INFORMED CONSENT AND GENETIC DATABASES: AN EXPLORATION OF THE AUTHORIZATION MODEL

by

Robin Zoe Hayeems

A thesis submitted in conformity with the requirements for the degree
Doctor of Philosophy,
Graduate Department of Public Health Sciences,
University of Toronto

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An Exploration of the Authorization Model

Robin Zoe Hayeems
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Abstract

In order to identify genes associated with common complex disorders, genetic databases are emerging worldwide and highlight the convergence of the fields of molecular genetics and public health. The nature of the methodology and technology required for this purpose necessitates careful examination of the process of informed consent. This study considered the authorization model as one approach to informed consent in the context of genetic database research. Using a conceptual framework grounded in moral theory, I argue that in order to suit this context, an evolution in the process of informed consent is warranted. A non-experimental, cross-sectional survey design was used to learn about the factors that influence potential research participants' willingness to authorize the use of various types of personal health information (PHI) under a range of conditions. Individuals who had pursued genetic testing for one of four late onset hereditary disorders were invited to participate in a 40 minute interview. Included in the interview guide was a previously piloted tool called the Health Care Information Directive (HCID). Quantitative data were analyzed using logistic regression and text data were analyzed using a content analysis.

199 individuals participated in this study. Key findings include: (1) genotype status, self-reported privacy level, and anonymization level are significant predictors of willingness

to authorize use of PHI, (2) type of PHI (genetic, non-genetic, family history information, information gleaned from a blood sample) is *not* a significant predictor of willingness to share PHI, casting doubt upon the genetic exceptionalism debate, (3) willingness to share health information is not significantly influenced by the nature of a specific research or administrative purpose for which it is requested, (4) the HCID tool can be simplified based upon these findings and still cohere with the principles of the authorization model, and (5) the concepts of trust, safeguards, altruism, and reciprocity are fundamental to understanding the factors that influence authorization and can be used to guide further exploration of the authorization model and the evolution of the informed consent process for the context of genetic database research.

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Table of Contents

	PAGE(S)
Chapter 1: Introduction	**1-24**
(A) Aims	2
(B) Background	
(i) Public Health Determinants, Prevention, and Promotion	2-4
(ii) Intersection of Public Health and Genetics	5-6
(iii) Public Health Genetics Research: An Example	7-13
(iv) Genetic Databases and the Eugenics Movement	14-19
(v) Informed Consent and Medical Privacy	19-21
(C) Chapter Overview	21-24
Chapter 2: Conceptual framework	**25-59**
(A) Bioethics, Research Ethics, and Public Health Ethics	
(i) Bioethics and Autonomy	26-29
(ii) Research Ethics and Autonomy	29-32
(iii) Public Health Ethics and Collective Interests	32-35
(B) The Concept of Privacy	35-38
(C) Overview of Conceptual Framework	38
(D) Moral Theory	
(i) Rights Theory	39-42
(ii) Ethics of Care	42-43
(iii) Communitarianism	43-45
(E) Conceptions of Autonomy	
(i) Traditional Autonomy	46-47
(ii) Relational Autonomy	47-51
(iii) Autonomy and the Citizen Role	51-54
(F) Autonomy and Trust	54-58
(G) Informed Consent – A Necessary Evolution	58-59

Chapter 3: Literature Review	**60-103**
Part I: Approach to Literature Review	61
Part II: Informed Consent – A Necessary Evolution	**61-81**
(A) Guiding documents, policies, and legislation	
(i) Founding Documents	61-64
(ii) The Canadian Context: Privacy Legislation	64-66
(iii) The Canadian Context: Informed Consent for Research	66-71
(B) Traditional Informed Consent in the Context of Biobank Research	
(i) Why it doesn't fit: theoretically	71-74
(ii) Why it doesn't fit: authorization bias	74-81
Part III: Alternate Consent Models	**82-94**
(A) Blanket Consent	82-83
(B) Presumed Consent	83-85
(C) Authorization	85-89
(D) Governance Structures	89-94
Part IV: Factors which influence participants' willingness to share PHI	**94-103**
(A) Type of Personal Health Information Requested	94-99
(B) Purpose for which Personal Health Information is Requested	100-101
(C) Type of Professional Requesting Personal Health Information	101-103
(D) Storage of Personal Health Information	103
Chapter 4: Research Question	**104-109**
(A) Rationale for Selecting the Authorization Model	105-106
(B) Research Question and Dimensions	106-109
Chapter 5: Methodology	**110-127**
(A) Study Design	111

(B) Recruitment	111-113
(C) Data Collection	
(i) The Interview Guide	114-116
(ii) The Interview	116-117
(iii) Data Tracking	117-118
(iv) Closure	118
(D) Data Analysis	
(i) Quantitative Analysis	118-124
a. Data Cleaning	119
b. Response Rates	119
c. Sample Characteristics	120
d. Identification of Key Variables	120-121
e. Exploration of Key Variables	121-122
f. Interpreting Relationships among Variables	123
g. A Predictive Model	123-124
(ii) Content Analysis	124-125
(E) Ethics Considerations	126-127
Chapter 6: Results	**128-174**
(A) Quantitative Findings	
(i) Response Rates	129-131
(ii) Sample Characteristics	131-134
(iii) Exploration of Key Variables	135-137
(iv) Interpreting Relationships among Key Variables	137-148
(v) Identifying Where Specific Difference Lie	148-160
(vi) A Predictive Model	160-161
(B) Content Analysis and Triangulation with Quantitative Findings	162-174
Chapter 7: Discussion and Conclusions	**175-215**
(A) Response Rates and Overall Sample Characteristics	176-181
(B) The influence of 'participant characteristics' on willingness to share Personal Health Information	
(i) Genotype	181-183
(ii) Phenotype	183

(iii) Population Group (iv) Self-reported Privacy Level	183-185 185-186
(C) The influence of 'information characteristics' on willingness to share Personal Health Information (i) Type of Personal Health Information (ii) Anonymization Level (iii) Purpose for which Personal Health Information is Requested	 186-188 189-191 191-193
(D) What underlies willingness to share Personal Health Information (i) Trust and Safeguards (ii) Altruism (iii) Reciprocity	 193-199 199-203 203-210
(E) **Conclusions:** How do these data inform the process of informed consent for genetic database research?	**211-216**
Chapter 8: Strengths and Limitations	**217-222**
Chapter 9: Future Directions for Research	**223-226**
Appendices	**227-300**
References	**301-318**

List of Tables

Table No.	Title	Page(s)
1	Characteristics of Genetic Databases Worldwide	11-13
2	Response Rates	131
3A	Sample Characteristics - Categorical Variables	134
3B	Sample Characteristics - Continuous Variables	134
4	Overall Predictors of Authorization	137
5A	Specific Predictors - Administrative Purposes	154-155
5B	Specific Predictors – Research Purposes	159
6	Predictive Model Scenarios	161
7	Content Analysis: Domains, Codes, and Definitions	163-164
8	Content Analysis: Interim Code Frequencies and Inter-Coder Concordance	167
9	Content Analysis: Final Code Frequencies and Sample Text	174

List of Figures

Figure No.	Title	Page
1	Willingness to Share Personalized Health Information: By Genotype	139
2	Willingness to Share Coded Health Information: By Genotype	140
3	Willingness to Share Aggregated Health Information: By Genotype	141
4	Willingness to Share Personalized Health Information: By Phenotype	143
5	Willingness to Share Coded Health Information: By Phenotype	144
6	Willingness to Share Aggregated Health Information: By Phenotype	145
7	Willingness to Share Personalized Health Information: By Population Group	146
8	Willingness to Share Coded Health Information: By Population Group	147
9	Willingness to Share Aggregated Health Information: By Population Group	148
10	Simplified Health Care Information Directive Tool	214

List of Appendices

Appendix No.	Title	Page(s)
1.1	Participant Groups and Recruitment Sites	228
1.2	Sample Invitation Letter	229
1.3	Sample Consent Form	230
1.4	HCID - Original	231
1.5	HCID – Modified for Genetics	232-233
1.6	HCID – Participant Copy	234-235
1.7	Sample Interview Guide (HBOC)	236-245
1.8	Study Questions, Variable, Instrument Link	246
1.9	Sample Participant Thank you Letter	247
1.10	Statistical Codes	248-263
1.11 (a-e)	REB Approval Letters	264-268
2.1	Effect of Anonymization Level (Research Purposes 1-6)	268-271
2.2	Effect of Anonymization Level (Admin Purposes 1-5)	271-274
2.3	Probability Estimates by Genotype	275-276
2.4	Probability Estimates by Phenotype	277-278
2.5	Probability Estimates by Population Group	279-280
2.6	Specific Predictors of Authorization	281-300

CHAPTER 1: INTRODUCTION

CHAPTER 1: INTRODUCTION

(A) Aims

Using relevant moral reasoning tools, existing literature, and a rigourous scientific methodology, this thesis aims to: (1) demonstrate why an evolution in the process of informed consent is warranted for the context of genetic database research and why the authorization model is a viable option to consider; (2) integrate the context of genetics into the Health Care Information Directive (HCID) tool, a tool that coheres with the principles of authorization, and to use this tool as part of a data collection instrument; (3) better understand the factors that influence individuals' willingness to share different types of personal health information under a range of conditions, and (4) relate findings to an ethically sound and pragmatic approach to informed consent in the context of genetic database research.

(B) Background

(i) Public Health: Determinants, Prevention, and Promotion

Public health has been defined as, "what we, as a society, do collectively to assure the conditions in which people can be healthy."[1] In Canada, many diseases have been controlled or almost eradicated with the advent of better living conditions, the availability of antibiotics, public health interventions such as immunizations, new technology, and universal health care. While mortality has been reduced and life span has increased, chronic and infectious diseases remain an important health care challenge. Given that we need to "assure the conditions" for health and not simply health itself, health care in Canada has shifted to appreciate the multi-dimensionality of health.[1] One advantage of

recognizing both the medical and non-medical determinants of health is that health promotion and disease prevention strategies that reflect a broad range of influences can be identified, implemented, and evaluated. Compared to a strictly medical approach to health challenges, a holistic approach is more likely to generate targeted and systematic improvements in the health of Canadians.

In 1974, Marc Lalonde, Minister of Health in Canada, put forward a comprehensive view on the determinants of health in *A New Perspective on the Health of Canadians.*[2] He outlined four elements that determine the health of Canadians: (1) human biology, (2) the environment, (3) lifestyle, and (4) the health care organization. Human biology refers to those aspects of physical and mental health that are determined by the organic structure and physiological functioning of the human body. More and more is being learned about the extent to which individuals' genetic constitution influences predisposition and susceptibility to disease. Environmental determinants include factors found in the physical environment such as quality of air, water, and soil, the safety of foods and drugs, waste disposal, and control of animal and insect vectors that transmit disease, to name a few. The category of environmental determinants has expanded to include the psychosocial environment: places where people live and work, as well as their levels of income, education, and social support. Lifestyle determinants relate to aspects of individuals' behaviour and surroundings that they control; this incorporates elements of both social responsibility and individual responsibility. Personal decisions about health behaviours result in favourable or adverse health consequences and play a major role in the health of populations. Finally, the way in which health care is organized, funded, and

delivered has tremendous influence on health outcomes. While the current system primarily alleviates the burden of ill health, medical error, budgetary constraints, and inaccessible care are noteworthy barriers.

Strategies used to promote health and prevent disease are a function of the aforementioned determinants of health. Key national and international documents in the late 1970s and early 1980s laid the groundwork for the field of *health promotion.* Some of these included the World Health Organization's (WHO) 1978 *Declaration of Alma Ata on Primary Health Care,*[3] the WHO's 1984 *Targets for Health for All by 2000,*[4] and the US's 1979 publication; *Healthy People: The Surgeon General's Report on Health Promotion and Disease Prevention.*[5] Motivated by these documents and a growing understanding of the concept and importance of health promotion in 1986, Canada's Minister of National Health and Welfare at the time, released *Achieving Health for All: A Framework for Health Promotion.*[6] Consequent to this publication, Health and Welfare Canada, the WHO, and the Canadian Public Health Association endorsed the Ottawa Charter for Health Promotion[7] which defined current concepts of health promotion and called for systematic and rigourous health promotion efforts in Canada. As articulated in the Ottawa Charter, health promotion approaches include five components: reorienting health services, enhancing personal skills, strengthening community action, creating supportive environments, and building healthy public policy. Specific strategies include education, communication, legislation, fiscal measures, community organizational change, community development, and local community action.

(ii) Intersection of Public Health and Genetics

While public health traditionally has focused on prevention and management of common, multifactorial conditions that affect large populations, genetic medicine has traditionally focused on the management of rare, single gene disorders that affect small groups of people. How then do the fields of public health and genetics intersect?

One answer is that both public health practice and genetic medicine utilize the technology of *screening* as a mode for 'secondary prevention.' *Disease prevention* falls into one of three categories. *Primary prevention* strategies aim to prevent disease before it happens, thereby reducing the incidence of disease. Classic examples of this approach include immunization programs, avoidance of risk behaviours like smoking, and using safety devices like seatbelts. *Secondary prevention* strategies aim to detect and treat disease at an early stage in order to improve health outcomes for affected individuals. Often this is achieved by using various screening technologies (e.g. mammography for breast cancer). *Tertiary prevention* strategies aim to reduce death and disease through medical treatment and rehabilitation of ill individuals.[1]

Whitby[8] defines *screening* as "the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly." The goal of screening is to identify which individuals in a community *probably* have the disease and which individuals *probably* do not so that early intervention may be initiated and better health outcomes achieved. Screening can apply to an entire population if individuals are all at risk for a given disease (mass screening) or can be

performed on selective sub-groups at increased risk of developing certain diseases. Population screening for tuberculosis in developing countries where the prevalence is high is an example of mass screening, whereas preconceptual genetic screening for Maple Syrup Urine Disease in the French Canadian population and for Tay Sachs disease in the Ashkenazi Jewish population are examples of selective screening.[1] Screening of a defined population is justified when (1) the disease causes significant morbidity and mortality, (2) there is an asymptomatic stage of the disease that is detectable by a test, (3) early intervention is known to affect health outcomes favourably, (4) the test is sensitive, specific, rapid, cost-effective, accessible, and acceptable to health care providers and the screened population with respect to invasiveness/risk, and (5) adequate resources within the health care system are available for appropriate diagnostic and therapeutic follow-up.[1]

A second answer is related to the underlying research enterprise that facilitates these clinical developments. The availability of draft sequences of the human genome has accelerated the isolation and characterization of common gene variants associated with susceptibility to common complex conditions. It is only with the convergence of molecular technologies and population-level risk factor and health outcome data that a clearer understanding of the complex gene-environment interactions underlying human disease can emerge. With this, pharmaceutical enhancement and more effective preventive strategies may ensue.[9] This progress requires not only sophisticated molecular technology and research methodology, but also buy-in from the population at large.

(iii) Public Health Genetics Research: An Example

While it is a fundamental goal of both traditional genetics research and public health genetics research to better understand human disease, the scope of the research questions posed by researchers in each field vary. When the scope of a research question shifts from one related to identifying the single cause of a rare disease affecting a small group of people to one that is related to identifying multiple risk factors associated with a common disease affecting large populations, researchers use different recruitment, data collection and analytic strategies.

For example, identifying risk factor genes with only modest predictive value requires the participation of very large samples. To further identify the interactions between genetic and environmental risk factors, molecular and epidemiological data need to be linked and statistically manipulated in sophisticated ways. Genetic databases have emerged as a mechanism through which to facilitate this complex methodology. One definition of a genetic database is: "a stored collection of genetic samples in the form of blood or tissue that can be linked to medical and genealogical or lifestyle information from a specific population, gathered using a process of generalized consent."[10] The primary goal of genetic databases is to collect DNA, to link it with medical and genealogical data, and to use this combined resource to search for genetic influences on common complex disorders such as heart disease, Alzheimer's disease, cancer, and mental illnesses. In turn, it is anticipated that these findings will lead to improved understanding of disease causation, improved pharmaceutical agents for risk reduction or therapy, and an overall reduction in disease morbidity and mortality.

In Canada for example, a plan is underway to develop a large, multi-generational, longitudinal research program to examine how genetic and environmental influences contribute to human development, aging, and health outcomes. Specifically, the Canadian Institutes of Health Research (CIHR) has proposed the Canadian Lifelong Health Initiative,[11] a merger between the Canadian Longitudinal Study on Aging[12] (CLSA) and the Canadian National Birth Cohort[13] (CNBC). The CLSA would contribute 50,000 Canadians older than age 40 who would be followed for 20 years. The CNBC would recruit 20,000-30,000 women prior to or early in pregnancy and follow these women and their children through development. A wide range of personal and medical information as well as biological samples would be collected.

Many other collections are ongoing in Europe and the United States.[14] Table 1 provides a synopsis of the primary features of the better known databases worldwide. All of these databases plan to search for susceptibility genes for complex disorders while attempting to improve public health and medical care in their respective region. In some cases it is also a priority to stimulate the local economy through expansion of the biotechnology sector. Despite this similarity among these databases with respect to their fundamental goals, they differ with respect to their approach to informed consent as well as the extent to which and conditions under which the private sector is involved in their operation and funding. The Utah Pedigree Database[15] (UPDB), for example, holds over nine million family and medical records from Utah families in order to analyze patterns of genetic inheritance and identify specific genetic mutations for cancer and a range of other diseases. Individuals are asked to opt-in to this database and only anonymized data are

available to interested external researchers. Should external researchers require identifiable data for their research, UPDB contacts potential participants for permission to release their contact information to the external researchers who then must contact individuals for explicit consent. The private sector can access anonymized data only. The UPDB is funded through the University of Utah's institutional and grant funds. It has been actively thriving with no known opposition for 30 years and is tightly linked with both the University of Utah and the Church of Latter Day Saints.

Similar to its interest in identify disease-causing genes, Iceland's Health Sector Database[16] (HSD) represents a very different phenomenon. To a large extent, the Icelandic controversy has set the stage for the ongoing debate about how best to manage public consultation, consent, data storage, and commercial interests in the realm of public health genetics research and therefore warrants a brief review. In December 1998, Iceland's Parliament, the Althing, passed 'the Database Act,'[17] a highly controversial law authorizing the development of a Health Sector Database to collect genetic and medical information already contained in various locations around Iceland as part of Iceland's national health system. As a result of the Database Act, Iceland is the only country in the world with laws authorizing collection and storage of the genetic heritage of an entire population by a private biotechnology corporation with rights to exploit the data as a commercial commodity. Databases that contain detailed medical information about every Icelandic person, both living and dead, dating back to 1915 are now linked together in a single centralized electronic database created and operated by a private biotechnology company, deCODE Genetics. Medical record data will be entered into this centralized

database prospectively.[18] While there is tremendous scientific potential for a resource such as this, there are a number of legitimate ethical concerns related to how it has been structured. For example, limited consultation with the public and academic communities was solicited. Rose[19] suggests that lack of consultation may have been related to (a) anticipated dissent from the academic community, and (b) an assumption that Icelanders, more fearful of earthquakes and volcanoes than the fruits of science and technology, would simply buy-in. As well, data collection operates under a model of presumed consent. While opting-out is a theoretical option, it is time-limited and lies with the participants' initiative. This approach includes no provisions for vulnerable populations (e.g. children, cognitively impaired) and does not reflect a genuinely voluntary approach to research participation. Finally, while personal data are stripped of identifying information, there is significant concern about how protective encryption measures are in a small population like Iceland.

Table 1 - Characteristics of Genetic Databases Worldwide						
Genebank Location	**General Description**	**Government Role**	**Commercial Involvement**	**Informed Consent**	**Opposition**	**Current Progress / Of Note**
Canadian ***Federal Initiative (CLHI)***[11] http://www.cihr-irsc.gc.ca/e/18542.html	Canadian Lifelong Health Initiative proposed to collect personal and medical information as well as biological samples to examine how genetic and environmental influences contribute to human development, aging, and health outcomes.	CIHR funded	None identified	Not established to date	None identified to date	Development in progress
Quebec ***CARTaGENE Project***[20] http://www.cartagene.qc.ca	To provide a comprehensive source of information on the genetic variation of a large population in Quebec; gene-hunting for common complex disorders, to develop predictive and diagnostic technologies	Provincially funded	None identified	Preliminary study description and consent form with layered options approach available for comment online: (http://www.cartagene.qc.ca/docs/InfoConsent_En.pdfdocuments)	None identified to date	Awaiting ethics approval and integrating the recommendations of the Quebec Ministry of Health and Social Services. Research and related ethical issues to be monitored by an independent body, the Institute of Populations Ethics and Governance (IPEG)
United States ***Utah Pedigree Database (UPDB)***[15] http://www.huntsmancancer.org/groups/ppr/	9 million Utah family and medical records in use to identify specific genetic mutations associated with cancer and other diseases.	Funded through University of Utah institutional and grant funds	Commercial researchers can access anonymized data only; otherwise not involved	Only anonymized data available for statistical analyses unless patient permits contact from external researchers	None	Thriving for 30 years; strong collaboration with academic centres and Church of Latter Day Saints
United States ***The Cancer Genome Atlas Project***[21] .http://cancergenome.nih.gov/index.asp	To further understand the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. Initial targets include lung cancer glioblastoma, and ovarian cancer	NCI/NHGRI funding and oversight	International Genomics Consortium & Translational Genomics Research Institute, of Phoenix, Ariz.,	Ethics, Law, and Policy Group (ELP) was created to guide approaches to consent, collecting relevant family and medical information	None identified to date	Pilot phase for study designs for three target cancers in progress; identifying centres from which to collect data

			will manage TCGA's biospecimen core resource.	and linking it to biospecimens, sharing TCGA data with external researchers, and intellectual property.		
United States ***NHANES III DNA Bank***[22] http://www.cdc.gov/nchs/nhanes.htm.	The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the US population that includes personal interviews, clinical, laboratory and radiological examinations. The associated DNA Bank contains over 7000 specimens In collaboration with NCI, genotyping for 87 variants of 57 genes known to be associated with cancer and other diseases is underway.	Federal funding and oversight	None identified	Separate consents for household survey, medical exam, and collection of DNA sample	None identified to date	In progress since early 1990s.
Iceland Health Database[16] http://www.decode.com/Population-Approach.php	Integration of three databases: the Iceland Health Database (IHD), genealogical records, and the DNA biobank to identify genes associated with common complex disorders	Legislation allowing construction of IHD and biobank passed by Parliament	DeCODE Genetics has exclusive commercial rights to the information in the IHD and authorization to construct biobank	Data protected by 3rd party encryption; presumed consent with opt-out for IHD, informed consent for biobank sample collection	Mannvernd voices significant opposition	License granted to access IHD in 1998 Biobank Act passed 2000 70,000 samples collected as of 2003.
United Kingdom ***UK Biobank***[23] http://www.ukbiobank.ac.uk/	DNA, medical records, lifestyle surveys collected from 500,000 volunteers aged 45-60yrs.	MRC, Wellcome Trust, Dept Health providing 45 million pounds to initiate project	None identified to date	General consent model with 10 key information points included (see Ch 2, p45-6)	Liberty, Genewatch UK	Began 2003, proceeding until 2013
European Union (Finland) ***GenomeEUtwin***	Aims to apply and develop new molecular and statistical strategies to analyze unique European twin and other population cohorts to define and	Funded by European Commission	None identified	Voluntary, opt-in,	None identified	Project started 1 Sep 2002. Project duration is 4 years

[24] http://www.genomeutwin.org/; personal comm	characterize the genetic, environmental and life-style components of obesity, migraine, coronary heart disease and stroke					
Estonia ***Estonian Genome Project***[25] http://scholarsportal.info.myaccess.library.utoronto.ca/pdflinks/0611181439130 8863.pdf	Aims to collect and integrate biological samples, medical records, and genealogical data on 1 million people in order to identify disease genes and deliver "genomic medicine" to Estonians	Estonian Genome Foundation responsible; Human Genes Research Act passed 2000	EGeen Inc. plans to market products to global pharmaceutical industry	Voluntary participation with restricted opt out option	No organized dissent but critics feel priority should be given to under funded health system instead of this endeavour	Pilot occurred in 2002; unexpectedly low number of samples collected (1000). Project expected to continue for 10yrs. EGF has promised participants specific information about their own genotypes and genetic risks over course of study
Latvia ***Latvian Genome Project***[26] http://bmc.biomed.lu.lv/gene/print/Latvian%20Genome%20Project-raksts%20Judith%20Sandor.doc	Medical, genetic and genealogical data	Latvian Genome Foundation (LGF); Human Genome Research Act passed 2002	LGF plans to market access to the database to global pharma industry	Voluntary, opt-in, agreement relates to provision of sample, collection of health and genealogical data, and use for statistical purposes.	None identified	Launched 2001, expected duration 10yrs
Sweden ***Vasterbotten region***[27]	Genetic and medical information from 70,000 40-60yr olds; samples from pre-existing 15 yr old heart study biobank	Swedish MRC granted commercial rights to the database and passed research guidelines	UmanGenomics has exclusive rights to genetic samples from existing medical biobank and rights to commercialize information derived; but only has access to coded samples	Informed consent required from previous donors for each new project	None identified; participation in region's health check-up program remains unchanged	In progress

(iv) Genetic Databases and the Eugenics Movement

While genebanks may make important contributions to our general understanding of disease and improve the public's health, there is considerable opposition to their existence and continued development. In addition to the research ethics concerns highlighted, in part by the Iceland Health Database, there is general opposition to genetic medicine's *reductionist* approach. Primarily, it is the historical and social context of *eugenics* that substantiates these latter objections. Reservations toward genetic medicine are fueled by the fear that systematized knowledge of the human genome might lead to "modern-day eugenics."[28] To appreciate the way in which today's genetic databases may be considered eugenic in nature, a brief history of eugenics is warranted.

Eugenics is a social philosophy which advocates the improvement of human hereditary traits through various forms of intervention. Historically, eugenics aimed to create healthier, more intelligent people, to save society's resources, and to lessen human suffering. Historical means of achieving these goals focused on selective breeding, while modern ones focus on prenatal testing and screening, birth control, and assisted reproductive technologies. Historically, eugenics has been used as a justification for coercive state-sponsored discrimination and human rights violations, such as forced sterilization of persons with genetic defects, the killing of the institutionalized and, in some cases, genocide of races perceived to be inferior.[29] Opponents argue that eugenics is not only immoral but is also based upon poor science.[30]

Selective breeding of human beings was suggested as far back as Plato in *The Republic:* "the best men should have intercourse with the best women as frequently as possible, and the opposite is true of the very inferior."[31] In the 1860s, Sir Francis Galton further defined these ideas, drawing on his cousin Charles Darwin's recent work, *Origin of Species.*[32] He then coined the term *eugenics,* derived from the Greek words *eu (good) and gen (birth)* in 1883.[33] Galton's fundamental argument was that "genius" and "talent" were hereditary traits in humans and since one could use artificial selection to exaggerate traits in other animals, one could expect similar results when applying such models to humans. He further refined his definition of *eugenics* in 1904 as: "the science which deals with all influences that improve the inborn qualities of race; and those that develop them to the utmost advantage."[34]

One of the earliest advocates of eugenic ideas in the United States was Alexander Graham Bell. Based upon the rate of deafness on Martha's Vineyard, he concluded that deafness was hereditary. He recommended a marriage prohibition against the deaf and proposed various immigration controls. Interestingly, his own wife was deaf. Following this and beginning with Connecticut in 1896, many states enacted marriage laws with eugenic criteria, prohibiting anyone who was "epileptic, imbecile, or feeble-minded" from marrying. As director of a biological research program at Cold Spring Harbor in 1898, Charles Davenport had access to the Eugenics Records Office and began to promote eugenics research. During this same time period, researchers attempted to demonstrate a heritable component to mental illness, then seen as a justification for state laws to prohibit marriage and force sterilization of the mentally ill. These laws were

upheld by the US Supreme Court in 1927 and by 1945, over 45,000 mentally ill individuals in the United States had been forcibly sterilized.[29]

Many other Western nations adopted some form of eugenics legislation around this time. In 1933, Germany passed a law allowing for the 'involuntary sterilization of hereditary and incurable drunkards, sexual criminals, lunatics, and those suffering from an incurable disease which would be passed onto their offspring."[29] Nazi Germany remains infamous for its eugenics programs in which extensive experimentation on live human beings, forcible sterilization, and systematic racial killing was rampant. Until the 1970s, sterilization programs also existed in Canada, Sweden, Norway, Finland, Denmark, Switzerland, UK, France, Estonia, and Iceland. Singapore practiced a form of eugenics that encouraged university graduates to marry in the hope that this combination would produce more intelligent children. While some countries, most notably Canada and Sweden, maintained eugenics programs until the 1970s, eugenics became almost universally condemned in response to Nazi abuses. High-school text books no longer included sections on eugenics and scientific journals changed their names and content to reflect an anti-eugenics postwar attitude.[29]

Developments in genetic, genomic, and reproductive technologies at the end of the 20th century, however, have raised many new ethical questions and concerns about what exactly constitutes the meaning of eugenics and what its ethical and moral status is. While medical geneticists and genetic counsellors are not motivated by eugenic goals in their daily work, the combination of advancing technology and society's threshold for

tolerating and financially supporting differences among human beings can make it difficult to ignore a eugenic flavour in the field today. Prenatal diagnosis and preconceptual genetic testing could be conceptualized as two examples of a modern day manifestation of eugenics. While the choices to use prenatal diagnosis itself and to manage potential 'bad news' that may follow are left to the parents, the very availability of the technology and its routine availability to women age 35 years and over compromises the genuine nature of this choice. A less subtle manifestation of eugenics in this context is the not uncommon belief that one aim of this technology is to reduce the birth rates of those with genetic diseases in the population and thereby reduce the emotional and financial burden of individuals with such conditions on caregivers and society in general.[35]

As more disease genes are being identified, identifying disease carriers through preconceptual genetic testing is becoming commonplace. Knowledge of carrier status prior to or during a pregnancy can be used to guide individuals' decisions about mating and reproduction in the first place and/or how to manage information generated from prenatal diagnosis that may ensue as a subsequent step. An oft-cited systemized approach to using preconceptual genetic testing to avoid the birth of unhealthy children is the *Dor Yeshorim Program* (Hebrew: "generation [that is] straight/reliable").[36] An organization that offers genetic screening to members of Orthodox Jewish communities for recessive traits that cause lethal or debilitating diseases common to Jewish people (e.g. Tay Sachs disease), it aims to reduce the incidence of these conditions. Because Orthodox Judaism generally frowns upon selective abortion, Dor Yeshorim argues that avoiding mating between carriers is a better alternative to reducing disease incidence than the lethality of

selective abortion. In opposition to the eugenics-oriented critique it has received, Dor Yeshorim argues that unlike historical eugenics which aimed to eradicate hereditary *traits*, their goal is to reduce the occurrence of homozygosity. Only interested in eliminating "active cases of the disease," they do not aim to eliminate *trait status* and do not test for dominant conditions on which mating has no effect.[37]

Genetic databases represent a further example of a systemized attempt to glean genomic knowledge which, in turn, could fuel technological developments with manipulative and potentially morally questionable outcomes. Based on the historical eugenics movement and the capacity for modern science to 'modify the human species,' attitudes towards genetic medicine and genetic databases, a recent manifestation of this trend, remain guarded. Specifically, the potential involvement of private industry in the development of and profits resulting from these initiatives exacerbates existing cultural resistance to the commodification of the body associated with biotechnology in general.[38]
There are also significant concerns regarding personal privacy (Chapter 2). Many are troubled by the ability of genetic databases to store information for long periods of time, and link it with other health records as well as data related to employment and insurance.

Pervading these concerns is that the emergence of genetic databases will lead to general public distrust of the enterprise of medical research.[39] Given the efforts in research ethics following widespread distrust following World War II (Chapter 2), it would be devastating to the enterprise of medical research to confront another such setback. When the medical research enterprise essentially relies upon a foundation of trust for its progress, any potential threat to this trust warrants deliberation. Navigating the practical

and ethical organization of these databases in order to maximize their benefit and minimize their harm is a daunting task. Examining the process of informed consent, a longstanding and fundamental component of human subjects research, is one way to address the tension between individual and public health interests. Since informed consent can be considered from both theoretical and pragmatic perspectives, it is well-suited to empiric research.

(v) Informed Consent and Medical Privacy

Canadians are ambivalent about the importance of informed consent for the use of health information for research. When asked about the nature of informed consent in a Saskatchewan survey,[40] 62.9% of respondents agreed that "To receive informed consent, health professionals would need to provide details of every anticipated use of health information." 71.4% agreed that "To receive informed consent, health professionals should not have to provide details of every anticipated use of personal health information on every occasion, but should be expected to make this information available on request..." There is evidence to suggest that this ambivalence pervades jurisdictions outside of Canada. In focus groups with members of the Japanese public, for example, views about informed consent for using archived information and biological samples varied widely. Views included unconditional use of information because of an implicit sense of trust in the research enterprise, to complying with reluctance, to wanting veto power and opt-out options, to the insistence on specific and individualized informed consent.[41] This ambivalence combined with the need to balance individual privacy

interests and necessary access to information by researchers creates moral tension and poses difficulties for setting consent policies.[42] [43]

In the conventional research setting, a traditional approach to informed consent (in which risks and benefits are known and explicitly described) can be used since health information is used for a specific and defined research purpose. In contrast, the inordinate number of research questions that will arise and can legitimately be addressed by genetic databases alone, compounded with their link to general health records, makes it impossible to specify future data uses. This context calls into question the traditional approach to informed consent. Not only are the feasibility and moral coherence of traditional consent questionable, there is also concern that requiring specific and continuing consent will inappropriately inhibit research.[44]

Relying on "blanket" and "presumed" consent models which, respectively, lack legal weight in Canada and are autonomy-limiting do not provide an adequate solution. As a policy alternative to existing consent models for genetic database research, Caulfield et al proposed a new ethical/legal framework called the authorization model. Whereas individual informed consent would be required for initial collection of biological material and/or personal health information (PHI), subsequent uses could be carried out under a model of pre-authorization.[44] The Health Care Information Directive (HCID) was developed as a tool by which to facilitate this authorization process.[45]

Innovative strategies are critical to the implementation of new Canadian privacy legislation, particularly because there currently exists no simple manner by which individuals can exercise control over all facets of their PHI. However, the need to protect privacy must be balanced with the need for the health system to collect information necessary to provide and evaluate health services. According to recent federal (PIPEDA)[46] and Ontario provincial (PHIPA)[47] legislation, individuals are required to have the "knowledge of" and "consent to" the collection, use, or disclosure of personal information. The form of consent depends on the sensitivity of the information and the circumstance under which it is obtained. Since the implementation of an authorization model would require legislative change in Canada,[44] careful consideration of its conceptual and practical components is warranted. Empiric data reported in this dissertation will contribute to our understanding of key factors to consider when crafting an approach to informed consent in the context of genetic database research.

(C) Chapter Overview

Chapter 2 provides the theoretical background and conceptual framework around which this investigation was conceived and structured. This chapter begins by providing a historical account of the principle of autonomy in the contexts of *Bioethics* and *Research Ethics* and highlights the shift in thinking to collective rather than individual interests warranted by the emergence of the field of *Public Health Ethics.* Given the investigation's emphasis on research participants' willingness to share personal health information, the complexity of the concept of *privacy* is then illustrated. The conceptual framework is then described by exploring a shift in the conception of *autonomy* through

the lenses of *Rights theory, The Ethics of Care,* and *Communitarianism.* Using these theoretical backdrops, autonomy is conceived of as *traditional*, *relational*, and as a function of the *citizen role*. Like the principle of autonomy, the concept of *trust* plays a central role in the medical research enterprise. This concept is defined and discussed with respect to its relationship with autonomy. The conceptual framework, ultimately, argues for a shift in the conception of autonomy in order to reconcile its inherent tension with trust. Since the process of *informed consent* provides a mechanism through which to respect autonomy and engage in a trusting relationship, the proposed conceptual shift in autonomy warrants a similar shift in how the process of informed consent is conceptualized and implemented for the context of genetic database research.

Chapter 3 reviews empiric literature as well as relevant historical, policy, and legislative documents related to the question of informed consent and genetic database research. Using these sources to highlight the differences between traditional clinical research for which the traditional approach to informed consent was conceived and the modern context of genetic database research, it is argued that the traditional model of informed consent simply does not suit this new context. Alternate models of informed consent that have been proposed and explored in the literature are reviewed. These include *blanket consent, presumed consent, authorization models, and governance structures*. Finally, what is reported in the literature about factors which influence research participants' willingness to share personal health information is reviewed. These factors include the *type* of personal health information requested, the *purpose* for which it is requested, the

type of professional requesting the information, and how the personal information is *stored.*

Chapter 4 provides a rationale for selecting the *authorization model* as worthy of further investigation and defines the research question at hand along with its specific dimensions.

Chapter 5 describes the methodology used to answer the research question at hand. This research used a non-experimental, cross-sectional survey design and collected data using a structured interview guide administered by the researcher. Study participants were recruited from Toronto area teaching hospital clinics that offer genetic testing for a spectrum of hereditary disorders (hereditary non-polyposis colorectal cancer, hereditary breast and ovarian cancer, hereditary hemochromatosis, and thrombophilia). Data were collected using a semi-structured interview guide which included the Modified Health Care Information Directive, a previously piloted tool that coheres with the principles of the authorization model. Quantitative data were analyzed descriptively and using logistic regression and text data were analyzed using a content analysis approach. Ethical considerations specific to the methodology of this research are explained.

Chapter 6 describes the results of this investigation. Quantitative findings are described and illustrated as appropriate. Findings from the content analysis are described and then triangulated with quantitative findings where appropriate. Key findings include: (1) genotype status, self-reported privacy level, and extent to which health information is anonymized are significant predictors of willingness to share personal health information,

(2) type of personal health information and purpose for which it is requested are *not* significant predictors of willingness to share personal health information, and (3) the concepts of trust, safeguards, altruism, and reciprocity are fundamental to understanding these influential factors and can guide the evolution of the informed consent process for the context of genetic database research.

Chapter 7 interprets the study findings in the context of related empiric literature and relevant theoretical underpinnings. It is organized into four sections: (1) response rates and overall sample characteristics, (2) the influence of 'participant characteristics' on willingness to share personal health information, (3) the influence of 'information characteristics' on willingness to share personal health information, and (4) what underlies willingness to share personal health information. Nine conclusions are offered, each of which provides a practical recommendation for how the process of informed consent might evolve for the context of genetic database research.

Chapter 8 describes the conceptual and methodological strengths and limitations associated with this investigation. And finally, *Chapter 9* suggests possible future directions for inquiry.

CHAPTER 2: CONCEPTUAL FRAMEWORK

CHAPTER 2: CONCEPTUAL FRAMEWORK

(A) Bioethics, Research Ethics, and Public Health Ethics

(i) Bioethics and Autonomy

It was in 1971 that the term 'bioethics' first appeared in the literature with Van Rensselaer Potter's book, *Bioethics: Bridge to the Future,*[48] in which he "proposes the term *Bioethics* in order to emphasize the two most important ingredients in achieving the new wisdom that is so desperately needed: biological knowledge and human values." Quickly, the term *bioethics* labeled all academic and professional efforts to address the ethical issues raised by developments in the biological sciences and their application to medical practice. Coining the term *bioethics* coincided with the establishment of institutions focused on the study of ethical issues in medicine. Now The Hastings Center, The Institute of Society, Ethics and the Life Sciences was established in 1969 in order to study and make recommendations on a wide variety of ethical challenges facing the medical field at the time. The Kennedy Institute of Ethics was then established in 1971 at Georgetown University in Washington, DC and was the first to offer a graduate program in bioethics. And in 1976, the Clinical Research Institute of Montreal created the Centre for Bioethics, the first of its kind in Canada.[35]

The modern field of bioethics is new enough that several of its founding members remain active contributors to its current literature. Daniel Callahan, co-founder and past director of the Hastings Center, provides a broad account of the origins of bioethics:

> "Bioethics can surely be spoken of as a child of the 1960s. Four developments were important: the opening up of once closed professions to public scrutiny, which

> happened strikingly with medicine; the fresh burst of liberal individualism, putting autonomy at the top of the moral mountain; the brilliant array of technological developments in biomedicine, ranging from the [contraceptive] pill and safe abortions to control of the beginning of life to control of dialysis and organ transplantation to hold off the end of life; and the renewed interest within philosophy and theology in normative ethics, pushing to one side the positivism and cultural relativism that seemed for a time in the 1940s and 1950s to have spelled the end of ethics as a useful venture."[49]

Notwithstanding the relatively modern and primarily North American beginnings of bioethics, the implicated values systems applied to medical care have ancient roots. Ancient Greek philosophers such as Aristotle and Plato considered issues related to personhood, virtuous behavior by physicians, and rules of medical practice. The first code of medical ethics dates back to fifth century Greece, when the *Hippocratic Oath*[50] was developed. Ancient physicians took this oath, promising to "first, do no harm" to their patients. Despite Hippocrates' teachings, medical practice did not begin to follow some norms of practice or set of regulations until religious movements influenced the field. Christian, Jewish, and Islamic teachings in the Middle Ages (500-1500 C.E.) began to provide ethical grounds for medical practice. *The Prayer and Oath of Maimonides*[51] (ca. 1200), for example, is attributed to the Jewish physician and philosopher, Moses Maimonides. It implores physicians to look upon the sick with empathy and respect, to accept the teaching of their elders in developing their medical skills, and to work to the benefit of all humankind.[35, 52]

In years to come, bioethics became formally integrated into professional codes of ethics. Percival's Code,[53] written by physician Thomas Percival in 1794, was the first code of medical ethics that was adopted by a professional group of physicians. It was eventually used as the starting point in the development of a code of ethics for the American Medical Association[54] which was adopted in June of 1847 and lays out the duties and obligations of physicians to their patients, of patients to their physicians, and of physicians to society and the field of medicine itself. The Canadian Medical Association adopted an almost identical code one year after its establishment in 1867.[35,55]

While the field of bioethics has evolved to include a range of sub-disciplines (e.g. research ethics, environmental ethics, organizational ethics), its historical roots were oriented in the domain of clinical ethics. Clinical ethics is centered around making value-laden decisions at the bedside for an individual in a particular context. The outcome of clinically-oriented ethical reflection is a practical judgment about what should be done for a particular individual at a particular time, taking into consideration their clinical condition, needs, life plans, strengths, and vulnerabilities. Roy[35] suggests that clinical ethics "works with patients' biographies to interpret the meaning of principles; that is to determine what principles command, permit, tolerate, or prohibit for this particular patient." Rebecca Cook[56] refers to this level of analysis as *microethical*; the level of analysis that applies ethical principles to how one person (e.g. the health care provider) treats another (e.g. the patient).

The integration of bioethics into mainstream medical institutions in the 1960s and 1970s coincided with the dramatic shift toward civil liberties and individual rights movements

of the time. This placed further emphasis on attending to individual interests in the clinical setting generally and fueled a further emphasis on patient-centered clinical care. In response to this shift as well as the emergence of guiding documents like the Belmont Report,[57] the doctrine of informed consent and the principle of respect for persons became ever more important in the clinical domain.[52]

Clinical ethics' past and present emphasis on autonomy is exemplified by a range of high-profile ethical/legal cases. For example, the US Supreme Court decision in Roe v. Wade in 1973 reflected the importance women place on the reproductive right to choice in the context of abortion. Louise Brown's successful conception through *in vitro* fertilization in 1978 opened the floodgates for reproductive rights to manifest through the use of assisted reproductive technologies. The beginnings of the HIV/AIDS pandemic in the 1980's raised ethical questions about medical confidentiality and privacy as well as the protection of the dignity of those infected. And in the 1970's and 80's, the widely publicized cases of Karen Ann Quinlan and Nancy Cruzan brought end-of-life issues into focus in the realm of clinical ethics and led to the advent of mechanisms such as advance directives.[52]

(ii) Research Ethics and Autonomy

Research ethics, a sub-discipline of bioethics, has throughout its recent history, been similarly focused on the principle of respect for persons and the doctrine of informed consent. A collection of historical research subject abuses in fact justifies research ethics' past and contemporary focus on autonomy. These illustrative events will be

reviewed in this section and their corresponding 'guiding documents' will be reviewed in Chapter 3 (Part II, Section A).

A colourful history of human subject research abuses opened on December 9, 1946, when an American military tribunal opened criminal proceedings against 23 German physicians and administrators for their willing participation in war crimes and crimes against humanity. Among the charges were that German physicians conducted medical experiments on thousands of concentration camp prisoners without their consent. Most of these subjects died or were permanently disabled following these trials.[58] As a direct result of this trial of 'the Nazi Doctors,' the Nuremberg Code[59] was established in 1948. It states that "the voluntary consent of the subject is absolutely essential." Although it was not legally binding, the Nuremberg Code was the first international document which advocated voluntary participation and informed consent (Chapter 3, Part II, Section A). Ongoing at the time as Nuremberg was the Tuskegee Syphilis Study (1932-1972)[60]. Conducted by the US Public Health Service, 600 low-income African American males were enrolled in a study to monitor the natural history of syphilis. 400 of these individuals were infected with syphilis but were never told of their diagnosis, even when penicillin (a proven cure) became available in the 1950s. This deception continued until 1972 at which point the study was publicized and stopped. Needless to say, many individuals died of syphilis over the course of these 40 years.

A third example of human subject research abuses occurred in New York City's Jewish Chronic Disease Hospital in 1963.[61] Interested in learning about the nature of the human

transplant rejection process, chronically ill patients who did not have cancer were injected with live human cancer cells. The physicians did not inform the patients as to what they were doing. The physicians rationalized their approach by suggesting that (i) they did not want to scare the patients and (ii) they thought the cells would be rejected. Concurrently (1963-1966), at Willowbrook State School in New York State, parents of mentally handicapped children in the institution gave consent for their children to participate in a study about the course of viral hepatitis and the effectiveness of an agent for inoculating against hepatitis.[62] Parents were provided with study information describing the drug administration as vaccinations. However, the children were deliberately infected with the hepatitis virus. There is evidence that the school only admitted children to the school whose parents gave permission for them to be in the study.

Similarly, research in psychology and social science at this same time was not without its ethical problems. The Milgram obedience studies[63] and the Stanford Prison Experiment[64] are paradigmatic experiments conducted on subjects who were deceived as to their role in the study. Similarly, the "Tearoom Trade" affair was a study conducted by Laud Humphreys in 1974 in which he spied on unknowing men engaging in anonymous sexual acts the in restrooms of public rest stops. He then tracked down the men's identities (using their license plates and public records) and interviewed them about their private lives and sexuality.[65]

These and other research studies were included in Henry Beecher's critical survey of twenty-two medical research projects conducted in the United States following World

War II.[66] Documented in his review was the evidence that many research participants were not aware that they were even involved in research, were not provided with information about potential study risks, and were not asked to consent to participate. As a result of these oversights, Beecher's paper emphasizes the importance of informed consent as well as the "presence of an intelligent, informed, conscientious, compassionate, responsible investigator."

While some have criticized the fields of bioethics and research ethics for being "damagingly preoccupied" with the notion of autonomy[67] and neglectful of ethical problems inherent in public health research and practice,[68] the evolution of their modern histories certainly justifies this preoccupation. However, as a result of the current debates around universal health care, the persistence of infectious disease, the recognition of the social and economic determinants of health, and the applicability of biotechnology to our understanding of common chronic disease, the fields of public health and public health ethics are gaining ground.[69]

(iii) Public Health Ethics and Collective Interests

A heightened interest in public health research and practice has engendered a scholarly focus in the area of Public Health Ethics. This new interest is reflected by extensive academic writing in the area, [70] [71] [72] [73] [74] efforts to develop public health ethics curricula for graduate education,[75] [76] [77] the emergence of public health ethics interest groups and forums at international gatherings,[78] and the development of a Public Health Code of Ethics.[79] Public Health Ethics attempts to ground ethical dilemmas that confront public

health practice and policy in principles that reflect collective interests and the common good. Public Health Ethics scholars have appropriately recognized the limitations of traditional ethical principles (autonomy, beneficence/non-maleficence, justice) in this context and have developed an expanded repertoire of reasoning tools to apply to the interests of the 'public.'

Difficult is the tension, however, between the predominant orientation in favor of civil liberties and autonomy found in bioethics and the communitarian orientation supporting the field of Public Health. While traditional bioethics can coherently apply its individualistic orientation to the problems of clinical medicine and research and Public Health Ethics can coherently apply a communitarian lens to its dilemmas, the real challenge for these converging fields is to guide our moral reasoning when individual and communitarian values come into conflict. Respecting individual privacy rights in the context of genetic database research presents one scenario in which a value tension requires resolution in order for this particular research enterprise to proceed harmoniously.

Public Health Ethics offers five conditions which can be applied to the tension between the public health goals of this type of research and the preservation of individual interests like privacy.[72] The *effectiveness* condition says that it is essential to show that infringing upon a moral consideration will protect or promote public health. Advocates of database research and molecular scientists would argue that understanding disease causation and improving treatment are contingent upon public participation and that individual liberties

should be respected but should not limit potential medical advances. Critics question the projected value of the research itself and defend intrinsic individual rights.

The *proportionality* condition is intended to show that the *probable* public health benefits of a program or intervention outweigh the infringed moral considerations. *Probably* genetic database research is a proportional approach to understanding certain diseases, but the true certainty of its benefits and risks remain unknown. While database research may be effective and proportional, the *necessity principle* says that it may not be necessary to infringe upon individual liberties in order to accomplish its goals. The ideal scenario would be to develop a protocol in which individual privacy rights remain intact while scientific research proceeds. Meeting the *least infringement* condition requires authorities involved in organizing and implementing database research to minimize infringement upon individuals. Data management strategies such as coding and anonymizing personal information and samples are examples of minimizing infringement on individual privacy. The extent to which these records are linked to identifiable clinical records remains controversial. Minimizing infringement is consistent with the *least restrictive means* principle that Upshur has applied to the context of database research.[70]

Finally, *public justification* is a key condition to establishing public trust in any public health initiative. The *transparency* principle[70] suggests that all stakeholders should be involved in public deliberations and that decision making should be accountable and free of political interference. While political context will inevitably shape certain outcomes,

an engaged and trusting public will mitigate this influence. Genetic databases vary in the extent to which they have engaged key stakeholders in their development. Many argue that concerns related to privacy infringement and community exploitation are a result of insufficient public consultation.[19]

According to the guidance of these conditions, it should be possible to achieve the public health goals of genetic database research while simultaneously preserving individual liberties. This reconciliation, however, requires moral reflection, empiric evidence, and engagement with the academic community as well as the general public.

(B) The Concept of Privacy

The *Oxford English Dictionary, Second Edition* defines privacy as "the state or quality of being *private*:

> 1a. The state or condition of being withdrawn from the society of others, or from public interest; seclusion; b. The state or condition of being alone, undisturbed, or free from public attention, as a matter of choice or right; freedom from interference or intrusion.
>
> 2a. Private or retired places; private apartments; places of retreat; b. A secret place, a place of concealment.
>
> 3. Absence or avoidance of publicity or display; a condition approaching to secrecy or concealment"[80]

As is reflected by this definition, privacy is a complex concept with a range of possible interpretations. Context largely determines whether privacy is manifesting as a moral value or a legal right. This section will focus on the moral value of privacy – both intrinsic and instrumental. The discussion of privacy legislation in Chapter 3 Part II Section A will reflect the interpretation of privacy as a legal right.

Some commentators believe that privacy has intrinsic value and defines one's essence as a human being. Included in this essence are individual dignity, integrity, personal autonomy, and independence. According to Bloustein,[81] respect for these values unifies the concept of privacy. From his perspective, an invasion of privacy is best understood as an affront to human dignity.

Others focus on the instrumental value that privacy affords. A context relevant to this research and consistent with an 'instrumental' emphasis is to orient privacy around control over personal information. Westin[82] for example, describes privacy as the ability to determine for ourselves when, how, and to what extent information about us is communicated to others. Parent[83] characterizes personal information as factual- facts that most people choose not to reveal about themselves related to health, salary, weight, and sexual preferences. Gavison[84] frames a similar interpretation of privacy as an issue of access; what others know about us and the extent to which they have physical access to us. She believes that one has perfect privacy when one is completely inaccessible to others. This level of privacy can be gained through secrecy, anonymity, or solitude. Opponents of the control/access viewpoints argue that conceiving of privacy as control

over/access to information is an insufficient interpretation because (1) a person can have privacy without having any control over others' access to their information and (2) privacy is not limited to the context of accessing personal *information* alone.[85]

A further interpretation of privacy links it with the intrinsic and instrumental value inherent in intimate and social relationships. Fried[86] argues that privacy has intrinsic value and is fundamental to one's development as an individual with a moral and social personality able to form intimate relationships involving respect, love, friendship, and trust. That privacy enables one to assert control over information about oneself in turn allows one to maintain varying degrees of intimacy. Love, friendship, and trust are only possible if people have privacy and afford it to others. Constructs such as love, friendship, and trust can be viewed as manifestations of the instrumental value of privacy. Rachels[87] extends this view beyond intimate relationships to a range of social relationships. By controlling who knows what about us and who has access to different levels of information, we can vary our behavior with different people so as to maintain control over social relationships. We invoke different levels of privacy depending on with which party we interact, balancing the advantages gained by releasing information against the possible risks of inappropriate use of the information we provide.

Petronio's Communication Privacy Management Theory[88] brings many of these perspectives together. Her theory suggests that individuals "develop a series of privacy rules regarding why, how, and to whom they will disclose private information based upon conceptions of information ownership, the risks and benefits of disclosure, and the nature

of the relationship between the parties sharing information." It is reasonable to speculate that these dimensions influence research participants' decisions regarding sharing PHI.

(C) Overview of Conceptual Framework

The conceptual framework that positions this research explores the tension presented by genetic database research as a transition from individual to population-based research ethics using three theoretical perspectives: Rights theory, Ethics of Care, and Communitarianism. To then justify a necessary evolution in the process of informed consent, these moral lenses will be applied to the concept of *autonomy* and its relationship with *trust*. The concept of privacy as previously introduced is woven into this exploration.

Specifically, I will attempt to illustrate how moral theory lays the groundwork for the shift in our thinking about the concept of autonomy. I will then describe the classic tension between the concepts of autonomy and trust, after which I will argue that these values are indeed compatible when autonomy is considered relational and trust is appropriately located. I will then propose that one way to, simultaneously, respect the principle of autonomy and express trust is to engage in the process of informed consent. Why this conceptual shift necessitates an evolution of the process of informed consent for the purpose of genetic database research will be described briefly in this chapter and elaborated upon in Chapter 3.

(D) Moral Theory

(i) Rights theory

That moral theory should be "rights-based" stems from the belief that the function of morality is to protect individual interests. According to liberal individualism, individual rights are the fundamental tools by which a given end is achieved. Given the individual rights-based origins of clinical and research ethics, it is appropriate to consider the theoretical underpinnings of this perspective. Beauchamp and Childress[89] suggest that "no part of the moral vocabulary has done more to protect the legitimate interests of citizens in political states than the language of rights." Bearing rights is both a source of personal protection and a source of dignity and self-respect.

