EJHG Open

European Journal of Human Genetics (2013) 21, 245–247

www.nature.com/ejhg

POLICY

Population studies: return of research results and incidental findings Policy Statement

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The Public Population Project in Genomics and Society (P^{3}G) is a not-for profit international consortium with members from more than 40 countries. Its objective is to lead, catalyze, and co-ordinate international efforts and expertise in order to optimize the use of population studies, biobanks, research databases, and other similar health and social science research infrastructures. The year 2011–2012 witnessed a plethora of special issues of journals on the return of results but few discussed the particular situation of population studies that serve as resources for future unspecified research. P^{3}G considers it important to propose a policy that distinguishes between the contexts of population research and disease (clinical) research involving patients and then delineates actual and future obligations. The objectives of this *Policy Statement* are to: (1) delineate the particular characteristics of population studies, (2) distinguish the circumstances surrounding access by researchers to such studies, and (3) develop a framework for the return of research results and incidental findings.
European Journal of Human Genetics (2013) **21,** 245–247; doi:10.1038/ejhg.2012.152; published online 11 July 2012

PUBLIC POPULATION PROJECT IN GENOMICS AND SOCIETY (P^{3}G)

P^{3}G is a not-for profit international Consortium with members from more than 40 countries. Its objective is to lead, catalyze, and co-ordinate international efforts and expertise in order to optimize the use of population studies, biobanks, research databases, and other similar health and social science research infrastructures so as to improve the health of individuals and populations. To achieve this, the Consortium is committed to:

1. providing global perspectives and strategic approaches to the optimization of data access and use;
2. catalyzing multidisciplinary and international scientific expert input;
3. engaging studies, cohort, and biobank resources/infrastructures and their users in dynamic knowledge-based exchange;
4. disseminating and valorizing knowledge relevant to the mission of P^{3}G; and
5. serving the needs of the P^{3}G programmes and their platforms.

P^{3}G brings the genomics, epidemiology, social science, ELSI (ethical, legal and social issues)/policy-making, and information technology communities together. Through its network of experts and platforms, P^{3}G is a resource for research.

The year 2011–2012 witnessed a plethora of special issues of journals on the return of results,[1,2] but only a few articles therein[3–6] discussed the particular situation of population studies that serve as a resource for future unspecified research. P^{3}G considers it important to underscore the unique character of such infrastructures and to propose a policy that distinguishes between the contexts of population research and disease (clinical) research involving patients and then delineates actual and future obligations. This is important, as the conditions under which participants are recruited and consented must be respected. Careful weighing of the effects of creating new obligations or expectations to say nothing of the capacity to meet them with the necessary professional integrity form the basis for this *Policy Statement*.

POLICY STATEMENT

Context and scope

This *Policy Statement* considers the issue of return of results in the specific context of population genomics and addresses possible modalities for such return.

The question of return of results presents unique characteristics when viewed through the lens of population studies. In general, participants in population studies are making a free and informed choice to contribute to future, yet unspecified, research hypotheses that will contribute to the advancement of science. Population-based studies serve multiple research hypotheses over a long period of time. Despite the anticipation of their eventual contribution to health care systems, they cannot be seen as a substitute for clinical research involving patients or for health care. The objective of these resources is to support research. Any confusion concerning their goals could jeopardize their existence due to the creation of unreasonable expectations.

Population studies operate in heterogeneous contexts. This affects the chain of custody in the collection, conservation, and use of the data and samples. The notion of 'population-based studies' includes a variety of different kinds of 'architectures' that has impacts on the capacity or appropriateness of returning results. Several actors are involved in this chain of custody: the biobank, the host institution, the participants, and the users (the researchers) with their own local Ethics Review Committee. What obligations are created and how they percolate through the chain of custody takes different forms.

Finally, the consent given by participants is an opportunity to create reasonable expectations for participants that are both consistent

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with the notion of maximizing benefits for future generations while recognizing their altruistic contribution to science. The presence of ongoing communication by the population study with participants is essential. Any return of results should be part of a mutual consensus between a population study and its participants.

This *Policy Statement* first defines the terms used throughout the document. It then presents its objectives and guiding principles before addressing the issues associated with:

- feedback at assessment and from laboratory analyses before storage;
- the modalities of returning general results to participants; and finally,
- the conditions and modalities of returning individual research results (IRRs) and incidental findings (IFs).

Note that countries may have legal requirements concerning the return of research results and IFs as well as access to personal data. Population studies and researchers should be aware of these obligations.

Definitions

Actionability: a finding is actionable if there is a recognized therapeutic or preventive intervention or other available actions that have the potential to change the clinical course of a disease or condition.

Analytic validity: an analytically valid finding is one that accurately and reliably identifies a particular genetic characteristic, such as a nucleotide sequence or a gene expression profile.

Baseline assessment: includes measurements such as blood pressure, lung function, bone density, height, weight, fat, and others.

Clinical significance: a finding is clinically significant when it is both analytically valid and reveals a well-recognized and significant risk of a serious health condition.

General results: aggregate results drawn from the analysis of data and samples of a group of research participants.

IFs: unforeseen findings concerning a research participant that have potential health or reproductive importance. They are discovered during the course of research but are outside its objectives.

IRR: results discovered during the course of research, which concern an individual participant, and have potential health or reproductive impact.

Lab analyses: analyses carried out on biological samples before storage.

Population studies: include population biobanks, longitudinal cohorts, social science, and genetic epidemiology research serving as a resource for future unspecified research.

Participants: individuals contributing their data and samples to a population study.

Policy Statement objectives

The objectives of this *Statement* are to:

1. delineate the particular characteristics of population studies;
2. distinguish the circumstances surrounding access by researchers to such studies; and
3. develop a framework for the return of research results and IFs.

