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INDIVIDUAL GENETIC RESEARCH RESULTS

Uncertainties, Conceptions, and Preferences

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Abstract
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This thesis contributes to the ethical discussion on how to handle incidental findings in biomedical research using sequencing technologies from a theoretical and an empirical perspective. Study I and II are theoretical studies that used conceptual analysis. Study I demonstrates that the argument for disclosure based on the principle of beneficence ignores the complexity and uncertain predictive value of genetic risk information. The argument neglects the distinction between an incidentally discovered disease and an incidentally discovered risk for disease with unclear predictive value. Study II investigates the proposal to let participants express their preferences to incidental genetic findings in the consent form. The study argues that this freedom of choice is problematic because it is uncertain whether the opportunity to choose in the consent phase enables people to express what they truly prefer. Participants might be steered to a specific answer depending on mood, triggered feelings, and the framing of the question.

The second part of the thesis is empirical and used both a qualitative and a quantitative approach. Study III investigates research participants' understanding of genetic risk and used a phenomenographic approach and focus group interviews. One result was that participants understood genetic risk in binary terms. This understanding involved an either/or concept of genetic risk. Participants tend not to understand genetic risk as a probability. They also interpreted the information in terms of their past, present, and future life. Study IV used a questionnaire with a stated preference technique called Discrete Choice Experiments (DCE) to investigate participants' preferences for genetic risk information. An effective preventive measure was the most important characteristic for research participants in their decision to be given genetic risk information. When the disease was life threatening, had a high penetrance probability, and had effective preventive measures, 98% of the participants wanted to know their incidental genetic risk information.

As genetic risk information has many different characteristics and includes many uncertainties, ethical discussions and empirical studies of people's attitudes and preferences need to explicitly engage the complexity of genetic incidental findings.

Keywords: Incidental findings, genetic risk information, research participants, risk perception, free choice, framing, conceptions of genetic risk, making sense of genetic risk, preferences for genetic risk information

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To Mina and Eliot

Front cover: illustration by Agnese Aizpuriete

List of Papers

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

I Viberg, J., Hansson, M. G., Langenskiöld, S., Segerdahl, P. (2014). Incidental findings: the time is not yet ripe for a policy for biobanks. *European Journal of Human Genetics*, 22 (4): 437-441.

II Viberg, J., Langenskiöld, S., Segerdahl, P., Hansson, M. G. (2016). Freedom of choice about incidental findings can frustrate participants' true preferences. *Bioethics*, 30 (3): 203-209.

III Viberg Johansson, J., Segerdahl, P., Hösterey Ugancer, U., Hansson M. G., Lagenskiöld, S. (2018). Making sense of genetic risk: A qualitative focus-group study of healthy participants in genomic research. *Patient Education and Counseling,*101 (3):422-427.

IV Viberg Johansson, J., Lagenskiöld, S., Segerdahl, P., Hansson M. G., Hösterey Ugancer, U., Gummesson, A., Veldwijk, J. (2018). Research participants' preferences for receiving incidental genetic risk information: a discrete choice experiment. *(In manuscript)*

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Contents

Abbreviations

IRR	Individual Research Results
IFs	Incidental Findings
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
NGS	Next Generation Sequencing
WES	Whole Exome Sequencing
WGS	Whole Genome Sequencing
GWAS	Genome-wide association studies
SCAPIS	The Swedish CArdioPulmonary bioImage Study
ACMG	American College of Medical Genetics and Genomics
DCE	Discrete Choice Experiment
TTT	Time-To-Think
NTTT	No Time-To-Think
RUT	Random Utility Theory
NGT	Nominal Group Technique
ASCC	Alternative Specific Constant C

Introduction

> "But it's unbelievable: I have a lower than average risk – not even the ordinary twelve percent, only 7.7. It is as if a very old, hissing pressure deep inside my body quickly seeps out and floats away. For a wonderful, absurd second, I believe I've been liberated from death." Lone Frank in *My Beautiful Genome*.

Receiving genetic risk information can be perceived as being 'set free' from fear a disease can give. Or, it can start emotional processes of guilt, sadness, and fear of what the future might bring (McAllister et al., 2007).

When research participants enrol in biomedical research, one motivation can be that they get an extensive health check-up. Disclosing health-related information such as blood pressure, lung function, and results from blood analysis (cholesterol and blood sugar) is uncontroversial and common practice in research. Genetic risk information, on the other hand, is often withheld (EpiHealth, 2011; UK Biobank, 2006). There is no agreement in the research community on how to handle results from genetic research (Bledsoe, Grizzle, Clark, & Zeps, 2012; Bredenoord, Kroes, Cuppen, Parker, & van Delden, 2011; Wolf, Lawrenz, et al., 2008). The current consensus is that information, if disclosed, should benefit participants. However, some argue that information can do harm for both participants and research (Bledsoe et al., 2012; Forsberg, Hansson, & Eriksson, 2009; Hens, Nys, Cassiman, & Dierickx, 2011; Juengst, Flatt, & Settersten, 2012).

Genetic research sometimes reveals unexpected (or incidental) genetic findings about participants. This circumstance involves several ethical positions and conclusions and it is difficult to see how to resolve these issues. This thesis assesses arguments for and against disclosing genetic incidental findings to research participants. Moreover, the thesis investigates the conceptions and preferences that research participants have when it comes to genetic findings about their genome sequence.

Background

Biomedical research is designed to include the investigation of common diseases (e.g., cancer, diabetes, dementia, depression, and cardiovascular diseases). This can be done by combining questionnaires, physical tests, biological samples, and population and disease specific registers. Biobank research and a rapidly growing number of biomedical research areas including genomics have identified many genes and a growing number of biomarkers associated with disease. Genetic testing for monogenic disorders (diseases caused by mutation in a single gene) are well established, but little is known about the complex risks associated with multifactorial disorders, where the predictive importance of individual elements – i.e., genetic, epigenetic, or environmental – will differ for different individuals. To examine disorders or diseases that depend on multiple genetic and environmental factors, research investigates many genes in combination.

Biomedical research using genomics

Biomedical research that collects biological samples in combination with other measurements is considered non-interventional. By observing the participants via collection of different data (questionnaires, physical measurement data, different imaging techniques, biomedical data, and genotyping), research aims to find associations between genes, lifestyle, and specific diseases. Of course, the overall aim is to determine diagnoses, to provide preventive treatments, and to treat common diseases.

When examining associations between genes, lifestyle, and specific diseases, researchers use technologies that rapidly read many DNA or RNA fragments simultaneously (high throughput sequencing technologies). New technologies such as next-generation-sequencing (NGS) are high-resolution, 'non-target' techniques that can detect variation throughout the whole genome and exome. With this technology, the whole genome and exome can be sequenced, which will generate an enormous amount of raw data requiring complex bioinformatics analyses to extract useful information. Depending on the aim of the test, the analysis will focus on the entire genome, exome, or selected parts (van El et al., 2013). This approach has greater potential to identify the genetic component of health problems. The challenge, however, is the handling of this

vast amount of information. When the research question is broad, an untargeted approach needs to be used, a situation that may mean incidental findings will be detected (Lohmann & Klein, 2014).

A genetic test intends to predict individuals' disease risks so that preventive measures can be taken before the disease manifests. However, this depends on the predictive ability of the test – i.e., whether the test can distinguish a group of people who have a higher risk of disease than others. However, NGS does not have overall predictive ability as such. The technique should rather be seen as 'one assay that consists of numerous tests' (Morgan, Chen, & Butte, 2010; Zimmern & Kroese, 2007). The predictive ability of a test is determined by three things: i) the incidence of the disease, ii) the frequency of the polymorphism, and iii) the association between variation and the disease. How many people have the disease and whether the variation is present or absent is the basis for calculating different risks (Table 1) (Janssens, Patch, & Skirton, 2015).

Table 1. The basis for calculating predictive ability of a genetic test.

		DISEASE		
		YES	**NO**	**TOTAL**
VARIATION	Present	a	b	$a + b$
	Absent	c	d	$c + d$
	Total	$a + c$	$b + d$	n

Table 1 and equations 1-3 are adapted from Janssens et al. (2015).

The association between a present variation and a disease is the key importance for making predictions. This means that the stronger the association is, the higher the risk difference is between people who have the gene variation and those who do not have it, also known as risk difference (equation 1):

$$\text{Risk difference: } (a/(a+b)) - (c/c+d)) \quad (1)$$

However, the risk of getting the disease (i.e., disease risk), for example, in a 10-year period, also depends on whether the disease is rare ($a + c$ has a small value) (equation 2):

$$\text{Disease risk: } (a+c)/n) \quad (2)$$

The risk can be low but still have a high association because the disease is rare. Moreover, the risk can be high even when the association is not strong because the disease is common.

A likelihood ratio is the ratio of the probability of a positive test in a diseased person to that in a non-disease person (equation 3):

$$\text{Likelihood ratio: } (a/(a+c))/(1-(d/(b+d))) \quad (3)$$

Because multifactorial diseases – e.g., cardiovascular diseases, type 2 diabetes, and asthma – are caused by interaction between genes and environmental risk factors, genetic variation has only a minor impact on the disease risk. Therefore, genetic tests for these common diseases are less robust than tests for monogenic disorders (Janssens et al., 2015). Factors other than genetics – e.g., environmental factors – better explain the disease onset for an actual individual.

When evaluating a genetic test in a clinical setting, it is relevant to consider the analytical validity, the clinical validity, and the clinical utility. The analytical validity is the ability to measure accurately and reliably the genotype of interest. Clinical validity is the ability of a genetic test to detect or predict a clinical disease. Clinical utility is measured by whether the test will lead to an improved outcome (Zimmern & Kroese, 2007).

Examples of research studies using biological samples

Large-scale population-based studies have been initiated worldwide over the past ten years. The UK Biobank, LifeGene, SCAPIS, The CHRIS, and the PGS study are just a few examples of on-going extensive research projects (Almqvist et al., 2011; Bergstrom et al., 2015; Lunshof et al., 2010; Pattaro et al., 2015; Sudlow et al., 2015). They all aim to develop knowledge that can improve treatments and diagnostics in a wide range of serious and life-threatening public diseases (e.g., cancer, heart disease, stroke, diabetes, depression, and forms of dementia). The projects aim to discover the reason why some people develop particular diseases and others do not.

Between 2006 and 2010, the UK biobank recruited 500 000 people aged between 40-69 years. In addition to biological samples such as blood, urine, and saliva, the biobank uses detailed information about the participants to follow their health. The research will link the participants' health records, the collected data, and mortality data. Blood samples will provide detailed information about the genetic make-up. The aim with the project is to investigate how people's genes interact with their lifestyle and environment to cause disease. Presently, the biobank is genotyping, but it plans to do whole genome sequencing and exome sequencing. The project does not generally provide feedback to individual participants about information derived from analyses of data. Participants receive limited individual feedback (e.g., blood pressure, body mass index, possible melanoma, or serious incidental findings noticed by radiographers). The participants do not get information related to the genetic analysis (Sudlow et al., 2015).

The Life Gene study in Sweden is another population-based project that follows individual health to study diseases (e.g., allergies, depression, infections, cardiovascular diseases, and cancer). To date, the study has recruited 52 107 participants and aims for 250 000 participants. Participants get some health-related information back such as haemoglobin, cholesterol, kidney

value, shortcut, and apolipoprotein A1 and B. However, no results from the genetic analysis are disclosed (Almqvist et al., 2011).

The Swedish CArdioPulmonary bioImage Study (SCAPIS) aims to prevent cardiopulmonary disease by identifying risk markers that allow prediction of the disease. The project involves extensive measurements of 30 000 Swedes aged 50–64. The project plans to do whole genome analysis. The participants will get some health-related information back. If serious incidental findings are made by radiographers, the participants are referred to a physician. However, no information from the genetic analysis will be disclosed (Bergstrom et al., 2015).

The Cooperative Health Research In South Tyrol (CHRIS) study follows 10 000 participants and investigates the genetic and molecular basis of age-related common chronic conditions and their interaction with lifestyle and environment in the general population (e.g., cardiovascular, metabolic, neurological, and psychiatric conditions). Unlike the other examples, the CHRIS study uses dynamic consent; that is, participants can change their consent answers online over time. The choices that can be made are about consent to different projects, data sharing, the permission to use samples and data in case of death and return of secondary/unexpected results. The participants are asked to state their preferences for receiving health threatening results including genetic incidental findings. However, if such findings are to be disclosed, the genetic counselling unit will be contacted. Participants are approached by a medical geneticist who undertakes counselling before results are tested and confirmed (Pattaro et al., 2015).

The Personal Genome Project is an international large-scale genomic sequencing project by Harvard Medical School. The project aims to sequence the genomes of 100 000 individuals and make their genetic information available as a resource for scientific discovery and public use. In addition to genomic sequence data from the biological samples, extensive self-reported questions regarding environment, physical traits, disease history, and psychiatric and behavioural information are included in an online database that is open to other researchers. The project uses open consent and potential research participants need to take an online training program and complete a questionnaire with a perfect score to ensure that they understand the risks associated with the fact that the project comprises unrestricted access to data. The participants will have a personal online profile where they will find out whether they have a clinically validated genetic variant (Lunshof et al., 2010).

Participants in genetic research

What these examples of studies have in common is that they are observational and do not involve interventions. The primary risk for participants in this kind of research is that sensitive personal information ends up in the wrong hands. Risks in biobank research are more of a psychological, social, or economic character. For example, if someone's information ends up in the wrong hands (insurance companies or employers), the individual can be discriminated against because of his or her genetic disposition.

A growing issue associated with this research is how incidental genetic research results should be handled: "a finding concerning an individual research participant that has a potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study" (Wolf, Lawrenz, et al., 2008, p. 219). Disclosed information to a participant can cause stigmatization and disturb relationships with family, friends, or colleagues (Eriksson & Helgesson, 2005). Another potential harm is the psychological burden of an overload of information. Information is considered harmful if a participant gets information that is not desired or the participant cannot interpret and it causes stress and anxiety (Hens et al., 2011). However, empirical studies show that many participants would like to receive individual genetic research results (Appelbaum et al., 2014; Kaufman, Murphy, Scott, & Hudson, 2008; Meulenkamp et al., 2010; Murphy Bollinger, Bridges, Mohamed, & Kaufman, 2014; Murphy et al., 2008).

Regulations in biomedical research

Informed consent is a central topic in biomedical ethics. Informed consent goes back to the debates of the European Enlightenment and it has its roots in liberal political theory, economic thought, and the social contract tradition. In contemporary bioethics, The Nuremberg Code of 1947 is generally seen as the first authoritative statement of consent. The code is a response to the abuses that were performed by the Nazi Germany regime and before and during World War II (Manson & O'Neill, 2007).

The code states that a voluntary consent from the human subject is essential. A freely given consent legitimates action that would otherwise be unacceptable. Informed consent provides assurance that there has been no coercion and autonomy is protected so that individuals can make voluntary choices. Informed consent is a two-way process. First, those who request consent must provide an explicit statement of the purpose of the research study and the effects, risks, and other relevant features of the procedure to those whose consent is sought. Second, those who are asked to consent must show explicitly that they understand this information and agree to the proposal (Manson & O'Neill, 2007).

The Declaration of Helsinki explicitly states what information a potential research participant should be given:

> In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately 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, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.
>
> After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.
>
> All medical research subjects should be given the option of being informed about the general outcome and results of the study (World Med Assoc, 2013).

In Sweden, the use and storage of samples and personal information is regulated by the Biobank Act (SFS 2002:297) and the General Data Protection Regulation (Regulation (EU) 2016/679). All research on stored identifiable biological material must be reviewed and approved by the Ethical Review Board according to the Ethical Review Act (SFS 2013:460). These acts regulate how human biological material is collected, stored, and used with respect to personal integrity.

