extramural Program were another story. In 1964, NIH was implicated in a lawsuit following the cancer studies at the Jewish Chronic Disease Hospital in New York. The defendant hospital argued that NIH, as funder of the project, ought to pay for damages to at least one of the plaintiffs. NIH lawyers managed to deflect this particular claim. To the Public Health Service (PHS), however, this was a clear sign of vulnerability to future lawsuits of the same kind. Introducing strict informed consent requirements was one possibility. Since 1962, such requirements were in place for trials involving unlicensed drugs. NIH leaders argued in favour of the more flexible group consideration model. In 1965, the National Advisory Health Council approved a resolution stating that any research institutions receiving PHS funding must provide prior review of research protocols by a committee consisting of "institutional associates" of the principal investigator (pp. 144–156). Since numerous research institutions also outside the US depended on PHS grants, ethics review rapidly became a widespread practice also internationally (Hedgecoe, 2012, p. 664). This marked the beginning of the paradigm of independent review which persists to this day.

Guidelines

The growing importance of research ethics as a means of regulating research becomes particularly apparent in the Declaration of Helsinki (DoH). In contrast to the Nuremberg Code, authored by judges and unmistakably legal in nature, the DoH was the work of medical doctors (Rothman, 1998, p. 59). Authored and adopted by the World Medical Association (WMA) in 1964, this document has become one of the most cited documents in research ethics as well as the one with which health care professionals seem to be most familiar (Höglund et al., 2010, p. 97). The fact that it has been revised several times over the years makes it very useful for tracking trends in the bioethical discourse.

The original DoH formulated its status rather modestly: "It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil, and ethical responsibilities under the laws of their own countries." (World Medical Association, 1964) Duties were either phrased in the passive or as incumbent on "the doctor", "the research worker", "the investigator", or "the investigating team". The level of abstraction was high: there were no rules that could be followed out-of-the-box. The judgment of the individual was emphasised throughout the document. By all appearances, its aim was to

remind individual doctors of duties that they, being doctors, ought to have already recognised as binding. In this sense, the norms it expressed were internal and moral rather than external and legal. Interestingly, however, a paragraph in the Nuremberg Code stating that everyone involved in carrying out an experiment have a non-transferable responsibility to assure the ethical quality of the subject's consent was not carried over to the DoH. Already, individual moral responsibility had begun to be ever so slightly deemphasized.

The first revision of the DoH (World Medical Association, 1975) was carried out in the wake of the Tuskegee syphilis study, the Willowbrook hepatitis study, and several other scandals (Hoff, 2003, p. 161). A requirement that research protocols be submitted for ethics review was now introduced. The committee was to be "specially appointed" and "independent", with no further specification of what this would entail. Informed consent requirements were elaborated. Guaranteeing the "ethical authenticity" of the consent rested with the RECs. This, some authors claim, was inevitable "after the scandals denounced by Beecher and Pappworth showed that it was impossible to rely on the moral integrity of experimenters" (Herranz, 1998, p. 137).

A peculiar tension also emerged with regard to the document's status. While still declaring itself "only a guide", it now asserted compliance with its rules and principles as a strict requirement for publication. The tension was relieved in the fifth revision with a forceful self-assertion: "No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this document." (World Medical Association, 2000) But the perhaps most salient feature of this revision was the level of detail in some of its instructions. Participants must be informed of

> the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. (World Medical Association, 2000)

There are similar rules governing the information to be passed to RECs and journals. Once a true declaration—a statement of the basic principles and values that ought to govern human subject research—the DoH has increasingly taken on the appearance of a legal document. Despite having retained its name over the years, it now aims to direct action rather than to serve as a base for moral deliberation. This is not necessarily surprising. Conceivably, like guidelines issued by many other organisations, the DoH has served at least partly to defend the autonomy of the medical profession

against governmental infringement (Hoff, 2003, pp. 183–188, Arnold and Sprumont, 1998, pp. 91–92). With scandals and incidents continuing to surface, it is no wonder that this form of defence has intensified over time.

Informed consent

The right to refuse to participate in medical research is a fundamental ethical principle. Its inception is often misattributed to the Nuremberg Code. In fact, the corresponding duty to ensure the voluntariness of the research subject was embedded in German law already in 1931—well before the Nazi doctors began their bestial and far from voluntary experiments (Hoeyer, 2008, p. 441). Even earlier, several codes mention voluntariness as crucial in human experimentation. Nevertheless, the Nuremberg Code of 1947 is a critical document both because of the emphasis it puts on voluntariness and because of its relative fame both within the research community and among the general public.

The requirement for informed consent was reiterated in the original DoH, according to which the doctor is obligated to obtain "freely given consent after the patient has been given a full explanation" or, in the case of non-therapeutic research, "free consent, after he has been fully informed" (World Medical Association, 1964). Since the Belmont Report, the procedure has been motivated by the principle of respect for persons: "Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied." (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) Of course, the threat of malpractice suits were also an important driving factor, at least in the US (Mulford, 1967).

Confusingly, there are two ways to understand informed consent. Understood in a substantial sense, informed consent constitutes an autonomous authorisation of an action (such as enrolment in research). This implies that the decision and the process that led up to it were in fact autonomous.[5] In a procedural sense, informed consent is the proper procedure for obtaining such authorisation. The distinction between the substantial and the procedural understanding is necessary because it is quite possible, for instance, to receive information without ever actually digesting it. Determining whether consent is informed in the procedural sense is typically easier. It is also more easily documented.

[5] Though autonomy is a central concept in bioethics and research ethics, there is no consensus on what it means to speak of an action as autonomous. Suggestions made by different authors include: individual, made with dignity, self-assertive, self-knowing, critically reflective, independent from external causation, free from obligation, or furthering one's interests. See O'NEILL, O. (2003) Some limits of informed consent. *J Med Ethics*, vol. 29, no. 1, pp. 4–7.

Informed consent can be divided into elements that serve both as criteria for the state of being substantially informed and as steps of the corresponding procedure. There are two "threshold elements": *competence* on part of the research participant to understand the necessary information, and *voluntariness*, which rules out any kind of coercion. Next, there are "information elements": *disclosure* of material information, *recommendation* of a plan, and *understanding* of information and recommendation. Finally, the "consent elements" comprise a *decision* and an *authorisation* of the plan that was decided upon (Beauchamp and Childress, 2001, pp. 77–80).

In the early years, the focus of bioethicists working on informed consent was on standards of disclosure. As one might expect, lawsuits were one of the main driving forces toward more demanding standards. The *professional* standard, which holds that what should be disclosed is determined by reference to reasonable medical practice (in effect, tradition), was gradually replaced by the *reasonable person* standard following a lawsuit in 1972 (Goldworth, 1999, pp. 394–395). The latter holds that any information about a procedure or research project which is likely to influence the decision of a "reasonable person" is to be disclosed, rather than merely those facts that the professionals themselves find important. Although there are clear benefits to this standard, it has been argued to be sometimes too static. In some contexts, a *subjective* standard that focuses on the actual concerns of a particular individual has been argued to be more reasonable. Since then, the concept of informed consent has been continuously refined, with focus gradually shifting from the duty to disclose information to that of making sure that the research participant understands it.

Regulatory bodies

With many biobanking projects growing into international undertakings, there is high demand for multinational governance and regulation. As we shall see in the next chapter, policy makers also put a lot of faith in the ability of higher-order bodies to cultivate public trust. Presently I will briefly describe a number of regulatory and advisory bodies that are relevant to the field of biobank research. Although not exhaustive, this list is sufficient to get an idea of the complexity of the situation.

- The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-governmental, non-profit organisation jointly established by WHO and UNESCO in 1949. It currently comprises over 55 member organisations. One of the many activities of CIOMS is to develop international guidelines for biomedical research (The Council for International Organizations of Medical Sciences, 2012).

- The European Conference of National Ethics Committees (COMETH) is a recurrent conference aiming to promote cooperation between national bioethics committees in Europe, providing aid in setting up such committees, and promoting public debate on bioethical issues (Council of Europe, 2012b).
- The European Group on Ethics in Science and New Technologies (EGE) is an independent multidisciplinary body advising the European Commission in legislation and policy making processes. Members are appointed on the basis of their expertise and serve in a personal capacity. Before issuing its opinions, EGE invites different stakeholders to roundtable meetings (European Group on Ethics in Science and New Technologies, 2012).
- The InterAcademy Panel (IAP), founded in 1993, is a global network of science academies. Its main aim is to help its members to advise citizens and public officials on the scientific aspects of critical global issues. IAP currently comprises 105 academies (InterAcademy Panel, 2012).
- UNESCO's International Bioethics Committee (IBC), created in 1993, monitors progress in life sciences to ensure respect for human dignity and freedom. It consists of 36 independent experts appointed by the Director-General. Through its working groups, IBC produces advice and recommendations that are adopted by consensus (United Nations Educational Scientific and Cultural Organization, 2012b).
- UNESCO's Intergovernmental Bioethics Committee (IGBC) was established in 1998. It consists of representatives from 36 member states elected by the General Conference. IGBC convenes at least biannually and offers advice to IBC on its recommendations (United Nations Educational Scientific and Cultural Organization, 2012a).
- The Council of Europe's Committee on Bioethics (DH-BIO) was established in 2012. It replaced the Steering Committee on Bioethics (CDBI), operative since 1992, as the body responsible for intergovernmental work on the protection of human rights in the field of biomedicine. The work of CDBI was material to the preparation of the Convention on Human Rights and Biomedicine, enacted in 1996 (Council of Europe, 2012a).
- The U.N. Inter-Agency Committee on Bioethics was established in 2003 to promote coordination and cooperation between a number of United Nations agencies, including UNESCO and WHO, and other international organisations within the field of bioethics (World Health Organization, 2013).
- World Commission on the Ethics of Scientific Knowledge and Technology (COMEST) is an advisory body and forum for reflection. COMEST was established by UNESCO in 1998. It comprises scholars from various disciplines as well as representatives for UNESCO's international science programmes and global science communities. The

mandate of COMEST is to formulate ethical principles for decision-makers (United Nations Educational Scientific and Cultural Organization, 2012c).

Critical events in biobank research

What follows is an overview of some of the most significant critical events in the history of biobank research. Compared to those in invasive research, there are two significant differences. First, the criticism has usually focused on *wrongs* rather than harms. Second, although some research projects have targeted minorities (and been criticised accordingly), these design decisions have been motivated by scientifically valid reasons rather than convenience. But informed consent ever seems to be at the forefront when explanations are sought as to why wrong was done.

The Alder Hey organ retention scandal

In 1999, the British House of Commons instigated an inquiry regarding the handling of organs from deceased children at the Royal Liverpool Children's Hospital NHS Trust (also known as Alder Hey). The inquiry was prompted by reports of allegedly substandard and possibly unlawful practices. The final report, published in 2001, revealed a long-standing practice of removing and retaining whole organs as a matter of routine without parental consent. This was in direct violation of the Human Tissue Act of 1961, according to which parents must be assumed to object to use of their child's body for therapeutic purposes, medical education or research unless there is good reason to believe otherwise (The House of Commons, 2001, p. 3).

Although much of the criticism focused on a particularly problematic era between 1988 and 1995, the practice of retaining whole organs stretched much further back in time. Since 1948, some organs—mainly hearts—had been routinely taken for purposes of research and education. Tissue samples were generally sufficient for these purposes, but since the fixation process was time consuming, returning these organs to the body in time for the funeral was often impossible. As a consequence, huge collections of organs were built over the years (pp. 5–7).

In 1988, a new Chair in Fetal and Infant Pathology was appointed. Shortly after entering office, the Chair issued an instruction that there was to be no disposal of human material whatsoever. He subsequently failed to conduct post mortem examinations in a timely fashion. A backlog consequently built up and was never resolved. Routine histological analysis was discontinued. Many reports were never finished, and judging from the large numbers of intact organs in store, many others had been fabricated. There was no system for keeping record of the incessantly growing

collection. Even though both the Executive Board at Alder Hey and the University of Liverpool were aware of many of these shortcomings as early as 1992, they took no action until three years later.

Despite that the practice at Alder Hey between 1988 and 1995 was questionable on almost every level—from the actions of individuals to lack of proper procedures to weaknesses in management—the lessons learned by the bioethics community centred around the failure to obtain consent, the paternalist tradition that made organ retention possible (or even normal practice), and the need for new regulations (Hall, 2001). The scandal directly contributed to the enactment of a new Human Tissue Act in 2004. Any removal, storage or use of human tissue without consent was made illegal and punishable by law. Interestingly, the parents phrased their concerns differently:

> The essence of their complaint is that they were deliberately misled into thinking that they were burying their deceased children intact, when in fact each child had been systematically stripped of his or her organs, a large majority of which remained stored and unused from 1988 to 1999. The inadequate handling strategy adopted by Alder Hey merely served to aggravate the situation to the extent that some families have faced numerous funerals as a result of organs being returned to them on a piecemeal basis over the past 14 months. (The House of Commons, 2001, p. 12)

Not that the failure to ask the parents for permission was unimportant. Indeed, many parents indicated that they would have been willing to donate their children's organs for research purposes, had they only been asked (Hall, 2001, pp. 455–456). Refusals, too, would have been normatively significant. But an even greater wrong resides in the fact that they were deceived as to their children's fate.

The Havasupai Indian tribe case

In 1990, researchers at Arizona State University collected blood samples from members of the Havasupai tribe in order to study possible genetic causes to the high prevalence of diabetes in this population. Later, the samples were reused in unrelated projects. After the tribe learned of the reuse in 2004, some of its members filed a $50 million lawsuit for, among other things, fraud, breach of fiduciary duty, negligence and trespass. They were particularly offended by the use of their blood to study the genetic basis of schizophrenia and the effects of inbreeding, as well as by evolutionary-genetics studies suggesting that the Havasupai, contrary to the tribe's origin story, had once migrated across the Bering Sea.

In the legal proceedings, the core question became whether these additional studies fell within the scope of the original consent. The aim of the project, as it was stated in the consent document, was to study "the

causes of behavioral/medical disorders". In 2010, the parties settled, with the University agreeing to pay $700,000 to the plaintiffs as well as issuing an official apology. The Havasupai case may well contribute to the already strong tradition of framing ethical concerns as matters of securing informed consent. It also seems to underpin the notion that "people have a right to control the uses to which their bodily tissues are put, regardless of whether those uses pose any risk." (Mello and Wolf, 2010, pp. 204–205)

Part of the disappointment of the Havasupai was related not to what kind of research was carried out but to what results were and were not produced. Since the 1960s, the tribe had suffered from a tremendously high prevalence of adult-onset diabetes. Many of the tribe's 650 members had had limbs amputated or were forced to undergo dialysis. To judge from interviews with tribe members, there was a widespread optimism that the research on diabetes in which they participated would actually produce results that would help them regain their health and allow them to continue to live on in the canyon. As it turned out, they waited in vain. Instead, they were presented with results that contradicted their cultural beliefs. The suggestion—though not wholly unfamiliar to the tribe—that the origin stories retold throughout the generations were false was considered a "hurt" against the elderly. Worse, perhaps, were the findings of significant inbreeding. As one member put it, "We say if you do that, a close relative of yours will die." (Harmon, 2010) But this, one might respond, is simply how research works: Results cannot always be predicted, and sometimes they provide knowledge that you would rather not have, consent or no consent.[6] Still, as I will argue in the discussion chapter, there are moral reasons to be sensitive to expectations that may cause incidents of this kind.

deCODE and the Icelandic Health Sector Database

In 1997, the US biotech company deCODE approached the Icelandic Ministry of Health with a proposition for establishing a new nation-wide database for health data, later to be known as the Health Sector Database (HSD). Together with two other databases—one with genetic data extracted from biological samples, the other containing genealogic data—it would allow researchers to approach the causes of common multifactorial diseases from a new perspective. By cross-referencing data from all three databases and "mining" it for correlations without a priori hypotheses, deCODE hoped to gain new knowledge where conventional hypothesis-driven methods had

[6] Similar harms may follow from teaching Mendelian inheritance patterns in biology class. My biology teacher once confided to me that a pupil from a previous year had deduced, on the basis of eye colour, that her father was unlikely to be her biological one. Though regrettable, such events are not usually seen as reasons to stop teaching genetics.

proven ineffective (Árnason, 2004, pp. 28–30, Rose, 2001, pp. 9–10, Gulcher and Stefánsson, 2000, p. 1827).

Before a contract could be negotiated, new legislation had to be passed. By all appearances, speed was of the essence:

> The first time that anyone other than deCode staff, key Health Ministry personnel, and senior members of the Government heard about the proposed HSD was at a meeting on 23 March 1998, six months after deCode had faxed a draft of the bill to the Government. That day, 15 experts were invited at 12 noon to a meeting to take place at 3 p.m. at the Ministry. There they were told about the forthcoming database bill; the participants at the meeting, and in particular the then Director of Public Health, demanded to see the written text.
>
> Two days later the text was made available – in confidence – to the 15 experts. Comments were to be sent to the Ministry before 12 noon the next day, giving the experts less than 24 hours to produce a considered opinion. On a number of occasions, not least in its evidence to the European Steering Committee on Bioethics, the Ministry has claimed wide professional consultation, but there was little evidence of this at the crucial early stages. Neither the Icelandic Medical Association nor the Specialists' Association reported any such consultation among their members. (Rose, 2001, p. 17)

The first bill caused considerable debate both in Iceland and internationally. A major source of disagreement was the plan to copy the contents of the medical records of the entire population into the HSD on the basis of "presumed consent" (Rose, 2001, p. 18).[7] In the final law, voted through in December, an opt-out provision was added. In theory, Icelanders were granted the right to decide whether to take part in the HSD. In practice, any data submitted to the database after a six month grace period would remain there indefinitely even after opt-out. As there were no special provisions for children, those under 18 would not be able to retract their data once they came of age (Rose, 2001, p. 25, Andersen and Arnason, 1999, p. 1565). However, deCODE and the Icelandic Medical Association later agreed to add an option of having one's data destroyed (Árnason, 2004, p. 33).

Confidentiality was another major source of concern that was partially addressed in the amendment. Once within the HSD, the data would be protected by encryption. In particular, there would be one-way encryption of personal identifiers.[8] Still, since the data might contain personal

[7] Other models were suggested for the genealogical and genetic databases. The former was part of the public domain, so there would be no consent, and no option of withdrawal. As to the latter, explicit, broad consent would be sought. See ÁRNASON, V. (2004) Coding and consent: moral challenges of the database project in Iceland. *Bioethics*, vol. 18, no. 1, pp. 27–49.

[8] In practice, this means that records for a known individual can be retrieved by someone who has access to the unencrypted personal identifier and the encryption key, whereas those who have access to the database but not the key can read the data but not identify the person to whom it pertains.

characteristics, there would still be a risk of inadvertently identifying someone on the basis of her data. This risk was minimised through a rule stating that no results would be pulled from the database in sets of less than ten individuals (Rose, 2001, pp. 20–21). Nevertheless, as critics pointed out, there would be no anonymity at the point when records were being entered (Árnason, 2004, p. 31, Andersen and Arnason, 1999, p. 1565).

A third concern was about freedom of research. The company that won the licence—ultimately, deCODE—was to fund the database and would in return be given monopoly control for 12 years. Third parties were granted the right to buy access, but only on the condition that their interests would not conflict with those of deCODE. Many critics believed that deCODE was thus granted an unreasonable amount of power, possibly to the detriment of independent research (Rose, 2001, p. 21).

Opinions differ on what "went wrong" in the Icelandic case. Legal experts have unsurprisingly emphasised the procurement of health data without prior consent as the most contentious issue, purportedly "as it has been seen as a breach of the principles contained in the Declaration of Helsinki and the Icelandic Patients Rights Act 1997." (Kaye and Martin, 2000, p. 1147) Philosophers have questioned whether "community consent" and data security could replace the need for individual consent (Árnason, 2004, p. 38). In other documents, the controversy is thought to show the importance of considering "public attitudes" (European Commission, 2012, p. 23)—that is to say, majority opinion. But this rather misses the mark because public support for the HSD was, and still is, remarkably high.

A more important point which is illustrated by the HSD controversy is that in the absence of proper public engagement, it is quite unclear what normative conclusions one is entitled to draw from surveys of people's attitudes. Although deCODE representatives have, in defence of the new law, described the debate as lively (Gulcher and Stefánsson, 2000, p. 1827), most of it took place only after it had been passed. And even *with* public engagement, there are marginalised groups to consider: children, the mentally disabled, the poor, and the illiterate, to name a few (Árnason, 2004, pp. 37–38). Public attitudes can be strategically important, but considering them does not absolve policy makers or researchers from their duty to consider the rights and needs of the few.

More attention should perhaps be awarded the fact that a commercial company was in effect allowed to dictate public policy, circumventing the consultation process that is usually regarded a hallmark of democracy. If this criticism is sound, people may have found a reason not to trust legislators and other policy makers to protect their interests.

LifeGene

In 2010, Karolinska Institutet and all other Swedish universities that comprise medical faculties joined forces to create LifeGene, a new population-based biobank and infrastructure for medical research into common diseases. Over the course of eight years, half a million Swedes between 18 and 45 years of age were planned to be recruited. To ensure representativeness, invitees were selected at random from the Personal Address Register and encouraged to invite their family and friends. Those who responded were invited to a test centre, where they got to answer a questionnaire, undergo a series of examinations (body composition, heart rate, blood pressure, waist/hip ratio, lung function and hearing), and have blood drawn to be stored in the biobank. Results from the physical examinations as well as serum cholesterol levels were returned to participants. This examination, referred to as a "health check", was promised to reoccur regularly.

While LifeGene resembles UK Biobank in many respects, it differs crucially from the Icelandic HSD. Perhaps most importantly, LifeGene, like UK Biobank, recruits by opt-in. Upon their first visit to the test centre, participants grant explicit consent for storage of material and data and its use in REC approved research. Those who wish to withdraw their consent later can also demand that their samples and data be destroyed. No single party has privileged access or commercial monopoly. Commercial companies are granted access only if they collaborate with a researcher at a Swedish research institute (LifeGene, 2010).

To the surprise and disappointment of the biobanking community, LifeGene was suspended in 2011 following an inquiry by the Swedish Data Inspection Board (Datainspektionen, 2011). The Board found that the project violated the Personal Data Act (Sveriges riksdag, 1998) by handling personal data, including sensitive data, without declaring a specific enough purpose. It was suggested that the Government or Parliament consider regulating this matter separately, as is the case with health data registers.

The matter was deemed important enough to warrant intervention by the Government. In February 2012, the Minister of Education and Research announced his intent to advance a new regulation that would allow Swedish universities to keep registers for population-based research (Utbildningsdepartementet, 2012). The bill was promptly criticised for being hastily concocted, underdetermining some issues and conflicting with existing laws and regulations. The Swedish Research Council observed that the proposed right to have one's data destroyed would conflict with the Archives Act. Besides that, they thought it unclear whether it would pertain also to data maintained by third parties, and to what degree it would be enforceable if it did. The Council also doubted whether consent expressed by participants could ever be *informed* in the relevant sense, especially when it

concerns procurement of future, and possibly sensitive, contents of medical records. Many people, it was argued, would likely be unable to foresee the consequences of such consent (Vetenskapsrådet, 2012a). The Swedish National Council on Biomedical Ethics (SMER) expressed similar concerns (Statens medicinsk-etiska råd, 2012). At the time of writing, the Government is yet to reach a decision on the matter.

The role of informed consent in biobank research

While the idea of informed consent was originally developed with invasive research in mind, that is, the kind that can cause bodily harm, it has come to play a key role also in biobank research. As we have seen, biobank research was a largely unregulated field little more than a decade ago, with samples being taken and used for research as a matter of routine. In the light of a number of groundbreaking discoveries and technological advances in genetics and genomics, there has been a perceived need for tighter regulation (Hoeyer, 2008, pp. 431–432). This is reflected in the fifth revision of the Declaration of Helsinki, carried out in Edinburgh in 2000, where the scope of the document was extended to cover biobank research (World Medical Association, 2000). Also in the Convention on Human Rights and Biomedicine (Council of Europe, 1997)—now ratified by many states within the European Union—biobank research is subsumed under human subjects research and thus subjected to the same restrictions as clinical trials. As a result, researchers are now considered both morally and legally obligated to obtain informed consent for research on biological samples.

Since its inception, interest for informed consent has grown tremendously. Today, it is one of the most debated issues in bioethics. Although conceivably a cumbersome solution to something that was not even considered a problem until the last decade, informed consent is consistently—and fascinatingly—picked out by RECs (Coleman and Bouesseau, 2008) and company policymakers (Hoeyer et al., 2005b) as the single most important matter in biobank research. American researchers testify that informed consent issues are the most common source of "considerable discussion" with their IRBs. Perhaps as a consequence, they generally feel that renewed consent is required for reuse of biobank samples. Interestingly, they also believe that this would be impossible in practice (Edwards et al., 2011, pp. 341–343).

From an organisational perspective, informed consent can be an attractive solution as it offers significant protection against litigation (Hoeyer, 2008, O'Neill, 2004). Usually not regarded a major threat in the Swedish context, this is quite a big deal internationally, and there are examples of Swedish companies following suit (Hoeyer et al., 2005a). Even when ethical rather than legal concerns are at the forefront, informed consent is attractive

because it allows a large array of issues—confidentiality, risk of discrimination, benefit sharing, to name a few—to be neatly subsumed under the question how the subject can be made to understand the stakes so that she can decide for herself. Many donors, in contrast, reject the view that a procedure of this kind absolves researchers from their responsibilities (Levitt and Weldon, 2005, pp. 317–318, Allen and McNamara, 2011).

Despite the triumph of informed consent in bioethics generally, there are some aspects of biobank research that have made it reasonable to look for alternative ways to protect research participants against harms and wrongs. Biobanks make it possible to pursue questions that "conventional" research cannot. A single blood sample can be stored almost indefinitely and reused in many different research projects. Over time, huge collections can be built, which makes it possible to identify and investigate for instance the impact of uncommon (but potentially important) risk factors. Furthermore, samples need not always be reanalysed. It is quite possible, and increasingly common, to store results from previous analyses in databases for future access.

