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Ethical implications of using biobanks and population databases for genetic suicide research

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Abstract

This article provides a review of the ethical considerations that drive research policy and practice related to the genetic study of suicide. As the tenth cause of death worldwide, suicide constitutes a substantial public health concern. Biometrical studies and population-based molecular genetic studies provide compelling evidence of the utility of investigating genetic underpinnings of suicide. International, federal, and institutional policies regulating research are explored through the lenses of the ethical principles of *autonomy, beneficence, non-maleficence*, and *justice.* Trapped between the Common Rule's definition of human subjects, and the Health Insurance Portability and Accountability Act's protected information, suicide decedent data occupy an ethical gray area fraught with jurisdictional, legal, and social implications. Two avenues of research, biobanks and psychological autopsies, provide tangible application for the ethical principles examining the risks to participants and their families. Additionally, studies surveying public opinion about research methods, especially broad consent, are explored. Our approach of applying the four ethical principles to policy, sample collection, data storage, and secondary research applications can also be applied to genetic research with other populations. We conclude that broad consent for secondary research, as well as next-of-kin at the time of autopsy, serve to satisfy privacy and confidentiality under the ethical principle of *autonomy.* We recommend ongoing ethical evaluation of research policy and practice.

Keywords

epidemiology; ethics; federal policy; genetics; HIPAA; suicide

1 | INTRODUCTION

According to the World Health Organization, nearly 800,000 people die of suicide annually (World Health Organization, 2017). Suicide is a global phenomenon, with 78% of suicide deaths occurring in low-income and middle-income countries in 2015 (World Health

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CONFLICTS OF INTEREST

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Organization, 2017). In the United States, suicide presents the 10th leading cause of death and the suicide rate has been increasing on a consistent basis (Kochanek, Murphy, Xu, & Tejada-Vera, 2016). This has been the case across age groups with an alarming rate increase for adolescents (Murphy, Mathews, Martin, Minkovitz, & Strobino, 2017). Given the prevalence and rising trend of its occurrence, suicide presents a critical public health concern requiring further research and prevention efforts.

Research on the environmental and genetic basis of suicide has confirmed that risk for suicide has a significant genetic component (Brent & Mann, 2005; Coon et al., 2013). Human subjects research including biometrical and molecular genetic studies of suicidal *behavior* have already been a focus of the scientific research community (Althoff et al., 2012; Roy & Segal, 2001; Roy, Segal, Centerwall, & Robinette, 1991). However, genetic investigation of postmortem tissue samples from *suicide death* cases have been rare. This type of analysis is useful when combined with population database records including familial history and medical records (Coon et al., 2018). Historically, this type of study has not been considered "human subjects" research, as decedents are not considered human subjects. However, due to growing concerns regarding consent, privacy, and confidentiality for biologically related individuals in the context of an era of increased digital documentation, the scientific community is calling for increased regulation and protection. This article reviews ethical barriers to research on suicide decedents, as well as on surviving family members who may share genetic and environmental precursors. Discussion includes a review of ethical principles and research regulations as well as application of these considerations to the forums of biobank and psychological autopsy research with suicide decedents. Genetic researchers may use the approach detailed here when applying ethical principles to other populations.

2 | ETHICAL PRINCIPLES AND CORRESPONDING POLICY RELATING TO GENETIC RESEARCH OF SUICIDE

In considering the ethical implementation of suicide genetics research efforts, it is helpful to begin with the four major ethical principles that provide the foundation for human subjects' research: *autonomy, beneficence, non-maleficence, and justice* (Beauchamp, 2001; Lynch, 2002). Autonomy pertains to an individual's choice to participate in research and requires an assurance of *privacy* and *confidentiality* (Beauchamp, 2001). *Privacy* is the right of an individual to choose which information they wish to share about themselves, which includes *consent. Confidentiality* protects identifying markers of the individual from unauthorized persons. We make a case in the following paragraphs that the standard of *autonomy* presents the greatest risk to participants in genetic research. Because *autonomy* includes the issues of *privacy*, *consent*, and *confidentiality*, it is here that the clinical researcher must be aware of related study design, data sharing, and data access issues.

Beneficence refers to the moral obligation to benefit others, while *non-maleficence* is the obligation not to harm others (Beauchamp, 2001). Finally, *justice* pertains to the equal opportunity to participate in and benefit from research. These final three principles are especially important in the consideration of research on vulnerable populations (Beauchamp,

2001; World Medical Association, 2013). While not designated as vulnerable populations by U.S. policy, (a) individuals at risk for suicide (e.g., relatives of decedents, or individuals with severe major depression) and (b) individuals who have died by suicide (decedents) demand attention to a complex web of ethical considerations.