There are no acts that regulate individual return of genetic results. However, guidelines have been issued by various institutes and organizations. A work group funded by United States' National Institutes of Health (NIH) recommends that researchers should disclose genetic information that reveals risks of serious health conditions that can be acted on (Wolf et al., 2012). The American College of Medical Genetics (ACMG) recommends investigating 56 known pathogenic variants in clinical diagnostics that preform exome and genome sequencing (Kalia et al., 2017). However, the ACMG emphasizes that it is not mandatory to inform the patient (Directors, 2015).

Participants' right *not to know* their incidental findings is also established by the Universal Declaration on the Human Genome and Human Rights:

> The right of each individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected (United Nations Educational Scientific and Cultural Organisation (UNESCO), 1997, Article 5c).

The right *not to know* is also recognized by The Council of Europe:

> Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed (The Council of Europe, 1997, Article 10).

According to the Presidential Commission for the Study of Bioethical Issues in the United States, incidental findings should have these features: accurate and good precision (analytical validity), causal association with pathology (clinical validity), actionable in clinical decision making (clinical actionability), medical implications for one's self or offspring (clinical or reproductive significance), and magnitude of doing potential harm (Presidental Commission, 2013).

Communicating genetic risk information

People become aware that they run an increased risk of developing hereditary disease in many ways. Some may become suspicious that a hereditary disease runs in the family when a close relative develops cancer in early age. Others may become aware of their increased risk through a genetic investigation. Alternatively, some become aware of the hereditary component when they participate in biomedical research. Thus, the starting point for individuals is very different.

In the clinical setting, genetic counselling provides information about a genetic condition. This process has two equally important parts. The first part is to provide knowledge of the diagnosis, prognosis, predictive value, and what it means to live with knowledge of having a risk. The principle is that this information must be adapted and communicated in a person-oriented way. The second part is to psychologically support the individual or family when processing this information and to support the course of action the individual or family find appropriate (Biesecker, 2001). Specifically, counselling should be non-directive and non-judgmental, supporting the families' process of decision-making and adjustments. The genetic counsellor should remain neutral and only supply knowledge and give psychological support to the individual or family when they make their decision (White, 1997).

Communicating genetic risk information has many dimensions. The concept of risk is complex and the language of genetics is not an everyday language and not always easy for people to assimilate (Armstrong, Schwartz, Fitzgerald, Putt, & Ubel, 2002; Covello & Peters, 2002). Moreover, people's psychosocial reactions to genetic counselling, genetic tests, and subsequent preventive measures need to be considered. Hereditary diseases concern not only the individual but also the entire family. The information creates many questions, concerns, and emotions (Allain, 2008; McAllister et al., 2007; Meiser & Halliday, 2002; Vansenne, Bossuyt, & de Borgie, 2009).

The ethical issue of individual genetic risk information

How to handle results from genetic research is an issue that has been lively debated from a variety of disciplinary perspectives for more than a decade (Bledsoe et al., 2012; Bredenoord, Kroes, et al., 2011; Christenhusz, Devriendt, & Dierickx, 2013; Eriksson, 2004; Wolf, Lawrenz, et al., 2008; Wolf, Paradise, & Caga-anan, 2008). To begin with, there is disagreement of what a genetic incidental finding is and how it manifests in research studies. The umbrella term 'individual research results' contains different types of results (e.g., blood pressure, blood fat, results of spirometry, and CT-scan). Genetic 'individual research results' (IRR) and incidental findings (IFs) are both findings that have potential health or predictive health importance for an individual. Typically, an incidental finding is defined as 'a finding concerning an individual research participant that has a potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study' (Wolf, Lawrenz, et al., 2008).

There has been criticism of the concept of IFs in genomic and genetic research, as is difficult to distinguish IFs from other findings because the nature of the research question in genomic studies can be very open ended or descriptive. That is, almost nothing (or everything) is 'incidental' because the research question inevitably looks for complex patterns of which the components may not be known at the outset (Cho, 2008). New forms of genetic sequencing blur the boundaries between research results and incidental findings, making what is 'incidental' unclear. The new technology of NGS blurs the boundaries between research and clinic as well, making the term 'incidental finding' confusing. Some use the term to mean something that the researchers only stumble upon in doing a restricted analysis of a specific region of the genome and not of the whole genome (Parens, Appelbaum, & Chung, 2013). Others suggest that researchers can avoid discovering incidental findings by using target sequencing and answering a specific clinical question instead of looking at the whole genome (Middleton et al., 2015). Others talk in terms of a duty to look for IFs that have clinical value in projects where the whole genome is sequenced (Gliwa & Berkman, 2013). Here, IFs are not incidental but are actively sought. In research that aims to discover something but also actively seeks for something else, that 'something else' is also named a secondary finding. For example, the ACMG recommends that clinicians search for findings that could have clinical relevance using a list of 56 gene variants. According to Tabor et al. (2014), approximately 1-3% of the participants will have one of the 56 genomic variants listed by ACMG. Sometimes, IFs are spoken of in more general terms. This general approach is probably because in many biomedical research projects it is not always known what part of the genome will be studied when participants provide informed consent. In the consent phase, it might be known what the study is about (e.g., cancer or diabetes) but not what specific locus will be investigated.

In summary, the concept IFs is not a unified concept as it is referred to by several names such as secondary findings, off-target results, unanticipated findings, or unsolicited findings. Using the term 'incidental findings' emphasizes the original intention of the researcher and not the nature of the finding. Therefore, there have been suggestions that the term might need to be renamed 'individual genomic results' (Parens et al., 2013). Another suggestion is that 'unsolicited findings' is a more appropriate term because data will be generated that are not related to the initial question (van El et al., 2013). In this thesis, the terms incidental findings, genetic risk information, and individual genetic results are used as synonyms.

Different types of arguments for and against disclosure

There are several ethical positions and much diversity of conclusions and suggestions on the question of disclosure of genetic incidental findings. The ethical issue of disclosure of IFs involves, for example, well established research ethical principles on how to treat and act towards research participants: respect for person, beneficence, and nonmaleficence (The Belmont Report, 1979). Notably, the principles of autonomy, principle of beneficence, and nonmaleficence occur in arguments both for and against disclosure of IFs (Tables 2 and 3).

Table 2. Examples of arguments for disclosure of incidental findings in research.

Type of argument	Argument for disclosure incidental findings
Principle of beneficence	Participants will benefit from knowing information that can prevent life-threatening diseases, help avoid bad conditions or be used in reproductive decision-making (Affleck, 2009; Christenhusz et al., 2013; Knoppers, Deschenes, Zawati, & Tasse, 2013; Wolf et al., 2012).
Principle of autonomy	Individuals can take control over their lives and mediate the outcome in the way they want to (Affleck, 2009; Wolf, Paradise, et al., 2008).
Principle of reciprocity	Research should give something back to participants to maintain reciprocity between researchers and participants. Research has a duty to give back to participants what belongs to them (Helgesson, 2014; Murphy et al., 2008).
Principle of rescue	If a researcher is in a position to mitigate with little risk to the overall research study, she/he should disclose information that indicates a risk of significant harm to the participants (Gliwa & Berkman, 2013).

Table 3. Examples of arguments against disclosure of incidental findings in research.

Type of argument	Argument against disclosure incidental findings
Principle of nonmaleficence	Disclosure can be harmful for participants since disclosure may cause anxiety. Participants might make decisions based on misunderstandings of the information. There is also a risk of the therapeutic misconception (Forsberg et al., 2009; Hens et al., 2011; Klitzman, 2006; Solberg & Steinsbekk, 2012).
	Participants risk to be harmed by getting information that is not about them or by getting not validated results since safety demands are lower in research compared to the clinic (Bledsoe et al., 2012).
Principle of nonmaleficence (future patients)	Disclosure can be harmful for future patients because it impedes the quality of the research due to extra costs (Bledsoe et al., 2013; Forsberg et al., 2009; Klitzman, 2006).
Principle of autonomy	Participants have the right *not to know* this kind of information (Andorno, 2004; United Nations Educational Scientific and Cultural Organisation (UNESCO), 1997).

Another kind of argument for disclosure is based on the principle of reciprocity. This argument is used in three ways. First, there is a duty to give something back to participants in return for their contribution to research. Second, there is a duty to give back to participants what belongs to them ('their' genetic information). Third, disclosure can also increase participation when people find that they can benefit from participating (Bollinger, Scott, Dvoskin, & Kaufman, 2012; Bredenoord, Onland-Moret, & Van Delden, 2011; Helgesson, 2014).

The 'duty to rescue' applies when one finds oneself in a position to mitigate harm to another without significant risk to oneself (Gliwa & Berkman, 2013). The 'duty to rescue' is nevertheless questioned because research has another purpose than health care (Forsberg et al., 2009; Ravitsky & Wilfond, 2006), and researchers are not trained in the counselling skills necessary to return individual results properly (Bledsoe et al., 2012).

The ethical value of satisfying one's preferences

In the ethical debate, a general consensus is that disclosed information should benefit participants (Affleck, 2009; Christenhusz, Devriendt, & Dierickx, 2012; Knoppers, Deschenes, Zawati, & Tasse, 2012; Wolf, Lawrenz, et al., 2008). However, there is no agreement that genetic information always will benefit participants as sometimes sharing such information can cause problems such as anxiety (Hens et al., 2011). One way to get past the disagreement about participants' personal utility of genetic information could be to let participants express whether they prefer to be informed about IFs. As proposed

and practised to a small extent, participants are asked in the informed consent whether they would like to be re-contacted about IFs (Appelbaum et al., 2014; Fabsitz et al., 2010; Murphy Bollinger et al., 2014; The CHRIS Study, 2011). This proposal seems appealing from an ethical perspective since it supports the right *not to know*. Furthermore, such an approach may empower participants' sense of autonomy.

Moreover, empirical studies show that many participants want to receive individual genetic risk information, especially if treatments or preventive actions are available for the condition they risk developing (Appelbaum et al., 2014; Kaufman et al., 2008; Meulenkamp et al., 2010; Murphy Bollinger et al., 2014; Murphy et al., 2008). Participants want genetic risk information because it may help them treat or prevent the disease, it may motivate a change of behaviour, it is interesting to learn more about one's genes, it creates a feeling of having control of one's life, and it can provide a basis to make a life plan (Bollinger et al., 2012).

Hence, consistent with the ethical principle of respect for autonomy, participants' rights, and what participants desires, a free choice about incidental findings could be motivated. Instead of discussing whether incidental findings should be disclosed or what findings should be disclosed, the discussion focuses on whether participants should be offered the choice to know or not know genetic incidental findings. The focus moves from what is beneficent for participants to know to what satisfies their preferences.

What people actually wish for is an empirical fact. However, according to value theories such as desire-satisfaction theory or preferentialism, it also has normative implications. Combined with a normative theory such as utilitarianism, it indicates what a right act is – i.e., doing what maximizes the satisfaction of preferences.

Fulfilment of participants' preferences can thus be advocated as a non-hedonistic value. The good is not maximizing health and minimizing pain or suffering, but fulfilling what a person prefers (Timmons, 2002). Fulfilling a person's preferences can be seen as an intrinsic value. For example, being given the opportunity to make a choice according to one's preferences could be seen as being recognized as a person who is capable of making choices (Dworkin, 1988). When participants make their own decision regarding incidental findings, it could empower them and it recognizes them as persons capable of knowing what is best for themselves.

Another reason to consider preferences is the belief that it leads to the best consequences for the participants. According to this view, participants are the best judges of what is best and respecting a person's preferences would thus have an instrumental value. Typically, people want what is good for them, and they are the ones who know that 'good' best (von Wright, 1997). If a participant finds it worrying to know genetic risk information, the person will benefit

from not knowing. Correspondingly, a person who finds genetic risk information empowering will benefit from knowing. And, presumably, the person who knows this best is the participant.

Rationale

With new technologies developed in the fields of genomic research, such as next generation sequencing technologies, research will have a rich informative material for finding associations between genes and disease development. It will thus be able to anticipate who runs a higher risk of getting, for example, cancer. This raises the ethical question how to handle incidental findings related to individual research participants. When researchers gain knowledge about individual participants' genomic makeup, should that information be disclosed to them? Moreover, when and how should disclosure of these findings take place?

There are several ethical positions and much diversity of conclusions and suggestions on the question of disclosure of genetic incidental findings. It is therefore important to scrutinize basic concepts of and assumptions about genetic risk information and human decision making. Furthermore, before a policy can be recommended and implemented, it is valuable to empirically study how people understand genetic risk and how and why they make trade-offs between risks and benefits regarding individual genetic risk information.

Aims

The overarching aim of this thesis was to contribute to the ethical discussion on how incidental findings in biobank research using whole genome sequencing should be handled.

The specific aims of each study are outlined below.

I To describe the different arguments for and against disclosure of genetic incidental findings and analyse whether they take into account the complexity and the unclear predictive value of genetic information.

II To investigate whether preferentialist arguments for giving participants' freedom of choice about incidental findings take into account psychological findings about decision making under risk and uncertainty.

III To explore research participants' qualitatively different ways of understanding genetic risk and how they make sense of genetic risk in their own lives.

IV To investigate research participants' willingness to receive incidental genetic risk information and the trade-offs they make between different aspects of genetic risk information.

Methods

This thesis investigates from two perspectives how to handle genetic incidental findings in biobank research when using whole genome sequencing. The first two studies are theoretical and used conceptual analysis. These two studies contribute to the ethical discussion by examining two common normative positions on how to handle incidental findings in genomic research. The second part of the thesis is empirical. The empirical part consists of a qualitative study with focus-group interviews and a quantitative study with a questionnaire with a stated preference technique. The methodological approaches used in Studies I-IV are summarized in Table 4.

Table 4. Design, data, participants, and analysis of the studies included in the thesis.

	Approach	**Material**	**Participants**	**Analysis**
I	Theoretical Prescriptive	The ethical debate from journals	-	Conceptual analysis
II	Theoretical Prescriptive	The ethical debate from journals	-	Conceptual analysis
III	Qualitative Descriptive	Focus group discussion	Research participants (n=16)	Phenomenographic analysis
IV	Quantitative Cross-sectional	Questionnaire Discrete choice experiment	Research participants (n=393)	Descriptive statistics Panel-mixed-logit models Relative importance Predicted uptake Interactions

Theoretical methods

The first two studies in this thesis analysed the arguments that have been used to support common normative positions on the question how to handle incidental findings in biobank studies. These studies do not argue for a particular answer to the normative question about how incidental findings should be handled in biobank research. Rather, they employ a form of conceptual analysis that confronts basic notions in the ethical debate with facts and findings that have or have not considered those notions. More specifically, Study I and II scrutinize basic concepts of and assumptions about genetic risk information and human decision making that characterize the ethical debate. The studies try to show that these concepts and assumptions are idealized and oversimplified: they fail to consider the complexity and uncertain predictive value of genetic risk information as well as the emotional processes that psychological research has demonstrated enter human decision making under risk and uncertainty.

Study I

This study assessed current arguments in the literature on incidental findings for and against disclosure. It was not intended to be a complete literature review, but an outline of the most important kinds of arguments needed to identify common assumptions about IFs in biobank research that can contribute to the unresolved diversity of conclusions and suggestions. Study I identified an analogy to IFs in imaging studies as responsible for an oversimplified concept of such findings in genetic research; that is, these studies neglect the complexity of genetic risk information. It also identified a problematic reliance on ethical principles such as the principle of beneficence, as it is difficult to know what is good or best when what is discovered is information with uncertain predictive value.