Biobanks, then, potentially allow research to be conducted with great efficiency. Their flip side is that building the required infrastructures, especially the pan-European or even global ones which are now envisioned, is costly. With one of the major strengths of biobanks being efficient reuse of samples, imposing additional costs in this step may impede not only individual research projects but even whole biobanking initiatives. When samples are held for long periods of time, getting in touch with donors to obtain renewed consent becomes increasingly difficult. Some will have died, others will have moved one or several times, and still others will fail to answer inquiries due to lack of time or interest. What we risk is significant dropout rates for reasons that have nothing to do with people's concerns about biobanks or biobank research. Quite clearly, the validity of research is at stake (Helgesson, 2012, p. 41). For these and other reasons, re-consent for each project in which a sample is used has been argued to be unfeasible (Boulton and Parker, 2007, p. 2187, Árnason, 2004, pp. 42–43, Ashburn et al., 2000, p. 3379, Stjernschantz Forsberg, 2012).

Broad consent

To meet these new challenges, *broad consent* has emerged as the new norm in biobank research in Sweden and increasingly also internationally. Instead of seeking separate consent for each new research project, researchers obtain one-time consent for using samples in a wide range of research projects, or even *all* kinds of medical research. Broad consent does not go quite as far as "blanket" consent, which allows any kind of research (Hansson, 2009, p. 10) or even any use, including for forensic and commercial purposes (Helgesson, 2012, p. 42). Broad consent thus acknowledges the importance of letting the

donor decide whether his or her samples are to be stored and used in research, and downplays that of knowing the precise aims and methods of the studies. Two supplementary safeguards are usually assumed, namely, that the research projects in question must be approved by RECs and that the research participant should have the right to withdraw her consent at any time (Helgesson and Johnsson, 2005). This model has been employed in Swedish legislation with regard to samples taken in health care (Sveriges riksdag, 2002). Several other countries have similar implementations (Hansson, 2009, p. 9).

The notion of broad consent has raised considerable controversy both within and outside the academic community. It is sometimes suggested that the difference between the views of proponents and opponents lies in how they balance "the social good generated by biobanking research against the ethical and legal requirement to obtain informed consent" (Caulfield, 2007, p. 210). This is a curious claim since placing ethics and law on one end of the seesaw already implies that whatever sits on the other is unethical and unlawful. Indeed, it is often a foregone conclusion that broad consent amounts to a "lowering of the traditional consent standards" (p. 215).

Two arguments against broad consent warrant closer scrutiny. The first concerns whether broad consent can be properly informed; the second, whether a practice of broad consent sacrifices the interests of the individual in a way that narrow—or project-centred—consent does not.

Can broad consent be informed?

Part of the criticism sustained by broad consent regards whether it should count as a form of informed consent. Some authors argue that such talk is misleading:

> There is no such thing as "general informed consent". The more general the consent is, the less informed it becomes. It is misleading to use the notion of informed consent for participation in research that is unforeseen and has not been specified in a research protocol. It is, however, another and an open question whether it is wise to require informed consent for all secondary research purposes. (Árnason, 2004, pp. 41–42)

The last sentence appears to concede that broad consent might sometimes be justifiable after all. We are thus invited to understand the first of Árnason's claims as one about proper use of language. But the criticism runs deeper (Helgesson, 2012, p. 43). The substantive state of "being informed" is usually regarded as crucial to autonomous decision-making. If broad consent, as Árnason claims, cannot be informed, it inevitably sacrifices autonomy for some other good. This is precisely what some opponents find

unsatisfactory (Caulfield, 2007, p. 213). Proponents of broad consent have met this objection squarely:

> [W]hat is appropriate information? If the information covers all issues that are relevant for a person's choice, then that person's consent is appropriately informed. If the risks and benefits are common to several studies, then general information on these studies might be sufficient for the donor of the sample to make an informed decision. (Hansson et al., 2006, p. 266)

It is reasonable to ask for what purpose information should be given. If a piece of information is not used by someone to make a decision, it is arguably irrelevant to that particular decision (Helgesson, 2012, p. 44). Rather than requiring that *all* donors be given a certain pre-defined set of information, it might then be more appropriate to give each donor only the facts that *he* desires. This is, in essence, to embrace a subjective standard of informed consent. Conversely, if donors are satisfied with the information given, it is hard to see, from the perspective of autonomy at least, why they should not be allowed to decide for themselves (Helgesson, 2012, p. 49, Shickle, 2006, p. 516). Insisting that they need to absorb some particular set of information in order to be autonomous is, on this view, merely another form of paternalism.

There is, however, one additional complication to consider. Consent, Onora O'Neill argues, is a propositional attitude, which makes it intransitive: Consent to one proposition *p* does not imply consent to whatever is entailed by *p* (O'Neill, 2003, pp. 5–6). This is most obvious with regard to causal relationships. Imagine a friend driving you to the train station. In a sense, you consent to his so doing, though this might seem a strange way to talk about an everyday situation. On your way there, you have an accident in which you are injured. Now, even though your injury is obviously causally related to your decision to go with him, you hardly consented to be injured.

Such intransitivity applies also to *logical* relationships. Since the logical implications of *p* may not be transparent to the one who consents, consent to *p* does not imply consent to propositions that are logically equivalent to *p* or implied by *p*. The events at Alder Hey illustrate this point. Organs, as we know, are composed by tissue. So it appears that if one is allowed to do anything with a particular set of tissues, one should be allowed to do anything with the corresponding organs as well. The parents disagreed: Although they had consented to unrestricted removal of tissue, they claimed to have never consented to the removal of whole organs. According to O'Neill, they were right. To them, "tissue" meant something else—biopsy material, perhaps—and *this* was what their consent was about. It follows that consent is never consent to a procedure as such, but always to a particular description of it. If matters turn out to differ ever so slightly from how they

were described, one could truthfully claim to have never consented to what took place (O'Neill, 2002a, pp. 154–155).

If O'Neill's reasoning is correct, consent to research (or even consent to *any* research) does not imply consent to, for instance, cancer research. Similarly, consent to unrestricted future access to medical records does not imply consent to access to any particular piece of information stored within. At first glance, this analysis would seem to warrant a sceptical position on broad consent. In fact, it cuts even deeper. The problem of intransitivity becomes most apparent in the case of broad consent simply because the number of conceivable implications is large. But it also follows that informed consent to a specific study proposal can never be consent to the study itself, only to a particular description of it. Since no imaginable description says everything about a study, there will always be facts that are unmentioned, underemphasised, or overemphasised. Such facts can be used to call the consent into question (Helgesson, 2012, p. 45). In fact, if optimal "uptake" of information is the goal, the description must be tailored to the target audience. This inevitably makes it partial in some respect or another (Murphy and Dingwall, 2007, p. 2227).[9]

Applying the principle of intransitivity of propositional attitudes has unexpected consequences. A patient who consents to being included in a randomised clinical trial, for instance, has not consented to the particular method of randomisation used, unless of course it was specifically mentioned. This is no mere quibble. Although objecting to some method of randomisation may be regarded idiosyncratic, it is not obviously irrational. The patient might simply have reasons to believe that some methods are less scientifically sound than others. If we dismiss this view, we do so for pragmatic reasons rather than moral ones. Consequently, if intransitivity poses a problem for broad consent, narrow consent is equally weak as a moral justification for doing research. Increased specificity cannot solve this problem.

It might be argued that this *reductio ad absurdum* is unfair. One does not, after all, need to claim that informed consent is a perfect procedure in order to see its value. But it does show that even if the participants are assumed to be competent and interested in learning, there is no objective way to decide what facts are necessary and sufficient for autonomous participation. Such things are determined by cultural and social conventions, and can always be

[9] The problem is not that maintaining a neutral stance is difficult, but that there is no such thing as a neutral stance. The patient information sheet issued by The National Biobank Council in Sweden, for instance, mentions the value of storing samples not once, but twice. On the one hand, this could be seen as a sign of bias towards research interests. On the other, redundancy may be crucial to secure the understanding of those patients that skimmed (or skipped) the first part of the sheet. Furthermore, no less than seven different usages are listed, though they could have been condensed to three (care, quality assurance, and research). The current design of the sheet may invoke a more vivid image; but it could also be argued to overemphasise the importance of donating. Who is to say?

challenged accordingly. Consent is not morally significant in the same way as contracts are legally binding. In contracts, stipulated definitions of procedures to be carried out are crucial, but such definitions lack *moral* weight in a consent situation unless all parties embrace them. This limits the kind of moral justification that consent can lend to action.

The greater good

Broad consent is a more recent invention than informed consent, having emerged only when the latter became impractical. It is tempting, then, to frame it as a deviation from the norm—as a trade-off between protecting individual interests and facilitating research. As opponents to broad consent are quick to point out, the very notion of trading the interests of the individual for some other good goes against the grain of a fundamental principle in bioethics: that of the primacy of the individual (Caulfield, 2007, p. 216). An often cited formulation of this principle is found in the Declaration of Helsinki: "In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests." (World Medical Association, 2008)

This objection does not necessarily hinge on what information is required for autonomous decision-making. It could be argued instead that broad consent does a worse job of protecting individuals against harm than narrow consent does, and that this difference is morally significant. In pursuing this argument however, opponents of broad consent face the fundamental choice of whether or not to view the principle of the primacy of the individual as absolute. If they do, they must also regard as unethical all non-therapeutic research that entails risks to participants, however small they may be (Helgesson and Eriksson, 2008, p. 54). This would include most biobank research. If they do not, they must concede that any increased risk that donors run by consenting broadly must be weighed against the risks of delaying research if that option is not allowed. I believe that most authors would choose the latter horn of the dilemma. If I am right, divergent conclusions are seen because different people weigh the benefits and risks differently.

On one extreme, one could argue that imposing more than *minimal* risk on donors is unacceptable regardless of potential benefits. Biobank research entails risks that are unknown—which includes the possibility that they might be more than minimal. Project-centred consent would then be required to ensure that the risks are voluntarily assumed. This argument can be responded to in two ways.

First, risks can be voluntarily assumed in many ways that are morally acceptable, not just through informed consent. In the case of broad consent, proper information implies telling donors that their samples might be used in research of which they do not approve. If this is done properly, the additional

risk can be accounted for (Helgesson, 2012, p. 45). The situation is analogous to signing a contract while knowing that the terms are likely to change and that one will be too busy to notice, only with a more generously formulated right to withdraw. This does not entail that seeking re-consent will never be necessary. Arguably, when the framework undergoes a fundamental change, this might be the right thing to do (Steinsbekk and Solberg, 2011).

Second, this is precisely why we need ethics review: to weed out projects that might impose risks that are unacceptable even though donors might be willing to take them. Broad consent does not imply broad REC approval (Hansson et al., 2006, p. 269). Regardless of what consenting model one settles on, leaving risk-benefit assessment to donors is irresponsible unless one can reasonably assume that all donors will be well equipped to make them. The crucial question is thus not whether donors have a right to make such assessments, but rather whether the researchers have a duty to.

The quest for public support

In policy making, *public trust* has become something of a buzzword: universally assumed to be crucial to biobank research, but rarely defined. When it is, it is usually taken to be reducible to, or at least involve, belief (Sutrop, 2007, pp. 191–193). Some authors define trust more generally as "judgement and action in conditions of less than perfect information" (Watanabe et al., 2011). Other times, it is apparently used as an umbrella term for several others: support for biobank research; confidence in the operation of biobanks (for instance with regard to confidentiality and data security); and willingness to contribute samples and data (European Commission, 2012, pp. 23–33). Given the lack of a shared definition, the moral significance of trust is not obvious, neither is how—or indeed, if—it should be supported.

Since research is important, morally justifiable policies must not only adequately protect the rights and interest of participants but also allow research to be carried out. In the case of biobank research, this implies that policies should be made compatible with continued public willingness to participate in research. Policy makers use tools such as attitude surveys to predict how people will respond. As a consequence, knowing what people think is important to policy making not because people matter (in themselves), but because their behaviour matters (instrumentally).

Some might find this characterisation unfair. Respect for the individual is after all a base requirement which is echoed in most, if not all, modern policy documents. But arguably, basing policy decisions on survey estimates of people's attitudes is not to respect them as persons—at least not those with minority opinions. Nevertheless, rather than seeing moral reasoning based on trust as distinct from that which is based on respect for persons, I hope to show later in this thesis how they can be integrated.

This chapter focuses on the role that public trust plays in public policy. This role, it turns out, is intimately related to the evidence we have for believing that trust is more or less prevalent. Before I turn to public trust in biobank research, however, I will draw some important lessons from a neighbouring context: health care. In particular, actions intended to cultivate trust in a system may not always succeed in cultivating a corresponding degree of trustworthiness.

Public trust in health care

The histories of medical research and health care run in parallel and continue to be intimately connected not least in the field of bioethics. Traditionally, research ethics has concerned itself with questions about disclosure, voluntariness and, more recently, informed consent. Trust, in contrast, has been more abundantly debated in medical ethics. Trust is often thought essential to doctor-patient relationships since it facilitates the consultation and thus ultimately improves health outcomes (Atteslander, 2006, Mechanic, 2004, Skirbekk, 2009). Not everyone, however, has been equally enthusiastic.

The three stances of public policy

In a paper on trust and public policy in the health care setting, Mark A. Hall (2005) distinguishes three different stances that public policy has taken toward trust, namely, the *predicated*, *supportive*, and *sceptical*:

> In its predicated stance, public policy (which includes ethics and law) takes the existence of trust as a factual premise for imposing a particular obligation. The reasoning is often formal and deductive, not instrumental or empirical: Because trust exists, therefore physicians, facilities, or insurers should do X, refrain from Y, or be liable for Z. The obligations do not depend on any assumptions about how they affect trust, only that there is trust. […] In contrast, the supportive stance is more proactive. Here, public policy seeks to promote trust with rules intended to maintain or increase trust where it exists, or to restore trust where it is threatened or diminished. Contrasting with both of these stances is a skeptical attitude about trust, one that believes trust does not exist or cannot be sustained or justified, and so uses the absence or illegitimacy of trust as a premise for a regime that institutionalizes distrust. (p. 157)

The predicated stance is arguably the most traditional. It makes no empirical assumptions regarding how certain actions will affect trust. It does, however, draw on study findings to the effect that despite a general decline in trust in medical professionals generally, people continue to trust their own doctors and are surprisingly willing to forgive mistakes (Hall, 2005, p. 160, Mechanic, 2004, p. 1418). Normatively, it holds that one ought to be at least as trustworthy as one is trusted. Sometimes, however, some gap may have to be tolerated: It is neither possible to live up to the "superhuman expectations" that patients occasionally have of their doctors, nor always advisable to dispel them (Hall, 2005, p. 160). This raises important questions. Why should we regard actual trust as the standard against which trustworthiness is to be measured? How do we decide how large a gap is acceptable? And how do we know when trustworthiness should be pursued, and when people should instead be disabused of their trust? The predicated

stance tends to cast the patient in a passive role and has therefore been accused of being paternalistic (p. 158).

For various reasons, the sceptical stance is rapidly becoming the prevailing attitude in the managing layers of health care organisations. Some associate trust with old-school paternalism and therefore see a tension between trust and autonomy (p. 157). A related position holds that trust is inherently irrational, blind, or naïve. Still others assume that trust in health care has long been on the decline and is now beyond repair (Shore, 2007). It is noteworthy that one can be sceptical about traditional trust relationships while acknowledging the instrumental value of more guarded forms of confidence, perhaps something resembling Cold War "synthetic trust" (Hall, 2005, p. 164). Regardless, the sceptical stance focuses not on securing trust, but on measuring performance and ensuring adherence to clear standards. Like the predicated stance, the sceptical stance could be understood as aiming for some kind of trustworthiness, albeit one more reminiscent of machine-like reliability than of human virtue.

Lastly, the supportive stance explicitly seeks to increase patients' trust in health care. What marks this stance apart is its emphasis on investigating and addressing patients' concerns. Its success depends on making the correct assumptions regarding what kinds of actions will actually increase trust. This is not always straightforward. For instance, confidentiality laws and other kinds of privacy protection have had little apparent effect despite concerns voiced by the public in these areas. Trust in doctors seems to depend more on other factors such as interpersonal skills and pre-existing conceptions of the "archetypal physician". This may be why such trust often survives despite the fact that it is occasionally violated (pp. 159–162).

Formalisation and institutionalised distrust

Over the last few decades, health care policy has increasingly come to rely on *formalisation* in an attempt to secure its trustworthiness. In practice, the importance of trust relationships is downplayed in favour of transparency, accountability and audit. The change has had profound consequences for how trust and trustworthiness are understood. Onora O'Neill writes,

> in the last twenty years in many parts of the world further measures have been introduced, which introduce more precise ways of securing better and more detailed compliance with externally imposed requirements, and so (it is supposed) increased trustworthiness. […] If trustworthiness can be guaranteed, then placing trust will be simultaneously risk-free and unnecessary. Formalisation has advantages that are constantly mentioned by its advocates: mutual clarity of expectations, clear performance targets, defined benchmarks of achievement, enhanced accountability. (O'Neill, 2002a, p. 130)

There is a certain ambiguity to the formalist agenda: It purportedly aims to secure the trustworthiness of the health care system and nurture a culture of trust, but simultaneously seeks to make trust redundant. Interestingly, it can be described so as to appear compatible with any of the three stances described above. This gives it considerable rhetorical power, but only at the cost of impoverishing both trust and trustworthiness. I will explain.

A crucial aspect of formalism is that it can be read by patients as a token of distrust: Health care professionals must be checked up on because they cannot be trusted to do their job. Conveying this attitude to the public entails a risk of undermining what little trust may still exist (Hall, 2005, p. 163). Then again, perhaps this is precisely the point, since what is desired is not trust in individuals, but trust in the system. The formalist agenda in public health policy can be likened to the use of institutionalised distrust to cultivate trust in democratic processes:

> [T]he democratic culture of trust is due precisely to the *institutionalization of distrust* in the architecture of democracy. Most of the principles constitutive of democratic order assume the institutionalization of distrust, which provides a kind of backup or insurance for those who would be ready to risk trust, a disincentive for those who would contemplate breaches of trust, as well as a corrective of the actual violations of trust, if they occur. In effect, the spontaneous, generalized culture of trust is likely to emerge. (Sztompka, 1998, p. 26)

By promising a more trustworthy system, more prevalent trust, and less misguided trust, formalism indeed seems to be the grand unification of the three stances. But this is exactly why it struggles to support its own weight. There are three problems to consider.

First, no matter how symbolic its intent, distrust can be a self-fulfilling prophecy. Ubiquitous checkups and overt suspicion have been found to undermine doctors' sense of self-worth, professional pride, and moral integrity—and thus their trustworthiness. Some, if not many, will learn to do exactly what they are paid for, or less if they can get away with it (O'Neill, 2002a, p. 134, Hall, 2005, p. 163). Furthermore, if monetary incentives are to steer doctors towards rather than away from better judgments, the chosen performance indicators must correlate near perfectly to actual quality of care. If the measurements fail to reflect some aspects of quality, one can safely assume that those aspects will not be properly attended to. Hence, quality will suffer. In both cases, a rich conception of trustworthiness is exchanged for a considerably shallower, reliability-centred one.

Second, while institutionalised distrust could give us at least some hope of securing trust in a system where the guardians are more easily trusted than the guarded, in reality, the opposite is often the case (O'Neill, 2002a, p. 138, Sutrop, 2007, p. 195, Hall, 2005, p. 159). Not only do oversight mechanisms imply additional levels of bureaucracy, potentially consuming resources that

could be put to better use; they may also propagate the problem of trustworthiness upwards in the hierarchy (O'Neill, 2002a, pp. 130–133). What we risk is increased distrust in the system as a whole.

Third, institutionalised distrust may not even enable people to place better whatever trust they have left. In the process of uprooting paternalism through greater emphasis on informed consent and autonomy, inflicting some collateral damage on traditional relationships of trust may have been inevitable. But arguably the problem with the traditional patient-doctor relationship was never trust *per se*, but rather the asymmetrical distribution of knowledge and power and the propensity of doctors to make use of that asymmetry (pp. 16–21). Today, the major challenge for many patients is not lack of information, but how to orient themselves in the abundance of it (Atteslander, 2006). It is therefore imperative that patients are allowed to trust medical professionals to help them with those matters that they are least equipped to deal with themselves.

Public trust in biobank research

Many authors portray the public as being uneasy about medical research in general and biobank research in particular. In the UK, recent scandals such as the retention of organs at Alder Hey and Bristol Royal Infirmary are thought to have severely damaged trust in health care and research (Burton and Wells, 2002, p. 5, Boulton and Parker, 2007, p. 2188, Ashcroft, 2000, Seale et al., 2005, Kaye and Martin, 2000, p. 1146, Hall, 2001, p. 456). In the US, whole books have been dedicated to the alleged "crisis" of trust in health care and research (Shore, 2007). Public trust in research is thought to be especially fragile given that people have been "sensitised by various biomedical research controversies" (Caulfield, 2007, p. 222).

In biobanking policy, contrary to what has been the case in public health policy, the supportive stance is conspicuously dominant (Asai et al., 2002, Ashburn et al., 2000, Ashcroft, 2000, Hansson, 2005, Tutton et al., 2004, Sutrop, 2007, pp. 190–191, European Commission, 2012, p. 31). This is perhaps not surprising given that the objectives and the means necessary to reach them differ significantly between these two fields. Everyone sooner or later needs health care, and most of us will seek it, trust or no trust. Biobank research, in contrast, depends on people's continued willingness to participate. Even a slight decline might threaten the whole enterprise by introducing selection bias (Hansson, 2009, p. 8, Stjernschantz Forsberg, 2012, p. 37). Trust is considered instrumentally valuable because it presumably entails a greater willingness to participate in research. For the same reason, many fear the erosion of public trust and so regard it a fragile foundation for a research enterprise (Allen and McNamara, 2011). It has been suggested that biobanks should be embedded in familiar and trusted

institutions such as universities, national research institutes and hospitals to improve their appearance of trustworthiness and thus their sustainability (European Commission, 2012, p. 31, Harris et al., 2012, p. 1110).

Even those who agree that trust is both desirable and feasible as a means to increase research participation may see reasons not to pursue trust indiscriminately. It has been argued that trust "reproduces the asymmetrical relationship between lay and expert", effectively running counter to the ideal of "knowledgeable, empowered citizens" (Ducournau and Strand, 2009, pp. 125–126). Others have made a distinction between "authentic" and "blind" trust, where the former would be based on information, critical reflection, and autonomy, whereas the latter amounts to "obeying the authorities without taking any responsibility" (Sutrop, 2007, p. 196). Exactly how much information processing and rational reflection a citizen can be expected to carry out to qualify as autonomous is of course an open question. Many people have a hard time piecing their lives together even without this additional burden. "Trusting" others in some matters is strategically rational and, from that point of view at least, arguably compatible with individual autonomy (Kihlbom, 2008, p. 148, Helgesson et al., 2005, p. 673).

There is a clear need to understand the concept of public trust better. What is it? Is it rational? How do we measure it? What difference does it make?

In order to avoid speaking in circles—explaining empirical findings through conceptions of trust and vice versa—I will begin by suggesting preliminary definitions of public trust and distrust. "Public trust" is, I suggest, the term we use to give voice to our confidence that public support for biobank research will continue. This concept differs significantly from that of a *trust relationship* (Study III), though there are connections between the two that need to be considered. Conversely, we speak of "public distrust" when we fear that public support is about to dwindle.

My definitions of public trust and distrust have three strengths. The first is that they capture the implicit assumption that biobank research is essentially trustworthy. The second follows—perhaps surprisingly—from their subjective character. By referring to public trust as a fact not just about the public but also about the one who seeks evidence of it, we avoid making undue assumptions about the psychological state of the public (if such talk even makes sense). The third and consequential advantage is that they highlight an asymmetry in how evidence of public trust on the one hand and distrust on the other are used in directing action. Whereas confidence regarding future public support for a desirable activity counts as a reason to continue on the present course, lack of such support does not become a reason to steer off it altogether, but rather to devise measures to *cultivate* support.

There is no doubt, then, that public trust is important to consider, though our ideas of what it is and what we should do with it may as of yet be rather

vague. In the following I will summarise some influential empirical studies that claim to assess the level of public trust. After that, I describe what role trust has in fact had in public policy.

Evidence of public trust

According to the 2010 Eurobarometer survey, Europeans are generally unfamiliar with biobanks. 34% claimed to have ever heard of them, and as few as 17% had actively engaged with the topic by discussing it or seeking out information about biobanks. Nevertheless, when asked whether they would be willing to provide information about themselves to a biobank, 46% answered in the affirmative. There are striking differences in willingness between countries, with the five Nordic countries found at the top of the list at 67-93% (European Commission, 2010, p. 61). This is usually presumed to be due to their long tradition of biobanking. Finding Iceland at the absolute top may seem surprising given the controversy that has surrounded the HSD (Health Sector Database). Intuitively, public support seems to be a poor measure of ethical acceptability. Alternatively, the bioethical account of the controversy has been misguided. The European Commission takes no stand on the matter (2012, pp. 23–26).

To get the general picture of what evidence of public trust is available, I will examine the state of matters in Sweden and the United Kingdom. Both countries have a long tradition of public surveys, but differ considerably in societal structure.

The United Kingdom

In 2000, the Wellcome Trust and Medical Research Council (2002) conducted interviews with members of the public in preparation for the establishment of a research biobank. The study gave a rather mixed picture of the attitudes of the British. There seemed to be a high level of trust in medical professionals overall, but there were also signs that this trust had begun to erode. More specifically, many subjects mentioned the events at Alder Hey and the case of Harold Shipman (a GP convicted of murder of 15 patients) as reasons to be more wary in the future. People seemed to have a generally supportive attitude toward medical research, regarding it "well-intentioned and strictly controlled". There were, however, various negative connotations: "animal testing, cloning, failure to seek consent from donors, lack of openness among researchers, and profit-making by pharmaceutical companies". Genetic research in particular was regarded as sinister and thought to be carried out for its own sake rather than for public benefit. The investigators found that the better people understood genetic research, the more positive their views. The use of biological samples in research was unfamiliar to many, but once informed of this practice, most thought it acceptable if accompanied by informed consent. Many preferred that their

samples be used for disease-specific projects rather than general research (pp. 6–7). Their hesitation about the latter seemed to be connected to fears of cloning, eugenics or other questionable uses. The involvement of health care personnel, in particular GPs, lent credibility to the project (p. 8).