Rights-based theory emphasizes that, in a democratic society, a certain space must be carved out within which an individual is protected and allowed to pursue personal projects. Rights that are entitled to fundamental protections include those related to life, liberty, expression, and property. Rights are justified claims that individuals and groups can make upon others or upon society. To have a right is to be in a position to determine, by one's own choices, what others are to do and need not do. *Legal* rights are claims that are justified by legal principles and rules and *moral* rights are claims that are justified by moral principles and rules. By this definition, a right is a justified claim or entitlement validated by moral or legal principles or rules. If a person possesses a right, others are legitimately constrained from interfering with the exercise of that right. If an individual is compromised in his/her ability to assert his/her rights, as in the case of children or

those with insufficient mental capacity, they need not lose their inherent rights. Rather, claims can be made on their behalf by authorized representatives.[89]

The fact that one individual's rights may impose constraints on another individual's behavior implicates a relationship between rights and obligations and therefore a relational component to rights-based theory more generally. "If X has a right to do or have Y, then X's right entails that some party has an obligation either not to interfere if X does Y or to provide X with Y."[89] If an institution has an obligation to provide some form of health care to its citizens, for example, then citizens can claim an entitlement to this health care. However, obligations do not always imply corresponding rights; this correlativity is imperfect. An individual's perceived obligation to give to charity, for example, does entitle the recipient to claim this gift as a right. Using the distinction between perfect and imperfect obligations helps to reason through the correlativity of rights and obligations. Justice is a perfect obligation and entails a correlative right; whereas kindness and charity are imperfect obligations and do not entail correlative rights. Mill argued that, "Justice implies something which is not only right to do and wrong not to do, but which an individual person can claim from us as a moral right. No one has a moral right to our generosity or beneficence because we are not morally bound to practice those virtues towards any given individual."[89] So obligations of justice are perfect and the correlativity thesis always holds but some obligations of beneficence (e.g. kindness, charity) are imperfect and may not have correlative rights.

The perspective that ethical reasoning should be rights-based is consistent with the belief that the function of morality is to protect individual interests rather than communal interests and that rights (rather than obligations) are our primary instruments to this end. Framed this way, rights precede obligations. The primacy of rights over obligations is endorsed by Robert Nozick[90] and Alan Gewirth.[91] Nozick suggests that "Individuals have rights and there are things no person or group may do to them without violating their rights."[90] He believes that all persons have the right to do as they choose and that an obligation not to interfere with this right follows from the right itself. That is, an obligation is derived from a right. Similarly, Gewirth argues that "respondents" have correlative obligations *because* "subjects" have certain rights:

> "Rights are to obligations as benefits are to burdens. For rights are justified claims to certain benefits, the support of certain interests of the subject or right-holder. Obligations on the other hand, are justified burdens on the part of the respondent or duty-bearer; they restrict his freedom by requiring that he conduct himself in ways that directly benefit not himself but rather the right-holder. But burdens are for the sake of benefits, and not vice-versa. Hence, obligations which are burdens, are for the sake of rights, whose objects are benefits. Rights then are prior to obligations in the order of justifying purpose..."[91]

Nozick's and Gewirth's accounts do not reject the correlativity thesis, rather they hold that obligations follow from rights, not the converse. Rights take precedence over obligations because, from this theoretical perspective, the purpose of morality is to secure liberties and benefits for a rights-holder.

While committed to the primacy of individual rights, rights theorists acknowledge that communal life and human relationships provide the necessary context for the development and assertion of the self.

(ii) Ethics of Care

According to the Ethics of Care, *caring* refers to care for, emotional commitment to, and willingness to act on behalf of persons with whom one has a significant relationship. Downplayed in this approach are Kantian rules, impartial utilitarian calculations, and individual rights.[89] The origin of the Ethics of Care was predominantly in feminist writings. Gilligan[92] maintained that women's moral development is typically different from men's. Through her empiric research with girls and women, she identified "the voice of care" which, she claimed, stresses empathic association with others, not based on "the primacy and universality of individual rights, but rather on a very strong sense of being responsible." While the 'rights-obligations' language does not characterize dialogue amongst ethics of care scholars, these scholars likely believe that moral action is more a function of an obligation (rooted in care and/or responsibility) than of a fundamental right. She claims that whereas men tend to see morality in terms of rights and justice, women tend to view morality in terms of care responsibilities driven by attachments to others. In their description of Ethics of Care, Roberts and Reich[93] emphasize that real people live in families and that traditional philosophical theories have ignored the family life in particular. Further, real caring relationships such as familial ones embody inequalities of power, capacity, judgment, information, and responsibility. Similarly, Baier[94] rejects traditional philosophy's emphasis on justice, rights, and

autonomy of free and equal agents. She argues that social cooperation requires negotiation among unequals in a relational network and, therefore, recommends that an ethic of love and trust be integrated. Unlike traditional philosopher's depiction of emotions, feelings, and inclinations as distracting impediments to moral judgments, the Ethics of Care downplays this "cognitive bias" by giving emotions and attachments a moral role.

(iii) Communitarianism

Communitarian ethics views that everything fundamental in ethics is derived from communal values, the common good, social goals, traditional practices, and cooperative virtues. Communitarians use these values, rather than those related to individual welfare, to guide social policy. They propose that we replace the language of rights with the language of common good and the community's way of life. Communitarianism and the Ethics of Care share an emphasis on relationships, but communitarianism brings the priority of relationships to the level of community, politics, and social welfare. In light of this scope, a range of meanings of *community* are acceptable to communitarians. *Community* can refer to the political state, a small community itself, an institution, or a family unit. Communitarians believe that what one ought to do is determined by the social roles assigned to or acquired by a person as a member of a given community.

Radical communitarians reject central tenets of rights-based theory; what Mill defended as *individuality* and what Kant called *autonomy.* They believe that rights-based theories fail to (1) appreciate the constructive role of cooperative virtues and the political state in

creating conditions of a good life, (2) acknowledge shared goals and obligations that come from communal ideas and responsibilities, and (3) understand the individual as constituted by and embedded in communal life and social roles.[89]

When individual rights and community interests are viewed as dichotomous (as radicals from each perspective would argue), tension looms. In order to reconcile this tension, moderate communitarians emphasize the importance of various forms of and roles within a community, but attempt to accommodate rather than reject components of liberal theories. As Friedberg[95] writes on liberalism, "It is impossible to think of human beings except as part of ongoing communities, defined by reciprocal bonds of obligation, common traditions, and institutions…The ideal (in liberals' accounts) of the autonomous person is that of an authentic individual whose self-determination is consistent with the requirement that he is, of course, a member of a community."

A liberal individualist theory, utilitarianism speaks to the construct of community as one that is an aggregate of individual interests. Given Public Health Ethics' emerging role in reconciling the tension between individual and community interests, it is worthwhile to consider some utilitarian ideals in working through this reconciliation. Originally proposed by Jeremy Bentham, the rule of utility stated that "the good is whatever brings the greatest happiness to the greatest number of people." After realizing that the morality of an action is not determined by the number of people made happier, but rather the quantity of happiness produced, Bentham dropped the misleading "greatest number" part of the principle, replacing the original formulation with the more direct "greatest

happiness principle." So appealing to the community at large is not a specific interest of utilitarians. As well, end-oriented in nature, utilitarians are less concerned with intentions, motivations, and process than are ethics of care and communitarian scholars. Given the importance of the trusting relationship between research investigators and participants, a theoretical lens that does not emphasize a relational, dialogical process is arguably not best-suited to understanding the context of genetic database research.[85] For these reasons, a utilitarian orientation was not further pursued as fundamental to this conceptual framework.

Essentially communitarian in nature with an emphasis on process as well as appealing to the greater good, the domain of Public Health Ethics has evolved to provide some moral guidance to the field of public health. While it has yet to achieve the theoretical rigor of classic moral theory, it offers reflective principles by which to consider quandaries relevant to public health research and practice. The Public Health Ethics principles of mutuality, solidarity, universality, and citizenry are integrated into the exploration of autonomy that follows.

(E) Conceptions of Autonomy

Implicit in the aforementioned description of moral theory is the concept of autonomy. The following section links the fundamental values of each moral theory with its respective conception of autonomy. Rights theory considers autonomy in its traditional sense, Ethics of Care scholars consider autonomy as relational, and Communitarians

consider autonomy as fundamental to the citizen role. The concept of privacy is woven into each of these perspectives.

(i) Traditional Autonomy

The concept and principle of respect for autonomy is fundamental to moral reasoning. The word *autonomy* is derived from the Greek *autos* ("self") and *nomos* ("rule," "governance," or "law"). It was first used to refer to the self-governance of independent cities, states, and nations. *Autonomy* has since been extended to individuals and has acquired a range of meanings including: self-governance, liberty, individual choice, freedom of will, and being ones' own person. Consistent among all traditional interpretations of *autonomy* are two conditions: (1) liberty (independence from controlling influences) and (2) agency (capacity for intentional actions).[89]

The principle of respecting autonomy requires an acknowledgement of a person's right to hold views, to make choices, and to act based on personal values and beliefs. Immanuel Kant and John Stuart Mill offer insight as to *why* such respect is owed to individuals. Kant argues autonomy should be respected because individuals have unconditional worth and the capacity to determine his/her own destiny. To violate a person's autonomy is to treat him/her as a mere means which runs in conflict with his/her capacity to determine his/her own destiny. Unlike Kant's moral imperative, Mill argues that respecting autonomy is due because personal convictions should drive individual life plans as long as they do not interfere with the freedom of others. Mill also argues that without security,

a society fails to provide a necessary condition for happiness or utility. Autonomy is necessary to ensure this sense of security which is, in turn, grounded in utility.[96]

One assertion of this traditional definition of autonomy can take the expression of individual rights. An assertion of autonomy that is fundamental to this research is the right to privacy- both the freedom and capacity to make individual choices about the collection, use, and disclosure of personal health information. Regardless of the consequences of a given privacy violation in the context of research ethics, rights theorists would support the protection of the fundamentally intrinsic value of privacy; protected not because its protection will produce good consequences but because a good or meaningful human life would be impossible without it.

(ii) Relational Autonomy

Feminist critiques of the traditional conception of autonomy argue that the capacities of the "self" cannot be adequately undertaken without attention to the rich and complex social and historical contexts in which agents are embedded. They point to the need to think of autonomous agents as not only rational but also emotional, creative, and feeling.[97] An appreciation for the "non-cognitive" elements of agency implicates relationships. With this in mind, *relational autonomy* can be understood to involve the explicit recognition of the fact that autonomy is defined and pursued in a social context and that social context influences the opportunities an agent has to develop and express his/her autonomy. This is consistent with the Ethics of Care both in its line of reasoning as well as the feminist orientation of the scholars supporting this view. Autonomy is not

viewed as an achievement of individuals, but rather as a function of social context. Advocates of this approach suggest that we need to explore a person's "social location" in order to properly understand his/her expression of autonomy.[98]

Fundamental to any relationship – and certainly those that occur in the context of research participation- is communication. Habermas' well known theory of *communicative action* can be understood as "a circular process in which the actor is two things in one: an *initiator,* who masters situations through actions for which he is accountable, and a *product* of the transitions surrounding him, of groups whose cohesion is based on solidarity to which he belongs, and of processes of socialization in which he is reared."[99] It is noteworthy that the conception of the individual in yet another context, communication theory, is understood to be a function of relationships.

Also fundamental to the notion of relationship is the principle of *reciprocity*. Specific to the medical care/research context, Knoppers and Chadwick[100] describe the reciprocity principle as one that supports the exchange of information between patient and provider or research participant and investigator. The investigator provides the potential participant with as much detail as possible with respect to study goals, potential benefits and risks, security measures, possible future uses, and potential for commercialization in order to equip him/her with the necessary information on which to base a decision that is consistent with his/her personal and cultural values as a participant. A frank and transparent discussion of these values and the participant's decision process is certainly encouraged and enhances the reciprocal nature of this exchange. Not only is it valuable

to honour reciprocity in order to explore and appreciate participants' contexts, it also serves as a guiding principle through which to assess and discuss participants' expectations regarding the extent to which researchers will communicate with them generally and disclose medically relevant findings that ensue from the research.

Another interpretation of the reciprocity principle extends beyond participant-investigator or interpersonal dyads to the community or population level. When genetic researchers consider founder effect and candidate gene studies in homogeneous populations, prior consultation with these communities is becoming an "ethical prerequisite." Again, this engages community members in a transparent process that considers important cultural values. An exchange of scientific information and cultural values can only enhance the collaboration among interested parties.[100]

Also emphasizing the relational nature of individuals, Rhodes[101] references Aristotelian notions of social bonds. She reminds us of the saying 'blood is thicker than water' and highlights four considerations to be granted moral weight in assessing and defining our autonomously-driven duties: family relationships, social relationships, the history of relationships, and the particulars of the relationship and situation. The moral weight that blood ties carry in defining our moral responsibilities is linked not only to the biological relationship but also to the social bonds implicated therein. Consistent with this reasoning, Kenan[102] speculates that advances in genetic technologies may fundamentally alter the way we view ourselves in relation to others. An obligation to reveal genetic information about oneself to their kin, for example, represents a shift away from the

traditional view of the autonomous self to a more "interdependent" self, in which the needs of significant others are considered an integral part of the self. This begins to question the primacy of rights over obligations.

An assertion of the right to privacy from this perspective would consider privacy from the perspective of a relationship – what is sacred and warranting protection between two or among many individuals. Not only would an assertion of privacy reflect what information is to be protected in the interest of a relationship, but also what information warrants sharing in order to preserve or enhance the trusting nature of a given relationship. Hallowell's[103] empiric study of women attending genetic counselling for hereditary breast and ovarian cancer supports this claim. Following a genetic counselling session, 40 women were interviewed. Women attended genetic counselling as a first step towards taking responsibility for their risks and were influenced by obligations to their kin. Women, reportedly, justified their actions almost exclusively in terms of the implications for others. Women perceived a personal responsibility to determine and manage their risks for the sake of past, present, and future generations; "maybe if I find out that I do have this gene…I can be more honest with myself and *honest with the family…*" Women *felt a duty to disseminate this information to their relatives*, and a responsibility to encourage them to act on it; "I mean I am not on a crusade to get everyone going (to screening), but I would like to think that (the family) thought it as important an issue as I do. I really do want (my sister) to go…she's got daughters you know…" Overall, genetic information was perceived as information about the family and, as such, women perceived an obligation to ensure that this information would be

shared with their kin. The principle of *mutuality*[100] speaks to a more open model of information sharing. Given the familial nature of genetic information, this principle justifies information sharing within families rather than one individual's discretionary control over access.

(iii) Autonomy and the Citizen Role

Not only is it argued that autonomy is a function of relationships, social bonds, and social duties, Corrigan[104] asserts that autonomy and free will should not be conceived of as politically innocent. She brings the relational conception of autonomy to the level of the population and the citizen's role within it. She describes concepts of biological or scientific citizenship which are active forms of citizenship and reflect assertions of autonomy in a pluralistic and political context. Specific to the enterprise of population-based research, she argues that the public "needs not only to know what is going on with respect to database research in general but expects to be given an opportunity at the outset to negotiate what counts as the common good…people want to make choices as citizens cognizant of common good, not simply as individual consumers." Consistent with the principle of *citizenry,* [100] this conception of autonomy reflects an inextricable link between individual agency and a commitment to the common good.

Chadwick links autonomy with the principle of *solidarity.*[105] Like Dworkin's concession that when "the claims of public utility are very significant, individuals are not justified in playing their [individual rights-oriented] trump cards,"[106] Chadwick argues that a right to refuse to participate in population-based genetic research should not necessarily override

the benefits this research could bring to others. She believes, on the contrary, that one has a duty to facilitate research progress and to provide knowledge that could be crucial to the health of others. Unlike Nozick[90] and Gewirth[91] who advocate for the primacy of rights over obligations, Chadwick's commitment to solidarity would lend itself to the converse rationale.

Hoeyer and Lynoe[107] advance an anthropological perspective that emphasizes social responsibility as fundamental to research participation. From their Swedish perspective, the historical interpretation of the 'welfare state' implies mutual responsibility: the state has the right to make health care decisions on behalf of its citizens, and the citizens are obliged, in a sense, to contribute to common efforts. Rhodes[108] believes so strongly in this civic duty that she goes so far as to propose a requirement for "every US resident to perform some research service every ten years…while each of us would be required to serve as a subject in some research study, we would be left the freedom to choose the particular project for our service from a national website…" The extent to which research participation can be considered a universal duty is debated in the literature. More moderate writers counter that while research participation is a valuable civic activity that should be encouraged and praised, it is akin to other community service roles like school-tutoring and volunteer fire-fighting and cannot therefore be required of everyone.[109] Williams[110] reminds us that there is considerable disagreement as to what constitutes desirable research and acceptable risk. A duty-bound system would subject some individuals to riskier research than others which could conflict with our

commitment to distributive justice. Viewing research participation in this light deems the use of Rhodes' conscription system as inappropriate.

Whether or not it is an absolute duty or a perceived civic responsibility, what motivates this interest in the common good? Some argue that research participants are driven by pure altruism.[111] Webster's Dictionary defines altruism as "the quality of unselfish concern for the welfare of others."[112] Altruists construe their donation of personal information and biological samples as 'gifts.'[113] With respect to genetic research in particular, the Human Genetics Commission endorses this motivation by suggesting that genetic knowledge may bring people into a special moral relationship with one another. The Commission proposes the concept of '*genetic solidarity and altruism*,' which promotes the common good (2.11): "*We all share the same basic human genome, although there are individual variations which distinguish us from other people. Most of our genetic characteristics will be present in others. This sharing of our genetic constitution not only gives rise to opportunities to help others but it also highlights our common interest in the fruits of medically-based genetic research.*" [114] Alternatively, Chadwick[105] suggests that a perceived duty to help others is motivated by *constitutive solidarity* in which individuals have an interest in common and by doing so, achieve a better outcome for themselves. For example, a group of individuals could collectively choose to enroll in a genetic database for the sake of the common good, and in turn, achieve better health care for themselves.

Modern thinking about the principle of *universality*[100] is rooted in the characterization of the genome itself as a shared resource. While it is a controversial expression, referring to the genome as the "common heritage of humanity" emphasizes its shared benefit to the public. The idea of the genome as a global public good, demonstrated by the creation of international, publicly accessible genebanks, is a manifestation of the universality principle. Regardless of the motivation to act in the interest of others, this conception of autonomy considers acting in the interest of others as a genuine component of what one desires for oneself.

Unlike individualists' protection of the intrinsic value of privacy, those committed to the principles of reciprocity, mutuality, citizenry, solidarity, and universality would be more inclined to share information than protect it in order to facilitate medical discovery for the common good. This reflects an emphasis on instrumental rather than intrinsic value of privacy. Conceived of this way, a willingness to share information comes from a desire to benefit others over and above, or in addition to, an autonomy-driven motivation to protect oneself. Ideally, one might conceive of a structure that both respects individuals' privacy rights *and* facilitates the use of individuals' information for the common good derived from medical discovery.

(F)Autonomy and Trust

The paradigm shift from traditional genetics research to public health genetics research warrants an exploration of the relationship between core values of the research enterprise: autonomy and trust. According to Webster's dictionary, to trust is to "believe in the

honesty and reliability of others, to have confidence or faith in, and to allow without fear."[115] Baier[116] describes trust as "a confident belief in and the reliance upon the ability and moral character of another person and a confidence that another will act with the right motives in accord with moral norms." Trust is fundamentally relational; it is placed in others whom we can rely on to take our interests into account. Trust is both interpersonal and systemic in the sense that it can be placed in individuals, groups, institutions, or social structures.[117]

In Plato's *The Republic,*[31] his older brother, Glaucon, argues that if one is not confident that others are sufficiently afraid of detection and punishment, one should expect others to harm or steal for their own self-interest. One should therefore act defensively and pre-emptively. In this view, trust manifests only if the 'trusted' is sufficiently afraid of punishment such that he/she does not act in his/her own self-interest.[118] More optimistically, Hume[119] appreciates that, in general, instincts are to care for loved ones and sympathize with others' feelings. He writes that "sympathy makes human beings mirrors of each other." This gives human beings a desire for company, the benefits of which can be gained from a union giving them a desire for company and the advantages this brings. Bailey's[118] interpretation of Hume[119] on trust is that, "love and sympathy of this kind would ensure that there would be more trust, and therefore more cooperation and peace generally…" In other words, people may act positively towards one another simply because they are loved.

While Plato argues that reliance on others is a function of fear of detection and punishment and Hume emphasizes the value of love and sympathy for reliance, Bailey[118] puts forth the notion of 'taking responsibility.' Trusting as a function of detection, punishment, love, or sympathy, is indirect. One cannot be genuinely trusted if he/she is relied upon *only* by resorting to such things. 'Taking responsibility' is part of being a friend, a partner, and a professional, for example. In a personal relationship, genuine trust cannot manifest unless the trustee believes that the trusted has taken responsibility for the particular, intimate role which they play in their life. Similarly, we may trust a doctor to prescribe appropriate treatment, and rely on her because she has taken responsibility for her role in our decisions about our health.

Trust flourishes between those who are positively linked to one another, whereas an individualistic conception of autonomy flourishes when we are least constrained by others and we have the 'space' to do our own thing. Trust belongs with relationships and mutual obligations; individualistic autonomy belongs with rights and (often) adversarial claims. Autonomy will continue to bear hard on relations of trust if understood as simply individualistic.[120] Hills,[121] however, describes Kant's emphasis on the idea that trust is not only crucial to help achieve the benefits of cooperation and joint ventures, but also to our fundamental respect for ourselves and others.

In order for public health genetics research to proceed in a morally coherent manner, the tension between autonomy and trust needs to be reconciled. Reconciling the tension between autonomy and trust requires shifting our conception of autonomy from one that

is starkly individualistic to one that is relational and, further still, reflective of the principle of solidarity. It also requires the recognition that the *locus of trust* for an individual, a community group, or a population engaged in medical research is a function of research context. For example, an individual considering participating in a research trial investigating a potential gene therapy likely places his/her trust in the principal investigator and/or physician affording him/her the opportunity. A family or small community invited to participate in a gene-hunting protocol might place its trust in a particularly well informed or invested family member, a community leader, or the institution executing the study. And a large population ascertained for a longitudinal cohort study examining genetic and environmental risk factors associated with a common disease might defer its trust to the governing structures built into the research enterprise itself. Governance structures could take the form of research ethics boards, policy statements, data guardians, or data safety monitoring boards.[122] [123]

Kass et al[124] provide empiric data to support how the locus of trust can vary. The US Advisory Committee on Human Radiation Experiments interviewed 100 outpatients about their experiences with and attitudes about research. They found that research participants place trust in (a) *physicians*, "To me, they are the doctors, and once I had gotten those doctors and I trusted them . . . it was pretty much up to them. I wanted to know what I was going to be going through as far as what to expect . . . but a lot of the little nitty-gritty detail, I did not even want to know." (b) *institutions*, "I think I've got the best treatment down there at [named hospital]. I don't think I could get any better." Similarly, "If it's not through [named hospital], I wouldn't touch it," and (c) *the research*

enterprise itself, ""They know what they're doing. They wouldn't have you do this if they didn't know what they were doing."

The concepts of autonomy and trust can be reconciled when both concepts, as well as the nature of the research context, are considered in tandem. Conceiving autonomy as individualistic is appropriate when the goals, risks, and potential benefits of research participation can be explicitly defined by an investigator in whom trust can be placed. However, autonomy must be conceived as relational or pluralistic when the goals, risks, and potential benefits of research participation cannot be explicitly defined by an investigator such that trust can only realistically be placed in social/governance structures which protect the common good. The process of informed consent is one mechanism by which to operationalize this reconciliation.

(G) Informed Consent – A Necessary Evolution

The process of informed consent is a fundamental part of maintaining the moral integrity of the medical research enterprise because it provides a practical mechanism through which researchers can respect the principle of autonomy and participants can express trust in a given research endeavor. Based on information they are given through the informed consent process, participants trust that study risks will be properly managed, that their participation is for good reason, and that the research will be carried our according to legal and ethical rules.[123] How autonomy is respected and trust is expressed, both philosophically and practically, is a function of the particular research context. As public health genetics gains ground as a new research context, an evolution of the process

of consent is warranted. Chapter 3 will explore the spectrum of consent models which have been applied to the area of genetic database research and will demonstrate why the traditional model of consent is not well suited to this context and why the authorization model is most worthy of further exploration.

CHAPTER 3: LITERATURE REVIEW

CHAPTER 3: LITERATURE REVIEW

PART I: Approach to Literature Review

In order to present a comprehensive review of the literature in this area of research, peer-reviewed indices (Pubmed, Psychinfo, and Bioethicsline) were carefully reviewed. Key-word and author-specific searches were conducted as appropriate for each of the following sections. References other than scientific journals (e.g. text) were identified through peer-reviewed papers as well as keyword/author searchers in the "University of Toronto Catalogue." Some materials were most accessible on the world-wide-web and were examined and downloaded accordingly (e.g. guiding documents, policy statements, legislation, and public opinion research). Searches were tailored to identify literature reflecting what is known about consent policies, approaches to informed consent for genetic research, and factors that influence patients' and research participants' willingness to share personal health information. Effort was made to synthesize the most current literature, rather than to provide a historical perspective on the evolution of these areas of research over time. Ultimately, this review presents salient and current research in this area and substantiates the goals of the proposed study.

PART II: Informed Consent – A Necessary Evolution

(A) Guiding Documents, Policies, and Legislation

(i) Founding Documents

Informed consent for research assumed priority in bioethics in the aftermath of World War II during which time individuals were used for medical experimentation without consenting or even being informed. This practice was universally condemned as a

violation of individual rights. As a consequence, the Nuremberg Code was established in 1947. It provided a core definition of consent: *"...the person should have the legal capacity to give consent...to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching or ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision."*[59] This coincided with Western societies' increasing emphasis on informed consent for patients undergoing any type of medical intervention.[68]

The commitment to autonomy is implied in the core conditions required by Nuremberg Code's definition of informed consent:

(1) There must be full disclosure of all relevant information, foreseeable risks, benefits, and interventions at a reasonable level that a person would require for decision-making. This is a legal requirement.

(2) The participant must demonstrate the capacity to understand the information disclosed and use this to reason through the foreseeable consequences of their decision to participate or not.

(3) The participant must understand the information provided. A demonstration of understanding beyond simply obtaining a signature must occur.

(4) The participant must come to a voluntary decision free from force, coercion or manipulation. There can be no threats, deception, or manipulation.

(5) Some representation of authorization, either verbal or written, must attest to the consent.[59]

While it remains the founding document that prescribes the conditions for ethical conduct of medical research, the Nuremberg Code does not consider conditions under which medical research with mentally compromised or pediatric populations can be undertaken, nor does it specify requirements for maintaining subjects' confidentiality.[56]

Other international documents that have evolved since this time similarly emphasize the importance of informed consent to participate in research and are more broadly conceived in their consideration of the range of ethical issues that may arise with human subjects' research. In 1964, the World Medical Association established recommendations guiding medical doctors engaged in medical research involving human subjects. The *Declaration of Helsinki*[125] governs international research ethics and defines rules for "research combined with clinical care" and "non-therapeutic research." It instructs that "research protocols should be reviewed by an independent committee prior to initiation" and that "each potential research subject must be adequately informed of the aims, methods, sources of funding, the possible conflicts of interest, institutional affiliations of the researchers, and anticipated benefits and potential risks of the study…"

The next landmark document in research ethics evolved in response to the Tuskeegee Syphilis Study. The United States created the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research in order to identify the basic ethical principles that should underlie the conduct of research involving human subjects and to develop guidelines which should be followed to assure that research is conducted in accordance with these principles. To accomplish this goal, this commission developed

the Belmont Report in 1979.[57] The three basic ethical principles reviewed in this Report include: (1) *Respect for persons* – Informed consent must be obtained and must reflect information, comprehension, and voluntariness; (2) *Beneficence* – the nature and scope of risks and benefits must be assessed in a systematic manner such that subjects are not harmed, risks are minimized, and benefits are maximized; and (3) *Justice* – the benefits and risks of research must be distributed fairly.

Some international statements have direct relevance to research involving banking biological material such as DNA. For example, the recently adopted UNESCO Declaration of Human Genome and Human Genetic Data[126]emphasizes the importance of "prior, free, informed, and express consent, without inducement or financial gain" of the person providing the genetic material. Similarly, the *World Medical Association Declaration on Ethical Considerations Regarding Health Databases*[127] declares that, "the right to privacy entitles people to exercise control over the use and disclosure of information about them as individuals....and that consent is needed if the inclusion of their information in a database involves disclosure to a third party."

(ii) The Canadian Context: Privacy Legislation

In Canada, federal and provincial laws regulate the government's collection, use and storage of personal information by both levels of government. These laws guide the type of information the government can collect, and how such information can be used in order to protect individuals' *legal right to privacy.* They also allow Canadian citizens to access, challenge and correct information about themselves. Every province and territory

in Canada (except for Newfoundland) has guidelines to protect personal information held by government departments and agencies. The provincial and territorial privacy acts guarantee individuals' rights to view and correct their personal information. The acts are administered and overseen by an independent commissioner or ombudsperson, with the authority to investigate complaints.[128]

Canada has two federal privacy laws: the *Privacy Act*,[129] and the *Personal Information Protection and Electronic Documents Act* (PIPEDA).[46] The federal *Privacy Act*,[129] in place since 1983, is overseen by the Privacy Commissioner of Canada and protects the personal information collected by government institutions. Essentially, the *Privacy Act* is a code of ethics for the government's handling of personal information. The *Privacy Act* ensures that Canadians can access information collected about them, and can challenge the accuracy of the information. Under its provisions, such information should be: (1) collected by government institutions in relation to operating programs or activities, (2) collected from the individual personally, (3) accurate and up to date, (4) subject to correction by the individual, and (5) used only for the purpose for which it was originally collected

PIPEDA[46] has been in place since 2004 and addresses the collection, storage and use of personal information by organizations in the *private* sector. Its provisions apply to information collected, used or disclosed by federally regulated agencies, such as telecommunications companies, broadcasters, airlines, banks, and federally regulated companies that conduct business online. PIPEDA also applies to provincially-regulated private-sector organizations, such as insurance companies and retail stores, unless the

province has passed "substantially similar" legislation. PIPEDA gives individuals the right to see and correct any personal information about them collected by companies in the course of their commercial activities. These provisions state that businesses must inform consumers about who is collecting the information, why the information is being gathered, and for what purposes it will be used. Under PIPEDA, personal information can be collected when it is: (1) gathered with the knowledge and consent of the consumer, (2) collected for a reasonable purpose, (3) used only for the reasons for which it was gathered, (4) accurate and up to date, (5) open for inspection and correction by the consumer, and (6) stored securely.

Substantially similar to the health information components of this federal legislation is Ontario's *Personal Health Information Protection Act, 2004* (*PHIPA*).[47] *PHIPA* governs the manner in which personal health information may be collected, used and disclosed within the health care system in Ontario. These legislated rules were designed to (1) give individuals greater control over how their personal health information is collected, used or disclosed and (2) provide health care professionals with a flexible framework to access and use health information as necessary in order to deliver adequate and timely health care.

(iii) The Canadian Context: Informed Consent for Research

Canadian law requires researchers to obtain informed consent for the use of identifiable health information and tissue for research purposes. Canadian courts view health information as closely tied to personal integrity and autonomy and, as such, advocate that research participants have the right to control what happens to their identifiable health

information. Personal health information is "identifying information" collected about an individual, whether oral or recorded. It includes information about an individual's physical or mental condition, including family medical history as well as any blood or body-part donations. "Identifying information" also includes health information that could identify an individual when used alone or in conjunction with other information.[130]

Long-standing Canadian common law principles and existing case law provide research participants with a legitimate expectation that personal health information will be kept confidential and not disclosed to third parties without their permission.[130] This obligation is further enforced by the Canadian Medical Association's *Health Information Privacy Code* which is premised by the "right of privacy is fundamental to a free and democratic society" and emphasizes and "patient's right to determine with whom he or she will share information and to know of and exercise control over use, disclosure, and access concerning any information collected about him or her."[131]

In Ontario, the general rule under *PHIPA* is that a health information custodian needs to obtain an individual's consent to collect, use and disclose personal health information unless the circumstance falls within the category of exceptions that allows the collection, use or disclosure without consent according to the discretion of an REB. The conditions under which informed consent may simply not be required include: (1) whether the research cannot be reasonably accomplished without access to the information, (2) the public interest in conducting the research and in protecting privacy, (3) whether obtaining consent directly is impracticable, and (4) whether adequate safeguards are in place to

protect the privacy of individuals and the confidentiality of their information. *PHIPA* also provides that consent is considered to be valid if it is knowledgeable, voluntary, related to the information in question, and given by the individual. Knowledgeable consent means that an individual must know why a health information custodian collects, uses or discloses his/her personal health information and that he/she may withhold or withdraw this consent.[47] *PHIPA* does not define how extensive a potential participant's knowledge must be; that is, is knowing that their data may be used for future research purposes sufficient, or must they know specifically what these uses may be? Furthermore, there is no specific provision within this legislation that separates genetic information from other types of personal medical information.

Guidance around obtaining informed consent in the Canadian medical research context is also provided by the Tri-Council Policy Statement: Ethical Conduct for Research Involving Human Subjects.[132] In 1998, The Medical Research Council (MRC – now Canadian Institutes of Health Research), Natural Science and Engineering Research Council (NSERC), and the Social Sciences and Humanities Research Council (SSHRC) all adopted the Tri-Council Policy Statement as a standard of ethical conduct for research involving human subjects. As a condition of funding, the councils require that researchers and their institutions, as a minimum, apply the ethical principles and the articles of the policy. The guiding ethical principles of the policy are: respect for human dignity, respect for free and informed consent, respect for vulnerable persons, respect for privacy and confidentiality, respect for justice and inclusiveness, balancing harm and benefits, minimizing harm, and maximizing benefit

Article 2.1(a) of the Tri-Council Policy states that research may begin only if: (1) prospective subjects or authorized third parties have been given the opportunity to give free and informed consent about participation; and (2) their free and informed consent has been given and is maintained throughout their participation in the research. Article 2.1(b) states that evidence of free and informed consent by the subject or authorized third party should ordinarily be obtained in writing. Where written consent is culturally unacceptable, or where there are good reasons for not recording consent in writing, the procedures used to seek free and informed consent shall be documented.

Section 8 of this policy statement applies to genetic research in particular. Because genetic research involves family members and/or the community, a potential tension exists between the interest of individuals in the study and the families who are thereby implicated. While the genetics researcher shall seek free and informed consent from the individual and report results to that individual if the individual so desires (Article 8.1), this process must be carefully executed in light of the aforementioned sensitivities of genetic information. Specific to the use of sensitive familial information in the form of databanks, Article 8.6 states that "...researchers who propose research involving the banking of genetic material have a duty to satisfy the REB and prospective research subjects that they have addressed the associated ethical issues, including confidentiality, privacy, storage, use of the data and results, withdrawal by the subject, and future contact of subjects, families and groups."

Finally, Article 10.3 applies the general principles of research involving identifying data of Section 2 to the specific case of tissue. Identification is a matter of sensitivity for individuals, families and members of groups. As such, Article 10.3(a) requires consent for the use of previously collected tissue from which persons may be identified; Article 10.3(b) provides an exception to the consent requirement when the tissue does not permit identification and poses no potential harms.

While respecting autonomy and obtaining informed consent for tissue collection and use are necessary steps in the research process, they do not speak to the issue of tissue ownership and property rights which is emerging as an increasingly complex and litigious domain. To date in the developed world, traditional property rights have not been bestowed upon human tissue. Doing so would strengthen the protections on individual autonomy, but in turn, would likely threaten researchers' ability to use stored tissue to its potential. A regulatory system that balances these interests has yet to be resolved in the American context.[133] Adding to this delicate balance is the necessary consideration of the commercial potential of tissue-based research. Would people consent to the use of their tissue if the result of pharmacogenomic research, for example, was that an expensive test is introduced to the market that is inaccessible through the health care system and grants significant profits to the researchers and commercial company? Based upon a number of legal cases that have brought this issue to the legal fore,[134] [135] various benefit sharing models have been proposed that would mitigate the imbalance in property interests between researchers and participants who donate biological samples for their research.[136]

While also beyond the scope of this discussion, the globalization of research generally and the exportation of tissue from the developing to the developed world that is implicated by this research warrants consideration.[137] Given the limits of informed consent and the poor adherence to exportation guidelines, Upshur et al[137] argue that engagement with communities from which tissue may be exported is necessary to foster legitimate and trusting research collaborations among developed and developing nations.

(B) Traditional informed consent and the context of biobank research

(i) Why it doesn't fit: theoretically

Canadian consent law and policy appears to flow directly from the traditional notion of autonomy. In *Ciarlariello v. Schacter,* the Supreme Court of Canada notes this connection where it states that, "it should not be forgotten that every patient has a right to bodily integrity. This encompasses the right to determine what medical procedures will be accepted and the extent to which they will be accepted...This concept of individual autonomy is fundamental to the common law..."[138] Over the years, the law has placed ever-more onerous disclosure and consent obligations on Canadian health care providers.[130] The doctrine of informed consent is even more rigorously interpreted in the research setting, "it is the most exacting duty possible, requiring 'full and frank disclosure' of all risks, no matter how remote, as well as other material information about the research."[139]

In traditional clinical research it is, arguably, appropriate to preserve this strict approach to informed consent. This approach requires full explicit consent for each use of

personally identifiable data. For each research project, potential participants would be told who wants to use their information and for what specific purpose. Permission would be sought for each use of individual information unless the nature of the research was considered exempt from this process as determined by an REB. This approach gives participants the most control over how their information is going to be used and makes researchers most accountable for their actions since each research endeavour needs to be explained upfront. It also maintains a direct link between researchers and participants. In a gene therapy trial, for example, the research question is defined, the study intervention is presented upfront, and its potential benefits and burdens are (generally) anticipated. Moreover, the subject is recruited based upon his/her individual eligibility and the research relationship is between a principle investigator and the individual subject him/herself. The core conditions of the traditional definition of consent (disclosure, capacity, voluntariness) can be met; an individualistic conception of autonomy is appropriate; and trust is placed in the principle investigator.

In the context of biobank research, full disclosure of research questions, methods, risks and benefits is not possible. The purpose for which health and lifestyle data may ultimately be used is simply not known at the time of its collection. The effort to collect this information is to create a research resource, not necessarily to answer a specific research question. As well, the nature of potential "informational harm" associated with data usage is different from the concrete and tangible physical harm that could result from a clinical trial. Potential for informational harm has been described in the context of genetic testing and research in the form of stigma,[140,141] psychological distress,[142,143,144]

altered family relationships,[145,146] and threatened insurability and employability status.[147,148] Conceptually speaking, the traditional model of informed consent is not consistent with the pluralistic conception of autonomy and the population-level locus of trust implicated by public health genetics research.

Further to these arguments, Caulfield and Reis[130] suggest that the nature of the relationship between the investigator and the participant could be considered fundamentally different in the contexts of clinical and non-clinical research. They put forth the argument that in the context of non-clinical research like biobank research, investigators do not have a fiduciary relationship with research participants because data are not necessarily collected in a clinical environment and participants are not necessarily seeking therapeutic help from researchers. For this reason, they argue that there could be less risk of exploiting the participant, reducing the researchers' obligation to a stringent informed consent process. However, UNESCO's policy on genetics is aimed at all forms of collection, regardless of where the collection process occurs[126] and statements from the WHO[149] and HUGO[150] do not make a distinction between data collected in clinical and non-clinical settings. Regardless of where information is collected for the purpose of research, participants donate their information and time in the hope that they are engaging in a trustworthy endeavour that will advance the public good. This necessitates compliance with an appropriate standard of consent. But what is deemed appropriate in this context remains unanswered.

In addition to the theoretical arguments against a traditional "full consent" approach, the empiric literature provides evidence to reject this approach. Not only is full consent in the context of longitudinal research incredibly time-intensive and potentially impractical, it may lead to substantive differences in the nature of the research population(s) recruited into studies. Recent studies examining how full consent models impact participation rates and participant characteristics in a range of non-clinical research studies reflect clear selection biases. This type of bias has been referred to as *authorization bias.*[151] Authorization bias is likely to result in a research sample that does not adequately represent the population of interest, thereby potentially distorting the findings and limiting their generalizability. What follows is a review of recent studies that reflect this phenomenon.

(ii) Why it doesn't fit: authorization bias

Research from Minnesota provides one example of a probable link between legislation requiring full explicit consent and authorization bias. In 1996, the Minnesota legislature passed a medical data privacy act requiring patient authorization for the use of medical records in research.[152] Yawn et al[151] studied the impact of this statute on a researcher's ability to obtain complete and representative data through a cross-sectional study of all patients visiting the outpatient clinic, emergency department, or hospital of the Olmsted Medical Center (OMC), for an appointment or admission during a one year period. Patients were asked to give consent for the use of their medical records for research. Of the 15,997 patients that were studied: 90.6% granted authorization, 3.6% refused authorization, 4.5% were undecided, and 1.3% was not asked. Since refusal rates were

found to be higher in older women and those with mental health problems, trauma, and ophthalmologic problems, the authors concluded that there is a chance of authorization bias.

Also interested in exploring the legislative change in Minnesota, Jacobsen et al[153] obtained a stratified random sample of patients encountered at The Mayo Clinic Rochester during the period 1994 through 1996. They then estimated the proportion willing to provide general authorization for medical records research. On the basis of data from administrative files, they compared demographic, diagnostic, and utilization characteristics for patients who provided authorization and those who did not. They found that women were more likely to refuse than men ($p=.067$), younger people more likely to refuse than older people ($p<.001$), and those who lived more remote from the clinic were more likely to consent than those who lived closer ($p=.001$). A trend was noted toward higher refusal rates among people with sensitive diagnoses (e.g. mental illness, infectious disease). They concluded that there is a possible bias and a threat to clinical understanding that could result in a failure to adequately inform patients and the public.

Despite these insights, existing legislation precluded the review of medical records of those patients refusing authorization. As a result, neither study can predict the bias that may occur in their overall sample frames. The Jacobsen study sample did not consist of patients currently undergoing assessment; diagnoses were historical and not validated by review of the medical record. As well, a high proportion of Rochester residents are

employed in the medical field, potentially increasing their understanding of the importance of medical records research. Finally, the reputation of the Mayo Clinic may have had an influence on patients' willingness to provide authorization. Therefore, these results may represent a "best-case" scenario.

McCarthy et al[154] also examined the impact of the Minnesota legislation in a health maintenance organization in the US. Upon seeking consent to conduct a study that would not have required consent prior to the implementation of the legislation (because it was considered minimal risk), they received only 26% approval. Based on these findings, they suggested that the legislation negatively influenced the ability to complete the study. They further concluded that efforts to protect patient privacy may come into conflict with the ability to provide timely health information that serves the public. The estimated cost of obtaining consent for this Mayo Clinic study was $1,000,000 U.S. for 214,000 patients. The anticipated cost of obtaining consent from everyone in Canada can be anticipated to be orders of magnitude higher.

In another effort to determine characteristics of consenting and non-consenting patients, Woolf et al[155] compared family practice patients invited to participate in a health services research survey. Among 1106 randomly selected, 33% did not give consent, 25% actively refused, and 8% did not answer. The remaining 34% of patients, which did consent, were older, included fewer women and African Americans, and reported poorer physical function than those who did not give consent ($P<.05$). On multivariate analysis, older age, male sex, and lower functional status were significant predictors of consent.

The authors concluded that patients who release personal information for health services research differ in important characteristics from those who do not, and therefore, that health services research restricted to patients who give consent may misrepresent outcomes for the general population. The authors acknowledge that placing the consent question at the end of their survey and using sophisticated consent language may have limited the internal validity of their study. Compared to Yawn's[151] population and Jacobsen's[153] population, the profile of this population was predominantly low-income and African American. The external validity of this study, therefore, was also limited.

Some jurisdictions require that all patients give written informed consent before enrollment in clinical registries. McKinney et al[156] investigated the feasibility of obtaining signed consent for the collection of identifiable data for a national pediatric clinical audit database. Consent was obtained from only 43% of admissions and was significantly greater among children who were more severely ill on admission ($p=.01$) and whose hospitals stays were longer than six days ($p=.002$). Consent rates were significantly poorer for children aged 10-14 ($p=.05$). The authors concluded that obtaining explicit consent for this purposes was pragmatically difficult since resources were limited and resulted in selection bias.

Motivated by the Scottish regulation that investigators "should seek express consent to disclose information, where identifiable data are needed for any purpose other than the provision of care or clinical audit,"[157] Al-Shahi et al[158] examined the differences between consenters and non-consenters invited to participate in a population-based cohort study

on brain arteriovenous malformations. Consenters were not significantly different from non-consenters in age, sex, or socioeconomic status, but were different in terms of clinical status and prognosis. Consenters were more likely to be independent, mobile, and candidates for interventional procedures than non-consenters. This reflects a bias in a cohort about which the natural history is trying to be elucidated, hence, limiting the generalizability of any relevant findings that emerge. Reflective of similar efforts to increase the stringency of the consent process in England, Junghans et al[159] evaluated the effect of opt-in and opt-out consent models using a randomized controlled trial among 510 patients with angina. The recruitment rate was 38% among those in the opt-in arm and 50% in the opt-out arm (p=.01). Patients in the opt-in arm had fewer risk factors (44% vs. 60% p = .05), less treatment for angina (69% vs. 82% p = .01), and less functional impairment (9% vs. 20% p = .02) than those in the opt-out arm. The authors conclude that requiring opt-in consent for research results in lower response rates and a biased sample and that for low-risk studies, should not be required.

Similarly, Tu et al[160] examined the impact of a full consent requirement on the Registry of the Canadian Stroke Network, a prospective registry based at 20 major stroke centers across Canada. Specifically, they examined the effectiveness of a comprehensive attempt to obtain informed consent on the overall participation rate and the characteristics of participating patients in that Registry. The overall consent rate among all potential participants was only 39% of 4285 eligible patients during phase 1 of the project and 51% percent of 2823 eligible patients during phase 2. Phase 2 was implemented because of the poor response rate in phase 1. Many patients died or left the hospital before they

could be approached for consent. Major selection biases were found; the in-hospital mortality rate was significantly lower among patients who were enrolled (7%) than among those who were not enrolled (22%) (relative risk of in-hospital death, 3.13; 95 percent confidence interval, 2.65 to 3.70; P<0.001). In this study, requiring written informed consent for participation in a stroke registry led to selection biases that rendered registry patients unrepresentative of the typical patient with stroke at each center. It must be noted that these findings speak only to the feasibility of consent-based registries for a cognitively impaired population in acute care. They do not speak to chronic conditions for which there may be more time to engage patients in a consent process. Moreover, data were not collected on reasons why patients refused to participate. Nonetheless, the authors suggest that these findings highlight the need for legislation on privacy and policies permitting waivers of informed consent for minimal-risk observational research.

Armstrong et al[161] extended Tu et al's[160] work by exploring the challenges associated with the HIPPA Privacy Rule[162] requirement of obtaining written consent for a follow-up telephone questionnaire following hospital discharge. They used a pre-test/post-test design to assess consent rate in two cohorts of patients eligible for an Acute Coronary Syndrome (ACS) registry at the University of Michigan. The pre-HIPPA consent process included telephone contact and verbal consent. The post-HIPPA consent process required mailed consent forms and written consent. Consent to follow-up in the ACS registry declined from 96.4% in the pre-HIPPA period to 34.0% in the post-HIPPA period (p<.01). Consent rates also varied depending on patient characteristics, reflecting a selection bias: those who returned written consent forms in the post-HIPPA period were

older, more likely to be married, and had lower mortality rates at 6 months. This approach reflects a strict interpretation of the HIPPA legislation and findings may vary where interpretation of this legislation varies.

In contrast, The Eastern Cooperative Oncology Group (ECOG)[163] accrued more than 7000 patients to studies using one of two consent forms for the storage and future use of samples left over from its therapeutic cancer clinical trials. The assent rate for the original banking consent statement was 89.4%, whereas that for the more detailed consent form was 93.7%. Higher assent rates were statistically significant for the detailed consent form versus the original consent form (P=.001), suggesting that increased patient protection does *not* result in decreased availability of biologic samples for future research purposes. Compared to the aforementioned studies with findings to the contrary, the ECOG population was already enrolled in therapeutic cancer trials when asked for further consent preferences. Testing a new approach to research consent with a population who has already "bought-in" to the research process does not reflect the same challenge as that undertaken by the other groups. This may be one explanation for this discrepancy.

With the exception of the ECOG study, the aforementioned studies indicate that authorization bias is a potential threat to the collection and interpretation of data required to set health policy and inform clinical choice. Anecdotally, O'Neill[164] has argued that "the complexity of the modern care environment, the vulnerability of acutely ill individuals at the time of approach, and challenges of excess information to be conveyed render true informed consent a heroic or impossible cognitive feat, even among

individuals with mature faculties." This is not necessarily grounds for rejecting the 'full consent' approach, rather it can be viewed as incentive for developing innovative consent strategies that respect both privacy and research interests.

Given that the condition of full disclosure cannot be met, that the nature of potential informational harms are different from physical harms implicated by "intervention-based" research, the significant potential for authorization bias, and the evolving conceptions of autonomy and trust, the traditional model of consent is not well suited to the context of public health genetics research. This incongruence is endorsed by the National Bioethics Advisory Commission (NBAC), which states that, "...applied to non-clinical research, the regulatory requirements seem to be either irrelevant or insufficient to provide protection."[165] Dr. Francis Collins, director of the National Human Genome Research Institute, similarly, notes that "the IRB guidebook is dusty and out of date for genetic research."[166]

For these reasons, alternate models of consent have been proposed. These include blanket consent, presumed consent, authorization, and governance models. How these models reflect the conceptual shift from traditional clinical genetics to public health genetics research will be considered.

PART III: Alternate Consent Models

(A) Blanket Consent

One interpretation of opt-in consent models is that participants make a one-time choice about all future uses of health information and/or tissue samples *without knowing* the specific uses to which it/they will be put. This interpretation has been referred to in the literature as *blanket consent.*[167] From a practical perspective, the use of opt-in consents would eliminate the need for database researchers to locate participants and obtain full consent for each data use. UNESCO's *Draft Report on Collection, Treatment, Storage, and Use of Genetic Data* states that "a system which required fresh consent would be extremely cumbersome and could seriously inhibit research... blanket consent covering all forms of future medical research might be preferable."[168] While a one-time consent would simplify the research process, blanket consents are necessarily vague and therefore are too general to carry legal weight. Moreover, they do not allow individuals to act meaningfully on their continuous right to control their health information.[169] As such, most types of blanket consent "fall short of true informed consent."[170] In line with these limitations, the American Society of Human Genetics' Policy on informed consent does not support a blanket consent approach. It states that,

> "Subjects involved in studies where the samples are identified or identifiable should indicate if their sample should be used exclusively in the study under consideration. If the sample is to be used more generally, subjects should be given options regarding the scope of the subsequent investigations, such as whether the sample can be used only for a specific disease under investigation, or for other unrelated conditions. It is inappropriate to ask a subject to grant blanket consent for all future

unspecified genetic research projects on any disease or in any area if the samples are identifiable in those subsequent studies."[171]

(B) Presumed Consent

In this model, individuals are presumed to want to participate in the research study and are typically given the opportunity to opt-out at any chosen time. The aims of a given study are widely publicized to its target population(s) so as to inform individuals of its existence. The means of opting out is straightforward and without consequence. Presumed consent can also refer to the situation in which a representative of a community consents to research on behalf of the entire community.[167]

Much of the controversy around genetic databases stems from the practice of presumed consent associated with the Icelandic Health Sector Database in particular. As was described in Chapter 1, the data for the genetic database is gathered on the premise of presumed consent. The directors of the Icelandic database project (deCODE Genetics) define presumed consent as "the consent of society to the use of health care information according to the norms of society."[172] Practically speaking, health data and biological samples are gathered automatically unless individuals specifically opt out. Taub et al[173] argue that the presumed consent standard can function as an effective safeguard only if concerned individuals are informed of the following: (1) the risks and benefits of the proposed research, (2) the fact that participation is optional, (3) the appropriate steps to follow to opt out, (4) their status as subjects unless they formally opt out, and (5) the contact information for a person who can further answer their questions and discuss the

research plans. It is the use of presumed consent without thorough community consultation and without explicit description of all of these safeguards that provoked international controversy and dissenting opinions from the academic community. While the majority of Icelanders support this endeavor perhaps for reasons related to a culturally-specific belief in science and technology, much of the existing dissent was substantiated by the fact that over 20,000 individuals (7% of the population) have opted not to participate in the bank.[19] Essentially, the directors of this initiative considered their "extensive community consultation and majority support" as a proxy for community consent. Dissenters considered the community consultation efforts to be inadequate and the presumed consent model to be morally untenable.

Given the implications database research has for a significant proportion of the population as well as the indirect risks it could impose on non-participating members of this population, community consultation is indeed essential. Both the Council of Europe *Convention for the Protection of Human Rights and Biomedicine* and the UNESCO Draft *Report on the Collection, Treatment, Storage, and Use of Genetic Data* call for appropriate public consultation in biomedical research. Critics of the Iceland database argue that there was insufficient community consultation and public debate around the approach to consent. In defense of the approach in Iceland, international guidelines and research publications differ in their definition of community consultation and consent. The definition has ranged from informing the public of database activities to including public opinion in the formative stages and decisions related to database development and protocol. Regardless of this definition, community consultation cannot be used as a

substitute for informed consent. It should precede and complement the process but not replace it.[173]

(C) Authorization

A range of "authorization" or "general permission" or "broad consent" or "stratified consent" models have been proposed in the literature. All of these approaches reflect the same basic premise: research participants would provide written consent for their personal health information to be used for the types of research with which they are comfortable; research participants would define the general boundaries for the use of their information at the time of its initial collection.[167]

Requiring full consent for any new research on previously collected information and/or sample(s) will usually make the research unfeasible, particularly in the context of genetic databases. Abandoning consent altogether, however, would remove the research subject's own check on the safety of the research, violate their dignitary interest in controlling their medical information and samples, and avail them to economic exploitation and potential harm. Authorization frameworks attempt to reconcile these tensions.

For example, NBAC recommends that consent forms be developed to include a range of options. These include: (a) refusing use of biological material in research; (b) permitting only unidentified use; (c) permitting coded use for some types of studies but not others with no future contact allowed; (d) permitting coded use for some studies with future contact allowed; and (e) permitting use for any kind of future study.[174] McGuire and

Gibbs[175] recommend a stratified consent process which presents potential participants with the option to release three levels DNA sequence data (multiple gene loci, single gene loci, no information). Associated with these levels is a decreasing risk to personal privacy at the cost of decreasing scientific knowledge. But personal choice and control over informational boundaries on the participants' behalf is maintained.