Guiding principles

This *Policy Statement* is consistent with P3G's *Charter of Principles* and aims to weigh the potential benefits and harms of the return of research results and IFs to participants in population studies. It includes consideration of the following principles:

- *Respect for persons* – the duty to respect the autonomy of research participants and protect those with reduced capacity. Respecting autonomy entails the provision of sufficient information to research participants so as to obtain their free, informed, and ongoing consent.
- *Beneficence* – the duty to maximize net benefits for research participants and for society as a whole, while advancing knowledge.
- *Non-maleficence* – the duty to minimize and prevent harm to research participants.
- *Reciprocity* – the duty to promote trust between researchers and research participants.

Feedback at baseline assessment and from lab analyses before storage

Findings emanating from the baseline assessment and lab analyses before storage as well as any subsequent assessments conducted by the population study for the purpose of enriching the research infrastructure are not research results. However, their return to participants constitutes a form of ongoing communication and feedback.

The description of the feedback process at baseline assessment should avoid the therapeutic misconception (ie, participants mistaking that baseline or subsequent assessments are equivalent to a medical checkup). Nevertheless, there should be a health professional involved as a member of the population study to ensure appropriate medical input in the overall process.

- Findings from baseline assessments should be returned to participants as soon as possible.
- Findings from lab analyses before the long-term storage of samples should be returned if they reveal a serious or life-threatening condition. Other data could also be returned, before storage, if participants have consented.
- When findings reveal an abnormal result during baseline assessment or lab analyses before storage, personnel should encourage participants to contact a physician. When life-threatening, critical values are found, immediate care should be provided for the participant.

Return of general results to participants: modalities

All efforts should be made to effectively communicate general results as a matter of transparency. They serve as the primary means of communication of research outcomes.

- As part of the ongoing communication between population studies and their research participants, general research results should be made available in an ongoing manner so as to inform participants of overall findings.
- Researchers accessing a population study should provide it with a description in lay language of their research as well as the results obtained, including negative results. Special attention should be paid by Ethics Review Committees to any result that may contribute to stigmatization. Researchers have a duty to actively promote the proper interpretation of research results, including their limits.
- Population studies can return general results via newsletters, websites, or other dynamic, interactive communications tools.

Return of IRRs and IFs to participants: conditions and modalities

No return of IRRs and IFs. There may be population studies where the policy is not to return individual results or findings, and this was consented to by participants at recruitment. This remains a viable option where appropriate. Researchers accessing the study population and their local Ethics Review Committee should be made aware of this policy.

For population studies with a no-return policy or where participants did not consent at recruitment to the return of findings but have, nonetheless, consented to recontact for updates and for further questions or collection of samples, such a period can create an opportunity to explain and introduce a return of results and Ifs policy and accompanying procedures, if the population study so chooses and with ethics approval. Indeed, upon recontact, participants could be provided with an option to consent (or not) to receiving such results. Moving forward, population studies with a no return policy could consider adding such an option to their consent process at recruitment.

Return of IRRs and IFs

Decision to return results: When consent to return results is present, one should consider whether the finding poses a material risk. Findings are material if they have:

1. analytical validity;
2. clinical significance; and
3. actionability.

Researchers, in collaboration with their local Ethics Review Committee, should consider returning IRRs and IFs to participants when they determine that the following criteria are met:

1. the participant has consented thereto in the initial consent form or at a later time;
2. the findings are analytically valid (ie, confirmed independently);
3. they reveal a significant risk of a serious health condition; and,
4. they are actionable.

Researchers, in collaboration with their local Ethics Review Committee, may consider returning IRRs and IFs when the above criteria are not satisfied, but when the following criteria are met:

1. the participant has consented thereto in the initial consent form or at a later time;
2. the findings are analytically valid (ie, confirmed independently);
3. they reveal an established risk of likely health importance to the participant; and
4. they have a likely therapeutic benefit.

The decision to return IRRs and IFs remains the responsibility of the researchers and the local Ethics Review Committee. Resources should be available for this decision-making process.

Communication of results. Contacting participants for the communication of material findings remains the responsibility of the population study. The population study should ensure the quality of the results, as well as the timeliness and appropriateness of the information returned to a given participant (including considerations related to the number of recontacts).

Procedures

Population studies should put in place policies and procedures that clarify and circumscribe the obligations and procedures arising from their return of results policy. These should be reflected in any material-transfer agreements and access policies for researchers. These policies should include the length of duration of any return of results policy and the degree of involvement of researchers. Attention should be paid to issues of feasibility and reasonability. Procedures should be in place in the population study for the communication of such results by a health professional.

CONCLUSION

The contents of this *Policy Statement* on the *Return of Research Results and Incidental Findings* were first discussed by P3G members in March 2010 at its annual meeting. At that time, the Centre of Genomics and Policy (McGill University) presented a *Points to Consider* document addressing emerging approaches to Return of Research Results and Incidental Findings and their implications for population studies. In October 2011, participants at a joint P3G/Making Connections Group meeting discussed a draft of the current document. That draft formed the basis of a *Points to Consider* document on the same topic by the Canadian Partnership for Tomorrow Project – a cohort recruiting hundreds of thousands of participants. The P3G Policy Statement will hopefully serve to guide and inspire other population studies as well.

ACKNOWLEDGEMENTS

We thank the P3G members and participants; the Making Connections Group; and the CPTP (Canadian Partnership for Tomorrow Project) ELSI Task Force. We would also like to thank our funders: Genome Canada/Genome Quebec; CIHR (Genetics), and the Canadian Partnership Against Cancer (CPAC).

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