Public attitudes to human genetic information were addressed in a poll commissioned by the Human Genetics Commission (2001) as part of a greater public consultation programme. Nine of ten respondents claimed to trust GPs to use human genetic information in medical databases responsibly. Three-quarters would trust the NHS (National Health Service) in this matter; three in five would trust the police; two in five would trust an Expert Government Scientific Advisory Committee or academic scientists; and one in five would trust private companies or the Government. Least trusted were insurance companies (7%), employers (5%), consumer groups (2%), and the general public (2%) (p. 40).

Sweden

During the last decade, the attitudes of the Swedish public to science have been assessed in a series of public surveys conducted by the non-profit organisation Vetenskap & Allmänhet (Public and Science) in collaboration with the University of Gothenburg. In 2006, when asked to what degree they trusted different kinds of professionals to handle their responsibilities, 48% of the informants claimed to trust scientists to a large or very large degree (on a five-point scale), as compared to 67% only a few years earlier. More trusted were health care professionals (79%), police officers (60%) and teachers (52%) (Vetenskap & Allmänhet, 2007a, pp. 7–8).

Interestingly, these observations are not obviously consistent with those in related reports. When asked about their trust in academic and commercial scientists respectively, people consistently profess greater trust in the former, with an all-time low (63%) in 2010 (2010b, pp. 8–9). The way the question is posed presumably matters. In particular, asking people to compare their trust in researchers with the trust they have in other professionals might yield different results than when they are asked to compare different kinds of researchers to each other.

Certain patterns of interpretation are worthy of note. A recent analysis concludes that there was a slight weakening of trust in researchers between 2002 and 2010, whereas trust in universities appeared to be stable (2012a, p. 7). One factor repeatedly suggested as an explanation for observed changes is recent media coverage. Causes for the apparent decline in trust in 2006 were sought in media exposure of research misconduct, a general weariness among the public with regard to alarmist tendencies in scientific reports, and a prevalent perception that scientific studies often contradict each other (2007b).

In the light of later findings, fears of faltering trust might have been exaggerated. In 2012, 86% of respondents claimed to trust researchers to a

large or very large degree (2012b, pp. 6–7). The authors explained this by reference to the media attention awarded the recent governmental proposition on research and innovation as well as on the absence of reports of scientific misconduct at the time.

It has sometimes been claimed that trust is fragile and likely to be shattered by "bad news" (2008). In retrospect, it can be doubted whether there was ever a true trend. The claim that alarmist reports and fraud have caused a decline in trust is also interesting given that medical research, which should be strongly associated with both, consistently enjoys a greater degree of trust than do the social sciences and the humanities (2010a, p. 21).

Six discourse frames of public policy

In 2003, Jones and Salter carried out a discourse analysis on the role of trust in governance of human genetics research in the UK. A decade later, their work remains highly relevant. The starting premise is that public trust serves both as a tool to reach political ends and as a thermometer of public life:

> Governance in its regulatory form is the political theatre where the pressures for change from the arenas of science and industry meet the inchoate needs, values and sensibilities of civil society. From this engagement result numerous, and frequently contradictory, political demands regarding the advancement of science, the promotion of the economy and the protection of the public interest. The task of regulation is to find a way of reconciling those demands. Public trust is the key measure of its political success or failure. If successful, public trust in the process of regulation, the decisions it reaches and the activity it regulates is maintained. If unsuccessful, then public trust declines and science and industry are thwarted in their ambitions. (Jones and Salter, 2003, p. 22)

The material consisted of 30 public policy documents of central importance. The authors identify six dominant discourse frames. In the following, I add some present-day examples to show how these frames apply to the current state of the debate. I thereafter discuss the significance of the fact that not all relevant issues are covered by them.

Mistrust and public ignorance

The first frame centres on the assumption that "non-scientists who do not trust science must be suffering from a deficit of information and understanding." (p. 30) More recently, the European Commission has stated that informing people better is paramount because in countries where few people are aware of biobanks, few are willing to participate in biobank research, and few express support for broad consent (European Commission, 2012, pp. 24–26). This line of thinking has been referred to as *the deficit model* because it explains the reluctance of the public in terms of its limited

knowledge or capacity for rational deliberation, the tacit assumption being that "to know science is to love it" (Sturgis et al., 2010, p. 166).

A version of the deficit model infuses the contemporary debate on informed consent. Informing someone, on this understanding, is accomplished by "educating" him or her through effective transfer of "objective" information. Misunderstandings arise when the information is incomplete, misleading, or badly written or when participants fail or refuse to produce the appropriate response. Consequently,

> [t]he solution to "misunderstanding" and "misconception" is then seen as lying in the more thorough informing of research candidates, of disabusing them of any "false" emotions they might feel about their participation, and, above all, of persuading them of the scientific account (Dixon-Woods et al., 2007, pp. 2213–2214).

Where an informational deficit exists, the remedy becomes a matter of improving the participant's information uptake by making it more comprehensive, clearer, more accurate, more relevant, more attractively packaged, etcetera. There is little empirical evidence that efforts of this kind are effective. In an experimental panel study, Sturgis et al (2010) investigated the effects of educational films on knowledge of and attitudes to different types of science as well as on trust in genetic scientists. Participants completed a questionnaire on three occasions: before, immediately after, and 4-6 months after the intervention. One of the two intervention groups watched a short film aiming to provide value-neutral, factual information. The second group watched a longer film covering also the legal and regulatory framework of genomic science. A control group completed the questionnaires without watching any film. The only observed effect of the interventions was a slight immediate increase in self-reported trust in the short-film group, and even this effect was temporary.

Accountability to a higher level of authority

Many of the documents reviewed emphasised the importance of multinational governance and regulation for public trust (Jones and Salter, 2003, p. 31).[10] Sometimes they explicitly referred to "higher-level bodies". The implication, apparently, was either that higher-level bodies would be more trusted than their lower-level counterparts, or that adding an extra level would somehow make the system as a whole more trusted.

[10] While regulation is usually understood as a set of formal rules, governance is a broader term that encompasses different kinds of intentional control of the actions of others through formal and informal bodies, documents and procedures as well as through everyday practice. See EUROPEAN COMMISSION (2012) Biobanks for Europe: A Challenge for Governance. Luxembourg: European Commission.

Today, given the difficulties that researchers collaborating across nation borders face when trying to navigate diverging legal frameworks and REC decisions, multinational governance may be necessary (European Commission, 2012, p. 45). The question how the public will react may thus be largely redundant. Some people may nevertheless find it easier to place trust if there is a clearly defined governance structure or body to speak for all that may have access to their data (Levitt and Weldon, 2005, p. 316). On the other hand, from what was said in the previous section about people's apparent preferences in placing trust, it can be doubted whether extra levels of authority would be conducive of trust. If anything, the presence or absence of interpersonal relationships of trust may be what decides the issue for many people (Studies I and II).

Management of conflicting interests

This frame is applicable ever since external governance replaced researchers' self-regulation (and thus their mandate to resolve conflicts internally). Most saliently, public and private interests are juxtaposed. Maintaining public trust is framed as a matter of having robust regulations that allow research to continue without sacrificing protection of individuals (Jones and Salter, 2003, p. 31). More recently, adequate data protection to ensure privacy and protection against potential misuse of information has been emphasised as necessary to sustain public trust in biobank research (European Commission, 2012, p. 29).

In a British study, participants in focus groups made a similar "sharp divide between the economic forces driving commercial companies and aimed at benefiting shareholders, and the health service that exists for the whole population." (Levitt and Weldon, 2005, p. 315) But not only commercial companies were suspected of having "an axe to grind". Patient groups and the scientists themselves were not above suspicion. Furthermore, promises of adequate regulation did not reassure the informants. Instead, they expressed scepticism regarding the possibility of enforcing them (p. 318).

Controlling science

This frame resembles the previous one in that it pertains directly to the perceived impotency of regulation. However, it focuses on a different threat, namely, that regulations will not keep pace with the advances in science. This risk is perceived as particularly great in controversial research fields such as human cloning (Jones and Salter, 2003, p. 32).

Other authors have noted that past experiences of racism and eugenics have left a trace of suspicion toward genetics, in particular from groups that have suffered in the past (Schwartz et al., 2001, McQuillan et al., 2006, Wong et al., 2004). These fears should perhaps not be too readily dismissed.

At the time of writing, tests purporting to assess "racial purity" are provided by at least one biotech company (Retassie, 2012).

Apart from such clearly unacceptable (and occasionally silly) uses, eugenics has, in a broad sense of the word, long been practiced in medicine. For instance, pre-implantation diagnostics for serious congenital diseases is often regarded as acceptable. Drawing the line against more questionable purposes is not always straightforward (Archer, 1998).

Transparency

It is usually assumed that a long-time practice of withholding information from the public has been instrumental in the erosion of trust. The response has been not only to provide open access to information, but to more actively advertise it (Jones and Salter, 2003, pp. 32–33). It has been more recently claimed that Europeans demand transparency with regard to the research aims and actors involved as well as feedback on research outcomes (European Commission, 2012, p. 31).

Critics have argued that transparency is nothing but a revised version of the deficit model where deficit of *knowledge* remains in the picture while deficit of *ability* is deemphasized. It has also been criticised for promising more than it can deliver. Beyond making information available, transparency does not contribute in any way to the deliberative process. Worse, the public is sometimes informed only after the relevant decisions have been made (Jones and Salter, 2003, p. 34).

Accountability and public consultation

In addition to transparency, public consultation has emerged as a relatively new strategy. It purportedly legitimises policies and engenders trust by involving lay people in the decision process. The strategy has faced criticism for being ineffectual since there is nothing that forces decision makers to actually respect the recommendations (Jones and Salter, 2003, p. 33).

The current stance of the European Commission is that care must be taken not to implement policies that lack public support. The need to involve patients is emphasised on many levels: as "partners in the research effort, especially in the areas of communication, advocacy and recruitment"; during the establishment phase of biobanks; in giving voice to their experiences regarding research needs; and as recipients of feedback "regarding use, sharing and transfer of samples" (European Commission, 2012, pp. 32–33). This trend is in line with the modern ideal of "empowered citizenship in a knowledge-based society", to be contrasted with the traditional dependence of lay people on the judgments of experts (Ducournau and Strand, 2009, pp. 125–126). It might, however, entail a risk of overemphasising the participation aspect:

> Commentators have suggested to adopt the term 'participant' rather than 'donor' to acknowledge the ongoing mutual nature of the relationship here described as established through biobanking and to avoid connotations to an over-and-done-with 'gift' […] We might, however, thereby overemphasise the element of participation. It is not an equal relationship and some donors will wish to limit their workload and obligations rather than enhance their influence on decision-making. Rather than emphasising participation I believe researchers should ask themselves what type of relationship specific donors have opted for when agreeing to participate. (Hoeyer, 2010, p. 350)

From this perspective, gifts are never over and done with; they are always interwoven with the obligations that pertain to a particular relationship. People who give gifts do so for a reason, and they want something in return (pp. 348–349). What emerges is a "gift relationship":

> Trust is an important factor in today's uncertain world but, rather than seeing trust as a measurable goal or performance indicator, we suggest that it needs to be seen as an emergent property of good social relationships that are built up over time. […] A 'gift relationship', embodying solidarity and trust, requires the establishment of a mutual relationship with obligations and expectations on both sides. This is the sort of evidence that people need in order to place their trust well. (Levitt and Weldon, 2005, p. 320)

Whenever we receive a gift, we are expected to *reciprocate* in a suitable manner. This is sometimes taken to imply that donors should receive results from the analysis of their samples or perhaps extra health checks (European Commission, 2012, p. 31, Gottweis et al., 2011, p. 739). But not everyone has such expectations. Neither is it clear that they, when present, should decide the issue. Very little can be said in the abstract about what reciprocal relationships are or must be like. After all, most meaningful relationships with other people involve some degree of reciprocity. Rather, the nature of a relationship becomes apparent in the responses that emerge as suitable ones.

Waning public trust—a matter of deficit?

This, then, is the policy makers' view of public trust in biobank research. But public trust has not always enjoyed the kind of attention it does today. To understand it properly, we must consider it against the background of the wider discourse on public support for science. According to Bauer and colleagues (2007), public trust is but the latest in a line of paradigms aiming to "sell" science.

Scientific literacy

The first paradigm frames the problem of lack of support for science in terms of deficit of *knowledge*. It was allegedly born in the 1970s in conjunction with public opposition to nuclear power. Central to its rhetoric is a

distinction between *objective* or *real* risk on the one hand and *subjective* or *perceived* risk on the other. The "scientific-institutional" view is considered better informed and thus objective, whereas the emotionally-laden views of the public are characterised as subjective. Arguably however, the former view tends to discount many potentially legitimate concerns. In the nuclear power case, people's concerns about morbidity, environmental damage, waste disposal, uranium mining, nuclear weapons, and many other things were largely ignored (Wynne, 2006, p. 214).

In this paradigm, the remedy against faltering support for science is to enhance the "scientific literacy" of the population. A literate public, it is suggested, would be more supportive of research programs and more likely (and able) to participate in public debates on science (Sturgis and Allum, 2004, p. 55). As we have seen, several of the discourse frames of biobank policy continue to make this assumption. But this time, it is not only knowledge of science *per se* which is thought lacking, but also of how it is regulated.

Public understanding of science (PUS)

From the mid 1980s, concern for public deficit of knowledge was partly replaced, or at least modified, by a growing awareness of the importance of public *attitudes*. In essence, the problem was now thought to be that people were "insufficiently in love with" science (Bauer et al., 2007, p. 84). Scientific interest for the correlation between knowledge and attitudes was growing; nevertheless, the presumption that "the more you know, the more you love it" still prevailed. New tools for promoting science emerged. Besides educating the public, one could now hope to "seduce" it through "market segmentation, profiling, targeted campaigning and message positioning"—just like one would market a commodity (p. 83). Recent emphasis on transparency and public consultation must be understood in this light.

Science and society

The last of the three paradigms involves a partial reversal of attribution of deficit. Scientific institutions, it is now thought, have held prejudiced views of the public, in particular regarding their capacity for understanding science. This has in turn led to misguided communication efforts, further contributing to the "crisis of trust". In the search for a remedy, the distinction between research and intervention has become blurred:

> The aim of analysis is to change institutions and policy. This agenda, academically grounded as it may be, often ends in political advice with a pragmatist outlook. […] Public deliberation and participation are the new "royal road" to rebuild public trust. (Bauer et al., 2007, p. 85)

As illustrated by the debate surrounding genetically modified (GM) crops in the UK, public consultation does not always imply genuine dialogue:

> [T]he British public was far from convinced of the benefits of GM crops and foods—not what the government hoped to hear. There were two responses: to attack the process on protocol for allowing environmental groups to have too much influence; or on outcome and to conclude that further dialogue was needed until the public had the "right" attitude. (p. 86)

Losing sight of the problem?

There are two main problems with the role attributed to trust in public policy. First, it is seen as yet another attitude to be engineered in order to maintain public support for research (Wynne, 2006, pp. 219–220). Commendable as these motives may be, I believe that such single-mindedness entails a risk of losing sight of the meaning of trust as well as of its moral relevance. This will be a main topic for discussion later in this thesis.

Second, despite considerable efforts to engage the public, some ethical concerns tend to fall outside the frame. Some attention to this phenomenon is warranted since it highlights one of the problems of trustworthiness.

A persistent fear of many people—and one that has inspired numerous books and movies—is the power of research to transform society, and not necessarily for the better (Levitt and Weldon, 2005, p. 319). Although the "Control of science" discourse frame touches upon these matters, it focuses on preventing illegal research rather than shaping future conventions. With policy makers and bioethicists firmly entrenched in familiar categories of pursuable issues—autonomy, privacy, confidentiality, etcetera—the public may find itself alone in facing many wider societal issues.

It might be argued that the solution is to be found in public consultation. But as observed by Jones and Salter, the policy discourse can be both oppressive and self-perpetuating:

> In order to have a sense that their concerns are engaged with, interested un-officials are forced to participate in the dominant political discourse of genetics and risk; in effect, this reinforces and reproduces the legitimacy of dominant frameworks. (Jones and Salter, 2003, p. 39)

Other authors have argued that the dominant discourse is oppressive in an even wider sense:

> even enlarged institutional discourses which recognize public ethical as well as risk-related concerns only serve to exacerbate public alienation and mistrust if, as they usually do, they impose their own definitions of what counts as an ethical issue, rather than recognizing the ethical concerns which people typically express […] For all their fashion-following language of

> upstream public engagement, they remain rooted in attention only to downstream impacts, and not to making upstream driving purposes, about the human ends of knowledge, not only its instrumental consequences, more accountable and humane. (Wynne, 2006, pp. 217–218)

To conclude, with proper governance in place, and even with public consultation, a number of issues remain to be addressed both within and outside of the dominant discourse frames. I will argue that this is where relationships of trust will have to do most of their heavy lifting. First, however, trust must be liberated from some of our expectations of it—most importantly, the one that it should be useful in our pursuit of public support for science. Once this is done, we can begin using it as a moral concept. It will then become evident that attention to, and respect for, precisely those expectations that *go beyond* or *challenge* social and cultural norms is an important part of what it means to be trustworthy.

Aims

The overarching aim of this thesis is normative: To examine how different normative positions with regard to the role of trust and individual responsibility in biobank research can be justified, and to test the strength of those justifications. I approach this aim through three related perspectives, each of which can be formulated as a pair of contrary statements:

1. The public tends to trust researchers and the research community *vs.* public trust is in short supply.
2. Trust is essential to research participation and therefore to the success of important research *vs.* trust poses a threat to autonomy and is obsolete in a society of enlightened individuals.
3. Ethically acceptable research depends on the researcher's individual moral competence *vs.* ethically acceptable research depends on regulation and oversight.

In Study I, I ask: How often do Swedish patients refuse to participate in health care-related biobank research? The question is justified by the reasonable assumption that if distrust were widespread, many people would refuse to participate when asked.

Study II asks: Do surveys accurately predict actual willingness to participate in biobank research? This is what we expect of instruments of measurement that we have reason to believe are reliable and valid. Consequently, failures to accurately predict behaviour must, unless resulting from flaws in individual surveys, count as a reason against relying on surveys in estimating trust.

Study III asks whether trust can be fairly described as either a disturbing element or something that should (or can) be cultivated for particular ends. I also seek a theoretical basis for my intuition that both trusting and being trusted is normatively significant in ways not captured by either of these views.

Finally, Study IV discusses to what degree researchers should be trusted or distrusted to take individual moral responsibility for their research. The dangers of both extremes are elucidated.

Methods

Bioethics is commonly characterised as a branch of applied ethics that deals with ethical questions in health care and biomedical research. As the word "applied" indicates, it is not primarily concerned with theory-building. Still, it somewhat misleadingly suggests that bioethics is about picking a theory and somehow grafting it onto reality to see what emerges. Though many bioethicists habitually approach problems from one or several moral theories, it is perfectly possible to practice bioethics without subscribing to any particular theory.

It would perhaps be more accurate to refer to bioethics as a kind of *practical* ethics, by which I mean ethics that deals with pressing real-life issues, as opposed to questions of mainly theoretical interest. A main task of the bioethicist is to critique normative positions—claims as to what should be done—by exposing inconsistent reasoning and unwarranted assumptions about facts, values, interests, duties, consequences of certain lines of action, etcetera.

To do ethics, understanding the difference between empirical, conceptual and normative claims is crucial. It can be illustrated as follows. A and B plan to have pancakes for dinner. A opens the fridge and looks into it. He then turns around and fixes B with an accusatory stare. "You forgot to buy milk," he says. How are we to understand this statement? First, A seems to claim that there is not enough milk in the fridge. This he finds out empirically, by looking. Second, A claims (implicitly) that milk is required to make pancakes. This is a conceptual issue that boils down to what we mean by pancakes. Third, A implies that their plans being upset is somehow B's fault. This is a normative claim, presumably resting on an agreement between A and B that whoever goes shopping is responsible for acquiring the requisite ingredients. Different methodology is required to challenge each kind of claim. In practice—even in academic work—they are often intermingled, and untangling them may require considerable effort.

Given that one of the tasks undertaken in this thesis—to address the question whether trust is abundant or in short supply—is clearly empirical, while the other two are conceptual and normative, it has been natural to approach them through very different methods, as described below.

Empirical methods

As I have described in the background chapters, a frequently used method to assess public trust is to conduct public surveys. An alternative approach, which I take in studies I and II, is to observe actual behaviour. To pre-empt an obvious objection, I do not claim that trust and "trusting behaviour" (if participation or cooperation can be described as such) amount to the same thing. But neither is it obvious that trust is accessible through introspection, which those that approach trust through surveys must presume. How these concepts relate to each other is a theoretical issue that must be addressed by different methodology, such as the one I employ in Study III.

Study I

Study I was designed to estimate the current (2005–2006) prevalence of "trusting behaviour" among Swedish patients with regard to storage of samples for future research. Theoretically, the best measure would have been the percentage of patients that did not refuse at least once during the study period. Investigating this ratio, however, would have involved tracking consent on a per-patient basis, potentially infringing on their privacy. I therefore settled for the second best measure: the percentage of *samples* for which consent was refused.

A peculiar feature of the Swedish system is that consent is presumed unless patients expressly refuse, first orally and later by filling out a "dissent form". It therefore made sense to calculate both the *preliminary* refusal rate on the basis of oral refusals and the *confirmed* refusal rate from the number of dissent forms submitted. At the time of the study, only a few years after the Biobank Act was passed in 2002, it was reasonable to assume that many patients would be under-informed about biobanks and their rights. We therefore had to consider the risk of overstating the theoretical (negative) correlation between refusal rate and trust. Furthermore, many health care institutions had not yet developed reliable routines, so actual refusal rates might be underestimated. On the other hand, if distrust were widespread, one could expect awakening awareness in the population and improving routines in institutions to manifest as an increase in refusal rates over time. A repeated cross-sectional approach was therefore deemed appropriate as it allowed a comparison of refusal rates between 2005 and 2006.

The lack of consistent routines across the country also entailed that not all data required for this study was available in central registers. We therefore used a top-down approach, beginning with Regional Biobank Registers (RBRs) across the country and working downwards through the hierarchy of biobank coordinators and individual laboratories. Full coverage was obtained in 13 of 21 locations (counties or central hospitals), and partial coverage in

an additional seven. The data was separated into series by sample type and location.

Outcome measures (preliminary refusals, confirmed refusals, dissent to specific uses of material, withdrawals of previous consent, undecided cases due to inability to consent, and unknown consent status due to system error) were expressed as ratios of the number of referrals. In each calculation, those (and only those) series for which the numerator was missing were excluded. We tested for change over time with Pearson's Chi-squared test for independence.

Study II

Study II compared factual participation rates in biobank studies to people's hypothetical willingness to participate based on survey estimates. In contrast to Study I, which was confined to the Swedish context, we extended the scope of Study II to include Iceland, the UK, Ireland, the US, and Singapore. By tracking references from contemporary literature on public attitudes to biobank research, we identified nine public surveys conducted in the past decade (1998-2008) that addressed hypothetical willingness to donate samples. Since many donors are also patients, we included two British surveys carried out on patients. Twelve biobank studies that reported participation rates were identified through published papers and by word-of-mouth. Only biobank studies with opt-in recruitment were included so as to eliminate the possibility of counting unaware donors among "trusting" ones.

Each survey was matched to one or more biobank studies based on country and approximate time frame (maximum gap of five years mid-enrolment), yielding a total of 22 pairs. In each pair, hypothetical and factual willingness was compared using Pearson's Chi-squared test for independence. A weakness with this design was that the observations were not independent. This was a deliberate trade-off. Due to the heterogeneity of the studies included, attempting any kind of summary measure would have been misleading. A one-to-one comparison setup would have been preferable, but with a single exception—namely, the pair of studies pertaining to the UK Biobank—none of the possible matches were unambiguously superior to any other. The resulting weakness was mitigated by seeking to explain the results of each comparison individually.

During the course of the study, several factors that could potentially influence people's willingness to participate in biobank research were identified. People who were approached as patients appeared on average to be more willing than the general public. A similar trend was observed for face-to-face recruitment as opposed to recruitment over mail or phone. Based on previous studies we expected genetic or commercial research as well as open-ended (as opposed to time-limited) storage of samples to be potential deterring factors. Controlling for all deterring factors was not

feasible given the small sample size. Instead, each comparison between survey and matching biobank study was presented separately, accompanied by a discussion on what factors could reasonably have contributed to the outcome.

Philosophical methods

The research question posed in Study I rests on the assumption that widespread distrust will show in high refusal rates. Only by making this assumption can one take low refusal rates as evidence of trust. Similarly, it is assumed in Study II that reliable and valid measures of trust—if such can be found—will also predict research participation. This is how the study raises the question whether surveys are in fact able to measure trust. So far, this is hypothetic-deductive standard fare.

The suspicion that many people are under-informed constitutes, as noted above, a potential objection to the conclusions drawn in Study I. This calls for a revision of the basic assumption: that widespread distrust will, unless people lack the knowledge necessary to allow them to act on it, entail high refusal rates. The question whether people in fact have such knowledge can then be the object of another empirical study. But imagine that we were to find that people are in fact very well informed, yet almost all agree to participate. Is this not conclusive evidence that there is trust? What could possibly still make us doubt? The question is not rhetorical, but aims to make a conceptual point.

Let us first note that even if a survey were to indicate that people are distrustful of research, this would not challenge the basic assumption that one who trusts will not participate, or cooperate, if given a choice. Faced with such evidence, we would perhaps begin to question the validity of the survey, or to suspect that people are somehow systematically coerced into participating in biobank research. But the core of our original assumption does not lend itself to testing. This is not to say that it is scientifically unsound; it is simply one that is not refutable through *empirical* counterevidence. The same goes for the claim that a valid and reliable measure of trust *is* one that predicts participation. To actually challenge or support these claims, one must take a theoretical position on the meaning of trust rather than provide new observations of what one takes to be trust. To dismiss the idea that trust can be assessed by observing behaviour, or to insist that surveys can measure trust without necessarily predicting behaviour, is to embrace a particular *model* of trust: one holding that trust resides in our minds. We are thus led to Study III, which aims to elucidate the concept of trust.