Some feel that asking potential participants to choose among too many options creates unnecessary complexity. Beskow et al[176] developed a consent document which addresses the option of future research by simply stating that "investigators would like to store remaining biological material for future research, describing plans for such research to the extent to which it is known, and offering participants the option of consenting or refusing to participate in what has been described." Similarly, O'Neill[177] believes that "more specific consent is not invariably better consent." Rather than presenting prospective participants with "an array of tick boxes and propositions for signature," she advocates for a layered approach in which individuals control the amount of information they choose to receive. More specific information underlying the initial layer of information would be provided in the form of fact sheets, brochures, or in-depth discussions. Even if an individual's judgment is based on limited information, if he/she is comfortable with his/her level of knowledge and choice, O'Neill believes this honours the goals of genuine, autonomous consent.

Greely[170] explores these ideas more comprehensively and describes an innovative framework that is intended to enable unforeseen research on previously collected samples and information without requiring new informed consent. This framework reflects a permission model and is similar to NBAC's proposal.[174]Although his proposal does not

stay within the current boundaries of the Common Rule,[178] additional safeguards are integrated into his framework to enhance research subject protection. When the specific research use for the information and/or sample(s) is known at the time of collection, informed consent for that particular use is required. When the specific research use is not known at the time of collection, researchers may ask participants for a general *permission* to use these data. The permission may be general (use for any subsequent research purposes) or narrow (use only for research related to genetics and heart disease). Additional safeguards included in this framework include: (1) research must be REB approved, (2) REB must require new informed consent if research deemed unusually sensitive to participants, (3) subject must be informed as to whether participation in unforeseen research will influence their participation in any other clinical or research program, (4) subject must exercise control over the extent to which he/she would like to be re-contacted should relevant information be identified over the course of study, (5) subjects must be notified of their right to withdraw at any time, (6) time limits on data storage must be made clear to participants, (7) participants must be informed of and approve any transfer or sharing of their information with third parties, (8) potential consequences to community group research must be highlighted, and (9) any contemplated commercial use of data must be disclosed to potential participants.

Included in The Ethics and Governance Framework for the UK Biobank is a description of the consent process that is planned for this particular collection of health information.[179] Because all future research uses are impossible to anticipate, consent will be sought for medical research "in general." Consent will be based upon an explanation of the following key points: (1) the fact that the Biobank is a long term research resource,

(2) the kinds of information that will be collected with options to avoid provision of any particular kind, (3) the fact that there will remain a link between the Biobank and individuals' personal health records, (4) the Biobank will be the legal owner of all samples and information, (5) the safeguards that will be in place to preserve data security, (6) that only research approved by Research Ethics Boards can access the bank, (7) that commercial entities may use the bank, (8) that participants may be recontacted over time, (9) that participants have the right to withdraw at any time, and (10) that the Biobank will remain engaged with participants through websites, newsletters, the media, and a contact person for participants' reference. A commitment to engaging research participants (as indicated by point #10) moves the research process in the direction of actually viewing participants as partners in the research relationship, perhaps meeting the condition of reciprocity.

In the Canadian context, Caulfield et al's authorization model is conceptually similar to Greely's permission model. According to Caulfield,[180] because the parameters of successful biobanks cannot satisfy the legal/ethical requirements for full consent in Canada, a legislated exception to consent is required. Legal weight for the authorization model would come from this new legislation. Research participants would, in authorizing use of their data and samples for defined purpose(s), relinquish their rights to traditional consent in this context. Further protections, such as those suggested by Greely,[170] could also be built into this model to afford research participants further protections. While Greely's model does not elaborate on what actual consent documents would look like, Caulfield's model lends itself to the Health Care Information Directive, a concrete decision tool by which to facilitate the authorization process.[45] A leading

scholar in the area of health information privacy and genetics research, Bartha Knoppers states, "It is my opinion that broad consent to longitudinal studies with authorization for future studies together with the protection of ethics review, ongoing communication of the project and the communication of general results is not a waiver of informed consent. It is a form of consent that is true to the very nature of biobanks."[181]

The Ethics Office of the Canadian Institutes of Health Research (CIHR) developed a Privacy Best Practices document to guide health researchers and REBs in making decisions about managing personal health information.[182] Their document recommends that when personal data are to be entered into a database for multiple research uses over an extended period of time, research participants should be informed of the following at the time of collection: (1) expected types of studies, (2) expected data types and purposes, (3) expected commercial uses, (4) data retention period, (5) the process overseeing the use and security of the data, and (6) the opportunity to authorize future uses of data with or without recontact. Recontact options could include being recontacted on a regular basis defined by the individual, not being recontacted at all, being recontacted for certain types of data uses but not others. It is innovative of CIHR to consider an authorization model as appropriate for database research and speaks to its potential viability in this context.

(D) Governance Structures

Some scholars have explored the idea that responsibility for and control of health information should not rest with the individual research participant but should rest with a governing or data monitoring body. According to Williams and Schroeder, [110] "the

individualistic focus of informed consent needs to be supplemented by pro-active forms of ongoing institutional governance. Much more attention must be paid to the duties pertaining to the custodians of genebanks and to the institutions that fund them."

Caulfield[44] suggests that one strategy for achieving a shift in responsibility is to waive consent altogether. Waiving consent defers judgments about data usage to a research ethics board (REB). Although not permitted by Canadian common law, certain provinces have legislation in place (e.g. Alberta's Health Information Act, Ontario's PHIPA) that allows access to identifiable health information without individual consent under specific circumstances and with REB approval.[183] Likewise, as stated in the Tri-Council Policy,[132] an REB can waive the requirement to obtain informed consent, provided that (a) the research involves no more than minimal risk to the subjects, (b) the waiver or alteration is unlikely to adversely affect the rights and welfare of the subjects, (c) the research could not practicably be carried out without the waiver alteration, (d) whenever possible and appropriate, the subjects will be provided with additional pertinent information after participation, and (e) the waivered or altered consent does not involve a therapeutic intervention. As well, an REB in the United States can waive the requirement of consent when certain conditions are met.[184]

While REBs can and should provide a critical role in the process of protecting human subjects in biobank research, there is evidence to suggest that the complexity of issues implicated by biobank research is beyond the scope of REBs' experience and expertise. A recent Canadian survey of 43 REBS reflects some the challenges that REBs face in managing research protocols involving biobanks. A fictional protocol involving the creation, use, and management of a genetic biobank was presented to these REBs. They

were asked: "Do you think that this protocol is ethically acceptable to your REB?" 23% refused the protocol categorically, 26% wanted the protocol to be reviewed by the PI before deciding, 26% required some form of modifications, 14% felt that the protocol was not within their mandate, 9% accepted the protocol with conditions, and only 1% accepted it without conditions.[185] In another study 44 Canadian biomedical REBs agreed to review a mock research protocol about functional neuroimaging which included a biobank component. 68% of the REBs rejected the protocol because it included a biobank, 23% approved it with conditions, 7% approved it unconditionally, and 2% did not answer. Among the 68% who rejected the protocol, 37% were concerned about access to medical records, 30% questioned the database altogether, and 30% felt that they were not sufficiently equipped to evaluate a study including a biobank.[186]

These two studies reflect some of the difficulties that REBs have in making decisions about appropriate use of biobanks in human subjects' research and support Auray-Blais and Patenaude's[187] interest in developing alternate approaches to biobank management. Williams and Schroeder[112] concur that ethics committees have the capacity to stop unethical or unwanted research from being undertaken but do not have the expertise to steer the usage and management of a biobank. To assist REBs, Auray-Blais and Patenaude propose the idea of a medical archivist to play the role of a data protection officer.[187] In their model, the archivist would hold the research protocol, the signed consents, and the data codes, and would be responsible for communicating with participants, withdrawing and destroying data as appropriate. Already trained in the area of medical records, familiar with hospital codes of ethics related to medical

privacy, and employed within medical centres, an archivist could indeed enhance the practical and ethical organization of biobank research.

In addition to the technical barriers to reviewing genetic database research, there is a sentiment in the literature that the fundamental process of REB review lacks accountability and transparency. Although ethical principles intended to be standards against which protocols are to be assessed are well articulated, REB guidelines for decision-making are vague regarding how to actually weigh risks and benefits. This leaves much to the discretion and integrity of volunteer members of the boards who may have some training in research ethics but are certainly not experts in the field. Zlotnik-Shaul[188] suggests that "the accountability of REBs may be improved in a number of ways: statutory codification of detailed standards; an enhanced model of self-regulation; accreditation of REBs; and certification of REB members." By making review procedures more explicit and expecting greater proficiency from board members, the overall accountability of REBs will be improved.[188]

With or without their limitations, REBs will remain fundamental to research review. Their presence, however, does not preclude the exploration of other structures which could supplement the role of the REB. For example, in addition to the requirement that all protocols pass through the relevant REB, The UK Biobank Ethics and Governance Framework describes a management and accountability model that operates at arms length from the day-to-day runnings of the biobank itself. This model includes a Board of Directors which is responsible for ensuring that all UK Biobank policies and activities conform to the Ethics and Governance Framework and managing corporate

issues such as conflicts of interest that could arise. It also includes an Ethics and Governance Council which operates independently of the Biobank and monitors its activities as they relate to the Ethics and Governance Framework, recommending revisions as necessary. The governance structure of this Biobank includes a Steering Committee which is responsible for advising the CEO and PI on the research directions and scientific objectives, and specific study protocols. In the interest of engaging participants and maintaining a transparent and accountable system, a variety of mechanisms are in place to communicate with participants regarding project developments and key findings (e.g. websites, help-lines, newsletters, public meetings). Furthermore, the Governance Framework may establish a participants' panel to represent the general views of the UK participant population.[179]

Winickoff and Winickoff[189] report on yet another possible governance structure. They describe the National Research Council's suggestion that for a worldwide collection of DNA, "a more sophisticated and complicated approach would be to form an international organization to serve as a trustee and fund-holder for all the sampled populations."[190] Under a trust agreement, the tissue donor formally expresses a wish to transfer his/her property interest in the tissue to the trust. This could be done using a permission form that includes a discussion of safeguards like those proposed by Greely.[170] The donor appoints a trustee of the property who has legal fiduciary duties to keep or use the property for the benefit of a specified party, the beneficiary. In this context, the general public serves as the beneficiary. The advantages of this model as articulated by the authors include: (1) charitable trusts are consistent with the (considered by some) altruistic nature of tissue donation, (2) the structure of the trust

can provide the donors with an advisory role in the trust, and (3) charitable trusts are not vulnerable to bankruptcy the way that private collections are and this is important for maintaining a sense of trust from the donors as well as the actual data for the longitudinal nature of the research.

While these governance structures are laudable, it is premature to monitor and implement them given the intended or infancy-stage of most biobanks described in the literature. Until theses collections are up and running, a more hands-on approach to obtaining donors' permission is required.

PART IV: Factors which influence participants' willingness to share PHI

(A) Type of PHI Requested

The requirement for informed consent typically varies according to the sensitivity of the information and the application for which it is intended. As sensitivity increases, so does the need for informed consent and stringent safeguards.

The extent to which genetic information is substantively different from non-genetic information such that it warrants different treatment with respect to privacy and consent practices is an ongoing debate. Neither current Canadian legislation[46] nor the report generated by The Ontario Provincial Advisory Committee on New Genetic Technologies[191] provides a concrete position on this issue.

Existing literature defines the parameters of this debate.[192,193,194,195] Those who believe in "genetic exceptionalism" first argue that genetic information has a unique capacity to predict an individual's medical future. While this is true for rare single gene disorders

such as Huntingon's Disease, the 'prophetic potential' of most genetic susceptibility tests is significantly less than 100% and is modified by environmental and lifestyle factors. In many cases, the predictive value of a genetic susceptibility test is no greater than that which is offered by non-genetic predictors such as cholesterol and hypertension levels. Conversely, those who argue that genetics is unique in its predictive power base this claim on the fact that DNA is stable over time. While it is true that DNA itself is stable over time, the clinical interpretation of a given mutation varies as more is learned about the functional and epidemiological properties of a given variant.

A second exceptionalist argument is that the capacity for genetic test results to divulge information about family members is unique to genetic testing. While genetic tests are unique in their capacity to predict vertical transmission of disease (parent to child), non-genetic tests predict transmission by mechanisms implicating shared environments or person-to-person contact. Infectious disease transmission is a classic example of non-genetic familial transmission of disease. Third, those who advocate for genetic anti-discrimination legislation in particular, argue that genetic information can be used to discriminate against and stigmatize individuals, families, and communities. While the eugenics movement is a unique historical illustration of genetic discrimination and there are anecdotal reports of insurance discrimination based on genotype in the US, insurance underwriters routinely rely on non-genetic medical information (HIV status, serum cholesterol levels) to determine rates for health, life, and disability insurance. Moreover, stigmatization of illness, particularly those which are poorly understood, has occurred for centuries.

Third, exceptionalists caution that genetic testing can cause serious psychological harm in the form of depression, anxiety, fear, and family discord. However, psychological harm can also be experienced upon receipt of non-genetic medical information such as a diagnosis of HIV or heart disease. There is also evidence to suggest that the psychological harm associated with genetic testing, if it exists at all, is something to which individuals adjust in the short term.

Further to the domains of 'prophecy,' familial implications, and psychological effects, Lemmens and Austin[196] suggest that these characteristics of genetic information *combined with* the volume of information that can be extracted from one sample, the speed of testing, and its link with computer technology warrants regulatory attentions. Rather than viewing genetic and non-genetic information as dichotomous or genetic information as exceptional, they argue that "the concerns raised by the advent of genetic testing are related more to what one can call an amplification of existing concerns about health information than to the specificity of genetics." While regulatory models that consider the context and nuances of genetic information are warranted, it is simplistic and likely not in our best interest to continue to exceptionalize genetic information.

Empiric data are beginning to emerge to inform this debate. In a Canadian public opinion survey, 58% of respondents felt that genetic information should be more strictly regulated than other health information. In follow-up focus groups, further discussion of this point

indicated that Canadians would be more disturbed if their personal genetic information was inadvertently publicized than if their general health records were publicized.[197]

Plantinga et al[198] surveyed 597 individuals with genetic and non-genetic conditions to compare their experiences, beliefs, and attitudes regarding the confidentiality of their medical information. While most participants felt that their family members should be aware of their medical condition (93%), they wanted to control that disclosure and did not want doctors sharing this information without their permission (72%). As well, most participants did not mind if doctors shared medical information with other doctors if it was for their benefit (79%), but the majority felt that doctors should be punished for releasing information without their permission (73%). The same population was also asked about medical records research. Kass et al[199] reported that regardless of whether individuals had genetic or non-genetic conditions, 31% were willing to have records used for research without prior informed consent, 71% thought a computerized research database was a good idea provided access was restricted to the person they authorized, and 86% thought an anonymous research database was a good idea. Interestingly, the views and experiences reported did not differ between those with genetic and non-genetic conditions. This study was limited by its comparison of genetic conditions with HIV status, a potentially more stigmatizing condition around which privacy concerns may be heightened, thereby distorting perspectives on genetic conditions alone.

Stegmayr and Asplund[200] surveyed 1409 individuals who participated in a WHO risk factor research study 11 years following their initial enrolment in this study. When asked

about their interest in participating in ongoing genetics studies. 93% gave consent for their blood samples to be used for academic genetic research provided an ethics board approved the study and their data would be anonymized. While this is encouraging, this population was already enrolled in a research study so it is not surprising that they demonstrated continued support for medical research.

Roberts et al[201] surveyed 63 employees at two workplaces in New Mexico in order to characterize perspectives on genetic research from community stakeholders. Workers rated protection of confidentiality of genetic information as very important (scale: 1 = not important, 9 = very important; mean =8.5) and storage of genetic information as less acceptable than that of non-genetic information ($p<.0001$). They also felt that reporting identifiable genetic information was much less acceptable than reporting aggregate information ($p<.0001$). This study is novel in its description of employee perspectives on this topic, but limited by its small sample size. Merz et al[202] conducted a retrospective medical record abstraction of hospital consent-to-treatment and release-of-information forms. They examined whether the forms are present in the records and, if so, whether they are signed by patients. The results suggest that patients who have sensitive information in their medical records (mental health, drug and alcohol use) or pay out of pocket for their care are less likely to consent to disclosure of their records.

Willison et al[203] surveyed and interviewed Ontario family practice patients about their preferred method of consent for the use of information from electronic medical records for research. Among other findings, patients made little distinction between identifiable

and anonymous data when authorizing its use for research. In a Saskatchewan survey,[40] however, 99% of respondents agreed that *unidentified* health information may be available for health services and evaluation research and 97% agreed that statistical and/or aggregate data could be widely available for planning, evaluating, reporting, and research purposes. Similarly, in a national opinion poll,[197] >90% of Canadians indicated comfort with sharing genetic information with researchers when personal identifiers are removed from the databases. This literature regarding preferences for the extent to which data are anonymized is complicated by a wide range of terminology reflecting the concept of anonymization. Data can be personalized, de-identified, stripped of identifiers, coded, linked, anonymized, encrypted, or aggregated. To streamline the interpretation of studies that reflect on research participants' preferences on how data are managed, it would be worthwhile to define and investigate participants' understanding of these terms in and of themselves. This is lacking in the literature. While anonymizing data indeed protects participants from being identified and therefore having information disclosed without consent, it also strips them of any opportunity for recontact should medically relevant information be gleaned as well as any claim to benefit sharing from commercially valuable discoveries derived from their anonymized tissues.

Existing data suggest that the sensitivity of personal health information is indeed a function of its degree of anonymity as well as the actual nature of the information in question. It is anticipated that the proposed study will help to identify if/when different privacy and consent practices are warranted for different types of PHI.

(B) Purpose for which PHI is requested

There is evidence to suggest that authorization to share PHI varies with the purpose for which it is requested. The aforementioned Saskatchewan survey found that regardless of the actual study purpose, 87% of Canadians agreed that "PHI should only be used for the specific purpose it was gathered, or for a purpose consistent with this."

In Willison et al's[203] study of Ontario family practice patients, research sponsored by private insurance firms generated the greatest concern and research sponsored by foundations the least concern. Nair et al[204] interviewed 17 patients whose primary physicians were taking part in a study that utilized de-identified individual level health information from their electronic medical records. Participants were asked to comment on their comfort with personal information sharing for research supported by four types of funders (pharmaceutical companies, software companies, insurance companies, government). Participants voiced the greatest concern related to uses by pharmaceutical and insurance companies. Funding from such commercial sources was deemed more acceptable if the company provided a proviso that they would interact with the researchers at "an arm's length."

Genetic studies targeting homogeneous ethnic groups aim to identify candidate genes for a range of medical conditions. In the context of specific ethnic population studies (e.g., Ashkenazi Jews), participants remain individually anonymous, but membership to the ethnic group does not. This lack of group anonymity has led to concern about the possibility of stigmatization and discrimination based on the results of the genetic

research. Schwartz et al[205] surveyed Jewish individuals about their attitudes regarding the practice of using stored DNA samples for genetic research. Specifically, attitudes about informed consent and willingness to participate in genetics research using stored DNA in different circumstances (i.e., clinical setting vs. research setting) and for different diseases/traits under investigation were ascertained. Overall, most respondents reported that written informed consent should be required and that they would be willing to provide such consent. Participants were most willing to provide consent, however, when the sample had been collected in a research rather than clinical setting. Participants were significantly less willing to participate in research that examined stereotypical or potentially stigmatizing traits as opposed to research that examined medical or mental illnesses.

(C) Type of Professional Requesting PHI

Whether or not authorization to share information varies with the type of provider requesting PHI is only touched upon in the literature. Carmen and Britten[206] conducted a qualitative study to explore family practice patients' expectations and attitudes concerning confidentiality of patients' medical records in general practice. 39 patients completed semi-structured interviews. Patients' expectations diverged considerably from actual practice. The majority of interviewees felt that administrative and secretarial staff should not have access to medical records. Some patients had reservations about a doctor not directly involved in their care having access to their records. They were unaware of the fact that practice staff had ready access to their medical records. Interviewees had particular concerns about recording of non-medical information in their records, and the

confidentiality of computerized records. The authors suggest that explicit negotiations about what and with whom information is shared would mediate the discrepancies identified in this study.

Schers et al[207] analyzed survey data from 644 participants from 35 general practices in the Netherlands about access to the medical record by the on-call general practitioner (GP) and by the practice assistant in relation to the perceived importance of this information for their personal doctor. 20% of the patients stated that the on-call GP should not have access to their entire medical record and 44% did not support full access for the practice assistant. Patient consent to the on-call GP accessing PHI ranged from 62% for life events to 93% for medication history; and to the practice assistant from 37% for home details to 82% for medication history. Patients distinguished between "medically oriented information" and "lifestyle and psychosocial information." This study was limited by the fact that more participants were older and had chronic illnesses. Since these characteristics were associated with more agreement to information access, participants' overall concerns related to confidentiality may have been underestimated. The authors concluded that patient consent to access their medical record should not be taken for granted and that research into how to segregate information is warranted.

Respondents in Roberts et al's[201] workplace study were asked to rate the acceptability of sharing genetic information with various individuals on a 9-point Likert scale (1 = not acceptable, 9 = very acceptable). Overall, respondents believed that "asking about genetic conditions" was appropriate by a personal physician (mean = 8.1) but

inappropriate for an insurer or an employer (mean = 2.6, 2.0, respectively). Canadians also express resistance to sharing genetic information with individuals who are not involved in health care or research. 49% would deny access to health care companies, 91% do not believe insurance companies have the right to access existing personal genetic information, and 90% feel that employers should not have access to genetic information of applicants or employees.[197]

(D) Storage of PHI

There appears to be particular concern about electronic storage of PHI.[208] Mandl et al[209] believe that electronic medical record systems can be both accessible and private if they are designed properly. In their design, (1) all medical information can flow freely among institutions using a common set of communication protocols and (2) patients are able to control and manage their medical information in the same way they mange their online investments and purchases. Specifically, they advocate that since patients may have preferences about how different aspects of their medical history are shared, they should be able to independently authorize its use by granting differential access to different individuals. For most patients, the appropriate degree of confidentiality will be a compromise between privacy and the desire to receive informed medical attention. Conceptually, this idea is consistent with the authorization model and could be facilitated by the HCID.

CHAPTER 4: RESEARCH QUESTION

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(A) Rationale for Selecting the Authorization Model

Caulfield and Ries[130] ask, "How can we reconcile the strict interpretation of Canadian consent law with the unique context of biobank research?" Biobank research creates unique consent issues that ask us to question whether a strict interpretation of consent law in fact serves the public interest. As has been described, several scholars argue that this context provides a justification for moving away from the traditional autonomy-centered view of the consent process. Since blanket and presumed consent models lack legal weight and are autonomy-limiting and since biobanks are too young to legitimately evaluate the role of governance structures, it seems most appropriate to further explore the authorization model. Lacking existing case law and a legal framework, a movement towards an authorization model would require a new piece of legislation or a leading judicial decision.

A movement towards the authorization model could be justified for three reasons. First, it is theoretically rigourous in so much as it enables potential research participants to (a) assert complete control over their PHI if they have preferences with respect to what type of information can be used when, (b) assert complete deference to biobank authorities if they are comfortable with their PHI being used under all conditions, or (c) remain involved in the decisions about how their PHI might be used over time, by revisiting choices and maintaining a level of reciprocity with the researchers. Second, it is practically feasible; tools and forms that are conceptually congruent with the premise of authorization have been suggested and/or piloted in the literature and appear to be

promising. The HCID is one example of this. Finally, other proposed models such as blanket consent, presumed consent, and governance structures are neither practically nor ethically viable at this point in time.

(B) Research Question and its Dimensions

Given this commitment to further explore the authorization model, this investigation aimed to better understand what factors influence research participants' authorization to share PHI under a range of conditions. The specific research question was:

> *How do **individuals who have pursued genetic testing** define the **conditions** under which they are willing to authorize the use of their **personal health information (PHI)** for administrative and research purposes?*

Important dimensions of this research question include

(a) *"Individuals who have pursued genetic testing"* refers to the patient populations that were recruited for this study. Participants were drawn from four clinical contexts, all of which provide genetic and non-genetic tests for diagnostic and/or surveillance purposes of adult onset disorders. These included: hereditary non-polyposis colorectal cancer (HNPCC), hereditary breast and ovarian cancer (HBOC), hereditary hemochromatosis (HH), and thrombophilia (THR). These conditions reflect a continuum from rare disorders caused by highly penetrant genes (HNPCC) to common disorders caused by a combination of genetic and non-genetic risk factors (THR).

This combination of clinical populations also reflects the conceptual shift from a disease entity likely to be targeted using traditional genetics research approaches to a disease

entity more likely to be targeted using public health genetics research approaches. More specifically:

(i) HNPCC is a very rare dominant condition caused, predominantly, by mutations in the MLH/MSH DNA repair genes. Only 5% of the colorectal cancer population carries mutations in MLH/MSH. MLH/MSH testing is available to eligible families in Ontario to assess personal and family risk for colorectal cancer and colonoscopy is widely used as a measure of surveillance. The penetrance of MLH/MSH mutations are considered to be very high and approaches 80%.[210]

(ii) HBOC is a rare dominant condition caused, in part, by mutations in the BRCA1/2 tumour suppressor genes. Only 5-10% of the breast cancer population carries mutations in BRCA1/2. BRCA1/2 testing is available to eligible families in Ontario to assess personal and family risk for breast and ovarian cancer and mammography is widely used as a measure of surveillance. The penetrance of BRCA1/2 mutations are considered to be high and range from 50-80%.[211]

(iii) HH is a common recessive condition caused by a mutation in the HFE gene and leads to organ damage from iron overload. Approximately 1/10 Caucasians carries an HFE gene mutation and approximately 1/200 Caucasians has HH. Both genetic (HFE genotyping) and non-genetic (ferritin, transferring saturation) tests are available to assess risk and assist diagnosis of HH. The penetrance of the "major" HFE mutation (C282Y) is considered to be moderate and ranges from 20-40%.[38] While the population carrier

frequency of THR and HH are similar (6%, 10%), disease expression is a function of both the gene penetrance and inheritance pattern.[212]

(iv) THR is a very common dominantly inherited tendency to develop venous blood clots which can be associated with mutations in the Factor V gene (called Factor V Leiden). Approximately 6/100 Caucasians carries the FVL variant and approximately 1/1000 Caucasians develops a venous blood clot in adulthood. Both genetic (FVL genotyping) and non-genetic (APC-R assay, ultrasound) tests are available to assess risk and assist diagnosis of THR. FVL status confers 4-6 fold risk to develop venous blood clot; this risk is compounded by transient risk factors such as estrogen use or prolonged periods of immobilization. Compared to other genetic variants, FVL is weakly penetrant.[213]

To reiterate, this sampling approach enables a comparison among the perspectives of those whose medical condition has the characteristics of a public health concern (e.g. thrombophilia) and those whose medical condition does not (hereditary non-polyposis colorectal cancer). In this way, the traditional genetics group (HNPCC) serves as a type of "control" or reference point from which to make comparisons with a population that would more likely be the focus of public health genetics inquiry.

(b) "*Conditions*" refer to the intended use for the health information collected (research purposes and administrative purposes) as well as the level at which the health information would be anonymized (identifiable, coded, anonymized).

(c) *"Personal Health Information"* refers to the types of health information that participants were asked to hypothetically share (genetic test results, non-genetic medical test results, family history information, and blood sample).

CHAPTER 5: METHODOLOGY

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(A) Study Design

This research used a non-experimental, cross-sectional survey design.[214] Survey data were collected using a structured interview guide which was administered by a research assistant. Interested in the predictive effect of specific variables on authorization to share health information, a quantitative approach was best-suited to this research question. The survey data were collected by an interviewer-administered questionnaire (in contrast to self-administered) for two reasons. First, the Modified HCID Tool is complex and required explanation to participants. Second, the interviewer involved in the data collection process could easily clarify misunderstandings, encourage participants to complete all interview questions, and ask participants to elaborate on responses that may have warranted further explanation or description. In light of the fact that the authorization model is a newly proposed approach to informed consent, the interviewer was encouraged to engage in dialogue with participants who offered descriptive perspectives on why they were or were not willing to authorize the use of different types of health information for different research and administrative purposes. As a supplement to the quantitative analysis of these findings, a content analysis of the dialogue that emerged between the interviewer and the participant enabled a richer understanding of survey responses.

(B) Recruitment

Toronto area hospitals which provide clinical services for some or all of the target populations were considered as recruitment sites. Following exploratory discussions with

Clinic Directors and Hospital Administrators, four hospitals were included in the sampling frame. Participants were drawn from: (1) Mount Sinai Hospital (MSH), (2) The University Health Network (UHN), (3) Sunnybrook Health Sciences Centre (SHSC), and (4) North York General Hospital (NYGH) (Appendix 1.1). Eligible patients were over age 18 and had pursued genetic testing for HNPCC, HBOC, HH, or THR. It was not possible to assess comfort with the English language at the time of recruitment, but it was assumed that those who indicated interest in participating by completing the consent process were comfortable in English.

With permission from the Clinic and/or Laboratory Director(s), eligible patients were identified using clinical and laboratory databases. In addition to having had genetic testing for HNPCC, HBOC, HH, or THR, and being over age 18, clinical records had to indicate that the patient had been notified of his/her genetic test result. All records were reviewed to confirm that this disclosure had occurred. Patients were excluded from the list of potential participants if (1) there was any indication that a patient had not been notified of his/her genetic test result or (2) there was any indication that the patient was deceased. Potential participant names and contact information was entered into a recruitment spreadsheet. Clinic physicians reviewed and approved the recruitment spreadsheet for their respective clinics. If physicians felt that it was inappropriate to send a study invitation package to particular individuals (e.g. currently unwell), this individual's name was deleted from the recruitment spreadsheet.

All eligible participants were recruited by way of a one-time invitation letter (Appendix 1.2) that was signed by the physician who ordered the relevant genetic test and approved participant inclusion. The letter introduced the study and asked interested participants to review and sign an enclosed consent form (Appendix 1.3). Individuals who signed and returned their consent forms by mail were contacted by telephone to discuss the study in more detail and arrange a time to complete the study interview. If participants had any questions or concerns about the study, they were discussed at this time. Participants were given the option to complete the study interview by telephone or in-person, at a time that was convenient for them. The study invitation package also included a participant copy of the HCID tool (Appendix 1.6) for participants to reference at the time of participation in the study interview. Some participants accidentally returned the "HCID Participant Copy" with their consent form. In this case, the form was mailed back to the participant to keep on hand for their scheduled interview. Some participants misplaced their HCID tool while waiting to schedule a study interview. In this case, a new HCID tool was mailed or emailed to the participant to keep on hand for their scheduled interview. Some consenting participant records provided an incorrect telephone number. In this case, a subsequent letter was mailed to the participant. This follow-up letter indicated that our records were incorrect with respect to their current phone number and asked them to contact the study office by telephone in order to arrange a time to complete the study interview.

(C) Data Collection

Step 1: The Interview Guide

The Health Care Information Directive (HCID) was developed to negotiate between purely passive models of consent (such as blanket and presumed consent models) and fully participatory models of consent (the traditional model in which individuals must be contacted for each unique use of their health information regardless of format). Since Caulfield's authorization model calls for a legislated exception to consent, the HCID may be an appropriate alternative to a traditional consent form and facilitate the process of authorization. While it may be impossible to determine all possible uses in advance using the HCID, it is possible for individuals to define the range of possible usages of their PHI and to specify the form of data acceptable to them.

The HCID integrates sensitivity of data with intended use. It presents the permutations and combinations of sensitivity and usage in a matrix that forms a table, similar to an advance directive. The goal of the HCID is to allow individuals to make informed choices regarding how their health information can be used. Recent HCID pilot data demonstrated that most data users and consumers of health services agreed that privacy and consent issues were complex and important, and that a tool such as the HCID is a good idea.[215] The row headings of the HCID move from "most essential to most discretionary" uses and the column headings illustrate the types of data from most identifiable to most anonymous. The matrix forms a range of options which individuals can, as in advance directives, block out which uses and types of data they do not wish to contribute (Appendix 1.4). The HCID has face validity as it integrates the important elements of health information that have been discussed in the literature. From an ethical

perspective, the directive increases patient autonomy, facilitates patient control over information, and fosters transparency.[216]

For the purpose of this study, the HCID was modified to enable a comparison among different levels of anonymization. The American Society of Human Genetics describes four ways to identify samples for research purposes: (1) anonymous: biological materials that were originally collected without identifiers and are impossible to link to their sources, (2) anonymized: biological materials that were originally identified, but have been irreversibly stripped of their identifiers and are impossible to link to their sources, (3) coded: biological materials that are unidentifiable for research purposes but can be linked to their source by use of a code. Decoding can only be done by a member of the research team, and (4) identified: biological materials in which identifiers such as name, patient number, pedigree location are attached and available to the researcher.[217] The HCID reflects three of these categories: (1) identifiable health information; (2) coded information; and (3) anonymized information. In addition to the degree of anonymity, the sensitivity of PHI may depend upon the actual nature of the information (e.g. genetic vs. non-genetic information). For the purpose of the proposed research, the HCID was further modified to include a comparison between genetic and non-genetic medical information (Appendix 1.5).

The interview guide (Appendix 1.7) was primarily designed to capture participants' responses to situations posed by the Modified HCID Tool. To better understand the factors that influenced participants willingness to authorize the use of their health information, contextual questions related to medical research and information privacy

were included in the interview guide. The interview guide was structured with continuous (e.g. strongly agree to strongly disagree) and categorical (e.g. yes/no) scales and was organized into eight sections: (A) interview logistics and sampling characteristics, (B) participants' experience with a given medical condition and genetic testing, (C) participants' experiences with and opinions about research in general, (D) the HCID tool itself which included an exploration of participants' willingness to share four types of personalized, coded, and aggregated health information for six different research purposes and five different administrative purposes, (E) participants' perspectives on administering the HCID in practice, (F) participants' perspectives on privacy in general, (G) participants' comfort and experience with computers, and (H) participants' demographic characteristics. Appendix 1.8 links the study question, the variables of interest and the particular question(s) in the interview guide.

Prior to data collection, the interview guide was pilot tested for readability with members of our research team. Suggested changes related to simplifying language on the HCID Tool and creating a "participant-friendly" version of the tool for participants to reference during the course of the study interview were incorporated.

Step 2: The Interview

In preparation for the interview, the research assistant completed Section A (*Interview Logistics* and *Sampling Characteristics*) *except for* the participants' genotype. The principle investigator entered participant genotype status following the study interview because Clinic Directors requested that the interviewer remain blind to this information during the interview given the sensitivity that some individuals perceive it to have.

Study participants completed a structured interview in-person or by telephone with the research assistant. In-person interviews took place at Toronto General Hospital, the Joint Centre for Bioethics, and Sunnybrook Health Sciences Centre. The interviews were 30-45 minutes in duration. At the outset of the interview, the interviewer reviewed the goals of the study and restated that the interview would be audio-taped. The interviewer addressed any questions that the participant had prior to conducting the interview. The interviewer assembled the recording equipment and conducted the interview.

In addition to completing the structured portion of the interview, interviewees were encouraged to elaborate upon their perspectives or share experiences related to sharing medical information that may have been triggered by the structures questions. The interviewer used relevant probes to elicit this information where appropriate.

Step 3: Data Tracking

In addition to recording the interview, the interviewer took notes during the study interview. In the event that there were technical recording difficulties, hand-written notes were used as a back-up data source.

Following the completion of the interview, participant responses were entered into a database that included variables for each interview item and sampling characteristic (condition, genotype, phenotype, recruitment site). Audio-tapes were reviewed for audibility and given to the transcriber for transcription. Approximately halfway through the data collection period, digital recording equipment became available to the researchers. From this point forward, study interviews were recorded digitally and

transcribed electronically. Transcripts were returned to the researchers for qualitative analyses.

Step 4: Closure

Follow-up letters were sent to participants to thank them for their contribution of time and insights (Appendix 1.9) and to close the research relationship that had been established. For participants' personal records, copies of participants' signed consent forms were included in this follow-up package.

(D) Data Analysis

(i) Quantitative Analysis

First, basic trends and distributions using descriptive analysis were identified. Interested in the factors that influence individuals' authorization of the use of personal health information, data were analyzed using binary logistic regression. Binary logistic regression is a generalized linear model used to quantify the effect of predictor variables on a particular outcome (e.g. authorization) when that outcome is categorical in nature and has two values (e.g. authorize use, do not authorize use). Non-parametric data such as these are free of the assumptions of normality. Logistic regression uses odds ratios to reflect the probability of a given outcome.[218] This analysis and data manipulation was facilitated by SAS 9.1 software.[219] Appendix 1.10 includes statistical codes used to facilitate this analysis.

Step 1: Data Cleaning

The complete dataset was examined for data entry and coding errors. Identifiable errors were corrected. Based upon the sample size, many demographic variables had a disproportionate number of categories. For this reason, cumbersome categories within the following variables were collapsed: ethnic background, relationship status, education, employment status, and income. These variables were recoded to reflect this simplification.

Step 2: Response Rates

Response rates were calculated by disease group (HNPCC, HBOC, HH, THR), and recruitment site (UHN, MSH, NYGH, SHSC) using simple frequency calculations. Frequencies were calculated for the following response categories: (a) invitation packages sent, (b) participation completed, (c) invitation packages returned by Canada Post, (d) returned and completed consent forms but interviews not scheduled, (e) withdrew, (f) declined, and (g) did not respond. Response rates were first tallied using "total interview packages sent" as an unadjusted denominator and then tallied using this denominator minus the number of packages returned by Canada Post as an adjusted denominator.

Although included in the response rate calculations, partial data collected from anyone who withdrew participation was excluded from the remainder of the analyses. As well, response rates were used to inform the extent to which each disease group was included in the overall analysis.

Chi-square tests of association were used to determine the presence of response bias according to four criteria known at the time of recruitment: gender, recruitment site, disease group, and genotypic status.

Step 3: Sample Characteristics

Categorical demographic variables were analyzed using frequency tabulations and continuous demographic variables were analyzed using means, standard deviations, and ranges. To the extent that outlying data presented a skewed interpretation of a particular question, rationale for its exclusion is provided.

Step 4: Identification of Key Variables

Key variables were identified based upon the study question:

> *How do **individuals who have pursued genetic testing** define the **conditions** under which they are willing to authorize the use of their **personal health information (PHI)** for administrative and research purposes?*

"Individuals who have pursued genetic testing" can be described according to (a) the population group from which they were recruited (HNPCC, HBOC, HH, THR), (b) their genotypic status (genotype positive or genotype negative), and (c) their phenotypic status (phenotype positive or phenotype negative). "Conditions" refer to (a) the level at which PHI is anonymized (personalized, coded, aggregated) and (b) the intended use of PHI (research purpose or administrative purpose). Finally, "PHI" refers to four different types of personal health information: (a) genetic test results, (b) non-genetic test results, (c) family history information, and (d) information gleaned from a blood sample.

Other key variables were identified based upon questions asked in the interview guide which helped to appreciate the context from which participants made the choices they did. These will be referred to as "contextual factors." Simple frequencies and measures of central tendency were used to describe some contextual factors and Chi Square tests of association were used to identify associations among other contextual variables. Key associations that emerged from this preliminary step informed more specific analyses.

Step 5: Exploration of Key Variables

The extent to which key variables predicted authorization for the use of PHI was explored. Three predictor variables reflected characteristics of the study participants. These included: (a) the population group from which they were recruited (HNPCC, HBOC, HH, THR), (b) their genotypic status (genotype positive or genotype negative), and (c) their phenotypic status (phenotype positive or phenotype negative). Two predictor variables reflected characteristics of the health information. These included: (a) the level at which the information is anonymized (personalized, coded, or aggregated), and (c) the type of information being requested (genetic test results, non-genetic test results, family history information, or information gleaned from a blood sample).

First, "Overall Predictors of Authorization" were examined. To determine the overall effect of participant predictor variables on authorization, research purposes 1-6 were collapsed and administrative purposes 1-5 were collapsed. Authorization for research purposes as a whole were compared to authorization for administrative purposes as a whole, but neither was examined at the level of the specific purpose for this initial step. Information types (genetic, non-genetic, family history, blood sample) and anonymization levels (personalized, coded, aggregated) were also collapsed in order to

create an initial impression of the effects of the participant predictor variables. Odds ratios for research purposes and administrative purposes ("odds of saying yes to sharing information for research purposes and odds of saying yes to sharing information for administrative purposes") were calculated for each level of genotype, phenotype, and disease group to determine the significance of each variable's effect on authorization. Odds ratios were also calculated for participant characteristics including self-reported privacy level, age, gender, and education. Each of these variables was considered as a predictor variable and as a covariate so that its true effect on authorization could be determined. Unadjusted and adjusted odds ratios, p values, and 95% confidence intervals were calculated for each comparison. The presence or absence of multicolinearity among all variables was assessed by comparing unadjusted and adjusted odds ratios.

Second, "Specific Predictors of Authorization" were examined. The first step in identifying specific predictors was to examine the effect of anonymization level. Odds ratios ("odds of saying yes to sharing information") were calculated for each specific research purpose (1-6), each specific administrative purpose (1-5), and each anonymization level (personalized, coded, aggregated) for each level of disease group, genotype, and phenotype. Subsequent to this step, each specific type of PHI (genetic non-genetic, family history, blood sample) and each level of each participant predictor variable described above was added to examine the data at its finest level of detail. As above, each of these variables was considered as a predictor variable and as a covariate so that its true effect on authorization could be determined. Unadjusted and adjusted odds ratios, p values, and 95% confidence intervals were calculated for each comparison.

Step 6: Interpreting relationships among variables

In order to interpret the aforementioned odds ratios, probability estimates and 95% confidence intervals were calculated for each predictor variable that warranted further exploration based upon the significance of its effect on authorization in Step 5. These probabilities were adjusted for age, sex, education, and self-reported privacy level. The probability estimates were plotted so that a visual representation of these findings could further assist interpretation. The probability plots for the variable which had the greatest overall predictive effect on authorization was examined closely to determine which specific factors are most salient for participants' asked about authorizing the use of their personal health information.

Step 7: A Predictive Model

The variables with the most significant effect on authorization were entered into a predictive model. A Generalized Estimation Equation (GEE) is a type of Generalized Linear Model (GLM) used to model data that do not fit a normal distribution. GEEs are used when data are correlated or "clustered."[220] Since each respondent had to respond to several questions, we used GEEs to adjust for repeated measurements. All of the logistics models were adjusted for correlation among observations and were adjusted for possible over or under dispersion. The Pearson Chi-square test (the ratio of Pearson deviance divided by degrees of freedom) was used as a test for goodness of fit.[221] The fitted model calculates the probability of answering "yes" to sharing information for each level of the predictive variables entered into the model. Upper and lower 95% confidence intervals were calculated and significant differences among probability scores were determined according to the extent to which confidence intervals overlap. A range

of scenarios entered into the predictive model presented enables a better understanding of the factors that influence research participants' willingness to share health information.

(ii) Content Analysis

Content analysis has been defined as "any technique for making inferences by objectively and systematically identifying specified characteristics of messages."[222] A content analysis of the dialogues that ensued between the interviewer and the interviewees was undertaken as a way to supplement and inform the quantitative findings. Transcripts from interviews with all participants from the HBOC and THR populations were included in this step of the analysis. Transcripts from interviews with individuals from the HNPCC and HH populations were excluded. Remarks from participants whose audiotapes were indecipherable, blank, or incomplete were also excluded from this step.

A list of codes was established at the outset of this analysis. Each code fell into one of four domains: Two of these four domains were deductively determined: (1) Those that were descriptive of participant characteristics (GENO, PHENO, POPN, AGE, PRIV) and (2) those that were descriptive of the health information and the purposes for which it might be used (ANON, PURP1-4, TYPE, REVISIT). Codes in the third domain were inductively-oriented; they were assigned to themes that recurred while reviewing the transcript content (TRUST, SAFEG, ALTR). Codes in the fourth domain emerged in response to an open-ended question about participants' reactions to the HCID Tool itself, "What did you think of this form?" with the specific probe related to the form's level of

detail (D-COLL, D-GUID, D-OK). All codes and the operational definitions are presented in Chapter 6, Table 7.

Unlike traditional content analysis in which the recording unit is typically a word or a short phrase, only participant comments that captured the specified *meaning/essence* of the code were included as analyzable text. The context in which these comments were made was used to inform their meaning. Robson[214] describes this type of content as *latent* and explains that unlike *manifest content* which reflects the presence or absence of single words, latent content requires inference or interpretation on the part of the coder. Inference on the part of the coder was further required in order to meet the expectation that content analysis categories be mutually exclusive.

All transcripts were reviewed and coded by hand by two individuals. Given the high-inference nature of this analysis, a concordance check was done at a preliminary stage. Once necessary revisions to category definitions and coding scheme were made, the text was recoded by the same two coders and re-checked for concordance.

The frequency with which each code occurred in each analyzed transcript was entered into a Content Analysis Worksheet. Simple frequencies were calculated to reflect the salience of each theme. Remarks that best illustrate each particular theme were selected and are reported in Chapter 6. Attention to these remarks enabled a more nuanced discussion of the meaningful factors that predict authorization to share health information and mitigate the tension between research and individual privacy interests.

(E) Ethics Considerations

Prior to commencing any component of this methodology, ethics approval was sought and granted from Research Ethics Boards at Mount Sinai Hospital, The University Health Network, Sunnybrook Health Sciences Centre, and North York General Hospital as well as from the University of Toronto Health Sciences I Research Ethics Board (Appendices 1.11a-e).

Participants' consent was obtained prior to study participation (Appendix1.3). This process included an explanation of the study purpose, procedures, risks, and voluntary nature. All participants were given the opportunity to ask questions about the study goals and interview process at the outset of and throughout their participation.

Participants were assigned identification numbers at the time of participation and their names were deleted from data collection materials in order to protect their privacy. While a link between participant name and identification number was created, it was stored in a separate research office and was not accessible to individuals outside of the research team. All data materials will be stored in a locked research office and destroyed in ten years.

Telephone and in-person interviews were conducted in private rooms. Audio-tapes and digital recordings were labeled with identification numbers only. Participants were assured that the information they provided in the interview would not compromise their current or future care at respective hospital sites.

There were no physical risks to participating in this study. While it was possible that there be some psychological or emotional reaction to a discussion of health information privacy, participants appeared to be willing to share personal experiences and opinions without any evidence of psychological or emotional distress. Trained as a genetic counselor, the principle investigator was available to debrief with participants should any follow-up have been required.

Financial compensation was not available for participants.

CHAPTER 6: RESULTS

CHAPTER 6: RESULTS

(A) Quantitative Findings

(i) Response Rates

Response rates were calculated overall, by disease group (HNPCC, HBOC, HH, THR), and by recruitment site (UHN, MSH, NYGH, SHSC) using simple frequency calculations (Table 2). Invitation packages were mailed to 1148 eligible individuals. 80 of these 1148 packages (7%) were returned by Canada Post because the address was incorrect. Since 80 individuals for whom study invitations were intended were in fact not informed of the study and did not have the opportunity to decide about participating, they were excluded from response rate calculations. Overall and specific group denominators were adjusted to reflect this reduction in the sampling frame.

Overall, 199 individuals participated (19%). Of this total, only eight individuals participated from the HNPCC population (13%). 96 individuals from the HBOC population participated (19%), the greatest proportion of which came from the UHN Site (69/96 or 72%). Only 10% of the HH population participated, the majority of which came from the NYGH Site (8/11 or 73%). Finally, 21% of the THR population participated, the greatest proportion of which came from the SHSC Site (62/84 or 74%). Given the low response from the HNPCC (n=8) and HH (n=11) populations, their data were included in the description of the Sample Characteristics, but excluded from the remainder of the analyses.

One individual from the NYGH HBOC population withdrew participation part way through the study interview as she "lost interest" in the topic. Partial data obtained from this individual were excluded from the analyses.

Seventeen individuals expressed interest in participating by returning their signed consent forms but were unable to schedule study interviews within the allocated timeframe. Multiple attempts were made by the principle investigator to schedule interviews for these potential participants but for reasons related to illness, vacation, employment and family commitments, interviews could not be scheduled. Seven of these individuals were from the HBOC population, nine were from the THR population, and 1 was from the HH population.

Eight individuals proactively "declined" by returning an unsigned consent form along with a note indicating that they were not able to or not interested in participating in the study. Five of these individuals were from the HBOC population and three were from the THR population.

Three individuals (two HBOC and one THR) were identified as deceased since the time that the recruitment list was assembled. These individuals may have been deceased at the time that the recruitment list was assembled but this was not indicated in their medical records. Alternatively, they may have passed away between the time of ascertainment and receipt of study invitation.

842 individuals did not respond to the invitation to participate (842/1068 or 79%). 82% of the HNPCC population did not respond, 78% of the HBOC population did not respond, 89% of the HH population did not respond, and 76% of the THR population did not respond. Chi-Square tests of association ruled out any potential response bias. There were no significant differences among participants and non-participants according to gender (X^2= 2.00, p=.15), recruitment site (X^2= 1.10, p=.77), disease group (X^2= 4.50, p=.21), and genotypic status (X^2= 3.00, p=.08).

Table 2 - Response Rates

Condition	Recruitment Site	***Participation Complete***	*Withdrew*	*Consent returned but unable to schedule*	*Declined*	*Deceased since recruitment list assembled*	*Invitation package returned by Canada Post*	*No response*	Total Invitations sent (unadjusted for returns)	**Total Invitations sent (adjusted for returns)**	"Unadjusted Response Rate" (%)	**"Adjusted Response Rate" (%)**
HNPCC	**MSH**	**5**	0	0	0	0	4	35	46	**42**	11%	**12%**
	SHSC	**3**	0	0	0	0	0	14	18	**18**	17%	**17%**
	Subtotal	**8**	0	0	0	0	4	49	64	**60**	12%	**13%**
HBOC	**UHN**	**69**	0	2	4	2	22	207	303	**281**	23%	**24%**
	SHSC	**10**	0	4	1	0	12	141	176	**164**	11%	**12%**
	NYGH	**8**	1	1	0	0	0	40	50	**50**	16%	**16%**
	Subtotal	**96**	1	7	5	2	34	388	529	**495**	18%	**19%**
HH	**UHN**	**3**	0	1	0	0	2	59	65	**63**	5%	**5%**
	NYGH	**8**	0	0	0	0	0	35	43	**43**	19%	**19%**
	Subtotal	**11**	0	1	0	0	2	94	108	**106**	10%	**10%**
THR	**UHN**	**22**	0	2	1	1	13	90	129	**116**	17%	**19%**
	SHSC	**62**	0	7	2	0	27	214	311	**284**	20%	**22%**
	NYGH	**0**	0	0	0	0	0	7	7	**7**	0%	**0%**
	Subtotal	**84**	0	9	3	1	40	311	447	**407**	19%	**21%**
TOTAL		**199**	1	17	8	3	80	842	1148	**1068**	17%	**19%**

(ii) Sample Characteristics

Table 3A and Table 3B describe the characteristics of this sample. As reflected by the response rates, the study sample consisted predominantly of individuals from the HBOC (48%) and THR (42%) populations. 61% of the sample was genotype positive and 54% of the sample was phenotype positive. The majority of participants were over the age of 50 (63%), female (77%), Caucasian (93%), married or common-law (72%), educated at a highschool level or higher (88%), and employed full time (53%). Of the people who responded to the question about household income (28%), the majority (67%) reported

earning more than $40,000 annually. Most participants had no prior experience as research participants (66%). Of those with prior research experience, the majority were from the HBOC population (71%).

Contextual factors that could influence participants' willingness to authorize the use of their personal health information for research purposes were considered. Years since clinical diagnosis (if phenotype positive) and years since genetic test results received could reflect the extent to which the recency of information influences willingness to authorize its use. Mean years since clinical diagnosis was 8.60 [sd = 8.50, range (1.43)]. Years since clinical diagnosis was not associated with sharing information for administrative purposes (p=.20), and years since clinical diagnosis was weakly associated with sharing information for research purposes (p=.03). For each extra year since clinical diagnosis, the odds of sharing information for research increased by 3% (OR = 1.03). Mean years since genetic test results received was 4.60 [sd = 3.40, range (<1,15)]. Years since genetic test results were received was not associated with sharing information for research or administrative purposes ($p_{administrative}$ =.13, $p_{research}$= .96). Two individuals reported years since received genetic test results as greater than 25. Since genetic testing was not available for any of the index conditions 25 years ago, these outlying responses were excluded from this descriptive analysis. The extent to which participants had been engaged in research prior to this study could reflect their general perspectives on sharing PHI for research. The majority of participants had no prior research experience (66%) and prior research experience was not associated with sharing information for administrative or research purposes $p_{administrative}$ =.97, $p_{research}$= .37). As indicated in Chapter 3, there is some literature that suggests that willingness to share health

information varies with how the data are ultimately stored. In this sample, 34% preferred electronic storage 36^% preferred traditional paper storage, and 30% had no preference. On a Likert scale, participants were moderately comfortable with computers [mean = 2.1, sd = 1.3, range 1,5]. Finally, the majority of participants (95%) did not feel entitled to share in any commercial gain that might come to the investigators or institutions conducting the research.

The extent to which participants considered themselves to be a "private person" or an "open person" may also inform the information sharing tendencies. On a Likert scale where 1 was "very private" and 5 was :"very open," mean self-reported privacy level was moderate [mean = 3, sd = 1.31, range (1,5)]. Understanding the relative importance participants place on the privacy of medical information compared to other personal information created another reference point for comparison. 45% of participants felt that the privacy of their medical information was less important than the privacy of their financial information, 37% felt it was equally important, and 18% felt that the privacy of their medical information was more important than the privacy of their financial information.

Table 3A – Sample Characteristics - Categorical variables

Variable	Levels	N	%
Condition	HNPCC	8	4
	HBOC	96	48
	HH	11	6
	THR	84	42
Genotype	Geno +ve	121	61
	Geno –ve	78	39
Phenotype	Pheno +ve	107	54
	Pheno –ve	92	46
Age	50 or over	125	63
	Less than 50	74	37
Gender	Male	46	23
	Female	153	77
Ethnicity	Caucasian	185	93
	Not Caucasian	14	7
Relationship Status	Married or Common Law	144	72
	Not Married or Common Law	55	28
Education	More than High school	176	88
	High school or less	23	12
Employment Status	Full-time	105	53
	Not Full-time	94	47
Household Income	$40,000 or more	37	19
	Less than $40,000	18	9
	Did not respond	144	72
Prior Research Experience	Yes	68	34
	No	131	66
Relative importance of medical info compared to financial info	Medical is more	35	18
	Medical is the same	74	37
	Medical is less	90	45
Data Storage Preference	Electronic File	68	34
	Paper File	72	36
	No preference	59	30

Table 3B - Sample Characteristics - Continuous Variables

	Mean	STD	Range
Years since clinical diagnosis	8.6	8.5	1,43
Years since genetic test results received	4.6	3.4	<1,15
Self-reported privacy level (Likert 1-5)	3	1.3	1,5
General comfort with computers (Likert 1-5)	2.1	1.3	1,5
Everyday use of computers (Likert 1-5)	2.7	1.6	1,5

(iii) Exploration of Key Variables

First, "Overall Predictors of Authorization" were examined. Odds ratios for collapsed research purposes and administrative purposes, collapsed information types, and collapsed anonymization levels were calculated for each level of genotype, phenotype, and population group to determine the significance of each variable's effect on authorization (Table 4). Individuals who were genotype negative were more willing to share PHI for research and administrative purposes than were individuals who were genotype positive [$OR_{research}$ = .62, 95% CI .41-.95, p=.03; OR_{admin} = .54, 95% CI .36-.81, p<.01]. Neither phenotype nor population group had a significant effect on participants' willingness to share PHI for research or administrative purposes.

