Biobanking and Ethics: How Much Information Should Be Accessible?

By

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Thesis

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

Master of Arts

in

Medicine, Health & Society

August, 2014

Nashville, Tennessee

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To my mom, Louise, and my daddy, Thomas, for teaching me the value of education and hard work--Their support is everything to me.

and

To my best friend, Sarah Wathen, for being there everyday.

ACKNOWLEDGEMENTS

The completion of this project would not have been possible without the support of Vanderbilt's Center for Medicine, Health & Society and the Center for Biomedical Ethics & Society. I have been fortunate to have the opportunity to build professional relationships with each member of the faculty in both centers, and for that I will always be eternally grateful.

I want to extend special thanks to Dr. JuLeigh Petty and Dr. Elizabeth Heitman for mentoring me throughout my undergraduate and graduate careers at Vanderbilt. JuLeigh's direction, flexibility, and constant encouragement inspired me to pursue my Master's with MHS and collaborate with the Center for Biomedical Ethics & Society to achieve advanced levels of academic training in clinical ethics. Liz's willingness to mentor me has, and continues to be, invaluable in every aspect of my career. She has taught me through example how passion, diligence, and mindfulness are necessary for success in ethics, and I aspire to embody these traits as a professional. I thank them for everything they have taught me and I look forward to collaborating with them in the future.

And, of course, thank you to all of my friends, family, colleagues, and baristas for seeing me through this process. The successful completion of this thesis would not have been possible without them.

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Introduction

"Tell me what you know about BioVU."

Response 1: "Just heard of it, but don't know what it is."

Response 2: "On a voluntary basis blood is drawn and the DNA is put in a database and stripped of identifying information for research purposes."

Response 3:"That's how Vanderbilt is trying to figure out DNA to help find treatments for specific individual people."

The preceding quotes reflect three different responses from patients concerning Vanderbilt's de-identified, DNA biobank BioVU. The variations presented here are prime examples of patients' confusion regarding Vanderbilt's biobanking practices. The exit-interview surveys that were conducted for this project originated from a series of questions that I had relating to Vanderbilt's efforts to ethically implement the biobank and how that implementation relates to Vanderbilt Medical Center's research practices pertaining to other research using leftover biospecimens collected from patients. At Vanderbilt, and other academic research hospitals, it is common practice to use any biospecimens for medical research. Upon their first encounter with Vanderbilt's registration system and annually thereafter, in order to receive treatment from Vanderbilt patients must sign the general Consent to Treat form that includes acknowledging that Vanderbilt may use any and all biospecimens remaining after clinical diagnosis or treatment for research. Rather than apply the same standards of regular tissue and other biospecimen collection, the standards for BioVU are different because

BioVU specifically concerns the collection of DNA. In addition to having patients sign the Consent to Treat form, Vanderbilt also presents patients with the option to opt-out of participation in BioVU. For the general consent to treat, the possibility to opt-out of having other biospecimens used for research is not made available. The inconsistency of these practices is troublesome to many who are aware of the discrepancy, including, but not limited to, Vanderbilt's Ethics Committee, patient educations, and others within the Vanderbilt community that had this issue brought to their attention. As a member of the Vanderbilt community who is concerned about this issue, I wanted to know whether patients are also aware that even if they opt-out of participation in BioVU that not only could their leftover blood and DNA be used for other types of research, but any and all other biospecimens collected from routine tests and procedures could be as well.

In 2013, Vanderbilt pediatrician Kyle Brothers and his colleagues (2013) published a study measuring patients' awareness of BioVU. Between 2009 and 2012, Brothers and his colleagues conducted three sets of patient exit-interviews. Beginning in 2009, they interviewed adult patients who were having their blood drawn at two of the busiest phlebotomy labs in Vanderbilt University Medical Center. These 68 adult interviews were later compared with a second cohort of 77 exit-interviews collected in 2011 in the same locations to compare whether awareness was affected by new institutional campaigns that sought to increase the visibility of BioVU. Between these two time periods, exit-interviews were also conducted to include awareness on part of parents of pediatric patients who

were having blood drawn at Monroe Carrell Jr. Children's Hospital at Vanderbilt. However, the focus of this study is on the adult cohorts since this project is revisiting awareness of adult primary care patients at Vanderbilt. The primary outcomes measured were:

(1) Awareness of the Vanderbilt DNA databank
(2) Awareness that leftover blood could be used for research
(3) Support for the biorepository (p. 351)

Brothers et al found that while 92.5% of all adults surveyed reflected support for DNA databank after being offered a brief description of the project, awareness was still low. Only 48.1% and 32.5% of people in the Adult 1 and Adult 2 cohorts had heard of BioVU previously; 34.3% and 50% were aware that leftover specimens could be used from research; 2.6% and 2.5% could recall their choice of opting-out of participating in BioVU. The authors concluded that "the opt-out procedures utilized by BioVU [were] not yet optimal" and hypothesized that by moving to a kiosk-based electronic consent process from the paper-based consent process would improve patients' awareness of BioVU. (Brothers et al, 2013).

The current research project is intended to be an extension of the previous study, and assesses whether kiosk-based consent processes implemented in Vanderbilt clinics in January of 2013 have increased awareness of BioVU. In addition to re-measuring awareness, there was interest in measuring patients' awareness of Vanderbilt's' research practices regarding the use of other biospecimens not pertaining to BioVU (Brothers et al, 2013). These ideas were

proposed to BioVU planners to start a conversation regarding what the next survey might look like and how the research could be of use to Vanderbilt and BioVU. BioVU planners were concerned that the new questions could confuse and/or anger patients The looming confusion would potentially originate from my asking questions related to BioVU in combination with questions related to tissue research in the same survey, thus causing patients to think that BioVU involved more than just banking DNA samples collected from leftover blood drawn for routine lab testing. The anger, on the other hand, was expected to result from patients' frustration with their biological materials being used for research as well as concern, if my questions were in fact misconstrued, that Vanderbilt had not been transparent in their consent practices. It was made clear that if questions regarding the use of other biological materials unrelated to BioVU were included in the study, collaboration with BioVU planners for this project would be more difficult since the questions were seen to pose a risk to the trust BioVU planners had built within the Vanderbilt and Nashville community.

The process of informing patients of BioVU will be explained in further detail, but until then attention should be focused on how and why. It seems that BioVU planners' interests for BioVU came before patient interests. BioVU planners have drawn significant attention their initiatives to raise community awareness and support for BioVU specifically. The goals of these efforts have been to increase awareness and patient access to information. Disappointingly, the evidence of increasing rates of awareness is unconvincing, especially since patients are not presented with adequate information about what BioVU is prior

to the time of deciding whether they agree to participate. This skepticism was not unfounded since previous informal interactions with friends, colleagues, and other acquaintances with varying levels of involvement with the Vanderbilt and Nashville communities concerning the ethics of biobanking practices almost always resulted in the question: “Biobanking? What’s that?” Because these questions were coming from generally well-educated, involved members of Vanderbilt University, Vanderbilt University Medical Center, and even from medical professionals at other surrounding hospitals, it was suspected that surveying the general patient population would confirm this skepticism.