3 | REVIEW AND UPDATES OF REGULATIONS GOVERNING HUMAN SUBJECTS AND GENETIC RESEARCH

3.1 | Declaration of Helsinki

Current U.S. policy for human subject research is historically rooted in international policy as well as decades of ethically impoverished research in the mid-20th century. With its most recent amendment in 2013, the Declaration of Helsinki details ethical standards for safe and fair treatment of research participants. In addition, it delineates ethical reasons for conducting research such as understanding "the causes, development, and effects of diseases" and improving "preventative, diagnostic, and therapeutic interventions" (World Medical Association, 2013). The Declaration also makes specific provisions for research with vulnerable populations (World Medical Association, 2013). The primary focus of the Declaration and of the following federal regulations is to protect participants from harm and to reduce the risks to which they are exposed. Awareness of these regulations across the international research community helps to protect research participants as well as their families.

3.2 | Common rule

Currently the principal federal regulation governing human subjects research is 45 CFR 46 from the Department of Health and Human Services. 45 CFR 46 Subpart A, also referred to as the Common Rule (Hakimian, National Cancer Institute, & National Institutes of Health, 2004), makes provisions for human subjects research including what constitutes a human subject (United States Department of Health & Human Services, 2016). 45 CFR 46.101 (b)(4) delineates that the study of "existing data, documents, records, pathological specimens, or diagnostic specimens" is not considered human subjects research provided that the data are either publicly available or are de-identified (Hakimian et al., 2004; United States Department of Health & Human Services, 2016). Thus, the ethical standards of *autonomy, beneficence, non-maleficence*, and *justice* do not need to be satisfied by the same strict standards applicable to human subjects research.

Although instituted in 1991, the Common Rule has not yet been updated to address technological advances or newer regulations such as the Health Insurance Portability and Accountability Act (HIPAA). The first updates to the Common Rule took effect on January 21, 2019 (United States Code, 2017). The major changes of the updated Common Rule include tailoring informed consent procedures to better benefit both participants and researchers, using broad consent for sharing and secondary use of identified biospecimens, streamlining institutional review board (IRB) oversight, and reducing burdensome review procedures for low-risk research (Hodge & Gostin, 2017; United States Code, 2017).

With these changes, data from banked biospecimens are now more readily available for research. As genomic research is critical for our understanding of risk for suicide and suicide behaviors, the Common Rule's increased clarity on biospecimen research could be a boon for suicide research efforts. But it is complicated: the updated rule does not address regulations for research of those who are most implicated—suicide decedents—who are not currently defined as human subjects by either the Common Rule or HIPAA.

3.3 | Health Insurance Portability and Accountability Act

HIPAA, another federal regulation, protects identifiable health information by making explicit provisions for *privacy* and *confidentiality,* which are ethical domains within the principle of *autonomy.* While human tissue samples are not definitively delineated within HIPAA, data associated with tissue samples are often considered protected health information (Hakimian et al., 2004). Use of that protected information requires study-specific participant consent (Wendler, 2006b). This HIPAA requirement can be waived, however. 45 CFR 46 makes provisions for expedited review of human subjects research if the research presents no more than minimal risk, or the research conducted is only slightly modified from previously approved research conducted within the last year (HHS, 2016). This, combined with additional procedures of ethics committee approval, as well as with a waiver of study-specific authorization, serve to satisfy the HIPAA requirements for study-specific participant consent (Wendler, 2006b). This effectively downgrades the requirement to broad initial consent, which acknowledges data sharing and secondary uses. Broad consent is less rigorous than study-specific informed consent; therefore, the clinical researcher may inherit data through sharing initiatives and never engage in consenting procedures with the participants directly.

Additional HIPAA provisions protect the health information of individuals for 50 years following death (United States Code, 2016). Thus, while not considered as human subjects by 45 CFR 46, certain types of decedent data are still protected by HIPAA. This series of procedural hurdles further highlights the legal gray area between human and non-human subjects research. Once again, the question of risk to study participants becomes salient. These policies provide a confusing ethical quandary to the clinical researcher in suicide genetics, whose data may include primary and secondary sources, as well as a mix of human subjects and non-human subjects.