Odds ratios were then calculated for participant characteristics including self-reported age, sex, education, and self-reported privacy level. None of participants' age, sex, or education level had a significant effect on the odds of sharing PHI for research or administrative purposes. Self-reported privacy level, however, did have a significant effect on willingness to share PHI. Specifically, participants who reported themselves to be "more open" were more likely to authorize the use of their PHI for administrative purposes (OR = 1.21, 95% CI 1.01-1.41, p=.04). While the odds of sharing PHI for research purposes was also higher for those who reported themselves to be "more open," this finding was not significant (OR = 1.11, 95% CI .94-1.30, p=.22). Since each of these variables was considered as a predictor variable and as a covariate, the reported effects of these variables on authorization preclude confounding effects. Given the relevance of this variable, the extent to which self-reported privacy level was associated with (a) interest in revisiting choices on the HCID Tool and (b) preference for data storage

mechanism (electronic versus paper format) were assessed. There was no association between privacy level and interest in revisiting choices ($X^2 = .79$, p=.94) and no association between privacy level and preference for data storage format ($X^2 = 13.42$, p=.10)/

The effect of anonymization level on authorization was considered next. Odds ratios were calculated for each specific research purpose (1-6), each specific administrative purpose (1-5), and each anonymization level [(a) personalized, (b) coded, and (c) aggregated] for each level of population group, genotype, and phenotype. 198 comparisons generated from these combinations are presented in Appendices 2.1 and 2.2. Willingness to authorize use of health information was directly related to its degree of anonymity. Participants were most willing to share aggregated data and least willing to share personalized data. Furthermore, they were more willing to share aggregated data than they were coded data and they were more willing to share coded data than they were personalized data. This pattern was highly significant and held true for all research and administrative purposes, both HBOC and THR populations, both genotypic states, and both phenotypic states. Of 198 comparisons made, only 12 (6%) were not significant at $p<.05$ level. There was no apparent pattern to the non-significant results.

Table 4 – Overall Predictors of Authorization

Purpose	Predictor	Level	OR unadj	lowCI unadj	upCI unadj	p_unadj	OR adj	lowCI adj	upCI adj	p_adj
Admin	*genotype*	*Genotype +ve*	*0.5564*	*0.3728*	*0.8305*	*0.0041*	***0.5420***	*0.3617*	*0.8123*	*0.0030*
Admin	genotype	Genotype –ve	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	*genotype*	*Genotype +ve*	*0.6357*	*0.4196*	*0.9632*	*0.0326*	***0.6224***	*0.4090*	*0.9471*	*0.0269*
Research	genotype	Genotype –ve	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	phenotype	Phenotype +ve	1.2563	0.8584	1.8387	0.2403	1.2742	0.8709	1.8645	0.2120
Admin	phenotype	Phenotype –ve	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	phenotype	Phenotype +ve	0.8770	0.5914	1.3005	0.5139	0.8814	0.5938	1.3083	0.5309
Research	phenotype	Phenotype –ve	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	population	HBOC	0.8412	0.5648	1.2529	0.3949	0.7738	0.5113	1.1711	0.2252
Admin	population	Thrombophilia	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	population	HBOC	1.0155	0.6775	1.5221	0.9408	0.9064	0.5943	1.3826	0.6484
Research	population	Thrombophilia	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	age	50 or over	0.9920	0.6677	1.4736	0.9681	0.9742	0.6512	1.4574	0.8988
Admin	age	Less than 50	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	age	50 or over	0.9199	0.6120	1.3828	0.6882	0.9254	0.6104	1.4028	0.7147
Research	age	Less than 50	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	sex	Female	0.9193	0.5814	1.4534	0.7187	0.9221	0.5815	1.4621	0.7301
Admin	sex	Male	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	sex	Female	1.2545	0.8020	1.9624	0.3205	1.2458	0.7921	1.9594	0.3416
Research	sex	Male	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	educ	</= HS graduate	1.1721	0.6337	2.1677	0.6128	1.0704	0.5715	2.0049	0.8318
Admin	educ	higher than HS	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Research	educ	</= HS graduate	1.2618	0.6577	2.4207	0.4842	1.2049	0.6202	2.3407	0.5823
Research	educ	higher than HS	1.0000	1.0000	1.0000		1.0000	1.0000	1.0000	
Admin	*privacy*		*1.1763*	*1.0095*	*1.3707*	*0.0375*	***1.1727***	*1.0046*	*1.3689*	*0.0436*
Research	privacy		1.1094	0.9483	1.2980	0.1948	1.1038	0.9418	1.2936	0.2228

(iv) Interpreting Relationships among Key Variables

In order to interpret the aforementioned odds ratios, the probability (and 95% confidence interval) of "saying yes" to sharing health information for each of the eleven purposes (six research and five administrative purposes) was calculated. Given the significant aforementioned effects of anonymization level and genotype status, each level of these

predictor variables was factored into the calculation of probability estimates. These probabilities were adjusted for age, sex, education, and self-reported privacy level. These probabilities are reported in Appendix 2.4 and plotted in Figures 1-3.

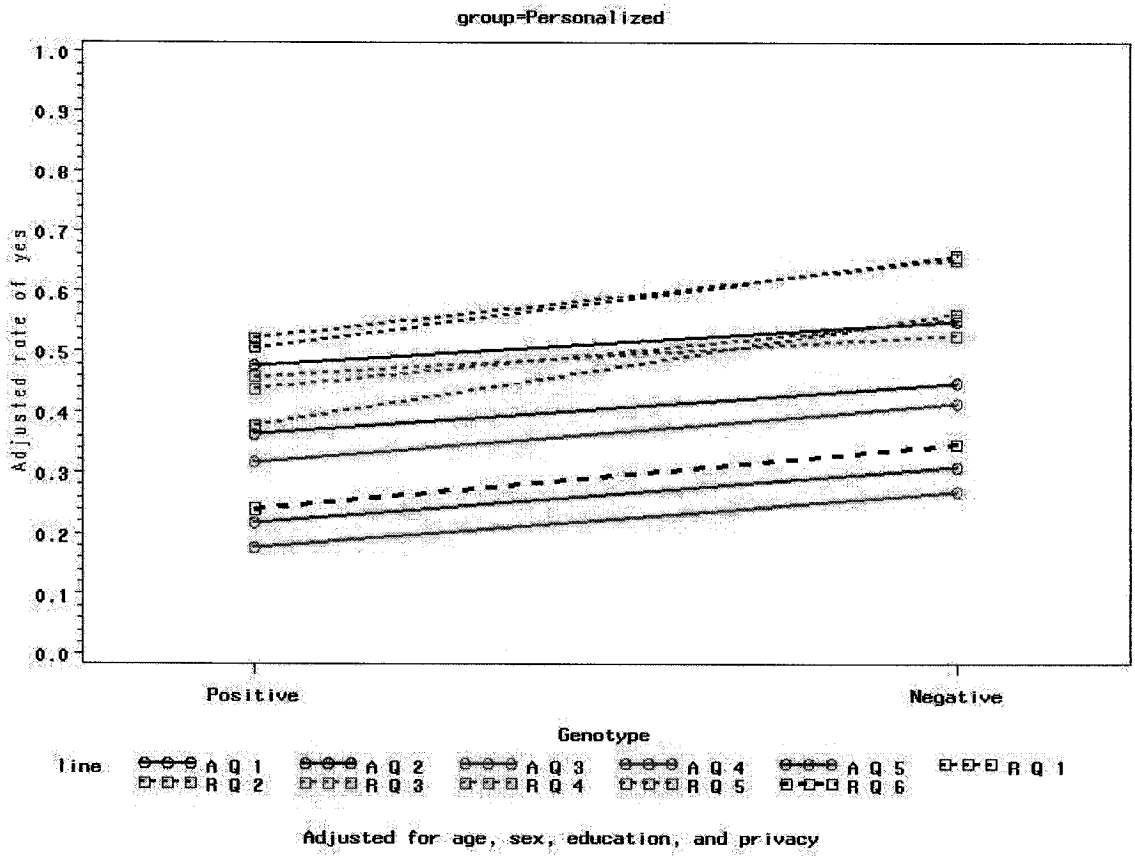
Figures 1-3 (and Appendix 2.3) reflect three overall trends: (1) participants who were genotype positive were less willing to authorize the use of their health information for all research and administrative purposes than were individuals who were genotype negative, (2) the probability that participants would share health information for research purposes was greater than the probability that they would share this information for administrative purposes, (3) participants were most likely to share aggregated health information followed by health information that is coded, followed by health information that is personalized.

When health information is personalized (Figure 1), research use is generally more likely to be authorized than administrative use. However, sharing health information for appointment reminder appears to be as likely as sharing it for research purposes and sharing health information for the purpose of government research appears to be as unlikely as sharing this information for other administrative tasks. From most to least permissive, the following sequence emerged: general and genetics research for HBOC or THR, appointment reminders, research on other conditions, controversial research, hospital tracking research, billing organization, hospital tracking administration, government research, hospital fundraising, government administration. While the sequence of permissiveness is worthy of comment in Chapter 7, the overlapping 95% confidence intervals suggest that the differences in these probability estimates are not

statistically significant. Interestingly, all probability estimates for sharing personalized information for administrative purposes were less than 0.50 (except AQ1) whereas most probability estimates for sharing personalized information for research purposes were greater and 0.50.

Figure 1:

Willingness to Share Personalized Health Information: By Genotype

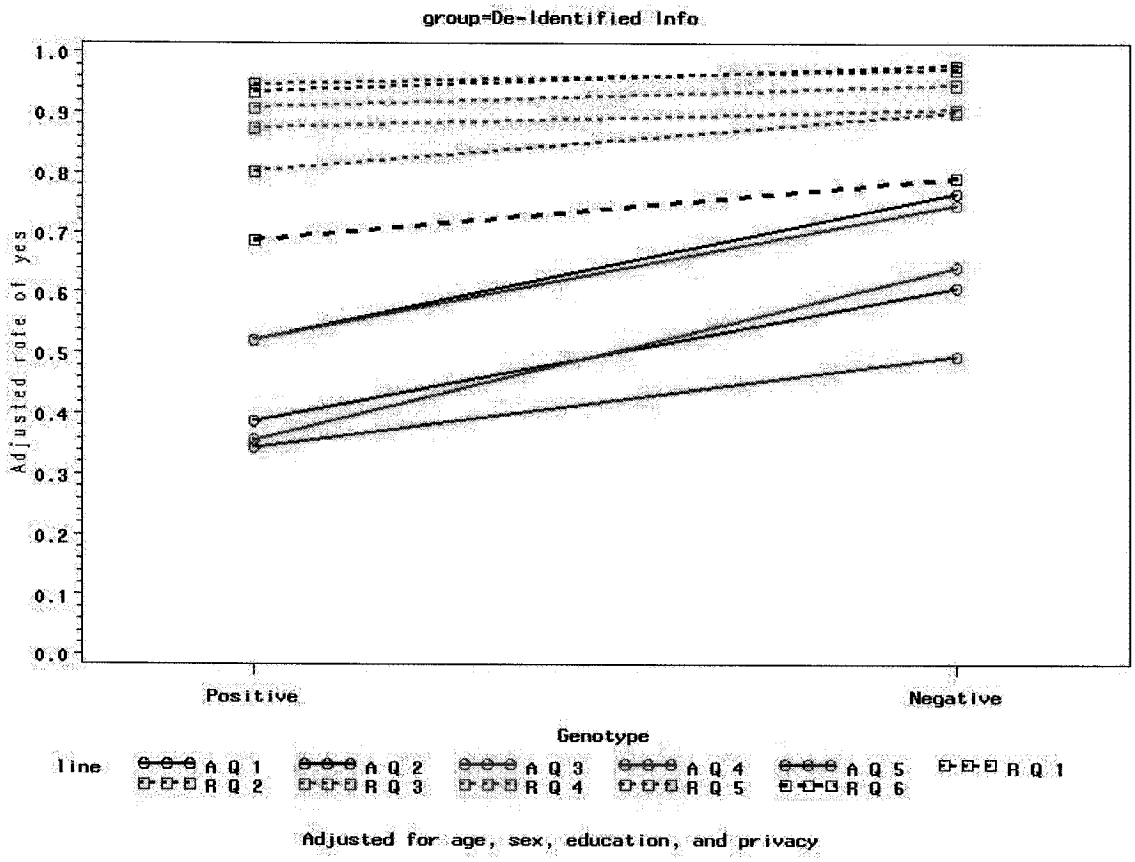


When health information is coded, the probabilities of sharing information for research purposes as a group are greater than they are for administrative purposes as a group (Figure 2). From most to least permissive, the following sequence emerged: general and genetics research for index condition, research on other conditions, controversial

research, hospital tracking research, government research, appointment reminders, hospital tracking administration, billing organization, government administration, hospital fundraising,. Based upon the confidence intervals, sharing coded health information for hospital fundraising purposes appears to be statistically significantly less likely than sharing coded information for general and genetics research on HBOC or THR, research on other conditions, and research in controversial areas.

Figure 2:

Willingness to Share Coded Health Information: By Genotype

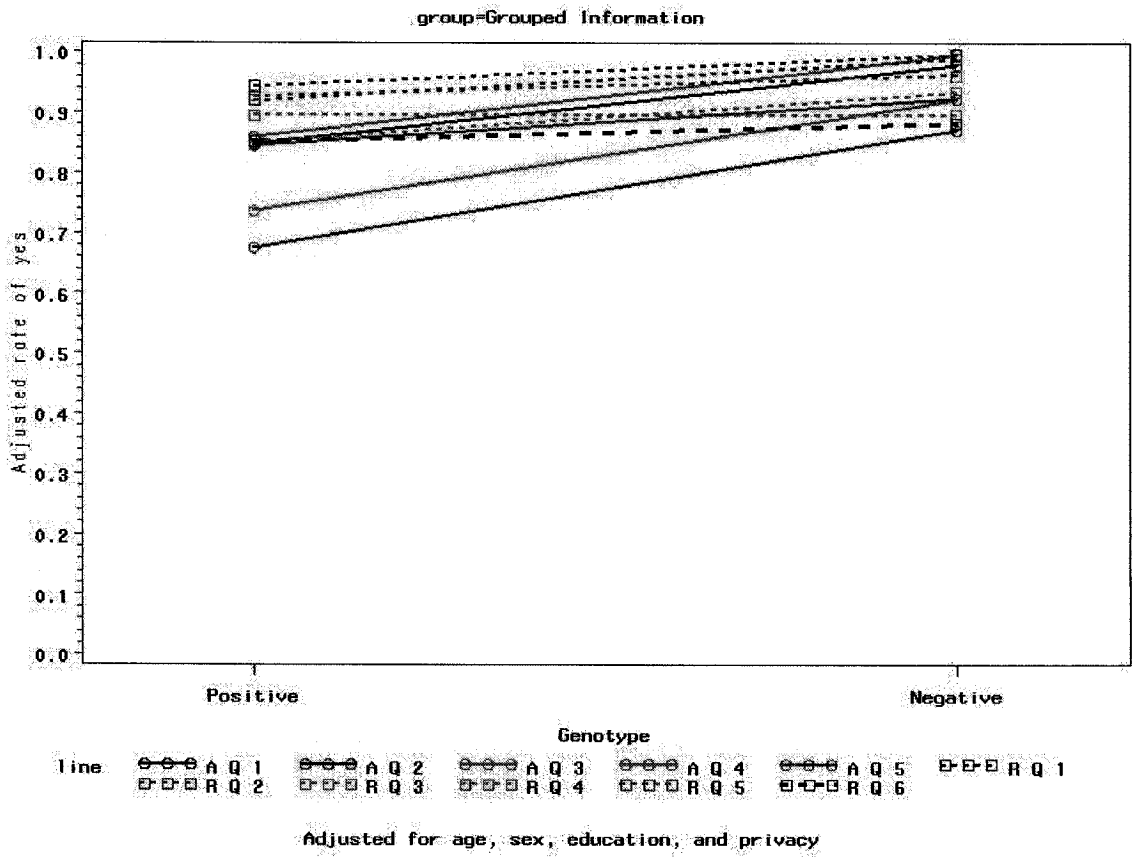


When health information is aggregated (Figure 3), the spread of probability scores is narrower. From most to least permissive, the following sequence emerged: general

research for HBOC and THR, genetics research for HBOC and THR and hospital tracking research, research into other conditions and controversial areas, hospital tracking administration, appointment reminders, hospital fundraising, government administration, billing administration. Again, while the sequence of permissiveness is worthy of comment in Chapter 7, the overlapping 95% confidence intervals suggest that the differences in these probability estimates are not statistically significant.

Figure 3:

Willingness to Share Aggregated Health Information: By Genotype



Since neither phenotype status nor population group were identified as significant predictors of authorization (Step 5), probability estimates for these variables will be reviewed briefly. Figures 4-6 and Appendix 2.4 depict probability plots and estimates for

both phenotypic states and Figures 7-9 and Appendix 2.5 depict probability plots and estimates for both population groups. For phenotypic states and population groups overall, probability to share health information for research purposes appears to be greater than that for administrative purposes. This is particularly salient when health information is coded (Figure 5, Figure 8). Overall, both phenotype positive and phenotype negative groups as well as HBOC and THR groups were more likely to share information for general and genetics research and less likely to share health information for billing organization, government administration and hospital fundraising purposes. Compared to the THR population, the HBOC population was as likely or less likely to authorize the use of their health information for various purposes. The effect of phenotypic status on probability of sharing health information for various purposes appears to be negligible.

Figure 4:

Willingness to Share Personalized Health Information: By Phenotype

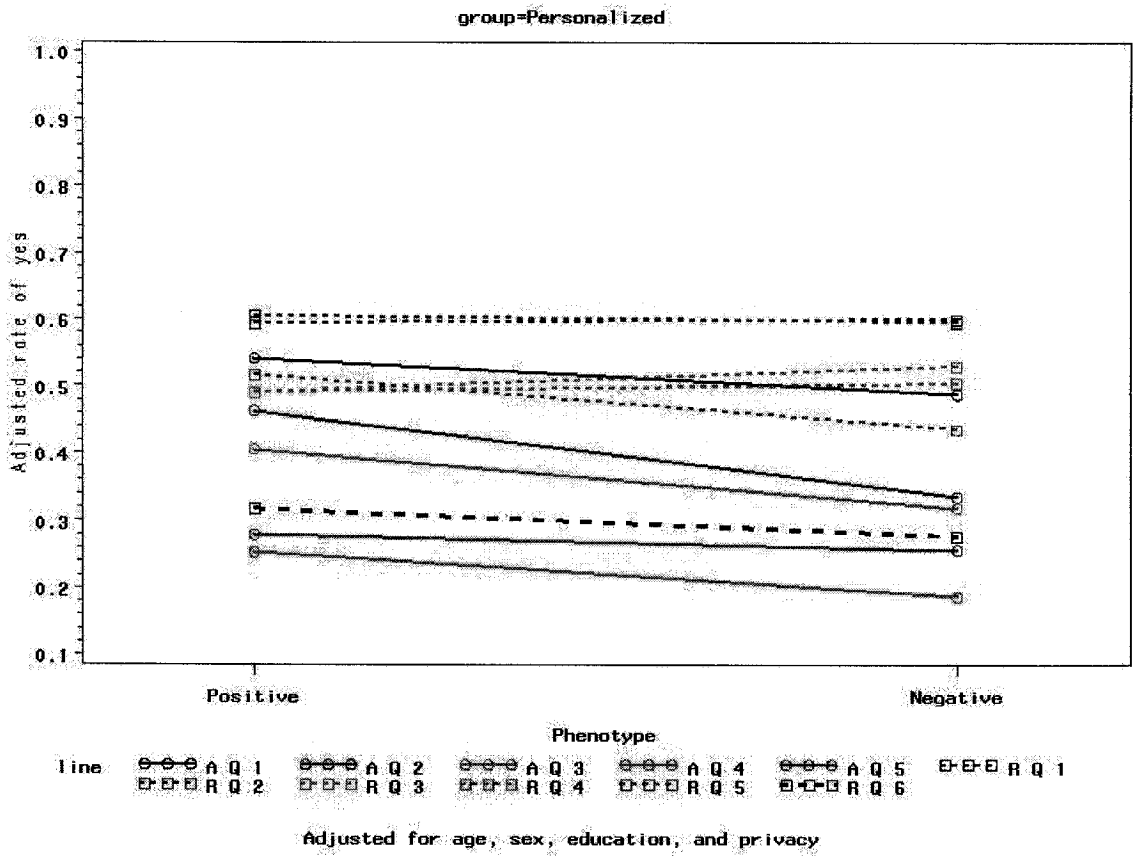


Figure 5:

Willingness to Share Coded Health Information: By Phenotype

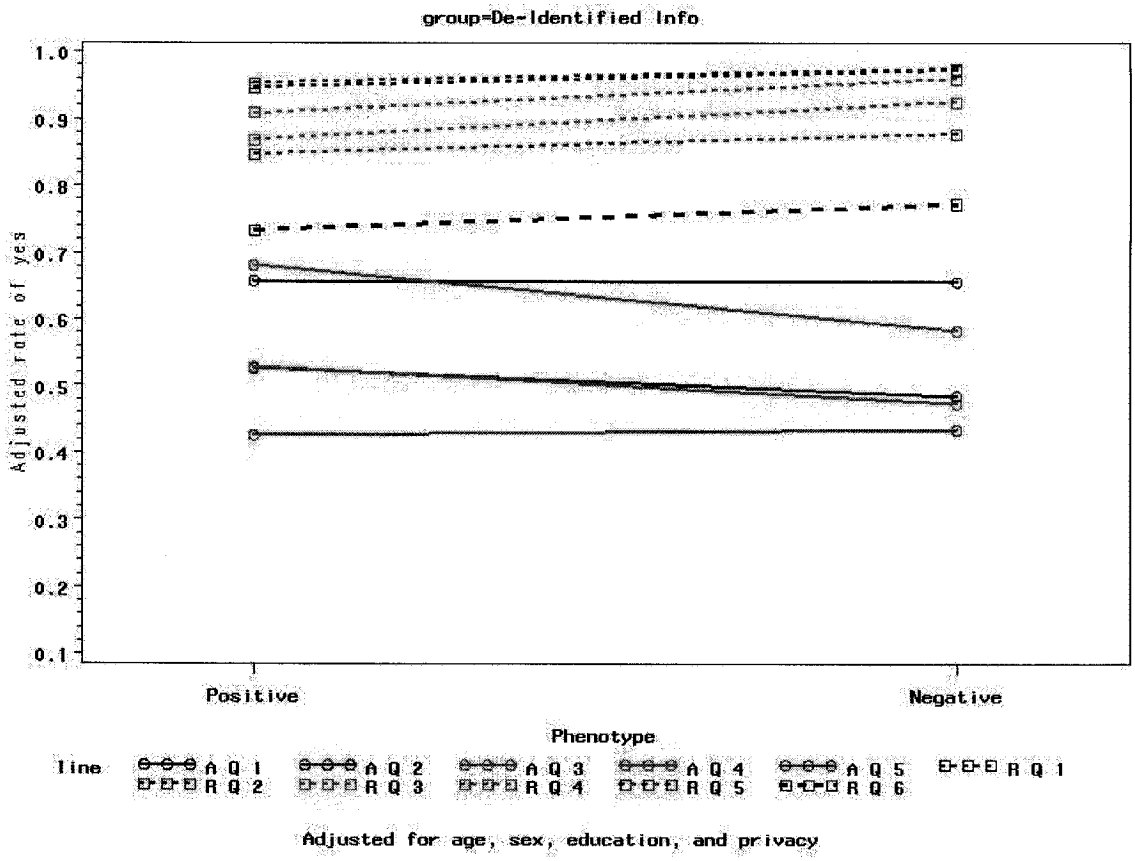


Figure 6:

Willingness to Share Aggregated Health Information: By Phenotype

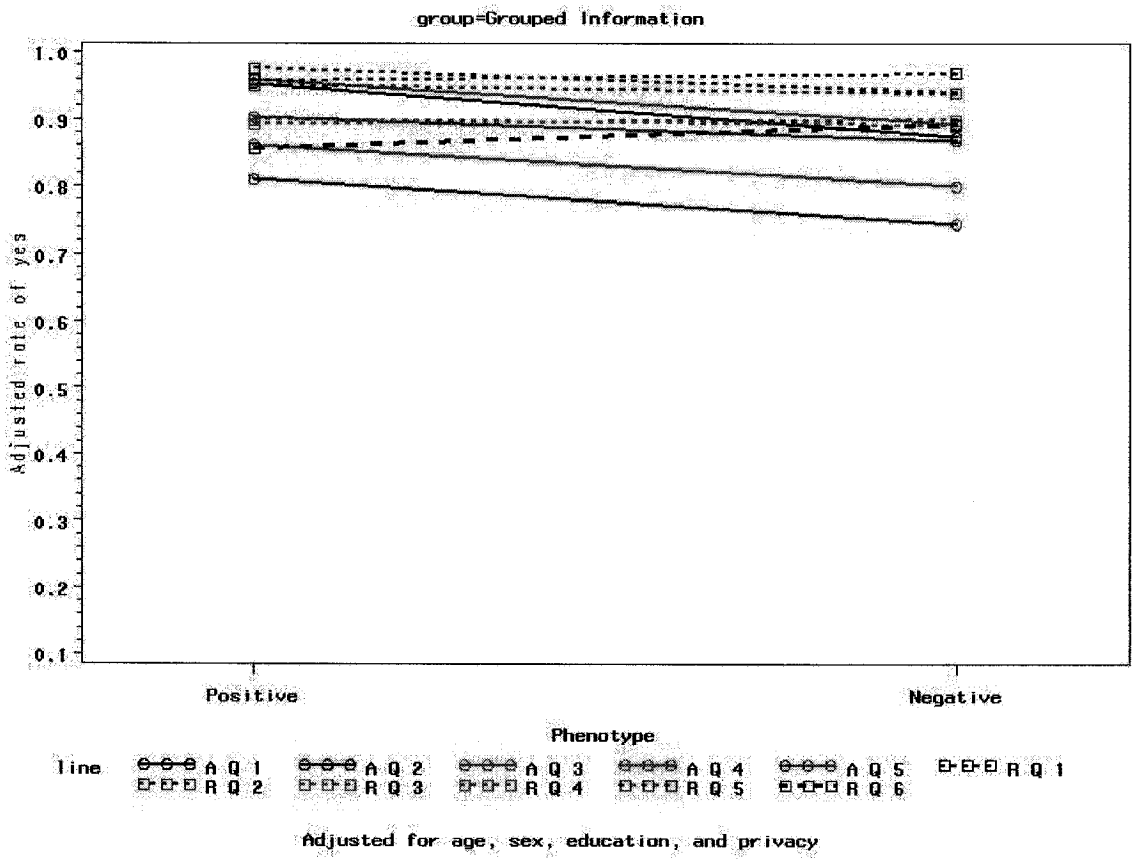


Figure 7:

Willingness to Share Personalized Health Information: By Population Group

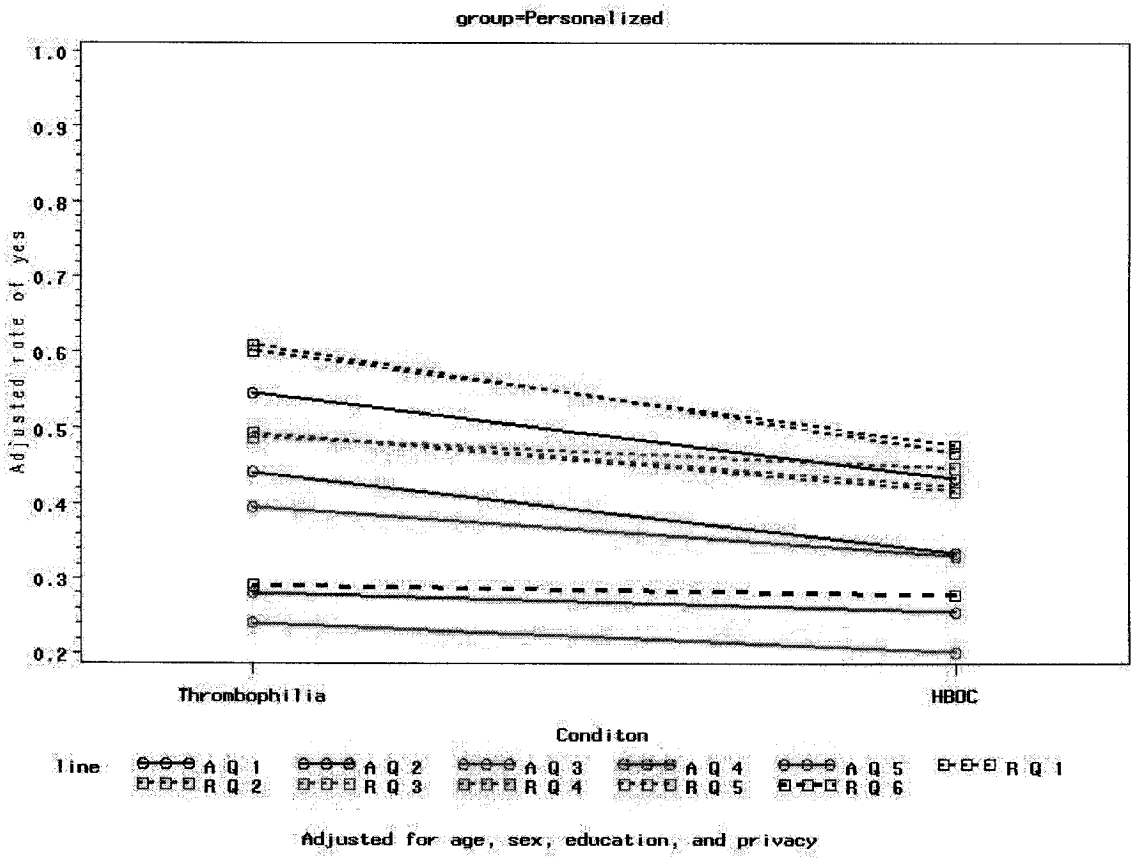


Figure 8:

Willingness to Share Coded Health Information: By Population Group

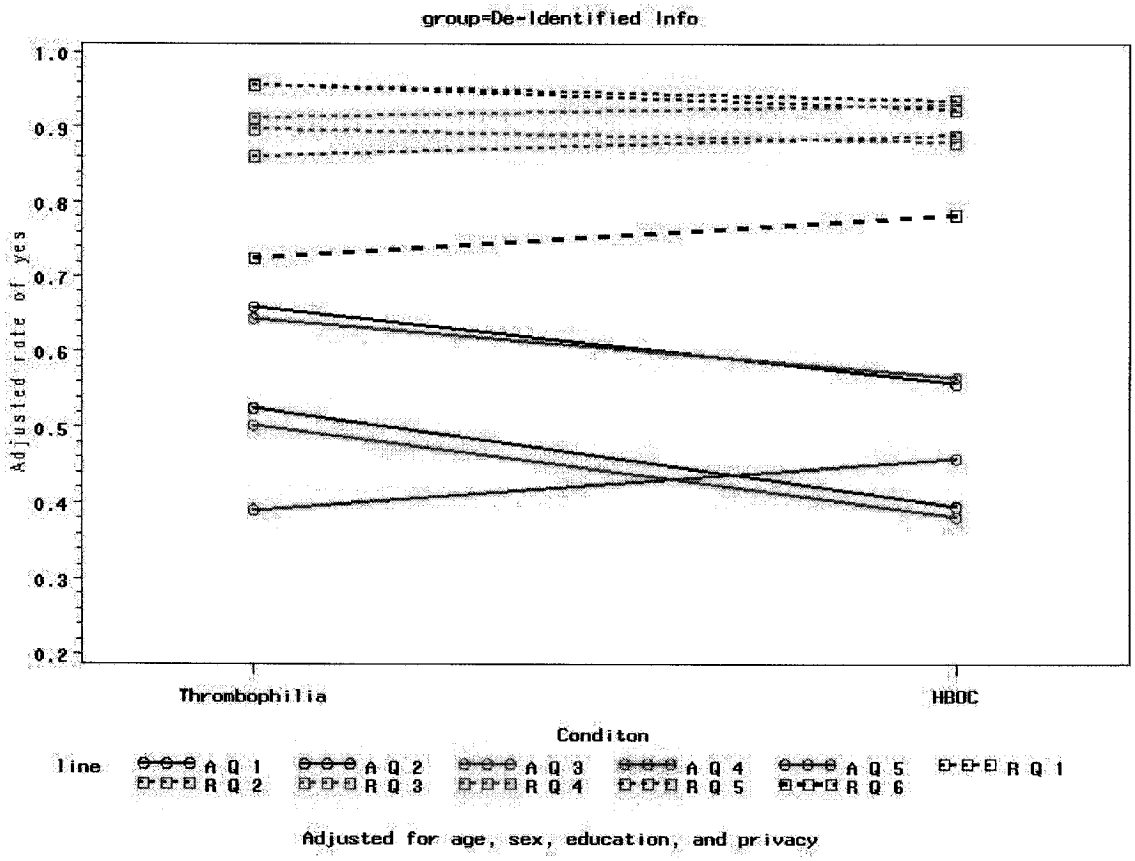
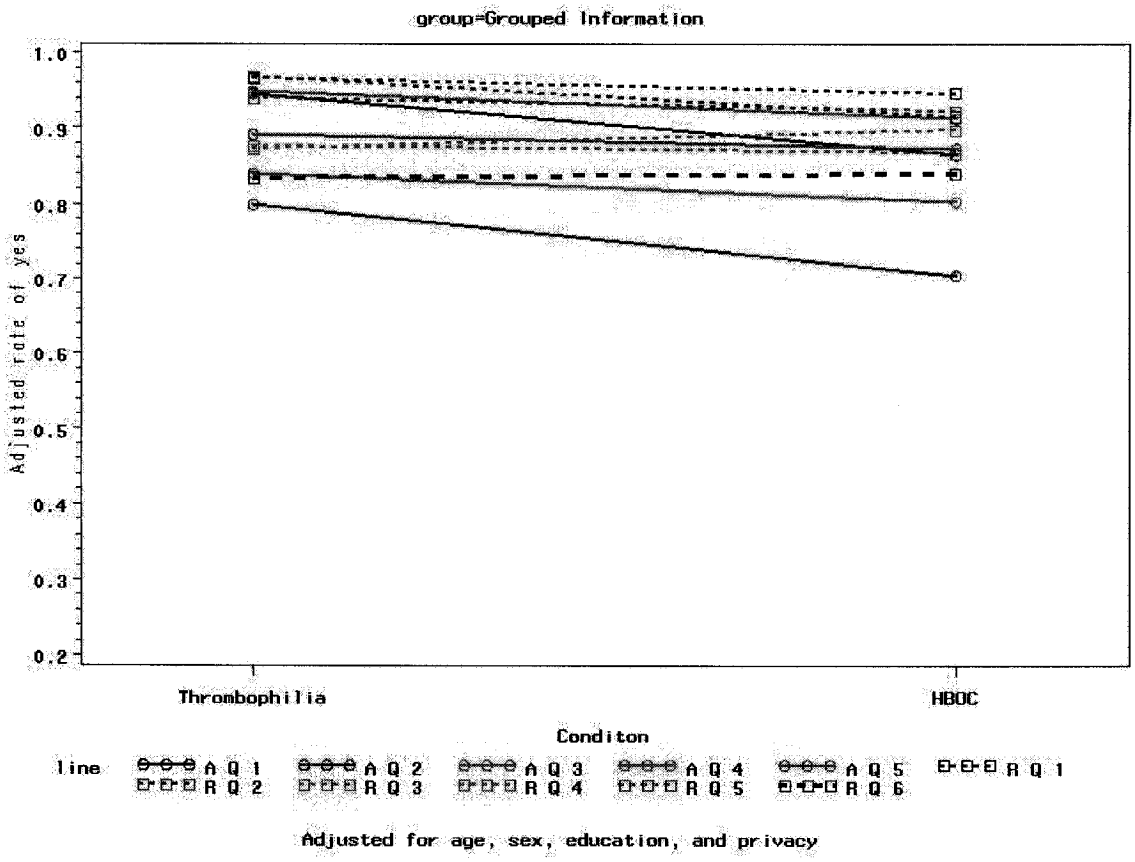


Figure 9:

Willingness to Share Aggregated Health Information: By Population Group



(v) Identifying where specific differences lie

Identifying the specific differences underlying the aforementioned overall findings required a further and finer level of analysis. Odds ratios were calculated for each specific research purpose (1-6), each specific administrative purpose (1-5), each anonymization level [(a) personalized, (b) coded, and (c) aggregated], each level of disease group, genotype, and phenotype as well as each specific type of PHI (genetic non-genetic, family history, blood sample). Self-reported privacy level, age, sex, and education were included as covariates in this step. A sampling of key significant results were extracted from Appendix 2.6 and reported in Table 5a and Table 5b to facilitate

presentation of these findings. Significant findings from this step in the analysis are presented by question posed to the research participant:

(a) Administrative Purpose #1: Would you permit administrative staff to have access to your health information to remind you of follow-up appointments and screening tests?

Genotype positive individuals were significantly less likely to share coded health information with administrative staff for the purpose of appointment reminder than were genotype negative individuals. This held true regardless of the type of information they were asked to share (OR_{gt} =.41, p = .02; OR_{ngt} =.30, p = .01; OR_{fhx} =.30, p = .01; OR_{bld} =.41, p=.02). Genotype positive individuals were also significantly less likely to share aggregated health information with administrative staff for this purpose than were genotype negative individuals. Again, this held true regardless of the type of information they were asked to share (OR_{gt} = .09, p = .02; $OR_{ngt,}$ = .09, p = .02; $OR_{fhx,}$ = .09, p = .02; OR_{bld} = .20, p = .03).

Individuals who reported themselves to be more open on the self-reported privacy scale were significantly more likely to share coded non-genetic test results and family history information (OR_{ngt} = 1.41, p =.03; OR_{fhx} = 1.50, p = .02) and personalized genetic test results (OR_{gt} = 1.30, p =.03) than were those who reported themselves to be less open on the self-reported privacy scale.

None of disease group, phenotype status, age, sex, or education level had a significant effect on authorization of any type of information for this purpose.

(b) Administrative Purpose #2: Would you permit administrative staff to have access to your health information to organize billing and payment for the services you receive?

Genotype positive individuals were significantly less likely to share coded health information with administrative staff for the purpose of organizing billing than were genotype negative individuals. This held true regardless of the type of information they were asked to share (OR_{gt} =.40, p = .01; OR_{ngt} =.41, p = .01; OR_{fhx} =.41, p = .01; OR_{bld} =.40, p=.02). Genotype positive individuals were also significantly less likely to share aggregated health information with administrative staff for this purpose than were genotype negative individuals. Again, this held true regardless of the type of information they were asked to share (OR_{gt} = .32, p = .01; OR_{ngt}, = .31, p = .01; OR_{fhx}, = .31, p = .01; OR_{bld} = .40, p = .03).

None of disease group, phenotype status, age, sex, education level, or self-reported privacy level had a significant effect on authorization of any type of information for this purpose.

(c) Administrative Purpose #3: Would you permit administrative staff to have access to your health information for hospital tracking and funding purposes?

Genotype positive individuals were significantly less likely to share coded health information with administrative staff for the purpose of hospital tracking and funding than were genotype negative individuals. This held true regardless of the type of information they were asked to share (OR_{gt} =.30, p = .01; OR_{ngt} =.40, p = .01; OR_{fhx} =.40, p = .01; OR_{bld} =.40, p=.02). Individuals who reported themselves to be more open on the self-reported privacy scale were significantly more likely to share personalized health information regardless of specific type requested (OR_{gt} = 1.41, p = .01; OR_{ngt}, = 1.41, p = .01; OR_{fhx}, = 1.32, p = .01; OR_{bld} = 1.41, p = .01) than were those who reported themselves to be less open on the self-reported privacy scale.

None of disease group, phenotype status, age, sex, or education level had a significant effect on authorization of any type of information for this purpose.

(d) Administrative Purpose #4: Would you permit administrative staff to have access to your health information for government tracking and funding purposes?

Genotype positive individuals were significantly less likely to share coded health information with administrative staff for the purpose of government tracking and funding than were genotype negative individuals. This held true regardless of the type of information they were asked to share (OR_{gt} =.30, p < .01; OR_{ngt} =.30, p < .01; OR_{fhx} =.31, p < .01; OR_{bld} =.31, p < .01). Genotype positive individuals were also significantly less likely to share aggregated health information with administrative staff for this purpose than were genotype negative individuals. Again, this held true regardless of the type of

information they were asked to share (OR_{gt} = .31, p = .03; OR_{ngt}, = .20, p = .02; OR_{fhx}, = .20, p = .02; OR_{bld} = .30, p = .03).

Individuals who reported themselves to be more open on the self-reported privacy scale were significantly more likely to share personalized health information regardless of specific type requested (OR_{gt} = 1.41, p = .01; OR_{ngt}, = 1.40, p = .01; OR_{fhx}, = 1.41, p = .02; OR_{bld} = 1.41, p = .01) than were those who reported themselves to be less open on the self-reported privacy scale.

Females were significantly more likely to share all types of aggregated health information for this purpose than were males (OR_{gt} = 4.70, p < .01; OR_{ngt}, = 4.11, p = .01; OR_{fhx}, = 4.21, p = .01; OR_{bld} = 3.62, p = .01).

None of disease group, phenotype status, age, or education level had a significant effect on authorization of any type of information for this purpose.

(e) Administrative Purpose #5: Would you permit administrative staff to have access to your health information for hospital fundraising purposes?

Individuals who reported themselves to be more open on the self-reported privacy scale were significantly more likely to share coded information for this purpose regardless of specific type requested (OR_{gt} = 1.41, p = .01; OR_{ngt}, = 1.41, p = .01; OR_{fhx}, = 1.41, p = .01; OR_{bld} = 1.41, p = .01) than were those who reported themselves to be less open on

the self-reported privacy scale. Similarly, those who reported themselves to be more open were significantly more likely to share personalized health information for this purpose ($OR_{gt} = 1.41$, $p = .01$; $OR_{ngt,} = 1.41$, $p = .01$; $OR_{fhx,} = 1.41$, $p = .01$; $OR_{bld} = 1.41$, $p = .01$) than were those who reported themselves to be less open on the self-reported privacy scale.

None of disease group, genotype status, phenotype status, age, sex, or education level had a significant effect on authorization of any type of information for this purpose.

Table 5A – Specific Predictors – Administrative Purposes

P	Q	Anon	Type	Predictor	Level	OR unadj	lowCI unadj	upCI unadj	p_unadj	OR adj	lowCI adj	upCI adj	p_adj
A	1	Coded	gt	genotype	Genotype +ve	0.8051	0.3817	1.6986	0.5693	0.3614	0.1559	0.8377	0.0176
		Coded	ngt	genotype	Genotype +ve	0.6944	0.3124	1.5437	0.3710	0.2704	0.1032	0.7087	0.0078
		Coded	fhx	genotype	Genotype +ve	0.7233	0.3324	1.5739	0.4142	0.2947	0.1181	0.7353	0.0088
		Coded	bld	genotype	Genotype +ve	0.7406	0.3470	1.5806	0.4375	0.3781	0.1628	0.8784	0.0237
A	1	Agg	gt	genotype	Genotype +ve	0.3820	0.1168	1.2497	0.1115	0.0899	0.0115	0.7014	0.0215
		Agg	ngt	genotype	Genotype +ve	0.3773	0.1154	1.2338	0.1069	0.0908	0.0116	0.7080	0.0221
		Agg	fhx	genotype	Genotype +ve	0.3774	0.1154	1.2349	0.1072	0.0885	0.0114	0.6900	0.0207
		Agg	bld	genotype	Genotype +ve	0.3460	0.1071	1.1181	0.0762	0.1828	0.0402	0.8322	0.0280
A	1	Coded	ngt	Privacy						1.4326	1.0362	1.9805	0.0296
		Coded	fhx	privacy						1.4682	1.0692	2.0161	0.0176
		Pers	gt	privacy						1.3046	1.0226	1.6644	0.0324
A	2	Coded	gt	genotype	Genotype +ve	0.7344	0.3801	1.4192	0.3584	0.3968	0.1965	0.8012	0.0099
		Coded	ngt	genotype	Genotype +ve	0.6998	0.3558	1.3764	0.3010	0.3772	0.1812	0.7854	0.0092
		Coded	fhx	genotype	Genotype +ve	0.7488	0.3828	1.4650	0.3983	0.3788	0.1843	0.7788	0.0083
		Coded	bld	genotype	Genotype +ve	0.7344	0.3801	1.4192	0.3584	0.4488	0.2247	0.8964	0.0232
A	2	Agg	gt	genotype	Genotype +ve	0.6920	0.3037	1.5769	0.3810	0.2962	0.1126	0.7792	0.0137
		Agg	ngt	genotype	Genotype +ve	0.6920	0.3037	1.5769	0.3810	0.2962	0.1126	0.7792	0.0137
		Agg	fhx	genotype	Genotype +ve	0.6830	0.2996	1.5571	0.3645	0.2907	0.1105	0.7645	0.0123
		Agg	bld	genotype	Genotype +ve	0.6451	0.2851	1.4594	0.2926	0.3534	0.1413	0.8839	0.0262
A	3	Coded	gt	genotype	Genotype +ve	0.7754	0.3875	1.5514	0.4722	0.3481	0.1587	0.7636	0.0085
		Coded	ngt	genotype	Genotype +ve	0.8192	0.4078	1.6458	0.5754	0.3744	0.1699	0.8250	0.0148
		Coded	fhx	genotype	Genotype +ve	0.8192	0.4078	1.6458	0.5754	0.3577	0.1628	0.7864	0.0105
		Coded	bld	genotype	Genotype +ve	0.7754	0.3875	1.5514	0.4722	0.4061	0.1890	0.8724	0.0209
		Pers	gt	Privacy						1.3562	1.0648	1.7275	0.0136
		Pers	ngt	Privacy						1.3496	1.0611	1.7165	0.0146
		Pers	fhx	Privacy						1.3426	1.0552	1.7082	0.0165
		Pers	bld	Privacy						1.3525	1.0628	1.7211	0.0141

Table 5a continued on next page

Table 5A ***(continued)***

P	Q	Anon	Type	Predictor	Level	OR unadj	lowCI unadj	upCI unadj	p_unadj	OR adj	lowCI adj	upCI adj	p_adj
A	4	Coded	gt	genotype	Genotype +ve	0.7458	0.3884	1.4319	0.3781	0.2925	0.1387	0.6165	0.0012
		Coded	ngt	genotype	Genotype +ve	0.8105	0.4204	1.5628	0.5306	0.3023	0.1426	0.6411	0.0018
		Coded	fhx	genotype	Genotype +ve	0.7831	0.4068	1.5072	0.4641	0.2965	0.1402	0.6272	0.0015
		Coded	bld	genotype	Genotype +ve	0.7458	0.3884	1.4319	0.3781	0.3363	0.1623	0.6969	0.0034
A	4	Agg	gt	genotype	Genotype +ve	1.0356	0.3991	2.6874	0.9427	0.2659	0.0803	0.8803	0.0301
		Agg	ngt	genotype	Genotype +ve	1.1644	0.4390	3.0883	0.7598	0.1971	0.0522	0.7445	0.0166
		Agg	fhx	genotype	Genotype +ve	1.1644	0.4390	3.0883	0.7598	0.1918	0.0506	0.7267	0.0151
		Agg	bld	genotype	Genotype +ve	1.0356	0.3991	2.6874	0.9427	0.2787	0.0852	0.9119	0.0346
A	4	Pers	gt	Privacy						1.3710	1.0687	1.7587	0.0130
		Pers	ngt	privacy						1.3670	1.0685	1.7488	0.0129
		Pers	fhx	privacy						1.3536	1.0569	1.7336	0.0165
		Pers	bld	privacy						1.3624	1.0644	1.7439	0.0141
A	4	Agg	gt	Sex	female					4.6958	1.6279	13.5449	0.0042
		Agg	ngt	sex	female					4.0895	1.3812	12.1087	0.0110
		Agg	fhx	sex	female					4.2548	1.4346	12.6194	0.0090
		Agg	bld	sex	female					3.6587	1.2750	10.4983	0.0159
A	5	Coded	gt	Privacy						1.3884	1.0816	1.7823	0.0100
		Coded	ngt	privacy						1.4114	1.0976	1.8151	0.0072
		Coded	fhx	privacy						1.3881	1.0810	1.7824	0.0101
		Coded	bld	privacy						1.3837	1.0789	1.7745	0.0105
A	5	Pers	gt	Privacy						1.3703	1.0668	1.7603	0.0137
		Pers	ngt	Privacy						1.3769	1.0751	1.7633	0.0113
		Pers	fhx	Privacy						1.3526	1.0550	1.7341	0.0172
		Pers	bld	Privacy						1.3625	1.0629	1.7464	0.0146

(f) Research Purpose #1: Would you permit researchers to have access to your health information for cancer/blood clotting research in general?

Genotype positive individuals were significantly less likely to share coded genetic test results with researchers for the purpose of general cancer/blood clotting research than were genotype negative individuals. (OR_{gt} =.30, p = .05). Genotype positive individuals were also significantly less likely to share personalized genetic test results (OR_{gt} =.50, p =

.03) and personalized family history information (OR_{fhx} =.50, p = .05) for this purpose than were genotype negative individuals.

None of disease group, phenotype status, age, sex, education level, or self-reported privacy level had a significant effect on authorization of any type of information for this purpose.

(g) Research Purpose #4: Would you permit researchers to have access to your health information for research in controversial areas (e.g. stem cell research)

Individuals who reported themselves to be more open were significantly more likely to share personalized non-genetic test and blood sample information for research in controversial areas ($OR_{ngt,}$ = 1.30, p = .05; OR_{bld} = 1.30, p = .05) than were those who reported themselves to be less open on the self-reported privacy scale.

Females were significantly more likely to share aggregated non-genetic test results for controversial research purposes than were males ($OR_{ngt,}$ = 8.01, p = .03).

None of disease group, genotype status, phenotype status, age, or education level, had a significant effect on authorization of any type of information for this purpose.

(h) Research Purpose #5: Would you permit researchers to have access to your health information for hospital tracking and funding purposes?

Genotype positive individuals were significantly less likely to share coded genetic test results for hospital tracking research than were genotype negative individuals (OR_{gt} =.41, p = .03). Genotype positive individuals were also significantly less likely to share personalized health information this research purpose than were genotype negative individuals. This held true for genetic test results, non-genetic test results, and family history information (OR_{gt} = .41, p < .01; $OR_{ngt,}$ = .50, p = .02; $OR_{fhx,}$ = .50, p = .02).

Individuals who reported themselves to be more open were significantly more likely to share personalized non-genetic test results, family history, and blood sample information for this research purpose ($OR_{ngt,}$ = 1.32, p = .04; $OR_{fhx,}$ = 1.32, p = .05; OR_{bld} = 1.32, p = .04) than were those who reported themselves to be less open on the self-reported privacy scale.

None of disease group, phenotype status, age, sex, or education level, had a significant effect on authorization of any type of information for this purpose.

(i) Research Purpose #6: Would you permit researchers to have access to your health information for government tracking and funding purposes?

Genotype positive individuals were significantly less likely to share personalized genetic test results with researchers for the purpose of government tracking research than were genotype negative individuals. (OR_{gt} =.51, p = .04).

Individuals who reported themselves to be more open were significantly more likely to share personalized health information for this research purpose (OR_{gt} = 1.41, p = .01; OR_{ngt}, = 1.41, p < .01; OR_{fhx}, = 1.41, p < .01; OR_{bld} = 1.41, p < .01) than were those who reported themselves to be less open on the self-reported privacy scale.

Females were significantly more likely to share all types of aggregated health information for this purpose than were males (OR_{gt} = 11.60, p < .01; OR_{ngt}, = 11.60, p < .01; OR_{fhx}, = 11.91, p < .01; OR_{bld} = 8.91, p < .01) as well as all types of coded information (OR_{gt} = 2.42, p = .03; OR_{ngt}, = 2.43, p = .02; OR_{fhx}, = 2.61, p = .02; OR_{bld} = 2.32, p = .04).

None of disease group, phenotype status, age, or education level, had a significant effect on authorization of any type of information for this purpose.

Table 5B – Specific Predictors - Research Purposes

P	Q	Anon	Type	Predictor	level	OR unadj	lowCI unadj	upCI unadj	P_unadj	OR adj	lowCI adj	upCI adj	p_adj
R	1	Coded	gt	genotype	Genotype +ve	0.6100	0.2153	1.7289	0.3525	0.2642	0.0715	0.9761	0.0459
		Pers	gt	genotype	Genotype +ve	0.6181	0.3305	1.1560	0.1320	0.4897	0.2580	0.9293	0.0289
		Pers	fhx	genotype	Genotype +ve	0.7444	0.3927	1.4112	0.3657	0.5186	0.2682	1.0029	0.0510
R	4	Pers	ngt	privacy						1.2731	1.0001	1.6206	0.0499
		Pers	bld	privacy						1.2719	0.9983	1.6207	0.0517
		Agg	ngt	sex	female					8.0281	1.2291	52.4387	0.0296
R	5	Coded	gt	genotype	Genotype +ve	1.1791	0.5483	2.5354	0.6732	0.3936	0.1667	0.9295	0.0334
R	5	Pers	gt	genotype	Genotype +ve	0.7727	0.4251	1.4046	0.3977	0.4165	0.2231	0.7778	0.0060
		Pers	ngt	genotype	Genotype +ve	0.8984	0.4928	1.6377	0.7265	0.4789	0.2557	0.8972	0.0215
		Pers	fhx	genotype	Genotype +ve	0.9650	0.5292	1.7596	0.9075	0.4755	0.2552	0.8860	0.0192
		Pers	ngt	privacy						1.2907	1.0086	1.6518	0.0426
		Pers	fhx	privacy						1.2802	1.0015	1.6365	0.0486
		Pers	bld	privacy						1.2915	1.0116	1.6490	0.0401
R	6	Pers	gt	genotype	Genotype +ve	1.0997	0.6009	2.0127	0.7579	0.5209	0.2805	0.9672	0.0389
R	6	Pers	gt	privacy						1.3680	1.0662	1.7553	0.0138
		Pers	ngt	privacy						1.4297	1.1136	1.8356	0.0050
		Pers	fhx	privacy						1.4070	1.0945	1.8089	0.0077
		Pers	bld	privacy						1.4195	1.1062	1.8216	0.0059
R	6	Agg	gt	sex	female					11.6023	2.6450	50.8944	0.0012
		Agg	ngt	sex	female					11.6023	2.6450	50.8944	0.0012
		Agg	fhx	sex	female					11.9232	2.7218	52.2314	0.0010
		Agg	bld	sex	female					8.8640	2.2845	34.3925	0.0016
R	6	Coded	gt	sex	female					2.3741	1.0831	5.2036	0.0308
		Coded	ngt	sex	female					2.4520	1.1167	5.3838	0.0254
		Coded	fhx	sex	female					2.6583	1.1970	5.9033	0.0163
		Coded	bld	sex	female					2.2935	1.0517	5.0016	0.0369

Following the completion of this series of questions, participants were asked about the extent to which they would like to revisit the aforementioned choices about sharing health information. 35% felt there was no need to revisit their choices, 8% wanted to revisit their choices in 5 years, 14% in three years, 6% in one year, 3% in six months, 22% every year, and 13% wanted to revisit their choices every time their information

could be used for a new purpose. Chi square tests indicated that the timeline for revisiting these choices (e.g. every time, annually, never) was not associated with population group (X^2=12.21, p=.41), genotypic status, (X^2=5.10, p=.51), or phenotypic status (X^2=2.11, p=.92).