Perhaps due to its importance in human interaction, trust has been studied in several different research fields. In experimental psychology, for instance,

subjects play "trust games" in which trusting behaviour can allegedly be observed (Bicchieri et al., 2011). One might, for instance, design an experiment to see what makes people cooperate with each other in a competitive game and, conversely, what makes them more likely to defect. To actually gain generalisable knowledge from such experiments, the psychologist needs a theory that predicts the outcome. Observations that go against expectations potentially count as reasons to revise the theory to accommodate for them. Psychologists investigate trust without necessarily claiming to observe it directly. Rather, trust is *operationalised* in trust games by exposing the players to cooperative and non-cooperative moves with varying degrees of risk and potential gain.

Of course, calling something "trust" does not yet make it trust. It is quite possible to claim that trust is something else than what the psychologist has studied without questioning the validity of her experiment. Put differently, a psychological experiment is designed to test a hypothesis regarding what people do in this or that circumstance, not to determine how we should speak of this or that kind of action. How well the word "trust" reflects what it refers to—in this case, a decision to cooperate—can be determined only by nailing down what trust *means*. This is where philosophy kicks in.

A similar line of reasoning may elucidate the relationship between philosophy and sociology. Though the sociologist may be interested in trust primarily as a variable that helps explain social interaction (Sztompka, 1998), he cannot avoid defining it, for instance as a mechanism for reducing complexity. This inevitably makes his theory susceptible to philosophical critique. Conversely, philosophers often support their accounts of trust with more or less well-founded empirical claims about its function in human endeavours. But the fact that disciplinary boundaries are routinely transgressed does not make them irrelevant. It only highlights the importance of distinguishing between empirical and conceptual claims.

Conceptual analysis

Conceptual analysis is a blanket term for a set of methodologies used in philosophical analysis. Its aim is to break down problematic concepts into smaller parts in order to better understand them. A popular—though by no means uncontroversial—approach is to construe the concept of interest in terms of a number of individually *necessary* and jointly *sufficient* criteria (Simpson, 2012, p. 550). The idea is that if such a set of criteria can be found, it will describe all instances of the concept and nothing but those. Philosophers work iteratively by drawing up examples, stipulating definitions, and subjecting them to critique through counterexamples. The process resembles hypothetic-deductive methodology: Substantial claims about a concept, just like empirical hypotheses, are falsifiable, and it is through falsification that the process moves forward (Føllesdal et al., 1993).

An important part of conceptual analysis is to nail down how the concept of interest relates to other important concepts in the context. For the purposes of this thesis, one such relationship is the one between trust and rationality. As rationality is important for autonomy, and autonomy is hard to ignore in contemporary bioethics, it seems reasonable to demand from an account of trust that it take a stand on whether trust can be rational. Answers to this question have generally—with some exceptions—taken one of two forms: "Trust is irrational because *p*", or "Trust is rational if/only if *p*". The reason given in *p* usually draws upon some theory of rationality and points to those aspects of trust (as it has been defined) that make it irrational or rational, respectively. One might, for instance, presume a conception of rationality holding that rational beliefs must be backed by evidence: facts or observations that make the belief likely to be true. If one's definition of trust entails that it is "resistant to evidence", that is, it prevails in the face of evidence of untrustworthiness, one is forced to conclude that trust is inherently irrational. I firmly reject that conclusion in this thesis.

In practice, conceptual analysis is rarely this tidy. Below, I will point out two difficulties that plagued my early work with trust. They are possibly representative of challenges posed by conceptual analysis in general, or they could be idiosyncratic. Regardless, they serve well as an illustration.

One or several concepts?

While analysing a concept, it is all too easy to disregard the fact that words often have different and more or less overlapping uses. Those that strike us as metaphorical ("I trust there will be rain today"), religious ("In God we trust") or sarcastic ("Trust him to do something like that!") generally present no problem. An account that tried to embrace them all would at any rate need to stretch itself thin enough to become irrelevant. Other times it may be less clear how we should think of a particular use of the word. Sometimes, "trust" means nothing more than a kind of detached confidence that some things are likely to happen because we can deduce from facts that they will, or because they have happened before in similar circumstances. Other times, one might be neither detached nor particularly confident, yet be said to trust. One might for instance trust a computer in the sense that one relies on it to do what it is meant to do. Some people do so to the extent that they fail to develop contingency plans, for instance by forgoing regular backups of their data, without thinking much of the matter.

Intuitively, the trust one might have in one's computer does not qualify as "real" trust. Opinions may of course differ on what qualities we should require of an instance of trust in order to call it "real". Thomas W. Simpson takes the ease with which counterexamples can be produced as a reason to be sceptical of the idea of trust as a single concept; yet he embraces in the end what he calls an "Ur-notion" of trust: "I trust someone when I rely on their freely cooperative behaviour." (Simpson, 2012, p. 558) This illustrates, I

think, how difficult it is to refrain from a single-concept analysis even when one considers such exercises futile.

In my analysis, I identify some instances of trust as more *paradigmatic* than others. Arguably, paradigmatic cases of trust are found in interactions between people.[11] Most of us develop a few deep relationships of trust within which we might be able to entrust matters that we could never entrust to anyone else. In contrast, we trust many people to do some things, like truthfully telling us the time when asked. What these distinctly different relationships share is the possibility of betrayal. (In contrast, it would not make sense to accuse a worn-out hard drive of betraying its owner, except figuratively or as a joke.) I have found it useful to begin with paradigmatic cases because these, at least, should be encompassed by a realistic account of trust.

Fundamental assumptions

Philosophers are obsessed with consistency. This is not in itself a bad thing. With training, spotting inconsistencies or contradictions in one's arguments and those of others becomes second nature, which greatly facilitates philosophical work. Deciding whether or when the fundamental assumptions behind one's work should be challenged is much harder, especially when defending it against opponents who share them. Two authors might debate whether trust is a belief or some other kind of attitude without realising that both have assumed it to be located within our minds. There is a considerable risk of one's attention being diverted away from trust as an aspect of human life toward the much narrower view of trust as a cognitive phenomenon, as something to be discovered in the human brain (Lagerspetz, 1998). I have attempted to avoid this pitfall by making very few assumptions about the psychology of the one who trusts, focusing instead on how trust is and can be used normatively.

Normative argumentation

As described earlier, normative statements are ones about what ought to be done rather than about the actual state of the world we live in. *Normative ethics* aims to produce such statements, whereas *descriptive ethics* tries instead to elucidate what norms actually infuse human practices. Bioethics tends to do a little of both. This thesis leans toward the normative.

[11] Of course, all trust between people is not paradigmatic. Sometimes, "trust" denotes polite hope or expectation ("I trust you have had a pleasant flight!") or grudging cooperation ("I guess I will just have to trust you.") We may speak of "placing trust" (like one places bets) in a person, which could mean that we rely on that person to do something, perhaps without developing contingency plans. The latter implies no particular degree of certainty—as any seasoned gambler knows, it all comes down to odds and payoffs.

How does one go about arguing what ought to be done? Let us first note that any normative position needs to be supported by concepts and facts, not necessarily in order to make it more persuasive, but to make it intelligible.[12] Even a bare-bones command such as "Do not kill!" presupposes at least an understanding of the concept of killing. More, one must know some crucial aspects of the conditions of human life to see why one would need to utter such a phrase in the first place. (In an ideal pacifist society, one would not.) Any statement about what we—as members of a profession, citizens in a society, or human beings—ought to do therefore has to say at least something about the world we live in.

Facts can also direct lines of inquiry in certain directions rather than others. Consider how the findings in Studies I and II are used to drive the investigation in Study III. The former two provide examples of behaviour that might be called "trusting". Further, they suggest that interpersonal relationships of trust are operative in such behaviour. They do not directly influence the conceptual analysis; rather, they act as reasons for assuming that a model of interpersonal trust can be *normatively relevant* in the context of sample donation.

Perhaps surprisingly to those unfamiliar with analytical philosophy or normative ethics, the same kind of empirical falsifiability that forms the backbone of the natural sciences is commonly regarded as a weakness in normative theories. Whenever a normative theory depends on the "truth value" of an empirical statement, it can also be refuted by empirical findings. By custom, therefore, ethicists involved in abstract theoretical work use empirical statements sparingly. In applied ethics, just like in everyday discussions, empirical statements are used much more generously to back one's claims: One should/should not do *x* because it is the case that *p*.

Besides the self-inflicted weakness of arguments of this form to empirical counterevidence—namely, evidence that *p* is false—there is another problem worthy of note. It could be argued that no proposition *p* is in itself a sufficient warrant for *x*. The connection between fact and normative claim may itself need justifying. Imagine for instance becoming witness to a child ripping the legs off an unfortunate insect. As any responsible adult would, you scold him: You should not do that (normative claim) because you are hurting the insect (fact). The answer comes promptly: Why should I not hurt it? You reply: Because it is wrong to inflict pain on others. Why is that wrong? The child asks. And so on, leading into a spiral of increasingly abstract (though not necessarily mistaken) justifications. And the discussion

[12] Though there have been attempts to formulate purely formal moral frameworks and statements—Kant's Categorical Imperative springs to mind!—those would hardly qualify as normative *positions*. A position is a position *on* something; an abstract framework would be a position on everything, which does not make sense.

does not end until both parties agree on a justification which will just *have to do*—or one of them gives up in frustration.[13]

The trick of normative argumentation, then, is to subject particularly shaky justifications—both one's own and those of others—to closer scrutiny while leaving passable ones alone. Which ones are which is not always obvious. In Study IV, I discuss the trend of institutionalising distrust in order to secure the trustworthiness of a system, in this case that of biomedical research. Several justifications that may seem good enough turn out to be questionable. For instance, arguments of the form "Researchers must be monitored since they have behaved badly in the past" begs several questions. Does bad behaviour in the past predict bad behaviour in the future? It may not, if what caused the behaviour was not the property of "being a researcher" but some other factor that no longer applies. Is oversight an effective means to prevent bad behaviour? There may be examples to the contrary. Furthermore, there may be other important values at stake. Does, for instance, institutionalised distrust have unintended side effects? If it does, it may be necessary to weigh those against its benefits.

[13] Sometimes, at least among philosophers, this "final" justification takes the form of a normative theory. But as often as not, philosophers disagree even on those.

Summary of Findings

Study I: Patients' refusal to consent to storage and use of samples in Swedish biobanks

In 2005–2006, an estimated 2.9 million samples were stored in clinical biobanks in Sweden. The proportion of samples for which preliminary (oral) refusal was expressed increased slightly from 0.139% to 0.149% (p=0.035). However, the confirmed refusal rate—defined as the fraction of samples for which a dissent form was signed and submitted—did not change significantly; if anything, there was a slight declining trend from 0.066% to 0.061% (p=0.062). Of all refusals, about three-fourths concerned storage, that is, constituted requests that the sample be destroyed or anonymised.

A model built on presumed consent and opt-out potentially entails a risk of patient-donors being under-informed about biobank research and their rights. Nevertheless, the low refusal rate and lack of a positive trend over time suggests that very few people are concerned about what risks storage of material may entail. Even fewer seem to be negatively disposed against research as such. We thus have at least one reason to doubt that distrust toward researchers or the research apparatus is widespread.

Study II: Hypothetical and factual willingness to participate in biobank research

Out of 22 pair-wise comparisons of hypothetical and factual willingness to participate in biobank research, twelve suggested that willingness to participate in biobank research may be greater than surveys predict, six indicated the converse relationship, and four showed no difference.

Given that the settings in which these studies took place varied widely, the small number of studies, and that the comparisons could not be regarded as independent observations, no further statistical analysis was performed. Instead, we sought to explain each observed difference individually. Notably, the three biobank studies with the lowest participation rates (10–26%) used relatively "impersonal" methods of recruitment (phone and mail) and recruited from the general population. Conversely, the three biobanks with the highest participation rates (88–99%) recruited patients face-to-face.

The same pattern was seen in the material from the Icelandic Cancer Project, which involved both patients recruited face-to-face (n=3817, 88% participation rate) and controls recruited by mail (n=1743, 82% participation rate). Post-hoc analysis reveals that this difference is statistically significant ($p<0.001$). Studies mentioning genetic research almost unequivocally displayed lower willingness than those that did not. This was true of both surveys and biobank studies, and seems consistent with findings from the US NHANES surveys that mentioning genetics can deter many people from participating. Against our expectations, commercial involvement and open-ended storage had no predictive value in this study.

Of the 18 pair-wise comparisons in which an apparent difference between hypothetical and factual willingness was found, 15 could be explained by taking these additional factors into account. The remaining three suggested that factual willingness to participate in biobank research is higher than the corresponding surveys would predict.

On the whole, the results of this study suggest that interpersonal relationships with health care personnel matter in people's decisions to take part in research. It also suggests that one may reason differently depending on whether one is expressing one's hypothetical attitudes or actually making a real-life decision. How important these factors are and whether the effect is mediated by trust, altruism, feelings of duty or something else entirely, are questions to which this study does not provide a definite answer.

Study III: Adequate trust avails, mistaken trust matters: On the moral responsibility of doctors as proxies for patients' trust in biobank research

Acknowledging the possibility that patients' trust in their doctors may influence their willingness to participate in biobank research, this study investigated the concept of trust from three perspectives: scope, rationality, and moral significance.

We do not always expect specific actions from those we trust. In health care, patients often trust their doctors across whole domains of interaction. A domain-oriented model of trust, unlike action-oriented ones, predicts the fact that patients do not always feel betrayed when their requests are denied. It also explains why patient-donors may not think much of extending their trust to cover matters of biobank research when recruited by people who normally care for their health.

Cognitive accounts of trust hold that trust is rational only if supported by sufficient evidence. They tend to ignore that the act of deciding what should or should not count as evidence in a particular context is itself a form of judging. Standards of rationality which are appropriate in a court of law are

not necessarily applicable to, for instance, the relationship between friends. The rationality of trust seems to be better captured by an analogy with emotions and perceptions. On this account, trust is adequate when three criteria are met: its focus of attention is a true property of the trustee; the one who trusts is not mistaken about her reasons for trusting; and trust is culturally or socially appropriate in the circumstances and given the roles and relationships involved.

Adequate trust involves normative expectations on the one trusted, but typically leaves the trustee some discretion regarding the precise actions to be taken. Fulfilling adequate trust is, if not always easy, usually morally unproblematic. Mistaken trust, on the other hand, raises the question of who should take responsibility for the harm that may follow. Doctors are typically ideally positioned to discover and compensate for mistaken trust that their patients place in them. Arguably, therefore, they have a Kantian imperfect duty to compensate for such trust. When doctors act as representatives for biobank research by recruiting their patients, several new factors that may give rise to mistaken trust must be taken into account. Doctors are obliged to develop their competence in their newfound role and watch out for tendencies to participate based on confused motives. Transferred into this new context, patients' trust in doctors to always act in their best interests may sometimes be inappropriate because the imputed duty conflicts with the duty to facilitate research. The most promising way to negotiate such expectations is through public engagement and debate.

Study IV: Making researchers moral: Why institutionalised distrust might not work

Research ethics—once a platform for declaring intent, discussing moral issues and providing advice and guidance to researchers—has developed over time into an extra-legal regulatory system, complete with steering documents, overseeing bodies, and formal procedures. Arguments in favour of more and better regulation often draw upon past atrocities committed in the name of research. Research regulation builds on a paradigm of institutionalised distrust, which implies that researchers must be distrusted and supervised so that public trust in the system as a whole may continue.

This paper examines some limitations of this approach. First, institutionalised distrust cannot be justified by past atrocities unless it is also taken to be a necessary or efficient means to prevent future ones; and there are several reasons to doubt that it is. Second, the efficacy of ethics review in safeguarding morally acceptable research depends on the moral competence and integrity of individual researchers. Third, ethics guidelines cannot, as it is sometimes assumed, educate or guide researchers to moral behaviour

unless they already have considerable capacity for moral judgment. Fourth, formalism is a potential threat to the moral competence and integrity of researchers by encouraging a blinkered view of ethical issues, replacing their internal motivation to act morally with external incentives, and alienating them to research ethics by subjecting them to contradictory demands.

It is concluded that the moral problem posed by inappropriate short-term behaviour on behalf of researchers is dwarfed by the long-term consequences of allowing their moral competence to deteriorate. Measures must therefore be taken to ensure that researchers are equipped to take their individual responsibility and not obstructed from doing so.

Discussion

What strikes me most about trust in the bioethical debate is that contrary to my initial expectations, it has in fact found its place, much like a fine piece of pottery might find a place in our homes: admired at first, then stowed away and forgotten, and finally rediscovered years later, only to end up as an ashtray.

Just like an ashtray can be very useful if one intends to smoke, trust can be immensely useful if one is to conduct public policy. (Obviously, smoking harms your body in a way that public policy need not, but bear with me.) Nevertheless, no matter how useful a piece of art can become, we may have aesthetic reasons to prefer that it remain a piece of art. Similarly, no matter how useful trust can be made, we might have moral reasons to abstain from using it in particular ways. Hence the question that I ask in the fourth and final section: What is proper use of trust?

As I remarked in Methods, normative questions of this kind may depend on empirical facts about trust; however, how trust can and should be approached empirically is contentious. In the next section, I will suggest a way to understand the findings of Studies I and II in the light of trust and public trust. I begin with a *naïve* interpretation. This is not to suggest that it is mistaken, only that it takes the findings at face value. In so doing, I aim to provoke a particular kind of critique that highlights the need for conceptual analysis before empirical evidence can be expected to reveal anything interesting about trust. This analysis is carried out in the second section. In the third, I attempt to bring the issue about public trust to a close before moving on to the normative question about the role of trust in biobank research.

A naïve interpretation

To one who fears a crisis of trust in biobank research, the results from Study I may appear too good to be true. With no reliable way of determining how many patients were actually asked whether or not they wanted their samples stored, one might suspect that the 0.1% refusal rate underestimates the prevalence of distrust. On the other hand, the apparent decrease in confirmed refusals over time suggests that if anything, patients grew less concerned about participating. This is intriguing, especially given that meanwhile, the

number of withdrawals from the PKU Biobank were rocketing, which would suggest a growing public awareness of biobanks. On the whole, Study I gives us no reason to believe that Swedish patients lack trust in biobank research.

Study II explored the value of surveys in predicting actual participation in biobank research. Most surveys underestimated actual participation rates. However, due to the small number of studies included, this finding may not be generalisable. Most discrepancies could be explained by differences in setting between studies. The most important factors in this regard were whether the respondents/donors were patients, whether they were approached in person rather than over mail or phone, and whether the samples were to be used for genetic research. But there was also a small residue that could not be explained by any of these factors. Since this was an exploratory study, it leaves us with a number of hypotheses regarding what factors contribute to people's willingness to participate in biobank research. Arguably, all of them *could* be false, but that would leave us nothing with which to explain why these surveys did so poorly what they promised to do.

A naïve interpretation, then, would be that fears of eroding trust in biobank research have been exaggerated, and that interpersonal relationships of trust are an important factor in people's willingness to contribute. In Sweden, insofar as people framed the controversy surrounding the forensic use of the PKU Biobank as a betrayal of trust, the effects seem to have been confined to the PKU Biobank itself. This observation parallels those made in Iceland, where despite the controversies surrounding deCODE and the Health Sector Database, public support for biobank research remains strong both in surveys and actual participation rates. Even in the UK, where the events at Alder Hey were initially thought to spell the doom of biobanking, the majority of non-participants in the UK Biobank decline for personal reasons (too busy, too unwell, too inconvenient, etcetera) rather than out of distrust for the endeavour as such. In settings more conducive of trust, in contrast, the problem of non-participation has been negligible. Conceivably, people do not consider biobank research as a monolithic system, but discriminate between different settings. This much, at least, has been claimed about people's relationship to science in general (Wynne, 2006, p. 212).

The idea that we are facing a "crisis of trust" in health care or society as a whole has become both widespread and insistent. It harmonises with social scientists' descriptions of social life in the post-modern society as "characterised by ambivalence, insecurity and disorder" (Miller and Boulton, 2007, p. 2202). Others have argued that the term "culture of suspicion" is more to the point because whatever views people may express about the trustworthiness of various actors, they obviously continue to place trust in them. We may claim, for instance, to distrust the food industry or the police, but nevertheless continue buying food at the supermarket or calling the

police when threatened (O'Neill, 2002b). If people claim to distrust an endeavour, yet go on to participate in it, would this not count as a reason to question their testimony?

But this might be to go too far. If trust is not a kind of behaviour—which numerous authors have argued it is not (Study III)—drawing conclusions about trust from participation rates must be, if not to compare apples and oranges, something akin to looking at apples and deciding that there must be oranges about. One might argue that just as we must keep survey estimates of trust and actual existence of trust apart, we should not confuse research participation with trust. As an example, some people who express distrust in science or scientists go on to donate samples anyway because they think that stalling medical progress would be worse (Ducournau and Strand, 2009, pp. 121–122). This would be a case of reliance, not trust. The same could be said about people who prefer interacting with the police over being left to the mercy of their assailants. Buying food, on the other hand, could hardly even qualify as reliance, let alone trust. If it did, what alternative action would count as non-reliance, or as an expression of distrust? So, it might be argued, what we sometimes speak of as "trusting behaviour"—that is, cooperation—may be only weakly correlated to trust, in particular in circumstances where cooperation is prudent in spite of one's misgivings.

But the sceptic now faces a problem. If the connection between trust and cooperation is as tenuous as it is claimed, why bother with the former at all, if the latter is what we need? I see two possibilities, both of which highlight the need for conceptual analysis.

First, one might imagine certain inertia in how declining trust manifests in behaviour. On this view, trust is just one of many factors that affect people's decision making. If people who previously participated with trust and confidence begin to do so reluctantly, speaking of an impending crisis of trust is not unreasonable, even though there may be no evidence of behavioural changes as of yet. This line of reasoning manifests in claims such as that "the reluctant acquiescence of the public in its knowingly inevitable, and relentlessly growing, dependency upon expert institutions (thus ambivalent 'as-if trust') has been stretched beyond breaking point" (Wynne, 2006, p. 212). People's distrust and other attitudes could also temporarily fail to manifest due to organisational factors. If participation rates are high only because consent is not properly obtained, the system is more fragile than it appears to be. But in order to judge just *how* fragile it is, and even more importantly, to prevent it from shattering, one still needs to pin down what is meant by "trust" or "distrust"—to find their place in human lives. Investigating statistical correlations between testimony and behaviour is simply not enough.

Second, one might argue that knowing what people think is valuable because it bears down on what we are allowed to do to them. However, even if one were to assume that surveys reliably reveal the views of the many, it

would not be immediately obvious that majority support can morally justify a policy that sacrifices the rights of individuals. At the very least, majority vote cannot decide whether *coercion* and *deception* are acceptable (they are not).

Basing policy decisions on people's attitudes makes more sense when other kinds of interests are at stake. This directly bears down on the debate on consent practices. Let us assume that a particular practice—broad consent, say—does at least not coerce or deceive people; we leave it an open question whether it serves their interests better than the alternatives. If, *ex hypothesi*, decisions commonly made by people in such a system turn out to fail the strictures of informed consent, should they still be respected? And what would it mean to respect these decisions, which are apparently made "on trust"? While empirical findings regarding people's attitudes and behaviour might give us reasons to reassess the moral status of various structures and procedures, including implementations of informed consent, the actual process of reassessment requires conceptual clarity.

The concept of trust

In this chapter I present the theoretical framework on which Study III was based. What I have sought is a concept of trust that both harmonises with everyday experiences of trust and is morally relevant in biobank research. As the most paradigmatic instances of trust are found in relationships between people, this is where I will start my inquiry.

My choice of paradigm is bound to raise questions of applicability. Admittedly, a model that focuses on trust relationships will necessarily differ from one that begins with the idea of "public trust".[14] The former is preferable for two reasons. First, understanding relationships of trust elucidates people's motives for participating in biobank research in ways that assessments of public trust—for instance through surveys—cannot. Counter to the common view that trust in biobank research must necessarily be more "impersonal" and "detached" than interpersonal trust, I intend to show through examples how the model I propose is very much applicable. Second, and more importantly, an analysis of relationships of trust does not begin by assuming that trust is a resource to be cultivated. Rather, we are led to ask what those who are engaged in trust relationships ought to do.

[14] I argued earlier that if public trust is to make sense, it must be understood as referring to the conviction that public support for an endeavour will continue.

Betrayal

It is widely held that trust can be betrayed, or at least let down, rather than merely disappointed (Baier, 1986, p. 235, Holton, 1994, p. 69, Nyquist Potter, 2002, p. 21, McLeod, 2002).[15] As the story goes, Immanuel Kant was so predictable in his habits that his neighbours could, in principle at least, tell the time of day by watching him come and go. Suppose that they had (somewhat oddly) actually come to rely on him as a clock rather than simply observing him with amusement. If he one day were to deviate from his habits, they could then imaginably be inconvenienced. But unless there was some peculiar agreement between them and Kant, one could hardly speak of him letting them down, let alone betraying them. And this, it is argued, is because Kant was not *trusted* in this matter (Jones, 2004, p. 6, Baier, 1986, p. 235).

While in some ways illuminating, this example does not quite nail down the precise conceptual relationship between trust and the possibility of betrayal. One could argue that not all instances of trust can be betrayed. While we may trust our children to carry out certain actions and refrain from others, we rarely speak of betrayal when they let us down. Conversely, on surface inspection, not all betrayal seems to be betrayal of trust. Unable to trust a particular car salesman, you might nevertheless decide to buy the car he is pitching. When the car promptly breaks down due to a flaw that he reasonably must have known about, would it be out of place to speak of betrayal, despite the fact that you did not trust him to begin with?

Therapeutic trust

It is true that we sometimes trust our children in spite of lingering doubt. But such an attitude, sometimes termed "therapeutic" trust (Jones, 2004, p. 5), clearly differs from what I like to call "paradigmatic" trust. Whereas the former is intended to foster a sense of responsibility and moral behaviour, the latter assumes that these faculties are already in place. This claim is conceptual, not causal. I do not claim that moral agency must be assumed *before* one can trust; only that imputing moral agency makes one's trust intelligible.

