"Duty" to recontact participants in a population based genetic database: the NUgene experience

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Genetic databases are generally created with the long-term goal of establishing genotype-phenotype correlations, and are explicitly NOT intended for participant benefit through the personal receipt of genetic information. In fact, most well-known genetic databases are set up to preclude the recontact of participants, both to protect confidentiality and because any genetic discoveries will likely have unclear implications in the near future. However, in general medical practice, recent years have brought an increasing sense of "rights" toward personal medical information; the question remains whether this "right" extends to control medical information obtained through research. If it does, study participants would need to be recontacted to reveal experimental genetic test results, or at least their availability. We will discuss our experience with the NUgene study, a longitudinal genetic database at Northwestern University created to assess the genetic components of common diseases. In summer 2001, prior to the start of NUgene recruitment, a planning committee met for over one year to discuss the project's format, including ethical aspects. The project's advisory committee felt strongly that recontact of study participants was *not* warranted. However, because of the broad and longitudinal nature of the project, the IRB requested a modified consent process for recontacting subjects. This consent allowed participants to opt for recontact under either of the following circumstances: (1) if more information was required for a future study or to participate in future research and (2) if "clinically significant results" were discovered through research examination. During the first year of the study, 808 participants were enrolled in NUgene. 92% opted for recontact regarding more information or future research and 96% opted for recontact for "medically significant" findings. A parallel ELSI study of NUgene participants examined informed consent, including recontact options. Of 200 surveyed participants, most had a good understanding (93% correct) that the purpose of the study was to benefit future patients, but they displayed a poorer understanding of whether they would learn specific personal health information from the study (62.6% correct). In-depth interviews with 109 participants suggested that approximately 1/3 of study participants *expected* to receive results and an additional 1/3 *hoped* to receive results. Respondents were also relatively open with regards to *how* they would prefer to be recontacted (e.g. mail, phone), but rarely provided reasons for their preferences. Such findings raise the issue of how participants interpret the option to be recontacted. We will discuss our experience in the context of available ethical and scientific literature, and raise additional questions for future research.

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Measuring the quality of informed consent (QuIC) of participants in a population-based genetic database

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Population-based genetic research studies are currently being undertaken to better understand complex, common diseases. Despite a large body of literature on the importance of informed consent in genetic research, there is little research data on this topic. Evaluating the informed consent process in this area can help to improve its effectiveness. The goals of this research were (1) to assess the knowledge and self-assessed understanding of participants in a population-based genetic study; (2) to identify predicting factors for participation and comprehension in population-based genetic studies. At the time of this abstract, interviews were conducted with 83 individuals who had enrolled in the NUgene project, a longitudinal study to associate medical information with genotype data at Northwestern University (43.5% of NUgene participants to date); data collection will continue to reach 200 subjects. Individuals were interviewed by telephone within 1-4 weeks of NUgene enrollment. Interviews consisted of: demographic questions, a modified version of the quality of informed consent measure (QuIC), and semi-structured questions about participation and understanding of NUgene (data presented separately). The QuIC is a measure designed to assess participants' knowledge and self-assessed understanding about essential components of informed consent, and validated in a population participating in cancer clinical trials. Summary knowledge scores and self-assessment scores for the modified QuIC were generated (ranging from 0-100). NUgene participants' self-assessed understanding was greater than their actual knowledge (90.1 vs. 68.7). Participants reported good understanding of the nature of the study (100), that the potential benefit is for future patients (99.4), and that participation is voluntary (90.9), and a reasonable understanding that the research is not intended to benefit them (75.0). Less understood concepts included: potential risks and discomforts (14.5), the experimental nature of the genetic testing (19.9), procedures to follow in the event of injury (37.2), and confidentiality issues (45.1). Education was the only variable found to predict higher knowledge (graduate degree, $p=0.03$). Caucasian ethnicity and income <$50,000 per year predicted higher self-assessed understanding ($p= 0.04$ and $p<0.01$, respectively). In contrast to the "therapeutic misconception" often seen in clinical research involving unproven treatments, NUgene participants report understanding that the purpose of the study is to benefit future patients and not to expect personal benefit. However, participants reported understanding more than knowledge scores indicated. Decreasing the gap between self-assessed understanding and actual knowledge is essential for truly informed consent. Identifying common misconceptions, such as potential risks of participation, can help genetic counselors, and others obtaining informed consent, to improve the process for population-based genetic research.

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Informed Consent for a Population Based Genetic Database: A qualitative assessment of understanding

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In November 2002, the NUgene project began recruiting subjects for a large, longitudinal genetic database; initial enrollment was primarily "self-referred" through media exposure, with a subsequent increase from general clinic patients. Concurrent with NUgene enrollment, we solicited interviewees to address attitudes about participation in NUgene. Semi-structured Interviews were conducted an average of 22 + 9 days after NUgene enrollment, and 107 transcribed interviews were analyzed, representing 44.6% of the overall NUgene enrollment. Subjects were 58% self-recruited, and mostly female (67%), Caucasian (83.5%), Christian (66.7%), married (48.1%), college educated (66.0%) and with household incomes > $50,000 (66.3%). Using a likert scale of 1-5 (5 being highest), interviewees generally considered themselves healthy, and comfortable with science (4.44 + .78) and genetics (4.03 + 1.15). Several themes emerged from the data, focusing around reasons for participation, beliefs regarding the risks and benefits of the study, expectations regarding results and ways in which participants would prefer to be recontacted if future studies or results become available. The majority of participants enrolled in NUgene in order to help mankind or the "general population" in some manner (>75%), to help find disease genes, treatments or cures, and/or to contribute to the overall knowledge of science or medicine. Less common reasons for participation were a personal interest in science or genetics, or in research participation in general. Many participants (~30%) clearly expressed a hope for personal benefit, often naming specific disorders or affected family members. Confidentiality protections of the study were described as good by most (>50%) study participants, and almost half specifically described one or more of the privacy protections associated with NUgene. While many were able to articulate the general privacy concerns, and a reasonable minority specifically cited concerns with employer (12%) or insurance discrimination (25%), most considered the risks to privacy low (25%) or none (~60%). With regards to the expectation for personal benefit, only 10% of participants explicitly stated they had no expectation for personal benefit. When asked whether they expected to be contacted with study results, respondents were split between having no expectation (42/107), being hopeful or open to the receipt of results (40/107) and stating clearly that they expected to be contacted with results (13/107); common explanations were if "something I need to know" or "something serious" was discovered. Over 75% of study participants felt that if a genetic test became available for their family they would wish to undertake it, and few caveats were mentioned. Overall, phone or mail were preferred for notification.

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