For this project, 61 adult patients were surveyed to answer the following questions:

(1) Are Vanderbilt patients aware of BioVU?

(2) Do patients actually know what BioVU is?

(3) Do patients realize their participation in BioVU?

(4) Do patients want more information?

(5) If the information is made available to them, will they access it?

The answers to these questions address the concerns that BioVU planners have expressed regarding the problem of confusion and *help to illustrate the source of that confusion*. BioVU planners have worried that giving patients too much information regarding BioVU will lead to confusion. It was hypothesized first that the confusion that BioVU planners cited as a reason to limit information is caused not by patients having too much information, but instead from having too little. In such case, is was hypothesized second that the confusion is a direct result of

BioVU planners decisions on which information is or is not necessary for patients to have regarding their participation in the project.

To address this hypothesis, this project seeks to meet three objectives: to provide a general overview of what biobanking is, address the implementation of Vanderbilt's biobanking practices, and measure current rates of patient awareness regarding BioVU. Pursuing these objectives will allow effective analysis of the current state of Vanderbilt's biobank through an ethically critical lens, followed by recommendations for how BioVU can improve patients' awareness and understanding of the project. In the context of BioVU in particular, it is appropriate to critically analyze some presumptions regarding BioVU's success, efficacy, and ethical practice. BioVU is a successful and nationally recognized DNA biobank, and it fulfills more ethical standards than is required by federal legislation. However, even in this context, the practice of informing patients of the project should not be revisited and cannot be improved.

Chapter II

Background

Biobanking

Shaw, Elger & Colledge (2014) conducted a systemic review of varying definitions of biobanks. After conducting interviews with 36 biobanking stakeholders, including project managers, pathologists, researchers, clinicians, lawyers, and ethicists, all with experience working with international biobanking, the authors found that most definitions agree that "biobanks are repositories of biological samples with accompanying linked data" (p. 226). The definition provided by the Swiss Academy of Medical Sciences (SAMS) is even more detailed. SAMS defines biobanks as "systematic collections of samples of human body substances (e.g. organs, tissue, blood, cells, etc.) and DNA as carrier of genetic information. Data that contain information on the donor (demographic data, type of disease, etc.), but also genetic data, are stored, either together with the samples or separately" (Shaw, Elger & Colledge, 2014, p. 226).

Multiple objectives underlie the goals of developing large-scale biobanks. Biobanks are developed for research purposes so that researchers have numerous samples of tissue, organs, blood, cells, or DNA at their disposal. With the samples being connected in some way to data from the participant's medical record, the intent is for researchers to be able to identify samples containing specific genomic characteristics that would be relevant to their research projects. Riegman and colleagues (2008) explain that enabling access to samples is the

key motivation in developing biobanks. Having high quality samples is the key motivating factor for inspiring large-scale multi-center research projects between varying research institutions. There were at least 179 biobanks in the United States as of 2011 according to Simon and colleagues (2011), and many hope to increase collaboration between researchers to further advance research efforts.

Ethical Concerns

Since biobanks are such a valuable resource for the advancement of research, scholars such as Widdows & Cordell (2011) state that they "require a rethinking of our ethical assumption and frameworks which have applied generally to other issues in ethics" because they are a new territory worthy of consideration (p. 207). Ethical concerns for biobanks have traditionally been related to privacy and identification of patients related to their biospecimen samples, informed consent, incidental findings in research, accountability to patients from whom the materials were derived and whether individuals whose materials have been used to develop effective treatments for their medical conditions and whether they will have access to new treatments. Biobanking is unique because it does not fit neatly into a singular focus area of medical ethics. It breaches barriers as the materials to build biobanks come from patients receiving clinical care, but the samples themselves are not classified as research subjects as traditionally defined in the realm of human subjects research. Because of this difference, the traditional standards applied to human subjects research do not apply with the same weight, especially in terms of obtaining

informed consent. This difference in common standards of informed consent in human subjects research is the key ethical problem that will be explored throughout the rest of this document.

Informed Consent

The evolution of informed consent practices pertaining to human subjects research formally after the Nuremburg Code established the first set of standard protections to be applied to research involving human subjects. The Nuremburg Code specified, “the voluntary consent of the human subject is absolutely essential” (Washington DC: US Government Printing Office, 1949). To improve and reinforce these expectations for obtaining consent from participants, the first version of the Declaration of Helsinki was drafted in 1964, expanding on the Nuremburg Code specifically to address those who may be considered vulnerable or have difficulties understanding the goals of the research they may contribute to. Since that time, As pitfalls were identified and caused problems for increasingly vulnerable persons, the Declaration has been revised and expanded.

In 1964, the Declaration specified that consent should not only be voluntary but also informed, and that research subjects should not be coerced by physicians who would benefit from the subject’s participation. It also allowed for consent to be obtained from legal guardians in cases of incompetent persons. At any time, the subject could withdrawal from the study. The revision that took place in 1989 further specified that informed consent could not be inferred from a

personal interaction between patient/subject and physician, but must be obtained in writing and/or formally documented.

The 2000-2004 revisions further began to emphasize respect and recognition for those who could not consent for themselves, such as minors and the physically and/or mentally incompetent. In such cases, consent should be obtained from legally authorized representatives. These vulnerable populations could only be included in research if and only if “the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons” (World Medical Association, 2008). The 2008 revision included that consent must be normally obtained, but may sometime be omitted in the interest of protecting the validity of a study where informed consent would compromise the outcome such as in cases of using identifiable human materials. Instead, researchers must go before a committee to have the requirement for informed consent suspended.

In the United States, protection for human subjects research is heavily influenced by the Belmont Report, which takes a principle-based approach advocating for (1) Respect for Persons, (2) Beneficence, and (3) Justice. Informed consent is addressed under the first principle of Respect for Persons, which equates to allowing participants to exercise their self-determination in choosing to participate in research studies. This requires researchers to provide appropriate information to the study’s potential participants, who may or may not choose to enroll in based on the information regarding risks and benefits provided to them before giving their consent to enroll. Human subjects research

in the United States is also guided by the “Common Rule” or HHS Regulations 45 CFR § 46 that outlines basic requirements and provisions for Institutional Review Boards, informed consent practices, and compliance. For informed consent, the “Common Rule” states at 46.116(a):

> An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence (Protection of Human Subjects, 2009).

Each subject should be provided with a statement that explicitly states the study is for research, the purposes of the research, duration of participation, description of potential risks and benefits, how records will be maintained, who to contact with questions and concerns, and the option of withdrawal or refusal at any time with no penalty to the participant.

Biobanking Meets Informed Consent

Biobanking practices regarding consent, however, are perplexing to researchers, ethicists, and regulatory officials alike since the concept is still

relatively new. Because biobanks are resources that collect samples to be used for future research, it is difficult to provide all relevant information regarding the types of studies and how exactly the collected materials may be used, if they are to be used at all. As noted by Shickle (2006) patients that agree to be participants are consenting to multiple things, such as allowing the collection of personal DNA and data, the collection of DNA and data to be used in ways other than testing, and also for research to be performed on the collected data and DNA. This can often prove to be a difficult feat in developing a more than adequate consent procedure because there is no way to describe detailed information regarding the research to be conducted on the collected materials at the time of recruitment. Despite this challenge, efforts to create successful biobanks have not been significantly affected.