Study II

The arguments for and against disclosure of IFs are mostly concerned with participants' rights and researchers' duties. However, one argument stands out. Since there is disagreement about whether it is beneficent for participants to know their IFs, the suggestion is that they should be given the opportunity to choose for themselves. The suggestion is to let them express their preferences in the consent they give. As in Study I, this study identified oversimplified assumptions in the debate, but in this case about preferences and decision making by discussing psychological findings about human decision making under conditions that resemble decisions about uncertain genetic risk information.

Empirical methods

The second part of this thesis focuses on research of participants' understanding of genetic risk and their preferences for receiving genetic risk information. Study III and IV consider the unclear predictive value of incidental findings in the design of the studies.

Study III investigate research participants' understanding of genetic risk and how they make sense of genetic risk information. The study gives helpful insight into what can be good to consider when communicating genetic risk to research participants. Moreover, the results of this study were valuable in developing the questionnaire for Study IV.

In Study IV, a questionnaire with a stated preference technique called Discrete Choice Experiments (DCE) was carried out to investigate research participants' preferences for genetic risk information. The questionnaire is constructed so that it takes into account the innate trade-offs in the decision, and the method enables investigating the relative importance of different information scenarios.

Study III

Theoretical framework

To better understand how research participants view genetic risk, a phenomenographic approach was chosen. This approach maps qualitatively different ways people think about, conceptualize, and understand phenomena. Developed in the end of the 1970s, phenomenography is designed to answer questions about thinking and learning and has its roots in education. The results from phenomenographical studies do not make statements about the world as such, but about people's conceptions of the world – how things appear to people. The method is not interested in 'correct' or 'true' conceptions, but all conceptions of reality, even 'mistaken' conceptions. The method can help reveal people's ways of thinking and facilitate learning, communication (Marton, 1986), and competence development within the health care sector (Larsson & Holmström, 2007). Central in phenomenography is relational thinking. In this view, thinking and understanding are about relations between the individual and that which he or she thinks about and understands. To gain an understanding of how people conceive a phenomenon, several sources of information can be used: written texts, drawings, or observing people's behaviour under a specific situation. The most common data collection is through interviewing (Marton, 1986). If we understand the relationship that exists between research participants and their understanding of genetic risk information, it can motivate pedagogical suggestions around communication of genetic risk information and might give us a better foundation for informed consent and survey development.

Setting

Study III and IV is a collaboration with the large research project Swedish Cardio-Pulmonary Bio-image Study (SCAPIS). SCAPIS aims to build a nationwide population-based cohort to study cardiovascular disease. The research programme will, among other methods, use whole genome sequencing technologies (Bergstrom et al., 2015).

Participants

Eligible participants for this study were individuals who had participated in SCAPIS and who were interested in being part of a focus group to share their experiences of and thoughts about receiving health-related information and possible genetic risk information.

In total, 16 research participants participated in this study in four focus groups. The groups were comprised of four women and two men, two women and two men, two women and one man, and one woman and two men. There were slightly more women than men. They were aged between 53 and 65 years (median 60.5). Demographics are given in Table 5.

Table 5. Demographics characteristics of research participants in Study III.

Background variables	***n***
Sex	
Female	10
Male	6
Age (years)	
50–54	3
55–59	4
60–65	9
Education level	
Compulsory school (9 years completed)	2
Upper secondary school (12–13 years completed)	5
Post-secondary and/or higher education	9

We tried to recruit participants representing all ages of the SCAPIS programme with both high and low levels of education and different experiences of disease and genetic diagnosis. One or two in each group had prior experience of severe diseases requiring extensive treatment (e.g., cancer or Parkinson's disease). Only one informant had experience of a close relative living with a monogenetic disorder (Huntington disease).

Procedure

The research nurses at SCAPIS informed incoming individuals who were about to start the SCAPIS research programme about this extra study. Those

who were interested signed a list and were contacted to set a date for the interview. The interviews were conducted in Gothenburg at the Sahlgrenska University Hospital and the room was familiar to the participants from when they first joined SCAPIS. The interviews were carried out in March and April 2016 by JVJ and UHU and were recorded and transcribed verbatim. The interviews were held primarily by JVJ, and UHU engaged occasionally by asking follow-up questions.

Data collection

Data were collected through focus group interviews with a semi-structured interview guide with open-ended questions. After these four focus group interviews, theoretical saturation was reached – the point where we did not gain any new insights. The interview guide was developed with recommendations from Krueger and Casey (Krueger & Casey, 2014). At the start of the interview, all participants were asked why they decided to participate in SCAPIS and go through all the tests. This open-ended question was easy to answer and, as an additional benefit, it encouraged the participants to be involved in the discussion early in the interview. To introduce the participants to the topic of discussion, the participants were asked to describe their experiences with the test. This transition question was also intended to encourage conversation about the key question: How the participants experienced and felt when they received health-related results from the tests. This part of the interview took around ten minutes. The key questions, the subject of the analysis later on, were about their thoughts about genetic risk information (Table 6).

Table 6. The main interview questions

Suppose that within this research project, with your consent of course, the researcher analyses your DNA for risk factors for cardiopulmonary diseases. With this method, researchers may find pathogenic variants that indicate your risk for other diseases.
1. Do you think that genetic risk information is different from the health-related information you have already received?
2. What do you think about the option of receiving genetic risk information?
3. When would you like to know?
4. When would you not want to know your genetic risk?

Probing questions were also asked to explore further the topic in question (Table 7). This part of the interview lasted between 47 and 77 minutes.

Table 7. Examples of probing questions

- Could you tell us more about it?
- Why/why not do you think that health-related information is different to genetic risk information?
- You mention that it is important that the genetic risk information should be *real*. Please tell me more about that.
- You said that preventive measures are important for you. Please tell me more about that.
- How do you think this information would make you feel?
- Why would it make you feel anxious?

Analysis

The transcribed interview data were analysed according the analysis process described by Stenfors-Hayes, Huld, and Dahlgren (Stenfors-Hayes, Hult, & Dahlgren, 2013). To assist in the sorting of the data, the software program NVivo 11 was used. The analysis focused on differences in how people think about the genetic risk. Data were not sorted as experience, thoughts, or opinions. Expressions that answer the question 'What are the different conceptions of genetic risk?' were selected and marked. The initial selected expressions (or quotations) from all interviews formed the basis for the analysis. The expressions were brought together into categories based on their similarities and differences. Expressions that appeared to reflect similar ways of understanding were grouped together by *how* they talk about genetic risk. After reading the grouped expressions (or descriptions) several times, the focus shifted to articulating *what* the descriptions meant. The content of each conception was scrutinized thoroughly and was given a representative label (descriptive category). As a last task in a phenomenographic analysis, an internal relationship among the categories was identified, also called outcome space (Larsson & Holmström, 2007; Stenfors-Hayes et al., 2013). This was visualized as a map of research participants' understanding of genetic risk (Figure 1).

Study IV

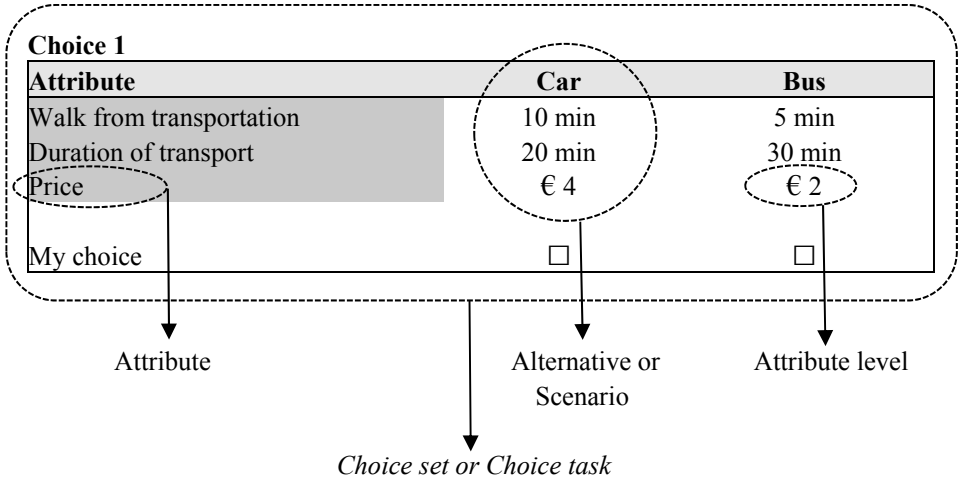
Theoretical framework

One approach to obtaining a better understanding of research participants' preferences for genetic risk information is to use a stated preference method such as Discrete Choice Experiment (DCE). DCE is an empirical method that was introduced into health economics in the early 1990s. The method aims to capture individuals' preferences in complex choice situations (Ryan, Gerard, & Amaya-Amaya, 2010). Using DCE, health economists have contributed to health policy by providing explicit measures of benefit valuation for assessment of alternative health interventions such as willingness to participate in

screening studies and preferences regarding the process or outcome of care. The method has the capacity to manage complex choice scenarios where each decision may carry both advantages and disadvantages for the individual. In this thesis, the DCE method enabled us to investigate participants' trade-offs between different aspects of genetic risk information (e.g., treatment availability, probability of getting the disease, and seriousness of the disease). Rather than just asking participants what they think is important and how much more important different aspects of genetic risk information are, this method gives knowledge about the relative importance of the different aspects based on their choices.

One great advantage with the DCE approach to eliciting individuals' preferences is that the data provided by the respondent are choice response variables (Hensher, Rose, & Greene, 2005). DCE is an attribute-based survey method and the theoretical basis is that preferences are deduced from individuals' choice behaviour. Individuals are asked to complete several choice tasks (Table 8). Each choice task consists of two or more situations ('alternatives' or 'scenarios'). The method assumes that individuals act or chose as if they were maximising their level of satisfaction. Individuals select the combination of aspects ('attributes' and 'attribute levels') in the situation that gives the highest level of utility.

Table 8. Example of a DCE choice set concerning alternative modes of transport to work.



DCE measures benefits (utility) and is based on the economic theory Random Utility Theory (RUT). The Utility (*'U'*) contains two components:

1. a systematic component (*'V'*) that can be specified as a function of the attributes of the alternative $V(X_{in,}\beta)$, and
2. a random component (ε_{in}) representing unmeasured variation in preferences.

V is the explainable component and ε is the unexplainable component. The categorical dependent variable is termed utility ('U') and is related to choices (equation 4) (Ryan et al., 2010). Utilities obtained from discrete choices models are measured on an ordinal scale. This implies that it is differences in utility that matters (Hensher et al., 2005).

$$U_{in} = V(X_{in}, \beta) + \varepsilon_{in} \quad (4)$$

Participants

The latest 1300 recruited research participants in SCAPIS over two years (years 2015-2016) were asked to participate. The participants were randomly assigned to one of two different groups. Half of the sample (n=650) were assigned to a group that were given seven days to consider their choices; that is, they had time-to-think (TTT) about their choices. The other half of the sample (n=650) were assigned to a group that had no time-to-think (NTTT) and had to answer right away after introduction of the questionnaire. The data from the TTT-sample and NTTT-sample are compared to see whether time for consideration impacts individuals' preferences. Results will be presented elsewhere and are not included in this thesis.

Regarding sample size, the following rule of thumb was used (equation 5) (Marshall et al., 2010):

$$\text{Sample size} > \frac{500l}{TA} \quad (5)$$

Equation 5 expresses that sample size depends on the number of choice tasks (*T*), the number of alternatives in a choice set (*A*), and largest number of levels in any attribute (*l*). The pilot of the DCE included 12 choice tasks with three alternatives each and the largest number of levels was five. Therefore, for this DCE at least 70 respondents were needed ((500×5)/(12×3) < 70). To conduct sub group analysis and use blocked design (asking people to only complete half of the choice tasks thereby limiting the burden on every single participant), we needed 420 (70×3×2=420) respondents. Because we anticipated a 65% response rate, 650 people were recruited for each group (TTT and NTTT).

In total, 393 of the 650 (60.5%) invited respondents started to answer the NTTT questionnaire. Respondents with >10% missing answers on their choice tasks were removed. Therefore, the final analysis used 351 questionnaires (89.3%): 58.8 years (range 50-66) was the mean age, 57.2% were female, 59.0% had university or higher education, and 84% reported that they were in good health.

Table 9. Demographical characteristics of the sample.

	No. (%) of the study cohort (n=351)
Mean age (SD)	58.8 (4.3)
Gender	
Male	42.5%
Female	57.3%
Other	0.3%
Highest educational level	
Primary school	10.8%
High school	30.2%
University or higher education	59.0%
Health literacy	
Inadequate	17.1%
Problematic	47.3%
Sufficient	34.8%
General health status	
Poor	2.0%
Average	14.5%
Good	83.5%

Procedure

Before Study IV could be performed, qualitative research work was done to make sure that the attributes in the final DCE were important in making the decisions and were possible of being traded (Coast et al., 2012). This qualitative research was performed in 2015 using both group interviews (focus groups included in Study III) and individual think-aloud interviews. This preparation phase can be described in three different stages:

1. First, a literature review was preformed to find out which features were important to participants and professionals when it comes to genetic risk information and incidental findings. Using PubMed and Web of science search, we identified 109 publications or which 29 articles were included in the review. Aspects important for participants and professionals were marked and were given a code. Codes were grouped into categories. The

aspects that were condition specific factors of the genetic risk information were set as the key attributes (grey area in Table 10).

Table 10. Aspects resulting from the literature review considered important in receiving or disclosing genetic risk information.

Code	Category
Risk numbers Analytical validity Confermed with other studies Expressivity Age of onset Clinical validity Severity of the disease Clinical actionable Reproductive impacted	Condition specific factors of the information
Different comunication means Degree of detail of the presentation of the information	How risk information is communicated
Different communicators	By whom the risk information is communicated
Agreement between parties/ informed consent Maintaining privacy	Duties and rights
Additional cost (time or money) for further follow up Additional risk to know, e.g., stress or anxiety	Additional effort and cost to know

2. To make sure that we had captured all the relevant attributes, we interviewed six geneticists on two occasions in a focus group setting. In the first meeting, the interview contained open-ended questions and used a semi-structured interview guide starting from a hypothetical case of an incidental finding. The transcribed material was thematically analysed: an initial reading followed by line-by-line coding. These codes were grouped into categories (Burnard, Gill, Stewart, Treasure, & Chadwick, 2008). A DCE prototype (a mere list of attributes and levels) was created based on the thematic content analysis. Attributes and levels were formulated by asking 'What in this material (codes and categories) describes a choice?' In the second meeting, the DCE prototype resulting from the first interview was presented and they were able to give their responses to the analysis.

3. To make sure that we had captured what is important for participants, focus group interviews were performed with research participants who were involved in the SCAPIS study and who could relate to the scenario of disclosure of IFs. The first part of the interview focused on research participants' own understanding of genetic risk (Viberg Johansson, Segerdahl, Ugander, Hansson, & Langenskiöld, 2017). After a ten-minute coffee break, the participants ranked the different aspects that they stated earlier as important in receiving risk information. Nominal Group Technique (NGT) was used to get an indication of what attributes are perceived as

the most to the least important (Hiligsmann et al., 2013). The group ranking of the attributes was then discussed in the group. After collecting ranking from all four groups, we calculated a total mean score of all the attributes. To narrow down the number of attributes to be relevant for a DCE, we compared and triangulated between the results from phase 1-3. The attributes were discussed thoroughly between the authors who were familiar with designing a DCE (JVJ and JV) and a genetic counsellor (UHU) and a geneticist (AG) who were knowledgeable of the relevance of the attributes for practice. Four attributes were finally selected for this DCE (Table 11). Relevant sub-populations who might differ in their preferences and attitudes were also identified. Initially, we thought of including the attribute 'severity of the disease' (levels: low, moderate, and high). What people conceive as serious was very much connected to their family history. They talked more about losing quality of life than about death and thought of serious diseases hindering life. Therefore, we changed this attribute to 'type of disease' (levels: life-threatening, disability, mental disease, and physical disease).