Further, while it is true in a sense that trust is essential to many relationships (McLeod, 2011), it can be doubted whether paradigmatic trust can ever be employed strategically like therapeutic trust can. When asked to give reasons for trusting, we generally understand the question as pertaining

[15] In ordinary language, both "disappointment" and "letdown" are used in a multitude of ways. The distinction made by these authors is a technical one that serves to illustrate that we are dealing with two different concepts: *disappointment* when things turn out differently than one would have hoped, and *letdown* as a description of a failure of another to respect one's trust. What is crucial is that trust can be let down or disappointed in a *moral* rather than a merely psychological sense. I will use these terms interchangeably to denote the moral concept unless I explicitly write otherwise.

to *epistemic* rather than *strategic* reasons. If we justify our trust by pointing out the goods that follow from it, we are describing something else. If, for instance, a friend of yours were to say that she trusts you not because you are trustworthy but because trust would be good for your relationship, you would likely feel distrusted rather than trusted (Hieronymi, 2008, pp. 230–231).

Expected betrayal

As to the shifty salesman, his deceit—assuming that he indeed deceived you—is indeed blameworthy and is likely to provoke both anger and indignation (or a lawsuit). But does this make it a case of betrayal?

On one extreme, "betrayal" could be taken to refer to your *feeling* of betrayal, which would make it purely subjective. But such a view would be tremendously problematic. First, as we have no privileged access to the feelings of others, we would then be unable to determine whether someone else has been betrayed; but arguably, we can. Second, using the word "betrayal" requires moral rather than empirical justification. While feelings can be ultimately explained in causal terms by pointing at synapses and neurotransmitters, someone who asks me why I feel betrayed is not expecting a lecture in neurophysiology. Neither would it be enough to simply point to my feeling: "I feel betrayed because that is how I feel!" He expects me to provide reasons, for instance by recounting what happened and arguing that things should have been done differently. Unless I can provide such reasons, I will not be able to convince him that I was betrayed. So, unless we already share a conception of betrayal, pointing to our feelings will not be very helpful.

One might instead be tempted to analyse betrayal along the lines of *wrongful frustration of another's wants.* But without further qualification, this would include many wrongs that we normally do not consider betrayals (assault and burglary, for instance). The specific kind of wrong which is betrayal seems to imply some kind of relationship with the other.

The car salesman, it might then be argued, is guilty of betrayal because he violated the duties implied by the *business relationship*. But one could imaginably have very divergent views of what such a relationship amounts to. Some businesspeople might claim that their dealings involve trust. To them, signs of untrustworthiness would be a deal-breaker. Others might see their work as a game where cheating is allowed as long as one gets away with it. To them, betrayal would be a non-issue. Still others might consider it more closely related to sport in that their actions and those of others are restricted by a "code of honour" or some other kind of mutual understanding of how the game is to be played. But a breach of a code of honour is arguably not betrayal as such but rather a form of misconduct.

Betrayal as an emotion

A common conception of betrayal thus presumes objectivity. But how can something that we experience as vividly as betrayal be anything but subjective? I will presently argue that the subjective-yet-objective character of betrayal can be rather well accounted for by describing it as an *emotion* in the sense intended by Ronald de Sousa (1987).

De Sousa develops his model of emotions through an analogy with perceptions:

> emotions belong to a broader class of *attitudes*, which share with beliefs a lack of specific organs and consequent encapsulation but share with perception the feature that they must be in some sense essentially perspectival. (p. 156)

In contrast to feelings, which are *felt*, we understand what it means to have a particular emotion only by reference to a set of *paradigm scenarios*:

> These are drawn first from our daily life as small children and later reinforced by the stories, art, and culture to which we are exposed. […] Paradigm scenarios involve two aspects: first, a situation type providing the characteristic *objects* of the specific emotion type […] and second, a set of characteristic or "normal" *responses* to the situation, where normality is first a biological matter and then very quickly becomes a cultural one. (p. 182)

Whereas the primitive instinctual responses that make emotions possible are innate, the emotions themselves are learned (pp. 181–182). The baby's first smile, unlike the smiles of a toddler, is not an expression of happiness or sociability. A counter-intuitive, but ultimately plausible consequence is that the one who experiences an emotion cannot determine what it is solely through introspection. The so-called "privilege of incorrigibility" that the subject may claim with regard to her feelings does not apply to her emotions. (How does indignation differ from resentment? Not by any particular *feel*.) By their association with paradigm scenarios, emotions become susceptible to objective assessment (p. 117). The only way of "having" an emotion is by acting it out in the culturally proper way and in response to the right kind of situation. Do it the wrong way, and other people will not understand what you are trying to express.

A consequence of applying de Sousa's model to betrayal is that the question whether or not we have been betrayed cannot be decided by reference to how we feel. Our shared conception of betrayal is formed by discussing scenarios, not by "comparing feelings". We now see why speaking of betrayal in the example with the car salesman puts significant strain on the concept without necessarily being out of place. The business relationship *can* be a relationship of trust, but only insofar as it resembles ones that we regard more paradigmatic. If the scenario is better described as

a case of risky reliance or a gamble, what we would call "betrayal" is merely a particularly strong move in whatever game is being played. The move can of course be illegal or immoral for other reasons, but betrayal will not be among them. Given such a description, the anger and indignation that follows will be nothing but a natural (though childish) reaction to losing. In any non-ideal case, betrayal, like trust, can be a more or less fitting description depending on what the relationship is like. Viewing these concepts as binaries—do you or do you not trust?— risks muddling rather than clarifying the issue.

Likewise, the distinction between therapeutic and paradigmatic trust is often not clear-cut in practice. As our children grow up we move, step by step, from the former to the latter in a slow, almost imperceptible process. To conclude, neither example constitutes a counterexample to the proposed analytic relationship between trust and betrayal, though they may appear as such if one forgets the fact that how well trust and betrayal fit their paradigms is a matter of degree.

Reality check

Before we move on, let us examine how my model of trust holds up so far in the context of biobank research.

In the chapter "The shaping of biobank ethics" I described some critical events in biobank research such as the Alder Hey organ retention scandal and the Havasupai Indian tribe case. In both cases, the question whether or not wrong was done was quickly reduced to a matter of whether some particular action fell within the "scope" of the original consent. Such discussions tend to be just as quickly reduced to quibbles: Are organs composed of tissue, and if they are, is tissue all there is to organs? Is research on schizophrenia a kind of medical or behavioural research, and if it is, are these descriptions fitting for such research? Whose opinion on these matters should prevail?

Given how these events played out, it is plausible to describe the relationships involved as relationships of trust. Speaking of betrayal also makes sense because it allows us to understand the claims that *moral wrong* was done. We do not necessarily have to agree; but neither is the notion of betrayal unintelligible. Some controversies might be avoidable by paying more attention to the expectations involved. Others can teach us valuable lessons for the future. Trust, then, can serve as an alternative perspective through which controversies can be approached.

Expectations

In philosophical analysis of trust, much attention has been awarded certain *formulas* such as "A trusts B to do *x*" (Nyquist Potter, 2002, p. 10). Abstract formulas are by their very nature both devoid of content and stripped of

context, and so by themselves say nothing at all about what kind of attitude trust is, or if trust even can be called an attitude at all. Nevertheless, they may give an impression of being illuminating since they draw attention to the remaining problematic component—"trusts". What if it could simply be supplanted with some other concept that we feel more comfortable with? If the truth value of the proposition is preserved, has not the riddle finally been solved? In fact, many authors have made attempts to redefine trust in terms of something else. According to Russell Hardin (2002),

> [t]rust is not a primitive, something that we just know by inspection, as the color blue might be a primitive, at least for ordinary people who do not think of it as a problem in optics. Rather, it is reducible to other things that go into determining trust. […] It is hard even to imagine a conception of trust that is nonreductive and still plausible. One might argue that joy is conceptually not reductive, although it is probably causally explicable in reductive terms. Trust is not merely an unvarnished emotion, however, in the sense that joy is. (p. 57)

To analyse trust, it is suggested, we should begin by considering it as a kind of belief, and then nail down those additional provisions that give trust its distinctive flavour. This would amount to investigating what kind of evidence typically backs "trusting beliefs". "A trusts B to do *x*" is thus analysed as "A believes that B will do *x* because *p*". Hardin identifies the crucial assumption on which trust is based as one of "encapsulated interest":

> I trust you because I think it is in your interest to attend to my interests in the relevant matter. This is not merely to say that you and I have the same interests. Rather, it is to say that you have an interest in attending to my interests because, typically, you want our relationship to continue. (p. 4)

I question neither that we sometimes have interests in attending to other people's interests nor that this can make us trustworthy (in some sense). But trust cannot *simply* (or exclusively) be a matter of having certain beliefs. If it were, it would not differ in any significant regard from the predictions that a psychologist makes about the behaviour of his research subject. (The criterion of encapsulated interest does not exclude such relationships since the subject might very well wish to continue the relationship.) Moreover, when the one we trust deviates from our expectations, speaking of betrayal would make no more sense than if the psychologist were to blame his subject for failing to conform to his theory (Lagerspetz, 1998, p. 80). Though Hardin says much about trust and trustworthiness, he unsurprisingly has little to say about betrayal. This oversight severely limits the applicability of his model.

Predictive and normative expectations

Another account of trust that tries to avoid this problem, but ultimately falls short, has been suggested by Pamela Hieronymi (2008). Its main weakness is that it makes significant assumptions about the psychology of the truster.

Much like Annette Baier (1986, pp. 235–237), Hieronymi argues that trusting another implies believing that she is reliable in her judgement and good in her will. But she recognises that predicting someone's future behaviour based on imputed good will (or any other psychological fact) cannot be to trust because it entails no vulnerability to betrayal. Indeed, it would be quite compatible with treating that person as one would an object (Hieronymi, 2008, p. 226).

Hieronymi argues, with Richard Holton, that someone who trusts takes a *participant stance* toward the other. The truster thus differs from the "confidence trickster" who relies on his victims' goodwill, yet cannot be said to trust them (Holton, 1994, p. 65, Hieronymi, 2008, p. 224). The participant stance is commonly described as a general attitude that we normally take only toward other people. It implies a readiness to take a range of *reactive attitudes* toward those people in response to their behaviour. We might, for instance, feel resentment toward those that hurt us, or gratitude to those that help us (Holton, 1994, pp. 66–67). The problems emerge when we try to answer *in abstracto* the question why we adopt those attitudes:

> [i]f I recognize that you are a creature that acts for reasons, and if I further allow your reasons to factor into my thinking and support my beliefs and decisions in something like the way my own will, it seems right to say that I adopt the participant stance towards you. If, further, I assume you are trustworthy and then take as central to my reasoning the reason given to you by the fact that I am relying on you, it seems plausible that this reliance would create the sort of vulnerability characteristic of the risk of betrayal. (Hieronymi, 2008, pp. 226–227)

The idea here seems to be that when I trust you, I expect you to regard my reliance on you as a reason to act; and in so doing, I risk betrayal. Of course, if this is to make sense at all, the influence that we expect our trust to have on the other must be of the right kind. What I think Hieronymi has in mind is something like Karen Jones's idea that trust implies an "expectation that the one trusted will be directly and favorably moved by the thought that we are counting on her" (Jones, 1996, p. 4). I cannot, so to speak, trust you without also believing that my trust makes a difference to you. By this, however, nothing much is gained. My trust is still reducible to beliefs, which are justified only by other beliefs, which in turn are about nothing but psychological facts about you. If I am mistaken about your reasons, I am still no more justified to feel betrayed than a psychologist whose subjects contradict his theory. The mistake is epistemic, so the blame should rest with me for drawing the wrong conclusions. If vulnerability to betrayal is a key

feature of trust, it is certainly not "created" by the kind of reliance or reasoning that Hieronymi has in mind.

Hieronymi's first mistake, just like Hardin's, appears to be that she implicitly takes the formula "A believes that B will *x* because *p*" as the logical starting point for analysing trust. She is thus misled into thinking that by nailing down *p*, the meaning of trust will become clear. But if betrayal is not a matter of mistaken beliefs, we should not expect to exhaust the meaning of trust by reference to beliefs. This does not mean that talk about good will or the participant stance is altogether mistaken. But no matter how consistent the analysis, it can never escape an inappropriate framing.

My suggestion is considerably simpler. To properly understand trust, we must make a distinction between *predictive* and *normative* expectations. The latter, unlike the former, are not primarily about what *will* happen but what *ought to* happen. Between people, to have normative expectations of someone is to make demands of him or her.[16] Trust involves both. However, what they are, and in particular what actions will count as honouring or letting down our trust, usually becomes apparent only after the fact. In this sense, trust is posthumous (Lagerspetz, 1998, pp. 22–23). When we are let down, it is the disappointment of the normative expectation, not the predictive one, which is our reason for rebuking the other: "You ought to have done *x*!" rather than "I thought you would *x*!" Though generally overlooked—or at least downplayed—by authors seeking to reduce trust to other concepts, some others have emphasised the role of normative expectations in trust (Jones, 2004, p. 6, Hollis, 1998, pp. 10–11).

As to "vulnerability", trust makes us vulnerable to betrayal only in the sense that actions that we describe as betrayal would not count as such unless we trusted. True, by relying on others, we might run risks that we would not otherwise have. But the risks become neither smaller nor larger by trusting as such, but by the actions that we take or fail to take (and even then, *not* relying on others can sometimes be riskier—as anyone who has hauled heavy furniture up a set of stairs well knows).

Discretionary powers

While trust is usually thought of as a matter of having certain expectations, and betrayal as a matter of disappointing them, trust is sometimes honoured precisely by *not* going along with the expectations:

> I would feel morally let down if someone who had promised to help me move house arrived announcing: "I had to leave my mother, suddenly taken ill, to

[16] The difference sometimes emerges in everyday language constructs, for instance in the phrases "expecting that" and "expecting of". For instance, we usually expect *that* prisoners will stay in prison, but rarely expect it *of* them. See HOLTON, R. (1994) Deciding to Trust, Coming to Believe. *Australasian Journal of Philosophy*, vol. 72, no. 1, pp. 63–76.

> look after herself in order to be here, but I couldn't break my promise to you." (Baier, 1986, p. 251)

Baier's initial expectations were unambiguous: She expected the other to stay true to her word. Nevertheless, fulfilling those expectations would cause Baier to feel let down. Intuitively however, her reaction is not merely a subjective "feeling" of being let down. The scenario can quite accurately be described as a betrayal of trust. How can that be?

Perhaps it is because preferences are amenable to change? After learning of the frail woman, Baier now prefers that the promise be broken. But this, I think, would be to misconstrue her point. Speaking of changing preferences seems to rather understate her reaction, as if implying that she could ever come to a different conclusion. Arguably, what have changed are not her preferences, but the scenario: Failing to show up as promised is no longer best described as promise-breaking, but as attending to someone in greater need. Whatever else Baier expected of the other, she certainly had hopes on her moral agency. Perhaps she also expected something like moral integrity, which implies being true to one's values and cleaning up one's own messes (McLeod, 2002, pp. 21–27). She also expected the other to recognise this. The other unfortunately expresses through her actions a contrary view of trustworthiness as simply being a matter of keeping one's promises.

Baier makes a related point in her analysis of trust as *entrusting.* Whenever we trust, she argues, we entrust something of value to the other, usually leaving some details of how it should be taken care of to the other's discretion (Baier, 1986, pp. 236–237). The logical form of trust, on this analysis, is "A entrusts B with valued item C". Conspicuously, this formula specifies no particular "*x*" that A expects of B. To endorse it is not to say that our expectations are *never* specific; rather, the formula aims to draw our attention to the valued item C, the identity of which logically precludes anything that we might think should be done with it. For instance, when parents leave their children in another's care, what is most important to them is that their children are involved, and the first (if not the only) thing that they expect the caretaker to do with their children is to take good care of them. Beyond this expectation, parents' ideas of what ought to be done are diverse and sometimes vague. Put differently, trust implies a demand on the other to know what ought to be done and to act accordingly, coupled with a firm belief that he will do just that, or at least the absence of contrary beliefs. It is when we distrust that we feel compelled to provide detailed instructions, checklists, etcetera.

It could of course be argued that Baier's formula does not capture all instances of trust, or even all interesting ones. Furthermore, it is not always intuitive; even in her own example on moving house, naming the valued item C is difficult. Nevertheless, recognising that it is at least sometimes applicable makes us see that whatever *specific* expectations we might have

on others whom we trust, they can only be *part* of what our trust means. One might, in a sense, "trust" one's spouse to remember the milk when she goes shopping, but when she forgets, speaking of betrayal seems harsh to the point of comical. This is not, as one might think, because the consequences are trivial, but because occasional lapses do not challenge the core of the trust relationship (McLeod, 2002, pp. 24–25).

Reality check

The expectation on the other to act as a moral agent and use his or her discretionary powers to determine what ought to be done is crucial to trust in biobank research. This is most readily seen by considering examples of overt distrust. In the study by Levitt and Weldon (2005), informants expressed concerns that researchers and other involved parties might be steered off proper conduct by their personal agendas. Arguably, it is not agendas *per se* that are problematic—everyone has them!—but the inclination to sacrifice other values. The pivotal point seems to be, then, whether researchers can be trusted to decide what parts of their agenda are compatible with proper conduct and which ones should be left aside.

Adam Hedgecoe (2012) provides another example of how the presumed character of the trustee is central to trust. In a field study on decision-making processes in British RECs, he found that "trust decisions" and "facework" plays an important part. Unlike in Sweden, inviting applicants to REC meetings is national policy in the UK. REC members generally regarded such meetings very important if not invaluable. Not only did they think it more efficient to ask for clarifications on the spot rather than engaging in a lengthy correspondence; they also saw these meetings as a complement to the written application because it allowed them to judge the trustworthiness of the applicant. Locally based RECs often had some experience of applicants from previous occasions, and those with a good track record could be given the benefit of the doubt. Conversely, as one informant put it, "[i]f you know somebody's a bit of a cowboy, you look at it more carefully." (p. 673)

Though interpersonal trust has been my focus so far, there is nothing in principle that prevents my model from being applied to trust in institutions as long as moral agency can be reasonably attributed. There is some empirical evidence that people in fact do this. In a qualitative study on the decision-making process of healthy volunteers to the Australian Cancer Study, Allen and McNamara (2011) found that the donors claimed to trust the research institution. Ostensibly, its reputation was crucial to their trust. Notably however, these donors conceived of the consent procedure as a "ritualized act creating a bond of trust and responsibility between themselves and researchers." In the end, the perceived moral agency of the institution hinged on that of the people constituting it. Individual moral agency was in

turn conceived of both as a commitment to act morally and as having some degree of freedom to do so.

Evidence, reason and justification

The way I have described trust thus far may seem to imply that trust can be employed rather arbitrarily. If you expect someone to "take good care of" your children without being able to specify what this entails beforehand, how can you ever hope to justify your trust?

Part of what has troubled philosophers about trust is that it appears to allow otherwise rational people to disregard *evidence*. Trust allows us, or so it is thought, to make decisions when evidence is in scarce supply, to willingly forgo it when it is available, and perhaps most importantly, to ignore it when it runs counter to our convictions. While some authors have concluded that trust is an "emotional" attitude and thus inherently irrational, others have attempted to fit trust into existing theories of rationality. This has been done in two ways. The first describes trust as a strategy that allows us to cooperate in ways that would otherwise be impossible. In such a scheme, the "rationality" of trust consists in its utility. I have already argued that such "trust" is too disingenuous to be the paradigm. The second considers the rationality of trust in terms of the rationality of the corresponding beliefs, thus subjecting it to the constraints of epistemic rationality. I will presently consider the latter option before arguing that the idea of justifying one's trust must be understood rather differently.

Seeking evidence for trust

On an epistemic view of trust, justifying one's trust in someone to "take good care of" one's children must be a matter of seeking evidence of the caretaker's trustworthiness. We thus invoke the image of looking through her credentials, reputation, observations of past behaviour, etcetera. But we soon realise that such evidence cannot be conclusive. People change, after all, so a good track record does not guarantee trustworthiness in the future. For all you know, exemplary behaviour in the past could be coincidental, or even a ruse to lull you into a false sense of security (Lagerspetz, 1998, p. 79). You begin to doubt. Some additional evidence must be found to restore your trust—but what could such evidence possibly look like? That which was previously unproblematic has now become problematic.

Now imagine that the caretaker in question is not a stranger, but your spouse. Hopefully, your history together has provided you with numerous examples of trustworthy behaviour. But trusting him or her still seems unwise for exactly the same reasons. Your inductive reasoning does not hold up to scientific rigour. Neither does the trust you have in the mother or father of your children to "take good care" of them lend itself to investigation through hypothetic-deductive methodology unless you can spell out some

concrete implications to test. Assume that you were—oddly—of the opinion that "taking good care" of your children implies nothing more than refraining from abusing them. It would then be possible to state a null hypothesis: He or she does abuse them. But what kind of experiment would you conduct to falsify it? It seems completely unreasonable to look for evidence for one's trust in the same way that the scientist looks for evidence for a theory. Some other conception of "evidence" is obviously needed.

Perhaps we should take as the norm not the scientist's conception of evidence, but the lawyer's? An example originally provided by Judith Baker (1987) that intends to problematise trust seems to assume as much. Olli Lagerspetz (1998) has pointed out how the example itself is problematic:

> A close friend of mine is being accused of a major crime—say, of working for a foreign intelligence agency. The available facts establish her guilt in the eyes of most people. Yet if she tells me she is innocent I will believe her rather than the others. […]
>
> The following image is now evoked. Facts are brought to my knowledge ('the evidence'). Reasonably, they ought to make me assume the existence of some further, unpleasant facts about my friend. However, add trust; and the scales are turned. In this picture, trust simply outweighs the evidence. We naturally ought to wonder how anyone who cares about correct judgment can let such things happen. Yet they do happen; and this is often cited as admirable rather than irrational. (p. 86)

The picture of trust "outweighing" facts indeed paints it as something irrational. We are led to think of ourselves as biased in favour of our friends in a sense that the court is not. But what this example shows is not bias in the usual sense of the word:

> [W]hen first presented with the would-be evidence, I do not even seriously consider the idea that my friend could be deceiving me. The difference between me and the others is then not just that we ask the same questions but are inclined to weigh the evidence differently. I do not even seriously ask certain questions. I believe that some other explanation can be given for the facts that others would cite against her. (pp. 86–87)

Similarly, trusting the mother of my children to care for them appropriately is part of what goes into our relationship. If I start asking for evidence, I inevitably change its nature. The case is not, as one might think, fundamentally different in "shallower" relationships of trust: If I ask a stranger to tell me the time, I will probably trust him to answer me truthfully, without asking for additional evidence. This is the essence of our relationship. One question that I would not seriously consider is whether he is a notorious liar. You might successfully convince me that he is (if I trust *you* more); but in this case, too, the relationship is changed into something else.

Lagerspetz refers to this as the *asymmetry* of trust: We use the word "trust" when there is, from a third-person perspective, a reasonable case for suspicion, but a conspicuous lack of it from the first-person view. Trust, then, may be "in the eye of the beholder. It is not 'there' as a neutrally recognisable state of affairs—say, a psychological state." (p. 45) This is probably true. Yet the same things can be said about many other kinds of observable behaviour. What counts as "normal" when hanging out with one's friends could conceivably be regarded crude at a gala dinner. From one perspective, one does exactly the same thing; from another, one most certainly does not. That no neutral description can be given of one's behaviour does not preclude critique of it. Similarly, an outside observer may not be able to trust like I do; yet he might come to understand *why* I trust, and argue that my reasons are bad ones. This indicates, I think, that trust, like behaviour and emotions, is not a private matter, but can be critiqued. I will now go on to investigate what such critique could amount to.

Reasons recast

If someone were to ask me why I trust a certain person, my response might take the form "I trust A because *p*." What is it that I do by so saying? To begin, we must understand *p* as aspiring to be a *rational* reason for trusting A; if we did not, what I just said would be meaningless.[17] We face a problem: If trust cannot be defeated by appeal to hard and cold facts (as it could not in Baker's court example), how can we ever argue that *p* is a better reason for trusting A than, say, *q*?

One solution would be to conceive of a divide between the activity of trusting and that of conjuring reasons for one's trust, where the latter but not the former could be subjected to objective critique. But this would, in a single stroke, re-enact the view of trust as irrational and conceive of any talk of trust as a pretence or afterthought. I believe that some other options remain to be explored. Before embarking on this mission, however, I will explain why I find it worth pursuing.

My main aim, as has been noted before, is normative. To that end, I pursue a model of trust which is clearly action-guiding. Now, my starting point is not, as one might assume, that we should distinguish between "rational" and "irrational" trust because the former but not the latter should be supported or honoured. Trust, in my view, implies a moral demand *regardless of whether it is adequate or mistaken*. But as I am about to argue, finding the proper way of responding to it does hinge on making this

[17] Arguably, "because" could also be understood in a causal sense, but this would make for some very odd conversations, except perhaps between neuroscientists ("I trust you because of a lesion in my Hippocampus!") or psychotherapists ("I trust you because I had a dominant father!")

distinction. Moreover, it might be easier to be trustworthy if one is able to distinguish between different kinds of mistakes.

Nothing of what I have said so far implies that trust cannot be justified by reasons. I firmly believe, however, that many attempts to postulate criteria for such reasons have tended to take too narrow a view on trust. Though we might occasionally justify our trust to others by presenting reasons that resemble good will or encapsulated interests, nothing of the sort is strictly required in order to trust. Lagerspetz (1998) makes a related point about reliance:

> To rely on others is to exercise judgment concerning the reasonableness of depending on them for some particular purpose. The judgment will take account of the risks and possible benefits involved, in the light of what one knows about the other person's competence, disposition, and so on. This is not to imply that all cases of reliance are outcomes of explicit reasoning. The point is that they can be assessed in terms of such reasoning. (p. 48)

Reasons are not causes. Rather, they are "the sorts of things that we give or receive, exchange and refuse." (O'Neill, 2002a, p. 91) Reasons can be criticised for being mistaken, insufficient, incomprehensible, deluded, incoherent, or just plain wrong. But to be any of these things, reasons must be of a recognisable form that makes it at least possible to *imagine* adopting them. In the case of trust, this constraint excludes prudential reasons, though such reasons may be perfectly valid for *relying* on others. Reasons that bear down on the perceived trustworthiness of the trustee are more promising candidates.