To help create some standardization in approaching consent models for biobanks, biological specimens that are collected without having any private, identifying information attached are exempt from the normal provisions of human subjects research. This is possible because the Office of Human Research Protection has specified that these remains do not meet the definition of a "human subject" as defined at 45 CFR § 46.102(d):

> Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains
>
> (1) data through intervention or interaction with the individual, or
>
> (2) identifiable private information (OHRP, 2008)

Thus, it is permissible for institutions and researchers to not develop an informed consent protocol for their biobanks. However, a consent protocol is still often used due to the perceived need to "satisfy public and other stakeholder expectations for being informed and given the opportunity to refrain from research participation" (Simon et al, 2011).

Consent is gathered in one of three ways: (1) general or blanket consent, (2) opt-in consent, or, most controversially, (3) opt-out consent. General or blanket consists of gathering consent from everyone who may come through a particular health care system, including from individuals who may never become participants. This approach is seen as problematic because it is difficult to inform participants adequately of the true nature of their participation because it is possible that they will never be participants and because of the chance for confusion or misunderstanding that the consent is for future purposes as well as current research efforts (Simon et al, 2011). Opt-in consent is a method through which systems give everyone as much information as possible for the potential participants to be able to make an informed decision. The problems associated with opt-in models are comparable to those associated with general or blanket consent.

The opt-out model of consent is arguably not a method of obtaining consent, but more so of gaining assent. Upon introduction to an opt-out biobank, patients are given the opportunity to decline participation. This is the trickiest of approaches to gaining consent for a number of reasons. First, it assumes that the patients realize they have a choice and can effectively say no. In turn, it also

assumes that the person filling out the paper work is competent to opt-out if they so choose. Most importantly, the ability for the patient to make an informed decision depends entirely and explicitly on the public availability of information, especially at the time of decision (Shickle, 2006). The availability of that information is entirely the responsibility of the sponsoring institution to decide what is and is not necessary or appropriate for patients to have at, before, or after that time.

BioVU

Vanderbilt's de-identified DNA biobank BioVU utilizes an opt-out model of participation. It has had a remarkable amount of success and is one of the largest DNA biobanks in the country. BioVU planning has been an ongoing effort since 2004, and as of mid-2012, BioVU had over 150,000 samples, with 600-800 new samples accrued daily (Vanderbilt University, 2014). In the literature, BioVU is most well known for its opt-out consent model and is often referred to as a case study in the opt-out approach. In 2011, BioVU planners explained the success of their approaches while boasting their commitment to ethical biobanking practices. Vanderbilt recognizes that the Office of Human Research Protections has granted exemption status to remaining biological materials such as tissues, organs, blood, etc. under 45 CFR § 46; however BioVU planners have attempted to apply the standards of the Belmont Report to BioVU to ensure ethical research practices in recruiting participants for BioVU.

To obtain samples for BioVU, DNA is extracted from leftover blood that would otherwise be discarded. In this method, , no interaction is needed with the patient as a research subject. While these samples undergo a de-identification process, each sample is linked to data collected from the patient's electronic medical record. The de-identified data collected from the EMR is referred to as the Synthetic Derivative (SD).

In applying the standards of the Belmont Report to BioVU, program planners received a great amount of multidisciplinary input from multiple committees and boards including,: the Medical Center Ethics Committee and the Medical Records Committee, as well as creating an institutional operations oversight committee established specifically for BioVU, and a Community Advisory Board also established specifically for the project. BioVU also underwent initial review and receives on going oversight of the resource and its use by the IRB (Pulley et al, 2010, p. 43).

Each of these groups contributed to the analysis and implementation of BioVU in compliance with the principles as outlined in the Belmont Report, first beginning with how patients who identify as potential participants would be notified of the program and asked whether they are willing to participate. In order to preserve the boundary between clinical care and research participation, Vanderbilt decided to implement a separate section within the normal patient registration procedures in order to gain consent for participation. To do this, the Consent to Treatment/Agreement to Pay form was expanded to include explanations that research on tissues and other biospecimens that are collected

from medical procedures and tests may be used in research. It also explicitly notifies patients of the DNA Databank. At the time of this writing, the form stated:

> I understand and agree that any specimens or tissues normally removed from my body by VUMC in the course of surgery, or medical treatment that would otherwise be disposed of may be retained, used for educational purposes or research, including research on the genetic material (DNA) or other information contained in those tissues or specimens (Pulley et al, 2010, p. 43).

Additionally, the section referring to BioVU participation offers an option to opt-out in the language as follows:

> I also understand that if I do not want DNA research to be done using my leftover blood, I need to check the box shown below (Pulley et al, 2010, p. 43).

A check box is shown followed by text instructing Vanderbilt not to use leftover blood for the DNA databank. It was argued that the text served to "distinguish health care from research related to practices and functions that may involve data or tissues" and to also preserve the boundary between practice and research. While it is understood from a practical standpoint by BioVU planners and the supporting oversight that "the Consent to Treatment form is not always read in its entirety by patients, and sometimes not read at all", the goal was still to distinguish BioVU from other research pertaining to the use of leftover biospecimens collected during medical procedures (Pulley et al, 2010, p. 43). BioVU planners argue that they have met the requirement of Respect for Persons by making this choice available.

BioVU planners met requirements for the principle of Beneficence based on the fact that the collection of samples has a decreased risk of harm to

individuals with a maximized benefit to the broader society. If we look at BioVU from a proportionality perspective, that is if we weigh the risks and benefits against each other, the perceived risks to participants are much less than the foreseen perceived benefits in research. For instance, because privacy is a common ethical concern in the history of the development of biobanking practices, Vanderbilt has sought to eliminate that concern via the Synthetic Derivative (SD) that completely de-identifies the samples before they are stored in BioVU. This is done through creating a second database structure that creates a de-identified copy of data from Vanderbilt's in- and out-patient electronic medical record system. If researchers wish to extract certain samples based on particular data fields, they can enter them into the SD database and locate samples that they need based on that approach (Pulley et al, 2010). Thus, the threat of the common ethical concerns are avoided, therefore giving more weight to the benefits that can come from having a large-scale biobank as a resource for research.

In terms of Justice, BioVU is unbiased and nondiscriminatory in terms of sample collection. Any and all patients that are 18 years or older who experience a laboratory blood-draw and who have also signed a consent to treatment form without indicating their wish to opt-out are potential inclusions. Since there cannot be any exclusions based on social or demographic data, Justice related concerns are non-issues since "the diseases are amenable to research in direct proportion to the proportion of individuals who are receiving health care for those disease and conditions" (Pulley et al, 2010, p. 46).