Table 11. Attributes and levels for the DCE.

Attributes	**Levels**
Type of disease	Life-threatening disease (ref.)
	Physical disability
	Mental disease
	Physical disease
Disease penetrance probability	5 out of 100 (ref.)
	30 out of 100
	80 out of 100
Preventive opportunities	Nothing (ref.)
	Operation
	Medication
	Lifestyle changes
Effectiveness of the preventive measure	0% (ref.)
	25%
	50%
	75%
	90%

After finding the important attribute, next step was to construct the pilot DCE and check face validity and comprehension of the questions. This was done through cognitive interviews (think aloud) with eight participants. During this step, the participants completed the questionnaire they were reading and thinking out loud (Cheraghi-Sohi et al., 2007; Ryan, Watson, & Entwistle, 2009).

A pilot of the survey (a paper version) was tested in a sample of 22 participants from the SCAPIS study. The pilot survey was used to make sure that the choice model could be estimated and that the levels contributed to the choice rather than dominated the choice. This analysis also helped us refine the experiment in preparation for the final study.

Data collection

The questionnaire consisted of three parts. The first part included demographic questions such as age, gender, education level, their estimated health, earlier experience with genetic tests, experience with severe disease in the family, and worries of being affected by a severe disease. The second part was the DCE. Participants were confronted with 15 different choice scenarios. Each scenario had two different situations. In each scenario, the participant had to select the preferred situation. Thereafter, participants were asked whether they would really like to know the outcome of the genetic test in the chosen situation or not (i.e., opt-out). Before participants were asked to complete the choice tasks, they received detailed information on the meaning of all attributes and levels as well as an explanation on how to complete a choice task, illustrated by two examples. Table 12 demonstrates a choice task without graphics. See Appendix 1 for the actual questionnaire.

Table 12. Example of choice task.

Imagine that you are getting genetic risk information from participating in the SCAPIS research program. In which situation would you prefer to receive information, situation 1 or situation 2?

	Situation 1	**Situation 2**
Type of disease	Life-threatening disease	Physical disability
Disease penetrance probability	5 out of 100	30 out of 100
Preventive opportunities	Operation	Medication
Effectiveness of preventive measure	75%	25%
Tick the dox of the situation that you prefer:	☐	☐

If you had the possibility to revive the information you preferred above, would you like to know it in real life?

☐ Yes

☐ No

Part three was about attitudes toward genetic risk information, questions about risk perceptions, health literacy, and numeracy. This will be published elsewhere and is not part of this thesis. The survey was online and constructed in Sawtooth Software SSI Web 8.4.8.

Analysis

Descriptive statistics were conducted using the Statistical Package for the Social Sciences (SPSS) version 24. The regression analysis was conducted using the Econometric software NLOGIT version 5. To investigate the preferences for receiving genetic test results, the data were analysed using panel-mixed-logit (p-MIXL) models, models that take into account preference heterogeneity and adjust for the multilevel structure of the data. See equation 6 for the model that was estimated.

$$U_{a,b} = V + \varepsilon = \beta_1 * type\ of\ disease_{disability_i} + \beta_2 * type\ of\ disease_{mental\ disease_i} + \beta_3 * type\ of\ disease_{physical\ disase_i} + \beta_4 * likelihood\ of\ disease_{30\ in\ 100_i} + \beta_5 * likelihood\ of\ disease_{80\ in\ 100_i} + \beta_6 * preventive\ measure_{operation_i} + \beta_7 * preventive\ measure_{medication_i} + \beta_8 * preventive\ measure_{lifestyle\ changes_i} + \beta_9 * effectivness_{25\%_i} + \beta_{10} * effectivness_{50\%_i} + \beta_{11} * effectivness_{75\%_i} + \beta_{12} * effectivness_{90_i} + \varepsilon \quad (6)$$

$$U_{opt-out} = \beta_0 * ASCC_i + \varepsilon$$

The relative importance of the attributes was estimated by the difference between the highest and lowest attribute level for each attribute. The largest difference value received a score of 1. That attribute represents the attribute that will be deemed most important by respondents. The other difference values were divided by the largest difference value resulting in a relative distance between all other attributes and the most important attribute. Predicted uptake for different hypothetical genetic test situations was calculated as equation 7.

$$\text{Predicted uptake: } 1/(1 + exp^{-V}) \quad (7)$$

Interactions were analysed using panel-mixed-logit (p-MIXL) models. Prior experience and worry of being affected by a severe disease was included separately in the models to see how they influenced the willingness to know incidental findings and the attribute effectiveness of the preventive measure.

Ethical considerations

Study I and II did not include human subjects and therefore ethical approval was not needed. Study III and IV were approved by the Regional Ethical Review Board in Gothenburg, Sweden (821:15, 610-16). The studies were conducted in line with Swedish law (SFS 2013:460) and the Declaration of Helsinki (World Med Assoc, 2013).

In Study III, written informed consent was given. All participants were informed of their right to decline to participate or to withdraw consent to participate at any time without any consequences. There was a risk identified that the participants might experience the interview unpleasant because of the questions raised by the moderator or comments by other participants. The questions might remind them about or awaken feelings about difficult experiences of illness in the family. Therefore, beside the information that they could cancel their participation and leave the room without any consequences, a genetic counsellor was present as an observer and with experience communicating complex risk information.

In Study IV, participants gave their informed consent when they chose to continue answering the online survey. The risk associated with Study IV was that the participants might experience the choice sets in the survey difficult and stressful. To minimize participants' burden, we designed the survey in four different blocks. This resulted in more people answering fewer choice tasks each. Participants may also experience that answering the survey helps them gain knowledge regarding genetic risk information and their own preferences. The focus groups and the think aloud interviews indicated that the participants thought that the topic of genetic risk information was important for research and society and found the topic interesting.

Summary of findings

Study I: Incidental findings: the time is not yet ripe for a policy for biobanks

Incidental findings are acknowledged to be an important ethical issue to consider in biobank research. Genome-wide association studies (GWAS) and disease-specific genetic research might reveal information not related to the research but relevant to specific participants. Study I focuses on genetic incidental findings. Disease risks can also be discovered in, for example, imaging studies (a blood vessel with thin walls can imply an increased risk for stroke), but this was not within the scope of the study.

This article presents the common arguments for and against disclosure of incidental findings (Table 13). After a review of arguments, the article argues that the discussion up until now has neglected the distinction between an incidentally discovered disease and an incidentally discovered risk for disease of unclear predictive value. The study elucidates this neglect in the ethical debate and shows how the arguments fail to address the more complex kinds of incidental findings that increasingly arise in biobank research.

Table 13. Argument for and against disclosure of incidental findings.

Arguments for disclosure	**Arguments against disclosure**
Disclosure is beneficent for individuals	Practical issues make disclosure unfeasible
Disclosure promotes autonomy	Disclosure can harm participants
Reciprocity requires disclosure	The relationship does not create a duty
Return of incidental findings accords with participants' wishes	Disclosure can harm research and prevent research from doing good

The arguments for disclosure depend very much on the hypothetical possibility that knowing genetic risk information might be beneficial for participants. In brief, if the information is valid and useful, participants who want to know should be informed. The study gives several examples of how idealized conditions are made: If results can enhance treatment, *if* they concern a material risk, *if* they have clinical utility, *if* they are life-saving, then they should be disclosed. The reason these conditions can be described as idealized is that

these properties are less self-evident in the case of multifactorial risk information. They only abstractly reflect what is required to make the principle of beneficence applicable. There is a tendency to conflate genetic risk information with information that is more characteristic of imagining studies, for example, in which the incidental findings may be a malign tumour, information that obviously should be communicated to the participant in accordance with the principle of beneficence.

The study also emphasizes the importance of empirical surveys when taking into account the complexity of genetic risk information. Many surveys of peoples' desire to be informed about IFs rely on a notion of risk communication as a form of communication about actual health and disease. Instead of asking potential participants whether they would want health relevant genetic risk information, to which they could hardly say no, they should be asked questions based on realistic presentations of risk information and what it means. Empirical methods are needed that capture the trade-offs that respondents might make when facing complex decisions. It is important to capture how they make trade-offs between, for example, risk of unproven predictive value, risk with low penetrance, and symptoms appearing after perhaps 30 years.

Study II: Freedom of choice about incidental findings can frustrate participants' true preferences

Ethicists, regulators, and researchers have struggled with the question whether incidental findings in genomic studies should be disclosed to participants. In the ethical debate, a general consensus is that disclosed information should benefit participants. However, there is no agreement on whether genetic information will always benefit participants or cause problems such as anxiety. One could get past this disagreement by letting participants express their preferences in the consent. This study argues that this freedom of choice is problematic.

The study discusses the preferentialist arguments that could be used to support a right for participants to decide and questions those arguments by drawing on psychological findings about people's reactions to probabilities and risks. This knowledge is then applied to the situation that participants in GWAS and disease-specific genetic research face when they are asked to make a decision about the future disclosure of genetic incidental findings.

Empirical psychological studies indicate that when it comes to decisions about risk, people tend to take the safe route rather than gamble. Moreover, their mood makes a difference in the decision, and small probabilities are overestimated and high probabilities are underestimated. Finally, presentation

of the risk matters. For example, different framings make people decide differently, even if the consequences are the same.

The study concludes that it is uncertain if the opportunity to choose in the consent phase enables people to express what they truly prefer. They might be steered to a specific answer depending on triggered feelings, mood, and the framing of the question in the information they are given.

Study III: Making sense of genetic risk: A qualitative focus-group study of healthy participants in genomic research

During the process of phenomenographic analysis, four descriptive categories of genetic risk were identified. Genetic risk may be understood as follows:

a) a binary concept,
b) an explanation (e.g., of symptoms),
c) a matter of revealing who I am (knowledge of oneself), and
d) as affecting life ahead.

One category was the 'binary concept' and it involves an either/or concept of genetic risk. It involves thinking that either you have the risk or you do not. Participants tend not to understand genetic risk as a probability. The levels of the likelihood of getting a disease were not considered useful, only whether one is at risk. When they described information worth knowing, their answers involved no probabilities. Rather, they talked about such risks as being 'real', 'important', and 'concrete'. The second way the participants conceived genetic risk was explanatory: their genome can explain why they get certain diseases and thus why their life unfolds in a certain way. The third way of understanding genetic risk was that it provides insight into a person's identity. Knowing one's genetic risk says something significant about who we are and where we come from. The last category was genetic risk as affecting future life. Genetic risk information can be a guide for the future, enabling individuals to plan and live their lives differently. It can be about changing life plans or taking appropriate measures in advance to prevent disease.

A further task in a phenomenographic study is to identify relationships among the descriptive categories. Category (a) concerns the nature of genetic risk itself. The other three categories of genetic risk (b, c, and d) relate genetic risk to time. Genetic risk is made sense of in terms of the participants' past, present, and future lives. The internal relationships can be visualized as a map of research participants' understanding of genetic risk (Figure 1).

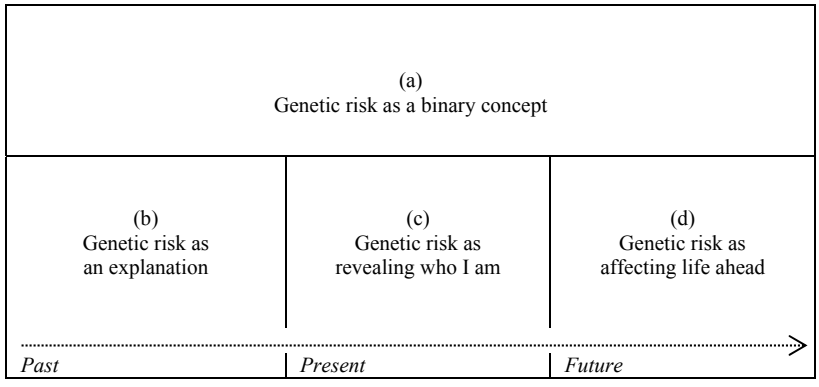


Figure 1. Outcome space: the study group's collective understanding of genetic risk.

Study IV: Research participants' preferences for receiving incidental genetic risk information: a discrete choice experiment

All attributes individually contributed to research participants' decision in knowing genetic risk information. Participants prefer being informed about a risk of having a life-threatening disease with a disease probability of 80 out of 100 and get information that can decrease the risk by lifestyle changes with a 90% effectiveness.

Participants prefer knowing their genetic risk over not knowing it. However, the standard deviation shows a large variation, which means that participants are heterogeneous towards knowing genetic risk (Constant ASCC, SD=±4.13, Table 14).

With respect to the relative importance of all the attributes, 'effectiveness of preventive measure' was most crucial for research participants in their decision to know about genetic risk. This was followed by 'preventive opportunities', 'disease penetrance probability', and 'type of disease'.

If genetic risk information were disclosed in biomedical research programs, research participants' interest to know would vary between 24% and 98% depending on the preventive measure opportunity and the effectiveness of the preventive measure. The combination that gives the highest rate (98%) is information about risk of getting a life-threatening disease, disease penetrance probability 80 out of 100, lifestyle changes as preventive opportunity, and 90% effectiveness of the preventive measure (Table 15).

Table 14. Participants' preferences for receiving incidental findings based on a panel-mixed-logit model.

	Estimate	SE	SD	SE
Constant ASCC	-2.77***	0.30	4.13***	0.25
Type of disease				
Life threatening (ref)	0.83***	0.10	0.96***	0.19
Physical disease	-0.25***	0.06	0.39***	0.10
Mental disease	-0.43***	0.06	0.57***	0.11
Physical disability	-0.14**	0.06	0.68***	0.09
Disease penetrance probability				
5 out of 100 (ref)	-0.86***	0.08	1.07	1.84
30 out of 100	0.07*	0.04	0.05	0.08
80 out of 100	0.79***	0.07	1.07***	0.07
Preventive opportunities				
None (ref)	-1.47***	0.14	0.68	0.12
Operation	0.21***	0.07	0.31**	0.14
Medication	0.34***	0.06	0.02	0.29
Lifestyle changes	0.92***	0.06	0.60***	0.06
Effectiveness of the preventive measure	0.04***	0.00	0.02***	0.00

*P<0.10; ** P <0.05; ***P<0.01

Table 15. Predicted uptake for the effectiveness of the preventive measure 90% and life-threatening disease, and different combination of preventive opportunity and penetrance probability.

	None	**Operation**	**Medication**	**Lifestyle changes**
5 out of 100	24%	89%	90%	92%
30 out of 100	40%	95%	96%	97%
80 out of 100	53%	96%	97%	98%

Discussion

The following discussion highlights key findings and topics in the four studies included in this thesis and asks what normatively can be learned from them. I also discuss the role of empirical research in ethics. The discussion ends with some methodological considerations about the empirical studies (Study III and Study IV).

Key findings and topics

What carries most weight for participants when they consider whether they want genetic risk information is whether there are preventive opportunities (Study III and IV). According to Study IV, the most important characteristic of genetic risk information for participants is that the preventive measure is effective. This is in line with an earlier study that demonstrated that one of the two main motivations to know genetic risk information is to find out what can be done to improve health (Sanderson et al., 2016).