3.4 | National Institutes of Health Genomic Data Sharing Policy

The governmental protections set forth in the Common Rule and HIPAA, however, have been surpassed in rigorousness by a trend in individual organizations which facilitate genetic research. Requirements from the National Institutes of Health Genomic Data Sharing Policy (GDS) provide one of the most notable examples for research conducted within the United States. While these only apply to certain NIH-funded research efforts, the NIH policy provides an example of a higher standard. The policy strives to enforce the ethical principle of *autonomy* on the use of genetic material, which is legally considered non-human subjects research (National Institutes of Health, 2014). Effective in 2015, GDS Policy requires researchers to maintain the standard of de-identification of data present in the Common Rule

as well as “to obtain participants’ consent for their genomic and phenotypic data to be used for future research and to be shared broadly” (National Institutes of Health, 2014).

While failing to rise to the study-specific standard of informed consent, as noted above, broad consent provides a level of autonomy in participants’ authorization to use their samples in future studies. Broad consent gives participants more autonomy than a waiver of consent (e.g., HIPAA waiver noted above) but less control than study-specific consent. The issue of broad consent as a research standard serves to further highlight the ethical quandaries faced by researchers when banked genetic material is acquired through means such as an autopsy or when phenotypic and demographic data is compiled by state government under statutory authority.

4 | SUICIDE DECEDENT RESEARCH: MEDICAL AUTOPSY

Acquisition of postmortem tissue samples by a medical examiner (ME) is often the means by which genetic research on death by suicide is conducted. The legal foundations regarding the use of biological samples in medical or forensic autopsy largely rely on statutory authority, which varies by state. Through an autopsy, the ME, coroner, or doctor acts in the public’s best interest by preventing further harm to others and/or satisfying the demands of justice (Lynch, 2002). ME offices often possess jurisdiction over suspicious deaths, which include suicide (Moore, Majumder, Rutherford, & McGuire, 2016). Frequently the samples acquired during an autopsy are stored under the auspices of promoting public health by creating potential for further genetic investigation which could yield new scientific insights (Moore et al., 2016). Such insights from secondary research could bolster suicide prevention efforts.

This use of samples from decedents for additional research, however, also delves into the more complex ethical gray area of the three subsets of *autonomy*: *privacy, consent*, and *confidentiality.* Many European countries and U.S. states permit the use of biobank and coroner’s data for secondary research if the data are irreversibly de-identified (Elger, Hofner, & Mangin, 2009), which only satisfies the issue of *confidentiality.* In large part, this is to prevent stigma and discrimination against living relatives of the decedent, who conceivably share a significant portion of the same DNA and therein have a privacy interest in how data are collected and used (Moore et al., 2016). However, de-identification does not address the *privacy* rights of the decedent or the issue of *consent.*

To address this, the ethical conversation is beginning to emphasize procuring consent from family members for secondary research on biological samples from decedents, as recommended by the National Association of Medical Examiners (NAME), the National Institutes of Health’s Genotype-Tissue Expression (GTEx) program and GDS, and the Swiss Academy of Medical Sciences (Elger et al., 2009; Moore et al., 2016; National Institutes of Health, 2014). Consent at the time of autopsy permits family members to endorse to what extent they wish to relinquish the right to privacy of the decedent’s biological material and will also allow family members to make their preferences known if evidence of a severe genetic risk is discovered, which helps satisfy the ethical quandary of duty to warn (Moore et al., 2016).

However, the practical limits of acquiring consent, such as ability to notify all family members with genetic interest of each research project, remain an area of contention. There are different definitions of who constitutes family for the purposes of authorizing research with decedent data. HIPAA regulations permit the personal representative of the decedent's estate to consent (HHS, 2016). NAME does not specify who constitutes "family" in their position paper (Middleton et al., 2013). GTEx, like HIPAA, recommends that the decision to consent is left to the "next-of-kin," which in a legal sense is the personal representative of the estate (Lonsdale et al., 2013). Ultimately, having a single point person to consent to broad use of the decedent's data for research provides more *autonomy* to the family than do consent waiver processes but less autonomy than contacting multiple family members of the decedent who may share genetic material.

5 | SUICIDE DECEDENT RESEARCH: BIOBANKS AND PSYCHOLOGICAL AUTOPSY

Legal and ethical considerations for suicide genetics research find practical application in two arenas: the biobank and the psychological autopsy. Each of these will be discussed, first in terms of the set-up and methods of each, then in relation to the four ethical principles (see Table 1), and finally in the context of public opinion. While a given research project may only utilize one of these resources, the ethical argument in support of research on suicide decedents is informed by an amalgamation of considerations from both.