Improvement

Pulley, Clayton, Bernard, Roden & Masys' analysis of BioVU intends to inform other institutions about the initiation of biobanks and the procedures that can be employed in order to protect the rights and welfare of the participating patient population while also protecting and preserving the potential success of such a valuable resource for the progress of genomic research. While BioVU planners have made efforts to inform patients of the practice and make them more aware of their involvement, they have also limited the information that patients receive about the biobank before deciding whether to participate. BioVU planners unanimously agreed that patients have a right to be informed of the project, but the degree to which patients are informed is not clear. Rid, Emanuel & Wendler (2010) express their concerns that this intuition alone raises several concerns:

> Clinical research is justified only when participants are protected from excessive risks. Yet it is often unclear whether the risks of research interventions are acceptable or excessive. Because no systematic framework exists for assessing research risks, investigators, funders, and institutional review boards (IRBs) currently rely on their intuitive judgment to make these determinations (p. 1472).

To address the problems associated with the use of intuition alone in evaluating the risks of clinical research, the authors proposed a 4-step method identified as the systematic evaluation of research risks (SERR) involving:

> (1) identify[ing] the potential harms posed by the proposed research intervention

(2) categoriz[ing] the magnitude of the potential harms into 1 of 7 harm levels on a harm scale
(3) quantify[ing] or estimate[ing] the likelihood of each potential harm
(4) compar[ing] the likelihood of each potential harm from the research intervention with the likelihood of harms of the same magnitude occurring as a result of an appropriate comparator activity (p. 1472).

This proposal was created in light of addressing intuition-based assessments of the risks posed by clinical research so that the influence of cognitive biases are minimized, thus furthering protection for potential research participants (Rid, Emmanuel & Wendler, 2010). While this method is not directly applicable to the practice of biobanking since the harm in collecting biospecimens from patients is so minimal, it does allow for the recognition of the need to revisit existing practices and procedures because the bias of those involved can inhibit abilities to recognize what is and is not harmful or is and is not appropriate.

Using quantitative and qualitative data collected from exit-interviews with Vanderbilt patients, I will show what patients know and what they expressed interest in knowing about BioVU. In doing so, I will also critique the power dynamic between BioVU planners and potential BioVU participants in that BioVU planners choose what and how much information is made available to participants. The main contributing factor to the confusion surrounding BioVU has been from how BioVU planners have decided to present the limited amount of information that was made available previously. Limiting the information that is made available to patients has been intended to address or avoid the problem of confusion, but it may actually have only made the problem worse. BioVU

planners believe that the current information available to patients helps them make decisions without burdening them with unnecessary details that may or may not be of direct interest to patients. It is here that it becomes clear that BioVU planners have exercised their own intuitions in order to make these determinations. With this bias becoming apparent, it is fair to revisit current BioVU structure and how patients are informed of the project before they become participants.

The goal of this project is not to rehash any of these debates about bias and disclosure, as most have been settled throughout the medical and bioethical communities that have been involved in the discussions. Instead, my goal is to offer a critical perspective of the process through which ethicists and researchers have come to justify biobanking “best practices” in informing patients and ensuring patient awareness of their involvement with biobanks with specific reference being made to Vanderbilt’s DNA databank, BioVU. Providing this critique will be useful not only for ongoing biobanking development efforts, but also for continuing ethical analyses that will improve the ways in which biobanks are implemented so that they can be utilized to provide better support for researchers.

Chapter III

Patient Awareness of BioVU

Methods

In April and May of 2014, I conducted exit interviews with adult patients outside the waiting areas for the Adult Primary Care Center and associated phlebotomy area who were either leaving from having their blood drawn or leaving from their appointments with their primary care providers. The survey design for this study was influenced by a previous survey instrument that was used by Brothers and his colleagues (2013) to measure patients' awareness of BioVU, awareness that leftover blood could be used for research, and support for the biorepository. Using similar methods inspired by the survey used by Brothers et al, I sought to reassess whether BioVU awareness has improved or remained stagnant and, if patients were familiar with BioVU, to identify what they knew about the project. Additionally, I wanted to ask patients whether they would be interested in having more information about BioVU and if they would be willing to access that information on a website should they have questions that could not be answered upon their first introduction to Vanderbilt University Medical Center's consent process.

These sites were chosen because they were similar to the sites selected in the study by Brothers and colleagues. The goal was to target a general sample of Vanderbilt's patient population. The sites chosen were also optimal because we were certain that every patient that came through the area had been notified of BioVU as a program and had been presented with the option to opt-out.

Additionally, these sites are some of few that had the BioVU informational brochures available to patients. When surveying, the interviewer (AS) would open by asking, “Are you leaving an appointment?” Potential participants were only eligible if they affirmed they were a patient leaving from a regularly scheduled primary care appointment or if they were having their blood drawn. I, then followed by asking, “Would you mind taking a few minutes to answer some questions for a research survey?” If the potential participants agreed to answer my questions, the interviewer the goals of the survey, the requirement for anonymity of records, and that they were free to end the interview at any time. As there was only one interviewer at any time, several potential participants could not be approached while exiting. It was not possible to record the number of people who could not be approached because it is not certain how many of them would have met the criteria as a potential participant. The interviewer did record the number of eligible persons approached whether they declined or agreed to continue with the interview. If patients agreed to participate, the interviewer continued with the survey that consisted of yes/no questions as well as some open-ended free text responses to be coded.

Results[1]

The data collected reflect the outcomes of 61 patient exit-interview surveys that were collected between April and May 2014. Of those who were approached, 100 people were eligible to complete the survey. Of those 100

[1] See Appendices for a complete list of tables and figures

people, 61 agreed to answer the questions about BioVU. When asked whether the patients had heard of Vanderbilt's DNA databank, BioVU, 50.8% claimed that had heard of BioVU. Of those 50.8%, only 25.8% expressed that they had seen some sort of advertisement for the project that they could recall. Across the population surveyed, there was an overwhelming amount of support expressed in favor of researchers at Vanderbilt using leftover, de-identified samples for BioVU research. In fact, no one expressed any feelings against research efforts. Only 13% of respondents had a neutral opinion when it came to BioVU.

Regardless of their awareness of BioVU, participants expressed an overwhelming amount of support for the research that is done by researchers that utilize BioVU as a resource. Of those who were in support of BioVU, 81% reported that they supported the use of BioVU samples because they will be used by researchers that are doing research that will lead to benefits for society. Eleven percent (11%) of participants expressed their support for BioVU in terms of their specific trust in Vanderbilt. The expression of trust for Vanderbilt is significant to the analysis of these objective findings and will be elaborated on later. As for those who expressed neutrality to BioVU, 12% stated that they felt that way because they did not know enough about the research that was being done through BioVU; 37% felt they did not know enough about BioVU in general to have an opinion; 25% were unsure of the benefits of the project; and 62% had other reasons for being neutral, such as them being in favor of research as long as their genetic materials were not used; despite the de-identification of BioVU

materials, they still expressed concerns about privacy, and worries about profits being collected from de-identified patient samples.