It is not surprising that information about risk of a life-threatening disease is preferred, a finding confirmed in other studies (Regier et al., 2015; Wynn et al., 2017). However, it is noteworthy that the level 'lifestyle changes' was more important than 'operation' and 'medication', a finding not in line with a previous discrete choice experiment study where medication was preferred over lifestyle changes. However, the combination 'lifestyle changes' and 'medication' was most preferred in that study (Regier et al., 2015).

A topic that became central in this thesis is the uncertainty of genetic risk information. It is common to distinguish between decisions made under *certainty*, under *risk*, and under *uncertainty* (Luce & Raiffa, 1957). If a decision is made under *certainty,* each alternative is known to lead to a specific outcome, so the decision strategy of maximizing and minimizing a given issue can be practiced by simply comparing the outcomes of the alternatives. To make a decision under *risk* means that the probability (in fact the distribution) of the outcomes is known. The value associated with each alternative (i.e., utility) is then usually derived from the statistical expectation of the alterna-

tives' outcomes (expected utility theory). The alternative that gives most expected utility is the best choice.[1] Finally, a decision under *uncertainty* is when the probabilities (i.e., the distribution) of the outcome of the different alternatives are not known.

Genetic risk information contains both risks and uncertainties. Genetic results can give known probabilities of a specific disease (outcome). This risk figure is based on how many people in a population having a specific gene variant also get the disease (penetrance). However, even though the probabilities are known, the strength of association between a specific variant and a specific phenotype (i.e., how well the variant explains or predicts the development of the phenotype) can be less clear. In addition, the outcome is not always known. For different individuals, diseases may have different expressions (phenotypes), prognosis, onset of the disease, additional risk factors affecting the risk, and effectiveness of prevention (Howard & Iwarsson, 2018). Therefore, decisions about genetic risk information, such as incidental findings, contain both the element of risk and the element of uncertainty, and this complexity needs to be considered in ethical discussions, in preference studies, and in genetic risk communication.

Considering how research participants value penetrance probabilities in their decision-making, the results from Study IV (Table 15) indicate that such probabilities are not so crucial for people's decision-making when prevention strategies are available. The probability that participants would like to know information about a life-threatening disease that can be prevented with lifestyle changes decreased very little, from 98% to 92%, when moving from the option of information with a penetrance probability of 80 out of 100 to information with a penetrance probability of 5 out of 100. However, when there is no preventive opportunity available, penetrance probabilities seem to be more important. When no preventive opportunity was available, the probability that participants would like to know information about a life-threatening disease decreased from 53% to 24% when moving from the option of information with a penetrance probability of 80 out of 100 to information with a penetrance probability of 5 out of 100.

The participants in Study IV seem to have made use of the penetrance probabilities in their decision-making only when no preventive opportunity was available. In addition, the participants seem to have focused on consequences and whether something *can be done* to prevent the disease from developing. Study III demonstrates that some participants tend not to understand genetic risk as a probability of getting a disease. They said that they only wanted to

[1]The strategy expected utility takes both probabilities and consequences into account. The expected utility of a gamble of 25% chance to gain $1000 and 75% chance to gain nothing is $250 ($0.25 \times \$1000 + 0.75 \times \$0 = \$250$). If the sure gain of not taking part of the gamble is $240, the gamble is still to preferred according to the theory of expected utility because it got a higher expected value ($250>$240).

know whether they had a risk, not any percentages. The level was not considered useful, only whether one is at risk. Several other studies have confirmed that the concept of genetic risk and its uncertainty is difficult to understand (Austin, 2010; Gordon et al., 2012; Linnenbringer, Roberts, Hiraki, Cupples, & Green, 2010; Sivell et al., 2008). A qualitative study by Biesecker et al. (2014) found that participants had three different perceptions of uncertainty in genomic sequencing. Most participants perceived uncertainty as a quality of the information and not of the sources of the information. Some connected uncertainty with the fundamental sources of the information, such as calculations of the probability that a gene variant is associated to disease. Others understood uncertainty in terms of limitations of the researchers' knowledge and interpretations of the data. Therefore, it is worth keeping in mind that research participants tend to avoid the uncertainty of genetic risk information as much as possible and instead focus on what seems more certain, namely, whether there are preventive opportunities or not.

Another topic in this thesis is the perhaps surprising fact that individual genetic risk information is not always as 'individual' as one may think. The personal utility of genetic risk information can be questioned. Knowing one's genetic make-up is not the same as knowing one's own probability of a disease. The goal of research is to seek generalized knowledge and risk figures are calculated from epidemiological data. The risk is therefore located outside particular individuals; that is, risk pertains to the population, not the individual (Edwards & Prior, 1997; Hollnagel, 1999).

In addition to the epidemiological basis of the risk calculations, the starting point of the risk communication is also an issue that makes individual genetic risk information less individual. In a patient-doctor relationship, the investigation starts with a problem (a phenotype or a family member affected by a hereditary disease). A genetic test can confirm the symptoms. In a participant-researcher relationship, however, the investigation starts with a result. The result will be less predictive without the connection to a phenotype. To best prevent disease, Burke et al. (2013) recommend assessing only those with a family history of, for example, breast cancer, instead of disclosing information about *BRCA* to asymptomatic women in the general population. In discussing return of genetic risk information to individual research participants, it is thus worth remembering that in the context of research, the information is less individual than might be assumed.

A further topic I want to highlight here is whether there are lessons to be learned from screening studies. Using whole genome sequencing on healthy research participants and actively seeking and considering disclosing IFs to participants resembles genetic screening. The two most important principles for a good genetic screening program is that the program is about an important health problem and that treatment or prevention can be offered (Andermann,

Blancquaert, Beauchamp, & Dery, 2008). The findings in Study III and IV support these principles. However, implementing screening methods is not without risks (Brodersen, Jorgensen, & Gotzsche, 2010). Some people will inevitably get false positive results and might unnecessarily undergo treatment or suffer from worries and anxiety. For example, having a false positive screening mammography result causes undesirable long-term outcomes (e.g., anxiety, worry, and bad sleeping pattern) (Brodersen & Siersma, 2013). In addition, some will get false negative results, which produces false security. When implementing screening programs, all important harms must be quantified and balanced against all potential good. An example of such calculation in mammography screening is that for every 2000 women invited for screening throughout ten years, one woman will have her life prolonged. In addition, ten healthy women will be over-diagnosed with breast cancer and will be treated unnecessarily. Additionally, it is likely more than 200 women will experience substantial psychological distress for months because of false positive results (Brodersen et al., 2010).

Patients receiving information about their risk for genetic conditions can also have strong psychological reactions (e.g., anxiety, worry, depression, and grief) (McAllister et al., 2007; Vansenne et al., 2009). Some of the participants who have the gene variation for a specific disease will get the disease. These participants can prepare or take preventive measures to affect disease outcome. However, some participants will not get the disease despite the gene variation. They might take unnecessary preventive measures or might be affected psychologically. Some of the participants will get the disease despite the absent gene variation. They might be lulled into false security.

A common response to the argument that disclosure should be practiced because it can be beneficent for participants is that disclosure also can be harmful. The response to the 'harmful argument' is that it is paternalistic to withhold information because it might cause anxiety and worry (Study I). Instead of using these arguments against each other, they could, in my view, be incorporated in a benefit-harm calculation of the kind that is used to assess screening programs. People's reactions and the actions they may or may not take will probably depend on the specific disease risk (e.g., for cancer or for Alzheimer's disease) disclosed. Therefore, it is probably impossible to propose general principles of disclosure that cover all diseases and characteristics of the information.

Another topic in the thesis is a tendency in the ethical debate to put perhaps too much weight on satisfying people's preferences (Study II). A fundamental ethical principle in research ethics (required by law and ethical guidelines) is to protect participants' autonomy via informed consent (SFS 2013:460; World Med Assoc, 2013). Through the informed consent process, participants can decide for themselves whether they want to participate in a study. In the light

of potential benefits and risks of harm, they can make their own choices according to their own preferences. To develop guidelines regarding return of genetic incidental findings, it is of value to better understand the preferences of research participants. Participants' views on benefits and risks and when benefits may outweigh harms in relation to different choices is valuable information. However, to what extent participants' preferences should be incorporated directly in the policy making process can be discussed. My view is that participants' preferences need to be considered. They are important stakeholders and their views are relevant to the ethical discussion and to policy making. However, their voice is not the only one. Other ethical values – e.g., potential harm due to false positive results, fairness to patients, and costs to disclose genetic risk information in a responsible manner – also need to be considered.

One reason why satisfying participants' preferences is given such weight is perhaps that it may seem to be a way of respecting autonomy. As presented in Study II, one argument for giving research participants an opportunity to express their preferences through consent is that it would acknowledge their autonomy. This proposal seems appealing from an ethical perspective. However, Manson and O'Neill (2007, p. 17) point out that the initial purpose of consent was not to maximize autonomy (understood as a property of the individual) but to protect research participants against grave wrongs by giving them the right to make choices that ought to be respected as autonomous. Such an idea of protection does not necessarily imply giving participants a choice of receiving individual results.

To give participants the opportunity to express their preferences regarding incidental findings is not, I would like to argue, to respect their autonomy, especially if one does not give them this choice because one is unsure whether the risk information will benefit them on any level (e.g., prevent disease). To do so is rather to transfer the difficulty to the participants, as if one is respecting them as persons by making them choose. Providing choice in the area of genetic risk information should, as Johnsson and Eriksson (2016) suggest, be understood as respecting a person's right to take responsibility for themselves and to empower them (to respect someone's authority). This way of framing the issue makes possible a different understanding of what is ethically at stake. Placing the burden on participants with information and choices that they did not ask for (or may not be able to make, I want to add) might not have anything to do with autonomy, but rather risks violating their integrity in the name of empowerment (Johnsson & Eriksson, 2016). I do not object to providing participants with an opportunity to express their preferences regarding IFs, I just want to point out that the ethical discussion might gain from not conflating the reasons for such a practice.

The role of empirical research in ethics

This thesis combines empirical studies and ethical reflection. Empirical studies can help ethicists identify relevant moral issues and describe people's beliefs and attitudes that can be relevant for a specific ethical issue. Invoking empirical findings in ethical deliberation is called empirical ethics. Empirical ethics can improve the context-sensitivity of ethical deliberation (Musschenga, 2005). Studies III and IV investigated research participants' understanding of and preferences for genetic risk information, exploring what this group of stakeholders might find relevant to focus on in the ethical discussion about how to handle individual research participants' genetic results.

Using empirical methodologies can open up a path out of the ethical impasse in the discussion about how to handle genetic risk information. It is not clear that people will have the same preferences to risk information with (i) early onset and high penetrance but with lack of medical treatment (e.g., Alzheimer's disease) and to risk information with (ii) low penetrance but high actionability (e.g., HFE-associated hemochromatosis). By investigating participants' conceptions of and preferences for genetic risk information, it becomes clear that the concept of genetic risk is complex and multidimensional. By using the empirical method of discrete choice experiments, we can, besides eliciting participants' preferences for genetic risk information, understand the heterogeneity of the preferences and get insights into what it can be associated to.

The results of Study IV make it clear that the complexity of genetic risk information needs to be taken much more seriously in the ethical discussion. Reliance on ethical principles (e.g., principle of beneficence) fails to consider the context-sensitivity of the ethical issues. Incidental genetic findings are different from incidental findings in imaging studies. This thesis thus indicates how ethical principles cannot always be applied to a new context and solve ethical issues in that new context. Handling IFs in genetic research is not simply an instance of a general approach to IFs.

This thesis does not solve the normative question how to handle genetic risk information about individual research participants. Rather, it emphasizes the complexity of genetic risk and proposes that this complexity needs to be taken into account in theoretical as well as in empirical studies. Instead of pushing the ethical discussion towards a normative suggestion for how individual genetic research results should be handled, we need to take a step back before we can move forward again. For example, more knowledge is needed about how people react to and live their lives with information about their genetic risks from research. This is necessary to better understand when genetic risk information will benefit and when it will harm participants.

Methodological considerations

This thesis contributes to the ethical discussion on how to handle incidental findings in biobank research that uses whole genome sequencing. The studies in this thesis used a mix of philosophical, qualitative, and quantitative methods, which is a strength of the thesis. However, there are methodological considerations and limitations with the empirical approaches used in this thesis that need to be discussed.

Trustworthiness of Study III

Credibility, transferability, dependability, and confirmability are all concepts that are used to judge the quality and trustworthiness of the results of a qualitative study (Lincoln & Guba, 1984, pp. 290-331). These were taking into consideration in this study.

Credibility can be described as the confidence of the truth of the data and the data's interpretations (Lincoln & Guba, 1984). Credibility was enhanced in this study by involving four researchers in the analysis process to define the categories by means of triangulation and consensus. The categories were discussed both in seminars and at international conference. This is a strength of the study. To capture as many understandings of genetic risk as possible, each focus group consisted of participants of different ages, education levels, and experience of illness and of genetic diagnosis. The participants were encouraged to speak freely about their experiences and thoughts, and they were reassured that this is a difficult and unexplored issue. However, there is a risk that focus group participants portray themselves as thoughtful and knowledgably individuals. Individual interviews would therefore be better at minimizing such a risk. We chose to do focus groups because the topic of genetic risk is widely unfamiliar to many of the participants. We thought it would be better to conduct the interviews in small groups so that the participants could explore their own thoughts in the light of others' ideas and thoughts. It seemed to work fine as the participants shared generously with their experiences and thoughts.

Transferability is about the extent to which the findings can be transferred to other contexts and populations (Lincoln & Guba, 1984). In order to make it possible for the reader to judge whether these results can be transferred to other contexts, a description of the study program and the participants was made. The result of this study may not be transferable to other age groups (e.g., people of reproductive age) or to specific patient groups. However, it indicates how healthy research participants who undergo an extensive health check-up understand genetic risk.

Dependability refers to the stability of data over time and over conditions (Lincoln & Guba, 1984). Dependability was enhanced by the fact that all interviews were conducted by the same researcher and with an interview guide with open-ended questions. Complete records were kept for all phases of the

research process (fieldwork notes, recordings, interview transcripts, and data analysis decisions). These records are saved in Uppsala University's storage of scientific data, Allvis.

Confirmability concerns whether the researcher can stay objective with respect to the data and the interpretations of the data. Confirmability was enhanced by involving researchers with different backgrounds and understandings of genetic risk. This reduced the risk that only one researcher's view dominated the results. The comparative part of the analysis was done individually by several researchers and was followed by joint discussions, checking the data, and rechecking the data. The risk of overlooking important aspects was therefore minimized. It also minimized the risk that results were dependent on who was performing the analysis.

Reliability and validity of Study IV

Reliability concerns the precision and consistency of measures (Bryman, 2016). Testing consistency of participants' answers can be done by asking the participants to perform the same choice twice within the same questionnaire. This type of testing was not performed in Study IV, but future research could benefit from such a strategy because the subject of genetic risk is quite complex. However, we tested whether the respondents made dominant choices based on the situation and not the attribute: they did not.

Validity concerns whether a measure of a concept really measures that concept. Validity can be divided into internal validity and external validity (Bryman, 2016). For good internal validity, the process of attribute development is very important, ensuring that the attributes are relevant in making the decision and can be traded (Coast et al., 2012). Choosing the final attributes in Study IV was done through literature review, focus group interviews, the ranking exercise Nominal Group Technique, triangulation with experts, presentations and discussions of the attributes at international workshops and conferences, and by performing cognitive interviews (think aloud). Moreover, we followed recommendations from Harrison et al. (2014) concerning how to frame risk as an attribute, design the opt-out option, and choose supplementary questions. All these activities contribute to ascertaining that the measure reflects the content of the concept in question. Finding the right attributes and levels was done through constant interaction with geneticists and participants. All this is a strength of the study.