5.1 | Biobanks

5.1.1 | Set-up and methods—Seen by many as beneficent to public health (O'Doherty et al., 2016; Porteri, Pasqualetti, Togni, & Parker, 2014; Wendler, 2006a), biobanks are comprised of genetic, phenotypic, and demographic data collected from diverse sources. These can include material collected from decedents during autopsy, donations from living patients with specific diagnoses such as cancer, and information from the general public (Mee et al., 2013; Murphy et al., 2009; O'Doherty et al., 2016). Regulations on biobanks vary, but common practice requires that research be subject to a thorough vetting process via an ethics committee, the data used for research be de-identified, and minimal risk be posed to those who have contributed samples (Wendler, 2006b). Such practices satisfy the requirements of the Common Rule and HIPAA, but do not necessarily achieve the standards set forth in the institutional policies discussed above.

5.1.2 | Ethical considerations—While legally appropriate, biobank research presents a persistent ethical dilemma related to *autonomy* due to issues of *privacy, consent*, and *confidentiality.* For living persons contributing samples for the first time, *privacy* and *consent* are together addressed through (a) an explanation of what information can be gleaned from the samples (*privacy*), and (b) each person's acceptance of a broad range of research interests for which the samples may be used (*consent*) (Murphy et al., 2009).

However, as noted above, broad consent does not meet the study-specific criteria set forth in HIPAA without several additional steps (Wendler, 2006b) nor does it satisfy ethical considerations related to individual choice regarding participation in the type of research

which may be conducted in the future. For example, four major biobanks were established in Ireland with the initial purpose of studying cancer (Mee et al., 2013). Expanding research objectives demonstrated a problematic use of broad consent, as many subjects did not wish to contribute to other medical interests, such as mental health research, but had already waived this right through acceptance of broad consent (Mee et al., 2013).

Irrespective of the type of consent, however, *confidentiality*, another component of *autonomy*, may remain the greatest risk of harm to participants. Improved technology continues to increase the risk that de-identified samples can be re-identified (National Institutes of Health, 2014). This could jeopardize confidential information either associated with the tissue samples or with risk identified via exposure of the genetic information of an individual.

Unlike *autonomy*, the remaining three ethical principles have neutral to positive implications for biobank research (Table 1). Both living individuals who have contributed to biobanks and the general public largely receive *beneficence* from the research efforts in the form of improved treatments and medications for multiple health conditions such as cancer and cardiac arrhythmia (MGH, 2017; University of Utah Health, 2017). *Maleficence* traditionally pertains to the risk of physical or mental harm to research participants. However, with bio-bank research, little risk of physical harm exists as data collection is often minimally invasive (Murphy et al., 2009). Finally, the ethical concern of *justice* continues to be better addressed as more people contribute to biobanks and as research findings are translated into actual interventions for public health across diverse communities. Increased global research efforts also further the potential for making access to the benefits of research more equitable. Applied in this context, an ethical argument begins to take shape that collective public benefit outweighs the present concerns of individual *autonomy*, especially when broad consent from the individual, or their next-of-kin, has been obtained.

5.1.3 | Public opinion—Public opinion of biobank research is often overlooked in the larger conversation among lawmakers and ethicists. However, multiple surveys have been conducted by researchers worldwide to assess both the public's general willingness to participate in biobank research as well as public opinion regarding their preferred level of consent. Seventeen of 20 studies found that at least 80% of respondents would be willing to participate in a biobank (Wendler, 2006a). A more recent review of 13 additional studies has observed a range of 34–96%, with an average of 59%, of respondents in favor of participating in a biobank (Johnsson et al., 2010). Although the average consensus of public opinion is positive, it remains clear that there is variability in the willingness to participate. Thus, it is at this level where an individual's right to *autonomy* is most relevant. With the exception of government-mandated autopsies, individuals are not compelled into participation in genetic research. An individual can best exercise dissent from participating in genetic research by never opting in.

Once subjects have agreed to participate in biobank research, the concern of the level of *consent* becomes relevant. Multiple studies assess the issue of the public's preference regarding level of consent with broad consent providing the most general option and study-specific informed consent providing the most limited option. These studies provide mixed

results. The investigation of Mee et al. into the four Irish biobanks showed that only 4 of 363 patients opted to be reconsented for each additional study which left 98.8% of participants authorizing broad consent (Mee et al., 2013). Wendler's (2006a) review of 30 studies on the topic yielded the combined results that 75–95% of those surveyed would be willing to provide one-time broad consent with the assurance that ethics committees would vet future research proposals (Wendler, 2006a). The most divided study regarding level of consent came from a U.S. study of 4,659 individuals broken into focus groups throughout the country that yielded a fairly equal split between those in favor of broad (48%) and specific (42%) consent (Murphy et al., 2009).

