

M8. FRAMEWORK FOR THE RETURN OF RESULTS TO PSYCHIATRIC GENOMICS RESEARCH PARTICIPANTS: WHAT SHOULD BE OFFERED?

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Background The increasing prevalence of genomic analysis (genome/exome sequencing and array-based measures) in psychiatric research generates complex novel challenges for investigators. A critical challenge is how to manage the clinically relevant information that can be generated with these technologies, such as risk for cancer, heart disease, or psychiatric disorders.

There is an emerging ethical consensus that genomics researchers have a duty to offer findings identified in the course of research that are clinically valid, medically important, and medically actionable. This consensus is mainly based on the beneficence argument that these findings may aid health care or life planning; and that it would be disrespectful to participants' autonomy to deny them the opportunity to decide whether to know this type of genomic findings. This has led to an increasing practice of returning results to individual participants in genomic research. However, there is little guidance about the return of results in psychiatric research, including what genomic findings should be returned and what is the scientific, ethical, and legal rationale for returning these.

Methods We conducted ethical and legal analysis of current return of results practices, relevant guidelines, and policies to generate a framework to guide determinations about the types of results that should be offered to psychiatric genomics research participants. The framework was developed for a genomic study with patient-participants suffering from treatment-resistant psychosis, but it is applicable to other psychiatric genomics research scenarios and populations.

Results Our analysis shows that, as in studies of other medical conditions, when resources allow, psychiatric genomics researchers should offer to return findings generated in the course of research that are clinically valid, medically important, and medically actionable (e.g., BRCA1/2 pathogenic variant). Notably, we conclude that due to potential benefit to participants, when resources allow, psychiatric genomics researchers should also offer to return "clinically valuable" genomic findings.

In this framework, clinically valuable genomic findings are those obtained in the course of research that, even if not medically actionable, have the potential to aid current or future health care because they: 1) are clinically valid findings that provide information about important health risks; 2) help corroborate or reject a psychiatric diagnosis; or 3) are rare variants of unknown significance in genomic loci known to be associated with a psychiatric disorder, particularly if consistent with a participant's known phenotypes.

Discussion Studies show that only about 4% of genome-wide association studies (GWAS) return findings to individual participants. This is in part because GWAS do not often generate findings with immediate clinical relevance. However, as large-scale GWAS identify more clinically relevant findings and genomic sequencing becomes more accessible and prevalent in psychiatric research, investigators will increasingly confront the challenge of having to manage clinically relevant findings in an ethically sound and legally valid fashion. This framework for the return of results in psychiatric

genomics research will help investigators make determinations about a key aspect of the return of results: what findings should be offered.

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