In summary, genotype positive individuals were less likely to share health information at each level of anonymization than were genotype negative individuals. Individuals who reported themselves to be more open were more likely to share health information than those who reported themselves to be less open. This held true for most administrative and research purposes and, in most cases, did not vary with disease group, phenotypic status, age, sex, education level, or the type of information requested. Many participants expressed interest in revisiting their choices about sharing health information at various time points but many were comfortable with their decisions for the long term.

(vi) A Predictive Model

The effects of genotype status and self-reported privacy level were identified as the most recurrent statistically significant predictors of authorization (Tables 5a,b). For this reason, each level of genotypic status (positive and negative) and each level of self-reported privacy level (1-5) were entered into a predictive model. The fitted model calculated the probability of answering "yes" to sharing information for each level of these two predictive variables. Table 6 presents a range of scenarios entered into the predictive model. The appropriate values for each scenario entered into the model generate probability estimates for sharing information under given conditions. At all

self-reported privacy levels (1-5), genotype positive participants were less likely to share health information than genotype negative participants. As self-reported privacy score increased ("very private" = 1, "very open" = 5), probability estimates increased at both genotype levels. Only when genotype positive individuals rated themselves as "very private ("1") and genotype negative individuals rated themselves as "open" ("4") or "very open" ("5") was the difference between genotype positive and genotype negative individuals statistically significant [P(geno+ve, privacy = 1) = .64; P(geno-ve, privacy = 4) = .83, {95% CI .78,.89}; P(geno-ve, privacy = 5) = .85, {95% CI .79,.90)].

For all regression models, there was no evidence of over or under dispersion or multicolinearity. With respect to goodness of fit, all models had non-significant Pearson Chi-square tests (ratios of Pearson deviance divided by degrees of freedom. were not significantly different from one).

Table 6 – Predictive Model Scenarios

Genotype	Privacy Level	P value	Upper CI	Lower CI
geno+ve	*1*	*0.64044*	*0.5057*	*0.7562*
	2	0.67182	0.5649	0.7635
	3	0.70173	0.6130	0.7775
	4	0.73001	0.6459	0.8003
	5	0.75654	0.6645	0.8298
geno-ve	1	0.76690	0.6542	0.8512
	2	0.79084	0.7074	0.8553
	3	0.81292	0.7486	0.8638
	4	*0.83317*	*0.7757*	*0.8782*
	5	*0.85162*	*0.7903*	*0.8973*

(B) Content Analysis and Triangulation with Quantitative Findings

Of the 199 interviews that were conducted and apparently taped, 13 tapes were inaudible to the transcriber and nine tapes were blank. Two of the inaudible tapes and two of the blank tapes emerged from the digital recording approach whereas the 18 other untranscribed interviews emerged from the traditional cassette recorder approach. While notes were taken during the interviews themselves, the interviewer recorded main ideas rather than specific remarks made by participants. Since they did not reflect direct participant responses, notes from these untranscribed interviews were not included in the content analysis. Transcripts from the 11 HH participants and eight HNPCC participants were excluded from this analysis. In total 158 transcripts were included in the content analysis.

Each coder reviewed 158 transcripts for four domains: (1) *participant characteristics* (GENO, PHENO, POPN, AGE, PRIV), (2) *health information characteristics* (ANON, PURP1-PURP4, TYPE, REVISIT), (3) inductively-oriented codes related to *sharing information for research and administrative purposes generally* (TRUST, SAFEG, ALTR), and (4) inductively-oriented codes related to *feedback on the HCID tool* (D-COLL, D-GUID, D-OK). Relevant text was coded and the number of instances of text reflecting each given code was tallied by Coder 1 and Coder 2. Table 7 provides definitions for each code.

Table 7 – Content Analysis: Domains, Codes and Definitions

Domain	Code	Definition
Participant characteristics	GENO	Any reference to the influence that being genotype positive or genotype negative has on sharing health information
	PHENO	Any reference to the influence that being phenotype positive or phenotype negative has on sharing health information.
	POPN	Any reference to the nature of a particular condition influencing willingness to share health information; something particular about breast cancer or thrombosis that makes people more or less willing to share health info or how having one of these conditions might compare to having a different health condition.
	AGE	Any reference an individual makes about their age being a factor in sharing health information
	PRIV	Any reference to being particularly "private" or "open" and its influence on sharing health information
Health information characteristics	ANON	Any reference to the way in which different levels of anonymization (personalized, deidentified, aggregated) influence willingness to share health information
	PURP1	Any indication that willingness to share health information for research purposes is different from sharing health info for administrative purposes
	PURP2	Any indication that willingness to share health information depends on the purpose *in general* for which it is requested (not a specific comparison between research and admin)
	PURP3	Any feelings about sharing health information for government purposes
	PURP4	Any feelings about sharing health information for fundraising purposes
	TYPE	Any reference to whether individuals are more/less willing to share different types of health information (genetic test results, non-genetic test results, family history info, blood samples)
	REVISIT	Any reference to when people would like to revisit their choices about sharing health information and what might lead them to change their minds

Sharing information generally	TRUST	Any comments about trusting or not trusting research/researchers or administration/administrators
	SAFEG	Any reference to mechanisms that are or should be in place to protect patients and/or research participants (e.g. consent, legislation, codes of ethics)
	ALTR	Any reference to individuals being motivated by altruism or a genuine interest in helping
Feedback on HCID Tool	D-COLL	Any reference to the suggestion that that the HCID tool is detailed and that columns/categories/rows in the HCID tool should be collapsed to simplify its use
	D-GUID	Any reference to the suggestion that that the HCID tool is detailed and that direct guidance or someone available to answer questions would simplify its use
	D-OK	Any reference to the suggestion that that the HCID tool is detailed but this level of detail was "ok" or "appropriate" from their perspective

Table 8 reflects the frequencies of each code as determined by each Coder. Coder 1 and Coder 2 were 100% concordant in assigning codes for 14/18 (78%) of the codes. Two "code-pairs" emerged as the explanation for discordant frequencies between coders. One code-pair emerged between PRIV *(any reference to being particularly "private" or "open" and its influence on sharing health information)* and ALTR *(any reference to individuals being motivated by altruism or a genuine interest in helping)*. Specifically, Coder 1 identified 37 instances of PRIV, whereas Coder 2 identified 41 instances of PRIV (90% concordant). Coder 1 identified 22 instances of ALTR, whereas Coder 2 identified 18 instances of ALTR (82% concordant). Coder 1 coded all four instances of the text that Coder 2 coded as PRIV as ALTR, and Coder 2 coded all four instance of this text as PRIV.

The second code-pair that emerged was between ANON *(any reference to the way in which different levels of anonymization (personalized, deidentified, aggregated) influence willingness to share health information)* and PURP1 *(any indication that willingness to share health information for research purposes is different from willingness to share health information for administrative purposes)*. Specifically, Coder 1 identified 60 instances of ANON, whereas Coder 2 identified 57 instances of ANON (95% concordant). Coder 1 identified 17 instances of PURP1, whereas Coder 2 identified 20 instances of PURP1 (85% concordant). Coder 2 coded all three instances of the text that Coder 1 coded as ANON as PURP1, and Coder 1 coded all three instance of this text as ANON.

For the PRIV-ALTR discordance, all instances of discordance were resolved by deferring to context and the nature of the interviewer's question that prompted the participants' remarks. For example, *"I'm in favour of whatever anybody can learn from me. I've got no secrets and I'm not big on keeping everything private" (171THR)* was coded as PRIV by Coder 1 and ALTR by Coder 2. Since at that moment the interviewer was asking the participant about the extent to which he considered himself to be a private or an open person, the final decision on the code for this particular instance of text was PRIV.

Similarly, for the ANON-PURP1 discordance, all instances of discordance were ultimately resolved by deferring to context and the nature of the interviewer's question that prompted the participants' remarks. However, resolving these discrepancies were more challenging given the implicit interaction between these two codes. That is, for

participants whose remarks fell into this discordant category, the extent to which they were willing to authorize the use of their health information depended upon *both* its level of anonymization and the purpose for which it was being collected. For example, *"I can see how knowing who I am could benefit the researchers, but for administrative staff, I don't see how it would benefit them to know who I am personally so aggregated would be ok for them" (097HBOC).* In all three instances, these participants were more willing to share their health information – be it personalized, coded, or aggregated- for research purposes and less willing to share personal health information for administrative purposes. Since ultimate purpose seemed to matter more to these three participants whose remarks were discordantly coded, the final decision on the code for these instances of text was PURP1.

Table 8 – Content Analysis: Interim Code Frequencies and Inter-Coder Concordance

Type of Code	Code Name	Coder 1 Freq (n)	Coder 2 Freq (n)	Concordance Rate
Participant characteristics	GENO	2	2	100%
	PHENO	1	1	100%
	POPN	9	9	100%
	AGE	12	12	100%
	PRIV	37	41	90%
Health information characteristics	**ANON**	60	57	95%
	PURP1	17	20	85%
	PURP2	39	39	100%
	PURP3	31	31	100%
	PURP4	24	24	100%
	TYPE	12	12	100%
	REVISIT	30	30	100%
Sharing information generally	TRUST	7	7	100%
	SAFEG	14	14	100%
	ALTR	22	18	82%
Feedback on HCID Tool	D-COLL	43	43	100%
	D-GUID	84	84	100%
	D-OK	31	31	100%

Table 9 presents final code frequencies and sample text for each code. Of the codes reflecting the participants' characteristics, PRIV *(any reference to being particularly "private" or "open" and its influence on sharing health information)*, occurred 39 times which is more than three times the frequency of any other participant-characteristic code. Some participants felt strongly about maintaining a high level of privacy, particularly in the context of health information, *"I think that sometimes medical info is intensely personal and that people who deal with it everyday like administrators and even sometimes researchers just take things for granted with test results; it is a piece of paper to them but it represents much more to the individual. It's just a whole sensitivity issue (136THR).* Others are not at all concerned about health information privacy and in fact,

view recent privacy legislation as a frustrating barrier to care and research, "*I don't think there is a privacy issue here at all. I think the more people that know the better off everyone's going to be. I think the new privacy act has gone too far" (106HBOC).* And others assume necessary protections are in place such that their information can be used to the extent that it is needed, but that their confidentiality is still maintained, "*I'm a fairly open person. As long as people consider confidentiality, I don't have a problem sharing information" (071HBOC).* Finally, some participants reflect upon the complexity of privacy and remain conflicted in their stance, "*Privacy. There are a lot of good things and a lot of bad things about it. It's hard to know where to draw the line" (146THR).*

While the frequency and richness of PRIV comments may be an endorsement of the predictive value of "self reported privacy level" identified in the quantitative analysis, it may also be an artifact of how the interview guide and analyses were structured. Data related to GENO, PHENO, POPN were collected at recruitment and not specifically inquired about during the interview. AGE was ascertained in a concluding demographics section of the interview; again, not an explicit discussion point. Participants' perspectives on privacy in general and as it related to various contexts were explored in more detail. This particular code, as a result of the design of the survey instrument, invited more comment than did the other participant characteristic codes. Not surprisingly, most of the PRIV comments came from individuals who described themselves as more "open" than "private" and many of these comments reflected this openness.

Of the codes reflecting the characteristics of the health information itself, there were 57 instances of ANON. ANON comments reflected a reluctance by many to share personalized health information because it was considered unnecessary to know individual names in order to accomplish a given research or administrative task. For example, *"Unless it is relevant to inform me of something, they can use my information for whatever decision they want to make without my name on it. I don't want them to use my name for just any purpose or for other researchers to have access to my name or for some other institution to force them to release my name" (042HBOC).* ANON comments also reflected a perceived benefit to individual tracing afforded by deidentified information should relevant health information be learned over time. For example, *"I feel quite strongly that no for personally identified, but fine with de-identified that can be traced back to me if need be. If there was something seriously wrong I would like to know" (159THR).* A significant variable in the quantitative analysis, the salience of ANON in the content analysis strengthens the finding that anonymization level impacts willingness to share health information.

There were 20 instances of PURP1, most of which highlighted the greater tendency of individuals to share health information for research purposes than for administrative purposes. For example, *"Anybody can have anything they want for research but I am not comfortable with admin staff having anything personalized. For whatever reason I trust a researcher more than I trust an admin person. I think this has to do with their level of accountability. When someone like a 'Kelly temp' person has only her job to lose by*

offending me through sharing confidential info it matters less to them than a physician or a researcher who is committed to caring for patients or to science" (147HBOC).

An increased willingness to share PHI for research purposes compared to administrative purposes was also identified in the quantitative analysis. There were 39 instances of PURP2, most of which reflected participants' interest in having some knowledge about the purpose for which their information might be used and some say in its use depending on this purpose. For example, *"If it for the right reasons and the right uses then that is ok, but if it is going to be used for stuff I am totally against – like a mom and a dad deciding they want a blue-eyed baby which I am dead against, then no, forget it" (152THR).*

There were 31 instances of PURP 3 and 24 instances of PURP4. While the purposes of government research/administration and hospital fundraising were not identified as a significant predictor variable in the quantitative analysis, many participants described considerable reluctance to the idea of sharing health information with the government, *"Just a little concern about government I guess my history with the government is that they collect information for one purpose and they tend to be very sloppy in the handling and use of it later, they can have very short memories using the information properly" (076HBOC)* as well as considerable reluctance to sharing specific health information with fundraisers, *"I don't think it's appropriate to ask people for money based upon certain test results or disease populations they may fall into" (110THR)*.

There were only 12 instances of TYPE. While comments were few in number and this variable (distinction among genetic, non-genetic, family history, blood sample

information) was not identified as a significant predictor of authorization in the quantitative analysis, some participants reflected concern about sharing genetic information, *I just feel that well everybody goes in for routine blood tests, but a genetic test is looking more closely at you, so I would be more careful about sharing it" (148THR)* and other participants did not make a distinction between sharing genetic and non-genetic information, *"Any blood test tells us something about our genes at some level so which type of information it is doesn't matter to me" (110THR).*

Finally, there were 30 instances of REVISIT. The majority of participants appeared to be comfortable with their choices about the types of PHI they were willing to share for a range of purposes for the long term, *"I don't think my answers would really change, so I'm thinking, you know, I don't think I need to revisit these particular questions" (031HBOC).* However, several participants indicated a preference to review their choices at various time points in the future. They anticipated that research projects and/or their health information may change and, in turn, their views on sharing health information may change, *"I would say yearly because you know, methods change and research opportunities change. Your opinions could change. Something tragic could happen with my health or otherwise and my opinions could change" (148THR).*

The inductively-oriented codes (TRUST, SAFEG, ALTR, D-COLL, D-GUID, and D-OK) will be elaborated upon in more detail in Chapter 7. It is noteworthy, however, to comment on respective frequencies of each of these codes. Comments identified as consistent with the meaning of TRUST, SAFEG, or ALTR emerged through the course

of the interviewer-participant dialogue. Participants were not specifically asked about these constructs; rather participants' reactions to or comments following various interview questions reflected these themes. While the insights reflected by these comments are very helpful to the overall understanding of the dataset (Chapter 7), comments of this nature did not occur with compelling frequency. Only seven respondents commented on the extent to which they trust the research and/or administrative process. Some are trustworthy, *"I trust [my doctors]. I have a history with them and I know that they are extraordinarily ethical" (056HBOC)* and some are not, *"It's a question of trust to be honest. It's the trust between in this case the patient and the whole medical community. And I think the trust in general in ordinary individuals like myself, has been eroded. Trust in politicians, trust in the media, trust in the medical community, trust in nothing. Part of it is because of accountability and transparency, but it's not just that. I think there's an element where there's a concern for standards being dropped—I prefer to air on the side of caution, until there is a level of trust that has been established" (034THR).*

Fourteen respondents made reference to safeguards that are or should be in place to protect patients and/or research participants. For example, *"I'm basing my trust in the researchers on some level of discipline and some type of formal code of conduct that they must have to follow" (077HBOC).* And 20 participants made reference to individuals being motivated by altruism or a genuine interest in helping. For example, "I made a commitment in my own mind to the medical world that because I was so blessed, that whatever I could do to assist I would do." (056HBOC)

In contrast, comments categorized in the *HCID Feedback* domain (D-COLL, D-GUID, D-OK) were directly solicited from all participants. All participants were asked for their thoughts about the HCID tool itself and were specifically probed on what they thought about its level of detail. Since 158 transcripts were included in the content analysis, it makes sense that 158 comments were identified as consistent with this domain. One advantage of having an interviewer complete the data collection tool *with* the participants is that missing data is minimized. Of the 158 transcripts reviewed, 43 respondents felt that the HCID tool was detailed and that its columns/categories/rows should be collapsed to simplify its use, *"There are too many columns and my answers are the same for all of them so you don't need all of them" (071HBOC).* 84 respondents felt that providing guidance to respondents in the process of completing the tool would simplify its use, *"yes, very helpful that you walked me through this process. I would not have completed it properly otherwise" (148THR).* And 31 respondents replied that the level of detail was "ok" or "appropriate" and did not offer further comment or suggestions, *"The form is clear and all of the columns help to be specific about how I want to share my information" (106HBOC).*

Table 9 – Content Analysis: Final Code Frequencies and Sample Text

Domain	Code	Freq(n)	Sample Text
Participant characteristics	GENO	2	"It would depend on the results. I mean, I'm looking at breast and ovarian cancer – if I had tested positive for the gene, I don't think I would want my name connected with it… but because I tested negative, I don't mind." (045HBOC)
	PHENO	1	"Since I've already had breast cancer, I'm not as concerned about insurance for example…it isn't really an issue, they can already write me off because I've had it….I would be more concerned that they could link back to me if I had not had breast cancer." (075HBOC)
	POPN	9	"I don't think having, being Factor V positive is a scandalous thing to be…If I had AIDS, I might not have answered the questions the same way." (110THR)
	AGE	12	"I think my age has been a big factor in some of the answers I gave because at this point I don't have to worry about job applications or buying insurance, but I think for anyone younger you would get a very different set of answers." (057HBOC)
	PRIV	39	"I'm a fairly open person. As long as people consider confidentiality and use information responsibly, I don't have a problem sharing it." (071HBOC)
Health information characteristics	ANON	57	"In general I don't really like anything out there with my name on it. I don't think it serves any purpose for it to have my name on it and you know, who knows where it's going. I'd prefer sort of de-identified information where information could be fed back to me if something came up that I should be aware of." (112THR)
	PURP1	20	"I am so for research, they can use whatever they want, but I don't want Joe Schmoe in accounts payable looking up my chart…" (113THR)
	PURP2	39	"I need to understand what they're doing, because if they take my information and sell it to someone, I would say no, but if they do it for medical research purpose, and then I have no problem. So my question would be what is the purpose? I need to understand why."(017HBOC)
	PURP3	31	"Anything that has to do with the government is sticky. I don't trust the government. Whether it is Martin, Harper, McGuinty, they are all out there to line their pockets, they don't do anything for us." (123THR)
	PURP4	24	"Stop, stop, stop begging me for money. Every hospital that I have gone to, they won't stop begging me for money."(116HBOC)
	TYPE	12	"I don't want my [genetic test results] released at all… I don't know still what the impact on insurance could be…and my children don't know anything about this and I wouldn't want them to inadvertently find out from anyone but me, when I choose to tell them. The less people that know about [these results] the better…people might treat me differently if they know I have it." (047HBOC)
	REVISIT	30	"I might have to say that every year it would have to be revisited… a lot can change with your health issues." (032THR)
Sharing information generally	TRUST	7	"It's a question of trust to be honest. It's the trust between in this case the patient and the whole medical community." (034THR)
	SAFEG	14	"I think often times it boils down to the ethics of the individual researcher or research assistant. I mean in theory the protocol goes by the ethics board, it looks in theory like it should be fine, but I think sometimes it is not." (136THR)
	ALTR	20	"I made a commitment in my own mind to the medical world that because I was so blessed, that whatever I could do to assist I would do." (056HBOC)
Feedback on HCID Tool	D-COLL	43	"It is not necessary to have all of these columns and rows; it would be easier to get through if you combined some of them."
	D-GUID	84	"It is very detailed and until I spoke to you I wasn't exactly sure what some of these columns meant. I would want someone around to ask questions to if I had to do this again."
	D-OK	31	"Yeah, very detailed, but it was pretty clear so I didn't mind it."

CHAPTER 7: DISCUSSION AND CONCLUSIONS

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(A) Response Rate and Overall Sample Characteristics

One interpretation of the low overall response rate is that health information privacy is not a paramount concern among these populations in particular. Since participants were drawn from clinical populations and have had genetic testing, they may understand and be comfortable with how their personal health information (genetic and non-genetic) may be used for future research and administrative purposes and therefore not feel the need to discuss these issues further in the context of this investigation. Quite the opposite interpretation could hold true as well. Non-respondents may in fact be particularly concerned about privacy and therefore want nothing to do with a study about the privacy of health information. While data were neither collected on participants' actual personal data nor what they have agreed to or not agreed to share in reality, the study invitation letter may have inadvertently led them to believe that they might be asked to share personal health information they were reluctant to share. While the hypothetical nature of this study is a limitation in other ways (Section E), it was hoped that individuals might have found safety in participating in a privacy study that collected perspectives on hypothetical situations. Despite the low overall response rate, no response bias was detected. This suggests that the findings are not related to anything idiosyncratic about this particular group of participants.

The response rates for the HNPCC and HH populations were particularly low. A low response rate in the HNPCC population could have been related to any of three factors: (1) only two clinical sites among the hospitals included in the sampling frame had

eligible patients to recruit, (2) the maximum number eligible to recruit from these sites was low in comparison to the HBOC and THR populations because of the relative rarity of HNPCC itself,[210] and (3) as a result of the rarity of this condition, eligible patients may feel over-recruited for research studies. Adopted from the economics literature, this phenomenon has been referred to as recruitment fatigue and may have been a force at play in the low response rate from this group.[223]

The low response rate among the HH population may have been a function of two factors: (1) only two clinical sites among the hospitals in the sampling frame had eligible patients to recruit and (2) it became apparent while reviewing eligible hematology patients' medical records that there was no explicit indication that patients had been notified of their genetic test results. The inclusion criteria included 'notification of genetic test results;' if this was not met, potential participants were excluded. Lack of notification could be related to the fact that many of these individuals tested positive for HH carrier status, a clinically insignificant finding. Particularly in a hematology setting where blood test results are often only followed if they bear clinical significance, non-disclosure of carrier status is not surprising. Whether or not this practice of non-disclosure of clinically insignificant genetic test results is appropriate is controversial[224] [225]and beyond the scope of this discussion.

Unfortunately, 17 individuals who were interested in participating in this study were not included in the data collection phase because we were unable to identify a convenient interview time. While this was a lost opportunity, 16/17 of these individuals were from

the majority populations (HBOC or THR), so it is unlikely that their data would have altered the overall findings.

The gender skew in favour of female participants (77%) reflects the relatively higher response rate from the HBOC population, a predominantly female population given its associated risks with breast and ovarian cancers. The literature is mixed regarding the extent to which gender influences willingness to participate in research in general. There is some evidence to suggest that in research on non-gender specific diseases, men are less likely to participate[226] and other evidence which suggests that men are more likely to participate.[227]

With respect to age, a small majority of participants were over the age of 50 (63%). There are three possible explanations for this: (1) there is some literature that suggests that older (particularly retired) individuals simply have more time to participate in research studies,[228] (2) the incidence of breast/ovarian cancer and thrombophilia increases with age[211, 213] so it is more likely for older people to be referred to the clinics from which the sample was recruited. Even though young age of onset is consistent with *hereditary* breast and ovarian cancer,[211] not everyone who qualifies for genetic testing in Ontario necessarily fits into this category. And (3) as indicated by the content analysis, older people appear to be less concerned about the privacy of their health information since employability and insurability are not of the same priority that they may be for younger individuals. For example,*" I think my age has been a big factor in some of the answers I gave because at this point I don't have to worry about job applications or buying*

insurance, but I think for anyone younger you would get a very different set of answers" (057HBOC).

As is commonplace for research studies whose participants have pursued genetic testing, the majority of participants were Caucasian, well educated, employed, and married or common-law.[229] Like most medical research, most research on ethical, legal, and social issues around genetics does not adequately reflect the views of minorities.[230] Wertz[231] suggests that in light of past experiences like the Tuskeegee Syphillis Study in which members of the African American population were badly mistreated [60] members of minority groups may hold considerably different views from those of the majority with respect to research participation. For example, Wertz[231] found that compared to Caucasian Americans, African Americans were less concerned about issues related to medical privacy, autonomy, and consent and were more concerned about the general welfare of their partners and family members. Pentz et al,[232] however, found that different ethnic groups had similar opinions; African American cancer patients were as likely as Caucasian cancer patients to agree to provide a biological sample for research purposes and to allow investigators to determine research use without contacting the patients again for consent. Interestingly, this is consistent with Wertz's finding that African Americans are not particularly concerned about medical privacy issues. Regardless of the implicated costs, it is important for researchers to be strategic about recruiting minority populations into policy-oriented research. The current study is limited in its ability to comment on the perspective of any minority group because it was, unfortunately, not designed to capture minority perspectives in particular.

Overall, contextual factors including years since clinical diagnosis, years since genetic test results received, and previous research experience did not have a significant effect on participants' willingness to share PHI for administrative or research purposes. The only context in which recency of genetic test results is examined with respect to its effect on sharing personal health information is the literature exploring probands' patterns of communicating BRCA and HNPCC genetic test results with family members. This literature is predominantly focused on who probands tell and why they tell[233 234 235] rather than the timeline to telling. In one study, however, the authors noted that most first degree relatives were informed of the proband's test result by 4 months from the time the result was received by the proband[236] and one study noted that 85% of sisters were informed of a proband's BRCA test results within one month of the proband receiving the result.[237] Based on this literature, however, one cannot assume that probands' readiness to share genetic test results with family members reflects a similar readiness to share this information with researcher and administrators. The effect of time since clinical diagnosis on willingness to share PHI is not explored in the literature to date.

While one might think that previous research experience could be associated with an increased willingness to share PHI with researchers generally, these data did not provide evidence to support this speculation. The scant literature on the extent to which prior research experience influences attitudes about research participation generally is mixed. Madsen et al[238] used structured questionnaires to investigate attitudes towards clinical research amongst cancer trial participants and nonparticipants, and compared results with those from previous studies amongst participants in noncancer trials. They found that

while 80% of participants in an irritable bowel disease study changed their attitudes towards research in a positive direction,[239] the majority of participants in a chemotherapy trial changed their attitudes about research participation following their participation in a negative direction. Perhaps the chemotherapy experience itself created more adversity for research participants than did the interventions involved in the IBD study.

Since these contextual factors were not particularly salient in these populations, literature on other contextual factors that may influence willingness to share health information was reviewed. One noteworthy study evaluated the process of recruiting women from a primary care physician network into a study on genetic counseling for breast cancer.[240] It also investigated predictors' of women's interest in participating in genetic counseling research. Among 340 participants, number of relatives with cancer, higher interest in pursuing BRCA1/2 testing, and lower degree of cancer worry were strong predictors of women's participation. However, interest in participating decreased as the number of study requirements increased. While psychological variables were not considered in the study at hand, it is interesting to note that cancer worry is a salient predictor or research participation.

(B) The influence of 'participant characteristics' on willingness to share PHI

(i) Genotype

Of the variables reflecting characteristics of the participants themselves (genotype status, phenotype status, population group), genotype status had the most compelling effects on participants' willingness to authorize the use of PHI. Overall, individuals who were

genotype negative were more likely to share PHI than those who were genotype positive. While there is some evidence to support an increased sensitivity among individuals who are genotype positive[241] which would support their reluctance to share PHI, there is also evidence suggesting that individuals who are genotype positive have more to gain from medical research[242] and therefore may be more willing to engage in research. This may be particularly true if the research is related to a potential treatment or a risk-reducing intervention such as a new breast or ovarian cancer screening approach. Such ambivalence is apparent within this study itself. The majority of participants are indeed genotype positive which could reflect a greater interest in research among this population compared to the genotype negative population. But when genotype positive individuals are asked about sharing particular PHI for various purposes, they are more reluctant to share it than their genotype negative counterparts.

While genotype status was the most salient 'participant characteristic' predictor of authorization in the quantitative analysis, the salience of this variable was not evident in the content analysis. Only two individuals made comments reflecting the impact of their genotype status on willingness to share information (Table 7): *"It would depend on the results. I mean, I'm looking at breast and ovarian cancer – if I had tested positive for the gene, I don't think I would want my name connected with it... but because I tested negative, I don't mind"* (045HBOC). At the request of some Clinic Directors, the interviewer was blind to the genotype status of the participants. Probing on the particular influence of genotype status was, therefore, not appropriate. This could be one

explanation for why the strong quantitative finding was not brought to bear in the content analysis.

(ii) Phenotype

The extent to which phenotype status predicted willingness to share PHI was negligible. Analogizing this variable with the aforementioned evidence about genotype status, one could speculate that those who are clinically affected have more to gain from research in order to reduce possible recurrence or, alternatively, those who are at risk but not yet clinically affected have more to gain from research from the perspective of prevention. Since only one person commented on this factor during the interview: *"Since I've already had breast cancer, I'm not as concerned about insurance for example...it isn't really an issue, they can already write me off because I've had it....I would be more concerned that they could link back to me if I had not had breast cancer"* (075HBOC), the effect of this variable was, by both methods of analysis, not compelling.

(iii) Population Group

Similarly, the population group (HBOC, THR) from which participants were recruited did not show a significant predictive effect on authorization to share PHI. While not as compelling as some themes apparent in the content analysis, comments reflecting the impact of the nature of one's condition were certainly more salient than those reflecting the impact of one's genotype. In all cases, participants' comments along this line compared their condition to one that might potentially be more stigmatizing. For example (Table 7): *"I don't think having, being Factor V positive is a scandalous thing to*

be...If I had AIDS, I might not have answered the questions the same way" (110THR). Because participants considered their condition to be less socially stigmatizing, they conveyed a general willingness to share PHI. Perhaps this general willingness to share given the low-stigma rating was a reason behind the quantitative responses given by other participants and helps to explain the low predictive value of this particular variable.

There are two noteworthy studies in the literature that examine patient perspectives on health privacy issues and compare perspectives among individuals with medical conditions which arguably, bear different degrees of stigma. Like the participants in this study, both of these other studies use HIV/AIDS as a reference point for comparison. Plantinga et al[198] interviewed 600 individuals with genetic and non-genetic conditions to explore perspectives and experiences related to medical privacy issues. Although participants' experiences did not differ significantly, compared to those in other disease groups, participants with HIV discussed confidentiality with their providers more often, signed documents pertaining to confidentiality of medical records more often, and benefited from providers withholding certain health information from others more often. All participants felt that information regarding HIV status, along with information related to abortion history and mental health, deserved protections over and above that which is provided by a general medical file. Page and Mitchell[243] surveyed 235 individuals about their perspectives on privacy, consent, and the use of health information for medical research. Participants represented three population groups: Multiple Sclerosis (MS), Mental Illness (MI), and HIV/AIDS. While this study was limited by the low response rate from the HIV/AIDS group, illness group was not found to significantly influence

participants' opinions on consent and health information disclosure for research purposes. Unlike Plantinga et al's[198] study which compared HIV/AIDS to purely physical disorders, Page and Mitchell's[243] use of MS and MI populations may reflect a level of stigma comparable to HIV/AIDS given the behavioural manifestations they bear; thereby minimizing the differences in opinion among these groups.

(iv) Self-reported Privacy Level

While as a group participants rated themselves to be moderately private overall, self-reported privacy level was a significant predictor of willingness to share PHI. As one would intuitively expect, those who rated themselves to be more open were more likely to share PHI than those who rated themselves to be more private. While self-reported privacy level was a significant predictor of willingness to share all types of health information under the majority of conditions, there was some evidence to suggest that medical information in general may be less sensitive than other types of personal information. As many as 45% of participants, for example, felt that the privacy of their medical information was less important than the privacy of their financial information and only 18% said that the privacy of their medical information was more important than the privacy of their financial information. Unlike the current study, Kass et al[199] found that self-reported privacy did vary by population group. The difference reported in Kass et al's sample was a function of the perspective individuals with HIV/AIDS, a notably more sensitive condition than those explored here.

One can only speculate as to how the concept of 'privacy' was conceived by study participants. While participants' response to the question, "...On a scale from 1-5, where

1 is 'very private' and 5 is 'very open,' how would you rate how private you are?" could reflect the intrinsic value participants place on privacy, the question was positioned *following* the completion of the HCID tool. Given the range of practical scenarios about information access presented in the HCID, more likely, it would be natural for participants to consider their answer to this question in a way that reflects the instrumental value of privacy. Had the self-reported privacy question preceded the HCID tool, a different meaning of self-reported privacy may have been derived. Regardless of how this particular question was asked and where it was placed in the course of the interview guide, the true meaning of a concept as complex as privacy could only have emerged from a nuanced discussion with study participants. While a deeper level understanding of the concept would be enlightening, data highlighting the concrete limits on access to personal health information under various conditions can shape practical solutions to managing informed consent for genetic database research.

(C) The influence of 'information characteristics' on willingness to share PHI

(i) Type of PHI

A fundamental motivation for modifying the HCID tool to suit the context of genetic information was to explore the extent to which individuals felt differently about sharing genetic and non-genetic health information. As reviewed in Chapter 3, debate abounds over whether and how to manage genetic information differently than other health information in terms of medical privacy and informed consent. What matters to patients or potential research participants should inform this debate. While there is some empiric literature on patients' and participants' perspectives on this issue (Chapter 3), the

exploration of the "type of information" variable in this investigation further informs this debate. The quantitative data in this study, across all population groups, and for all administrative and research purposes explored demonstrated that *type of PHI* was not a significant predictor of authorization. Interestingly, these data support the existing literature that suggests that genetic information is not necessarily perceived to be more sensitive or requiring of special considerations.

While there were some remarks to the contrary identified in the content analysis, they occurred in only a minority of transcripts and were not specific to sharing information with researchers or administrators in particular. Of the few comments that were made about treating genetic information differently than other PHI, some participants' reflected a reluctance to make decisions about sharing information that has implications for their family members because that decision is for the family unit or those particular individuals to make. How privacy rights for an individual within a family unit are protected while at the same time the interests of the family unit are best served is an ongoing tension in clinical practice as well as the academic literature.[244] It is also relevant to the governance of genetic databases which (as discussed in Chapters 1 and 3) explicitly capitalize on the homogeneity (i.e. relatedness) of particular communities. It is for this reason that the expectations implicit in the reciprocity principle can extend beyond participant-investigator dyads to the community or population level. The "ethical prerequisite" of prior consultation with these communities is an example of this extension of principle.[100]

While this overall finding of genetic 'nonexceptionalism' is limited by the study's low overall response rate, it suggests that individuals who have had genetic testing do not feel more strongly about protecting their genetic information than their non-genetic health information. This casts doubt upon the argument that genetic information needs to be considered fundamentally different from other medical information and by extension, warrants special treatment with respect to privacy and consent legislation and practice. Particularly for multifactorial disorders which are the predominant focus of genetic databases, genetic and non-genetic risk factors and associated tests will become increasingly indistinguishable. Treating all medical information with similar professional standards will simplify the provision of care and the conduct of research and will, evidently, respect many patients' wishes.

The finding that genetic information may not need to be treated differently from other health information lends itself to triangulation with the suggestion captured in the content analysis that the HCID tool would benefit from simplification by collapsing various columns/rows/categories (see D-COLL code in Chapter 6, Table 8 and Table 9). 43 participants endorsed this suggestion but were not specific about which variables to collapse to achieve this simplification. Based on the quantitative finding that authorization does not vary with *type* of PHI requested, it would seem reasonable that the four sub-categories of this variable (genetic test results, non-genetic medical test results, family history information, information gleaned from blood sample generally), be collapsed and this variable eliminated from the HCID tool. This and other feedback about the HCID tool (yet to be discussed) has been integrated into Chapter 7 Section E.

(ii) Anonymization Level

The effect of anonymization level on participants' willingness to share health information presents an interesting point for discussion. Quantitatively, the data suggest that participants from both population groups, of both genotypes and both phenotypes are more willing to share aggregated than coded data and more willing to share coded data than personalized data. This makes intuitive sense and is pervasive across all types of information and purposes for which it might be requested. Page and Mitchell's[243] findings support this notion; the only condition under which the majority of their participants believed that consent could be waived was if their health information was anonymized (i.e. aggregated). Quite similar to the study at hand, Whiddett et al[245] surveyed 200 primary care patients about their attitudes towards sharing different categories of health information with different classes of recipients. Level of anonymity was a significant predictor of willingness to share in this population as well. Interestingly though, the participants in this study were more willing to share non-identifiable data with researchers than with administrators, but less willing to share identifiable data with researchers than with administrators. Whiddett et al's interpretation of this finding emphasized that willingness to share health information with all recipients (practitioners, researchers, administrators, other organizations) increases as identity is removed. Other than indicating that participants were most willing to share with practitioners, followed by researchers and administrators, followed by external organizations, they did not elaborate upon the specific finding that suggested that participants differentially share differently anonymized data with administrators and researchers. One speculation, as identified in the content analysis of the current study, was that for practical reasons,

administrative staff may in fact need access to identifiable data for the purposes of appointment bookings and billings, whereas researchers do not need identifiable data to carry out their investigations and analyses.

While this quantitative finding was pervasive and compelling, the content analysis reflected the value participants placed on coded data in particular. For example (Table 8), *"In general I don't really like anything out there with my name on it. I don't think it serves any purpose for it to have my name on it and you know, who knows where it's going. I'd prefer sort of de-identified information where information could be fed back to me if something came up that I should be aware of."* Of 57 comments made about the extent to which anonymization level influenced willingness to share information, 35 of them reflected the heightened value participants placed on coded information because of the potential for relevant health information gleaned from research to be fed back to them.

What is interesting about this finding is that while sophisticated mechanisms have been developed to code and secure data and biological tissue entered into biobanks, it is virtually impossible for data to remain completely anonymized in such databases. While controversial, there are four fundamental reasons why some level of linking must be maintained: (1) The very nature of biobanks is that they are ongoing, prospective data collection resources. While biological samples may be collected only at the outset, health and lifestyle data may very well be entered over an indefinite period of time. Complete anonymization would prevent the ability to link existing data in the database with

incoming data entered into the database. (2) Participants have the right to withdraw their data from a given biobank at any given time. Without some link between who this person is and their data in the database, withdrawal is not feasible. (3) Some consent or authorization models in particular may afford participants the opportunity to learn about ongoing studies and findings that might be relevant to their personal health care. And (4) Should research participants ultimately "win" property rights to their biological samples once the data ownership debate resolves, being a beneficiary of any commercial gain requires that a link between the data and the individual be maintained. Without creating a link between these interested individuals and their data, these commitments cannot be honoured. If coding data is the most pragmatic approach to managing it in a biobank context, these data provide some reassurance that many research participants are in fact comfortable with the idea of coded data and many even value it over other forms of data manipulation. To some extent, participants' stated preference of a de-identified coding system that facilitates contact and feedback reflects an interest in a *reciprocal* relationship. This is a fundamental finding and will be discussed in more detail in Section D.

(iii) Purpose for which PHI is Requested

As was reviewed in detail in Chapter 6, data on participants' willingness to share PHI for six research purposes (general research on index condition, genetic research on index condition, research on health conditions other than index condition, research in controversial areas, hospital tracking research, and government research) and five administrative purposes (appointment reminders, billing organization, hospital tracking,

government tracking, hospital fundraising) were collected. At all levels of anonymization (personalized, coded, aggregated), the probability that participants would share health information for research purposes was greater than the probability that they would share health information for administrative purposes. Within the research domain, the probability of sharing PHI was typically greater for general and genetics research than for hospital tracking and government research, for example, but these differences were not statistically significant. Within the administrative domain, government administration and hospital fundraising were least likely to garner support from participants, but again, differences were not statistically significant.

The content analysis corroborated this general finding. Implicit in many remarks was that participants simply believe in the process of research and are slightly skeptical of administrative staff, *"I am so for research, they can use whatever they want, but I don't want Joe Schmoe in accounts payable looking up my chart..."* What underlies this willingness to share PHI for research purposes in particular has been gleaned from the content analysis as well as the literature and will be explored in Section D. Other than a sentiment of distrust in government-related activities (see Section D(i)), the content analysis did not identify differential preference for sharing PHI for specific research or specific administrative purposes. It is possible that this sample did not have the power to detect differences in sub-categories of research and administrative purposes since this is a fine level of analysis, but is also conceivable that other than the general distinction between research and administrative purpose, study participants do not feel strongly about the purpose for which their PHI is shared.

Based on the statistically non-significant results related to sub-categories of 'purpose,' the lack of text identified as specific to information sharing preferences based upon specific purpose for which information might be used, and the suggestion that the HCID is detailed and would be simplified by collapsing variables, it seems reasonable to collapse "purpose for which PHI is requested" into two general domains: research purposes and administrative purposes. This eliminates the six specific research purposes and five specific administrative purposes from the HCID Tool. Similar to the feedback regarding "type of PHI," this feedback has also been integrated into Chapter 7 Section E.

(D) What underlies willingness to share PHI

(i) Trust and Safeguards

Among those who made specific comments, participants conveyed a sense of trust in researchers, *"I just trust researchers, I really just trust them."* as well as trust in the research process overall, *"I think that they have rules and reviews in place; if it seems like bona fide research, then I trust the process."* Scholarly commentary[246] and empiric literature[247] on the topic of trust and mistrust in the research enterprise is mixed.

After reviewing empiric data from Australia, Mulligan and Braunack-Mayer[247] suggest, not surprisingly, that trust conferred upon the health system by its consumers enables researchers, in a transparent and accountable manner, to pursue important epidemiological research. Recognizing that their success is, largely, at the mercy of this trust, consumers insist on high standards of data security and confidentiality. In this

Australian review, the authors conclude that public confidence in health services is high and breaches of confidentiality occur infrequently.

While the data in the current study do not specifically reflect the perspectives of a range of ethnic groups, much of the empiric literature on 'trust in research' in general focuses on ethnic minority perspectives. Given the exploitation of some of these marginalized groups in the early years of human subject research, an emphasis on their views on the topic of trust in research is certainly justifiable. Barata et al,[248] for example, offer a valuable cross-cultural perspective on the issue of trust and medical research. They examined Portuguese Canadian and Caribbean Canadian immigrants' perceptions of health research and informed consent procedures using focus group discussions. Trust and mistrust emerged as salient themes during the focus groups with both ethnic groups, but how each group articulated the relevance of trust/mistrust was different. The Portuguese participants emphasized establishing interpersonal trust and voiced their suspicion of strangers (not of researchers per se), but were generally willing to partake in the hypothetical study described. Caribbean participants were more concerned about the safety of the research and were reluctant to participate in the hypothetical study because of concerns related to group discrimination.

Asai et al[249] engaged men and women from the general population in Osaka in focus groups in order to explore their attitudes about participating in medical research and compared these 'patient' perspectives with those of physicians. Trust in individuals' physicians or researchers was a fundamental reason for participating in a given research

project. However, mistrust in physicians and the health care system as a whole were expressed repeatedly. Unpleasant and painful experiences as well as clinical mistakes were cited as reasons for mistrust. Participants felt that this clinical mistrust would indeed extend to the research context.

Finally, motivated by the apparent under-representation of African-Americans among medical research participants in the US, Shavers et al[250] surveyed 91 African-Americans about potential impediments to participation in medical research studies. Chi-square tests and multiple logistic regression analyses were used to examine the association between race, issues related to trust in medical researchers, and the willingness to participate in medical research studies. African-American respondents were somewhat less willing to participate if they attributed high importance to the race of the physician when seeking routine medical care, if they believed that minorities or the poor bore most of the risks of medical research, and if they were aware of the Tuskegee Syphilis Study. These characteristics resulted in less trust in medical researchers.

Reflections on various legal cases have also raised consciousness to the issue of trust in the research enterprise. In *Greenberg vs. Miami Children's Hospital*[135] for example, a group of individuals and non-profit organizations had donated body tissue and genetic information to a researcher in order to facilitate his discovery of the gene related to Canavan disease. Upon isolation of the gene, a patent was issued to the investigators' institution for the genetic sequence. The research institution then began negotiating exclusive licensing agreements and charging royalty fees, thereby restricting public

accessibility of Canavan disease testing. The restricted use imposed by the cost of the test prompted Dan and Debbie Greenberg, parents of children affected by Canavan disease, to file suit on October 30, 2000. Similar to the *Moore vs. the Regents of the University of California* case,[134] the Florida court found no property interest for the biological samples and genetic information that was voluntarily given to the researchers because these were considered donations to researchers without any expectations of return. This judicial outcome has been criticized as a double standard and as a violation of fairness, equity, and justice owed to research participants. Merz et al consider it unfair to "patients contributing to the research enterprise for their investments to be wholly appropriated by firms or universities with no commitment to share profits equitably or to return to those patients something of value that they can both access and afford."[251] Commentators now point to this perceived double standard and infringement on justice as a legitimate source of public mistrust in the biomedical research enterprise.[136] If fundamental ethical principles are upheld by neither investigators nor the judicial system, trust in the research enterprise will continue to decline.

While the quantitative analysis did not reveal a statistically significant difference in willingness to share health information for government purposes, text identified in the content analysis convincingly conveyed this reluctance as one which is rooted in mistrust. While only 31/199 comments related to government use were identified, the views that were expressed were not ambivalent. For example (Table 9), this individual expressed unequivocal mistrust in the government: *"Anything that has to do with the government is sticky. I don't trust the government. Whether it is Martin, Harper, McGuinty, they are*

all out there to line their pockets, they don't do anything for us" (123THR). Whiddett et al[245] asked primary care patients with whom they would share general and sensitive health information. In order from most to least likely to be a recipient of this information were doctors, nurses, emergency room personnel, immediate family members, receptionists, pharmacists, health care researchers, community health workers, government health agencies, private health insurers, and government agencies in general. A reluctance to share with government entities appears to be consistent among limited data reported in the literature. While trust per se was not explored or discussed in Whiddett's study, it is reasonable to conjecture that, like it did in the current study, it may have played a role in the choices made by this group of participants.

Trust is certainly a nuanced phenomenon in this context so sensitivity on the part of researchers is required in order to develop strategies that tap into the most salient concerns about research participation among different participant and ethnic groups. In order to engender and maintain the trust that is fundamental to the success of research, both our data and the literature suggest that various *safeguards* are integral to the process and expected by study participants. Established but ever-modifiable safeguards include the informed consent process, data security measures, and consultations with research ethics boards. Those who develop, monitor and evaluate such safeguards must have an appreciation for the fact that the research process implicates partnerships; partnerships between investigators and participants, among investigators, within and among institutions, and within and among communities.

As discussed in Chapter 2, to trust is to "believe in the honesty and reliability of others, to have confidence or faith in, and to allow without fear"[115] or "a confident belief in and the reliance upon the ability and moral character of another person and a confidence that another will act with the right motives in accord with moral norms."[116] Relying on the ability and moral character of another person to act in accordance with moral norms places tremendous responsibility on that other person. It is this demonstration of responsibility and accountability that engenders and maintains the confidence of those bestowing trust. This is consistent with Bailey's notion of 'taking responsibility.'[118] Genuine trust in the context of a relationship cannot manifest unless the trustee believes that the trusted has taken responsibility for the particular role which they play in their life. In the same way that one may trust a doctor to prescribe appropriate treatment because she has taken responsibility for her role in the decisions about an individual's health, respecting individuals' dignity and *privacy*, appreciating the context from which they come, including them in decisions about research participation, and abiding by the rules of ethical research in a transparent and genuine manner put researchers in a position to take the responsibility for research participants that is expected of them.

Given the necessity of trust to the participant-researcher relationship, it is difficult to conceive of autonomy without a relational component. Kahn states that, "adequate protections will never be achieved unless there is a trust relationship between the researchers, their institutions, and the people whom we are asking to participate, along with the groups that they represent."[252] Active communication, a shared commitment to moving a research initiative forward, and a genuine belief that participants are partners in

the process – all consistent with a relational interpretation of autonomy – is fundamental to the success of these ventures.

(ii) Altruism

Many participants were inclined to share PHI simply because they trusted the initiatives or individuals to which they granted access. In addition, while not captured by the quantitative findings, many participants' comments suggested that they were motivated to share their health information for research purposes purely by altruism. For example, *"I made a commitment in my own mind to the medical world that because I was so blessed, that whatever I could do to assist research or other patients I would do."* It is consistent with the public health ethics principle of *solidarity* that research participants might be motivated purely by altruism. This notion was introduced in Chapter 2 but based upon the salience of this concept in the content analysis, it warrants further discussion.

In his thoughtful paper, Richard Tutton[253] considers how the public might conceive of the biological samples that they donate to genetics research, and whether the concepts of 'gift' and 'gift relationship' apply to this context. Tutton's exploration comes in response to the ethical guidelines for managing the UK Biobank which were developed and published by the Medical Research Council (MRC).[254] In discussing these guidelines, MRC draws upon Richard Titmuss'[255] work on blood transfusion when it refers to donating biological samples to genetic databases and says that, "this is preferable from a moral and ethical point of view, as it promotes the 'gift relationship' between participants and researchers and underlines the altruistic motivation for participation in research."[254]

In his book, *The Gift Relationship,* [253] Titmuss makes significant contributions to British policy on blood donation and transfusion. One of these contributions came from his use of Marcel Mauss' *gift theory.*[256] In his writings, Mauss argues that a "gift is an important force for solidarity." He observed that in many cultures, it is not necessarily "property or wealth or things economically useful that are exchanged, but rather acts of politeness: parties, rituals, festivals." While these exchanges appear to be voluntary, they are rooted in obligations, "to refuse to give...just as to fail to accept is tantamount to declaring war; it is to reject the bonds of alliance and commonality." Other scholars support this interpretation. Mary Douglas states that, "a gift that does not enhance solidarity is a contradiction,"[257] and Lewis Hyde suggests that "any exchange be it of ideas or of goats will tend toward gift if it is intended to recognize, establish, and maintain community."[258] Williams and Schroeder[110] remind researchers, however, that participants' altruism must be matched with a moral responsibility to use resources for the common good.

Titmuss felt that the blood donor system in the UK should be organized around the principle of voluntary donation. People who gave blood did so from a sense of altruism with no expectation of anything in return. Furthermore, he argues that it should be the responsibility of the social institutions to encourage the expression of altruism in order to foster relations of community. Interestingly, Titmuss integrates some empiric data from a survey examining attitudes and motives of almost 4000 blood donors in England. He asked survey respondents why they became blood donors and classified their responses into one of 14 categories. The category with the greatest number of responses (26%) was altruism. These individuals expressed a general desire to help with no expectation of any

personal gain for themselves. The next most popular category was 'general appeal' which referred to those who had been influenced by the media (18%), followed by 'personal appeal' which referred to those who had been influenced by friends or family to donate (13%). And as many as 10% reported being motivated by a sense of 'reciprocity;' they had received or knew of people who had received transfusions and wanted to reciprocate.

To supplement his academic discussion of Titmuss'concepts, Tutton[253] describes empiric evidence that he gathered in Orkney, a group of Islands off the north coast of Scotland. As part of the European Human Genome Diversity Project, geneticists collected blood samples from 157 volunteers from the Orkney population in order to delineate the genetic roots of the population that lived on these islands thousands of years ago. Tutton interviewed 15 of these participants in order to gather their perspectives on research participation. Like Titmuss, Tutton first asked respondents to explain why they opted to participate in the genetic diversity project. Some of Tutton's respondents expressed an interest in helping the researcher, "If somebody is to offer genuine research on the subject and he can't get people to help him then it's no use, so it's reasonable to help if it's genuine research" and others expressed an interest in helping their community, "I took part because I'm a true Orcadian and I thought I ought to do something to help Orkney, to do my little bit." Others were quite specific about what they were hoping to contribute to, "My mother was an MS sufferer and there was a lot of that in Orkney so I would like to help so they learn more about that." While motivated to help research specific to their personal cause, the researcher, or the community itself, none of these individuals

describes any expectation of outcomes either in general or for themselves personally. In terms of Titmuss' conceptualization of the 'gift relationship,' these responses could indeed be interpreted as expressions of altruism.

While Tutton's research certainly provides richer evidence for expressions of altruism among research participants than the current study, both converge on the idea that altruism and a sense of solidarity are important motivations for research participation. Further to the relational conception of autonomy reflected by the value research participants place on trust, participants' remarks related to altruism and solidarity endorse the idea that autonomy can be considered even more pluralistic in nature and could perhaps be conceived of as a function of citizenry. Corrigan suggests that one way to operationalize this notion of citizenry is to integrate citizens into the formative stages of research so that they have a voice in negotiating what counts as its common good; "...people want to make choices as citizens cognizant of common good, not simply as individual consumers."[104] In this way, individuals' personal decision to participate in a given research endeavour would be linked with their genuine belief in its collective good.