Speaking of reasons presumes objectivity. Interestingly however, the question whether my trust in you is adequate or mistaken cannot be settled with appeal to whether you are "in fact" or "objectively" trustworthy. Granted, the fact that we are talking of trustworthiness does imply that we share some conception of it. But to conceive of it as a property that people have would imply that it is possible to reach consensus on what a trustworthy person is like, just like we might agree on what it means to be short, industrious, or temperamental. We do have virtue theories of trustworthiness, but trust in our daily lives does not depend on how well the trustee embodies such ideals. It is the other way around: Through our experiences of trust—and perhaps to an even greater degree, those of betrayal—we conceptualise trustworthiness.

Trusting another, then, is not simply to see a property that others fail to see. Trust implies that there is room for genuine disagreement, not merely imprecise measurements. I will now suggest a way of understanding such disagreements.

Justifying emotions

Trust shows more than passing resemblance with emotions. We know what they are through their association with paradigm scenarios, of which there is ample supply in literature, plays, movies, and everyday life. They are justified by reasons, and occasionally, but not always, involve certain modes of expression. They involve seeing things in ways that those who do not share them may not agree with. I find the analogy useful because it elucidates how trust is expressed, described, discussed, and critiqued in our interactions with others. We are thus invited to understand its normative significance.

First, however, I will consider another aspect that trust shares with emotions: the one of *perception.* Every justification of trust, just like every justification of an emotion, involves a way of perceiving the other. In the case of trust, one might draw attention to some skill that the trustee possesses, or to a relational property, such as being a friend. According to de Sousa (1987), emotions have a similar logical structure:

> Emotions having targets typically involve a *focus* of attention, which is the apprehension of some (real or illusory) *focal property* of the target. Under certain conditions, which define the standard case, the focal property is also the *motivating aspect* of these emotions. (pp. 116–117)

The question "Why do I trust you?" typically addresses the focal property. The question "Why do I *really* trust you?" would bring out the motivating aspect, if I could only answer it. Adequate trust implies that the two answers are identical, or at least that the former can be inferred from the latter. But if we are to talk about trust at all, both the focal property and the motivating aspect must constitute *intelligible rationalisations* of trust. If someone for instance claims to trust his doctor because she wears green socks, we would not understand what he means in the absence of some clever story that explains why doctors wearing green socks are particularly trustworthy. What we question here is the relevance of the focal property.

Motivating aspects may also be problematic. If I take a drug that makes me perceive others as trustworthy, we might say that its effects have caused a state that I refer to as trust. The answer to the question "Why do I really trust you?" would be "Because of the drug." But since the effects of a drug cannot be a reason for trusting—such effects cannot be a reasons for anything at all, though they might cause many things—a drug-induced state can never qualify as trust. At best, it might mimic trust.

We can express these constraints in terms of a *formal object*:

> For each emotion, there is a second-order property that must be implicitly ascribed to the motivating aspect if the emotion is to be intelligible. This essential element in the structure of each emotion is its *formal object.* (p. 122)

I might for instance fear a dog because of its bared teeth and low growl. (I am not sure whether it makes sense to say that these things *cause* my fear, but they would certainly be among the reasons I would give you if you asked me.) In so doing, de Sousa says, I implicitly ascribe the formal object, *frightening*, to those features. Some other person faced with the same dog might remain quite unimpressed. Nevertheless, he would probably be able to understand why *I* find the dog frightening. My fear is then intelligible without being shared.

The formal object of trust is trustworthiness. Understanding someone's trust without sharing it is a matter of recognising what the other sees in the trustee, without necessarily agreeing that this property makes the trustee trustworthy.

But, one might now object, have I not just reintroduced the idea that I refuted in the previous section, that trust is something that deviates from a "neutral" approach to facts and evidence? No, because there is no such thing as a neutral approach. To distrust, or to question another's trust, is also to take a perspective. Depending on the context, the latter perspectives might be the ones that are in need of explaining.

Adequate and mistaken trust

With the limits of trust firmly in place, I return to the question of adequate and mistaken trust. There are three principal kinds of the latter:

1. **Misplaced trust:** The focal property is illusory, that is, the beliefs and assumptions that would make the trustee trustworthy in the sense intended by the truster are false.
2. **Irrational trust:** The focal property is neither equal to nor inferable from the motivating aspect, meaning that the truster is mistaken about what her reasons for trusting actually are, possibly (but not necessarily) because of some kind of self-deception.
3. **Inappropriate trust:** The instance of trust is inappropriate according to the prevailing cultural or social norms and given the current circumstances.

My taxonomy here differs slightly from the one I employed in Study III. There, I lumped together category (2), *irrational* trust, with cases that would perhaps be better called "not-quite-trust": those that would be more accurately described in other terms. The example of confusing trust and obedience that I used in the paper would appear to belong to the latter category. The practical implications, however, remain the same.

The first kind of mistaken trust, which I refer to as *misplaced* trust, is the one that philosophers usually focus on. As an example, one might trust one's doctor because one perceives her as competent in the relevant area of expertise, even when this is in fact not the case. The focal property fails to

qualify as the motivating aspect because it is not there. To understand this kind of trust is to find a candidate for the motivating aspect which is both an intelligible rationalisation for trust and makes the illusion intelligible. The motivating aspect might be an observation from which the focal property can be (mistakenly) inferred. To critique someone's trust on these terms is to argue that the inference is mistaken. Note that even though I have rejected attempts to *reduce* trust to beliefs, I do not see a similar problem with claiming that trust *involves* beliefs, no more than I see problem with claiming that relationships involve beliefs. (My relationship to my father would for instance not be what it is if I did not believe him to be my father.)

As an example of the second kind of mistaken trust, I might believe that I trust my doctor because I perceive her as competent, whereas the real reason is that she reminds me of my mother. Despite that both focal property and motivating aspect are intelligible rationalisations of trust,[18] this kind of trust is *irrational* since a resemblance with my mother would be no reason to believe the doctor competent in medical matters. This is the most elusive of the three because it could well occur without any overt signs of irrationality. What takes place might then strike no one as particularly problematic. We understand this kind of trust by imputing a motivating aspect which is unrelated to the focal property. Doing so is nigh impossible unless one knows the truster well. And even then, since this kind of critique would involve questioning her rationality, is not likely to be well received.

Lastly, trust can be *inappropriate*. As an example, it would not be appropriate to trust my plumber to take care of my children while I go shopping, regardless of whether he is an excellent babysitter. This is not a question of what we have contractually agreed upon. We often expect people to do more than what we could possibly agree on in advance. To understand this kind of trust is to recognise it as a breach of a social code rather than, say, disorganised behaviour. To critique it is to point out that the expectations must be renegotiated.

Reality check

It is usually assumed in the bioethical debate that trust is a substitute for true knowledge. It has been claimed, for instance, that "on the psychological level, the trusting person is in an intermediary state between knowledgeable and ignorant" and that trust is "judgment and action in conditions of less than perfect information." (O'Neill, 2004, p. 271) The problem with these claims is that the authors are implicitly taking a stand on what kinds of

[18] Someone might object that being *a mother* could not reasonably be an intelligible rationalisation of trust— after all, not all mothers are trustworthy! Crucially, however, I am not speaking of *a* mother but of *my* mother. I trust her because she is *my mother*—and that is all. I do not need to refer to some specific facts about her to justify my trust. This is indeed a form of subjectivity, but it does not amount to sheer projection. An outside observer might still agree that my reason is valid for me, though he might not be able to adopt it for himself.

reasons are legitimate for agreeing to participate: those based on knowledge about the study. If participants are found lacking in this respect, they must, on this view, "trust". But this is not to make a neutral observation of their psychological states, but rather to express concern over their decision-making. From the authors' perspective, it is sub-par. From the participants' perspective, it is probably quite sufficient. In my view, they are not necessarily any more (or less) trusting than those who would qualify as "fully informed". The association might have arisen from a mere contingency: Those who express suspicion rather than trust are more likely either to pay more attention to details before they make a decision or to outright refuse.

To judge from Hedgecoe's (2012) study discussed earlier, the reasoning employed by REC members when assessing the trustworthiness of applicants during face-to-face meetings follows quite closely the logical structure of trust that I have suggested. In particular, they paid attention to a well-defined set of focal properties (what Hedgecoe terms "trust-warranting" ones): *clarity* of thought, *openness* in communicating their research, and *receptiveness* to comments and suggestions (p. 675). In many other kinds of trust relationships, these properties would not be the first ones to come to mind. But in the ethics review context, they make perfect sense. Would not a researcher who embodies them also be likely to do his or her research conscientiously? The fact that the list is not exhaustive does not count against the rationality of REC members or against my model. It only shows that what the focal property of one's trust amounts to is ultimately a subjective matter. Other RECs with other experiences might well demand other kinds of evidence of trustworthiness.

My analysis of adequate and mistaken trust can be used to identify different sources of disappointment that may have to be handled differently. In Study III, I considered trust between patient-donors and doctors who act as representatives for biobank research, arguing that all three kinds of mistaken trust are conceivable. Furthermore, the Alder Hey incident involved, to judge from how returning of the remains was handled, some amount of *misplaced* trust. The Havasupai case, on the other hand, appears to mainly concern *inappropriate* trust in researchers to attend to the donors' needs like a doctor would.

Trust and duty

In my analysis of betrayal I argued that we understand what it is, including the fact that it is wrong, by reference to a number of paradigm scenarios that form part of our cultural heritage. I will presently argue that the same holds for trust. We cannot understand someone's trust without recognising our duty to respect it and attend to it. This duty must be understood in a wider

sense than merely as an imperative to refrain from betrayal. In the words of Lagerspetz (1998),

> calling someone's attitude 'trust' is never just making a neutral, empirical point about her mental states, behaviour, or the like. It is to claim that we must respect the expectations she has on us. (p. 161)

In my vocabulary, our duty to respect the other's expectations manifests in culturally shared paradigm scenarios of trust.

It might now be argued that telling stories of trust being let down does not prove that letting someone down is wrong any more than we can prove the wrongness of lumbering by telling stories about talking trees. But this objection misconstrues how paradigm scenarios work in our moral language. They are not arguments designed to prove a point. Most are not designed at all, and even those that are could be more accurately described as *illustrating* a point. Stories about betrayal are inextricably linked to the common-sense view of betrayal as a moral wrong: Unless we had either, we would not have the other. Hence, to recognise an event as betrayal *is* to dress it as a moral wrong. Similarly, saying that someone's trust was let down implies that some kind of wrong was done.

But are there not cases where there is trust but no duty to fulfil it? If someone trusts me to rob the bank for him, this hardly imposes on me a moral obligation to do so. However, to qualify as trust, this example requires some shoehorning. For one thing, we need a more vivid background story; one in which rebels fight against a dictatorship will do.[19] In such a story, there could be room for trust. The rebels might, for instance, trust each other to fight for a common cause. But then it is not obvious why there would *not* be a duty to partake in the robbery or at least stand aside while one's brethren do their dirty business. In other scenarios involving would-be bank-robbers, there is usually precious little trust. This is not an empirical assumption but a conceptual point: To expect of someone to actually carry out the action of robbing the bank—in the sense that one *demands* it of him—is not to give him the kind of leeway that I argued to be an essential feature of trust. In contrast, if one has reason to assume that the other in fact intends to rob the bank, one could conceivably trust him to do it *well.*

Someone might argue that this defence fails to address the main point of the objection. Even if we agree that betraying trust is morally wrong by definition, the same cannot be said about disappointments that do not constitute all-out betrayals. When we feel that letting someone down would be morally wrong, the argument goes, this is only a matter of contingent fact. Though breaking a promise of moderate importance out of forgetfulness could be construed as a disappointment of trust, the moral wrong would

[19] I owe this example to Olli Lagerspetz.

arguably reside in the fact that the self-imposed duty of keeping the promise was violated. Similarly, a doctor may let down a patient's trust by failing to disclose relevant side-effects of a proposed treatment; but would this not rather be a case of violating one's professional duties, or perhaps of failing to respect the patient's autonomy?

While it does appear that the wrong done by letting someone down can sometimes be described in other terms, there are other examples that make the idea of a wider duty of respecting trust plausible. Imagine two friends conversing. One of them plans to marry, but is yet to spread the news. The other promptly goes to tell a third person about it. Most readers would probably agree both that he let his friend down and that what he did was morally wrong. Why is this? The example does not indicate that the listener made any promises. Still, we get the feeling that what was being divulged was a secret, and that the decision to pass it on was not his to make. Perhaps there was, then, some *implicit* promise or agreement? But this would beg the question how it is supposed to be inferred. Unless we have already recognised the piece of news as a secret, it would not make sense to say that one has implicitly agreed not to spread it. But why would it be a secret? The answer, I think, is that we understand this case intuitively since we share a number of paradigm scenarios which it resembles. The words "secret" and "agreement" become applicable only when we recognise which course of action would be proper.

One might still wonder in what sense responding properly to trust is a *moral duty* rather than, say, a matter of etiquette. One might also wonder what we can say about proper responses to *mistaken* trust. Is it even possible to draw up some principles in the abstract?

The puzzle becomes less of a puzzle, I think, if we employ a Kantian view on duty. Given the intricacies of Kant's moral theory, a brief summary of some of its crucial features is necessary.

Autonomy of the will

Many readers will no doubt be familiar with the abyss that separates Kant's theory from consequentialist ones such as the one championed by John Stuart Mill. Kant, contrary to Mill, makes a sharp distinction between moral actions and those that pursue interests. On his account, even beneficent actions are not necessarily moral. More, he explicitly refutes the idea that the morality of an action depends on its consequences. To act morally is, according to Kant, to act on our moral duties. Whatever could this mean?

Today we tend to think of duties as something that binds us or constrains us from acting as we wish. The word "duty" has thus acquired a distinctive negative flavour. But in Kant's theory, duties are not bonds in any ordinary sense of the word. First, they would not bind us unless we happened to have desires that could operate independently of moral demands. According to Kant, a perfect rational creature could impossibly be distracted from acting

morally, and so would—paradoxically—not know of any duty. In this sense, her will is *autonomous.* The idea of duty emerges only because we, as rational creatures, are imperfect (Johnson, 2008). Second, unlike legal or social demands, moral duties are not devised by someone else, but arise from a process known as *self-legislation.*

The term "self-legislation" has given rise to much confusion. According to a common interpretation (that O'Neill argues to be mistaken), self-legislation is the act of prescribing one's own principles for oneself, independently of any authorities. On this reading, the process becomes arbitrary, which rather defeats its purpose. According to O'Neill (2002a), the "self" in "self-legislation" only refers to Kant's view that the moral law is not derived from anything else—not from a dictator's edict, a person's inclination, or even any conception of the good. Consequently, it cannot be a product of our desires either (p. 85).

If the moral law is not arbitrary, must it not adhere to some kind of *standard*, such as the standards of rationality? Kant claims to the contrary that there are no antecedently given standards (imprinted in our minds or otherwise) from which to derive it. Kant's idea is straightforward: autonomy of the will is simply the principles of thought in general. Moral principles "presuppose merely what it takes to be a principle at all" (pp. 90–92), namely, that they should provide reasons for action and be fit as laws for all:

> Autonomy in thinking is no more – but also no less – than the attempt to conduct thinking (speaking, writing) on principles on which all others whom we address could also conduct thinking (speaking, writing). Autonomy in action is no more – but also no less – than the attempt to act on principles on which all others could act. (p. 94)

If we speak but do so without structure, others will not be able to follow our train of thought. We then fail to provide them with reasons to adopt our way of thinking. Similarly, if we act out of no discernible principle, we fail to provide others with reasons to act as we do. So what exactly are these principles that rational thought and action presume?

Even though Kant's moral theory is notoriously obscure, it has become famous even among non-philosophers through its central principle, which he named the *Categorical Imperative.* It is an imperative because it commands us, and it is categorical because it does so unconditionally, without regard to what we would like to do. A *hypothetical* imperative, in contrast, is one which commands (or advises) under certain conditions: "If you are feeling cold, close the door." The Categorical Imperative is usually capitalised in order to distinguish it from the similarly named linguistic construct. "Close the door!", for instance, is a categorical imperative in the sense of being an unconditional command, but it is not *the* Categorical Imperative (Johnson, 2008).

Kant gave several different versions of the Categorical Imperative which he nevertheless regarded logically equivalent. One of them, known as the Formula of Autonomy, urges one to "choose only in such a way that the maxims of your choice are also included as universal laws in the same volition." (O'Neill, 2002a, p. 84) In theory, any action can be tested against this principle to see whether it is permissible. A number of actions that we usually think of as morally reprehensible are thus ruled out:

> Killing and coercing, injury and violence, manipulation and deception, torture and intimidation, enslaving and forced labour are all principles that cannot be willed as universal laws: those who seek to act on these principles cannot coherently will that everybody else do the same. Putting the matter generally, any principle of action whose universal adoption would destroy, damage or undermine capacities for action for some or for many cannot be willed as a universal law. The rejection of principles that cannot be principles for all is, on Kant's view, the basis of human duty. (pp. 87–88)

A morally permissible maxim of action is one which can be made universal, that is, can be acted on while coherently willing that everybody else adopt it as well. One cannot coherently will that everyone adopts a maxim of coercion, for any use of effective means of coercion will undermine the victim's capacity for coercing others in turn. This makes a maxim of coercion forbidden (pp. 86–89). Promising without intention to keep one's promise is another example. If promise-breaking were a universal law, making promises would be meaningless, as no one could ever expect us to keep them.

The impossibility of willing universal coercion or promise-breaking is, according to Kant, due to a *contradiction in conception*. We cannot possibly conceive of these as universal laws, for anyone who acts on them will always undermine someone else's capacity for doing the same. Any such act is an exception made for oneself and thus immoral. But the moral law also rejects maxims that are, strictly speaking, conceivable as universal laws but nevertheless cannot be *willed* without contradiction. "Willing", in the Kantian sense, is not a matter of mere desiring or wanting; "it requires the exercise of practical reason and focusing oneself on the pursuit of that end." (Johnson, 2008) This includes willing the means necessary to further one's willed ends.

The prime example of a maxim that cannot be universally willed is *indifference*. As everyone knows from experience, human beings have plans and projects. But according to Kant, this is not merely a contingent fact about humans. As imperfect rational beings, there is one end that we *must* pursue: our own happiness. But since we at least occasionally need assistance from others, willing a universal maxim of indifference would entail that many people would not receive the help they need to pursue their interests. Such a maxim therefore fails to be moral due to *contradiction in*

the will. As a result, we have an *imperfect duty* to contribute to the happiness of other people (Johnson, 2008, O'Neill, 2002a, pp. 88–89).

The duty of trustworthiness

In Study III, I claimed that someone who is trusted has an imperfect duty to respect the other's trust either by fulfilling it or compensating for it. In Kantian terms, we have a duty not to be indifferent to the other's trust. What ultimately instantiates the duty is that the trusted one is by definition in a unique position to further the ends of the truster.

When the other's trust in us is adequate, fulfilling it is morally unproblematic. This is not to say that it is always easy or straightforward, only that we know what we morally ought to do. Our duty is not *caused* by adequate trust, whatever that would mean. Rather, part of what it *means* to be trusted adequately is that we agree on what ought to be done. The problems emerge when the other's trust strikes us as mistaken. Being regarded as someone with god-like properties—as parents might be by their children, or as doctors are occasionally by their patients—is sometimes flattering but not always comfortable. Surely one cannot be obligated to live up to such expectations?

Surely not. But consider the feeling for a moment. Why, exactly, is there discomfort? Is it not because the other's trust is *unwelcome*? And why would that be, unless it entailed some additional responsibilities (that mere belief could not)? At the very least, you now face the decision whether or not to dispel the other's trust. Either way, there will be consequences for which you are partly responsible.

The kind of justification we demand of trust is intimately connected to the trustee's responsibility to attend to it. Richard Holton (1994) provides a vivid example:

> [W]hether we can bring ourselves to trust will partly depend on whether we think it is right to do so: whether or not we think the trust appropriate or justified. Sometimes this will be because it is only my belief that it is appropriate to trust you that leads me to think that you are reliable. For instance, I might think it appropriate to trust you to do a certain thing only if you invite me to do so; and it might be that very invitation that leads me to think you reliable, since it signals a readiness to take on the responsibilities that my trust would bring. (p. 72)

Clearly, when Holton speaks of a readiness to take on certain responsibilities, and of trusting on the basis of that readiness, he invokes both the epistemic and the normative character of trust. This is what makes an appeal such as "Trust me!" meaningful from both perspectives:

> The person who says it invites us to take a stance: the stance of trust. Sometimes that is enough to make us accept the invitation: perhaps because

> we had not realized it was open to us; perhaps because we thought we had already taken it but had not; perhaps because their acknowledgement that we would need to take this stance signals their acceptance of the responsibilities that would accrue to them as a result, or simply because it make the trust appropriate in a way it would not have been before. (pp. 75–76)

If you doubt my claim that there will be rain today, I add nothing of value by simply reasserting it. But "Trust me!" is not similarly redundant. When uttered in the right circumstances (notably, ones over which I have some control), it conveys something more, namely that I am ready to assume the responsibilities implied by being trusted. It is to acknowledge that trust implies a normative expectation—a demand—which can be both burdensome and unwelcome but also morally appropriate in the circumstances. It also serves to reassure you that I will at least not let you down out of ignorance of the fact that I am trusted. The fact that the phrase "Trust me!" *can* be used to deceive does not render it useless, let alone meaningless. On the contrary, if readiness to be trusted can be faked, it must also be possible to express it genuinely.

In the light of Kant's perfect and imperfect duties, the distinction between betrayal and disappointment suddenly makes sense. It is not that the former implies ill will while the latter does not. Rather, to betray is to regard the other as *insignificant*, unworthy of respect or attention. One who betrays knows all too well that she is trusted, and uses this trust to her own ends. She thus violates a perfect duty. In contrast, someone who fails to take the steps necessary to fulfil someone's trust—perhaps because she disapproves of being trusted in that particular way, or does not recognise the situation for what it is—lets the other down. This is a violation of an *im*perfect duty. We have thus found a moral reason to take the other's trust seriously, even when we think it mistaken.

Public trust revisited

Trust, on my understanding, differs significantly from *public* trust. The latter I defined earlier as the "attitude" that policy makers impute to the public to represent their confidence that public support for some endeavour—in this case, biobank research—will continue. If the two are irreconcilable, one might ask why I chose this approach in the first place. How could my model ever be used to critique evidence of public trust, let alone be of any use in policy making?

A proper answer to these questions begins by questioning the grounds on which they are asked. I did not really "choose" my approach; it became what it is because my first concern was to make sense of everyday use of the

word. If one begins one's analysis by asking how the concept can be made useful in policy making, one's field of view is already blinkered.

Nevertheless, my model does have its uses. Presently, I will use it to throw light on "public trust". From this aggregate concept I will weed out a number of phenomena that have very little to do with trust but which are sometimes included in the construct. Findings taken to imply distrust can sometimes be more plausibly explained in other terms, for instance as scepticism regarding the usefulness of whatever is proposed or as reactions to perceived wrongs that cannot be met squarely by reproaching the wrongdoer. This work has normative implications. First, if it turns out that public surveys cannot assess trust proper, we have one less reason to award them moral consideration. Second, if people's trust in biobank research can be better identified and understood through other means, this should count as a moral reason to pursue those means.

Utility

Several of my objections concern the way public trust is operationalised. The Eurobarometer surveys, for instance, assess trust by asking whether one supposes that the people in question "are doing a good job for society" (European Commission, 2006, p. 45, European Commission, 2010, p. 75). This of course begs the question what exactly is measured and what conclusions we are justified to draw from the measurements. I do not know the answer, but based on findings from other surveys, I will hazard a guess.

Many people think of medical research as more useful or important than other kinds of science. In 2009, more than 90% of Swedes thought it important to conduct world-leading research on cancer, whereas only about 20% regarded philosophy as important (Vetenskap & Allmänhet, 2010a). It is hardly a coincidence that testimonies of trust follow roughly the same pattern. In these surveys, respondents are asked to agree or disagree with statements such as "Increasing research funding improves society to the benefit of all" and "Swedish research is internationally competitive". These are rather strong cues to respondents that *bringing societal benefit* and *being competitive* are what researchers should be trusted to do. Arguably, many other possible ways of trusting them are excluded by this framing.

Whereas Vetenskap & Allmänhet tries—but ultimately fails—to make a distinction between trust and other kinds of optimism, the Eurobarometer attempts to avoid it altogether, seemingly by design:

> Saying 'doing a good job for society' is likely to express a view that the actor is both competent and behaves in a socially responsible way. Thus, 'doing a good job' constitutes a proxy measure of trust and confidence. (European Commission, 2010, p. 75)

What is sought here is, from my point of view at least, not trust but a kind of confidence that would make research participation hypothetically prudent. Though evidence of such confidence may be comforting to policy makers, it is not clear that it has any moral import. Furthermore, if it is as sensitive to media attention as has been claimed, one might also ask whether it is a suitable basis for large enterprises.

Familiarity

Why then not simply ask about trust directly? As illustrated by the survey conducted by the Human Genetics Commission (2001), this approach leads to a different set of problems. At first glance, being trusted by a mere two-fifths of the British population seems to be bad news for academic scientists. But is it? If we ask someone whether she trusts scientists, and whether she trusts GPs, can we be certain that we are measuring the same *kind* of trust in both cases?

I believe the right answer is "no". While asking about trust in GPs is likely to evoke responses informed by existing relationships of trust, few people have such relationships with scientists. With luck, the respondent is optimistic about science as a whole and is not too much deterred by the thought of entrusting sensitive data to people she does not know. A less than perfect score does not necessarily reflect distrust, only the fact that many people cannot bring themselves to trusting unknown entities. As an aside, I believe that British scientists should not be disheartened by receiving a mere 38%, but rather be inspired by the fact that millions of strangers have such faith in what they are doing that they are prepared to entrust them with their genes, especially with only 34% of the British having ever heard of biobanks (European Commission, 2010, p. 81).