Despite low patient awareness of BioVU as a project, when patients were prompted to remember whether they had opted out of allowing Vanderbilt to use their leftover blood for DNA research, 48% of people said they agreed to allow Vanderbilt to use their leftover blood, 11% declined, and 41% were unable to recall their response. Additionally, when asked whether they would like to have more information made available to them 57% said yes. Ninety-one percent (91%) wanted to know how the research is benefiting the community, 85% wanted to learn more about the studies using BioVU samples, 65% were interested in learning more about the de-identification process, and 65% wanted to know who has access to the samples.

Since it was hypothesized that patients would express interest in learning more about BioVU, they were also asked whether they had heard of and would visit a BioVU website designed for the sole purpose of learning about BioVU. Prior to the creation of the website, finding specific information related to BioVU was more difficult, especially for patient populations. Only 5% of people had heard of the BioVU website. For those who had not, 63% planned to visit the website, 10% said they had no plans to do so, and 26% said they might. 73% also thought that it would be of use to them to have a feature on the website where they could ask questions about the information listed on the BioVU website should they have additional concerns.

Discussion

It was found that slightly more than half of patients interviewed were aware of BioVU, but when asked what they knew about BioVU only two-thirds of them could provide accurate descriptions of BioVU's practices. Some descriptions were more accurate than others. Some patients could recite the key factors, with the most impressive response being:

> It is Vanderbilt's collection of DNA samples that are extracted from leftover blood. They remove all personal information. They asked me about this when I was filling out my paperwork.

This participant not only realized what BioVU was, but could also recall privacy practices and where she was first notified of the program. However, while responses such as these are most desired by BioVU stakeholders, they were rare. Figure 1 illustrates respondents' confusion concerning the project is evident. Most interestingly, there were several patients that confused BioVU with Vanderbilt's personalized medicine marketing campaign. Since both projects are related to DNA, this is not that surprising. There were also others that claimed to have heard of BioVU, but then admitted to knowing nothing about it other than hearing the term. It is likely that some of these recorded responses were from people who did not want to risk looking uninformed about BioVU. Although some argue that patients' confusion over biobanking arises because of the similarity between biobanking and the collection of other biospecimens for research, I would argue that the confusion was solely related to current BioVU practice since

the interview questions related only to BioVU rather than including research using other biospecimens.

The problem of confusion is not unique to BioVU. Almost 40% of articles on biobanking in Google scholar contained the word "confusion." Although this is a rough measure, it suggests that confusion is a common concern among researchers.[2] Of these hits, the confusion being referred to differs from article to article, based on what the main focus is in terms of ethical problems of interest, be it privacy, informed consent, or normative practices and procedures regarding how the biobanks are managed.

For instance, a study conducted by Halverson & Friedman Ross (2012) found that a group of 45 self-identified African Americans were confused about biobanking practices on three accounts: (1) reasons for consenting to participation in biobanks, (2) how the research is or is not related to clinical care, and (3) mistrust and misunderstanding about the meaning of the research findings. For Knoppers (2005), confusion in biobanking is based on the language used to explain identifiability of samples and how the terms are often inconsistent with each other. Knoppers explains:

> While international bodies are more explicit in their guidance on "genetic" data, confusion still reigns due to the use of different taxonomies and overall, the failure to anticipate the need for rules for population biobanks and ongoing longitudinal studies. Moreover, the terminology used to describe samples and data is still confusion and there is no clarity (p. 9).

[2] On July 15, I went to Google Scholar's homepage to conduct an advanced search for the terms "biobanking" and "confusion" to appear anywhere in the article limited between the years of 2000 and 2014, a total of 3,100 results were found. A search for "biobanking" with the same parameters yielded 7,650 articles.

Biobanking practices are still new and in development and lacking a standardized language; however Knoppers argues for a move towards standardizing norms in biobanking to decrease this confusion.

Additionally, Hoeyer's (2008) review of the biobanking literature focuses on confusion based on the original establishment of biobanks as well as the laws that surround their practice. He explains that the "biobank problem" has been influenced by inconsistent consent requirements, and the development of new laws has contributed to considerable confusion regarding biobanks. He also notes that while there are increasing calls for harmonization of biobanking practices, it remains unclear as to who should lead the effort. E.M. Meslin (2010) speaks to this well, explaining how the varying interpretations of how the Common Rule and regulations regarding consent requirements amplify confusion in the US. However, it is also important to note that revisions that have been made to the Declaration of Helsinki and the development of the International Conference on Harmonization have "created a certain amount of confusion with respect to international standards" as well (Meslin, 2010, p. 209).

While these are only a few examples, the number of hits in the brief history of biobanking literature is nothing short of impressive. It is clear that biobanking practices are confusing on multiple accounts, both nationally and internationally. In addressing the problem of confusion, it is not my goal to address every possible issue that biobanking practices globally could develop, since most medical and research practices do elicit some level of confusion among lay people, as is their nature since this type of knowledge is embedded in

the sciences. I do not expect, nor do I propose that, we do everything necessary to avoid any confusion since this is an impossible task. Rather, I look at the problem of confusion in specific reference to BioVU.

From my discussions with BioVU planners at the beginning of this project, it became clear that confusion was a major concern. BioVU planners and others in the Vanderbilt community that identify as stakeholders expressed concerns regarding my involvement in a project that would ask patients about BioVU. Before I settled on the measures on which this project is based I had originally wanted to ask patients whether they understood that even if they declined to allow BioVU to store their de-identified DNA samples, their biological specimen could still be used for other research. It was expressed by BioVU planners that making this distinction this would potentially confuse patients and cause some unnecessary anxiety on the part of the patients.; thus my original proposal was revised.

On my alternative path of investigation, I could identify what it is about BioVU's practice that is confusing to patients. BioVU and its processes are complex and difficult to understand: even members of the Vanderbilt community who are blasted with BioVU's successes are not necessarily aware of what it is or how it works. Despite this fact, if any of them also receive their care from Vanderbilt, it is likely that they are participants. In asking those who knew, or claimed to know about BioVU, I followed with the statement: "Tell me what you know about BioVU." In using this phrasing rather than asking what patients knew

about BioVU, required patients to formulate a response and define BioVU in their terms.

When asked whether patients supported, opposed, or were neutral about Vanderbilt-collected DNA from their leftover blood samples, the support was remarkably high. BioVU's contribution to societal benefit was the biggest motivating factor cited by patients regarding their reasoning for supporting biospecimens research. Interestingly, trust in Vanderbilt also played a role in patients' support for research. With no prompting by the interviewer, 11.3% of patients suggested trust and investment in Vanderbilt as something that made them believe in the research being done. In this section of the survey, patients could list multiple reasons for their interest or disinterest in supporting research using de-identified DNA samples from BioVU. While no one overtly opposed research using leftover biospecimens, a small number of patients expressed feelings of neutrality concerning research using BioVU as a resource because they did not feel like the research either directly affected them or they did not have enough information to pass judgment. A few patients suggested that they do not necessarily oppose research done through BioVU, but they could not admit full support because they did not want their genetic materials to be used. Acknowledgement and appreciation for societal benefit was not enough to convince them to participate in the project. This response may be of the minority opinion, but it is important to note that this patient preference cannot be met by Vanderbilt's current research standards pertaining to the use of blood, tissues, or any other specimens collected in the clinical setting that fall outside the scope of

BioVU. It is this small population of patients that are identified as patients that could potentially be upset by the fact that any and all of their biospecimens can be used for research, and thus it is their trust in Vanderbilt's system that is being violated.