Public opinion, while not unanimous, generally supports researcher preference for broad consent. Additionally, public opinion cites concerns held in common with researchers such as the inconvenience of being repeatedly contacted for ongoing study-specific informed consent (Mee et al., 2013). Other concerns that may not be in line with the concerns of researchers include limiting the topics of secondary research as well as the use of the samples by for-profit pharmaceutical companies (Johnsson et al., 2010; Wendler, 2006a). A bridge over these concerns is for researchers to dutifully explain the parameters of broad consent before enrolling participants. This allows the participants to only accept these conditions if they do not possess concerns regarding secondary research uses. It should be noted that these studies largely survey individuals about their own willingness and preferences related to biobanks, not their opinions related to others or decedents.

5.2 | Psychological autopsy

5.2.1 | Set-up and methods—In addition to the survey of public opinion on biobank research, participant response to psychological autopsies provides insight into ethical considerations specifically relevant to suicide research. First coined as a term by Shneidman in 1969 (Jacobs & Klein-Benheim, 1995), psychological autopsies include medical findings, mental health profiles, and interviews with surviving family that serve to reconstruct the psychological and social state of the decedent (Brent, Perper, Kolko, & Zelenak, 1988; Cooper, 1999; Jacobs & Klein-Benheim, 1995). Family members are identified by the researcher and contacted via phone, mail, or in-person to gauge their interest in participating in the interview (Beskow, Runeson, & Asgård, 1991). Provisions for the participants' wellbeing during and after the interview are a critical part of study design (Beskow et al., 1991; Wong et al., 2010).

5.2.2 | Ethical considerations—Most of the ethical debate regarding this method centers on the concerns for care of the surviving family who are interviewed (Beskow et al., 1991; Cooper, 1999), which falls under the principle of *non-maleficence.* Beskow et al. investigated *non-maleficence, beneficence*, and respect for *autonomy* as it related to surviving interviewees (Table 1). The authors concluded that study design and judicious assessment of what information to include in final publication satisfied these requirements (Beskow et al., 1991). An additional investigation also held that the ethical principles were indeed satisfied when following these standard methods (Cooper, 1999). The final principle of *justice* has also been established as psychological autopsies have been conducted worldwide with diverse populations.

5.2.3 | Public opinion—Conclusions drawn from multiple studies of the psychological autopsy method, wherein surviving family members were able to provide feedback on the interview process, provide a source of public opinion. While not representative of the population as a whole, these surveys provide a primary source opinion from individuals who have experienced both the death of a loved one and the research interview. Survey results show the family member acceptance rate for participating in a research study was consistently high in multiple settings (Beskow et al., 1991; Brent et al., 1988). Additionally, qualitative responses to participating in research have been observed across studies to be perceived by the participants as beneficial and/or positive (Beskow et al., 1991; Cooper, 1999; Wong et al., 2010). Of the participants who responded positively, common themes emerged, such as a gratitude for the opportunity to contribute to scientific knowledge, ability to aid future prevention efforts, and personal benefit during the grieving process (Beskow et al., 1991; Wong et al., 2010). While not a substitute for consent for the use of biological data of the deceased, the positive response of the majority of family members to the psychological autopsy procedure implies a willingness to further scientific understanding. This understanding serves to inform suicide prevention efforts in the future, providing public *beneficence.*

6 | CASE STUDY: SUICIDE RESEARCH IN THE STATE OF UTAH

To better conceptualize the ethical intersection of genetic research, suicide research, and the issue of *autonomy*, work being conducted in the State of Utah provides a concrete example. Utah is currently ranked fifth in the nation for suicide (Centers for Disease Control and Prevention, 2016) with a rate of 24.5 per 100,000 for persons aged 10 and older compared to the national rate of 15.7 (Department of Health, 2017). Male Utah residents aged 10 years and older possess the alarming rate of 36.9 (Department of Health, 2017). Despite prevention efforts, the suicide rate continues to rise annually (Department of Health, 2017).

Utah presents somewhat unique setting for conducting suicide research. First, Utah State Law authorizes the collection of postmortem samples with identifiable health information by the centralized office of the state ME for the purpose of conducting autopsies to determine the cause of death in a variety of situations including suicide (Centers for Disease Control and Prevention, 2017). The centralization of the ME makes it possible to conduct state-wide analysis of public health issues without encountering questions of jurisdiction.