While research participants in this study and Tutton's study describe altruistic motivations for participating, implicit in some of their remarks is a sense of duty or obligation to behave this way. While genuine expressions of altruism are not necessarily a function of obligation, scholars link this apparently unselfish interest in the community or common good with an obligation for such. In contrast to rights' theorists who advocate in favour of the primacy of rights over obligations, scholars who believe in

solidarity and pluralistic conceptions of autonomy argue that, for the sake of the collective good, obligations supersede individual rights. Specifically, Chadwick believes that individuals have a duty to participate in research in order to improve knowledge that could contribute to the health of the population.[105] Rhodes' conscription system that requires, "every US resident to perform some research service every ten years…" is another example of an unbridled commitment to this idea of civic duty.[108] While some individuals may certainly be motivated to participate in research by pure altruism, both these data and the literature suggest that banking on pure altruism as the explanation for participatory behaviour may be overly simplistic. More realistically, participants' perceived duty to help is motivated not only by altruism, but by constitutive solidarity in which individuals have an interest in common and by contributing to this interest, achieve a better outcome for themselves.[105] In this way, what citizens want for others is akin to what they want for themselves. This pluralistic conception of autonomy bears little resemblance to the traditional individualistic conception of autonomy.

(iii) Reciprocity

Knoppers and Chadwick[100] describe the reciprocity principle as one that supports the exchange of information between patient and provider or research participant and investigator. Their interpretation of reciprocity is oriented around the exchange of information that precedes study participation; a discussion of study goals, benefits, risks, security measures, possible future uses, and potential for commercialization which enables potential participants to make an informed decision that is consistent with his/her personal/cultural values. While this exchange is important in and of itself, it also sets the

stage for a discussion of participants' expectations regarding the extent to which researchers will communicate with them generally and disclose medically relevant findings that ensue from the research. The data gathered in the current study speaks more to the latter manifestation of reciprocity between participant and researcher; that which relates to participant expectations and data management.

The principle of reciprocity is relevant to the data gleaned from this study in four fundamental ways.

(a) First, many participants were explicit about the value of sharing coded health information because of the potential for them to be recontacted should medically relevant information come to light. While the quantitative data suggested a greater willingness to share anonymized health information than coded health information, when reasons were articulated for sharing differentially anonymized information, greater value was placed on the opportunity for recontact. A recent issue of the American Journal of Bioethics presents a series of commentaries on if, why, and how to provide genetic research results to study participants. The commentaries respond to Ravitsky and Wilfond's[259] 'results-evaluation approach' that uses the criteria of analytic validity and clinical utility to assess the value of the anticipated findings as well as the study context and meaning ascribed to the information by study participants in order to guide the investigators' decision about the disclosure of research results. The authors reject the option of making disclosure decisions based upon researcher preferences which do not consider participant perspectives and reject the option of autonomy-oriented decisions because leaving the disclosure decision entirely to the discretion of research participants is an inappropriate

responsibility to place on them. Ravitsky and Wilfond describe the *results evaluation framework* as honouring the principles of autonomy, beneficence, justice, and reciprocity.

The commentaries that follow the presentation of this framework highlight a range of concerns with this framework in particular and offer other valuable insight to navigating decisions about research results disclosure. Some of these perspectives are presented here. Dressler and Juengst,[260] for example, criticize Ravitsky and Wilfond's interpretation of the reciprocity principle; "the more intense the relationship [between the investigator and the research subject] the stronger the obligation for reciprocity." While Dressler and Juengst argue that a reciprocal relationship is indeed appropriate in this research context the researcher's commitment to his participants should most certainly not be a function of the duration or intensity of their relationship. Rather, all participants should be treated equitably. Others disagree with the premise that researchers *should* engage in a reciprocal relationship with participants at all and believe that the research relationship is contractual and the researcher compensates and protects the subject in exchange for their participation.[259]

Ossorio[261] questions the appropriateness of a 'clinician-style' obligation of researchers to provide research results. Just because (1) research participants may want to receive individual results, (2) researchers may want to return results as a way of validating participants' important contributions to research, (3) genetic research results may constitute important information about oneself; and (4) the opportunity for participants to make this choice enhances their self-determination, a researcher is not necessarily obliged to disclose this information. Results disclosure does, however, become obligatory if

researchers take on the role of clinician in this context. In the clinician role, investigators indeed have a duty to recontact participants should information posing real or imminent harm be discovered. Pervading this question generally is the ever-blurring lines between the role of the investigator and that of the clinician.[262] How the principle of reciprocity is operationalized for the clinician, the researcher, and the clinician-researcher remains a point for debate.

Rothstein[263] weighs-in with more pragmatic feedback suggesting that excessive reliance on objective criteria like clinical utility and analytic validity undervalues the subjective interests of research subjects. He also argues that rather than researchers and institutional review boards (IRBs) making decisions about disclosure once the results are obtained, study subjects should be presented with a tiered-model of decision making about possible research findings during the informed consent process. But Parker[264] and Klitzman[265] suggest that truly understanding the meaning that study participants assign to potential findings a priori is not realistic. If the decision about disclosure is made during the informed consent process, it is difficult to discuss the true meaning of the potential findings before they are known.

Similarly, some of the respondents in Tutton's research reflected an interest in learning more about their *own* ancestry from the results of the genetics study. For example, "I was interested in my own family because they used to say there was a lot of Spanish blood in me…I thought this answer might come out of this test." In part, this interest in personal information could be attributed to the geneticist's offer to provide participants with information specific to their particular samples. From the geneticist's perspective, Tutton found that most participants were only interested in general community-related findings,

but some individuals did want individualized feedback. Tutton does not elaborate upon any form of informed consent process that may (or may not) have specified the researcher's intent with respect to feeding personally relevant information back to participants. Regardless of what was formally discussed, some participants conceive of their participation in this data collection as a reciprocal relationship based around the exchange of blood samples for information about their family genealogies. In addition to altruism, an interest in reciprocity appears to have motivated this group of participants.

While fundamental questions remain unanswered, highlighting the practical and theoretical challenges related to if, why, and how genetic research results should be disclosed to research participants through academic debate is an important step towards resolving this difficult question.

(b) While not expressed by these participants, maintaining a personal link with their data enables research participants to be potential beneficiaries of commercial gain that may come from research findings, assuming they retain some level of property rights to the data they contributed to the research. This particular example of reciprocity could be interpreted to overlap with the notion of constitutive solidarity – individuals are motivated to contribute to a research interest, in part, to achieve a better outcome for themselves.

(c) Both quantitative data and participants' comments indicated a compelling interest in revisiting choices about what information they would be comfortable sharing over time. While 35% of the sample felt no need to revisit their choices, 44% of the sample expressed interest in revisiting their choices within the first year of making them.

Periodic contact with researchers was valued by participants in order to learn more about the nature of the ongoing research and in order to reassess the extent to which they remain interested as a participant. Many reasoned that what information they would be comfortable sharing under various conditions may change as their medical histories change. For example, "I might have to say that every year it would have to be revisited… a lot can change with your health issues." The frequency with which participants wanted to revisit their choices on the HCID was not associated with self-reported privacy level.

While interest in revisiting choices was not explicitly articulated by participants as a mechanism of control, it is reasonable to infer from this finding that some participants were comfortable relinquishing control to researchers and administrators while others preferred to retain some level of control over their health information. Similarly, Plantinga et al[198] found that whereas people are happy to share personal medical info with others, they want the ability to control and authorize such disclosures. As was previously discussed, controlling personal information is one way to operationalize the instrumental value of privacy. Also presented previously was the idea that relationships of trust are only possible if people have privacy and afford it to others. It follows then that allowing research participants to assert control over their health information is one way to foster the necessary trust between investigator and participant. As suggested by Petronio's Communication Privacy Management Theory[88] individuals "develop a series of privacy rules regarding why, how, and to whom they will disclose private information based upon conceptions of information ownership, the risks and benefits of disclosure, and the nature

of the relationship between the parties sharing information." Data from this study certainly support an influential role for these dimensions on research participants' decisions regarding sharing PHI.

(d) Finally, text identified in the content analysis suggests that completing the HCID Tool would be simplified if guidance was provided. While participants were not probed on from whom this guidance might come, their message suggested that the presence of an engaged professional would facilitate the process of defining the conditions under which they would be willing to share various types of health information. There is some literature suggesting that patients are reluctant to share health information with providers and administrative staff who are not directly involved in their care.[206] Whether participants' interest is in having a professional engage in a dialogue over each decision implicated by the HCID or in simply having a professional available as a resource should questions arise while completing the Tool was not gleaned from the data. Any level of engagement between participant and professional at this juncture is a representation of reciprocity.

These four examples of reciprocity: (1) interest in being recontacted should relevant medical information arise from research, (2) interest in benefit sharing of profits that ensue from research, (3) interest in revisiting choices made about research participation and information sharing, and (4) interest in professional guidance on completing information directives such as the HCID reflect the importance of the investigator-participant relationship. As previously discussed, trust is fundamental to maintaining this

relationship and implementing safeguards to foster and protect this trust is necessary. Honouring the aforementioned interests in reciprocity expressed by participants, in turn, provides one way to implement safeguards necessary to preserve a trusting relationship among interested parties.

Given the nuances in the data collected in the current study and Tutton's study suggesting that participants' motives are not purely altruistic, but also reflective of the principles of solidarity and reciprocity, the *gift relationship* conceptualization of research participation may be oversimplified. Madsen et al[239] found that study participants were motivated by both personal interests in improved (cancer) treatment as well as an interest in helping future patients. Again, motivation to participate in research appears to be layered. While interested in helping future patients, Madsen's population were self-interested and did not feel that they had an ethical obligation to participate, despite the necessity of *some* cohort of people to participate in order to identify, in this case, best treatment options. Rossel[266] articulates this tension as that in which a person is willing to accept a good (cancer treatment) procured by a social activity (clinical trial), but is unwilling to participate in this activity that is a prerequisite for obtaining the good. He refers to these individuals as 'free-riders.' For an equitable and just medical research enterprise to flourish, 'free-riders' should be reminded of Knoppers and Chadwick's[100] socially conscience perspective on solidarity.

(E) Conclusions: How do these data inform the process of informed consent for genetic database research?

(1) *Genotype status* is a significant predictor of willingness to share PHI. Genotype positive individuals are less likely to share personal health information at each level of anonymization for both research and administrative purposes than are genotype negative individuals. While genotype positive individuals may have plenty to gain from genetic database research (e.g. prophylactic or tailored pharmacogenomic approaches), researchers need to be sensitive to a potential reluctance among individuals in this population to share health information. A low overall response rate in this study may further reflect this population's reluctance to participate in research. To mediate these concerns, researchers need to ensure that rigourous safeguards related to information privacy are in place for participants and that a reciprocal relationship is developed with participants to foster and preserve trust in the research initiative.

(2) Individuals who report being more open on a *self-reported privacy* scale are more likely to share personal health information than individuals who report themselves to be more private. This appears to hold true for sharing information for both administrative and research purposes and across all population groups. Perhaps a reflection of the instrumental value of privacy, research participants' have a desire to maintain some level of control over their personal health information. This may manifest as decisions about what information to share under which circumstance at the time an initial request is made as well as an interest in revisiting choices made about information sharing over time.

(3) As significant predictors of authorization, genotype status and self-reported privacy level were combined into a *predictive model* which generated probability estimates for sharing health information under various circumstances. Combining salient predictor variables of this kind can help researchers design authorization models to suit their particular populations and research questions. Models such as this may also help researchers predict the likelihood of a given population's willingness to participate in research, a potentially useful factor in crafting rigourous study designs.

(4) *Type of personal health information requested* is not a significant predictor of willingness to share PHI. This quantitative finding suggests that these participants do not differentiate between genetic and non-genetic information in terms of their willingness to share it for research and administrative purposes. While a small minority of participants provide comments to the contrary, the data overall cast further doubt on the argument that genetic information is exceptional. This suggests that informed consent practices need not be tailored to particular characteristics of genetic information as they are not substantively different enough from those of other types of health information. Combined with study participants' suggestion to simplify the HCID Tool by collapsing columns, this finding motivates the elimination of the *type of personal health information (genetic, non-genetic, family history, blood sample)* variable from the Simplified HCID Tool. This change is reflected in the revised model illustrated in Conclusion 7.

(5) While individuals are significantly more willing to share personal health information for research purposes than for administrative purposes, their willingness does not

significantly vary according to six different research purposes and five different administrative purposes explored. From this finding, one could speculate that individuals are comfortable participating in genetic database research without necessarily knowing the specific purpose for which their data may be used. Combined with study participants' suggestion to simplify the HCID Tool by collapsing columns, this finding motivates the elimination of the sub-categories of the *purpose* variable from the HCID Tool, leaving only a distinction between research and administrative purposes as important to assess. This change is reflected in the revised model illustrated in Conclusion 7.

(6) The quantitative analysis indicates that individuals are more willing to share aggregated health information than coded health information and more willing to share coded health information than personalized health information. This finding held true across all types of health information, all purposes for which it might be requested, and all population groups. However, text examined in the content analysis suggests that many participants value the idea of coded data (in contrast to aggregated data) to enable the possibility of receiving medically relevant information gleaned from research. Strategies for data storage should be made explicit to potential participants in genetic database research and participants should be given the opportunity to understand the benefits and costs associated with each approach to data security. The strength of this quantitative finding combined with the discrepancy identified in the content analysis motivates its inclusion in the Simplified HCID Tool.

(7) Based on the findings informing Conclusions 1-6, a simplified version of the HCID Tool is proposed. The revisions to the tool used in this study include: (a) removal of the *type of personal health information* variable, (b) collapsing the *purpose for which personal health information requested* sub-categories into research and administrative purposes generally, (c) addition of three qualifying variables to provide investigators with some context from which potential research participants might be coming: genotype status (if known/relevant), self-reported privacy level, and interest in periodic contact with researchers to revisit choices and/or learn of any medically relevant findings. While pilot testing is necessary, this version is simpler, likely less cumbersome to complete, and better targeted with respect to factors that influence participants' willingness to share health information for research and administrative purposes. Figure 10 illustrates the simplified HCID Tool.

Figure 10: Simplified Health Care Information Directive Tool

	Willing to share *personalized* health information for		**Willing to share *coded* health information for**		**Willing to share *anonymized* health information for**	
	Yes	No	Yes	No	Yes	No
Research Purposes						
Administrative Purposes						
Genotype Status	+ve __ -ve ___					
Privacy Level (1 is very private, 5 is very open)	1 2 3 4 5					
Maintain Periodic Contact with Researchers	Yes __ No __					

(8) Greater willingness to share health information for research purposes compared to administrative purposes appears to be related to individuals' sense of *trust* in researchers as individuals as well as the *safeguards* built into the research process overall. The role of a trusted professional requires taking responsibility for others and demonstrating accountability for actions. Respecting a relational conception of autonomy and abiding by the rules of ethical research in a transparent and genuine manner can facilitate this role. While this message is not a new contribution to the literature, the existing resistance to the idea of genetic database research makes it particularly important that researchers in this field take these findings seriously in the design and implementation of their research in order to foster and maintain necessary trust of participants.

(9) While some individuals appear to be motivated by altruism to participate in research, these data, theoretical commentary, and related empiric literature suggest that interest in research is more complex than pure altruism. While individuals may indeed have a genuine interest in the common good, they also have expectations of the researchers (e.g. guidance), the research process (e.g. some level of control over others' access to personal health data), and management of the ultimate research findings (e.g. recontact regarding medically relevant information). These findings suggest that rather than a purely altruistic interest in research, individuals have a reciprocal interest in research. While a minority of savvy research participants may bring these expectations to the researchers' attention, researchers would do well to proactively negotiate these domains with potential participants and in so doing, honour the reciprocal nature expected of their research relationship.

(10) Data generated through this study offer a better understanding of the factors that influence research participants' willingness to authorize the use of their personal health information. These data suggest that preferences for sharing personal health information and motivations that underlie these preferences cannot be explained by one phenomenon. In response to participants' preferences, a revised HCID Tool has been proposed. Since the authorization model affords research participants the opportunity to assert complete control over their health information, complete deference to research authorities, or to negotiate the terms of a reciprocal relationship with research authorities, this model provides the flexibility needed to capture the complexity of research participants' interests. While further evidence from a non-hypothetical research setting is indicated, these data support further consideration of the authorization model as a viable approach to informed consent in the context of genetic database research. Further refinement of this approach is warranted prior to the legislative change required to accommodate this model of informed consent.

CHAPTER 8: STRENGTHS AND LIMITATIONS

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Given the interpretive nature and the complex theoretical underpinnings of bioethics, research ethics, and public health ethics, conducting empiric research that attempts to bridge these domains is a daunting task. While the conceptual framework behind this investigation attempted to simplify this complexity by honing in on concepts fundamental to informed consent (privacy, autonomy, trust), integrating the various domains of bioethics and relevant moral theory resulted in a complex justification for a research endeavour. While the exercise of this integration is arguably a strength of this investigation, the complexity and interpretive nature of the resultant framework may ultimately limit the coherence of the empiric findings. Academic in nature, it is not always straightforward to operationalize moral theory and ethical reasoning. While the process of informed consent was conceived of as a practical mechanism through which to grapple with moral questions, some theoretical arguments are simply difficult to fit into a practical mould. As well, the field of Public Health Ethics is young. While it is only through critical evaluation, empiric challenge, and academic scrutiny that this field will mature, it does not yet provide the same moral anchor to a research question that traditional moral theory might. While this investigation makes a valuable contribution to the developing literature on Public Health Ethics, its conceptual grounding is vulnerable to the existing criticism related to the theoretical immaturity of this field generally.

While a cross-sectional survey design is an appropriate approach for ascertaining potential research participants' perspectives, the data this approach generated are limited by the fact that they are hypothetical in nature. Rather than learning what people 'might'

do in given circumstances, findings would be more generalizable if research participants' 'actual' decisions in similar circumstances were sought. There is literature to support the notion that hypothetical interest in genetic testing, for example, is significantly greater than actual uptake.[267] When 'push comes to shove' and a *real* decision needs to be made in a clinical or research context, it may very well be different from the decision that the individuals themselves might have anticipated making. While a real-time test of the HCID Tool in a potential research participant population might have provided a more accurate reflection of willingness to share health information, the feasibility of this option was explored with two groups of investigators and was not supported. Investigators were reluctant to burden their potential participants with more paperwork and admitted to a concern about the impact a discussion about medical research and information privacy might have on their recruitment potential. On the other hand, the hypothetical nature of this study could be interpreted as a strength because it might have mitigated the potentially threatening nature of any real-time commitments to health information sharing preferences.

The choice of HNPCC, HBOC, HH, and THR as populations from which to sample was deliberate in its attempt to represent a spectrum from rare single gene disorders to common multifactorial disorders, the former representing a more traditional genetics research approach which would capitalize on small populations with very limited eligibility criteria and the latter representing a public health genetics approach which would use large populations with broadly defined eligibility criteria. Poor response rates from the HNPCC and HH populations in particular limited the ability to interpret the

findings as a reflection of this spectrum. While HBOC and THR represent rare and common conditions, respectively, these clinical groupings did not appear to influence participants' willingness to share health information. Had data from the other clinical groups been robust enough to include in the analysis, subtle gradations across this spectrum may or may not have been apparent. While the selection of individuals who had pursued genetic testing was deliberate in order to capitalize on their familiarity with genetic information and explore the relevance of genotype status, individuals who have pursued genetic testing are certainly not the only category of individuals who might one day be candidates for genetic database research. In fact, a lay person with no prior knowledge about genetics could easily be invited to participate in a genetic database and his/her perspective on sharing health information for this purpose would be similarly valuable and likely more generalizable than the perspectives obtained in this study.

Both the content and design of the interview guide as well as its mode of administration warrant discussion. The fundamental challenge with respect to the design of the interview guide was its attempt to incorporate the HCID as both a data collection tool *as well as* an instrument for participant comment. Since Goel and Upshur's version of the HCID[45] had been piloted[215] and systematically modified based upon this feedback and factors relevant to the context of genetics research, a logical next step was to implement it on a larger scale. Since the Modified HCID proved to be detailed and somewhat cumbersome to complete in the context of these study interviews, its role as data collection tool was prioritized over soliciting feedback throughout the course of the interview. While the intention was to collect feedback on the nature of the tool itself over

the course of completing it, completing the instrument itself became the focus of this section of the interview. Feedback on the tool was also limited by the fact that the solicitation of feedback, in part, was left to the discretion of the interviewer. While it was necessary for the interview to be administered by a researcher assistant (and not self-administered) in order to guide the participant through the questions and ensure completion of quantitative questions, additional open-ended questions specific to the tool and/or more explicit probes would have helped the interviewer meet this goal. Since transcription of interviews lagged behind the pace of completing the interviews themselves, making timely modifications to the interview guide was challenging. Finally, given the moral complexity of the conceptual framework grounding this investigation, more attention to participants' perspectives on concepts including trust, safeguards, altruism, and reciprocity would have facilitated a richer analysis of the meaning of these findings. Only through nuanced discussions of these complex concepts could this insight be gained and the interview guide was simply not structured to achieve this goal.

Although a logistic regression approach was appropriate for identifying the predictive effects of a range of variables on a categorical outcome variable, the quantitative analysis was limited by a low overall response rate. This, in turn, made fine-level variable comparisons difficult due to small cell size. Variable levels were collapsed where necessary to facilitate an appropriate level of analysis. While missing data was mitigated by using an interviewer-guided tool, the absence of some data precluded some fine-level analyses. The aforementioned limitations related to the data collection process (feedback

on HCID left to the discretion of the interviewer, transcription lag) compromised the potential richness of the qualitative data. Had the interview guide been designed with more specific probes and had transcripts been examined earlier in the process, a broader and deeper level of understanding of the factors that influence participants' willingness to share personal health information would have been ascertained.

CHAPTER 9: FUTURE DIRECTIONS FOR RESEARCH

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Variables identified as bearing influence on participants' willingness to authorize the use of personal health information warrant further exploration. While genotype status appears to be an important predictor variable, genetic test results per se do not seem to command special treatment with respect to information sharing. Does this mean that it is appropriate for researchers to inquire about potential participants' genotype at the outset of an investigation in order to guide their assessment of the extent to which they are comfortable sharing health information? Being careful to respect appropriate privacy boundaries while *not* exceptionalizing genetic information may prove to be a difficult balance to strike. Further empiric evidence on how to navigate this tension could help to inform the practical application of these particular findings to the process of informed consent for genetic database research.

A more nuanced understanding of the meaning of *privacy* for study participants would help to interpret the motivations underlying their decisions on the HCID tool. While it may not be realistic to integrate this type of discussion into the actual process of informed consent, richer qualitative data on how individuals' conception of privacy plays into their decisions about information access and control.

The simplified version of the HCID tool warrants piloting and further evaluation as a viable approach to informed consent in a real-time research setting. While investigators and participants could find this approach threatening to their recruitment and personal privacy, respectively, it is important to capture any relevant difference between

hypothetical willingness to share health information and actual willingness to share health information.

Evidence from this study highlighting participants' interest in a reciprocal relationship with investigators combined with current literature on how best to meet participant and investigator interests in this regard (AJOB series 2006:6) suggests that developing and evaluating various strategies for navigating the particulars of this relationship (e.g. how to manage data coding, interest in results disclosure, interest in revisiting choices about information sharing, interests in commercial benefit-sharing) are warranted.

Governance structures reviewed in Chapter 3 provide one mechanism for overseeing researchers' commitment to engendering trust, maintaining rigourous safeguards, and engaging participants as partners in the research process. While data in this investigation cannot speak directly to the viability of governance structures, the value of trust, safeguards, and reciprocity articulated by study participants suggests that governance structures should continue to be developed, implemented, and evaluated. As these structures mature and the process of informed consent continues to evolve, confidence in the management of ethical considerations for human subjects in the context of genetic database research will grow.

These study findings place additional responsibilities on researchers. Exploring researchers' perspectives on the feasibility of managing these responsibilities and

suggestions for how to integrate them into their existing priorities would make a pragmatic contribution to this body of literature.

Since the authorization model affords research participants the opportunity to assert their desired level of control over personal health information and could be implemented into practice using a more refined version of the HCID tool, exploration of the legislative changes in Canada required to accommodate this model of informed consent is warranted.

APPENDICES

Appendix 1.1 – Participant Groups and Recruitment Sites

	Index Condition			
	Hematology		Oncology	
PATIENTS	**VTE**	**HH**	**HBOC**	**HCC**
Genotype +ve & Phenotype +ve	***FVL+ve & VTE***	***HFE+ve & HH***	BRCA1/2+ve & BC/OC	MLH/MSH+ve & CC
Genotype +ve & Phenotype -ve	FVL +ve No VTE	HFE +ve No HH	BRCA1/2 +ve No BC/OC	MLH/MSH +ve No CC
Genotype *True –ve* & Phenotype -ve	FVL -ve No VTE	HFE -ve No HH	BRCA1/2 -ve No BC/OC	MLH/MSH -ve No CC
Recruitment Sites	UHN, NYGH, MSH		UHN, SW, NYGH	MSH, SW

Appendix 1.2 – Sample Invitation letter

University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

Name & Address
Date
Dear

RE: INVITATION TO PARTICIPATE IN STUDY ON MEDICAL PRIVACY

The Primary Care Research Unit in the Department of Family and Community Medicine at the University of Toronto and the Joint Centre for Bioethics at the University of Toronto are conducting a study of the 'Health Care Information Directive (HCID).' The goal of the HCID is to allow individuals to make informed choices regarding how their personal health information can be used. ***The HCID aims to ensure that sensitive health information is used ethically.*** In this study, the HCID is applied to the specific context of genetic information.

As an individual who has had genetic testing, we are inviting you to take part in this study. Participating in this study involves completing a 40 minute interview with a research associate. The interview can be done in-person or by telephone, at your convenience. We recognize that while you have likely been approached to participate in a number of research studies, your input regarding medical privacy practices would be very valuable.

Participation is voluntary and all data collected as part of this project will remain strictly confidential. Those choosing to participate will not be identifiable in any of the reports based on this research. Moreover, individuals remain free to stop their participation at any time.

If you would like to participate, please read and sign the enclosed consent form. Please return this form by mail in the self-addressed envelope provided. Once your consent form has been received, you will be contacted to arrange an interview time. Please keep the YELLOW and GREEN sheets included in your package. These will be necessary at the time of the interview.

If you have any questions, please contact Robin Hayeems (Research Associate) by e-mail at robin.hayeems@uhn.on.ca or by telephone at 416-480-6100*7194

Thank you for your consideration.

Yours truly,

Physician Name, MD, FRCPC

Head, Division of _____

Appendix 1.3 – Sample Consent Form

University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

CONSENT FORM

The collection, use, and disclosure of personal health information:

The Health Care Information Directive applied to Genetics

Principal Investigator: Dr. Upshur

Study Objectives:

This research project involves interviewing people who have had genetic testing for *Factor V Leiden (FVL)*. We are interviewing people who have had genetic testing for *FVL* to gain a better understanding of individuals' preferences related to the privacy of their medical information. Your opinion on this topic will help us to test the Health Care Information Directive (HCID), a new strategy developed to improve current privacy and consent practices in healthcare settings.

This study is carried out under the direction of the Primary Care Research Unit in the Department of Family and Community Medicine, Sunnybrook & Women's College Health Sciences Centre and the Joint Centre for Bioethics at the University of Toronto. The Principal Investigator is Dr. Upshur.

Procedures:

I understand that I will participate in a face-to-face or telephone interview with a research associate. The interview will ask me about various types of personal health information and my preferences for whether or not certain types of health information should be kept private or should be shared with other people. The interview will also ask me for my opinion on the HCID, a new privacy tool. The interview will take approximately 40 minutes to complete. I understand that I can withdraw my participation at any time. Refusal to continue with the interview will in no way affect my ongoing medical care. The interview will be audio-taped and transcribed verbatim. All transcripts and audio-tapes will be kept in a secure locked office and destroyed ten years following the end of the project. Only members of the research team will have access to the data. My name or any other identifying information will not be recorded without my consent. All my responses are completely confidential. There are no physical risks to participating in this study.

I have been given a copy of this consent form. If I have questions about taking part in this study, I can contact physician who is in charge of this study at the Family Practice Unit, Sunnybrook site, Dr. Ross Upshur (416-480-4753). Or, if I have any concern about the way in which this study is conducted I can talk to someone who is not involved with the study at all, but who can advise me on my rights as a participant. I may contact the Research Ethics Office at the University Health Network (416 946-4438).

I have read and understood the above information and agree to conduct the interview.

Subject Name	Signature	Date
Witness Name	Signature	Date
Investigator Name	Signature	Date

Appendix 1.4 – The Health Care Information Directive (Original)

	Personal Health Information	Registration Information	De-identified Data	Aggregated Statistical
Patient care (access by caregivers, such as physicians, nurses, physiotherapists etc. next of kin, advocate, legal representatives)				
Continuity of care Between Health Care Providers and Administrative levels Reminders for follow ups and screening tests etc				
Payment (hospital/fee for service)				
Administrative management (institutional and governmental/provincial)				
Continuous Quality Improvement, peer review				
Research Epidemiological Study Disease Registries				
Hospital fund raising (mail-outs)				
Deriving profit from data as a research product Marketing				

Appendix 1.5 – HCID Modified for Genetics

RESEARCH ***Would you permit researchers to access this information for research related to:***	**A** **Personalized Health Information**				**B** **De-Identified Information** (test results w/o identifiable info but linked to personal information)				**C** **Grouped Information** (test results w/o identifiable info and grouped)			
	Genetic Test Result (a1)	Mammo-gram or ultrasound Report (a2)	Family Hx of br/ov ca (a3)	Blood sample itself (a4)	Genetic Test Result (b1)	Mammo-gram or ultrasound Report (b2)	Family Hx of br/ov ca (b3)	Blood sample itself (b4)	Genetic Test Result (c1	Mammo-gram or ultrasound Report (c2)	Family Hx of br/ov ca (c3)	Blood sample itself (c4)
Q1. Breast/ovarian cancer in general	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q2. The genetics of breast/ovarian cancer in particular	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q3. Conditions other than breast/ovarian cancer (e.g. diabetes)	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q4. Controversial areas (e.g. stem cells, population-specific, mental health)	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q5. Hospital tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

Q6. Governmental tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

ADMINISTRATIVE ***Would you permit administrative staff and/or to have access to this information…***	**A** **Personalized Health Information**				**B** **De-Identified Information** (test results w/o identifiable info but linked to personal information)				**C** **Grouped Information** (test results w/o identifiable info and grouped)			
	Genetic Test Result (a1)	Mammo-gram or ultrasound Report (a2)	Family Hx of br/ov ca (a3)	Blood sample itself (a4)	Genetic Test Result (b1)	Mammo-gram or ultrasound Report (b2)	Family Hx of br/ov Ca (b3)	Blood sample itself (b4)	Genetic Test Result (c1)	Mammo-gram or ultrasound Report (c2)	Family Hx of br/ov Ca (c3)	Blood sample itself (c4)
Q1. To remind me of follow-up appointments and screening tests	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q2. To organize billing and payment for the services I received	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q3. For hospital tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q4. For government tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q5. For hospital fundraising purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

RESEARCH	**Appendix 1.6 – Participant copy**				**B**				**C**			
Would you permit researchers to access this information for research related to:	**Personalized Health Information**				**De-Identified Information**				**Aggregated Information**			
	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself
Q1. Breast/ovarian cancer in general	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q2. The genetics of breast/ovarian cancer in particular	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q3. Conditions other than breast/ovarian cancer (e.g. diabetes)	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q4. Controversial areas	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q5. Hospital tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q6. Governmental tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

ADMINISTRATIVE *Would you permit administrative staff and/or senior hospital administrators to have access to this information…*	**A**				**B**				**C**			
	Personalized Health Information				**De-Identified Information**				**Aggregated Information**			
	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself	Genetic Test Result	Mammo/ US Result	Family History	Blood Sample Itself
Q1. To remind me of follow-up appointments and screening tests	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?
Q2. To organize billing and payment for the services I received	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?
Q3. For hospital tracking and funding purposes	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?
Q4. For government tracking and funding purposes	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?
Q5. For hospital fundraising purposes	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?	Yes No ?

Appendix 1.7 – Sample Interview Guide

HEALTH CARE INFORMATION DIRECTIVE APPLIED TO GENETICS
INTERVIEW TOOL
SECTION A

Interview Logistics	
Date of Interview	
Location of Interview	☐ In-person (location _____) ☐ Telephone
Start Time	
End Time	
Participant's ID#	
Consent Received	☐ Yes ☐ No
Interviewer Initials	
Sampling Characteristics	
Recruitment Site	☐ MSH ☐ UHN (Thrombo / FOCC) ☐ NYGH ☐ SHSC (TSRCC / Hem)
Condition	☐ Thrombophilia ☐ Hemochromatosis ☐ HNPCC ☐ HBOC
Genotype	☐ Genotype +ve ☐ Genotype True –ve
Phenotype	☐ Phenotype +ve (if HBOC pop'n, specify if breast ca OR ovarian ca) ☐ Phenotype –ve

"Thank you for agreeing to participate in this study. I am going to ask you a series of questions related to personal health information and medical privacy. Many of these questions will help us to explore the value of a new type of consent tool called the Health Care Information Directive. A tool like this gives patients like you the chance to specify which types of medical information you are willing to share with whom and for what purpose. I will explain each section as we go along.
The package that you received included a couple of pages that will be necessary to complete the interview. You should find a YELLOW sheet and a GREEN sheet. Please have these sheets handy as well as a pen or pencil.
Do you need a minute to gather these things together?
Do you have any questions before we begin? If you do not have any questions now but think of a question once we get started, please stop me and ask.
Let's get started..."

Section B.

To start out, we would like to ask you a few questions about your experience with breast/ovarian cancer and/or genetic test result related to hereditary breast/ovarian cancer.

1. *[If clinically affected]* In what year were you diagnosed with breast/ovarian cancer? _____ [□ 98]

2. *[All]* In what year did you learn of your genetic test results related to hereditary breast/ovarian cancer?

3. From which health care provider did you learn of your *cancer diagnosis **and/or** genetic test results* and what were the circumstances? (e.g. family doctor, specialist, genetic counsellor, nurse) [□ 98 □ 99]

4. *[If clinically affected]* Have you ever been admitted to hospital because of a breast/ovarian cancer diagnosis?
   (01) □Yes (02) □ No [□ 98 □ 99]

5. *[All]* Has a close family member ever been admitted to hospital because of a breast/ovarian cancer diagnosis?

   (01) □ Yes (02) □ No [□ 98 □ 99]

6. Has a close family member ever passed away as a result of breast/ovarian cancer?
   (01) □ Yes (02) □ No [□ 98 □ 99]

Section C.

Next, we would like to ask you a few questions about your beliefs about research in general:

1. (a) Have you ever participated in research related to breast/ovarian cancer?
   (01) □ Yes (02) □ No [□ 98 □ 99]

   (b) If so, do you recall what this research project is/was about? [□ 98 □ 99]

2. We are interested in the extent to which you agree or disagree with the following statements.
   A score of "1" means that you *strongly agree* and a score of "5" means that you *strongly disagree. Make sense?*

	Strongly Agree				**Strongly Disagree**	
(a) In general, I do not mind if research findings are linked to my personal medical records in order to help interpret what they mean	1	2	3	4	5	[□ 98 □ 99]
(b) I do not mind if researchers outside of *PMH/NYGH* have access to my health information or blood sample for their research purposes if I have provided consent	1	2	3	4	5	[□ 98 □ 99]
(c) I would like to be contacted by the researchers or my doctor if medically relevant information is learned through the process of research	1	2	3	4	5	[□ 98 □ 99]
(d) I do not feel entitled to share in any financial gains that may come to the researchers or the institutions involved in this research	1	2	3	4	5	[□ 98 □ 99]

Section D: Script for Interviewer - *Explanation of HCID*

"Now we are going to walk through the Health Care Information Directive tool. It will take a few minutes to explain this tool before we start. (If telephone interview) You will need to follow along with your copy since we are doing this by phone.

First we will look at the YELLOW sheet. The YELLOW sheet is about the various types of personal information you might be willing to share with RESEARCHERS. If you have participated in a research study before, it may help you to keep that study in mind as we go through these questions.
When we are finished with the YELLOW sheet, we will move on to complete the GREEN sheet. The GREEN sheet is about the various types of personal information you might be willing to share with ADMINISTRATORS.

Let's start with the YELLOW sheet. You can see that there are 3 columns, labeled A, B, and C.

- **Column A** refers to *personal information*. This includes your specific genetic test result, your specific mammogram or ultrasound result, your specific family history of breast/ovarian cancer, and your blood sample itself. For the purpose of this column, all of this information would be labeled with your name.
- **Column B** refers to *de-identified information*. This means that your genetic test results, your specific mammogram or ultrasound result, your specific family history of breast/ovarian cancer, and your blood sample itself are labeled with an ID number and not with your name. However, there remains a master sheet that links your name to your number in the event you need to be identified in person for some reason.
- **Column C** refers to *aggregated information*. This means that your genetic test results, your specific mammogram or ultrasound result, your specific family history of breast/ovarian cancer, and your blood sample itself are stripped of any identifying information and grouped with results that belong to other people. There is no way to trace this information back to you individually.
- **So, to summarize, column A refers to information that has your name attached, column B refers to information that has an ID number attached but not your name, and column C refers to information that is grouped and cannot be traced back to you.**

Next, you can see that there is a list of questions along the left hand side of the page. I am going to ask you each of these questions about *each type* of information listed in columns A, B, and C. For example, Question #1 will ask you:
(a) if you would permit researchers to access your genetic test result identified by your name for research related to breast/ovarian cancer
(b) if you would permit researchers to access your mammogram/ultrasound report identified by your name for research related to breast/ovarian cancer
(c) if you would permit researchers to access your family history of breast/ovarian cancer identified by your name for research related to breast/ovarian cancer,
(d) if you would permit researchers to access your blood sample identified by your name for research related to breast/ovarian cancer
...and then we will proceed with Column B in which all of the above types of information would be identified by an ID # instead of your name.

Your answer to each question can be "yes," "no," or "undecided." I will be ticking the boxes in each column as we go on my copy of the tool. It may help you to follow along with a pencil and tick the boxes on your copy as we go as well.

We will go through each type of information in each column for each question. This is a lot of questions and may seem confusing. Do you have any questions before we begin? Does this make sense to you? If you don't have any questions now but have questions once we get started, please stop me and ask. Here we go..."

RESEARCH ***Would you permit researchers to access this information for research related to:***	**A** **Personalized Health Information**				**B** **De-Identified Information** (test results w/o identifiable info but linked to personal information)				**C** **Grouped Information** (test results w/o identifiable info and grouped)			
	Genetic Test Result (a1)	Mammo-gram or ultrasound Report (a2)	Family Hx of br/ov ca (a3)	Blood sample itself (a4)	Genetic Test Result (b1)	Mammo-gram or ultrasound Report (b2)	Family Hx of br/ov ca (b3)	Blood sample itself (b4)	Genetic Test Result (c1	Mammo-gram or ultrasound Report (c2)	Family Hx of br/ov ca (c3)	Blood sample itself (c4)
Q1. Breast/ovarian cancer in general	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q2. The genetics of breast/ovarian cancer in particular	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q3. Conditions other than breast/ovarian cancer (e.g. diabetes)	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q4. Controversial areas (e.g. stem cells, population-specific, mental health)	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q5. Hospital tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q6. Governmental tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

ADMINISTRATIVE ***Would you permit administrative staff and/or to have access to this information…***	**A** **Personalized Health Information**				**B** **De-Identified Information** (test results w/o identifiable info but linked to personal information)				**C** **Grouped Information** (test results w/o identifiable info and grouped)			
	Genetic Test Result (a1)	Mammo-gram or ultrasound Report (a2)	Family Hx of br/ov ca (a3)	Blood sample itself (a4)	Genetic Test Result (b1)	Mammo-gram or ultrasound Report (b2)	Family Hx of br/ov Ca (b3)	Blood sample itself (b4)	Genetic Test Result (c1)	Mammo-gram or ultrasound Report (c2)	Family Hx of br/ov Ca (c3)	Blood sample itself (c4)
Q1. To remind me of follow-up appointments and screening tests	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q2. To organize billing and payment for the services I received	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q3. For hospital tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q4. For government tracking and funding purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?
Q5. For hospital fundraising purposes	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?	☐ Yes ☐ No ☐ ?

Note to interviewer: As you go along ask respondent to comment further on "undecided" items:
**Record responses to these questions in table below.

Undecided Item	Why do you think you are undecided with respect to _____ at this point in time? (e.g. need more info, unsure, wrong timing	What additional information or circumstance would enable you to make a decision with respect to _____ with which you would be more comfortable (e.g. more explanation, prefer to consult with doctor/family member)
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		
☐ Research ☐ Admin Q__ Category A B C		

Section E

We would now like to ask you a few additional questions about the form we just reviewed:

1. If this form were to become a standard part of medical practice, how often would you like to revisit the choices you made?

   (01) ☐ every time this information could be used in research so the exact purpose is clear to me

   (02) ☐ in 6 months (04) ☐ every year (06) ☐ in 5 years

   (03) ☐ in 1 year (05) ☐ in 3 years (07) ☐ no need to revisit

   [☐ 98 ☐ 99]

2. If this form were to become a standard part of medical practice, where would you prefer to complete it?

   - ❑ at the OHIP office when I renew my OHIP card [01]
   - ❑ at my doctor's office (GP___ specialist__ other __) [02.1.2.3]
   - ❑ at home before my medical appointment [03]
   - ❑ on the computer (OHIP office ___ doctor's office ___ home ___) [04.1.2.3]

   [☐ 98 ☐ 99]

3. Assuming only those whom you authorize could access this information about your *cancer/genetic test result*, would you prefer that it be stored in a secure electronic file or a secure paper file?

   (01) ☐ Electronic

   (02) ☐ Paper

   (03) ☐ Doesn't matter

   [☐ 98 ☐ 99]

4. In general, what do you think of this form? (probes: too detailed, good amount of detail, prefer to have say in all of these options, no need to review all of these options, etc)

Section F.

We would now like to ask you a few questions about your beliefs related to privacy in general

1. We are interested in whether you consider yourself to be a private person or not. On a scale from 1-5, where 1 is 'very private' and 5 is 'very open,' how would you rate how private you are? [☐ 98 ☐ 99]

   Very Private *Very Open*

1	2	3	4	5

2. Would you say that the privacy of your medical information is more, less, or of the same importance as the privacy of your: [☐ 98 ☐ 99]

	More Important	Less Important	Same Importance
(a) financial information (e.g. salary, taxes, investments, debt)			

(b) intimate relationships (e.g. relationship status, sexual orientation)			
(c) family life			

Section G.

In this section, we would like to ask you a few questions about your comfort and experience with computers

1. On a scale from 1-5, where 1 is 'very comfortable' and 5 is 'very uncomfortable,' how would you rate your comfort with using computers in general? [☐ 98 ☐ 99]

Very Comfortable **Very Uncomfortable**

1	2	3	4	5

2. On a scale from 1-5, where 1 is 'almost always' and 5 is 'almost never,' how often do you use computers for everyday things like banking, ordering tickets, making airline/hotel reservations etc.? [☐ 98 ☐ 99]

Almost Always **Almost Never**

1	2	3	4	5

****

Section H. Demographics

Finally, to wrap things up, we have a few questions to ask you about yourself

1. In what year were you born? _____ [□ 98 □ 99]

2. *[Interviewer: Is respondent male or female?]*
   (01) □ Male (02) □ Female

3. Which one of the following best describes your ethnic background?
   (01) □ White/Caucasian (04) □ First Nations
   (02) □ Black/African Canadian (05) □ Other: _____
   (03) □ Asian/Pacific Islander [□ 98 □ 99]

4. Which one of the following best describes your relationship status?
   (01) □ Single (05) □ Divorced
   (02) □ Married (06) □ Separated
   (03) □ Partner (07) □ Other: _____
   (04) □ Common Law [□ 98 □ 99]

5. What is the highest grade level that you have completed?
   (01) □ Less than high school (06) □ University degree
   (02) □ Some high school (07) □ Some postgrad training
   (03) □ High school graduate (08) □ Postgrad or prof'l degree
   (04) □ Vocational School/College (09) □ Other: _____
   (05) □ Some University [□ 98 □ 99]

6. Which one of the following best describes your employment status?
   (01) □ Full-time (03) □ Not employed
   (02) □ Part-time (04) □ Retired [□ 98 □ 99]

7. Which best describes your total household income last year before taxes?
   (01) □ Less than $20,000 (04) □ $60,000-$79,000
   (02) □ $20,000-$39,000 (05) □ greater than $80,000
   (03) □ $40,000-$59,000 (06) □ No response [□ 98 □ 99]

8. Do you work in any of the following fields?
   (01) □ Health care (03) □ Law (05) □ No
   (02) □ Computers (04) □ Government [□ 98 □ 99]

9. In general, would you say your health is:

(01) □ Excellent (04) □ Fair

(02) □ Very good (05) □ Poor

(03) □ Good (06) □ Don't know

[□ 98 □ 99]

****

"We have completed the interview. Do you have any questions at this point? Do you have any additional comments or perspectives on this topic that you would like to share?"

Comments/Additional Notes:

'I'd like to thank you again for your time. We really appreciate your input."

Appendix 1.8: Study Question-Variable-Instrument Link

*How do **individuals who have pursued genetic testing** define the **conditions** under which they are willing to authorize the use of their **personal health information (PHI)** for administrative and research purposes?*

Portion of Study Question	Variable of Interest	Interview Guide Item(s)
INDIVIDUALS WHO HAVE PURSUED GENETIC TESTING	Condition	p.1 Section A Sampling Characteristic 1
	Genotype	p.1 Section A Sampling Characteristic 2
	Phenotype	p.1 Section A Sampling Characteristic 3
	Context Factors	p.2,7-9 Sections B, C, E, F, G, H
CONDITIONS	Research purpose	p.4 Section D Research Q1-Q6
	Administrative purpose	p.5 Section D Administrative Q1-Q5
	Anonymization level A - personalized	p.4-5 Section D Column A
	Anonymization level B – coded	p.4-5 Section D Column B
	Anonymization level C - aggregated	p.4-5 Section D Column C
PERSONAL HEALTH INFORMATION	Type 1 - Genetic Test Result	p.4-5 Section D Columns A1,B1,C1
	Type 2 – Non-genetic Test Result	p.4-5 Section D Columns A2,B2,C2
	Type 3 – Family History	p.4-5 Section D Columns A3,B3,C3
	Type 4 – Information gleaned from Blood Sample	p.4-5 Section D Columns A4,B4,C4

Appendix 1.9 – Sample Participant Thank You Letter

Address

Date

Dear

On behalf of our research team at Sunnybrook and Women's Health Sciences Centre and The University of Toronto, I am writing to thank you for your participation in the research study about the *Health Care Information Directive.* As promised, please find enclosed a copy of the consent form that you signed for your records.

We are in the process of compiling data collected from a number of teaching hospitals in the Toronto area and hope to be able to use these data to inform privacy and informed consent policy in Ontario.

We are truly grateful for the time and insight you dedicated to this project.

Should you have any questions about this research, please do not hesitate to contact me at anytime (416 480-6100*7194).

Thanks again.

Sincerely,

Robin Hayeems, MSc, ScM
Doctoral Student, University of Toronto
Primary Care Research Unit, Sunnybrook and Women's College Health Sciences Centre

Encl (1)

Appendix 1.10 – STATISTICAL CODES

This program performs summary statistics and analysis for 'CONDITION.' Analogous programs were run for 'GENOTYPE' and 'PHENOTYPE.'

```
*libname from 'libname path';
libname from 'C:\Documents and Settings\rahim\My Documents\Rahim\Robin Hyeems\June 06';

data dat; set from.datajune15; run;
proc format ;
value yesnof 1='Yes'
        2='No ';
value conditnf /* Condition */
    1 = 'Thrombophilia'
    2 = 'Hemochromatosis'
    3 = 'HNPCC'
    4 = 'HBOC'
    98 = 'N/A'
    99 = 'missing' ;
value genotypef /* Genotype */
    1 = 'Genotype +ve'
    2 = 'Genotype True -ve'
    98 = 'N/A'
    99 = 'missing' ;
value phenotypf /* Phenotype */
    1 = 'Phenotype +ve'
    2 = 'Phenotype -ve'
    98 = 'N/A'
    99 = 'missing' ;
value fA /* Is respondent male or female? */
    1 = 'male'
    2 = 'female'
    99 = 'missing' ;
run;

* table 2B;
data temp; set dat;
  if a1 in(98 99) then a1=.;
  aa=2006-a1;
  label aa='Years since clinical diagnosis';
  if a2 in (99) then a2=.;
  aa2=2006-a2;
  label aa2='Years since genetic test results received';

  label d1='Self-reported privacy level (Likert 1-5)';
  label e1='General comfort with computers (Likert 1-5)';
  label e2='Everyday use of computers (Likert 1-5)';
run;
title'Years since clinical diagnosis';
proc freq data=temp; tables aa; run;
proc means data=temp; var aa; run;


title'Years since genetic test results received';
proc freq data=temp; tables aa2; run;
proc means data=temp; var aa2; run;

proc freq data=temp; tables d1 e1 e2; run;
proc means data=temp; var d1 e1 e2; run;

data temp ; set dat;
```

```
if f1 in(98 99) then f1=.;
if f2 in(98 99) then f2=.;
if f3 in(98 99) then f3=.;
if f4 in(98 99) then f4=.;
if f5 in(98 99) then f5=.;
if f6 in(98 99) then f6=.;
if f7 in(98 99) then f7=.;
run;
proc freq data=temp ;
  tables f3-f7 ;
run;


data dat1; set dat;
access_for='Research          ';
question = 'Q 1';
group = 'Personalized         ';
subgroup='Genetic test results '; response = r1_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = r1_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = r1_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_c4;abc='Blood sample itself  ';output;

question = 'Q 2';
group = 'Personalized         ';
subgroup='Genetic test results '; response = r2_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r2_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = r2_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r2_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = r2_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r2_c4;abc='Blood sample itself  ';output;

question = 'Q 3';
group = 'Personalized         ';
subgroup='Genetic test results '; response = r3_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r3_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r3_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = r3_b1;abc='genetic test results ';output;
```

```
subgroup='Mammogram/ultrasound '; response = r3_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r3_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r3_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r3_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r3_c4;abc='Blood sample itself ';output;

question = 'Q 4';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r4_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r4_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r4_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_c4;abc='Blood sample itself ';output;

question = 'Q 5';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r5_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r5_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r5_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r5_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r5_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r5_c4;abc='Blood sample itself ';output;

question = 'Q 6';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r6_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r6_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r6_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r6_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
```

```
subgroup='Genetic test results '; response = r6_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r6_c4;abc='Blood sample itself  ';output;

access_for='Administrative    ';
question = 'Q 1';
group = 'Personalized         ';
subgroup='Genetic test results '; response = adm1_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm1_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm1_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_c4;abc='Blood sample itself  ';output;

question = 'Q 2';
group = 'Personalized         ';
subgroup='Genetic test results '; response = adm2_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm2_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm2_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm2_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm2_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm2_c4;abc='Blood sample itself  ';output;

question = 'Q 3';
group = 'Personalized         ';
subgroup='Genetic test results '; response = adm3_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm3_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm3_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm3_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm3_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm3_c4;abc='Blood sample itself  ';output;
```

```
question = 'Q 4';
group = 'Personalized        ';
subgroup='Genetic test results '; response = adm4_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm4_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = adm4_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm4_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = adm4_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm4_c4;abc='Blood sample itself  ';output;

question = 'Q 5';
group = 'Personalized        ';
subgroup='Genetic test results '; response = adm5_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm5_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm5_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = adm5_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm5_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm5_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = adm5_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm5_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm5_c4;abc='Blood sample itself  ';output;
run;
data dat2 ; set dat1;
if response in (3 11 98 99) then response = .;
age = 2006-f1;
if age le 0 then age=.;
if f5 in(1 2 3)          then educ='high school graduate or less';
else if f5 in(4 5 6 7 8 9) then educ='higher than high school    ';
else educ='';
if f7 in(1 2)       then income='#39,000 or less';
else if f7 in(3 4 50) then income='$40,000 or more';
else income='';
if a2 in(98 99) then year_genetic_test_result=.;
else year_genetic_test_result=2006-a2;
if year_genetic_test_result lt 0 then year_genetic_test_result=.;
if conditn in(1 4);
sex=f2;
if sex = 99 then sex = .;
run;

data adj ; set dat2; run;
data p;
 conditn=1;
 predict='yes';
 access_for ='Administrative'; group = 'De-Identified Info ';
```

```
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Administrative'; group = 'Grouped Information';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Administrative'; group = 'Personalized ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Research '; group = 'De-Identified Info ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;

access_for ='Research '; group = 'Grouped Information';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;

access_for ='Research '; group = 'Personalized ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;
run;

data p1;
conditn=4;
predict='yes';
access_for ='Administrative'; group = 'De-Identified Info ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Administrative'; group = 'Grouped Information';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Administrative'; group = 'Personalized ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output;

access_for ='Research '; group = 'De-Identified Info ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;

access_for ='Research '; group = 'Grouped Information';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;

access_for ='Research '; group = 'Personalized ';
question = 'Q 1'; output; question = 'Q 2'; output; question = 'Q 3'; output;
question = 'Q 4'; output; question = 'Q 5'; output; question = 'Q 6'; output;
run;

data unadj; set dat2 p p1 ; run;

title'Unadjusted ORs for CONDITION';
proc sort data=unadj; by access_for question group ; run;
proc logistic data=unadj desc;
  class conditn;
  by access_for question group ;
  model response = conditn /CLODDS=PL;
  ods output OddsRatios=or;
  output out=out p=pred l=l95 u=u95;
```

```
 format response yesnof. conditn conditnf.;
run;

data out1 ; set out ; if response = . ; if predict='yes';
keep access_for question group response pred predict conditn l95 u95;
run;

data t1; set out1; if conditn = 1 ;
if group = 'Personalized      ';
personalized=pred;
run;
data t2 ; set out1; if conditn = 1 ;
if group = 'Grouped Information';
information = pred;
run;
data t3 ; set out1; if conditn = 1;
if group = 'De-Identified Info ';
identified = pred;
run;
data t ; merge t1 t2 t3; by access_for ; run;
data t1; set out1; if conditn = 4 ;
if group = 'Personalized      ';
personalized=pred;
run;
data t2 ; set out1; if conditn = 4 ;
if group = 'Grouped Information';
information = pred;
run;
data t3 ; set out1; if conditn = 4;
if group = 'De-Identified Info ';
identified = pred;
run;
data tt; merge t1 t2 t3; by access_for ; run;

data ttt ; set t tt;
if conditn=1 then g='Thrombophilia';
if conditn=4 then g='HBOC        ';
drop conditn;
run;
data ttt; set ttt; conditn=g; drop g; run;
proc sort data=ttt; by access_for question; run;

title;
symbol1 i=j v=star c=black height=2. width=2;
symbol2 i=j v=square c=black height=2. width=2;
symbol3 i=j v=circle c=black height=2. width=2;
legend value=star 'personalized' value=square 'information' value=circle 'identified' ;
axis2 label=(A=90'Unadjusted rate of yes') order=(0 to 1 by 0.1);
axis1 label=('Conditon') order=('Thrombophilia' 'HBOC') offset=(15,15);
proc gplot data=ttt ; by access_for question;
plot (personalized information identified)*conditn/
    overlay haxis=axis1 vaxis=axis2 legend=legend1;
run;
quit;

data out1; set out1;
if access_for='Administrative' and question = 'Q 1' then line='A Q 1';
if access_for='Administrative' and question = 'Q 2' then line='A Q 2';
if access_for='Administrative' and question = 'Q 3' then line='A Q 3';
if access_for='Administrative' and question = 'Q 4' then line='A Q 4';
if access_for='Administrative' and question = 'Q 5' then line='A Q 5';
if access_for='Research' and question = 'Q 1' then line='R Q 1';
```

```
if access_for='Research' and question = 'Q 2' then line='R Q 2';
if access_for='Research' and question = 'Q 3' then line='R Q 3';
if access_for='Research' and question = 'Q 4' then line='R Q 4';
if access_for='Research' and question = 'Q 5' then line='R Q 5';
if access_for='Research' and question = 'Q 6' then line='R Q 6';
if conditn = 1 then condition = 'Thrombophilia';
if conditn = 4 then condition = 'HBOC        ';
drop conditn;
run;

proc sort data=out1; by group line; run;
symbol1 i=j v=circle  c=black line=1 width=2 height=1;
symbol2 i=j v=circle  c=blue  line=1 width=2 height=1;
symbol3 i=j v=circle  c=green line=1 width=2 height=1;
symbol4 i=j v=circle  c=red   line=1 width=2 height=1;
symbol5 i=j v=circle  c=purple  line=1 width=2 height=1;

symbol6 i=j v=square  c=black line=2 width=2 height=1;
symbol7 i=j v=square  c=blue  line=2 width=2 height=1;
symbol8 i=j v=square  c=green line=2 width=2 height=1;
symbol9 i=j v=square  c=red   line=2 width=2 height=1;
symbol10 i=j v=square c=purple line=2 width=2 height=1;
symbol11 i=j v=square c=black line=33 width=2 height=1;
title;
axis2 label=(A=90'Unadjusted rate of yes') order=(0.2 to 1 by 0.1);
axis1 label=('Conditon') order=('Thrombophilia' 'HBOC') offset=(15,15);
proc gplot data=out1 ; by group;
plot pred*condition=line/
    haxis=axis1 vaxis=axis2 ;
run;
quit;

****************************** adjusted;
proc sort data=adj; by access_for question group ; run;
proc means data=adj mean; var age; run;

proc genmod data=adj desc;
by access_for question group ;
class conditn id educ sex /* d1 income*/;
model response = conditn age educ sex d1 /*b2_a b2_b b2_c b2_d income a2*/
            /*year_genetic_test_result*/ /d=b link=logit scale=p;
repeated subject=id / type=exch modelse;
estimate 'HBOC        ' intercept 1 conditn 1 0 age 53/;
estimate 'Thrombophilia' intercept 1 conditn 0 1 age 53/;
ods output GEEModPEst=ods2;
ods output Estimates=e;
*ods output ConvergenceStatus=con2;
format response yesnof. conditn conditnf. sex fa. ;
run;
data e ; set e ;
pred=exp(estimate)/(1+exp(estimate));
l95=exp(lowercl)/(1+exp(lowercl));
u95=exp(uppercl)/(1+exp(uppercl));
run;

data t1; set e; if label='HBOC';
if group = 'Personalized      ';
personalized=pred;
run;
data t2 ; set e; if label='HBOC' ;
if group = 'Grouped Information';
information = pred;
```

```
run;
data t3 ; set e; if label='HBOC';
if group = 'De-Identified Info ';
identified = pred;
run;
data t ; merge t1 t2 t3; by access_for ; run;
data t1; set e; if label='Thrombophilia' ;
if group = 'Personalized      ';
personalized=pred;
run;
data t2 ; set e; if label='Thrombophilia' ;
if group = 'Grouped Information';
information = pred;
run;
data t3 ; set e; if label='Thrombophilia';
if group = 'De-Identified Info ';
identified = pred;
run;
data tt; merge t1 t2 t3; by access_for ; run;

data ttt ; set t tt; run;
proc sort data=ttt; by access_for question; run;

title;
symbol1 i=j v=star c=black height=2. width=2;
symbol2 i=j v=square c=black height=2. width=2;
symbol3 i=j v=circle c=black height=2. width=2;
legend1 value=star 'personalized' value=square 'information' value=circle 'identified' ;
axis2 label=(A=90'Adjusted rate of yes') order=(0 to 1 by 0.1);
axis1 label=('Condition') order=('HBOC' 'Thrombophilia') offset=(15,15);
footnote  'Adjusted for age, sex, education, and privacy';
proc gplot data=ttt ; by access_for question;
plot (personalized information identified)*label/
    overlay haxis=axis1 vaxis=axis2 legend=legend1;
run;
quit;

data e1; set e;
if access_for='Administrative' and question = 'Q 1' then line='A Q 1';
if access_for='Administrative' and question = 'Q 2' then line='A Q 2';
if access_for='Administrative' and question = 'Q 3' then line='A Q 3';
if access_for='Administrative' and question = 'Q 4' then line='A Q 4';
if access_for='Administrative' and question = 'Q 5' then line='A Q 5';
if access_for='Research' and question = 'Q 1' then line='R Q 1';
if access_for='Research' and question = 'Q 2' then line='R Q 2';
if access_for='Research' and question = 'Q 3' then line='R Q 3';
if access_for='Research' and question = 'Q 4' then line='R Q 4';
if access_for='Research' and question = 'Q 5' then line='R Q 5';
if access_for='Research' and question = 'Q 6' then line='R Q 6';
run;

proc sort data=e1; by group line; run;
symbol1 i=j v=circle  c=black line=1 width=2 height=1;
symbol2 i=j v=circle  c=blue  line=1 width=2 height=1;
symbol3 i=j v=circle  c=green line=1 width=2 height=1;
symbol4 i=j v=circle  c=red   line=1 width=2 height=1;
symbol5 i=j v=circle  c=purple  line=1 width=2 height=1;

symbol6 i=j v=square  c=black line=2 width=2 height=1;
symbol7 i=j v=square  c=blue  line=2 width=2 height=1;
symbol8 i=j v=square  c=green line=2 width=2 height=1;
symbol9 i=j v=square  c=red   line=2 width=2 height=1;
```

```
symbol10 i=j v=square c=purple line=2 width=2 height=1;
symbol11 i=j v=square c=black line=33 width=2 height=1;
title;
axis2 label=(A=90'Adjusted rate of yes') order=(0.2 to 1 by 0.1);
axis1 label=('Conditon') order=('Thrombophilia' 'HBOC') offset=(15,15);
proc gplot data=e1 ; by group;
plot pred*label=line/
    haxis=axis1 vaxis=axis2 ;
run;
quit;

data out1(drop=response predict); set out1;
unadj_probability=pred;
unadj_lowercl=l95;
unadj_uppercl=u95;
label=condition;
drop pred condition l95 u95;
run;

data e1; set e1;
adj_probability = pred;
adj_lowercl=l95;
adj_uppercl=u95;
drop estimate stderr alpha lowercl uppercl chisq probchisq pred l95 u95;
run;
proc sort data=out1; by access_for question group label; run;
proc sort data=e1; by access_for question group label; run;
data cond; merge out1 e1; by access_for question group label; run;
```

APPENDIX 1.10 - STATISTICAL CODES CONT'D.