Trust is crucial for the success of any major research project. The creation of BioVU, and the idea that Vanderbilt should notify its patient community of the program, is founded on the notion of trust and maintaining trust between institution and the surrounding community. AS noted by Widdows and Cordell:

> If participants withdraw the biobank fails and if this happens early in the process then the substantial set-up costs will be lost and there will be no gain at all—therefore ensuring that participants and the wider public are appropriately engaged with biobanks and that trust between these groups is maintained is crucial (Widdows & Cordell, 2011, p. 215).

This threat has influenced the practices and procedures of all of the biobanks around the world. Engaging in public and community awareness practices have been useful in order to gain trust in from the community at large. Vanderbilt has done its best to create the most ethical model of practice for our opt-out system, but there is still an opportunity to improve the system that exists. BioVU's practices regarding informing or notifying patients can be improved. Rather than coddle the existing trust patients have in Vanderbilt as cited by the survey participants, Vanderbilt should strive to continue to build trust and increase its transparency of research practices and ongoing patient participation in projects patients have agreed to participate in.

O'Neill (2004) acknowledges that trust and accountability play a major role in debates regarding ethics and healthcare settings. She argues that it is often believed that:

> In a mature society…we should not take matters on trust, but rather establish robust system of accountability, so replacing trust with structures that secure proper control and reporting (p. 269).

However, O'Neill rejects the notion that trust can be eliminated from the institutional setting by way of accountability since trust will always exist at some form or level. If not at the level of patients in a medical institution, then it will be at the level of those responsible for oversight, regulations, and accountability. It does not matter that the number of "layers of control, process, measurement and informed consent we add, we have in the end to decide whether to place—or refuse—trust" (O'Neill, 2004, p. 271). Therefore, the important issue at hand is that Vanderbilt needs:

> …To consider which forms of accountability best support which relations of trust. (…) The would-be eliminators of trust are neither accurate nor coherent when they suggest that all trust must be blind trust and so should be eliminated. The serious question is how we can support well-judged trust that enables people to gain enough evidence—never, and necessarily never, total evidence—to judge whether to place or refuse trust. What would it take for us to have forms of accountability that allow people to make intelligent and informed judgments about where to place their trust? (O'Neill, 2004, p. 271)

For BioVU to fully respect the trust that they so heavily claim to value, then they must fully recognize their accountability as the persons that Vanderbilt has entrusted to allow potential participants, Vanderbilt patients, to make an

intelligent and informed decision. To this point, it can only be argued that very few patients, based on the evidence that I have collected, are informed in making that decision.

Of nearly half of the patients interviewed who acknowledged having heard about BioVU, 41% could not remember whether they agreed to participate. This is problematic for BioVU planners because patients cannot recall their status as participants in the project. If BioVU planners want to advocate that patients are aware, then it should be easier for them to remember whether they agreed. The ease in forgetting about participation in the project could be attributed to the brevity of information with which BioVU is introduced and limited time in which patients are asked to fill out general paperwork for the first time. At the time of deciding whether to opt-out of BioVU, patients are presented the box shown in Figure 2.

To this point, BioVU planners have been operating from the standard of the reasonable person in addressing informed, opt-out consent. The reasonable person standard serves as the foundation of informed consent policies, and practice in medicine is sourced from law. According to this standard, it is required for information to be disclosed as “determined by reference to a hypothetical reasonable person”. In medicine, whatever a reasonable person would want to or should know about potential risks of medical procedures should be disclosed. As noted by Beauchamp and Childress, this standard is not so well developed that it is able to avoid encounters with conceptual, moral, and practical difficulties since no one has been able to carefully define exactly what a “reasonable person”

looks like. This abstraction makes it increasingly complex for physicians, researchers, and project managers to really discern what a reasonable patient should be told (Beauchamp & Childress, 2009, 123).

Often it is the case that, unless otherwise specified by federal or institutional policies and regulations, the responsibility of discerning what information is necessary for patients or researcher subjects to know falls on those who take ownership of the consent practice. This is precisely what has happened with BioVU. Since the general consent procedures that apply to human subjects research, as explained earlier, do not apply to biobanking practices, BioVU and other biobanking planners alike have the freedom to determine what their potential recruits get to know prior to their participation.

In the case of the current consent language, very little is shared prior to patients approaching the kiosks on which the document appears. Since the launch of kiosk-based paperwork in Vanderbilt clinics, opt-out rates have increased. In 2007 opt-out rates were at approximately 5%, but in 2013 after the 2012 launch of the kiosks the opt-out rates increased to nearly 16% for the adult patient population. It is not clear to BioVU planners and stakeholders why these rates have increased so significantly, but a few explanations can be inferred. Prior to the kiosks, patients were presented with the same paperwork by a person and may not have read through the paperwork with the same attention. The most positive assumption is that patients assented to participation in BioVU because of their trust in Vanderbilt. However, the kiosks make disclosures more visible to patients, thus helping patients pay more attention to what they are

actually signing. Since the BioVU document is more visible than it was previously, those who are opting out are likely doing so for one of two reasons: (1) they understand what BioVU is and do not want to participate or (2) they do not fully understand and say “no” because they are unsure of what exactly they are agreeing to. If patients are opting out due to the latter, those are the patients that require more information to make an informed decision. It could be the case that if they were given more information, they may choose to participate, thus benefiting BioVU’s goals.

Weir (2004) asks two questions when discussing the “Reasonable Person Standard of Disclosure” in the context of storing human biospecimens for use in genomic research:

> (1) What information should be disclosed to prospective participants so that they will know a research study involves DNA banking?
> (2) What information should be disclosed to prospective participants about a research team’s DNA banking practices so that they will have a sufficient understanding of the long-term implications of providing a blood or other tissue sample for a study? (p. 239)

Weir argues that informed consent literature has not focused on concerns about appropriate disclosure and consent involving the use of tissue samples derived via surgery and various clinical tests that are banked to be used indefinitely for research purposes which may or may not have to do with the reasons why the tissues or biospecimens were obtained from patients in the first place. The argument presented here is that the reasonable person standard is the most appropriate standard to apply to consent practices based on common general assumptions of minimal competency of information, prescriptively identifying risk

and liability, and also reflecting self-determination. In the context of biobanking research, the reasonable person standard applies to what concerns or questions a reasonable person may or may not have in the context that he or she may be agreeing to provide a blood sample to be stored in a biobank. Weir identified eight interests and concerns that should be included in the information given to reasonable persons "placed in the situation of a prospective research participant":

(1) Will my tissue sample [my DNA sample] be identified or traceable to me when it is being studied in the lab?
(2) What are the chances that information derived from my stored sample will get into the wrong hands?
(3) It is my tissue sample, right?
(4) Can I withdraw my personal involvement from this research study at any time?
(5) How long do you plan to keep my banked sample?
(6) If you find out something clinically important about me from my banked sample, will you tell me?
(7) Will other people have access to my DNA sample and data in the future?
(8) Will you or other scientists use my stored tissue sample for secondary research studies with different purposes? (Weir, 2004, p. 244)

The answers to these questions are what would satisfy the reasonable person standard in terms of biobanking research, especially since these would also serve as the appropriate standard to hold to which investigators should be held if they were to be collecting materials directly from participants for specific research studies.