If the initial purpose of the sample was to satisfy the ME's autopsy, a secondary use of the sample can be justified for research purposes as this is in keeping with the ME's jurisdiction to better understand the cause of death (e.g., the genetic predisposition for suicide; Centers for Disease Control and Prevention, 2017). As discussed above, familial or next-of-kin consent for sample use is not a current legal requirement in the United States, as decedents do not constitute human subjects (HHS, 2016).

Utah State Law also specifically addresses the sharing and use of identifiable health data in the Utah Health Data Authority Act. Use of these data is allowed when an individual has consented to their use or when the disclosure is specifically for research during a designated period of time at an organization with its own IRB (Hakimian et al., 2004; Utah Health

Code, 2016). This allows for population database records to be connected to medical records and to autopsy reports, providing researchers with an understanding of phenotypic expressions in addition to genetic data available through tissue samples.

Facilitated in part by the research-friendly benefits of a centralized ME's office and to state laws permitting certain exceptions to fully de-identified data, Utah is home to the Utah Population Database (UPDB). The UPDB provides researchers not only with data typical of a biobank database, but also with extensive data on genealogical pedigree structures, linking families back 11 generations (University of Utah Health, 2017). Public records and hospital claims data from two major medical institutions within the state are also linked to the genetic and pedigree data, to total representation of 8 million people (University of Utah Health, 2017). For additional assurance of confidentiality, however, the UPDB de-identifies these records before all secondary research commences.

Research using this database has contributed to multiple genetic discoveries related to colon cancer, breast cancer, melanoma, and cardiac arrhythmia (University of Utah Health, 2017). Pairing genetic data of individuals who died by suicide with population data from UPDB provides researchers with raw data of maximum utility to identify unique genetic markers of suicidal risk. As delineated above, the primary ethical dilemma of this research relates to the principle of *autonomy.* Thus, this research can best be substantiated if it is demonstrated that the research satisfies the other three ethical principles by doing no harm, producing the prospect of notable public benefit, and being equitable in the methods of inclusion for the study.

7 | CONCLUSION

With ethical considerations often outpacing legal regulations, the NIH's GDS Policy and GTEx program recommendations provide important harbingers to the future of genetic research in the United States. The line between human subjects research and non-human subjects research continues to be obscured by the need for an intermediary category to encapsulate human tissue and its associated phenotypic data. Ethical considerations specifically pertaining to *autonomy* will only continue to grow in importance as technological advances make re-identification of de-identified genetic data easier. In fact, the NIH cited this risk as a reason behind their GDS requirement to procure broad consent from biobank donors (National Institutes of Health, 2014).

While provisions have been made to satisfy the legal demands of this unique intersection between human tissue and human subjects research, the traditional ethical problem of *autonomy* persists. Broad consent for use of genetic material provides an important and realistic first step in the ethical access of data, but it inadequately addresses *autonomy* for close biological relatives in the case of working with decedent data. Broad consent from next-of-kin at the time of autopsy may be an appropriate next step.

Based on the utility of biobank research and the significant need to better understand the genetic causes of public health crises such as suicide, a true ethical consideration must rise above the façade of person-specific *autonomy* in favor of obtaining knowledge that can

benefit the whole. This must be achieved while continuing to protect individual subjects, by improving current standards of de-identifying data, continuing to seek independent approval for research via ethics committees, and promoting dialogue to refine the ethics of psychiatric genetic research on suicide. The clinical researcher is well-advised to understand the procedures used to obtain their data, including secondary data, as well as to uphold the four ethical principles in their work. Consulting with other professionals and staying abreast of national policy changes is crucial as technological advances continue to pose new ethical dilemmas and afford us new scientific opportunities.

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REFERENCES

Althoff RR, Hudziak JJ, Willemsen G, Hudziak V, Bartels M, & Boomsma DI (2012). Genetic and environmental contributions to self-reported thoughts of self-harm and suicide. American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics, 159b(1), 120–127. 10.1002/ajmg.b.32010

Beauchamp TL (2001). Principles of biomedical ethics UK: Oxford University Press.