Indirection

The Human Genetics Commission survey asked people whom they would trust to use human genetic information held in medical databases responsibly, and provided them with a list of potential trustees from which to choose. This peculiar design decision did yield some interesting findings, such as the one that the police seem to be more trusted than scientists. Those of us who are not English might be amused by the thought of entrusting the stereotypical London bobby with one's genetic data as well as one's bodily safety. But the theoretical value of such exercises remains unclear. In fact, there might be a problem of validity here that resembles the one that looms over questions addressing general attitudes toward science. The problem with the latter, it has been argued, is that

> people will answer in idiosyncratic ways because there is no unequivocal focus in the wording of an individual question. Thus, some people may respond to a question that asks about the contribution of science and

> technology to modern life thinking about nuclear power, while others respond on the basis of their views about mobile phones. (Allum et al., 2008, p. 39)

Similarly, it is quite unclear what "trusting" the police, the government, employers, consumer groups, or the public with one's genetic data amounts to. (Would you trust the police to do scientific research? Would you trust the public to identify criminals? Would you trust the government to do *anything at all* with your DNA?) The lack of a plausible scenario in which these actors are likely candidates forces the respondents to make assumptions to make sense of the comparison, and to rephrase the question to match those assumptions. One possible way of rephrasing it—though by no means the only one—is this: Who do you think would be least likely to use your DNA for sinister purposes, if they discovered it accidentally? But this may already depart from what the survey was intended to measure.

Reproach

The kind of trust one has (or can claim to have) in family members, neighbours, one's doctor, or one's children's teachers differs in a crucial respect from the kind one might have (or claim to have) in unspecified, unnamed, faceless scientists or research institutions. This is not merely to point out that the latter kinds of relationships leave less room for trust; it is to say that to the degree that there is trust, it will play out differently.

In a trusting relationship, trust is not automatically destroyed by disappointments. Already as small children, we are taught a number of rituals—displaying righteous anger and shame, apologising, forgiving, and making amends—that help us avoid such disasters. However, when the transgressor is unknown or otherwise unavailable, such rituals are useless. Insofar as we feel let down by a scientist found guilty of misconduct or fraud, we lack some of the usual means of resolving the incident. In this context, surveys must be seen as something more than just tools for assessing people's views. Informants, far from being passive objects to be studied, express their views actively. An alternative arena has emerged where scenarios of trust and disappointment can be played out.

I now suggest the following: Whereas the words used in the survey determine what the outside observer sees—if the question is about "trust", should we not interpret a low score as a token of distrust?—they are much more loosely related to what the informant intends to express. This is far from obvious, especially if one's view of trust is restricted to a pure cognitive (belief-oriented) model. If beliefs about future behaviour based on someone's track record were all that there is to it, being let down by unknown scientists would indeed count as a reason to distrust scientists generally and, by extension, to down-rate the science community in surveys. But it follows from my analysis of trust that this need not be the case. The

proper response to being let down, by a first-time offender at least, is not distrust. Just as heads of state do not immediately reach for their nuclear weapons in times of crisis, we do not typically declare our distrust if we intend to keep the relationship going. Rather, we respond by placing blame through emotions ranging from gentle admonishment to more severe reproach. In day-to-day interactions, these emotions can be expressed verbally, but also through tone of voice, posture, and sanctions. In surveys, the sole mode of expression is the act of ticking a box, and the one indicating "low trust" may often be the one that closest resembles one's sentiment. If this alternative interpretation is at least partly correct, we can see why the effects of misconduct on public trust depends to such a great degree on the time passed since the last scandal.

Conformity

The Wellcome Trust and Medical Research Council (2002) made an important observation when they told people about their plans to establish a biobank for genetic research:

> Initial response among the general public was generally favourable but unconsidered: respondents tended not to think through the project's implications. Issues raised in the statements subsequently prompted concerns and fears, but further information and discussion of these issues tended to restore positive views. (pp. 7–8)

Indirectly, two things are suggested: first, that there is a fine line between favourable and unfavourable views, where a few words could tip the balance either way; and second, that proper information will allay people's concerns. This interpretation harmonises with other observations to the effect that people, when given sparse descriptions of complex ethical issues and little time to deliberate, tend to opt for a precautionary response (European Commission, 2010, p. 64). Such a response is not necessarily very firmly rooted in their attitudinal structures. Consequently, the problem with low participation rates in some European countries is usually framed in terms of lack of information or awareness (2012, pp. 24–26).

Another possibility, however, is that the respondents conformed to the investigator's expectations. Klaus Hoeyer (2003) carried out an anthropological study on the recruitment of people into large-scale biobank, the Medical Biobank, in Västerbotten County, Sweden. Recruitment to this biobank took place in a setting familiar to many people—the local health care centre—in conjunction with health checks to which people were called at the age of 40, 50 and 60. After being examined, the patients were asked for an (optional) extra blood sample to be stored in the biobank and used in the future for research purposes (pp. 232–233). A key finding was that many

participants neither read the information sheet nor asked many questions about the research. Hoeyer found, however, that

> [t]he interviews raise questions left unarticulated by the donors during the examination. Perhaps informants either felt obliged to look for answers out of simple courtesy or maybe they wished to appear 'ethical'. It seems that to appear 'ethical' you must be willing to rationalise your acts. The interview imposes ethical demands on its research subject. It does not suffice to show a general concern and offer your blood to the nurse. You must know, be informed, and take a rationally justified stand on the developments of biomedical research. (p. 239)

In effect, if being suspicious or concerned is framed as being more "ethical" or "rational" than trusting, people will endeavour to be suspicious or concerned. Although one would expect this effect to be more pronounced in qualitative studies, a survey conducted in 2002 on people who had previously donated blood to a biobank suggests a similar pattern of response (Hoeyer et al., 2004). Research on survey technique has revealed that people often respond to questions out of courtesy, even when they have very little interest in or knowledge of the issue (Pardo et al., 2002, p. 13).

When we are asked a question, we tend to go along with whatever assumptions are necessary to understand why it is being asked. For example, if I am asked whether I would "feel respected" by a certain practice, I must, in order to understand the question, assume that the practice is ethically significant. Similarly, if a fact is presented to me as an ethical issue, I will naturally begin looking for reasons to be concerned. If I am invited to voice my concerns, it is no wonder if I come to do just that.

Proper use of trust

I described in the background chapters how research ethics has developed into a framework for regulation, complete with legislators (policy makers), documents (guidelines), arbitrators (RECs), and procedures (informed consent). This approach to ethics, however understandable in the light of recurrent transgressions of human rights, brings its own set of problems. Study IV focused mainly on ethics review and guidelines, concluding that neither is effective unless the researchers already possess significant capacity for moral deliberation. In a sense, this is to invoke the language of trust: Not only are researchers trusted by research participants, but also by those who evaluate their research. At least some RECs are very explicit about this (Hedgecoe, 2012). This entails, if we apply my model of trust, that researchers must respect the trust of at least two other actors.

In this section, I take a slightly different route toward the same conclusion by considering the relationship between trust and consent. I begin by

presenting an example of what being informed and consenting could mean to donors. Thereafter, I investigate the normative significance of trust for informed consent. In my view, there is no contradiction between the two. To the contrary, I will argue in favour of a conception of morally acceptable consent that *implies* trust. I conclude by considering a number of biobank controversies in this light.

Opt-in, opt-out, and the meaning of research participation

In the conclusion to Study I, my co-authors and I suggested that our findings of extremely low levels of dissent to biobank research among Swedish patients could be a reason to consider moving to an opt-out system. In an editorial response, Graeme Laurie (2008) advised caution in this respect, not least because of the "considerable ethical controversy" surrounding the Icelandic Health Sector Database (HSD) despite its widespread public support.

In the history of biobanking, HSD is an odd duck. Given the combination of presumed consent, commercialisation—with monopoly even—and new legislation (drafted by the company itself and then steamrolled through), the ensuing turmoil came as no great surprise. With its provision that data already submitted could not be removed, the opt-out system as initially devised promised more than it could deliver. Following the agreement that granted patients an unqualified right to withdraw their data, opting out still required some effort. Critics claimed that this was a deliberate strategy to reduce dropout (Rose, 2001, p. 20). To make matters worse, people seemed to be under-informed of their rights. Just before the law was passed, polls indicated that only 13% of the population felt they had "a good grasp" of it (Andersen and Arnason, 1999). Afterwards, leaflets were distributed to Icelandic households, but many claimed to have never received them (Rose, 2001, p. 24). In short, there was much to be criticised besides the opt-out design itself.

That opt-out *can* be implemented in a way that makes it unreasonably difficult for people to exercise their right does not by itself prove that opt-out as such is morally unacceptable. In deciding between opt-in and opt-out, it has been argued that the risk of including people against their will must be weighed against the risk of excluding people who do want to participate. Opt-in arguably increases the latter risk since people might drop out for practical reasons rather than because of any particular concerns. By making participation the default option, this could be partly avoided (Forsberg et al., 2010). On the other hand, given the criticism sustained by the Icelandic system, it has been suggested that opt-in might sometimes yield better coverage (Árnason, 2004, p. 39). Which design is superior in this respect seems to be an open empirical question.

Aside from pragmatic reasons for preferring one model over another, arguments can be based on how either model respects participants' autonomy. One argument for opt-in goes as follows:

1. A procedure of informed consent makes substantially informed consent possible;
2. substantially informed consent is instrumentally valuable because it enables autonomous choices;
3. autonomous choices are valuable intrinsically, instrumentally, or both.

The weakest link in the chain, I think, is found in step (1). Empirical evidence suggests that a procedure of informed consent is surprisingly often insufficient to make people substantially informed. In Sweden, only 65% of donors to the Medical Biobank in Umeå were aware some years later that they had donated blood, though all of them had signed informed consent forms (Hoeyer et al., 2005b). Notably, some donors do not bother to read the information given to them due to lack of time, patience, or interest (Hoeyer, 2003). Similar observations have been made outside Sweden. In the Australian Cancer Study, most donors paid little attention to the methods used, many did not realise that it involved genetic research, and some could not even recall donating a blood sample. Perhaps most surprisingly, "none of the participants understood that the sample was to be stored for an indefinite period of time for possible use in future studies." (Allen and McNamara, 2011) Even ambitious attempts at informing people better may ultimately fail to secure an "adequate" level of understanding. In the Biobank Japan Project, despite a multimodal approach (brochures, DVDs, and face-to-face discussion), 35% of participants did not remember the information given (Watanabe et al., 2011, p. 360). This seems to be consistent with the findings of Sturgis and colleagues (2010) that the effects of educational films on knowledge, attitudes, and trust may be limited.

What should we make of these findings? One gets the impression that understanding was markedly better in Japan (opt-in) than in Iceland (opt-out). Of course, since it is not obvious that the cited studies measure the same thing, a straight-off comparison would be methodologically problematic. But even if we assume that there is in fact a true difference in favour of opt-in, one problem remains. If even serious efforts to inform participants succeed in no more than two-thirds of cases, on what moral grounds are the remaining third enrolled? We are forced to one of two conclusions: Either a large minority—or sometimes, a majority—of biobank donors participate non-autonomously, or substantially informed consent cannot be the only route to autonomous decision-making. Onora O'Neill (2003) chooses the former horn of the dilemma; this poses no problem to her since she also argues that autonomy, as usually conceived in bioethics, is not

a fundamental value anyway. In her view, there is still value to informed consent, but it lies elsewhere:

> Our aim in seeking others' consent should be not to deceive or coerce those on the other end of a transaction or relationship: these are underlying reasons for taking informed consent seriously. (p. 6)

Informed consent, on this view, provides reasonable protection against coercion even when conclusive evidence of voluntariness is hard to find. Similarly, a requirement that all important facts be disclosed makes deception less likely, but scarcely guarantees that anyone is actually informed in a substantial sense. Quite obviously, the responsibility of the researcher or research representative cannot end here; but this may be all that the procedure can carry.

I believe that there is more to be said in this matter, and thus I will pursue the idea of an alternative route to autonomous participation. Informed consent remains in the picture, but acts as a vehicle rather than a criterion. For reasons that will become clear shortly, the *meaning* that research participants attribute to their participation is crucial.

I begin with a contrasting case. In her study of people's views on the Icelandic HSD, Hilary Rose (2001) encountered several people who had a "succinct grasp" of its implications but nevertheless did not act on what they knew:

> One young woman […] said "Well I don't want to know if I am going to die of a heart attack when I'm 40 and I don't want anyone else to know either". When I asked her what she was going to do about opting out she replied that she "almost certainly wasn't going to bother, it seemed all a bit unreal". (p. 24)

I am left with two intuitions. First, there is a striking ambiguity to this case that leaves me wondering what the informant is actually saying. There might be a hidden clarity to her reasoning, but she does not convey it. Either way, we are left in the dark as to what participation *meant* to her.

Meaningful actions, on a minimal understanding of meaningfulness, are ones for which reasons can be given. Scratching one's head is a meaningful action if it relieves one of an itch, while a tic that looks the same is not. Similarly, not bothering to opt out because one has better things to do might be minimally meaningful, whereas not bothering because it seems "unreal" is not. But why not? Because this answer merely raises another set of questions that must be answered before it can be understood: In what way did it seem unreal? Was the scenario so nightmarish that it became disorienting? Or was it simply not important enough to warrant further attention?

Second, if there is such a thing as an autonomous decision, this one is not it. Lack of information was not the problem, or at least not the main problem. What is crucial is that, based on what the informant knew and believed of the HSD, she *gave voice* to her resentment but did not *act* on it. On a superficial level, this might be seen as prudent; perhaps she wanted the hassle of filling out forms even less than she wanted to participate. If this was indeed the reason, her decision was arguably meaningful. But it is not yet autonomous. To see why, we need to scratch away the veneer of first-order preferences.

One way of scratching is by employing Gerald Dworkin's (1988) theory of autonomy. Autonomy, according to Dworkin, is

> a second-order capacity to reflect critically upon one's first-order preferences and desires, and the ability either to identify with these or to change them in light of higher-order preferences and values. By exercising such a capacity we define our nature, give meaning and coherence to our lives, and take responsibility for the kind of person we are. (p. 108)

Autonomy implies meaning but is a narrower concept since not all actions for which reasons can be given qualify as autonomous. As an example, one might desire to smoke while simultaneously desiring not to have that desire (p. 108). Some people who smoke non-autonomously still find some meaning in it. Others continue out of habit; still others, to avoid cravings. The weaker concept of meaning may still be useful because reasons can be readily asked for, given, and discussed, whereas reflection on and adjustment of motivational structures cannot be observed directly.

On Dworkin's view of autonomy, the woman interviewed by Rose arguably failed to act autonomously because she did not alter her motivational structure to match her decision. This is at least one plausible way of interpreting the unresolved tension in her testimony. While one can have reasons for abstaining from action, what we see in this case is passivity in a more fundamental sense. The opt-out system might be to blame. Had she been asked explicitly, she could imaginably have refused, or else found some reason to agree. Instead, she just went with the flow for no apparent reason at all.

The meaning of participation, then, depends partly on whether it results from acting, from refraining from acting, or more extremely, from *doing nothing*. Meaning can be found only in the first two. The "default position" lens sees the choice between opt-in and opt-out as merely a matter of whether non-participation or participation should be the default position. Through this lens, these designs appear to be perfect opposites; but they are not. Quite apart from pro and con arguments based on risk-benefit evaluation, one could argue that explicit consent has an edge because it evokes the language of responsibility. More specifically, it presents the

participant with the opportunity to contribute to the public good rather than the one to refuse such contribution.

Explicit consent can also allow participants to confer responsibility on researchers (Allen and McNamara, 2011). This, too, is an example of a meaningful action. In such circumstances, research participation can be properly understood as an act of trust. This is an important point; unfortunately, it is not uncomplicated. I will return to it shortly.

Morally acceptable consent

In bioethics, popular understanding of autonomy differs significantly from Dworkin's view. The most influential account holds that "an autonomous person who signs a consent form without reading or understanding the form is qualified to act autonomously, but fails to do so." (Beauchamp and Childress, 2001, p. 58) From this perspective, many donations to the Swedish Medical Biobank would count as mistakes rather than meaningful actions (Hoeyer and Lynöe, 2006, p. 17). The same could be said about the Australian Cancer Study and the Biobank Japan Project. Interestingly, this is the deficit model in a new guise. As described earlier, this term refers to our tendency to describe views and decisions that run counter to those of experts in terms of lack of knowledge or competence. Only this time, people's eagerness and naïveté rather than their distrust is what we think is in need of explaining. In my view, we need to do better than this uneasy wavering between polar opposites. But first we need a clearer view of it.

The wavering results, I suggest, from attempts to fit a square peg into a round hole. When cast in the role of the peg, donors must navigate a novel situation shaped by academics' views on what it means to be informed, while attempting to find meaning along the way. In conformity with the paradigm of the deficit model (Wynne, 1991, Sturgis et al., 2010), experts are seen as informed by default. Thus, if participation on certain terms but not on others is advisable from the expert's point of view, any deviation from this standard will be read as either distrust or naïveté. Our worry about the abundant evidence of such deviations is moderated by a quaint hope that with time and effort, participants will come to adopt the experts' point of view, and then go on to make a decision that is both truly informed and cooperative.

As noted by Dixon-Woods et al. (2007), the deficit model, when applied to informed consent, presumes a stimulus-response sequence where any failure of interpretation can be attributed to "noise or "interference". Participants are characterised as passive recipients of information that is expected to "do" something to them. Their contribution to the comprehension process is discounted, which may lead to misdirected efforts to increase understanding by technical means such as "clear writing, leaflet

design, and full disclosure" (p. 2214). Even when one is aware that this approach blinkers one's view, it is surprisingly hard to resist.

A related critique has been phrased by Manson and O'Neill (2007) against overuse of "conduit and container metaphors" in situations where they might be obscuring rather than illuminating:

> The use of metaphors supports certain inferences, or metaphorical entailments. If information *about* certain things is *conveyed* in the process of communication – rather than generated, negotiated, constructed or produced – then it seems evident that there is some kind of stuff that is *about* other things, that is possessed, stored, transmitted, broadcast, and so on. Yet the ways in which the conduit/container metaphors support certain entailments, and thereby structure our thought, may not be obvious to speakers. Such structuring is *implicit* in the use of the metaphors, not an explicit part of our understanding of, or our talk about, communication. (pp. 38–39)

In ancient Rome, to inform was literally to *shape*. Much like the potter moulded clay into various utensils, teachers shaped their pupils into worthy citizens. These are examples of processes of *information*. Arguably, neither can be intelligibly described as transferring or transmitting something to the ball of clay or pupil in question. Of course, these images too could be criticised for picturing donors as passive recipients. But at least the teacher-pupil case necessarily involves a kind of communication (presumably two-way) that cannot be achieved through informed consent documents or leaflets aimed at the general public. Other authors have argued that "public understanding of science represents an interactive process between lay people and technical experts rather than a narrowly didactic or one-way transmission of information packages." (Wynne, 1991, p. 114) This does not show that communication with a researcher or a research representative is necessary in order to become informed, but it does raise the question.

Many people think of their health as a private matter that they are reluctant to share with anyone but their family and, possibly, their doctor. Biobank research, in contrast, implies centralisation of potentially sensitive data into large repositories from which it will be available to a lesser or greater number of strangers. Some authors have argued that informed consent is important here because it allows people to maintain control over matters of personal integrity (Caulfield, 2007, p. 223) or over the uses to which donated material is put (Winickoff and Winickoff, 2003, p. 1181). In contrast, some people see it as an act of *handing over* control to others (Levitt and Weldon, 2005, p. 317, Ducournau and Strand, 2009, pp. 121–122, Hoeyer and Lynöe, 2006, p. 19). The result might be a form of apathy:

> public understanding of science is extremely demanding, and unless the motivation is very high […] it may well be reasonable for lay people to decide not to be drawn into this open-ended and socially uncertain activism and to opt instead for "apathy" or a seemingly uncritical trust in a particular

> source of advice, even if it is partial in some way. The judgment whether or not to show an interest in science therefore is a social one, tied to judgments of one's own power (or powerlessness) to act in one's social environment. (Wynne, 1991, p. 118)

Still, even with regard to those who resist attempts to "draw them in", there are important distinctions to be made between apathy, powerlessness and autonomously chosen inattention to detail. At one extreme,

> when confronted with informed consent, donors inclined to trust the authorities are caught in what Bateson (1972) calls a double bind. If they accept, they engage in a contractual relationship which lightens the authorities' responsibility; if they decline donation, they cannot perform their duty as citizens […] For citizens who at once wish to encourage good research and fear the implications of insufficient balancing of corporate interests, etc., this is a lose/lose situation. (Hoeyer and Lynöe, 2006, p. 19)

That people do choose to participate, then, does not prove that their participation is unproblematic. Between the problem of "informing" participants adequately and the risk of unwittingly pressuring them into cooperating, morally acceptable consent might seem unachievable. Yet people continue to consent to biobank research, and many find it meaningful to do so. As observed by Allen and McNamara (2011), the participants in the Australian Cancer Study "felt anything beyond purely superficial information was irrelevant and therefore immaterial to their decision to participate." Despite their limited understanding of the study, however, they still claimed to "have acted in a self-determined manner and expressed satisfaction that they had control and that consent was theirs to give and withdraw." They quite obviously rejected the notion that they were giving up their control by consenting. Instead, they saw the consent procedure as valuable because it allowed them to "confirm themselves as morally responsible actors who establish a relationship of trust with the research institution and confer responsibility upon this institution." Many were motivated by altruism or their identity as morally responsible citizens. Arguably, their decision to allow such values to outweigh any concerns they might have had was autonomous. Even though the informants "liked the idea of signing a form that 'sealed a deal'", the meaning of the process went well beyond agreeing to certain propositions. It became a "symbolic act" where the declaration of trust and transfer of responsibility to the institution was paramount. The authors suggest that narrow and broad consent would have been equally effective in this regard, whereas presumed consent would not have provided participants with this opportunity to "declare their trust and their identity as moral actors in their community."

I will now make four claims. First, Allen and McNamara's example can be understood as a case of trust. Second, and perhaps more controversially,

the consent given is morally acceptable. Third, these two facts are related rather than coincidental. Fourth, as will become evident in the final section, taking this perspective reveals some of the researchers' responsibilities that might otherwise remain unnoticed.

To bolster my first claim, it would perhaps be enough to refer to the participants' self-reported trust in the institution. But that would go against the grain of my view that we recognise trust first and foremost by considering the type of situation, not the words uttered. So I will instead point to some characteristics that I associate with trust: a conspicuous *lack of concern* that may strike an outside observer as naïve; *normative expectations* on the researchers to do their part (use the samples to do good research, for instance); and *lack of specific expectations* about the actions to be taken. In my view, this is quite enough to speak of trust.

My second claim regarded moral acceptability. Though this is not the place for a full-fledged analysis, I at least owe the reader a brief sketch of what I think this amounts to. To begin, morally acceptable consent implies that the decision is in some sense made autonomously, perhaps in the way suggested by Dworkin. One does not necessarily need a lot of information to make autonomous decisions, though as a general rule being knowledgeable makes it easier to further one's ends. Crucially, however, autonomous decisions are also meaningful. This is, I think, just another way of formulating Manson and O'Neill's analysis of the process of becoming informed as involving attribution of meaning. This in turn presumes two-way communication and negotiation rather than "transfer" of any stuff referred to as "information". With these constraints in mind, I suggest three conditions for morally acceptable consent:

1. **Agreement in sentiment:** The agreement and whatever is agreed on must be taken seriously by both parties.
2. **Trust:** The encounter can be plausibly described in terms of trust.
3. **Adequacy:** Mistaken trust, when it occurs, is corrected or compensated for.

This schema elaborates my third claim by suggesting that morally acceptable consent implies trust. Some additional comments may be called for. To begin, condition (1) does not, I think, distinguish morally acceptable consent from other kinds of consent, but rather explicates part of what consent means. "Consent" literally means agreement in sentiment—or harmony—which rules out any kind of subterfuge, including deception, coercion, and betrayal. The latter is something of a special case: While it could be seen as a form of mistaken trust, I prefer to reserve the latter term for instances that are problematic in the situation where they are expressed, not just after the fact. Condition (2) is in a sense pragmatic, aiming to expose telltale signs of future controversy. I am not thereby suggesting that anything like a

foolproof algorithm for avoiding controversy can be built on trust. But it does follow that we should watch out not just for signs of apprehension or uneasiness but also of apathy and suspicion. Finally, condition (3) entails that the parties must agree on many things that could never be specified in a contract, and that any disagreements are sorted out. This is by far the most demanding of the three conditions. Notably however, it does not rule out accidental disappointments. The way I understand the Australian case, it passes all three conditions.

One might now be concerned that my account excludes the very ideal case of informed consent. If someone were to truly embody this ideal, surely her consent would be acceptable, but would not trust then be redundant? But the latter assumption would be mistaken. Trust, as I have described it, is neither a matter of refraining from acquiring knowledge nor an attitude that compensates for lack of knowledge. Conceivably, these misconceptions stem from the contingent association that was pointed out by Lagerspetz: Trust appears to be redundant when "all" facts are on the table because in such situations, *there is no room for suspicion* even from the viewpoint of an outside observer. That said, even a seemingly ideal case may turn out to leave room for such suspicion. Once a research participant is fully informed, does she not face the decision whether or not to trust the researchers to do what they have promised to do? Through sleight of hand, the need to speak of trust has been made to reappear.

Controversies in the light of trust

In one of the background chapters I presented several examples of critical events—incidents, controversies, and other kinds of conflicts—in biobank research. The number of possible framings of any critical event is large (and perhaps infinite?)—so to actually learn something from them, one has some picking and choosing to do. In this concluding section, I will view them through the lens of trust. Rather than attempting to "do them justice", as a historian would, I use them to illustrate some of the theoretical and normative points made in this thesis. I aim to show how my model of trust and trustworthiness can reveal some responsibilities that a legalistic, contract-centred approach leaves unarticulated. Although our first concern should be not to coerce or deceive, more is expected of moral agents—researchers included—than attending to one's negative duties. To treat people as ends in themselves, we must occasionally assist others to further their ends, especially when we are in a unique position to do so.

Forensic use of the Swedish PKU Biobank

My first example is also the most straightforward. Following the murder of the Minister of Foreign Affairs in 2003, the prosecutor requested that samples be released from the PKU Biobank in order to verify the identity of

the prime suspect. The responsible body, Karolinska Institutet, complied. From one perspective, what took place was completely reasonable, especially given that the PKU Biobank is unique in its near-complete coverage of Swedes born in 1975 or later. From another, allowing the police to access samples collected for purposes of care and quality assurance is no less a betrayal (condition (1)) than it would be to allow them to access suspects' medical records. The National Board of Health and Welfare subsequently recommended that samples be released only under court order (TT, 2004).