Following this standard of consent in biobanking practices would classify as the gold standard. However, as expressed previously, this is not by any means the standard across the board. BioVU does answer all the questions in ways that are available to patients, but which are difficult to locate. BioVU can advocate that it makes information available to patients, and the website only adds to this availability, but the order of events that occur in communicating that information is not necessarily well managed. Based on the data collected, BioVU planners have failed in keeping patients aware of both BioVU as a project let alone their involvement with it.

BioVU currently does not meeting the standard for adequately informing members of the general patient population of their involvement in BioVU. Additionally, based on the results of this survey, there are a significant number of people who fall under the category of lay patient populations who express interest in having more information when the topic is explicitly brought to their attention. It is apparent that BioVU's interests for potential participants are not consistent with actual patient interests. This is not to suggest that the information has not been available, but it has not been accessible or easily delivered to patients. For instance, a person filling out the general paperwork for the first time may have a specific question regarding how the information is de-identified so they may assess whether they trust the methods that are being used. While front desk staff has been prompted to give them the brochures that cover the most common questions, the brochures contain limited information. Additionally, patients may not even be aware that they can ask more specific questions. In

fact, it would potentially be more beneficial to BioVU to provide more adequate information because some patients will say no simply because they do not have enough information and are not presented with ample opportunity to express their questions or concerns.

Information at the time of decision-making is limited, and can easily be forgotten. However, when presented with the option of having more information about BioVU, 57.4% said they would be interested. While this is not everyone, this is enough of an interest for it to be worth it, on the part of BioVU planners, to make information more accessible to patients. Svalastong, Allgaier, Martinelli & Gajovic (2014) have explained that public discussions, engagement, and dialogue between science and society are crucial for successful, sustainable projects that lead to important scientific advances being developed. Knowledge that is shared about complex and potentially controversial topics is constantly being developed, and the Internet is a useful resource that allows a lot of information to be made readily available to the public. BioVU recognizes this and has been motivated to make information that was previously inaccessible to patient populations available on the website. Many of the patients interviewed were interested in having additional information. As the results show, there are enough people interested in knowing more that merit BioVU's efforts to create an easily navigable, intelligible website.

The creation of this website has definitely been a step in the right direction, but there is still more that we can do. In order to be more effective BioVU should further embrace the fact that "communication is not a one way street but ideally a

dynamic dialogue that produces new insights into the issues" (Svalastog, Allgaier, Martinelli & Gajovic, 2014, p. 55). Since BioVU planners have placed value in public acceptance of the project they also should recognize that public acceptance of scientific knowledge is key to legitimacy in the process of decision-making. Creating better opportunities for dialogue would be more valuable than simply creating a website that places information out there for those who may be interested in learning more. However, as Svalastog, Allgaier, Martinelli & Gajovic argue,

> The delegation of public communication of innovative scientific knowledge to public relations experts adds a further source of distortion of the communication process. Although communication aims at dialogue, this is frequently not achieved due to the variety of communications involved and their different goals (p. 54).

When space is actually created for dialogue, it is here that legitimization of the decision-making process can occur. With the current set-up, BioVU's consent process does not allow much of a dialogue. Should patients express any interest or concern regarding their participation at the time of decision-making, they are not presented with enough information unless they ask someone at the front desk, whereupon they will be provided a brochure like the one shown in Figures 3.1 and 3.2, which provides vary basic information in a question and answer format. The need for this brochure could be decreased if BioVU planners give more information that a reasonable person would want to know when Figure 2 appears on the kiosk screen.

Chapter IV

Conclusion

Since nearly half of the patients interviewed for this project were unaware of BioVU, BioVU should consider taking a new approach in raising patients' awareness of the program. The intention to implement and maintain an ethical biobanking procedure should be applauded, but there is room for improvement. Confusion, trust, and giving patients the information necessary to make an informed decision concerning their agreement to participate in BioVU have been themes throughout this analysis, all of which can be easily addressed by giving more information to patients at the time of making their decision to participate in or opt-out of BioVU. Brochures, advertisements, and website access do only so much to inform patients of the project, especially since this information is only found if the patient goes looking for it after accepting or declining participation.

Based on the number of survey respondents patients who were interested in having more information about BioVU, it would not be a wasted effort to offer more information before they are presented with the consent language at the kiosk. Rather than propose a drastic restructuring of BioVU procedures, it is more appropriate for BioVU to take these results into account and seriously consider revising the consent language as if BioVU were operating from an opt-in model. The electronic documents should be treated as such so that patients are truly given a convenient opportunity to make an informed decision regarding their participation in BioVU.

Since the rates of general approval for research using leftover biospecimens were so high, it can be expected that the opt-out rates will not change much. In fact, providing slightly more information may be beneficial to BioVU if the opt-out decrease is due to an increase of patient understanding of what BioVU is and what it does. Even if the opposite is true, BioVU and Vanderbilt should be able to take pride in the fact that they are able to deliver the information necessary for patients to make autonomous, informed decisions.

The kiosk-based consent language should expand beyond simply notifying patients that their leftover blood will be used for DNA research in BioVU. At the very least, it needs to be stated that:

(1) BioVU is Vanderbilt's DNA biobank

(2) Leftover blood samples will be used to extract the patient's DNA

(3) A de-identified record of the patient's medical history will be linked to the sample

(4) The samples will be stored indefinitely to be used for research

This information is present both in BioVU brochures and on the BioVU website, but is not conveniently available without patient prompting, assuming that front desk staff are available at the time. While it is true that there will be many patients that do not care about whether their materials will be used for research, nor are interested in this seemingly excess information, it is most fair to everyone if this information is presented for those who will want it.

Appendix

A. Tables

Table 1. Patient Awareness of BioVU		
	Yes	No
Have heard of BioVU	50.8%	49.2%
Have seen BioVU advertisements	25.8%	74.2%

Table 2. Opinions About Using Leftover Blood for Research	
Support	86.9%
Oppose	0%
Neutral	13.1%

Table 2.1 Reasons for Supporting BioVU Research	
Research might benefit me or my family someday	9.4%
BioVU samples will be used to benefit society	81.1%
I trust research being done at Vanderbilt	11.3%
The collection of genetic samples will help scientists conduct research on why some people get sick and others don't	17%
Other	13.2%

Table 2.2 Reasons for Neutrality Towards BioVU Research	
I do not know enough about the research being done by BioVU	12.5%
I do not know enough about BioVU in general	37.5%
I am unsure how this will benefit me or society	25.0%
Other	62.5%

Table 3. Information Patients Desire About BioVU	
How research is benefiting the community	91.4%
The studies that are using BioVU samples	85.7%
How the samples are de-identified	65.7%
Who has access to the samples	65.7%
Other	2.9%

B. Figures

Figure 1. What Patients Knew About BioVU

"Vanderbilt uses left-over blood to extract DNA to be used for research."