Beskow J, Runeson B, & Asgård U (1991). Ethical aspects of psychological autopsy. Acta Psychiatrica Scandinavica, 84(5), 482–487. [PubMed: 1776502]

Brent DA, & Mann JJ (2005). Family genetic studies, suicide, and suicidal behavior. American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 133c(1), 13–24. 10.1002/ajmg.c.30042

Brent DA, Perper JA, Kolko DJ, & Zelenak JP (1988). The psychological autopsy: Methodological considerations for the study of adolescent suicide. Journal of the American Academy of Child and Adolescent Psychiatry, 27(3), 362–366. 10.1097/00004583-198,805,000-00016 [PubMed: 3379020]

Centers for Disease Control and Prevention. (2016). Stats of the State - Suicide Mortality by State: 2014 Retrieved from https://www.cdc.gov/nchs/pressroom/sosmap/suicide.htm

Centers for Disease Control and Prevention. (2017). Coroner/ME Laws - Publications by Type - Public Health Law Utah: Author Retrieved from https://www.cdc.gov/phlp/publications/coroner/utah.html

Coon H, Darlington T, Pimentel R, Smith KR, Huff CD, Hu H, … Gray D (2013). Genetic risk factors in two Utah pedigrees at high risk for suicide. Translational Psychiatry, 3(11), e325 10.1038/tp.2013.100 [PubMed: 24252905]

Coon H, Darlington TM, DiBlasi E, Callor WB, Ferris E, Fraser A, … Gray D (2018). Genome-wide significant regions in 43 Utah high-risk families implicate multiple genes involved in risk for completed suicide. Molecular Psychiatry 10.1038/s41380-018-0282-3

Cooper J (1999). Ethical issues and their practical application in a psychological autopsy study of suicide. Journal of Clinical Nursing, 8(4), 467–475. [PubMed: 10624264]

Department of Health. (2017). IBIS-PH - Complete Health Indicator Report - Suicide Retrieved from https://ibis.health.utah.gov/indicator/complete_profile/SuicDth.html

Elger BS, Hofner M-C, & Mangin P (2009). Research involving biological material from forensic autopsies: Legal and ethical issues. Pathobiology: Journal of Immunopathology, Molecular and Cellular Biology, 76(1), 1–10. 10.1159/000178150

Hakimian R, National Cancer Institute, & National Institutes of Health. (2004). National Cancer Institute Cancer Diagnosis Program: 50-state Survey of Laws Regulating the Collection, Storage, and Use of Human Tissue Specimens and Associated Data for Research: U.S. Department of Health and Human Services, National Institutes of Health.

Hodge JG Jr., & Gostin LO (2017). Revamping the US federal common rule: Modernizing human participant research regulations. JAMA, 317 (15), 1521–1522. 10.1001/jama.2017.1633 [PubMed: 28241195]

Jacobs D, & Klein-Benheim M (1995). The psychological autopsy: A useful tool for determining proximate causation in suicide cases. The Bulletin of the American Academy of Psychiatry and the Law, 23(2), 165–182. [PubMed: 8605401]

Johnsson L, Helgesson G, Rafnar T, Halldorsdottir I, Chia KS, Eriksson S, & Hansson MG (2010). Hypothetical and factual willingness to participate in biobank research. European Journal of Human Genetics, 18(11), 1261–1264. 10.1038/ejhg.2010.106 [PubMed: 20648060]

Kochanek K, Murphy S, Xu J, & Tejada-Vera B (2016). Deaths: Final data for 2014. National Vital Statistics Reports, 65(4), 1–121.

Lonsdale J, Thomas J, Salvatore M, Phillips R, Lo E, Shad S, … Young N (2013). The genotype-tissue expression (GTEx) project. Nature Genetics, 45(6), 580–585. [PubMed: 23715323]

Lynch MJ (2002). The autopsy: Legal and ethical principles. Pathology, 34(1), 67–70. [PubMed: 11902450]

Mee B, Gaffney E, Glynn SA, Donatello S, Carroll P, Connolly E, … Giles FJ (2013). Development and Progress of Ireland's biobank network: Ethical, legal, and social implications (ELSI), standardized documentation, sample and data release, and international perspective. Biopreservation and Biobanking, 11(1), 3–11. 10.1089/bio.2012.0028 [PubMed: 24845249]

MGH. (2017). Overview & history Boston, MA: Massachusetts General Hospital Retrieved from http://www.massgeneral.org/research/about/overview.aspx

Middleton O, Baxter S, Demo E, Honeywell C, Jentzen J, Miller F, … Stacy C (2013). National Association of Medical Examiners position paper: Retaining postmortem samples for genetic testing. Academic Forensic Pathology, 3(2), 191–194.