One challenge was how to choose levels of the attribute disease penetrance probability. One finding in the qualitative Study III was that participants did not want to know risk figures; they only wanted to know if they were at risk and for what disease. Despite this binary thinking, participants were forced to make choices based on levels (5, 30, and 80 out of 100). This might have made it more complicated to people to complete the choice tasks. One alternative that has been used in other studies is to include 'high' and 'low' as levels for

the attribute, but this would create other problems as we would not know how people interpreted these descriptive levels.

As far as possible, established and validated instruments were included for risk perceptions, health literacy, and numeracy. When this was not possible, the research group developed questions (i.e., their estimated health, earlier experience with genetic tests, experience with severe disease in the family, and worries of being affected by a severe disease). This was made for participants' estimated health, earlier experience with genetic tests, experience with severe disease in the family, worries of being affected by a severe disease, and attitudes to genetic risk information.

External validity concerns whether the findings of a study can be generalized beyond the specific context (Bryman, 2016). In Study IV, the sample was consecutively recruited participants in SCAPIS during 2015-2016. This sample was a random sample of the general population of Gothenburg in the age span of 50-64 years old. The study population for Study IV is therefore people with this specific age span and who are interested in participating in biomedical research. Selective participation is a general concern in population studies. The SCAPIS pilot study was conducted in Gothenburg and had a total target population of 24 502 individuals. Of these, 2243 were randomly selected from six residential areas. The overall participation rate was 50% (68% in high socioeconomic status areas and 39% in low socioeconomic status areas). The following sociodemographic variables were associated with participation: higher socioeconomic areas, Sweden as a country of birth, not living single, university education, employed as an occupational status, and higher age. Participants and non-participants also exhibited clear differences with respect to disease history overall, although history of cardiovascular disease did not differ markedly (Bjork et al., 2017). Compared to the SCAPIS pilot study, Study IV included more female participants (57.3% compared to 50.0%) and more participants with university education (59.0% compared to 35.4%). There is selection bias in SCAPIS compared to the general population and in Study IV compared to SCAPIS study. When testing, the differences in preferences in Study IV were partly associated with education level. University education influenced negatively the overall willingness to know genetic risk information (Constant ASCC=1.92***, result not presented). However, the willingness to receive genetic risk information among participants with university education was not affected by the effectiveness of the potential preventive measures.

In Study IV, the participants were asked to complete an online survey. People with limited computer access or experience might therefore not answer the survey. This makes the external validity weaker. For those participants who informed us about their difficulties, a paper version of the survey was sent out. The paper version was sent to four participants, and two of them returned their answers. A benefit with using electronic data collection was that the online survey could provide attribute explanations if participants needed them while

making their choices. All data were immediately collected as the survey was completed, which minimized typing mistakes when manually inputting data. Moreover, participants could not misunderstand that only one choice between situations A and B should be made, because the online survey forced them to select only one of the alternatives.

A previous study compared preferences in a paper-based survey and in an online survey and found that they were similar (Determann, Lambooij, Steyerberg, de Bekker-Grob, & de Wit, 2017). Therefore, we added the data from the paper version of the survey to the data from the online survey. However, the same study recommended including fewer choice sets per respondent to minimize respondents' fatigue when answering an online survey. One concern of Study IV is that 15 choice sets might be a bit demanding for some participants.

Another concern of external validity when collecting stated preferences is to what extent stated preferences equal revealed preferences (Ryan et al., 2010). All studies on stated preferences struggle with hypothetical bias. Because participants are not bound to their hypothetical choices, there may be differences between what they say they will choose and what they actually would choose. Revealed preferences would be preferable to solve that issue, but it is not always possible. It is still of interest to conduct research that gives insight into research participants' stated preferences in order to understand the complexity of genetic incidental findings and to get input before developing a policy for disclosure of genetic risk results. Stated preference data give a good start when considering new disclosing strategies where little data exist for observed revealed preference.

Conclusions and implications

This thesis studied how research participants understand the concept of genetic risk and what characteristics of genetic risk information they find interesting to know about (or less interesting). It also contributes to the ethical discussion about incidental findings by emphasising the importance of more seriously taking into account the complexity of genetic risk information in ethical discussions as well as in empirical investigations. The main conclusions and implications of the thesis are stated below.

- Ethical arguments for disclosure of incidental findings rely on beneficial-sounding provisions that do not reflect the complexity of genetic incidental findings. Since this neglect probably contributes to the irresolvable character of the ethical debate on incidental findings, the uncertainties in genetic risk information need to be generally acknowledged as a starting-point in ethical discussions.

- It seems attractive to let participants in genomic research express their preferences to incidental findings in the consent form. However, it is uncertain if this opportunity enables them to express what they truly prefer. They might be steered to a specific answer through triggered feelings, mood, and the framing of the question on the consent form.

- Research participants understand genetic risk so as to make it meaningful in their lives. To make sense of the complex information and to make important decisions, they interpret the information in terms of their past, present, and future life. Risk communication may be enhanced by tailoring the communication to these lay conceptions.

- Participants make use of probabilities in their decision-making only when no preventive opportunities are available. Their decision-making focuses on whether something can be done to prevent the disease that might develop. Moreover, research participants prefer information about risks that can be reduced through lifestyle changes (compared to ‘no preventive opportunity’, ‘operation’, and ‘medication’). Since genetic risk information has many characteristics, empirical studies of attitudes and preferences need to explicitly engage with this complexity.

Future Research

The results of this thesis give rise to several suggestions for future studies. The concept of genetic risk information contains both possible benefits and harms to participants. Healthy research participants' reactions, the actions they may or may not take, and changed quality of life as a result of knowing genetic risk information need to be balanced against each other. To improve benefit-harm analysis, more research is required to better understand the actual benefits and harms of genetic risk information.

More research is also needed about research participants' conceptions of and preferences to genetic risk information in different age groups, for example, during reproductive age. Furthermore, future research needs to investigate participants' revealed preferences to genetic risk information in research programs where they could express their preferences through consent. Their choices as well as what influences their preferences and how they react to revealed information need to be investigated.

Another issue that needs to be studied is what causes preference heterogeneity. In Study IV, preference heterogeneity was revealed. A further research task is to investigate what influences that heterogeneity. Risk perception might be relevant in explaining differences in preferences between individuals. What one person perceives to be a high risk might be considered a moderate risk by someone else. Such differences in risk perception might cause differences in preference structures.

Epilogue

> "All things are so very uncertain, and that's exactly what makes me feel reassured." Too-ticky, *Moominland Midwinter* by Tove Jansson.

Contrary to what Too-ticky expresses, I did not feel reassured during my journey as a doctoral student. I felt that there were so many uncertainties. I questioned whether I had understood my research area. I doubted that my writing was good enough. I did not trust that I was the right person to investigate this question. I am not a geneticist, psychologist, genetic counsellor, health economist, or philosopher. Could a prosthetist/orthotist like me perform research about this issue? I struggled a lot with just understanding my research question. I did not understand how, despite there being so many ethical positions and conclusion, there were still no solutions to the ethical issue: How to handle genetic incidental findings? I asked myself, what am I missing? I mixed up my personal uncertainty, that of my own ability, and the uncertainties surrounding the research itself. I have been very frustrated during these years, struggling with how to carry on with my theoretical work. I thought that I would balance the different ethical arguments and resolve the ethical issue. Voila! But, it did not work like that. I am grateful that one of my supervisors taught me it was ok to be uncertain. He said that if I allow myself to wander around in the unknown, soon enough I will start to recognize what surrounds me. First, I did not understand what he meant. Second, I became a bit annoyed. But in the end, I am glad I trusted him, because it came true. When the day came, I realized that by allowing myself to live with the uncertainty, it turned out that the concept of uncertainty became both my method and the main result of my thesis.

Many times during my graduate training, I have been confronted with the question: 'So, what do you think, should incidental findings be disclosed?' In the beginning, I thought that, at least with time, I would be able to provide a *yes* or *no* answer to that question. However, with time, I found that the purpose of my research was not to resolve the normative issue of disclosing genetic incidental findings. I have now come to a point when I can relax and say that *I do not know*. Instead, the purpose of my work was to get to the core of the question and show its complexity. In other words, my mission was to expose the uncertainties that lie behind the different ethical arguments that, at first glance, seem so clear and certain. Today, I can finally say that all these things are so very uncertain, and that's exactly what makes me feel reassured.

Sammanfattning (Summary in Swedish)

Att ta emot genetisk riskinformation kan uppfattas på olika sätt. Vissa människor reagerar med lättnad att de hade mindre risk än vad de befarade. Andra drabbas av sorg och oro inför framtiden. Vissa drabbas av skuld. De känslomässiga reaktionerna är olika.

En av anledningarna till att människor tackar ja till att delta i medicinska forskningsstudier, kan vara att de får genomgå en omfattande hälsokontroll. Det är brukligt att deltagarna får tillbaka hälsorelaterad information såsom blodtrycksvärden, lungfunktion eller blodvärden. Genetisk riskinformation har å andra sidan inte lämnats ut på rutin.

Biomedicinsk forskning som undersöker de vanliga folksjukdomarna (såsom cancer, diabetes, demens, depression eller hjärt- och kärlsjukdomar) kombinerar frågeformulär, fysiska tester, insamling av biologiskt material och jämför med olika registerdata. Forskningsdeltagarens blodprov används för att identifiera en individs DNA. Genom att undersöka sambandet mellan genvariationer, hur människor lever, och specifika sjukdomar är förhoppningen att hitta verktyg för att diagnostisera, förebygga och behandla de vanliga folksjukdomarna. Denna form av gentester resulterar i en enorm mängd data om respektive deltagare. Med hjälp av denna information beräknas vilka individer som har högre risk att drabbas av till exempel cancer. En etisk fråga i samband med denna forskning är hur denna genetiska riskinformation (kallas även genetiska bifynd) ska hanteras. Bör fynd som kan vara relevanta för en deltagares hälsa, men som är bortom syftet med forskningsstudien, återrapporteras till deltagaren?

Inom forskarvärlden råder det konsensus kring att information som lämnas ut till forskningsdeltagare ska vara till deras nytta. Vissa argumenterar dock för att denna information kan vara till skada för deltagarna och forskningen. Det finns flera olika etiska positioner och många olika slutsatser och förslag på huruvida deltagare ska få denna information.

Det övergripande syftet för denna avhandling var att bidra till den etiska diskussionen om hur genetiska bifynd bör hanteras inom biomedicinsk forskning.

Syftet med Studie I var att beskriva de olika etiska argumenten för och emot att återföra genetiska bifynd till forskningsdeltagare, samt att analysera om argumenten tar hänsyn till den komplexitet och osäkerhet som informationen rymmer. Studien undersökte argumenten för och emot återförande av genetiska bifynd i teoretiska artiklar från vetenskapliga tidskrifter. Det vanligaste

argumentet för att återföra denna information var att informationen kan vara till deltagarnas nytta. Detta argument undersöktes närmare genom begreppsanalys. Studien identifierade en problematisk analogi med avbildningsstudier (exempelvis röntgen). I avbildningsstudier kan ett bifynd vara att forskaren upptäcker en tumör. Detta är information som uppenbarligen bör återföras enligt principen om att göra gott. Genetiska bifynd är inte information om sjukdomstillstånd utan information om risk för sjukdom. Studien identifierade en överdriven tillit till etiska principer. En vanlig etisk princip som *att göra gott* blir mindre hjälpsam när det är svårt att avgöra vad detta goda är. Eftersom genetiska bifynd är riskinformation med osäkert prediktivt värde, så blir det oklart vad som här vore *att göra gott*.

Syftet med Studie II var att undersöka om argumentet att ge forskningsdeltagare ett fritt val gällande genetiska bifynd tar hänsyn till psykologiska faktorer vid beslutfattande under risk och osäkerhet. Argumentet om att ge deltagare ett fritt val skiljer sig från de argument som undersöktes i Studie I. Istället för att bekymra sig om informationen gör gott, flyttas fokus till att låta deltagarna själva välja. Förslaget innebär att deltagarna i samband med samtyckesprocessen får välja om de vill veta hälsoavgörande genetiska bifynd. Även i Studie II studie genomfördes en begreppsanalys som identifierade ett förenklat antagande gällande preferenser och hur mänskligt beslutsfattande ser ut vid beslut som handlar om osäker information. Tidigare psykologiska studier har visat att när det kommer till att ta beslut under risk så tenderar människor att ta det säkra före det osäkra. Människors humör gör också skillnad vid beslutsfattande. Människor tenderar att överskatta låga sannolikheter och underskatta höga sannolikheter. Vidare har det visats att hur man presenterar risk påverkar människors beslut även då konsekvenserna är desamma. Studiens slutsats är att det är osäkert om möjligheten att ge deltagare ett eget val i samband med samtycket verkligen ger dem möjlighet att säga vad de faktiskt föredrar. Det är troligare att de styrs till ett specifikt svar genom triggade känslor, humör eller helt enkelt hur frågan är formulerad.

Syftet med Studie III var att kvalitativt undersöka hur forskningsdeltagare själva förstår genetisk risk. Sexton deltagare intervjuades i 4 grupper. Materialet analyserades med en fenomenografisk ansats. I analysen identifierades 4 olika kategorier. Den första och mest framträdande kategorin var att deltagare förstod genetisk risk som ett binärt begrepp, som ett ”antingen eller”: antingen har man en sjukdomsrisk eller så har man den inte. När de beskrev vilken information som var värd att veta innehöll beskrivningarna inte sannolikheter utan de sa att de ville ha information om risker som är ”på riktigt”, ”verkliga”, och ”konkreta”. Den andra kategorin var att genetisk risk ger en förklaring till varför livet blev som det blev. Tredje sättet att förstå genetisk risk var att se risken som en inblick i en persons identitet. Genetisk riskinformation kan säga något om vilka vi är och varifrån vi kommer. Den sista kategorin var att genetisk risk kan påverka vårt framtida liv. Deltagarna såg informationen som en sorts föraning om framtiden. De tänkte att de genom att veta sin genetiska risk

fick möjlighet att planera sitt liv och vidta lämpliga åtgärder för att förebygga sjukdom. Slutsatsen av studien var att forskningsdeltagare förstår risk så att risken blir något meningsfullt för dem i deras liv. För att ge mening åt den komplexa informationen och kunna fatta beslut, tolkar de informationen i termer av dåtid, nutid och framtid. Riskkommunikation skulle kunna förbättras genom att ta i beaktande dessa förståelser och därmed möta deltagarna.

Syftet med Studie IV var att undersöka forskningsdeltagares vilja att återfå genetisk riskinformation. Studien baserades på en web-enkät som 351 personer svarade på. Enkäten var utformad med en hälsoekonomisk metod som heter Discrete Choice Experiment. Metoden innebär att deltagare får välja mellan två olika situationer. Detta upprepades 15 gånger. Fördelen med denna metod är att man kan beräkna hur mycket viktigare en aspekt av den genetiska riskinformationen är (t.ex. att det finns en förebyggande åtgärd) i jämförelse med en annan aspekt (t.ex. sannolikheten att få sjukdomen). Det visade sig att deltagare vill få riskinformation som kombinerar följande aspekter: risken gäller en livshotande sjukdom; sannolikheten att drabbas är 80 av 100; risken kan minskas genom en livsstilsförändring; förändringens effektivitet är 90 %. Om samtliga ovanstående kriterier är uppfyllda är sannolikheten att en deltagare vill få informationen 98 %. Studien kunde också visa att deltagare använder sig av sannolikheter i sina beslut bara då det inte finns någon preventiv åtgärd tillgänglig. Deras beslutsfattande fokuserar främst på om det finns något som kan minska risken för sjukdom.