This program performs analysis for PREDICTIVE MODELS

```
libname from 'C:\Documents and Settings\moineddinr.SMHPC9223\My Documents\Rahim\Robin Hyeems\June 06';
*%inc 'C:\Documents and Settings\moineddinr.SMHPC9223\My Documents\Rahim\Robin Hyeems\data_march25.sas';
data dat; set from.datajune15; run;
proc format ;
value yesnof 1='Yes'
        2='No ';
value conditnf /* Condition */
    1 = 'Thrombophilia'
    2 = 'Hemochromatosis'
    3 = 'HNPCC'
    4 = 'HBOC'
    98 = 'N/A'
    99 = 'missing' ;
value genotypef /* Genotype */
    1 = 'Genotype +ve'
    2 = 'Genotype -ve'
    98 = 'N/A'
    99 = 'missing' ;
value phenotypf /* Phenotype */
    1 = 'Phenotype +ve'
    2 = 'Phenotype -ve'
    98 = 'N/A'
    99 = 'missing' ;
value fA /* Is respondent male or female? */
    1 = 'male'
    2 = 'female'
    99 = 'missing' ;
value agef 2='<50 '
       1='>/-50 ';
value educf 1='> high school'
        2='</- high school';
run;


data dat1; set dat;
access_for='Research        ';
question = 'Q 1';
group = 'Personalized       ';
subgroup='Genetic test results '; response = r1_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r1_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r1_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r1_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r1_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r1_c4;abc='Blood sample itself  ';output;

question = 'Q 2';
group = 'Personalized       ';
```

```
subgroup='Genetic test results '; response = r2_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r2_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r2_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r2_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r2_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r2_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r2_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r2_c4;abc='Blood sample itself ';output;

question = 'Q 3';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r3_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r3_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r3_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r3_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r3_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r3_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r3_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r3_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r3_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r3_c4;abc='Blood sample itself ';output;

question = 'Q 4';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r4_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = r4_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = r4_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r4_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r4_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r4_c4;abc='Blood sample itself ';output;

question = 'Q 5';
group = 'Personalized        ';
subgroup='Genetic test results '; response = r5_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = r5_a4;abc='Blood sample itself ';output;
```

```
group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = r5_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r5_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = r5_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r5_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r5_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r5_c4;abc='Blood sample itself  ';output;

question = 'Q 6';
group = 'Personalized          ';
subgroup='Genetic test results '; response = r6_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r6_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = r6_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r6_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = r6_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = r6_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = r6_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = r6_c4;abc='Blood sample itself  ';output;

access_for='Administrative     ';
question = 'Q 1';
group = 'Personalized          ';
subgroup='Genetic test results '; response = adm1_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = adm1_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_b4;abc='Blood sample itself  ';output;

group = 'Grouped Information   ';
subgroup='Genetic test results '; response = adm1_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm1_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm1_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm1_c4;abc='Blood sample itself  ';output;

question = 'Q 2';
group = 'Personalized          ';
subgroup='Genetic test results '; response = adm2_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself  '; response = adm2_a4;abc='Blood sample itself  ';output;

group = 'De-Identified Info    ';
subgroup='Genetic test results '; response = adm2_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_b3;abc='Family Hx of br/ov ca';output;
```

```
subgroup='Blood sample itself '; response = adm2_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm2_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm2_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm2_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm2_c4;abc='Blood sample itself ';output;

question = 'Q 3';
group = 'Personalized       ';
subgroup='Genetic test results '; response = adm3_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm3_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm3_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm3_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm3_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm3_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm3_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm3_c4;abc='Blood sample itself ';output;

question = 'Q 4';
group = 'Personalized       ';
subgroup='Genetic test results '; response = adm4_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm4_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm4_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm4_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm4_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm4_c2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm4_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm4_c4;abc='Blood sample itself ';output;

question = 'Q 5';
group = 'Personalized       ';
subgroup='Genetic test results '; response = adm5_a1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_a2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm5_a3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm5_a4;abc='Blood sample itself ';output;

group = 'De-Identified Info   ';
subgroup='Genetic test results '; response = adm5_b1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_b2;abc='Mammogram or UultraS ';output;
subgroup='Family Hx of br/ov ca'; response = adm5_b3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm5_b4;abc='Blood sample itself ';output;

group = 'Grouped Information  ';
subgroup='Genetic test results '; response = adm5_c1;abc='genetic test results ';output;
subgroup='Mammogram/ultrasound '; response = adm5_c2;abc='Mammogram or UultraS ';output;
```

```
subgroup='Family Hx of br/ov ca'; response = adm5_c3;abc='Family Hx of br/ov ca';output;
subgroup='Blood sample itself '; response = adm5_c4;abc='Blood sample itself ';output;
run;

data dat2 ; set dat1;
if response in (3 11 98 99) then response = .;
age = 2006-f1;
if age le 0 then age=.;
if age ge 50 then age_cat=1;
else if age lt 50 then age_cat=2;
if age=. then age_cat=.;
if f5 in(1 2 3)          then educ=2;
else if f5 in(4 5 6 7 8 9) then educ=1;
else educ='';
if f7 in(1 2)       then income='#39,000 or less';
else if f7 in(3 4 50) then income='$40,000 or more';
else income='';
if a2 in(98 99) then year_genetic_test_result=.;
else year_genetic_test_result=2006-a2;
if year_genetic_test_result lt 0 then year_genetic_test_result=.;
if conditn in(1 4);
sex=f2;
if sex = 99 then sex = .;
run;


data dat2; set dat2 ;
keep access_for question group conditn sex genotype phenotyp age_cat
   educ d1 response subgroup id;
run;

data dat3; set dat2; if conditn = 4 then conditn=2; run;

%macro p(lab=,conditn=, sex=, genotype=, phenotyp=, age_cat=, educ=, d1=, out= );
data &out; run;
proc genmod data=dat3 desc;
class conditn genotype phenotyp id educ sex age_cat;
model response = conditn genotype phenotyp age_cat educ sex d1
            /d=b link=logit ;
repeated subject=id / type=exch modelse;
format response yesnof. ;
estimate "lab" intercept 1 /*conditn &conditn sex &sex*/
          genotype &genotype /*phenotyp &phenotyp
          age_cat &age_cat educ &educ*/ d1 &d1;
ods output Estimates=&out;
run;
%mend;

%p(genotype=1 0, d1=1  ,out=p);
%p(genotype=1 0, d1=2  ,out=o);
data p; set p o ; run;
%p(genotype=1 0, d1=3  ,out=o);
data p; set p o ; run;
%p(genotype=1 0, d1=4  ,out=o);
data p; set p o ; run;
%p(genotype=1 0, d1=5  ,out=o);
data p; set p o ; run;

%p(genotype=0 1, d1=1  ,out=o);
data p; set p o ; run;
%p(genotype=0 1, d1=2  ,out=o);
data p; set p o ; run;
```

```
%p(genotype=0 1, d1=3  ,out=o);
data p; set p o ; run;
%p(genotype=0 1, d1=4  ,out=o);
data p; set p o ; run;
%p(genotype=0 1, d1=5  ,out=o);
data p; set p o ; run;

data p1; set p;
  p=exp(estimate)/(1+exp(estimate));
  lowercl=exp(lowercl)/(1+exp(lowercl));
  uppercl=exp(uppercl)/(1+exp(uppercl));
run;
proc print data=p1 noobs;var p lowercl uppercl; run;
```

Appendix 1.11(a): REB Approval Letter – University of Toronto

UNIVERSITY OF TORONTO
Office of the Vice-President, Research and Associate Provost
Ethics Review Office

PROTOCOL REFERENCE #13046 December 9, 2004

Dr. R. Upshur
Sunnybrook & Women's College HSC
2075 Bayview Ave.
Toronto, ON M4N 3M5

Ms. R. Hayeems
134 Ava Rd.
Toronto, ON M6C 1W1

Dear Dr. Uphsur & Ms. Hayeems:

Re: Protocol entitled, "The Collection, Use and Disclosure of Personal Health Information: The Healthcare Information Directive Applied to Genetics" by Dr. R. Upshur (supervisor), Ms. R. Hayeems (PhD candidate)

ETHICS APPROVAL **Original Approval Date: December 9, 2004**
Expiry Date: December 8, 2005

We are writing to advise you that a member of the Health Sciences I Research Ethics Board has granted approval to the above-named research study, for a period of **one year**, under the Board's expedited review process. Ongoing projects must be renewed prior to the expiry date.

The following documents (received Nov. 30, 2004) have been approved for use in this study: Invitation Letter to Patients, Invitation Letter to Providers, Patients Survey/Interview, Providers' Survey/Interview, Patients Consent Form, and Providers Consent Form. Participants should receive a copy of their consent form. We acknowledge receipt of the UHN, SWCHSC and NYGH REB approval letters for this study; please provide our Office with copies of annual renewals as soon as they become available. Please provide our Office with a copy of the MSH REB approval letter as soon as it becomes available.

During the course of the research, any significant deviations from the approved protocol **(that is, any deviation which would lead to an increase in risk or a decrease in benefit to participants)** and/or any unanticipated developments within the research should be brought to the attention of the Ethics Review Unit.

Best wishes for the successful completion of your project.

Yours sincerely,

Marianna Richardson

Marianna Richardson
Ethics Review Coordinator

xc: Dr. N. Kreiger, Chair Health Sciences I Research Ethics Board
Prof. K. Dominick, Graduate Coordinator, Public Health Sciences

Simcoe Hall 27 King's College Circle Toronto Ontario M5S 1A1
Telephone 416/ 978-3165 Fax 416/ 946-5763 email: ethics.review@utoronto.ca

Appendix 1.11(b): REB Approval Letter – North York General Hospital

OFFICE OF THE
RESEARCH ETHICS BOARD

Tel: 416-756-6828
Fax: 416-756-6822
E-mail: daddeo@nygh.on.ca

NORTH YORK GENERAL HOSPITAL
Including the IODE Children's Centre

September 29, 2004

Robin Hayeems, MSc, ScM
Genetic Counsellor
Adult Genetics Program
University Health Network
200 Elizabeth St, 3ES 401B
Toronto ON M5G 2C4

Dear Ms. Hayeems:

Re: The Collection, use, and disclosure of personal health information: The Health Care Information Directive applied to genetics

The above-named protocol and the consent form were reviewed at a meeting of the North York Research Ethics Board on June 22, 2004. The Board requested that the following changes:

- The consent form must reflect North York General Hospital information
- Study sites must be outlined

The above changes were submitted to the REB and reviewed on September 29, 2004. A quorum was maintained. Full board approval has been granted for one year.

If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives annual re-approval. The REB must also be notified of the completion or termination of this study and a final report provided.

If, during the course of the research, there are any serious adverse events, changes in the approved protocol or consent form, or any new information that must be considered with respect to the study, these should be brought to the immediate attention of the Board. As the Principal Investigator, you are responsible for the ethical conduct of this study.

The REB of NYGH functions under the guidance of the Tri-Council Policy Statement and the ICH/GCP Guidelines.

Sincerely,

Anne Summers MD, BSc, FRCPC, FCCMG
Chief and Medical Director, Genetics Program
Chair, NYGH Research Ethics Board

September 28, 2004
Date of Approval

September 28, 2005
Expiry Date

AS:da

Appendix 1.11(c): REB Approval Letter – Sunnybrook Health Science Centre

MEMORANDUM

SUNNYBROOK & WOMEN'S
Sunnybrook and Women's College Health Sciences Centre

To: Dr. R. Upshur
Primary Care Reaserch Unit
Room E349b

From: Philip Hébert MD

Date: September 29, 2004

Subject: **The Collection, Use and Discovery of Personal Health Information: The Health Care Information Directive Applied to Genetics**

Research Ethics Board
Sunnybrook Campus

The Research Building
2075 Bayview Avenue,
Room ST 33,
Toronto, ON,
Canada M4N 3M5
Tel 416.480.4276
Fax 416.480.5814

The Research Ethics Board of Sunnybrook and Women's College Health Sciences Centre operates in compliance with the Tri-Council Policy Statement, the ICH/GCP Guidelines and Division 5 of the Food and Drug Regulations.

Project Identification Number: 198-2004
Approval Date: September 29, 2004

The Research Ethics Board of Sunnybrook & Women's College Health Sciences Centre has conducted an expedited review of the research protocol referenced above on the above captioned date and approved the involvement of human subjects as specified in the protocol and the Information sheet/consent form. Please have this printed with the Sunnybrook and Women's logo at the top.

The quorum for approval did not involve any member associated with this project.

Should your study continue for more than one year you must request a renewal on or before one year from the approval date. Please advise the Board of the progress of your research annually and/or any adverse reactions or deviations which may occur in the future.

The above Project Identification Number has been assigned to your project Please use this number on all future correspondence.

Philip Hébert, MD PhD FCFPC
Chair, Research Ethics Board
/mp

Appendix 1.11(d): REB Approval Letter – Mount Sinai Hospital

Research Ethics Board

600 University Avenue, Room 1003B
Toronto, Ontario, Canada, M5G 1X5
t: (416) 586-4875 f: (416) 586-4715
www.mtsinai.on.ca

June 24, 2004

Dr. Katherine Siminovitch
Department of Medicine
Mount Sinai Hospital
Room 656A
600 University Avenue
Toronto, Ontario

Dear Dr. Siminovitch:

RE: MSH REB # 04-0055-E
The Collection, Use, and Disclosure of Personal Health Information: The Health Care Information Directive applied to Genetics

The above named protocol, Patient Consent Form (dated 13 May, 2004), the Provider Consent Form (dated 13 May, 2004) and all Invitation Letters, Survey and Interview Guides received on 25 February, 2004 have received expedited review by the Mount Sinai Hospital Research Ethics Board. The proposal is approved for the next 12 months. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The REB should be notified of the termination of this study and a final report provided.

If, during the course of the research, there are any serious adverse events, changes in the approved protocol or consent form or any new information that must be considered with respect to the study, these should be brought to the immediate attention of the Board. As the Principal Investigator, you are responsible for the ethical conduct of this study.

Sincerely,

Ronald Heslegrave, Ph.D.
Chair, Mount Sinai Hospital Research Ethics Board

24 June, 2004
Date of Initial REB Approval

24 June, 2005
Expiry Date of REB Approval

Appendix 1.11(e): REB Approval Letter – University Health Network

University Health Network
Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

University Health Network Research Ethics Board
700 University Avenue
8th Floor South Room 8-18
Toronto, Ontario, M5G 1Z5
Phone: 416-946-4438
Fax: 416-595-9164

May 13, 2004

Ms. Robin Hayeems / Dr. Katherine Siminovitch
ES 3-401C
TGH

Dear Ms. Hayeems:

RE: UHN REB # 04-0115-AE
The Collection, Use, and Disclosure of Personal Health Information: The Health Care Information Directive Applied to Genetics

The above named submission has received expedited review by the University Health Network Research Ethics Board. Any concerns and revisions requested have been addressed to the satisfaction of the REB. The Protocol (received February 24, 2004), the Patient Consent Form (dated May 13, 2004), the Provider Consent Form (dated May 13, 2004), the Invitation Letter to Patients, the Invitation Letter to Providers, the Electronic Survey for Providers, the Interview Guide for Providers, the Thrombophilia Interview Questions, the Hemochromatosis Interview Questions, the Hereditary Breast/Ovarian Cancer Interview Questions and the Questions to follow completion of HCID (all received February 24, 2004) are approved for the next 12 months. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The REB must also be notified of the termination of this study and a final report provided.

If, during the course of the research, there are any serious adverse events, changes in the approved protocol or consent form or any new information that must be considered with respect to the study, these should be brought to the immediate attention of the Board. As the Principal Investigator, you are responsible for the ethical conduct of this study.

Sincerely,

Ronald Heslegrave, Ph.D.
Chair, University Health Network Research Ethics Board

13 May, 2004
Date of Initial REB Approval

13 May, 2005
Expiry Date of REB Approval

The University Health Network REB operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines and REB requirements as defined in Canada's Food and Drug Regulations, Division 5.

Appendix 2.1 Effect of Anonymization Level (Research Purposes 1-6)

Purpose	Question	Comparison	OR	95% L CI	95% U CI	P value
R	1	a hboc vs b hboc	0.6480	0.5417	0.7753	0.0000
		a hboc vs c hboc	0.5738	0.4713	0.6986	0.0000
		b hboc vs c hboc	0.8855	0.8155	0.9615	0.0038
		a Thro vs b Thro	0.5216	0.3423	0.7949	0.0025
		a Thro vs c Thro	0.4738	0.3043	0.7376	0.0009
		b Thro vs c Thro	0.9084	0.7557	1.0919	0.3060
R	2	a hboc vs b hboc	0.6769	0.5717	0.8014	0.0000
		a hboc vs c hboc	0.5980	0.4960	0.7208	0.0000
		b hboc vs c hboc	0.8834	0.8144	0.9582	0.0028
		a Thro vs b Thro	0.6003	0.4231	0.8517	0.0042
		a Thro vs c Thro	0.5497	0.3787	0.7980	0.0017
		b Thro vs c Thro	0.9157	0.7661	1.0946	0.3334
R	3	a hboc vs b hboc	0.6125	0.5031	0.7456	0.0000
		a hboc vs c hboc	0.5400	0.4368	0.6676	0.0000
		b hboc vs c hboc	0.8817	0.8119	0.9576	0.0028
		a Thro vs b Thro	0.4509	0.2697	0.7540	0.0024
		a Thro vs c Thro	0.3615	0.2082	0.6277	0.0003
		b Thro vs c Thro	0.8016	0.6242	1.0295	0.0833
R	4	a hboc vs b hboc	0.6330	0.5220	0.7676	0.0000
		a hboc vs c hboc	0.5389	0.4351	0.6675	0.0000
		b hboc vs c hboc	0.8514	0.7740	0.9365	0.0009
		a Thro vs b Thro	0.4651	0.2828	0.7650	0.0026
		a Thro vs c Thro	0.3973	0.2339	0.6748	0.0006
		b Thro vs c Thro	0.8542	0.6819	1.0699	0.1702
R	5	a hboc vs b hboc	0.6309	0.5187	0.7674	0.0000
		a hboc vs c hboc	0.5326	0.4276	0.6635	0.0000
		b hboc vs c hboc	0.8442	0.7633	0.9337	0.0010
		a Thro vs b Thro	0.4934	0.2919	0.8338	0.0083
		a Thro vs c Thro	0.3104	0.1682	0.5727	0.0002
		b Thro vs c Thro	0.6291	0.4464	0.8866	0.0081
R	6	a hboc vs b hboc	0.5643	0.4454	0.7151	0.0000
		a hboc vs c hboc	0.4463	0.3417	0.5830	0.0000
		b hboc vs c hboc	0.7909	0.6991	0.8947	0.0002
		a Thro vs b Thro	0.4927	0.2802	0.8663	0.0140
		a Thro vs c Thro	0.2816	0.1436	0.5525	0.0002
		b Thro vs c Thro	0.5716	0.3807	0.8582	0.0070

Appendix2.1AnonymizationlevelR1-6 ***(continued on next page)***

Appendix 2.1 Effect of Anonymization Level (Research Purposes 1-6) *(continued)*

Purpose	Question	Comparison	OR	95% L CI	95% U CI	P value
R	1	a Genotype +ve vs b Genotype +ve	0.5996	0.4965	0.7241	0.0000
		a Genotype +ve vs c Genotype +ve	0.5345	0.4368	0.6540	0.0000
		b Genotype +ve vs c Genotype +ve	0.8915	0.8208	0.9682	0.0064
		a Genotype -ve vs b Genotype -ve	0.7369	0.5826	0.9321	0.0109
		a Genotype -ve vs c Genotype -ve	0.6796	0.5239	0.8815	0.0036
		b Genotype -ve vs c Genotype -ve	0.9223	0.8245	1.0316	0.1567
R	2	a Genotype +ve vs b Genotype +ve	0.6386	0.5375	0.7587	0.0000
		a Genotype +ve vs c Genotype +ve	0.5693	0.4728	0.6856	0.0000
		b Genotype +ve vs c Genotype +ve	0.8915	0.8224	0.9664	0.0053
		a Genotype -ve vs b Genotype -ve	0.7679	0.6168	0.9559	0.0181
		a Genotype -ve vs c Genotype -ve	0.7082	0.5532	0.9065	0.0062
		b Genotype -ve vs c Genotype -ve	0.9222	0.8245	1.0316	0.1567
R	3	a Genotype +ve vs b Genotype +ve	0.5552	0.4492	0.6863	0.0000
		a Genotype +ve vs c Genotype +ve	0.4768	0.3801	0.5982	0.0000
		b Genotype +ve vs c Genotype +ve	0.8587	0.7824	0.9425	0.0013
		a Genotype -ve vs b Genotype -ve	0.7155	0.5540	0.9241	0.0103
		a Genotype -ve vs c Genotype -ve	0.6481	0.4877	0.8614	0.0028
		b Genotype -ve vs c Genotype -ve	0.9058	0.8033	1.0214	0.1065
R	4	a Genotype +ve vs b Genotype +ve	0.5950	0.4889	0.7241	0.0000
		a Genotype +ve vs c Genotype +ve	0.5119	0.4137	0.6332	0.0000
		b Genotype +ve vs c Genotype +ve	0.8603	0.7835	0.9448	0.0016
		a Genotype -ve vs b Genotype -ve	0.7144	0.5453	0.9360	0.0147
		a Genotype -ve vs c Genotype -ve	0.6000	0.4359	0.8259	0.0017
		b Genotype -ve vs c Genotype -ve	0.8398	0.7079	0.9963	0.0452
R	5	a Genotype +ve vs b Genotype +ve	0.5770	0.4659	0.7146	0.0000
		a Genotype +ve vs c Genotype +ve	0.4421	0.3463	0.5643	0.0000
		b Genotype +ve vs c Genotype +ve	0.7662	0.6765	0.8677	0.0000
		a Genotype -ve vs b Genotype -ve	0.7243	0.5593	0.9380	0.0145
		a Genotype -ve vs c Genotype -ve	0.6363	0.4730	0.8561	0.0028
		b Genotype -ve vs c Genotype -ve	0.8785	0.7592	1.0166	0.0820
R	6	a Genotype +ve vs b Genotype +ve	0.5256	0.4087	0.6759	0.0000
		a Genotype +ve vs c Genotype +ve	0.3710	0.2776	0.4959	0.0000
		b Genotype +ve vs c Genotype +ve	0.7059	0.6072	0.8207	0.0000
		a Genotype -ve vs b Genotype -ve	0.6784	0.5084	0.9052	0.0084
		a Genotype -ve vs c Genotype -ve	0.5960	0.4315	0.8232	0.0017
		b Genotype -ve vs c Genotype -ve	0.8785	0.7592	1.0166	0.0821

Appendix2.1AnonymizationlevelR1-6 *(continued on next page)*

Appendix 2.1 Effect of Anonymization Level (Research Purposes 1-6) ***(continued)***

Purpose	Question	Comparison	OR	95% L CI	95% U CI	P value
R	1	a phenotyp +ve vs b phenotyp +ve	0.6055	0.4681	0.7831	0.0001
		a phenotyp +ve vs c phenotyp +ve	0.5093	0.3831	0.6770	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.8412	0.7295	0.9700	0.0173
		a phenotyp -ve vs b phenotyp -ve	0.6542	0.5436	0.7874	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.6147	0.5058	0.7469	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.9395	0.8832	0.9994	0.0479
R	2	a phenotyp +ve vs b phenotyp +ve	0.6590	0.5275	0.8235	0.0002
		a phenotyp +ve vs c phenotyp +ve	0.5590	0.4344	0.7194	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.8482	0.7395	0.9730	0.0188
		a phenotyp -ve vs b phenotyp -ve	0.6792	0.5687	0.8113	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.6352	0.5266	0.7662	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.9351	0.8787	0.9952	0.0347
R	3	a phenotyp +ve vs b phenotyp +ve	0.5709	0.4300	0.7579	0.0001
		a phenotyp +ve vs c phenotyp +ve	0.4512	0.3283	0.6200	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.7903	0.6709	0.9310	0.0049
		a phenotyp -ve vs b phenotyp -ve	0.6143	0.4990	0.7563	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.5698	0.4587	0.7079	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.9276	0.8689	0.9902	0.0242
R	4	a phenotyp +ve vs b phenotyp +ve	0.6037	0.4611	0.7905	0.0002
		a phenotyp +ve vs c phenotyp +ve	0.4788	0.3524	0.6507	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.7931	0.6725	0.9353	0.0059
		a phenotyp -ve vs b phenotyp -ve	0.6364	0.5206	0.7780	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.5727	0.4616	0.7104	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.8998	0.8296	0.9760	0.0109
R	5	a phenotyp +ve vs b phenotyp +ve	0.6672	0.5267	0.8452	0.0008
		a phenotyp +ve vs c phenotyp +ve	0.4997	0.3749	0.6660	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.7489	0.6276	0.8937	0.0013
		a phenotyp -ve vs b phenotyp -ve	0.5835	0.4608	0.7389	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.4813	0.3700	0.6261	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.8249	0.7339	0.9272	0.0013
R	6	a phenotyp +ve vs b phenotyp +ve	0.6144	0.4665	0.8093	0.0005
		a phenotyp +ve vs c phenotyp +ve	0.4434	0.3186	0.6170	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.7216	0.5913	0.8806	0.0013
		a phenotyp -ve vs b phenotyp -ve	0.5438	0.4161	0.7107	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.4170	0.3078	0.5649	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.7668	0.6652	0.8839	0.0003

Appendix 2.2 Effect of Anonymization Level (Admin Purposes 1-5)

Purpose	Question	Comparison	OR	95% L CI	95% U CI	P value
A	1	a hboc vs b hboc	0.7658	0.6616	0.8865	0.0004
		a hboc vs c hboc	0.7034	0.5966	0.8293	0.0000
		b hboc vs c hboc	0.9184	0.8541	0.9876	0.0217
		a Thro vs b Thro	0.8702	0.6932	1.0924	0.2308
		a Thro vs c Thro	0.7521	0.5502	1.0281	0.0741
		b Thro vs c Thro	0.8643	0.6975	1.0710	0.1826
A	2	a hboc vs b hboc	0.7163	0.5967	0.8599	0.0003
		a hboc vs c hboc	0.6008	0.4834	0.7466	0.0000
		b hboc vs c hboc	0.8387	0.7481	0.9402	0.0025
		a Thro vs b Thro	0.8472	0.6896	1.0409	0.1145
		a Thro vs c Thro	0.6842	0.4808	0.9736	0.0350
		b Thro vs c Thro	0.8076	0.6062	1.0759	0.1442
A	3	a hboc vs b hboc	0.6811	0.5653	0.8206	0.0001
		a hboc vs c hboc	0.5363	0.4284	0.6713	0.0000
		b hboc vs c hboc	0.7874	0.6948	0.8922	0.0002
		a Thro vs b Thro	0.6426	0.4510	0.9155	0.0143
		a Thro vs c Thro	0.4911	0.3081	0.7830	0.0028
		b Thro vs c Thro	0.7643	0.5794	1.0083	0.0572
A	4	a hboc vs b hboc	0.5660	0.4404	0.7274	0.0000
		a hboc vs c hboc	0.4059	0.3029	0.5438	0.0000
		b hboc vs c hboc	0.7171	0.6162	0.8345	0.0000
		a Thro vs b Thro	0.5335	0.3234	0.8800	0.0139
		a Thro vs c Thro	0.3597	0.1891	0.6843	0.0018
		b Thro vs c Thro	0.6743	0.4706	0.9661	0.0317
A	5	a hboc vs b hboc	0.5635	0.4354	0.7293	0.0000
		a hboc vs c hboc	0.4147	0.3079	0.5584	0.0000
		b hboc vs c hboc	0.7359	0.6332	0.8552	0.0001
		a Thro vs b Thro	0.8391	0.6117	1.1511	0.2768
		a Thro vs c Thro	0.3224	0.1561	0.6660	0.0022
		b Thro vs c Thro	0.3843	0.2021	0.7305	0.0035

Appendix2.2AnonymizationlevelA1-5 ***(continued on next page)***

Appendix 2.2 Effect of Anonymization Level (Admin Purposes A1-5) ***(continued)***

A	1	a Genotype +ve vs b Genotype +ve	0.8024	0.7027	0.9163	0.0011
		a Genotype +ve vs c Genotype +ve	0.7053	0.5987	0.8309	0.0000
		b Genotype +ve vs c Genotype +ve	0.8790	0.8003	0.9654	0.0070
		a Genotype -ve vs b Genotype -ve	0.7828	0.6318	0.9698	0.0251
		a Genotype -ve vs c Genotype -ve	0.7507	0.5966	0.9446	0.0144
		b Genotype -ve vs c Genotype -ve	0.9590	0.8825	1.0422	0.3242
A	2	a Genotype +ve vs b Genotype +ve	0.7657	0.6561	0.8936	0.0007
		a Genotype +ve vs c Genotype +ve	0.6126	0.4978	0.7538	0.0000
		b Genotype +ve vs c Genotype +ve	0.8001	0.6990	0.9158	0.0012
		a Genotype -ve vs b Genotype -ve	0.7406	0.5558	0.9868	0.0403
		a Genotype -ve vs c Genotype -ve	0.6458	0.4802	0.8685	0.0038
		b Genotype -ve vs c Genotype -ve	0.8720	0.7452	1.0205	0.0878
A	3	a Genotype +ve vs b Genotype +ve	0.6812	0.5703	0.8136	0.0000
		a Genotype +ve vs c Genotype +ve	0.5209	0.4162	0.6519	0.0000
		b Genotype +ve vs c Genotype +ve	0.7646	0.6693	0.8736	0.0001
		a Genotype -ve vs b Genotype -ve	0.6617	0.4916	0.8905	0.0064
		a Genotype -ve vs c Genotype -ve	0.5728	0.4108	0.7988	0.0010
		b Genotype -ve vs c Genotype -ve	0.8658	0.7459	1.0049	0.0580
A	4	a Genotype +ve vs b Genotype +ve	0.5847	0.4614	0.7410	0.0000
		a Genotype +ve vs c Genotype +ve	0.3946	0.2943	0.5290	0.0000
		b Genotype +ve vs c Genotype +ve	0.6748	0.5705	0.7981	0.0000
		a Genotype -ve vs b Genotype -ve	0.5262	0.3546	0.7808	0.0014
		a Genotype -ve vs c Genotype -ve	0.4563	0.3000	0.6943	0.0002
		b Genotype -ve vs c Genotype -ve	0.8672	0.7476	1.0060	0.0600
A	5	a Genotype +ve vs b Genotype +ve	0.6398	0.5103	0.8021	0.0001
		a Genotype +ve vs c Genotype +ve	0.4036	0.2995	0.5437	0.0000
		b Genotype +ve vs c Genotype +ve	0.6308	0.5209	0.7638	0.0000
		a Genotype -ve vs b Genotype -ve	0.5818	0.3927	0.8618	0.0069
		a Genotype -ve vs c Genotype -ve	0.4454	0.2840	0.6984	0.0004
		b Genotype -ve vs c Genotype -ve	0.7656	0.6118	0.9580	0.0195

Appendix2.2AnonymizationlevelA1-5 ***(continued on next page)***

Appendix 2.2 Effect of Anonymization Level (Admin Purposes A1-5) ***(continued)***

A	1	a phenotyp +ve vs b phenotyp +ve	0.8096	0.6800	0.9639	0.0176
		a phenotyp +ve vs c phenotyp +ve	0.7067	0.5673	0.8804	0.0020
		b phenotyp +ve vs c phenotyp +ve	0.8729	0.7677	0.9925	0.0381
		a phenotyp -ve vs b phenotyp -ve	0.7875	0.6796	0.9125	0.0015
		a phenotyp -ve vs c phenotyp -ve	0.7260	0.6141	0.8582	0.0002
		b phenotyp -ve vs c phenotyp -ve	0.9219	0.8513	0.9984	0.0456
A	2	a phenotyp +ve vs b phenotyp +ve	0.7810	0.6495	0.9392	0.0086
		a phenotyp +ve vs c phenotyp +ve	0.6514	0.5080	0.8352	0.0007
		b phenotyp +ve vs c phenotyp +ve	0.8340	0.7081	0.9823	0.0297
		a phenotyp -ve vs b phenotyp -ve	0.7397	0.6047	0.9049	0.0034
		a phenotyp -ve vs c phenotyp -ve	0.5988	0.4735	0.7572	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.8095	0.7039	0.9310	0.0031
A	3	a phenotyp +ve vs b phenotyp +ve	0.6685	0.5290	0.8447	0.0007
		a phenotyp +ve vs c phenotyp +ve	0.5412	0.4057	0.7220	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.8096	0.6907	0.9491	0.0092
		a phenotyp -ve vs b phenotyp -ve	0.6828	0.5587	0.8344	0.0002
		a phenotyp -ve vs c phenotyp -ve	0.5293	0.4143	0.6763	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.7752	0.6736	0.8922	0.0004
A	4	a phenotyp +ve vs b phenotyp +ve	0.6080	0.4521	0.8176	0.0010
		a phenotyp +ve vs c phenotyp +ve	0.4226	0.2905	0.6147	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.6950	0.5590	0.8641	0.0011
		a phenotyp -ve vs b phenotyp -ve	0.5396	0.4088	0.7123	0.0000
		a phenotyp -ve vs c phenotyp -ve	0.4038	0.2946	0.5535	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.7484	0.6433	0.8706	0.0002
A	5	a phenotyp +ve vs b phenotyp +ve	0.6448	0.4803	0.8656	0.0035
		a phenotyp +ve vs c phenotyp +ve	0.3968	0.2668	0.5900	0.0000
		b phenotyp +ve vs c phenotyp +ve	0.6154	0.4748	0.7976	0.0002
		a phenotyp -ve vs b phenotyp -ve	0.6083	0.4680	0.7905	0.0002
		a phenotyp -ve vs c phenotyp -ve	0.4295	0.3129	0.5897	0.0000
		b phenotyp -ve vs c phenotyp -ve	0.7062	0.5903	0.8448	0.0001

Appendix 2.3 Probability Estimates by Genotype

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
f/u appt	Coded	geno -ve	0.8993	0.8604	0.9283	0.7660	0.4506	0.9289
	Coded	geno +ve	0.7665	0.7261	0.8025	0.5212	0.2301	0.7986
	Agg	geno -ve	0.9838	0.9616	0.9932	0.9799	0.8572	0.9975
AQ1	Agg	geno +ve	0.8737	0.8407	0.9007	0.8478	0.4503	0.9743
	Pers	geno -ve	0.6817	0.6278	0.7311	0.5509	0.3090	0.7709
	Pers	geno +ve	0.6172	0.5727	0.6597	0.4774	0.2434	0.7218
billing	Coded	geno -ve	0.8117	0.7641	0.8515	0.6085	0.3489	0.8185
	Coded	geno +ve	0.6617	0.6175	0.7032	0.3885	0.1777	0.6513
	Agg	geno -ve	0.9188	0.8826	0.9446	0.8702	0.6123	0.9661
AQ2	Agg	geno +ve	0.7957	0.7569	0.8298	0.6755	0.3281	0.8987
	Pers	geno -ve	0.5723	0.5167	0.6262	0.4486	0.2395	0.6777
	Pers	geno +ve	0.4828	0.4377	0.5282	0.3632	0.1720	0.6103
hsp trck	Coded	geno -ve	0.8633	0.8196	0.8978	0.7457	0.4657	0.9080
	Coded	geno +ve	0.7101	0.6681	0.7489	0.5220	0.2672	0.7658
	Agg	geno -ve	0.9968	0.9773	0.9995	0.9967	0.9625	0.9997
AQ3	Agg	geno +ve	0.8747	0.8420	0.9015	0.8587	0.5345	0.9698
	Pers	geno -ve	0.5765	0.5205	0.6306	0.4149	0.2118	0.6517
	Pers	geno +ve	0.4685	0.4240	0.5134	0.3170	0.1399	0.5699
gvt trck	Coded	geno -ve	0.8345	0.7877	0.8726	0.6423	0.3618	0.8505
	Coded	geno +ve	0.6333	0.5887	0.6757	0.3579	0.1626	0.6153
	Agg	geno -ve	0.9545	0.9247	0.9729	0.9226	0.6106	0.9891
AQ4	Agg	geno +ve	0.8641	0.8301	0.8922	0.7363	0.3484	0.9358
	Pers	geno -ve	0.4732	0.4171	0.5299	0.2691	0.1173	0.5049
	Pers	geno +ve	0.3541	0.3120	0.3986	0.1769	0.0662	0.3943
fundr	Coded	geno -ve	0.7128	0.6587	0.7615	0.4949	0.2577	0.7343
	Coded	geno +ve	0.5862	0.5408	0.6302	0.3456	0.1564	0.6007
	Agg	geno -ve	0.9188	0.8826	0.9446	0.9230	0.6787	0.9855
AQ5	Agg	geno +ve	0.8448	0.8090	0.8750	0.8450	0.5498	0.9605
	Pers	geno -ve	0.4704	0.4149	0.5266	0.3086	0.1347	0.5615
	Pers	geno +ve	0.3560	0.3134	0.4011	0.2182	0.0803	0.4712

Appendix2.4-ProbabilityEstimatesbyGenotype ***(continued on next page)***

Appendix 2.3 Probability Estimates by Genotype *(continued)*

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
dis res	Coded	geno -ve	0.9575	0.9282	0.9752	0.9782	0.8894	0.9960
	Coded	geno +ve	0.8866	0.8548	0.9121	0.9339	0.7297	0.9867
	Agg	geno -ve	0.9968	0.9776	0.9995	0.9962	0.8676	0.9999
RQ1	Agg	geno +ve	0.9686	0.9486	0.9810	0.9438	0.6325	0.9939
	Pers	geno -ve	0.7426	0.6908	0.7884	0.6590	0.4155	0.8401
	Pers	geno +ve	0.6066	0.5609	0.6505	0.5063	0.2613	0.7482
gen res	Coded	geno -ve	0.9446	0.9127	0.9653	0.9717	0.8312	0.9958
	Coded	geno +ve	0.9006	0.8702	0.9245	0.9464	0.7241	0.9916
	Agg	geno -ve	0.9968	0.9776	0.9995	0.9895	0.3410	0.9999
RQ2	Agg	geno +ve	0.9833	0.9669	0.9916	0.9201	0.0825	0.9993
	Pers	geno -ve	0.7492	0.6973	0.7948	0.6542	0.4076	0.8388
	Pers	geno +ve	0.6394	0.5940	0.6824	0.5213	0.2700	0.7623
other res	Coded	geno -ve	0.9178	0.8811	0.9438	0.9462	0.7761	0.9889
	Coded	geno +ve	0.8657	0.8317	0.8937	0.9063	0.6991	0.9758
	Agg	geno -ve	0.9840	0.9621	0.9933	0.9346	0.4905	0.9953
RQ3	Agg	geno +ve	0.9668	0.9465	0.9796	0.8505	0.5358	0.9656
	Pers	geno -ve	0.6634	0.6086	0.7141	0.5540	0.3245	0.7626
	Pers	geno +ve	0.5553	0.5092	0.6005	0.4387	0.2218	0.6818
controv	Coded	geno -ve	0.8816	0.8402	0.9134	0.9043	0.6734	0.9774
	Coded	geno +ve	0.8476	0.8121	0.8775	0.8740	0.6183	0.9674
	Agg	geno -ve	0.9615	0.9335	0.9780	0.8958	0.3406	0.9931
RQ4	Agg	geno +ve	0.9686	0.9486	0.9810	0.8943	0.3354	0.9930
	Pers	geno -ve	0.6304	0.5746	0.6829	0.5257	0.2925	0.7483
	Pers	geno +ve	0.5679	0.5217	0.6130	0.4583	0.2261	0.7102
hsp trck	Coded	geno -ve	0.8896	0.8495	0.9201	0.8994	0.7085	0.9705
	Coded	geno +ve	0.7844	0.7450	0.8191	0.8010	0.5454	0.9310
	Agg	geno -ve	0.9808	0.9579	0.9913	0.9613	0.5859	0.9977
RQ5	Agg	geno +ve	0.9689	0.9491	0.9812	0.9272	0.2596	0.9978
	Pers	geno -ve	0.6775	0.6232	0.7274	0.5621	0.3264	0.7727
	Pers	geno +ve	0.5022	0.4566	0.5477	0.3788	0.1751	0.6366
gvt trck	Coded	geno -ve	0.8133	0.7652	0.8535	0.7919	0.5428	0.9242
	Coded	geno +ve	0.7284	0.6861	0.7670	0.6872	0.4127	0.8729
	Agg	geno -ve	0.9448	0.9130	0.9654	0.8828	0.3945	0.9886
RQ6	Agg	geno +ve	0.9415	0.9166	0.9593	0.8506	0.2643	0.9890
	Pers	geno -ve	0.5318	0.4750	0.5877	0.3464	0.1605	0.5948
	Pers	geno +ve	0.4115	0.3670	0.4575	0.2404	0.0917	0.4980

Appendix 2.4 Probability Estimates by Phenotype

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
f/u appt	Coded	pheno-ve	0.8174	0.7738	0.8542	0.6563	0.3516	0.8706
	Coded	pheno+ve	0.8203	0.7808	0.8541	0.6582	0.3404	0.8779
	Agg	pheno-ve	0.8750	0.8367	0.9054	0.8724	0.5412	0.9754
AQ1	Agg	pheno+ve	0.9527	0.9279	0.9693	0.9540	0.7267	0.9939
	Pers	pheno-ve	0.6181	0.5671	0.6667	0.4883	0.2483	0.7339
	Pers	pheno+ve	0.6635	0.6172	0.7069	0.5405	0.3037	0.7603
billing	Coded	pheno-ve	0.7051	0.6556	0.7501	0.4845	0.2509	0.7252
	Coded	pheno+ve	0.7351	0.6907	0.7751	0.5264	0.2781	0.7624
	Agg	pheno-ve	0.8174	0.7738	0.8542	0.7447	0.4392	0.9157
AQ2	Agg	pheno+ve	0.8673	0.8315	0.8965	0.8100	0.4973	0.9483
	Pers	pheno-ve	0.4522	0.4012	0.5043	0.3353	0.1535	0.5838
	Pers	pheno+ve	0.5748	0.5271	0.6212	0.4632	0.2473	0.6938
hsp trck	Coded	pheno-ve	0.7306	0.6823	0.7739	0.5825	0.3224	0.8036
	Coded	pheno+ve	0.8014	0.7607	0.8367	0.6814	0.4163	0.8651
	Agg	pheno-ve	0.8886	0.8522	0.9169	0.8930	0.6257	0.9766
AQ3	Agg	pheno+ve	0.9523	0.9272	0.9690	0.9604	0.8333	0.9916
	Pers	pheno-ve	0.4670	0.4163	0.5185	0.3188	0.1414	0.5708
	Pers	pheno+ve	0.5489	0.5010	0.5960	0.4050	0.2038	0.6442
gvt trck	Coded	pheno-ve	0.6939	0.6431	0.7404	0.4732	0.2402	0.7185
	Coded	pheno+ve	0.7251	0.6805	0.7656	0.5280	0.2926	0.7516
	Agg	pheno-ve	0.8833	0.8459	0.9126	0.7994	0.4309	0.9545
AQ4	Agg	pheno+ve	0.9141	0.8832	0.9374	0.8612	0.5375	0.9707
	Pers	pheno-ve	0.3580	0.3096	0.4094	0.1863	0.0706	0.4086
	Pers	pheno+ve	0.4369	0.3897	0.4852	0.2531	0.1090	0.4842
fundr	Coded	pheno-ve	0.6408	0.5890	0.6895	0.4339	0.2150	0.6821
	Coded	pheno+ve	0.6311	0.5834	0.6763	0.4254	0.2153	0.6664
	Agg	pheno-ve	0.8528	0.8123	0.8857	0.8679	0.5700	0.9702
AQ5	Agg	pheno+ve	0.8932	0.8595	0.9196	0.9038	0.6664	0.9779
	Pers	pheno-ve	0.3876	0.3384	0.4393	0.2565	0.1025	0.5103
	Pers	pheno+ve	0.4144	0.3673	0.4632	0.2794	0.1186	0.5276

Appendix2.5-ProbabilityEstimatesbyPhenotype *(continued on next page)*

Appendix 2.4 Probability Estimates by Phenotype *(continued)*

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
dis res	Coded	pheno-ve	0.9448	0.9159	0.9641	0.9728	0.8284	0.9962
RQ1	Coded	pheno+ve	0.8881	0.8542	0.9149	0.9457	0.7705	0.9891
	Agg	pheno-ve	0.9864	0.9678	0.9943	0.9691	0.6068	0.9984
	Agg	pheno+ve	0.9739	0.9536	0.9855	0.9582	0.8180	0.9915
	Pers	pheno-ve	0.6666	0.6159	0.7138	0.5991	0.3419	0.8112
	Pers	pheno+ve	0.6568	0.6094	0.7013	0.5942	0.3496	0.7995
gen res	Coded	pheno-ve	0.9420	0.9127	0.9619	0.9745	0.8023	0.9972
RQ2	Coded	pheno+ve	0.8971	0.8641	0.9228	0.9520	0.7531	0.9923
	Agg	pheno-ve	0.9864	0.9678	0.9943	0.9401	0.0988	0.9996
	Agg	pheno+ve	0.9905	0.9750	0.9964	0.9768	0.8043	0.9977
	Pers	pheno-ve	0.6809	0.6303	0.7276	0.5955	0.3327	0.8129
	Pers	pheno+ve	0.6856	0.6387	0.7291	0.6053	0.3589	0.8077
other res	Coded	pheno-ve	0.9304	0.8990	0.9525	0.9588	0.8078	0.9923
RQ3	Coded	pheno+ve	0.8478	0.8099	0.8793	0.9085	0.6840	0.9785
	Agg	pheno-ve	0.9755	0.9537	0.9872	0.8902	0.5390	0.9825
	Agg	pheno+ve	0.9718	0.9511	0.9839	0.8986	0.5397	0.9853
	Pers	pheno-ve	0.6186	0.5669	0.6678	0.5279	0.2928	0.7512
	Pers	pheno+ve	0.5817	0.5330	0.6289	0.4899	0.2694	0.7144
controv	Coded	pheno-ve	0.8989	0.8630	0.9262	0.9254	0.6878	0.9859
RQ4	Coded	pheno+ve	0.8285	0.7891	0.8618	0.8687	0.6086	0.9657
	Agg	pheno-ve	0.9674	0.9435	0.9814	0.8992	0.2129	0.9966
	Agg	pheno+ve	0.9645	0.9419	0.9785	0.8928	0.4368	0.9889
	Pers	pheno-ve	0.5994	0.5473	0.6494	0.5039	0.2607	0.7452
	Pers	pheno+ve	0.5875	0.5386	0.6348	0.4904	0.2627	0.7222
hsp trck	Coded	pheno-ve	0.8440	0.8027	0.8780	0.8780	0.6778	0.9610
RQ5	Coded	pheno+ve	0.8104	0.7702	0.8450	0.8469	0.6220	0.9489
	Agg	pheno-ve	0.9728	0.9502	0.9853	0.9388	0.2858	0.9983
	Agg	pheno+ve	0.9742	0.9541	0.9857	0.9500	0.4949	0.9973
	Pers	pheno-ve	0.5352	0.4831	0.5865	0.4356	0.2153	0.6847
	Pers	pheno+ve	0.6044	0.5563	0.6505	0.5163	0.2877	0.7382
gvt trck	Coded	pheno-ve	0.7781	0.7313	0.8187	0.7728	0.5109	0.9172
RQ6	Coded	pheno+ve	0.7482	0.7043	0.7875	0.7338	0.4751	0.8935
	Agg	pheno-ve	0.9528	0.9254	0.9704	0.8926	0.3081	0.9936
	Agg	pheno+ve	0.9344	0.9067	0.9543	0.8560	0.3341	0.9860
	Pers	pheno-ve	0.4373	0.3857	0.4903	0.2771	0.1112	0.5402
	Pers	pheno+ve	0.4779	0.4298	0.5265	0.3169	0.1418	0.5659