"It is a DNA bank at Vanderbilt."

"They use my blood, but don't know what for. If Vanderbilt asks for it, they can have it."

"It is Vanderbilt's collection of DNA samples that are extracted from left-over blood. They remove all personal information. They asked me about this when I was filling out my paperwork."

"Participants are enrolled on a voluntary basis when blood is drawn, DNA is extracted and put into a database after being stripped of identifying information for research purposes."

"Vanderbilt asks permission to collect DNA for research."

"Just heard about it, but I don't know what it is."

"I have heard of BioVU, but I don't know much about it."

"I signed a consent form for [Vanderbilt] to use leftover blood specimens for research."

"[Vanderbilt] takes leftover blood to save for research."

"I signed something saying its okay for [Vanderbilt] to use extra blood for something."

"They take leftover blood samples and do studies with it after removing identifiers."

"[Vanderbilt] uses it to study DNA."

"[Vanderbilt] saves blood for testing for research."

"They use leftover blood to collect DNA and [Vanderbilt] de-identifies it."

"I signed a form and gave consent for leftover blood to be used for research."

"Leftover blood is used to help further research."

"[Vanderbilt] uses excess blood for DNA research."

"They are trying to collect people's DNA to be used for research. The DNA has been de-identified."

"It is a DNA bank that I signed a form about."

"I didn't know it was called BioVU, but I signed a waiver giving the project permission."

"I know nothing except that I agreed to have samples taken that are submitted to the DNA databank."

"I know nothing. They asked if they could use my DNA for something."

"I signed a sheet of paper saying they could use my blood for something so [Vanderbilt] could show me compatible drugs."

"Mapping process to pair drugs and different therapies to individuals."

"Vanderbilt is trying to figure out people's DNA so they can help find treatments for specific individuals."

"I received a letter telling me about some of the research being done at Vanderbilt and I read about it there."

"Saw the information on the brochure."

"Not much, just heard of it."

"I have only heard of it, but don't know what it is."

G.

Figure 2. BioVU Consent Language

BioVU Form:

DNA Research:

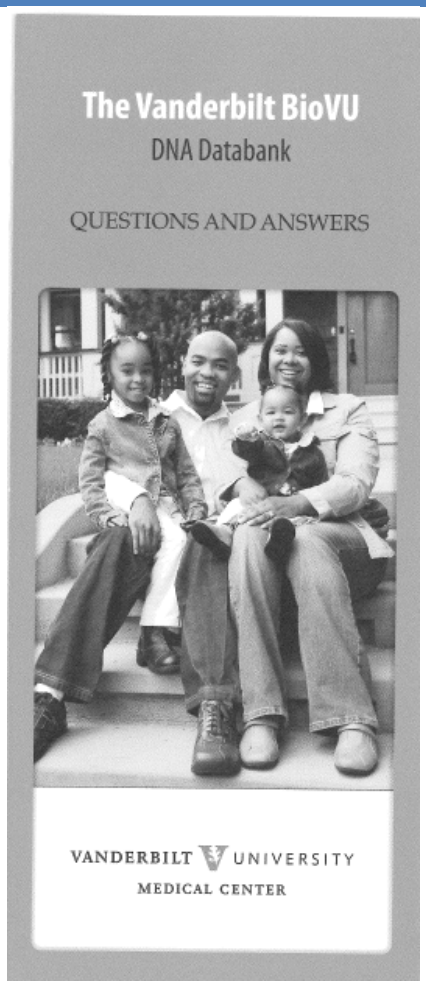
Leftover blood from tests, treatment, or surgery may also be used for DNA research through the Vanderbilt **BioVU** Program. If I do not what my leftover blood to go to the Vanderbilt BioVU Program for DNA research, I must check the box below. If I have questions or want further information on **BioVU**, I may call 866-436-4710.

☐ I do NOT want blood left over from tests, treatments, or surgery to be used for th Vanderbilt BioVU Program for DNA Research.

Patient/Legal Representative_____Date_____
(Relationship to Patient)_____

H.

Figure 3.1 BioVU Brochure 2014 (Front and Back Covers)



I.

Figure 3.2 BioVU Brochure 2014 (Inside Information)

VANDERBILT BIOVU

QUESTIONS AND ANSWERS

1. What is the Vanderbilt BioVU Program?

We are collecting DNA from adults and children who are patients at Vanderbilt to learn how differences we inherit affect health. Learning more about this could help us to improve health care for everyone.

2. What is DNA?

DNA is how people store information we inherit from our parents that directs how we grow and develop. The information is contained in pieces called genes.

3. How does Vanderbilt get DNA from patients?

When blood is drawn from a patient, it is used for the tests that were ordered. We get DNA from the blood that is left over after the tests are done. This blood would normally be thrown away.

4. What will Vanderbilt do with the DNA?

The first thing Vanderbilt will do is to put a code on the DNA and then enter it into a specially protected computer. This computer can then match the DNA with information about the person's health that is contained in the medical records here. Researchers will not be able to tell who the information applies to, because the code removes the information about the DNA that would identify it with one single person. But researchers will be able to study how differences in the genes affect health. Researchers may sometimes send the DNA to another Vanderbilt-approved institution or facility for research related services, such as doing a laboratory test to find particular genes in the DNA.

5. Will anyone know that this is my DNA?

NO. No one will ever know who the DNA belongs to. Vanderbilt researchers, insurance companies, employers, and law enforcement agencies will not be able to get information about a any one person's DNA. The purpose of putting the code on the DNA is to make sure that each person's privacy is protected.

6. How does Vanderbilt tell me about this program?

Patients treated at Vanderbilt are given forms that tell them about the project and how they may opt out, if they choose. There are also brochures and posters located in patient areas. If you have questions, you can call 866-436-4710.

7. What if I do not want my DNA to be used this way?

You may check the box on the opt-out form or call 866-436-4710 to opt out. We would like to collect all leftover blood but recognize that some people will not want their blood used. If you feel this way, you can simply opt out. Your doctors will not know if you opt out, and you will get the same care either way. If you opt out, our computer system will remember this choice and will prevent your blood samples from being used for research.

8. Will someone let me know if something different is found in my DNA?

NO. Because we will not know whose DNA is whose, it will be impossible to give anyone results about his or her DNA. On the other hand, we hope that learning more about how genes work will help make everyone's health care better, including yours.

9. What other concerns do people have?

Some people have worried that DNA could be used for cloning. This project does NOT involve cloning. Some people have wondered if it requires taking more blood. It does NOT require the drawing of any additional blood. Others have wondered if there is an extra cost. You will NOT have to pay anything extra.

10. Who makes sure Vanderbilt is using the DNA the way they are supposed to?

This project will be watched over by three groups: (1) our research review board; (2) a separate group of scientists, ethicists, and people who work at the medical center; and (3) a group from the community.

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