Huvudslutsatsen i denna avhandling är att både den etiska diskussionen och den empiriska forskningen om attityder och preferenser kring genetisk riskinformation behöver ta fasta på den osäkerhet som utmärker genetisk risk information.

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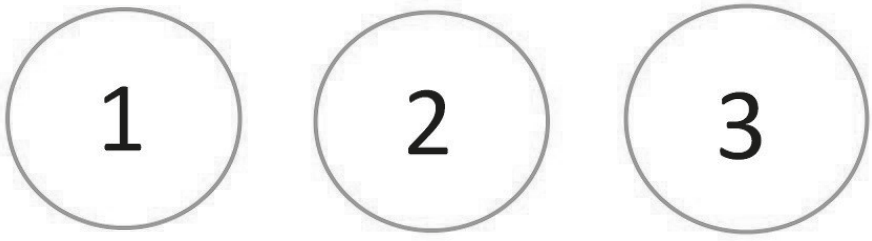
Appendix 1: The questionnaire in Swedish

Skulle du vilja få personlig information om genetisk risk?

Du deltar i SCAPIS och har genomgått mätningar och lämnat prover. Forskarna i detta SCAPIS projekt kommer inte att analysera dina gener (arvsanlag eller DNA). Men vi önskar att du föreställer dig att de gör en sådan analys för att hitta risker för sjukdom.

Om forskarna skulle genomföra en genetisk analys, skulle du i så fall vilja få information om din genetiska risk för sjukdom? Det är huvudfrågan vi önskar besvara med vår forskning. Enkäten är uppdelad i tre delar:



Bakgrundsinformation om dig

Hypotetiska valsituationer

Din uppfattning om och attityd till risk

Enkäten tar ca 30 minuter. Vi är intresserade av dina personliga tankar och önskemål, så det finns inte något rätt eller fel svar. Dina svar kommer att behandlas konfidentiellt och kommer inte användas för andra ändamål än denna undersökning och inte lämnas ut till obehöriga.

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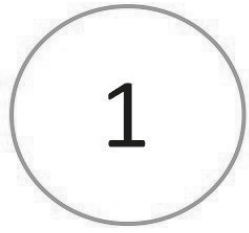


Bakgrundsinformation om dig

Vilket år påbörjande du SCAPIS-studien?

- 2014
- 2015
- 2016

Vilket år är du född?

19 [ ]

Vad är ditt kön?

- Man
- Kvinna
- Annat

0% 100%

Vad är din högsta avslutad utbildning?

- Grundskola, folkskola, realskola eller liknande
- 2-årig gymnasieutbildning eller fackskola
- 3- eller 4-årig gymnasieutbildning
- Universitets- eller högskoleutbildning kortare än 3 år (inklusive fristående kurser)
- Universitets- eller högskoleutbildning 3 år eller längre
- Annat

Vad är din huvudsakliga sysselsättning just nu?

- Yrkesarbetare
- Egen företagare
- Studerande
- Pensionär (ålders-, avtal, sjuk- och förtidspensionär)
- Långtidssjukskriven (mer än 3 månader)
- Tjänstledig eller föräldraledig
- Arbetssökande eller i arbetsmarknadspolitisk åtgärd
- Hemarbetande, sköter hushållet
- Annat

0% 100%

Har du tagit ett genetiskt test tidigare?

- Ja
- Nej

0% 100%

För vilka sjukdomar har du tagit ett genetiskt test för?

- ○ Följande sjukdomar:
- ○ Jag vet inte, det var för en annan studie
- ○ Jag vill/kan inte uppge detta

0% 100%

Hur bedömer du ditt allmänna hälsotillstånd? Är det:

- Mycket bra
- Bra
- Någorlunda
- Dåligt
- Mycket dåligt

0% 100%

Har du eller någon i din nära familj drabbas av allvarlig sjukdom de senaste 5 åren?

- Ja
- Nej, inte vad jag känner till

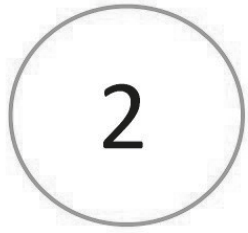
0% 100%

Jag eller någon i min närmast familj har drabbats av följande allvarliga sjukdomar de senaste 5 åren:

Tänker och oroar dig för att du eller någon i din nära familj ska drabbas av allvarlig sjukdom?

- Varje dag
- Mer än 1 gång i veckan, men mindre än varje dag
- Mer än 1 gång i månaden, men mindre än 1 gång i veckan
- Mindre än 1 gång i månaden
- Aldrig

0% 100%



Hypotetiska valsituationer

Vilken typ av genetik riskinformation vill du veta? Nu kommer vi presentera ett antal alternativ. Med varje val kommer du att ställas inför två situationer (situation 1 **eller** situation 2). Försök att välja det alternativ som du skulle föredra om du verkligen var tvungen att välja. Efter det får du möjlighet att svara om du skulle vilja veta genetisk riskinformation. Du får också svara på hur säker du känner dig med ditt svar.

0% 100%

Instruktioner för att förstå valsituationerna

Valsituationerna är uppbyggda med fyra aspekter som förekommer i flera olika kombinationer. För att du ska förstå dessa aspekter får du en beskrivning på några sidor vad de innebär. Blir du osäker under tiden du svarar, kan du sätta muspekaren över den information du vill läsa mer om för att klargöra vad vi menar. De olika aspekterna är:

- Typ av sjukdom
- Sannolikhet för sjukdom
- Förebyggande åtgärd
- Åtgärdens effektivitet

0% 100%

Instruktioner för att förstå valsituationerna

Typ av sjukdom du har risk för: Anger vilka konsekvenser sjukdomen får på dig. Olika typer av sjukdomar eller tillstånd kan drabba dig på grund av genetisk risk.

Livshotande sjukdom: Om du insjuknar är sjukdomen livshotande och du kommer troligen dö i förtid. Därför är behandling av sjukdomen avgörande. Dessa sjukdomar kan ibland botas, men inte alltid.

Funktionshinder: Innebär att du blir hindrad eller ”handikappad” i din vardag (t.ex. arbete, städning, familje- och fritidsaktiviteter) och du kan uppleva smärta och obehag. Du kan behöva hjälp i vardagen av andra i din närhet. Du kan uppleva problem med promenader, tvätta och klä dig själv eller kanske du har problem med din förmåga att höra och/eller se. Behandling för dessa sjukdomar är främst hjälpmedel och smärtlindring, annars finns ingen behandling som gör att du blir botad.

Mental ohälsa: Innebär att din mentala hälsa blir påverkad. Du kan få problem med att komma ihåg, planera och tänka strukturerat. Dessutom kan en sådan sjukdom leda till psykiatrisk sjukdom eller ändra din personlighet. Du kan behöva hjälp i vardagen av andra i din närhet. Behandling av dess sjukdomar är möjlig, men det finns ingen behandling som gör att du blir botad.

Fysisk ohälsa: Dessa fysiska tillstånd är inte livshotade och leder sällan funktionshinder. Däremot innebär dessa sjukdomar en försämring av ditt allmänna hälsotillstånd som kan påverka din livskvalitet och behöva behandling. Exempel på sjukdomar är diabetes, högt blodtryck eller allergier.

0% 100%

Instruktioner för att förstå valsituationerna

Sannolikheten för sjukdom: Om du får ett svar från det genetiska testet att du löper risk för sjukdom är det inte säkert att du drabbas av sjukdom. Sannolikheten att drabbas av sjukdom kan presenteras på flera sätt. Ett sätt är att beskriva hur många människor av 100 som har samma typ av genvariant som du och som sedan kommer bli drabbad av sjukdom. De olika situationerna innehåller följande sannolikheter:

Instruktioner för att förstå valsituationerna

Förebyggande åtgärd: En del sjukdomar går att förebygga. Genom att vidta åtgärder kan man påverka riskens storlek. Det betyder inte att risken helt försvinner, men att den minskar. Följande olika nivåer kommer att finns i din valsituation:

Operation: Du bli inlagd minst 1 dygn på sjukhuset för att utföra den förebyggande operationen. Du får räkna med en tid för att kroppen ska läka. Operationen medför risk för komplikationer.

Medicin: Du behöver inte gå regelbundet till sjukhuset utan du kan hämta ut medicinen på närmaste apotek. Du kan behöva ta medicinen resten av ditt liv. Det kan ta tid att få rätt dos inställt. All medicinering innebär risk för någon form av biverkningar.

Livsstilsförändring: Du behöver ändra på dina levnadsvanor. Det kan innebära att du ska ändra kost (ändra innehåll, sluta med viss föda eller minska kaloriintag), sluta med t.ex. rökning eller alkohol. Det kan även innebära att du måste ändra din fysiska aktivitet. Du kan behöva ändra ditt sömnmönster.

Ingenting: Det finns ingen åtgärd för att minska din risk för sjukdom.

Instruktioner för att förstå valsituationerna

Åtgärdens effektivitet: Olika åtgärder har olika förmåga att minska risken. Om du vidtar en åtgärd är det möjligt att risken minskar. Detta innebär att några av dem som skulle ha fått sjukdom kommer inte få den pga. den förebyggande åtgärden. Antalet individer som inte blir sjuka pga. att de vidtar förebyggande åtgärd beror på antalet personer som får sjukdomen. T.ex. om 30 personer av 100 får sjukdom och alla 100 vidtar en förbyggande åtgärd vars effektivitet är 50 %, då kommer 15 av 30 inte längre får sjukdom. De olika nivåerna för de olika riskerna är följande:

Ingen minskad risk: Då det inte finns någon förebyggande åtgärd för att minska risken för sjukdom kommer inte risken att kunna minskas

25 % effektivitet

50 % effektivitet

75 % effektivitet

90 % effektivitet

0% 100%

TIPS: Om du vill i valsituationen påminna dig om vad alternativen innebär kan du placera muspekaren på alternativet så kommer innehållet upp i en grå ruta:

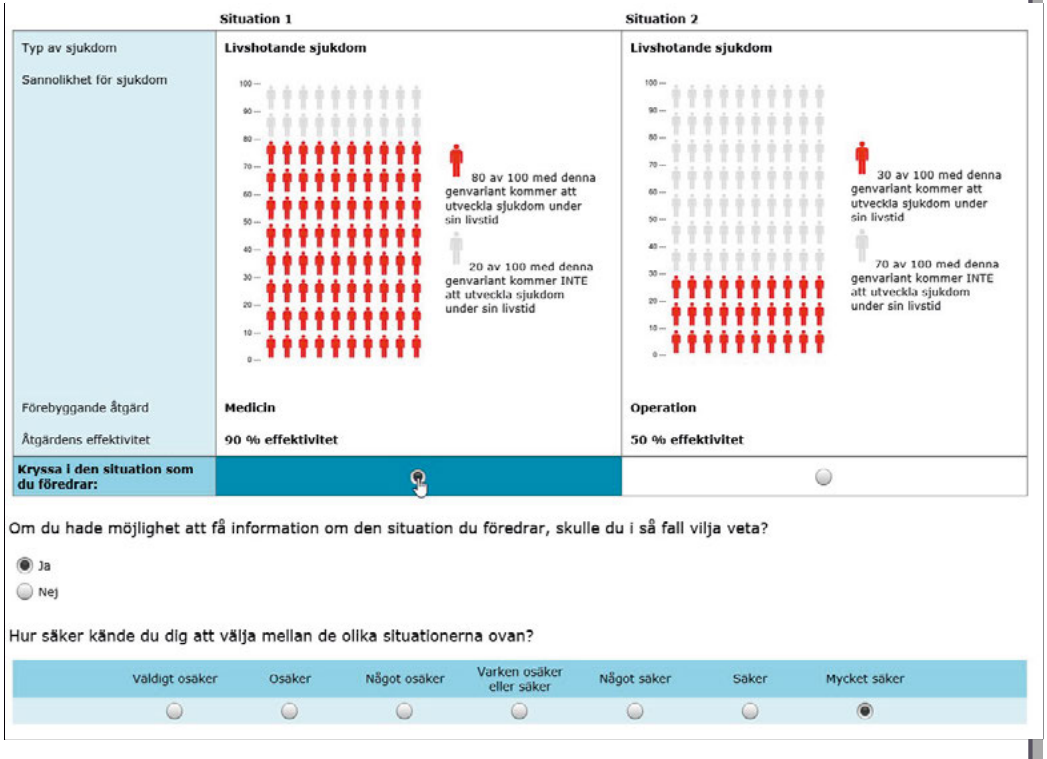
0% 100%

EXEMPEL 1 av 2

Här nedan ser du **ett exempel** på hur valsituationen kommer att se ut. Vid detta exempel har personen valt **Situation 1**, dvs att personen föredrar om den genetiska risken handlar om:

- Livshotande sjukdom
- när sannolikhet för sjukdom är **80 av 100**
- den förebyggande åtgärden är **Medicin**
- och den har **90 % effektivitet** att minska risken.

Personen har svarat **Ja** till att veta Situation 1 och känner sig mycket säker på sitt val och har därför markerat **Mycket säker**.

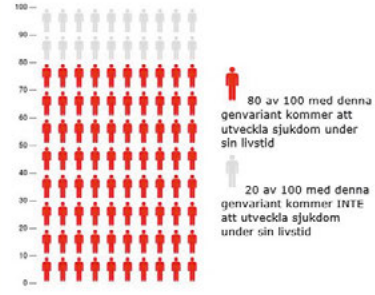
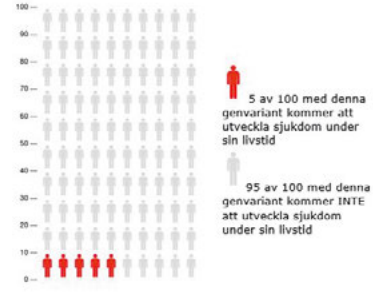


EXEMPEL 2 av 2

Här nedan ser du **ett nytt exempel** på hur valsituationen kommer att se ut. Vid detta exempel har personen valt **Situation 1**, dvs att personen föredrar om den genetiska risken handlar om:

- Livshotande sjukdom
- när sannolikhet för sjukdom är **80 av 100**
- den förebyggande åtgärden är **Livsstilsförändring**
- och den har **25 % effektivitet** att minska risken.

Personen har svarat **Nej** till att veta Situation 1 och känner sig något säker att hon/han föredrar Situation 1 framför Situation 2 och har därför markerat **Något säker**.

	Situation 1	Situation 2
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom		
Förebyggande åtgärd	**Livsstilsförändring**	**Operation**
Åtgärdens effektivitet	**25 % effektivitet**	**90 % effektivitet**
Kryssa i den situation som du föredrar:	◉	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
◉ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	◉	○	○

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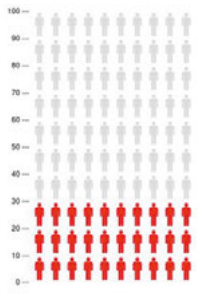
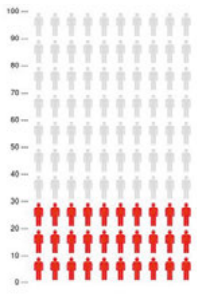
Nu får du börja välja!