Moore QL, Majumder MA, Rutherford LK, & McGuire AL (2016). Ethical and legal challenges associated with public molecular autopsies. The Journal of Law, Medicine & Ethics, 44(2), 309–318. 10.1177/1073110516654124

Murphy J, Scott J, Kaufman D, Geller G, LeRoy L, & Hudson K (2009). Public perspectives on informed consent for biobanking. American Journal of Public Health, 99(12), 2128–2134. 10.2105/ajph.2008.157099 [PubMed: 19833988]

Murphy SL, Mathews TJ, Martin JA, Minkovitz CS, & Strobino DM (2017). Annual summary of vital statistics: 2013–2014. Pediatrics, 139(6), e20163239 10.1542/peds.2016-3,239 [PubMed: 28814547]

National Institutes of Health. (2014). NOT-OD-14–124: NIH Genomic Data Sharing Policy Obtained from https://grants.nih.gov/grants/guide/notice-files/not-od-14-124.html

O'Doherty KC, Christofides E, Yen J, Bentzen HB, Burke W, Hallowell N, … Willison DJ (2016). If you build it, they will come: Unintended future uses of organised health data collections. BMC Medical Ethics, 17(1), 54 10.1186/s12910-016-0137-x [PubMed: 27600117]

Porteri C, Pasqualetti P, Togni E, & Parker M (2014). Public's attitudes on participation in a biobank for research: An Italian survey. BMC Medical Ethics, 15, 81 10.1186/1472-6939-15-81 [PubMed: 25425352]

Roy A, Segal N, Centerwall B, & Robinette C (1991). Suicide in twins. Archives of General Psychiatry, 48(1), 29–32. 10.1001/archpsyc.1991.01810250031003 [PubMed: 1984759]

Roy A, & Segal NL (2001). Suicidal behavior in twins: A replication. Journal of Affective Disorders, 66(1), 71–74. [PubMed: 11532534]

Shneidman ES (1969). Suicide, lethality, and the psychological autopsy. International Psychiatry Clinics, 6(2), 225–250. [PubMed: 5810563]

United States Code. (2016). Health Insurance Portability and Accountability Act 45 CFR 160, 162, 164

United States Code. (2017). Federal policy for the protection of human subjects: Final rule. Federal Register, 82, 7149–7274. [PubMed: 28106360]

United States Department of Health & Human Services. (2016). 45 CFR 46 | HHS.gov. Retrieved from https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

University of Utah Health. (2017). Utah population database overview Retrieved from https://healthcare.utah.edu/huntsmancancerinstitute/research/updb/

Utah Health Code. (2016). Utah Health Code Title 26 Chapter 33a Section 109 Retrieved from https://le.utah.gov/xcode/Title26/Chapter33A/26-33a-S109.html?v=C26-33a-S109_2016051020160510.

Wendler D (2006a). One-time general consent for research on biological samples. BMJ, 332(7540), 544–547. 10.1136/bmj.332.7540.544 [PubMed: 16513715]

Wendler D (2006b). One-time general consent for research on biological samples: Is it compatible with the health insurance portability and accountability act? Archives of Internal Medicine, 166(14), 1449–1452. 10.1001/archinte.166.14.1449 [PubMed: 16864754]

Wong PWC, Chan WSC, Beh PSL, Yau FWS, Yip PSF, & Hawton K (2010). Research participation experiences of informants of suicide and control cases: Taken from a case–control psychological autopsy study of people who died by suicide. Crisis: The Journal of Crisis Intervention and Suicide Prevention, 31(5), 238–246.

World Health Organization. (2017). Suicide fact sheet Retrieved from http://www.who.int/mediacentre/factsheets/fs398/en/

World Medical Association. (2013). WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects 2013 available at https://www.wma.net/policies-post/wma-declaration-of-helsinkiethical-principles-for-medical-research-involving-human-subjects/

TABLE 1

Ethical Considerations in Biobank and Psychological Autopsy Research

Ethical principle	Pros	Issues for Consideration
Biobank research		
Autonomy	• Confidentiality is treated through de-identification	• Privacy concerns of decedent and Relatives • Issues of study-specific informed consent versus broad consent for future research
Beneficence	• Promotes critical insight and discoveries	
Maleficence	• Minimally invasive to living persons and not invasive to decedents	• Limited with respect to issues of autonomy
Justice	• Increased consortium/global efforts to genetic research efforts	• Emphasis on European ancestry populations remains prevalent
Psychological autopsy research		
Autonomy	• Family members of decedent opt in to the psychological autopsy	• Family members are contacted based on decedent records
Beneficence	• Interviews provide qualitative data and highlight bio-psychosocial and phenotypic data	
Maleficence	• The majority of family members contacted opt in to participate	• The invitation to participate, discussing deceased may be distressing to family members
Justice	• Psychological autopsies have been performed worldwide with cultural considerations relevant to each study	