Appendix 2.5 Probability Estimates by Population Group

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
f/u appt	Coded	HBOC	0.7930	0.7488	0.8312	0.5574	0.2318	0.8402
	Coded	THR	0.8378	0.7943	0.8736	0.6601	0.3417	0.8790
	Agg	HBOC	0.8800	0.8430	0.9092	0.8650	0.4826	0.9778
AQ1	Agg	THR	0.9520	0.9230	0.9704	0.9454	0.7076	0.9920
	Pers	HBOC	0.5974	0.5472	0.6455	0.4341	0.1935	0.7104
	Pers	THR	0.6836	0.6318	0.7312	0.5460	0.2984	0.7729
billing	Coded	HBOC	0.6907	0.6420	0.7354	0.3953	0.1619	0.6886
	Coded	THR	0.7538	0.7044	0.7973	0.5255	0.2774	0.7616
	Agg	HBOC	0.8160	0.7735	0.8520	0.7044	0.3440	0.9155
AQ2	Agg	THR	0.8675	0.8266	0.8999	0.7996	0.4940	0.9422
	Pers	HBOC	0.4737	0.4239	0.5240	0.3345	0.1437	0.6010
	Pers	THR	0.5680	0.5140	0.6204	0.4424	0.2300	0.6782
hsp trck	Coded	HBOC	0.7421	0.6957	0.7836	0.5659	0.2788	0.8146
	Coded	THR	0.7831	0.7356	0.8242	0.6442	0.3794	0.8429
	Agg	HBOC	0.9036	0.8698	0.9294	0.9124	0.6324	0.9844
AQ3	Agg	THR	0.9390	0.9074	0.9603	0.9484	0.7879	0.9891
	Pers	HBOC	0.4841	0.4341	0.5345	0.3300	0.1393	0.5998
	Pers	THR	0.5299	0.4762	0.5829	0.3956	0.1953	0.6382
gvt trck	Coded	HBOC	0.6720	0.6227	0.7179	0.3822	0.1646	0.6601
	Coded	THR	0.7267	0.6754	0.7726	0.5029	0.2666	0.7378
	Agg	HBOC	0.8989	0.8641	0.9256	0.8036	0.3965	0.9622
AQ4	Agg	THR	0.8902	0.8516	0.9198	0.8398	0.4915	0.9660
	Pers	HBOC	0.3790	0.3311	0.4294	0.2022	0.0735	0.4476
	Pers	THR	0.4019	0.3496	0.4565	0.2413	0.1006	0.4749
fundr	Coded	HBOC	0.6755	0.6265	0.7210	0.4588	0.2140	0.7253
	Coded	THR	0.5750	0.5201	0.6281	0.3906	0.1869	0.6411
	Agg	HBOC	0.8605	0.8219	0.8919	0.8726	0.5336	0.9762
AQ5	Agg	THR	0.8765	0.8360	0.9081	0.8909	0.6343	0.9746
	Pers	HBOC	0.3898	0.3415	0.4403	0.2551	0.0953	0.5268
	Pers	THR	0.3932	0.3414	0.4475	0.2814	0.1175	0.5352

Appendix2.6-ProbabilityEstimatesbyPopulationGroup ***(continued on next page)***

Appendix 2.5 Probability Estimates by Population Group *(continued)*

Purpose	Anon	Level	unadj P	unadj L CI	unadj U CI	adj P	adj L CI	adj U CI
dis res	Coded	HBOC	0.8929	0.8578	0.9202	0.9243	0.6679	0.9867
RQ1	Coded	THR	0.9270	0.8935	0.9506	0.9568	0.8182	0.9909
	Agg	HBOC	0.9766	0.9556	0.9878	0.9458	0.5353	0.9962
	Agg	THR	0.9789	0.9563	0.9899	0.9650	0.8085	0.9945
	Pers	HBOC	0.6119	0.5613	0.6601	0.4777	0.2252	0.7421
	Pers	THR	0.6885	0.6357	0.7368	0.6019	0.3534	0.8071
gen res	Coded	HBOC	0.9010	0.8669	0.9272	0.9359	0.6493	0.9914
RQ2	Coded	THR	0.9264	0.8925	0.9502	0.9565	0.7739	0.9930
	Agg	HBOC	0.9870	0.9691	0.9946	0.9148	0.0320	0.9997
	Agg	THR	0.9879	0.9683	0.9955	0.9679	0.6198	0.9982
	Pers	HBOC	0.6359	0.5854	0.6835	0.4679	0.2133	0.7404
	Pers	THR	0.7129	0.6607	0.7601	0.6098	0.3607	0.8123
other res	Coded	HBOC	0.8906	0.8553	0.9182	0.9298	0.7083	0.9863
RQ3	Coded	THR	0.8638	0.8219	0.8971	0.9119	0.6987	0.9788
	Agg	HBOC	0.9766	0.9556	0.9878	0.8973	0.5009	0.9870
	Agg	THR	0.9642	0.9380	0.9795	0.8717	0.4991	0.9789
	Pers	HBOC	0.5660	0.5151	0.6156	0.4218	0.1955	0.6865
	Pers	THR	0.6031	0.5489	0.6549	0.4939	0.2681	0.7223
controv	Coded	HBOC	0.8500	0.8105	0.8825	0.8791	0.5702	0.9755
RQ4	Coded	THR	0.8625	0.8203	0.8961	0.8963	0.6679	0.9738
	Agg	HBOC	0.9687	0.9458	0.9822	0.8669	0.1377	0.9963
	Agg	THR	0.9547	0.9262	0.9725	0.8761	0.3867	0.9875
	Pers	HBOC	0.5806	0.5298	0.6298	0.4477	0.2020	0.7219
	Pers	THR	0.5796	0.5243	0.6330	0.4877	0.2550	0.7259
hsp trck	Coded	HBOC	0.8395	0.7991	0.8731	0.8895	0.6695	0.9697
RQ5	Coded	THR	0.8036	0.7573	0.8429	0.8612	0.6487	0.9542
	Agg	HBOC	0.9740	0.9523	0.9859	0.9222	0.2167	0.9980
	Agg	THR	0.9673	0.9419	0.9818	0.9395	0.4263	0.9969
	Pers	HBOC	0.5484	0.4975	0.5983	0.4163	0.1838	0.6932
	Pers	THR	0.5805	0.5265	0.6327	0.4942	0.2659	0.7250
gvt trck	Coded	HBOC	0.7903	0.7460	0.8287	0.7828	0.5113	0.9254
RQ6	Coded	THR	0.7059	0.6539	0.7530	0.7247	0.4583	0.8912
	Agg	HBOC	0.9553	0.9292	0.9720	0.8396	0.2112	0.9903
	Agg	THR	0.9157	0.8806	0.9411	0.8344	0.3099	0.9826
	Pers	HBOC	0.4667	0.4157	0.5184	0.2780	0.1021	0.5660
	Pers	THR	0.4268	0.3738	0.4816	0.2910	0.1229	0.5460

Appendix 2.6 Specific Predictors of Authorization

P	Q	Anon	Type	Pred	Level	OR unadj	lowCI unadj	upCI unadj	p_unadj	OR adj	lowCI adj	upCI adj	p_adj
A	1	Agg	bld	genotype	Genotype +ve	0.3460	0.1071	1.1181	0.0762	0.1828	0.0402	0.8322	0.0280
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0611	0.7082	1.5897	0.7737
				age						1.0004	0.9539	1.0491	0.9877
				sex	female					0.7610	0.1955	2.9620	0.6936
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7872	0.1445	4.2890	0.7820
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Agg	fhx	genotype	Genotype +ve	0.3774	0.1154	1.2349	0.1072	0.0885	0.0114	0.6900	0.0207
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0653	0.7038	1.6123	0.7649
				age						0.9914	0.9418	1.0436	0.7423
				sex	female					0.8126	0.2029	3.2552	0.7695
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7817	0.1379	4.4307	0.7808
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Agg	gt	genotype	Genotype +ve	0.3820	0.1168	1.2497	0.1115	0.0899	0.0115	0.7014	0.0215
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0670	0.7030	1.6197	0.7606
				age						0.9941	0.9455	1.0453	0.8178
				sex	female					0.8053	0.2026	3.2013	0.7584
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7421	0.1320	4.1733	0.7350
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Agg	ngt	genotype	Genotype +ve	0.3773	0.1154	1.2338	0.1069	0.0908	0.0116	0.7080	0.0221
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0666	0.7018	1.6208	0.7628
				age						0.9926	0.9445	1.0432	0.7696
				sex	female					0.8040	0.2019	3.2016	0.7570
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7490	0.1332	4.2110	0.7428
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Coded	bld	genotype	Genotype +ve	0.7406	0.3470	1.5806	0.4375	0.3781	0.1628	0.8784	0.0237
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3495	0.9965	1.8275	0.0527
				age						1.0288	0.9944	1.0645	0.1022
				sex	female					0.8202	0.3003	2.2401	0.6990
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6094	0.1717	2.1622	0.4433
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Coded	fhx	genotype	Genotype +ve	0.7233	0.3324	1.5739	0.4142	0.2947	0.1181	0.7353	0.0088
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4682	1.0692	2.0161	0.0176
				age						1.0158	0.9804	1.0524	0.3859
				sex	female					0.8917	0.3198	2.4865	0.8266
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5806	0.1590	2.1203	0.4107
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Coded	gt	genotype	Genotype +ve	0.8051	0.3817	1.6986	0.5693	0.3614	0.1559	0.8377	0.0176
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	

				privacy						1.3147	0.9743	1.7740	0.0735
				age						1.0304	0.9961	1.0658	0.0826
				sex	female					0.7940	0.2916	2.1622	0.6518
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6306	0.1784	2.2294	0.4742
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Coded	ngt	genotype	Genotype +ve	0.6944	0.3124	1.5437	0.3710	0.2704	0.1032	0.7087	0.0078
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4326	1.0362	1.9805	0.0296
				age						1.0126	0.9767	1.0498	0.4965
				sex	female					0.9459	0.3365	2.6596	0.9161
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5381	0.1458	1.9856	0.3522
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Pers	bld	genotype	Genotype +ve	0.6802	0.3682	1.2566	0.2184	0.8009	0.4329	1.4816	0.4793
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2437	0.9776	1.5822	0.0758
				age						1.0099	0.9837	1.0368	0.4619
				sex	female					0.6255	0.2885	1.3563	0.2347
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.0461	0.3803	2.8771	0.9305
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Pers	fhx	genotype	Genotype +ve	0.6923	0.3744	1.2803	0.2411	0.7599	0.4085	1.4135	0.3859
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2513	0.9834	1.5922	0.0682
				age						1.0027	0.9767	1.0293	0.8430
				sex	female					0.6189	0.2841	1.3485	0.2272
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.1159	0.4048	3.0761	0.8321
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Pers	gt	genotype	Genotype +ve	0.6724	0.3623	1.2480	0.2085	0.6818	0.3656	1.2716	0.2285
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3046	1.0226	1.6644	0.0324
				age						1.0045	0.9782	1.0314	0.7410
				sex	female					0.6246	0.2867	1.3605	0.2361
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.0269	0.3706	2.8457	0.9593
				educ	higher than high school					1.0000	1.0000	1.0000	
A	1	Pers	ngt	genotype	Genotype +ve	0.7027	0.3781	1.3059	0.2645	0.7556	0.4048	1.4103	0.3787
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2700	0.9950	1.6210	0.0548
				age						1.0069	0.9804	1.0340	0.6140
				sex	female					0.6887	0.3163	1.4995	0.3475
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9530	0.3449	2.6331	0.9260
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Agg	bld	genotype	Genotype +ve	0.6451	0.2851	1.4594	0.2926	0.3534	0.1413	0.8839	0.0262
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0751	0.7814	1.4790	0.6565
				age						1.0187	0.9828	1.0560	0.3103
				sex	female					1.8990	0.7521	4.7949	0.1747
				sex	male					1.0000	1.0000	1.0000	

				educ	high school graduate or less					0.5877	0.1630	2.1191	0.4166
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Agg	fhx	genotype	Genotype +ve	0.6830	0.2996	1.5571	0.3645	0.2907	0.1105	0.7645	0.0123
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0767	0.7797	1.4867	0.6537
				age						1.0144	0.9775	1.0528	0.4484
				sex	female					2.0431	0.7976	5.2340	0.1366
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5823	0.1587	2.1372	0.4150
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Agg	gt	genotype	Genotype +ve	0.6920	0.3037	1.5769	0.3810	0.2962	0.1126	0.7792	0.0137
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0784	0.7797	1.4914	0.6485
				age						1.0162	0.9796	1.0541	0.3916
				sex	female					2.0008	0.7845	5.1026	0.1465
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5616	0.1536	2.0533	0.3831
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Agg	ngt	genotype	Genotype +ve	0.6920	0.3037	1.5769	0.3810	0.2962	0.1126	0.7792	0.0137
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0784	0.7797	1.4914	0.6485
				age						1.0162	0.9796	1.0541	0.3916
				sex	female					2.0008	0.7845	5.1026	0.1465
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5616	0.1536	2.0533	0.3831
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Coded	bld	genotype	Genotype +ve	0.7344	0.3801	1.4192	0.3584	0.4488	0.2247	0.8964	0.0232
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2570	0.9683	1.6317	0.0858
				age						1.0232	0.9936	1.0536	0.1261
				sex	female					1.5377	0.7022	3.3676	0.2820
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5501	0.1921	1.5753	0.2656
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Coded	fhx	genotype	Genotype +ve	0.7488	0.3828	1.4650	0.3983	0.3788	0.1843	0.7788	0.0083
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3147	1.0060	1.7181	0.0451
				age						1.0184	0.9878	1.0499	0.2412
				sex	female					1.7423	0.7818	3.8829	0.1745
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5087	0.1740	1.4871	0.2169
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Coded	gt	genotype	Genotype +ve	0.7344	0.3801	1.4192	0.3584	0.3968	0.1965	0.8012	0.0099
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2610	0.9704	1.6385	0.0827
				age						1.0227	0.9930	1.0534	0.1356
				sex	female					1.5479	0.7044	3.4014	0.2767
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5417	0.1882	1.5595	0.2558
				educ	higher than high school					1.0000	1.0000	1.0000	
A	2	Coded	ngt	genotype	Genotype +ve	0.6998	0.3558	1.3764	0.3010	0.3772	0.1812	0.7854	0.0092
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2954	0.9882	1.6981	0.0609

				age							1.0104	0.9804	1.0413	0.5030
				sex	female						1.7294	0.7788	3.8403	0.1784
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						0.5100	0.1744	1.4920	0.2189
				educ	higher than high school						1.0000	1.0000	1.0000	
A	2	Pers	bld	genotype	Genotype +ve	0.6894	0.3813	1.2463	0.2182		0.7420	0.4111	1.3393	0.3220
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							1.2524	0.9903	1.5837	0.0603
				age							1.0017	0.9766	1.0276	0.8935
				sex	female						0.6747	0.3301	1.3788	0.2805
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						1.2632	0.4827	3.3057	0.6340
				educ	higher than high school						1.0000	1.0000	1.0000	
A	2	Pers	fhx	genotype	Genotype +ve	0.7043	0.3890	1.2753	0.2472		0.7014	0.3864	1.2734	0.2438
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							1.2580	0.9940	1.5920	0.0561
				age							0.9947	0.9696	1.0204	0.6844
				sex	female						0.6716	0.3263	1.3824	0.2798
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						1.3629	0.5183	3.5841	0.5303
				educ	higher than high school						1.0000	1.0000	1.0000	
A	2	Pers	gt	genotype	Genotype +ve	0.6608	0.3654	1.1951	0.1706		0.6856	0.3805	1.2352	0.2089
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							1.2290	0.9727	1.5528	0.0840
				age							1.0011	0.9760	1.0269	0.9313
				sex	female						0.7234	0.3557	1.4712	0.3713
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						1.0818	0.4182	2.7981	0.8712
				educ	higher than high school						1.0000	1.0000	1.0000	
A	2	Pers	ngt	genotype	Genotype +ve	0.6845	0.3783	1.2386	0.2103		0.6863	0.3796	1.2409	0.2129
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							1.2546	0.9918	1.5871	0.0585
				age							0.9986	0.9734	1.0244	0.9121
				sex	female						0.7198	0.3519	1.4727	0.3681
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						1.2011	0.4580	3.1503	0.7095
				educ	higher than high school						1.0000	1.0000	1.0000	
A	3	Agg	bld	genotype	Genotype +ve	0.5584	0.1828	1.7059	0.3065		0.0840	0.0107	0.6630	0.0188
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							0.9524	0.6219	1.4584	0.8224
				age							0.9848	0.9353	1.0369	0.5610
				sex	female						1.1697	0.3263	4.1933	0.8099
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						0.4748	0.1016	2.2183	0.3437
				educ	higher than high school						1.0000	1.0000	1.0000	
A	3	Agg	fhx	genotype	Genotype +ve	0.6277	0.2017	1.9537	0.4215		0.0000			
				genotype	Genotype True -ve						1.0000	1.0000	1.0000	
				privacy							0.9434			
				age							0.9748			
				sex	female						1.3235			
				sex	male						1.0000	1.0000	1.0000	
				educ	high school graduate or less						0.4461			
				educ	higher than high school						1.0000	1.0000	1.0000	

A	3	Agg	gt	genotype	Genotype +ve	0.6277	0.2017	1.9537	0.4215	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9431			
				age						0.9751			
				sex	female					1.2639			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.4395			
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Agg	ngt	genotype	Genotype +ve	0.6277	0.2017	1.9537	0.4215	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9431			
				age						0.9751			
				sex	female					1.2639			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.4395			
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Coded	bld	genotype	Genotype +ve	0.7754	0.3875	1.5514	0.4722	0.4061	0.1890	0.8724	0.0209
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2729	0.9654	1.6783	0.0872
				age						1.0051	0.9747	1.0364	0.7457
				sex	female					0.8531	0.3576	2.0354	0.7203
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8067	0.2546	2.5559	0.7150
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Coded	fhx	genotype	Genotype +ve	0.8192	0.4078	1.6458	0.5754	0.3577	0.1628	0.7864	0.0105
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2785	0.9673	1.6899	0.0842
				age						1.0024	0.9717	1.0341	0.8787
				sex	female					0.9091	0.3782	2.1852	0.8313
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7939	0.2485	2.5358	0.6968
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Coded	gt	genotype	Genotype +ve	0.7754	0.3875	1.5514	0.4722	0.3481	0.1587	0.7636	0.0085
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2779	0.9679	1.6871	0.0836
				age						1.0043	0.9737	1.0359	0.7859
				sex	female					0.8551	0.3569	2.0485	0.7254
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7954	0.2492	2.5389	0.6990
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Coded	ngt	genotype	Genotype +ve	0.8192	0.4078	1.6458	0.5754	0.3744	0.1699	0.8250	0.0148
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3084	0.9867	1.7349	0.0619
				age						1.0017	0.9708	1.0337	0.9137
				sex	female					0.9029	0.3754	2.1717	0.8196
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7605	0.2373	2.4366	0.6449
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Pers	bld	genotype	Genotype +ve	0.7959	0.4414	1.4353	0.4480	0.6654	0.3651	1.2128	0.1835
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3525	1.0628	1.7211	0.0141
				age						1.0075	0.9821	1.0337	0.5657
				sex	female					0.6334	0.3090	1.2985	0.2125

				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4737	0.5510	3.9418	0.4398
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Pers	fhx	genotype	Genotype +ve	0.8881	0.4917	1.6041	0.6940	0.6352	0.3471	1.1626	0.1412
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3426	1.0552	1.7082	0.0165
				age						1.0071	0.9813	1.0336	0.5913
				sex	female					0.6728	0.3267	1.3857	0.2824
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4688	0.5488	3.9308	0.4440
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Pers	gt	genotype	Genotype +ve	0.7800	0.4331	1.4047	0.4078	0.5999	0.3288	1.0947	0.0959
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3562	1.0648	1.7275	0.0136
				age						1.0057	0.9803	1.0319	0.6621
				sex	female					0.6213	0.3026	1.2755	0.1947
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4971	0.5579	4.0170	0.4230
				educ	higher than high school					1.0000	1.0000	1.0000	
A	3	Pers	ngt	genotype	Genotype +ve	0.8712	0.4834	1.5700	0.6464	0.6890	0.3784	1.2546	0.2232
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3496	1.0611	1.7165	0.0146
				age						1.0069	0.9815	1.0329	0.5992
				sex	female					0.6474	0.3160	1.3261	0.2346
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4538	0.5440	3.8848	0.4556
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Agg	bld	genotype	Genotype +ve	1.0356	0.3991	2.6874	0.9427	0.2787	0.0852	0.9119	0.0346
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0316	0.6960	1.5292	0.8767
				age						1.0033	0.9588	1.0499	0.8871
				sex	female					3.6587	1.2750	10.4983	0.0159
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.3460	0.0853	1.4029	0.1373
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Agg	fhx	genotype	Genotype +ve	1.1644	0.4390	3.0883	0.7598	0.1918	0.0506	0.7267	0.0151
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0302	0.6863	1.5465	0.8859
				age						0.9974	0.9511	1.0458	0.9131
				sex	female					4.2548	1.4346	12.6194	0.0090
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.3258	0.0771	1.3765	0.1272
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Agg	gt	genotype	Genotype +ve	1.0356	0.3991	2.6874	0.9427	0.2659	0.0803	0.8803	0.0301
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0758	0.7214	1.6041	0.7202
				age						1.0023	0.9572	1.0494	0.9229
				sex	female					4.6958	1.6279	13.5449	0.0042
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.3308	0.0797	1.3734	0.1277
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Agg	ngt	genotype	Genotype +ve	1.1644	0.4390	3.0883	0.7598	0.1971	0.0522	0.7445	0.0166
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	

				privacy						1.0305	0.6855	1.5493	0.8850
				age						0.9980	0.9516	1.0466	0.9328
				sex	female					4.0895	1.3812	12.1087	0.0110
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.3193	0.0757	1.3469	0.1201
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Coded	bld	genotype	Genotype +ve	0.7458	0.3884	1.4319	0.3781	0.3363	0.1623	0.6969	0.0034
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2903	0.9920	1.6784	0.0574
				age						0.9953	0.9666	1.0249	0.7536
				sex	female					1.2722	0.5753	2.8137	0.5521
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5260	0.1850	1.4953	0.2281
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Coded	fhx	genotype	Genotype +ve	0.7831	0.4068	1.5072	0.4641	0.2965	0.1402	0.6272	0.0015
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2966	0.9943	1.6907	0.0551
				age						0.9926	0.9636	1.0226	0.6261
				sex	female					1.3743	0.6146	3.0731	0.4386
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5189	0.1805	1.4921	0.2235
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Coded	gt	genotype	Genotype +ve	0.7458	0.3884	1.4319	0.3781	0.2925	0.1387	0.6165	0.0012
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2961	0.9948	1.6886	0.0547
				age						0.9945	0.9656	1.0243	0.7153
				sex	female					1.2822	0.5765	2.8516	0.5422
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5171	0.1802	1.4844	0.2203
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Coded	ngt	genotype	Genotype +ve	0.8105	0.4204	1.5628	0.5306	0.3023	0.1426	0.6411	0.0018
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3393	1.0219	1.7554	0.0343
				age						0.9937	0.9642	1.0241	0.6830
				sex	female					1.3337	0.5975	2.9767	0.4821
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.4930	0.1710	1.4214	0.1905
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Pers	bld	genotype	Genotype +ve	0.8777	0.4768	1.6159	0.6754	0.6148	0.3330	1.1350	0.1199
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3624	1.0644	1.7439	0.0141
				age						1.0124	0.9862	1.0393	0.3551
				sex	female					0.7101	0.3456	1.4591	0.3515
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9089	0.3454	2.3916	0.8465
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Pers	fhx	genotype	Genotype +ve	0.9779	0.5288	1.8086	0.9433	0.5688	0.3060	1.0574	0.0745
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3536	1.0569	1.7336	0.0165
				age						1.0130	0.9864	1.0404	0.3414
				sex	female					0.7528	0.3630	1.5610	0.4454
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9182	0.3484	2.4202	0.8630

				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Pers	gt	genotype	Genotype +ve	0.8382	0.4545	1.5457	0.5719	0.5390	0.2910	0.9982	0.0494
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3710	1.0687	1.7587	0.0130
				age						1.0111	0.9848	1.0381	0.4110
				sex	female					0.6880	0.3337	1.4186	0.3111
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9273	0.3506	2.4522	0.8790
				educ	higher than high school					1.0000	1.0000	1.0000	
A	4	Pers	ngt	genotype	Genotype +ve	0.9474	0.5139	1.7465	0.8625	0.6202	0.3357	1.1459	0.1272
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3670	1.0685	1.7488	0.0129
				age						1.0108	0.9847	1.0376	0.4216
				sex	female					0.7330	0.3570	1.5051	0.3975
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8864	0.3370	2.3315	0.8069
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Agg	bld	genotype	Genotype +ve	0.8149	0.3408	1.9486	0.6454	0.5176	0.2017	1.3282	0.1708
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9382	0.6670	1.3197	0.7142
				age						1.0050	0.9669	1.0447	0.7989
				sex	female					1.5953	0.5833	4.3630	0.3629
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8918	0.2209	3.5993	0.8722
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Agg	fhx	genotype	Genotype +ve	0.8884	0.3672	2.1494	0.7929	0.4338	0.1610	1.1689	0.0987
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9364	0.6612	1.3261	0.7111
				age						1.0012	0.9621	1.0419	0.9524
				sex	female					1.6905	0.6116	4.6727	0.3115
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8598	0.2104	3.5131	0.8334
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Agg	gt	genotype	Genotype +ve	0.8884	0.3672	2.1494	0.7929	0.4338	0.1610	1.1689	0.0987
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9364	0.6612	1.3261	0.7111
				age						1.0012	0.9621	1.0419	0.9524
				sex	female					1.6905	0.6116	4.6727	0.3115
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8598	0.2104	3.5131	0.8334
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Agg	ngt	genotype	Genotype +ve	0.8884	0.3672	2.1494	0.7929	0.4338	0.1610	1.1689	0.0987
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9364	0.6612	1.3261	0.7111
				age						1.0012	0.9621	1.0419	0.9524
				sex	female					1.6905	0.6116	4.6727	0.3115
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8598	0.2104	3.5131	0.8334
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Coded	bld	genotype	Genotype +ve	1.5021	0.8100	2.7855	0.1966	0.5690	0.2991	1.0823	0.0856
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3837	1.0789	1.7745	0.0105
				age						1.0073	0.9800	1.0353	0.6050

				sex	female					1.2174	0.5691	2.6045	0.6121
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2624	0.4363	3.6522	0.6673
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Coded	fhx	genotype	Genotype +ve	1.5768	0.8481	2.9316	0.1501	0.5302	0.2771	1.0144	0.0553
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3881	1.0810	1.7824	0.0101
				age						1.0053	0.9779	1.0335	0.7060
				sex	female					1.2483	0.5822	2.6766	0.5688
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2432	0.4280	3.6110	0.6890
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Coded	gt	genotype	Genotype +ve	1.5021	0.8100	2.7855	0.1966	0.5115	0.2674	0.9782	0.0427
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3884	1.0816	1.7823	0.0100
				age						1.0067	0.9793	1.0348	0.6369
				sex	female					1.2271	0.5721	2.6317	0.5991
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2536	0.4317	3.6402	0.6777
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Coded	ngt	genotype	Genotype +ve	1.5768	0.8481	2.9316	0.1501	0.5469	0.2853	1.0481	0.0690
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4114	1.0976	1.8151	0.0072
				age						1.0046	0.9771	1.0328	0.7479
				sex	female					1.2773	0.5949	2.7425	0.5301
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2145	0.4172	3.5358	0.7215
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Pers	bld	genotype	Genotype +ve	0.9671	0.5253	1.7805	0.9145	0.6592	0.3547	1.2250	0.1875
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3625	1.0629	1.7464	0.0146
				age						1.0139	0.9865	1.0419	0.3233
				sex	female					0.8086	0.3849	1.6991	0.5750
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8797	0.7147	4.9437	0.2008
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Pers	fhx	genotype	Genotype +ve	1.0444	0.5662	1.9262	0.8895	0.6033	0.3242	1.1227	0.1107
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3526	1.0550	1.7341	0.0172
				age						1.0154	0.9876	1.0440	0.2808
				sex	female					0.8333	0.3962	1.7527	0.6308
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8273	0.6944	4.8086	0.2221
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Pers	gt	genotype	Genotype +ve	0.9240	0.5011	1.7039	0.8002	0.5759	0.3090	1.0733	0.0823
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3703	1.0668	1.7603	0.0137
				age						1.0123	0.9849	1.0405	0.3817
				sex	female					0.7852	0.3725	1.6551	0.5250
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.9334	0.7319	5.1078	0.1835
				educ	higher than high school					1.0000	1.0000	1.0000	
A	5	Pers	ngt	genotype	Genotype +ve	1.0117	0.5503	1.8601	0.9701	0.6451	0.3482	1.1955	0.1637

				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3769	1.0751	1.7633	0.0113
				age						1.0110	0.9840	1.0388	0.4279
				sex	female					0.8443	0.4024	1.7718	0.6546
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8162	0.6899	4.7811	0.2269
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Agg	bld	genotype	Genotype +ve	0.7654	0.1248	4.6950	0.7727	0.3147	0.0324	3.0538	0.3187
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2778	0.6224	2.6234	0.5041
				age						0.9562	0.8712	1.0494	0.3448
				sex	female					0.6713	0.0622	7.2453	0.7426
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.2200	0.0249	1.9441	0.1732
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Agg	fhx	genotype	Genotype +ve	1.1605	0.1599	8.4250	0.8830	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2494			
				age						0.8968			
				sex	female					0.7147			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1972			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Agg	gt	genotype	Genotype +ve	1.1605	0.1599	8.4250	0.8830	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2496			
				age						0.8962			
				sex	female					0.6955			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1963			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Agg	ngt	genotype	Genotype +ve	0.5802	0.0517	6.5174	0.6592	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3500			
				age						0.8648			
				sex	female					1.1833			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.0948			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Coded	bld	genotype	Genotype +ve	0.6100	0.2153	1.7289	0.3525	0.3954	0.1216	1.2854	0.1229
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8301	0.5552	1.2412	0.3643
				age						0.9630	0.9179	1.0102	0.1225
				sex	female					1.1529	0.3646	3.6450	0.8086
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8792	0.2030	3.8067	0.8633
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Coded	fhx	genotype	Genotype +ve	0.7544	0.2567	2.2172	0.6084	0.3203	0.0840	1.2215	0.0955
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8365	0.5423	1.2903	0.4194
				age						0.9529	0.9031	1.0055	0.0785
				sex	female					1.0521	0.2954	3.7464	0.9376
				sex	male					1.0000	1.0000	1.0000	

				educ	high school graduate or less					0.7739	0.1717	3.4880	0.7386
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Coded	gt	genotype	Genotype +ve	0.6100	0.2153	1.7289	0.3525	0.2642	0.0715	0.9761	0.0459
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8287	0.5525	1.2428	0.3634
				age						0.9592	0.9131	1.0077	0.0981
				sex	female					1.1732	0.3675	3.7451	0.7874
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8721	0.1983	3.8342	0.8562
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Coded	ngt	genotype	Genotype +ve	0.6701	0.2327	1.9300	0.4583	0.2904	0.0763	1.1055	0.0699
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8372	0.5456	1.2847	0.4161
				age						0.9466	0.8973	0.9986	0.0443
				sex	female					1.3070	0.3968	4.3054	0.6598
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8595	0.1910	3.8680	0.8436
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Pers	bld	genotype	Genotype +ve	0.7068	0.3766	1.3266	0.2801	0.5376	0.2825	1.0232	0.0588
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1707	0.9130	1.5012	0.2141
				age						0.9960	0.9689	1.0239	0.7765
				sex	female					1.0483	0.4961	2.2155	0.9016
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2146	0.4201	3.5117	0.7197
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Pers	fhx	genotype	Genotype +ve	0.7444	0.3927	1.4112	0.3657	0.5186	0.2682	1.0029	0.0510
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1960	0.9291	1.5395	0.1647
				age						0.9864	0.9582	1.0154	0.3548
				sex	female					1.1251	0.5271	2.4013	0.7607
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2410	0.4246	3.6270	0.6931
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Pers	gt	genotype	Genotype +ve	0.6181	0.3305	1.1560	0.1320	0.4897	0.2580	0.9293	0.0289
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1526	0.9006	1.4750	0.2592
				age						0.9930	0.9662	1.0207	0.6180
				sex	female					0.9457	0.4477	1.9974	0.8836
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3506	0.4668	3.9071	0.5793
				educ	higher than high school					1.0000	1.0000	1.0000	
R	1	Pers	ngt	genotype	Genotype +ve	0.7979	0.4256	1.4957	0.4813	0.5648	0.2958	1.0781	0.0833
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1828	0.9215	1.5183	0.1875
				age						0.9939	0.9667	1.0218	0.6639
				sex	female					1.0536	0.4983	2.2275	0.8913
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2166	0.4205	3.5200	0.7176
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Agg	bld	genotype	Genotype +ve	0.5732	0.0510	6.4371	0.6520	0.6285	0.0527	7.5020	0.7136
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4118	0.5465	3.6467	0.4763

				age						0.9886	0.8851	1.1042	0.8393
				sex	female					1.6917	0.1206	23.7319	0.6964
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.2180	0.0120	3.9689	0.3035
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Agg	fhx	genotype	Genotype +ve	1.1585	0.0713	18.8152	0.9176	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6652			
				age						0.9196			
				sex	female					3.5518			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1195			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Agg	gt	genotype	Genotype +ve	1.1585	0.0713	18.8152	0.9176	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6716			
				age						0.9189			
				sex	female					3.4817			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1177			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Agg	ngt	genotype	Genotype +ve	1.1728	0.0722	19.0495	0.9107	0.0000			
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6686			
				age						0.9190			
				sex	female					3.4583			
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1186			
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Coded	bld	genotype	Genotype +ve	0.6880	0.2387	1.9827	0.4886	0.6081	0.2014	1.8360	0.3777
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8091	0.5364	1.2205	0.3126
				age						0.9785	0.9341	1.0251	0.3599
				sex	female					1.3550	0.4258	4.3121	0.6070
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3196	0.2526	6.8937	0.7424
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Coded	fhx	genotype	Genotype +ve	0.7632	0.2597	2.2424	0.6231	0.5182	0.1559	1.7225	0.2834
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8313	0.5391	1.2817	0.4028
				age						0.9871	0.9402	1.0364	0.6016
				sex	female					1.2901	0.3677	4.5258	0.6908
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.0045	0.1880	5.3673	0.9958
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Coded	gt	genotype	Genotype +ve	0.6880	0.2387	1.9827	0.4886	0.4446	0.1363	1.4497	0.1789
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8098	0.5359	1.2237	0.3165
				age						0.9760	0.9307	1.0234	0.3148
				sex	female					1.3883	0.4339	4.4425	0.5803
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2964	0.2458	6.8362	0.7596
				educ	higher than high school					1.0000	1.0000	1.0000	

R	2	Coded	ngt	genotype	Genotype +ve	0.7632	0.2597	2.2424	0.6231	0.5091	0.1518	1.7079	0.2743
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8201	0.5298	1.2694	0.3735
				age						0.9664	0.9184	1.0170	0.1893
				sex	female					1.5782	0.4789	5.2012	0.4533
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2297	0.2276	6.6435	0.8101
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Pers	bld	genotype	Genotype +ve	0.7343	0.3849	1.4008	0.3487	0.5650	0.2918	1.0941	0.0904
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2129	0.9397	1.5656	0.1383
				age						0.9959	0.9681	1.0245	0.7745
				sex	female					1.2556	0.5866	2.6876	0.5578
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4197	0.4634	4.3498	0.5396
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Pers	fhx	genotype	Genotype +ve	0.6901	0.3600	1.3229	0.2639	0.5862	0.3011	1.1411	0.1160
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2240	0.9458	1.5842	0.1245
				age						0.9984	0.9700	1.0276	0.9137
				sex	female					1.4114	0.6559	3.0371	0.3782
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3338	0.4345	4.0939	0.6147
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Pers	gt	genotype	Genotype +ve	0.5900	0.3095	1.1247	0.1090	0.5434	0.2818	1.0477	0.0686
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1511	0.8943	1.4815	0.2745
				age						0.9905	0.9630	1.0187	0.5051
				sex	female					1.1528	0.5406	2.4582	0.7128
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.6098	0.5269	4.9183	0.4034
				educ	higher than high school					1.0000	1.0000	1.0000	
R	2	Pers	ngt	genotype	Genotype +ve	0.8182	0.4300	1.5570	0.5410	0.6007	0.3092	1.1671	0.1326
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2279	0.9495	1.5878	0.1175
				age						0.9943	0.9664	1.0230	0.6923
				sex	female					1.2820	0.5989	2.7442	0.5224
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3991	0.4562	4.2905	0.5569
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Agg	bld	genotype	Genotype +ve	1.1481	0.2255	5.8471	0.8679	0.6796	0.1153	4.0059	0.6695
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.5575	0.7911	3.0664	0.1999
				age						0.9803	0.9053	1.0614	0.6233
				sex	female					0.6115	0.0601	6.2236	0.6778
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.2228	0.0277	1.7934	0.1582
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Agg	fhx	genotype	Genotype +ve	1.7407	0.2838	10.6761	0.5492	0.3055	0.0307	3.0368	0.3116
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6873	0.7863	3.6208	0.1793
				age						0.9553	0.8680	1.0512	0.3486
				sex	female					0.7082	0.0618	8.1205	0.7816

				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1926	0.0199	1.8660	0.1551
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Agg	gt	genotype	Genotype +ve	1.7407	0.2838	10.6761	0.5492	0.3076	0.0310	3.0559	0.3142
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6902	0.7868	3.6312	0.1785
				age						0.9552	0.8678	1.0514	0.3491
				sex	female					0.6927	0.0605	7.9321	0.7679
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1915	0.0197	1.8600	0.1542
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Agg	ngt	genotype	Genotype +ve	1.7625	0.2873	10.8114	0.5403	0.3063	0.0309	3.0389	0.3122
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.6859	0.7860	3.6161	0.1798
				age						0.9551	0.8679	1.0510	0.3470
				sex	female					0.6877	0.0601	7.8677	0.7633
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.1934	0.0199	1.8759	0.1564
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Coded	bld	genotype	Genotype +ve	1.2143	0.4969	2.9676	0.6702	0.6255	0.2390	1.6373	0.3392
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8523	0.5959	1.2190	0.3814
				age						0.9715	0.9322	1.0124	0.1695
				sex	female					1.0769	0.3767	3.0790	0.8900
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.8073	0.2230	2.9231	0.7444
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Coded	fhx	genotype	Genotype +ve	1.3710	0.5502	3.4165	0.4982	0.5494	0.1987	1.5191	0.2484
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8743	0.6048	1.2638	0.4749
				age						0.9767	0.9360	1.0192	0.2778
				sex	female					0.9948	0.3242	3.0527	0.9927
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6712	0.1823	2.4709	0.5488
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Coded	gt	genotype	Genotype +ve	1.2143	0.4969	2.9676	0.6702	0.4866	0.1782	1.3286	0.1598
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8525	0.5955	1.2205	0.3835
				age						0.9693	0.9295	1.0109	0.1459
				sex	female					1.0939	0.3810	3.1403	0.8675
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7953	0.2177	2.9051	0.7290
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Coded	ngt	genotype	Genotype +ve	1.3514	0.5425	3.3663	0.5178	0.5479	0.1964	1.5287	0.2505
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.8648	0.5955	1.2559	0.4454
				age						0.9615	0.9198	1.0050	0.0820
				sex	female					1.1838	0.4047	3.4625	0.7580
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.7657	0.2062	2.8438	0.6901
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Pers	bld	genotype	Genotype +ve	0.8480	0.4633	1.5521	0.5929	0.6493	0.3522	1.1972	0.1666
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	

				privacy						1.2108	0.9534	1.5376	0.1167
				age						1.0012	0.9752	1.0279	0.9281
				sex	female					0.9159	0.4378	1.9160	0.8155
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3429	0.4899	3.6813	0.5666
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Pers	fhx	genotype	Genotype +ve	0.8833	0.4813	1.6210	0.6888	0.6230	0.3359	1.1554	0.1332
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2541	0.9854	1.5959	0.0657
				age						1.0055	0.9788	1.0329	0.6900
				sex	female					0.9835	0.4665	2.0737	0.9651
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2757	0.4637	3.5101	0.6372
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Pers	gt	genotype	Genotype +ve	0.7619	0.4164	1.3943	0.3778	0.5666	0.3061	1.0491	0.0707
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.1964	0.9424	1.5188	0.1409
				age						0.9991	0.9731	1.0258	0.9468
				sex	female					0.8546	0.4076	1.7920	0.6775
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.4474	0.5261	3.9823	0.4739
				educ	higher than high school					1.0000	1.0000	1.0000	
R	3	Pers	ngt	genotype	Genotype +ve	0.9519	0.5198	1.7433	0.8732	0.6848	0.3705	1.2658	0.2270
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2205	0.9604	1.5510	0.1032
				age						0.9995	0.9735	1.0263	0.9711
				sex	female					0.9179	0.4387	1.9205	0.8200
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.3470	0.4912	3.6942	0.5628
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Agg	Bld	genotype	Genotype +ve	1.5696	0.3410	7.2248	0.5627	0.9831	0.2050	4.7151	0.9830
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3216	0.6881	2.5384	0.4024
				age						1.0010	0.9334	1.0734	0.9782
				sex	female					4.9450	0.9436	25.9146	0.0586
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6233	0.0548	7.0877	0.7031
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Agg	Fhx	genotype	Genotype +ve	1.5696	0.3410	7.2248	0.5627	0.9612	0.2002	4.6141	0.9605
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3182	0.6884	2.5240	0.4045
				age						1.0006	0.9333	1.0727	0.9869
				sex	female					5.0504	0.9656	26.4148	0.0550
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6339	0.0558	7.2007	0.7131
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Agg	Gt	genotype	Genotype +ve	1.5696	0.3410	7.2248	0.5627	0.9831	0.2050	4.7151	0.9830
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3216	0.6881	2.5384	0.4024
				age						1.0010	0.9334	1.0734	0.9782
				sex	female					4.9450	0.9436	25.9146	0.0586
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6233	0.0548	7.0877	0.7031

				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Agg	Ngt	genotype	Genotype +ve	1.1772	0.2311	5.9973	0.8443	1.2513	0.2323	6.7409	0.7942
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4159	0.6852	2.9258	0.3477
				age						1.0102	0.9366	1.0895	0.7935
				sex	female					8.0281	1.2291	52.4387	0.0296
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.4489	0.0348	5.7917	0.5393
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Coded	bld	genotype	Genotype +ve	0.9224	0.3933	2.1633	0.8526	0.7303	0.3060	1.7429	0.4788
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9095	0.6530	1.2667	0.5746
				age						0.9908	0.9548	1.0281	0.6232
				sex	female					1.4117	0.5457	3.6521	0.4771
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.1630	0.2926	4.6236	0.8302
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Coded	fhx	genotype	Genotype +ve	0.9224	0.3933	2.1633	0.8526	0.7598	0.3163	1.8251	0.5389
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9352	0.6693	1.3065	0.6944
				age						1.0003	0.9640	1.0380	0.9867
				sex	female					1.3116	0.4889	3.5186	0.5900
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.0047	0.2520	4.0062	0.9947
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Coded	Gt	genotype	Genotype +ve	0.8502	0.3663	1.9735	0.7057	0.6867	0.2898	1.6270	0.3931
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9140	0.6597	1.2664	0.5889
				age						0.9934	0.9579	1.0302	0.7210
				sex	female					1.3643	0.5304	3.5093	0.5194
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.1749	0.2969	4.6499	0.8183
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Coded	ngt	genotype	Genotype +ve	0.9224	0.3933	2.1633	0.8526	0.7757	0.3225	1.8655	0.5705
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9320	0.6660	1.3043	0.6813
				age						0.9889	0.9524	1.0268	0.5623
				sex	female					1.4730	0.5657	3.8357	0.4277
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.1196	0.2800	4.4762	0.8731
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Pers	bld	genotype	Genotype +ve	0.9854	0.5352	1.8146	0.9624	0.7287	0.3931	1.3508	0.3149
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2719	0.9983	1.6207	0.0517
				age						1.0083	0.9816	1.0357	0.5474
				sex	female					1.1784	0.5660	2.4535	0.6609
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.9018	0.6286	5.7543	0.2551
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Pers	fhx	genotype	Genotype +ve	1.0154	0.5520	1.8677	0.9608	0.7429	0.4006	1.3776	0.3455
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2539	0.9848	1.5965	0.0664
				age						1.0109	0.9838	1.0387	0.4335

				sex	female					1.0401	0.4960	2.1810	0.9170
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.9782	0.6554	5.9703	0.2261
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Pers	gt	genotype	Genotype +ve	0.9099	0.4963	1.6682	0.7601	0.7062	0.3828	1.3026	0.2654
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2476	0.9815	1.5859	0.0708
				age						1.0038	0.9775	1.0309	0.7784
				sex	female					1.0144	0.4887	2.1058	0.9693
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.2265	0.7371	6.7252	0.1559
				educ	higher than high school					1.0000	1.0000	1.0000	
R	4	Pers	ngt	genotype	Genotype +ve	1.1184	0.6081	2.0569	0.7188	0.8801	0.4762	1.6266	0.6835
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2731	1.0001	1.6206	0.0499
				age						1.0035	0.9771	1.0307	0.7958
				sex	female					1.0727	0.5165	2.2276	0.8507
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.1082	0.6974	6.3724	0.1863
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Agg	bld	genotype	Genotype +ve	0.7561	0.1233	4.6370	0.7625	0.8877	0.1398	5.6367	0.8995
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2568	0.5979	2.6421	0.5465
				age						1.0067	0.9281	1.0919	0.8723
				sex	female					2.4976	0.3504	17.8012	0.3610
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.3963	0.0312	5.0272	0.4752
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Agg	fhx	genotype	Genotype +ve	1.7407	0.2838	10.6761	0.5492	0.2932	0.0303	2.8419	0.2898
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0633	0.4959	2.2800	0.8747
				age						0.9676	0.8859	1.0569	0.4649
				sex	female					4.8454	0.6868	34.1847	0.1134
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5669	0.0443	7.2520	0.6626
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Agg	gt	genotype	Genotype +ve	1.1481	0.2255	5.8471	0.8679	0.6645	0.1137	3.8820	0.6499
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3338	0.6680	2.6631	0.4143
				age						0.9737	0.9005	1.0528	0.5038
				sex	female					3.0324	0.5155	17.8376	0.2198
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.6695	0.0575	7.7960	0.7487
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Agg	ngt	genotype	Genotype +ve	1.7407	0.2838	10.6761	0.5492	0.3013	0.0311	2.9158	0.3002
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0648	0.4940	2.2950	0.8727
				age						0.9678	0.8855	1.0578	0.4708
				sex	female					4.6810	0.6629	33.0566	0.1217
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.5549	0.0433	7.1154	0.6510
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Coded	Bld	genotype	Genotype +ve	1.1791	0.5483	2.5354	0.6732	0.4728	0.2060	1.0851	0.0772

				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9685	0.7152	1.3115	0.8360
				age						1.0002	0.9674	1.0341	0.9902
				sex	female					1.2940	0.5287	3.1670	0.5725
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2947	0.3316	5.0557	0.7101
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Coded	fhx	genotype	Genotype +ve	1.4026	0.6382	3.0827	0.3997	0.4417	0.1851	1.0536	0.0654
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9861	0.7218	1.3470	0.9297
				age						0.9985	0.9647	1.0335	0.9334
				sex	female					1.2424	0.4880	3.1628	0.6490
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.1712	0.2964	4.6278	0.8217
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Coded	Gt	genotype	Genotype +ve	1.1791	0.5483	2.5354	0.6732	0.3936	0.1667	0.9295	0.0334
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9709	0.7162	1.3161	0.8489
				age						0.9992	0.9662	1.0334	0.9639
				sex	female					1.3069	0.5317	3.2123	0.5596
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2726	0.3238	5.0018	0.7300
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Coded	ngt	genotype	Genotype +ve	1.3737	0.6380	2.9581	0.4171	0.4957	0.2152	1.1417	0.0992
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						0.9886	0.7281	1.3425	0.9417
				age						0.9963	0.9633	1.0305	0.8314
				sex	female					1.3119	0.5345	3.2200	0.5535
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.2851	0.3283	5.0303	0.7187
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Pers	bld	genotype	Genotype +ve	0.8854	0.4873	1.6087	0.6896	0.5191	0.2805	0.9610	0.0369
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2915	1.0116	1.6490	0.0401
				age						0.9910	0.9652	1.0175	0.5025
				sex	female					1.0099	0.4865	2.0965	0.9788
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8622	0.6426	5.3966	0.2521
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Pers	fhx	genotype	Genotype +ve	0.9650	0.5292	1.7596	0.9075	0.4755	0.2552	0.8860	0.0192
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2802	1.0015	1.6365	0.0486
				age						0.9914	0.9651	1.0184	0.5277
				sex	female					0.9650	0.4598	2.0252	0.9249
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8420	0.6333	5.3572	0.2621
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Pers	gt	genotype	Genotype +ve	0.7727	0.4251	1.4046	0.3977	0.4165	0.2231	0.7778	0.0060
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2631	0.9878	1.6152	0.0626
				age						0.9843	0.9583	1.0109	0.2453
				sex	female					0.9553	0.4572	1.9957	0.9031
				sex	male					1.0000	1.0000	1.0000	

				educ	high school graduate or less					2.0430	0.6972	5.9862	0.1927
				educ	higher than high school					1.0000	1.0000	1.0000	
R	5	Pers	Ngt	genotype	Genotype +ve	0.8984	0.4928	1.6377	0.7265	0.4789	0.2557	0.8972	0.0215
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.2907	1.0086	1.6518	0.0426
				age						0.9837	0.9576	1.0105	0.2301
				sex	female					1.0462	0.5018	2.1811	0.9041
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.8768	0.6416	5.4899	0.2503
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Agg	bld	genotype	Genotype +ve	1.6579	0.5056	5.4364	0.4041	0.9298	0.2674	3.2330	0.9088
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3001	0.7701	2.1950	0.3260
				age						1.0115	0.9575	1.0686	0.6824
				sex	female					8.8640	2.2845	34.3925	0.0016
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.0431	0.1035	10.5129	0.9714
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Agg	fhx	genotype	Genotype +ve	2.0954	0.5910	7.4291	0.2520	0.6759	0.1768	2.5836	0.5669
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3330	0.7669	2.3170	0.3082
				age						1.0037	0.9474	1.0634	0.8991
				sex	female					11.9232	2.7218	52.2314	0.0010
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9858	0.0934	10.4107	0.9905
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Agg	gt	genotype	Genotype +ve	2.0954	0.5910	7.4291	0.2520	0.6994	0.1834	2.6668	0.6006
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3377	0.7670	2.3331	0.3052
				age						1.0045	0.9478	1.0645	0.8804
				sex	female					11.6023	2.6450	50.8944	0.0012
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9576	0.0907	10.1090	0.9713
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Agg	ngt	genotype	Genotype +ve	2.0954	0.5910	7.4291	0.2520	0.6994	0.1834	2.6668	0.6006
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3377	0.7670	2.3331	0.3052
				age						1.0045	0.9478	1.0645	0.8804
				sex	female					11.6023	2.6450	50.8944	0.0012
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					0.9576	0.0907	10.1090	0.9713
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Coded	bld	genotype	Genotype +ve	1.5368	0.7731	3.0553	0.2203	0.6291	0.3069	1.2893	0.2055
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0488	0.7972	1.3796	0.7337
				age						1.0052	0.9756	1.0358	0.7323
				sex	female					2.2935	1.0517	5.0016	0.0369
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.7108	0.4452	6.5738	0.4343
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Coded	fhx	genotype	Genotype +ve	1.5716	0.7812	3.1614	0.2049	0.5143	0.2421	1.0925	0.0837
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0694	0.8070	1.4171	0.6402

				age						1.0011	0.9705	1.0325	0.9469
				sex	female					2.6583	1.1970	5.9033	0.0163
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.6183	0.4136	6.3328	0.4892
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Coded	gt	genotype	Genotype +ve	1.5368	0.7731	3.0553	0.2203	0.5659	0.2723	1.1761	0.1271
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0666	0.8085	1.4071	0.6482
				age						1.0038	0.9738	1.0346	0.8071
				sex	female					2.3741	1.0831	5.2036	0.0308
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.6542	0.4279	6.3943	0.4657
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Coded	ngt	genotype	Genotype +ve	1.6399	0.8193	3.2824	0.1624	0.5951	0.2855	1.2407	0.1662
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.0711	0.8101	1.4162	0.6297
				age						1.0020	0.9718	1.0331	0.8976
				sex	female					2.4520	1.1167	5.3838	0.0254
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					1.6312	0.4208	6.3236	0.4791
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Pers	bld	genotype	Genotype +ve	1.1500	0.6286	2.1037	0.6501	0.6480	0.3495	1.2013	0.1683
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4195	1.1062	1.8216	0.0059
				age						1.0040	0.9780	1.0307	0.7667
				sex	female					1.2922	0.6171	2.7058	0.4966
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.3308	0.8001	6.7902	0.1209
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Pers	fhx	genotype	Genotype +ve	1.2197	0.6631	2.2435	0.5230	0.5571	0.2982	1.0407	0.0665
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4070	1.0945	1.8089	0.0077
				age						1.0031	0.9765	1.0304	0.8223
				sex	female					1.3715	0.6464	2.9099	0.4105
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.4115	0.8237	7.0600	0.1083
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Pers	gt	genotype	Genotype +ve	1.0997	0.6009	2.0127	0.7579	0.5209	0.2805	0.9672	0.0389
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.3680	1.0662	1.7553	0.0138
				age						1.0030	0.9769	1.0297	0.8263
				sex	female					1.2757	0.6080	2.6768	0.5196
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.3940	0.8198	6.9909	0.1104
				educ	higher than high school					1.0000	1.0000	1.0000	
R	6	Pers	ngt	genotype	Genotype +ve	1.2378	0.6751	2.2696	0.4904	0.6470	0.3480	1.2032	0.1690
				genotype	Genotype True -ve					1.0000	1.0000	1.0000	
				privacy						1.4297	1.1136	1.8356	0.0050
				age						1.0022	0.9762	1.0289	0.8710
				sex	female					1.3373	0.6386	2.8002	0.4408
				sex	male					1.0000	1.0000	1.0000	
				educ	high school graduate or less					2.2774	0.7798	6.6510	0.1323
				educ	higher than high school					1.0000	1.0000	1.0000	

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