0% 100%

(1 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Funktionshinder**	**Funktionshinder**
Sannolikhet för sjukdom	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Medicin**
Åtgärdens effektivitet	**90 % effektivitet**	**90 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
○ Nej

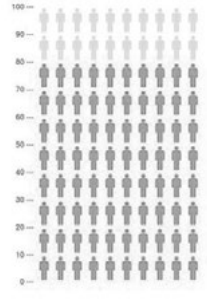
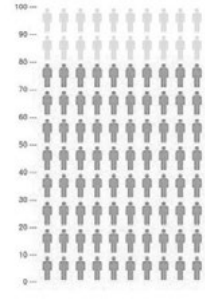
Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

0% 100%

(2 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Fysisk ohälsa**	**Mental ohälsa**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Medicin**
Åtgärdens effektivitet	**75 % effektivitet**	**75 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

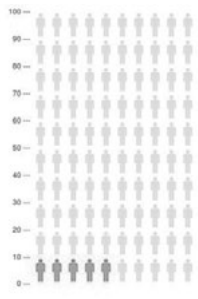
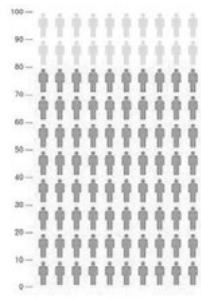
Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

0% 100%

(3 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Mental ohälsa**
Sannolikhet för sjukdom	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Operation**	**Livsstilsförändring**
Åtgärdens effektivitet	**50 % effektivitet**	**90 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

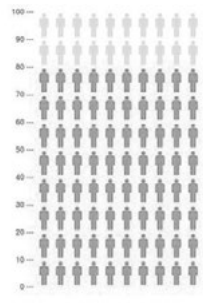
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(4 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Mental ohälsa**	**Fysisk ohälsa**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Ingenting**	**Ingenting**
Åtgärdens effektivitet	**Ingen minskad risk**	**Ingen minskad risk**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

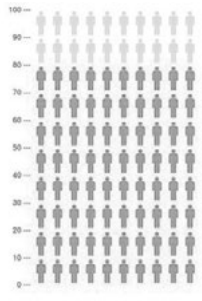
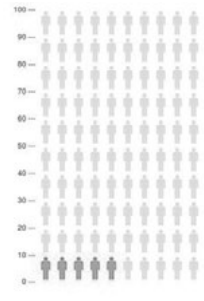
- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

(5 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Operation**
Åtgärdens effektivitet	**25 % effektivitet**	**90 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

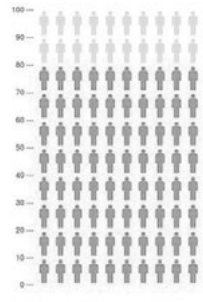
Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

0% 100%

(6 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Operation**
Åtgärdens effektivitet	**90 % effektivitet**	**50 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

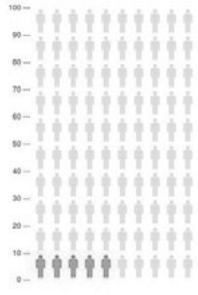
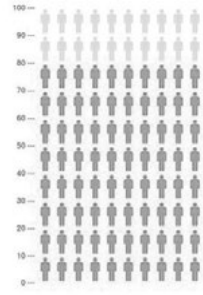
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(7 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Operation**
Åtgärdens effektivitet	**75 % effektivitet**	**25 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

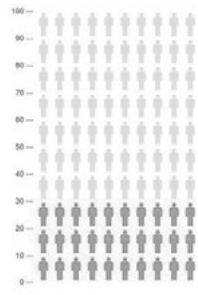
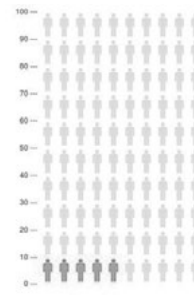
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(8 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Operation**
Åtgärdens effektivitet	**50 % effektivitet**	**75 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

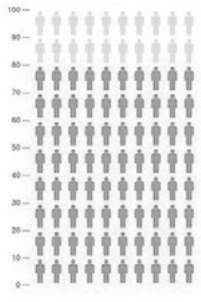
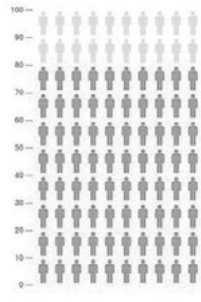
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(9 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Fysisk ohälsa**	**Fysisk ohälsa**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Operation**
Åtgärdens effektivitet	**25 % effektivitet**	**50 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

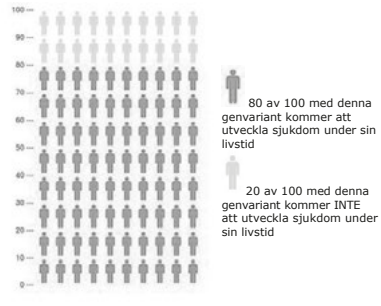
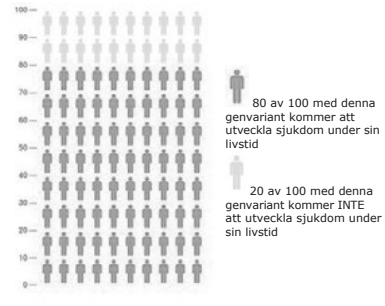
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(10 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Funktionshinder**	**Funktionshinder**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Livsstilsförändring**
Åtgärdens effektivitet	**75 % effektivitet**	**75 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

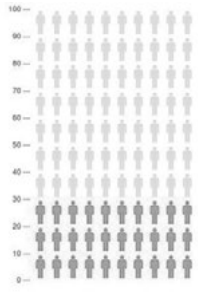
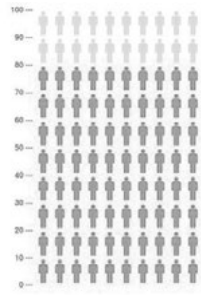
Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

0% 100%

(11 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Livsstilsförändring**	**Operation**
Åtgärdens effektivitet	**90 % effektivitet**	**50 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

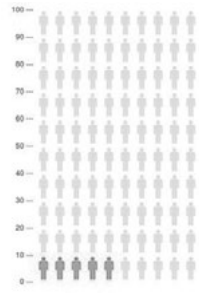
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(12 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Fysisk ohälsa**
Sannolikhet för sjukdom	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Operation**
Åtgärdens effektivitet	**25 % effektivitet**	**75 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

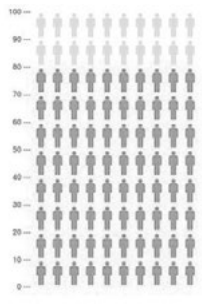
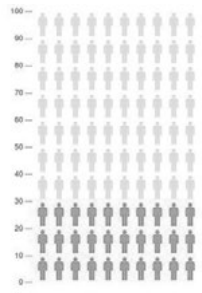
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(13 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Fysisk ohälsa**	**Funktionshinder**
Sannolikhet för sjukdom	 80 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 20 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Ingenting**	**Ingenting**
Åtgärdens effektivitet	**Ingen minskad risk**	**Ingen minskad risk**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

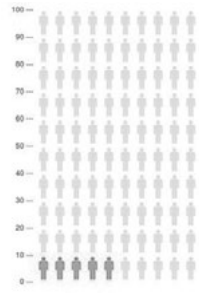
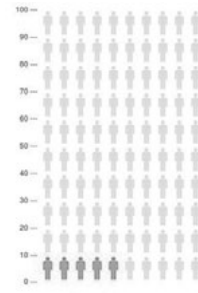
- ○ Ja
- ○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

(14 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Mental ohälsa**	**Fysisk ohälsa**
Sannolikhet för sjukdom	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Livsstilsförändring**
Åtgärdens effektivitet	**25 % effektivitet**	**50 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

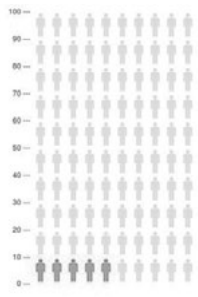
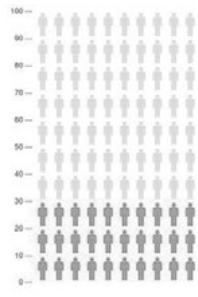
Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

◀ ▶

0% 100%

(15 av 15)

Föreställ dig att genetisk riskinformation kommer att erbjudas till dig i och med din medverkan i SCAPIS. I vilken situation föredrar du att veta denna information, i situation 1 **eller** situation 2? Kryssa den ruta som representerar ditt val:

	Situation 1	**Situation 2**
Typ av sjukdom	**Livshotande sjukdom**	**Livshotande sjukdom**
Sannolikhet för sjukdom	 5 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 95 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid	 30 av 100 med denna genvariant kommer att utveckla sjukdom under sin livstid 70 av 100 med denna genvariant kommer INTE att utveckla sjukdom under sin livstid
Förebyggande åtgärd	**Medicin**	**Operation**
Åtgärdens effektivitet	**75 % effektivitet**	**90 % effektivitet**
Kryssa i den situation som du föredrar:	○	○

Om du hade möjlighet att få information om den situation du föredrar, skulle du i så fall vilja veta?

○ Ja
○ Nej

Hur säker kände du dig att välja mellan de olika situationerna ovan?

Väldigt osäker	Osäker	Något osäker	Varken osäker eller säker	Något säker	Säker	Mycket säker
○	○	○	○	○	○	○

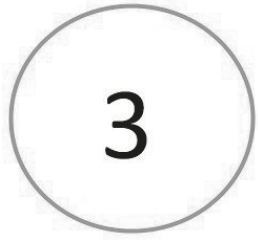
◀ ▶

0% 100%

Hur svårt var det att välja?

- Inga val var svåra
- Vissa val var svåra
- Flesta val var svåra
- Alla val var svåra

0% 100%



Din uppfattning om och attityd till risk

Slutligen har vi några frågor som handlar om din attityd och uppfattning av risker. Vi vill också att du svarar på några frågor som handlar om din förståelse av hälsoinformation och risksiffror.

Nedan presenteras några påståenden som gäller genetisk risk. Markera det alternativ på varje rad som stämmer bäst överens med ditt svar:

	Stämmer inte alls 1	Stämmer dåligt 2	Stämmer delvis 3	Stämmer bra 4	Stämmer precis 5
Om jag vet min genetiska risk kan jag förbygga att allvarligt sjukdom drabbar mig	○	○	○	○	○
Jag är inte säker på att det skulle hjälpa mig att veta min genetiska risk	○	○	○	○	○
Jag tror att min familj skulle bli hjälpt om jag vet min genetiska risk	○	○	○	○	○
Jag tycker det är meningslöst att veta min genetiska risk	○	○	○	○	○
Jag skulle leva mitt liv annorlunda om jag visste min genetiska risk	○	○	○	○	○
Jag skulle bli orolig om jag visste min genetiska risk	○	○	○	○	○
Om jag vet min genetiska risk så lär jag mig mer om mig själv	○	○	○	○	○
Jag skulle bli rädd om jag visste min genetiska risk	○	○	○	○	○
Om det var möjligt att få tillbaka genetisk riskinformation så skulle jag vilja få det	○	○	○	○	○

Föreställ dig att 100 individer genomför ett genetisk test som du skulle kunna göra i SCAPIS. Hur många av dem tror du kommer ha **risk** för genetisk sjukdom?
Uppge en siffra mellan 0 till 100:

Vad tror du **din** risk för genetisk sjukdom är? Uppge mellan 0-100 %:

Hur skulle du beskriv din risk för att drabbas av genetisk sjukdom i ord. Välj något av följande:

- Extremt liten risk
- Mycket låg risk
- Låg risk
- Möjlig risk
- Trolig risk
- Rätt hög risk
- Hög risk
- Mycket hög risk
- Extremt hög risk

0% 100%

Ibland kan risker presenteras i siffror. Vi är intresserade av vad du anser är hög och låg genetisk risk. Det finns inget rätt eller fel svar. Skriv en siffra mellan 0-100 % som du tycker representerar ordet:

Hög risk:

Extremt hög risk:

Möjlig risk:

Trolig risk:

Extremt liten risk:

Mycket låg risk:

Rätt hög risk:

Låg risk:

Mycket hög risk:

Rätt låg risk:

0% 100%

Vi är intresserade av att veta hur du tänker om din hälsa och att ta risker. Berätta om något av följande passar in på dig?

	Instämmer helt 1	Instämmer mycket 2	Instämmer till stor del 3	Instämmer måttligt 4	Instämmer lite 5	Instämmer väldigt lite 6	Instämmer inte alls 7
Jag tycker att jag tar väl hand om min kropp	○	○	○	○	○	○	○
Jag vill inte behöva tänka på konsekvenserna för min hälsa i allt jag gör	○	○	○	○	○	○	○
Det är viktigt för mig att organisera mitt liv så att jag kan njuta av god hälsa senare	○	○	○	○	○	○	○
Om det handlar om min hälsa så ser jag mig själv som en person som undviker risker	○	○	○	○	○	○	○
Osäkerhet på konsekvenserna av en medicinsk åtgärd är generellt sett något man får räkna med	○	○	○	○	○	○	○
Min hälsa betyder allt för mig.	○	○	○	○	○	○	○

0% 100%

Vi är intresserade av att veta hur du tänker om din hälsa och att ta risker. Berätta om något av följande passar in på dig?

	Instämmer helt 1	Instämmer mycket 2	Instämmer till stor del 3	Instämmer måttligt 4	Instämmer lite 5	Instämmer väldigt lite 6	Instämmer inte alls 7
När jag ser tillbaka på mitt liv tycker jag generellt sett att jag faktiskt tog risker med min hälsa	○	○	○	○	○	○	○
Om läkaren inte kan försäkra mig om vilka potentiella konsekvenser en medicinsk åtgärd kan få så skulle jag helst inte genomgå den	○	○	○	○	○	○	○
När det gäller min hälsa kommer säkerheten först	○	○	○	○	○	○	○
För att kunna njuta av god hälsa nu och i framtiden är jag villig att offra mycket	○	○	○	○	○	○	○
Andra säger att jag riskerar min hälsa på grund av mina vanor	○	○	○	○	○	○	○
Jag är inte så noga med min hälsa	○	○	○	○	○	○	○
Generellt sett skulle jag säga att jag inte har särskilt stora problem med att genomgå en riskabel operation	○	○	○	○	○	○	○

0% 100%

Här kommer några påståenden som handlar om att ta del av information som har med hälsa, sjukdomar och sjukvård att göra. Vi har förstått att ibland kan information om hälsa och risker vara svårt att förstå. Vi är nyfikna på dina erfarenheter. Markera det alternativ på varje rad som stämmer bäst överens med ditt svar:

	Stämmer inte alls 1	Stämmer dåligt 2	Stämmer delvis 3	Stämmer bra 4	Stämmer precis 5
Jag kan hämta information från flera olika informationskällor såsom, tidningar, internet, böcker, hälso- och sjukvården, familj och vänner m.m.	○	○	○	○	○
Jag kan välja ut just den information som jag behöver från en mängd informationskällor.	○	○	○	○	○
Jag kan förstå informationen och dela med mig av den till andra.	○	○	○	○	○
Jag kan bedöma om informationen är trovärdig.	○	○	○	○	○
Jag kan med hjälp av informationen planera och avgöra vad jag behöver göra för att förbättra min hälsa.	○	○	○	○	○

0% 100%

Slutligen vill vi be dig svara på några frågor om dina erfarenheter och känslor om siffror. Skatta nedan hur du uppfattar dig själv gällande följande frågor:

	Inte alls bra 1	2	3	4	5	Extremt bra 6
Hur bra tycker du att du är på att arbeta med bråktal?	○	○	○	○	○	○
Hur bra tycker du att du är på att räkna ut hur mycket en tröja kommer att kosta om det är 25 % rabatt?	○	○	○	○	○	○

	Aldrig 1	2	3	4	5	Mycket ofta 6
Hur ofta tycker du att sifferinformation är användbart?	○	○	○	○	○	○

0% 100%

Tack för din medverkan!

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