The Medical Biobank

During his fieldwork in Västerbotten County, Sweden, Klaus Hoeyer found that none of the people he observed—regardless of whether or not they agreed to participate in the Medical Biobank—paid much attention to the consent form (Hoeyer and Lynöe, 2006, p. 16). To them, it definitely did not play the part of ritual. To the degree that there was a "symbolic act", it was found in the bodily interaction:

> When people transfer blood and sign the consent form, very few words are usually exchanged on the matter. Donors rarely ask questions beyond "Where should I sign?" and medical examinations are characterised by non-verbal bodily interaction between the patient and the nurse […] Sometimes, the needle is already in the arm when nurses ask whether they should take an extra sample for research besides the ones to be used for the medical examination. This situation, where the nurse is active and the people are passive, preparing themselves for test results concerning their susceptibility for disease, does not encourage intellectual inquiry concerning research purposes. Both parties are involved in creating an inter-subjective atmosphere (p. 18).

This case must be understood against the background of the Swedish welfare system where individuals are "enmeshed in a set of duties and responsibilities in a state–citizen relationship in which healthcare plays a central part." (p. 18) People are *cared for* by doctors and nurses; they are *called* to check-ups; and now, they are allowed the opportunity to *reciprocate.* In this setting, informed consent is not only alien, but constitutes a fundamental change in the nature of the relationship—from one of exchange to a contractual one—and calls for a reinterpretation of the authorities' responsibilities to match. Hence, even though one might be inclined to describe this as a case of trust, one can also suspect a Batesonian double bind in action (p. 19).

I do not know how this ambiguity is to be resolved. Fortunately, I do not need to in order to make my point: People who are confused by contradictory demands—through a double bind or otherwise—cannot truly consent. To trust under such circumstances would be irrational (Study III)

and thus fail condition (3), whereas consenting without trusting would fail condition (2). This highlights the need to be careful not to overemphasise participation as a civic duty, even when there is no outright coercion.

Swedish clinical biobanks

Conceivably, the threat of a double bind looms over biobanks in Swedish health care more generally. There is also the perhaps more pressing problem of research representatives—in this case, doctors—being unaware of what participation in clinical biobanks might entail. The Biobank Act (Sveriges riksdag, 2002) does not, for instance, distinguish between academic and commercial research (though it does state that each project must be approved by an REC). And even when disclosed to patients, commercial involvement can be masked by the familiarity of a health care setting (Winickoff and Winickoff, 2003, p. 1180).

In my analysis, non-disclosure of material information fails condition (1) or (3). To be able to see this, we need to consider how a patient might phrase her critique, should the missing fact be later discovered: "You never told me that *p*!" What is implied here is either that *p* was withheld (which would amount to deception) or that the doctor did not realise that *p* ought to be disclosed (which is a failure of competence).[20] Morally acceptable consent in this context thus requires that doctors have some basic knowledge of the Biobank Act. They must also be able to apply this knowledge to real-life situations. Admittedly, this duty cannot always receive priority, but neither should it be forgotten.

The moral justifiability of the system as a whole is quite another matter. When new responsibilities are imposed on doctors, there is always a risk that they will go unmet. On the other hand, doctors are already bound by a multitude of laws, regulations, and expectations, so why should they not be able to handle another? But part of the explanation why the system works despite its complexity (and that of the rule framework that governs it) lies in tradition and culture. Doctors embody to varying degree a number of professional virtues that help them navigate the various legal and moral claims placed on them (Beauchamp and Childress, 2001, pp. 30–31). Even in unfamiliar waters, running aground is surprisingly rare. From this perspective, introducing new areas of responsibility can be problematic unless they are covered by existing virtues and role responsibilities. To ensure a trustworthy system, the Biobank Act is simply not enough; what is needed is first and foremost a cultural change. In particular, biobank research

[20] Note that in my adaptation of de Sousa's analysis of the structure of emotions to the case of trust, what I am modelling are not the *cognitions* involved in trust but rather the way we *reason* about trust. Since I am not making claims about anyone's mental states, I need only argue that these are forms that arguments about trust, betrayal and disappointment might take. Luckily, the latter is easier. See DE SOUSA, R. (1987) *The Rationality of Emotion*. Cambridge, Massachusetts: The MIT Press.

cannot just borrow credibility from health care; the involved actors must agree on a view of it as an integrated part of the health care system.

deCODE and HSD

Intuitively, the grudging acceptance expressed by the young Icelandic woman who "wasn't going to bother" opting out of the HSD does not give the impression that the consent was morally acceptable. As it happens, it fails condition (2) because it involves distrust, or perhaps apathy, rather than trust. It possibly also fails condition (1) since the "participant" does not take the (implicit) agreement seriously. This, I argue, is a risk that we run with opt-out systems.

A case could also be made for opt-in for reasons related to professional autonomy and trust. From one point of view, after the new law had been passed, Icelandic doctors had no choice but to hand over their patients' records to deCODE. From another, doing so could well be framed as an act of betrayal (failure of condition (1)), at least from the viewpoint of those patients who had not quite grasped what was about to happen beforehand and came to regret their inaction later. Critics also suggested that if patients came to believe (rightly or wrongly) that everything they said would go into the HSD, many of them would stop talking openly (condition (2)); conversely, doctors might start keeping shadow records to protect them (Rose, 2001, p. 19). Though speculative, neither scenario is implausible. Whatever else one might think about opt-in systems, they at least do not pose similar threats to the trust between patient and doctor (Árnason, 2004, p. 46).

The Havasupai case

From the legal perspective, the crucial question in the Havasupai case was whether the research that had been carried out fell within the scope of the original consent. Also from an ethical perspective, the case may seem to illustrate the indispensability of informed consent: Had the Havasupai been allowed to consent to each particular use of their blood samples, they would not have felt violated, and the lawsuit would never have taken place.

I find this interpretation of the controversy unsatisfactory. This is not merely because a general requirement for narrow consent would be devastating to biobank research, although that might be true as well. The main problem is rather that no matter what kind of consent is obtained, strategies of this kind provide no guarantee against adverse events—though they may be able to deflect any consequent legal claims. Of course, speaking of this particular case, it is at least conceivable that the researchers *could* have predicted the findings of inbreeding and migratory patterns that the Havasupai found offensive. The possibility of reaching such conclusions *could* have been stated in an informed consent sheet (even though doing so

might also have counted as an insult). But all this is *ad hoc*. Nailing down general principles that are useful in practice is that much harder.

Often, people's concerns about research results and their possible uses cannot be addressed at the level of informed consent. People may be concerned about eugenics, but there is no way that eugenic uses of genetic knowledge can be predicted, let alone prevented, by those who write informed consent documents. It does not even help to say that eugenics is a "possible" consequence. In the absence of a plausible causal chain, this would amount to mere guesswork. People with seemingly unrelated concerns may come to contribute indirectly, in less than obvious ways, to what they despise. An animal rights activist, for instance, would probably be appalled to learn that "the identification of specific gene sequences might lead to animal experimentation […] as the developments in functional genomics make cross-species comparison swift and promising" (Hoeyer and Lynöe, 2006, p. 17).

Approached through the lens of trust relationships, in contrast, this case becomes rather clear. It does not quite seem to be a case of betrayal, as the Havasupai would have it. At the very least, there is still room for some optimism that the researchers never intended to betray or exploit, but (perhaps naïvely) attempted to do as much research as possible within the limits of the agreement. Obviously, however, there was a fundamental *dis*agreement as to what the agreement entailed: The Havasupai trusted the researchers *inappropriately* to solve their diabetes problems—research rarely, if ever, produces such quick fixes—and *misplaced* their trust in them to respect their taboos. Their consent thus failed condition (3).

We are thus shown the necessity of being sensitive to cultural perceptions—in this case, the particular stigmas that the Havasupai associate with mental illness and inbreeding, and the importance of their origin stories remaining undisturbed. The researchers, on this account, should have considered refraining from doing research that could offend, harm or hurt the donors, or, if they were initially unaware of what their results would be, end it when things became clearer. Although I am not in a position to judge whether the harm done to the Havasupai outweighs the scientific value of the published results, I believe that the question is justified. Even more importantly, the researcher must be the one to ask it.

Future Work

No matter how many pages are written on a topic, there always seems to be more work that needs doing. Perhaps Robert M. Pirsig (1974) was right in observing that for each hypothesis successfully tested, many more suggest themselves. My thesis, at least, leaves many questions unanswered.

Some questions arise from the limitations of my studies. To wit, my empirical findings are but tiny pieces in a much larger puzzle. They could be criticised for providing only weak evidence that interpersonal relationships matter to decisions to take part in research. One could certainly desire more complete, robust and convincing evidence for or against the presence of trust in biobanking. I suspect that the additional payoff, in terms of practical moral implications, from such inquiries would be limited. Other questions may be more important to consider. For instance, given the great interest that policymakers have shown for public trust, empirical and normative work on the role that public trust plays and should play in their decision making is much needed.

My conceptual analysis of trust was crucial in this thesis. Since few analyses age well, I cannot hope for its permanence. Nevertheless, whatever one may think about my account of trust, at least it shows how conceptual analysis can make a difference to one's normative conclusions. In my mind, deciding how an instance of human interaction should be described and finding out what one ought to do are two sides of the same coin. My aim has not been to show that we actually, in real life, infer duty from trust. Rather, it has been to argue that such inferences, when they are made, are morally valid. I have chosen to understand the connection between trust and duty in terms of Kantian imperfect duties. Employing other theories might yield different results. Bioethicists who are not too keen on Kant might want to explore such possibilities.

Finally, I have hinted at a few possible practical applications of my account of trust. Conceivably, many others remain to be investigated. More could be said, perhaps, about the relationship between researchers and RECs and the moral significance of trust in this relationship. One could also ask how RECs are in turn trusted, and if so, by whom and in what sense. Their decisions can be criticised for being opaque and occasionally idiosyncratic. What if they were required to follow a strict procedure where only facts accessible to all and principles dictated by a governing body were allowed into the discussion? Could we then trust them to make moral judgments, or

would consistent rule-following be the best we could hope for? I suspect that if one were to apply my model of trust to this context, one would find that the trustworthiness of RECs in fact *depends* on them being autonomous. This is, at least, an intuition that I think is worth pursuing.

Conclusions

After many years in the shadow of other ethical concepts such as autonomy, trust has enjoyed a renaissance of sorts within the field of biobanking. Sadly, with policymakers and most authors focusing on the vague concept of *public trust* and how it can be cultivated, the discourse has been impoverished. In my view, trust has been employed as a tool rather than taken seriously as a moral concept. Perhaps the moral aspect has been considered redundant as long as we have a robust framework of guidelines, ethics review and informed consent. But there are limitations to each one of these pillars. Guidelines and ethics review do not guarantee morally acceptable research unless the researcher has moral competence and integrity, and the justificatory power of informed consent is limited unless the participant finds meaning in his or her participation.

In this thesis I have defended a view of trust that encompasses conceptual, empirical and normative aspects. A number of conclusions can be drawn from each perspective. I also feel justified in making one methodological point.

Throughout my work with trust it has become clear that no single conception of trust is superior across all situations. It has become just as clear, however, that not every logically consistent conception is morally significant. Viewing trust as an attitude or belief, for instance, does not explain why betrayals and disappointments should be reasons to blame the trustee rather than the truster. I have suggested that our understanding of trust in the moral sense is informed by culturally shared paradigm scenarios of trust. Those scenarios have certain features in common. Most importantly, they imply that there are certain normative expectations that must be respected. What this means depends on whether the particular instance of trust is adequate or mistaken. Respecting adequate trust is by definition morally unproblematic (though not necessarily easy). When trust is mistaken, in contrast, there are always some ambiguities that need to be resolved before the duties of the trustee become clear. I have suggested that the possibility of trust being misplaced, irrational or inappropriate brings out three corresponding duties:

1. Endeavour to be at least as trustworthy as you are trusted. When you cannot live up to people's expectations, dispel the illusion that you can.

2. Be wary when a situation apparently involving trust is ambiguous, for instance when it could just as well be described in terms of obedience or duty, since this can be a sign of undue influence.
3. Be sensitive to normative expectations, especially in unfamiliar encounters. When they are implicit, seek to make them explicit. When they are inappropriate, seek to renegotiate.

In policy work, empirical evidence of trust is in high demand. There are two reasons for this. First, trust—or at least *public* trust—is a criterion for successful policy. Second, the common perception that people in post-modern society are becoming less trusting has instilled fears in the research community that participation in biobanks will decrease, which could threaten the scientific validity of studies. What policy makers are interested in, then, is not trust *per se*, but rather *public support* for biobanking. The empirical studies that I conducted as part of this thesis suggest that people are more willing to participate in biobank research than many surveys predict, and that speaking of a "crisis of trust" may thus be an exaggeration, at least in the contexts in which these studies took place. Existing relationships of trust may be crucial, not least when people are recruited in the context of health care.

Now to my methodological point. One way to approach trust empirically has been through public surveys. In contrast, whether people in fact participate in research depends partly on other factors than those that determine how they respond to questionnaires. My point is then not merely that people's behaviour cannot be accurately predicted by surveys; this is already a known fact. It is rather that morally significant trust is recognised in interactions between people, not by observing certain outcomes such as research participation. We thus have reason to doubt whether surveys, even perfectly reliable and internally valid ones, can ever assess the kind of trust that matters most. Surveys will likely continue to play an important part in assessing public knowledge and attitudes, but it is not clear that elevating "public trust" to a criterion of success for public policy is morally justifiable.

Trust provides a lens through which the moral acceptability of various practices can be assessed, including research and the interactions that lead up to research being conducted. Given the various difficulties with "fully" informing donors and the limited justificatory power of consent, the wisdom of relying on procedures is questionable. I have suggested that morally acceptable consent involves adequate trust, whereas lack of trust or mistaken trust indicates a possible moral problem. Researchers and research representatives must therefore take donors' trust seriously. This is in many ways more demanding than a legalistic reading of informed consent.

The theoretical reasoning that grounds my view of morally acceptable consent can be extrapolated to the process of ethics review. Not all ethical issues can be handled at this level, especially not those that arise during the

course of a project. Further, researchers are experts in their own fields and thus best positioned to foresee future uses of their findings. When approving projects, RECs place trust in the researchers' moral capacities, unless they act against better judgment. Personal knowledge of applicants should not be seen as an impediment to independent judgment, but may actually improve RECs' decisions.

To conclude, no amount of documents, formal procedures and oversight can relieve researchers of their individual moral responsibility. One way to understand this responsibility is to pay attention to how one is trusted, by research participants, RECs, or society at large.

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Summary in Swedish – Sammanfattning

Vilken roll bör förtroende spela i biobanksforskning? Är det något som vi måste odla (ungefär som vi odlar potatis)? Eller är det etiskt relevant av någon annan anledning? Hur förhåller sig förtroende till forskarens individuella moraliska ansvar? I den här avhandlingen närmar jag mig de här frågorna genom både empiriska (erfarenhetsbaserade) och filosofiska (analyserande och argumenterande) metoder. Avhandlingen består av fyra artiklar och en så kallad kappa (ramberättelse).

Jag drar fyra övergripande slutsatser:

1. I motsats till vad man befarat verkar det som att människor verkligen har förtroende för biobanksforskning. Detta gäller i synnerhet i Sverige, men skulle också kunna gälla i andra länder.
2. I begreppet förtroende ryms det normativa förväntningar, det vill säga förväntningar om vad som *bör* göras snarare än vad man *tror* kommer att göras. Den som har någons förtroende har också ett moraliskt ansvar att hantera förväntningarna. Detta ställs på sin spets i situationer där det upplevs att förtroendet bygger på missförstånd eller när förväntningarna är orimliga.
3. Man måste skilja mellan förtroende mellan personer och det som ibland kallas ”allmänhetens förtroende” för forskning. Allmänhetens förtroende brukar man försöka mäta med hjälp av attitydundersökningar. Oftast är målet att få en uppfattning om hur villig befolkningen är att delta i forskning under olika förutsättningar. Påstådda effekter på ”allmänhetens förtroende” används sedan för att legitimera samhällets reglering av verksamheten. Men det här förtroendebegreppet är inte så väl lämpat för att identifiera forskarens moraliska plikter.
4. Forskaren kan aldrig avsäga sig sitt individuella moraliska ansvar. Även om det finns regler och riktlinjer, forskningsetisk prövning och procedurer för att inhämta informerat samtycke, kommer etiska överväganden alltid att behöva göras av den enskilda forskaren under loppet av ett forskningsprojekt. Forskaren måste alltid fråga sig hur han eller hon bör agera för att vara *värd* forskningsdeltagarnas förtroende snarare än för att *få* det. På detta sätt kan forskningen bli mer moraliskt acceptabel.

Biobanker är samlingar av prover tagna från människor. Till en biobank hör även en databas där man lagrar olika sorters information om provgivarna, till exempel om deras sjukdomar och levnadsvanor. Biobanker har länge använts i sjukvården för utbildning och kvalitetssäkring. Exempelvis måste en patolog granska tusentals prover i sitt mikroskop för att bli skicklig på att bedöma avvikelser, och för detta behövs provsamlingar. Det är också viktigt att spara vissa prover för att man senare ska kunna gå tillbaka och kontrollera att de har bedömts rätt. Ibland vill man göra nya analyser för att få en säkrare diagnos. Biobanker kan även användas för forskning. I det senare fallet är syftet inte att ta reda på information om enskilda individer, utan att leta generella samband som kan förklara uppkomsten av olika sjukdomar. På detta sätt läggs grunden för nya behandlingsmöjligheter i framtiden.

I Sverige lämnar patienter ibland prover som sparas i en biobank. Det rör sig främst om vävnadsbitar, cellprover (till exempel de som tas vid gynekologiska undersökningar), blodprover för immunologisk analys (för att påvisa reaktioner mot vissa smittämnen) samt prover för genetisk analys. De flesta ”vanliga” blodprover sparas endast under kortare tid (högst två månader) för kvalitetssäkring. När ett prov tas som kan komma att sparas längre, ska patientens läkare efterfråga patientens samtycke till att det sparas och används för vård, kvalitets- och utvecklingsarbete, undervisning samt forskning. Om patienten invänder mot något av detta noteras det i journalen. Han eller hon får därefter fylla i en så kallad ”Nej-talong”. Landstingets biobankskoordinator ser sedan till att provet kastas eller att dess användning begränsas enligt patientens önskemål. Förutom biobanker som innehåller prover som samlats in genom hälso- och sjukvården finns det även sådana som är kopplade till specifika forskningsprojekt. Relativt nyligen har man även börjat bygga större biobanker som samlar in prover direkt från allmänheten och som används i många forskningsprojekt.

Med den tekniska utvecklingen följer nya möjligheter. Biobanksforskare kan idag utvinna mängder av information ur prover, inte minst om provgivarnas genetiska anlag. Med hjälp av kraftfulla datorer kan information om provgivares gener, livsstil, omgivningsfaktorer, sjukdomar med mera analyseras för att hitta samband som förklarar uppkomsten av både folksjukdomar och ovanliga sjukdomar. För detta krävs det stora mängder provgivare. De största biobankerna har redan samlat prover från miljontals människor. Eftersom detta är oerhört kostsamt måste man kunna återanvända insamlade prover och data i flera olika forskningsprojekt. Det pågår flera samarbeten mellan forskare världen över för att göra detta på effektivast möjliga sätt.

Parallellt med denna utveckling kan man se en gradvis förändring i det sätt som biobanker och biobanksforskning regleras. För femton år sedan var biobanksforskning i det närmaste oreglerat. Idag finns det strikta regler för hur biobanker får inrättas, hur insamlandet av prover ska gå till, hur ett

informerat samtycke ska se ut och hur forskningen ska granskas, med mera. Ett stort antal nationella och internationella organ arbetar med att utfärda nya riktlinjer för forskning. Tyvärr blir dessa allt mer komplicerade och svårbegripliga. Ett antal etikprövningsnämnder ansvarar för att granska alla forskningsprojekt för att se till att de är etiskt acceptabla. Detta kunde i bästa fall vara ett forum för etisk diskussion mellan forskaren och nämnden. Tyvärr ägnas en stor del av tiden åt att utforma informationsblad till provgivaren.

Vad är det då som dessa regleringsmekanismer är tänkta att skydda oss mot? Till skillnad från forskning som görs direkt på människor, till exempel genom att låta deltagarna ta olika sorters mediciner och observera effekterna, innebär biobanksforskning inga direkta fysiska risker. Till största del har debatten i stället handlat om provgivarnas integritet. Man behöver till exempel både regler och tekniska lösningar för att hindra att skadlig information hamnar i orätta händer. Det är lätt att föreställa sig vad som skulle kunna hända om försäkringsbolag eller arbetsgivare fick tillgång till stora mängder information om ens hälsa. Men det finns även etiska frågor som berör forskningen som sådan. Kanske bör man inte forska på allt som man kan forska på. Samtidigt kan den medicinska forskningen förhindra sjukdom, lidande och förtida död. Olika människor kan ha olika syn på vilka forskningsområden som är moraliskt acceptabla. Hur olika intressen ska balanseras är en av de många frågor som diskuteras i bioetiken.

En viktig fråga för beslutsfattare är att säkerställa ”allmänhetens förtroende”. Detta är förståeligt eftersom biobanksforskning är beroende av att många människor vill bidra med prover. Attitydundersökningar som påstår sig mäta allmänhetens förtroende får därför stor uppmärksamhet. I samband med olika kriser och skandaler har man sett sjunkande nivåer av förtroende, vilket har skapat en osäkerhet bland beslutsfattarna. För att undvika en förtroendekris har man sett det som nödvändigt att införa alltmer heltäckande reglering, nationsövergripande styrning och bättre insyn i beslutsprocesserna. Det har även blivit vanligare att engagera allmänheten i diskussioner om hur forskningen ska regleras för att vinna människors förtroende.

Jag kommer nu att återge huvuddragen i artiklarna.

Studie I. I denna studie undersökte jag och mina medförfattare hur vanligt det är att patienter i Sverige invänder mot att deras prover sparas eller används. Under 2005–2006 togs knappt 3 miljoner biobanksprover i Sverige. I drygt 0,1% av fallen invände patienten muntligen mot lagring av provet. Hälften av dessa skickade in en Nej-talong. Andelen varken ökade eller minskade signifikant från 2005 till 2006. Vi drog slutsatsen att det åtminstone i detta sammanhang saknas övertygande tecken på en förtroendekris.

Studie II. I denna artikel undersökte vi huruvida faktiskt deltagande i biobanksforskning är större än vad man kan förvänta sig utifrån resultat från

attitydundersökningar. Vi jämförde resultat från attitydundersökningar utförda i Sverige, Island, Storbritannien, Irland, USA och Singapore med faktisk deltagandefrekvens i biobanksstudier utförda i samma länder under samma tidsrymd. I flertalet fall var faktiskt deltagande större än vad man kunde vänta sig. Särskilt hög deltagandefrekvens (88–99%) sågs i studier där provgivarna tillfrågades ansikte mot ansikte i en vårdsituation. Omvänt deltog få (10–26%) i studier där provgivare rekryterades från den allmänna befolkningen per brev eller telefon. Vi drog slutsatsen att förtroenderelationer spelar roll för människors beslut att delta i biobanksforskning.

Studie III. Denna studie syftade till att besvara frågan: Vad innebär ”förtroende” i en situation där en patient lämnar prover och får frågan av sin läkare om de ska sparas?

Förtroende innebär långt ifrån alltid att man har specifika förväntningar om vad som bör göras. Snarare är våra förväntningar ofta kopplade till våra respektive roller. En läkare som inhämtar samtycke för forskning kan till exempel förväntas ha viss kompetens på området och vara beredd att föra en opartisk diskussion om forskningens fördelar och nackdelar.

En fråga som måste ställas är hur det kan vara rationellt att ha förtroende. Det är ofta svårt att peka på vad vi har för faktaunderlag för att lita på någon. Vi argumenterar i denna studie för att man kan likna förtroende vid *känslor*. Känslor är visserligen subjektiva, men de fyller också en social funktion och kan därför bli föremål för kritik. Känslor kan uppstå på felaktiga grunder eller vara olämpliga i sammanhanget – vilket alla som någon gång skrattat vid fel tillfälle är plågsamt medvetna om. Det följer av liknelsen med känslor att förtroende kan vara antingen adekvat eller problematiskt.

Den som har någons förtroende (läkaren i det här fallet) har ofta de bästa förutsättningarna för att upptäcka eventuella problem i förtroenderelationen. Han eller hon har därför ett ansvar för att missuppfattningar korrigeras eller att orimliga förväntningar tas upp till diskussion. Vissa motsättningar kan behöva diskuteras på samhällsnivå och inte endast i den aktuella situationen.

Studie IV. I denna studie undersökte vi på vilket sätt reglering och kontrollmekanismer kan förväntas säkerställa moraliskt acceptabel forskning. Vi fann ett antal viktiga begränsningar. För det första fungerar forskningsetisk granskning bara om forskare kan antas vara moraliskt ansvarstagande. En del av nämndernas ledamöter är själva forskare, och forskarnas redogörelser för vad som är god forskning är ofta vägledande när forskning på nya områden ska bedömas. För det andra är etiska riktlinjer lämpliga varken för att styra forskarnas beteende eller för att fostra deras moral. Om de används som styrmedel kommer det alltid att uppstå fall där det moraliskt rätta är att gå mot dem. Ansvarstagande riskeras alltså att bestraffas medan moralisk lathet belönas. Som ett sätt att fostra forskarnas moral misslyckas de eftersom moraliska överväganden krävs för att tolka dem. Man förutsätter alltså det som man avser att fostra. För det tredje finns

det risker med en byråkratisering av etiken. När forskarna tvingas fokusera på ett smalt urval av etiska problem riskerar de att bli ouppmärksamma på sådana som inte kan förutsägas. Starka yttre incitament för att agera på ett sätt som är ytligt korrekt kan undergräva forskarnas inre motivation att göra det rätta. Med de hundratals dokument som forskarna ska förhålla sig till är motstridiga krav oundvikligt, vilket kan leda till att de fjärmar sig från etiken. Sammanfattningsvis måste regelverken utformas så att forskarna uppmuntras till att ta sitt ansvar snarare än hindras från att göra det.

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