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Genetic forum

Focus group discussions on secondary variants and next-generation sequencing technologies

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ABSTRACT

The clinical application of new genetic technologies will be and already is of great benefit to children with unexplained developmental disabilities or congenital anomalies. In most cases, it will be their parents who, together with medical professionals, make decisions about what should be disclosed and how the information will be used. We conducted eight exploratory focus group discussions with stakeholders to provide a broad sketch of concerns and ideas around the communication of results from next-generation sequencing technologies involving children. Stakeholders included those with (grand-) children of various ages and those without children; those involved professionally with genetics and those who were not; and a range of ages. Participants were asked to focus on which secondary variants they would and would not want disclosed about their (hypothetical) children or themselves. While the literature often concentrates on the medical and scientific characteristics of secondary variants, focus group participants were also interested in factors involving the parent-child relationship and the broader context. This resulted in more flexibility surrounding the types of secondary variants disclosed to parents than much of the literature currently supports. In addition, participants would on occasion use the same factors to argue opposing positions. The "Family Illness Paradigms model" can help explain this seeming contradiction. This model emphasises the importance of how the family reacts to personal and family experiences of disease and loss, more than the fact of having these experiences.

1. Introduction

Thanks to rapidly falling costs, the widespread clinical implementation of whole genome and exome sequencing (WGS and WES, respectively) is imminent [Hayden, 2014]. Some are already using WGS and WES in clinical diagnosis [Choi et al., 2009; Lupski et al., 2010; Worthey et al., 2011]. However, as has often been noted, reports of falling sequencing costs regularly lose sight of invariably high analysis and follow-up costs [Mardis, 2010].

One of the potential causes of high analysis and follow-up costs is the phenomenon of so-called secondary variants or incidental findings. Secondary variants introduce costs at various levels: longer pre-test counselling and informed consent discussions; confirmation of analytical and clinical validity and clinical utility; potential post-test discussions with colleagues, Institutional Review Boards or their equivalents, and patients or research participants; plus follow-up costs in primary healthcare. A key step in the development of standard discussion protocols, informed consent procedures, and panels or filters is the investigation of which secondary variants various stakeholders deem worthy of identifying and disclosing and on what basis.

As in a previous study [Christenhusz et al., 2014], we focus here on the particular issue of the disclosure of secondary variants to parents. A qualitative research method was chosen. This allows the emergence of new themes that are relevant to the research participants, a vital step when investigating a new topic. The question of disclosure to parents was focussed on, as it is children with heritable diseases who will be and already are a key beneficiary of the clinical application of new genetic technologies [Boycott et al., 2014]. In most cases, it will be these children's parents who, together with medical professionals, make decisions about what should be disclosed and how the information will be used. Only one official guideline has been published to date on the issue of secondary variants arising from genetic testing, that of the American College of Medical Genetics and Genomics (ACMG) in April 2013 (with revisions published in a press release

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Table 1
Socio-demographic characteristics of the focus group participants and their children. Note that some participants expressed familiarity with genetic diseases in more than category (family history, studies, or work), so that the numbers in the final column exceed the number of participants.

Focus group	Reason for recruiting this particular group	Recruitment strategy	Number and gender of participants	Age range	Children per participant	Familiarity with genetic diseases
		Number of contact people and group composition		Nearest 5 years	Median number and age range	Number through family history, studies, or work
Parents of young children	Parents with children of a certain age; not involved with genetics professionally	2 contact people delegated; 2 acquaintance groups	4 women, 2 men	26–45	3 children (under 5 years of age, primary school age)	2 family history; 3 through studies; 2 through work; 2 no familiarity
Parents of teenagers and young adults	Parents with children of a certain age; not involved with genetics professionally	2 contact people delegated; 2 acquaintance groups + 1 stranger	3 women, 3 men	36–55	2–3 children (teenagers, over 18 years of age still at home and left home)	5 family history; 1 through studies; 1 through work; 1 no familiarity
Immigrant parents (5 Asian, 1 Middle Eastern, 1 East European)	Parents with a non-Belgian ethnic background; not involved with genetics professionally	Integration office of the province of Flemish-Brabant; strangers + 1 married couple	4 women, 3 men	26–45	2 children (under 5 years of age, primary school age, teenager)	4 family history; 1 through studies; 3 no familiarity
Clinical genetics centre staff	Parents and involved with genetics professionally	1 staff member delegated	4 women, 1 man	36–55	2 children (all ages)	1 family history; all through studies; all through work
Bio-informaticians	Involved with genetics professionally	1 staff member delegated	7 men	26–55	4 participants with no children; 3 participants with a mean of 2 children (all ages)	4 family history; 6 through studies; 6 through work
Biological sciences master students	Not parents; younger than other groups; familiar with medicine and genetics through studies	3 masters classes approached	4 women, 2 men	18–25	0 children	3 family history; 6 through studies; 4 through work
Genetics PhD students	Not parents; involved with genetics professionally	Fellow PhD students	4 women, 3 men	18–45	0 children	3 family history; 6 through studies; 6 through work; 1 no familiarity
Grandparents	Asked to focus on their grandchildren; older than other groups; not involved with genetics professionally	2 contact people delegated; 2 sets of siblings and 2 strangers	4 women, 2 men	46–75	4 grandchildren (under 5 years of age, primary school age), 2 adult children	2 family history; 1 through studies; 3 no familiarity

on 1 April 2014) [Green et al., 2013]. Other guidelines are currently being drafted. The ACMG guideline recommends that a list of secondary variants (confirmed mutations associated with serious conditions judged to have clinical utility) be checked every time WGS or WES is conducted in a clinical setting, regardless of the patient's age. This appears to contradict existing guidelines prohibiting the genetic testing of children for adult-onset conditions [Borry et al., 2009; Clayton et al., 2014]. The ACMG justified the policy change by arguing that secondary variants are qualitatively different to primary genetic test results, because disclosure of secondary variants can provide significant information to the child-patient's family (specifically, the child-patient's parents) that would not be known otherwise [Evans, 2013]. One of the aims of the present study was to investigate whether the time of onset of a genetic condition is considered to be a relevant factor to parents in secondary variant disclosure discussions, and thus indirectly investigate whether participants support previous or emerging guidelines.

In contrast to other published qualitative studies, we did not divide our focus groups according to medical professionals and lay people. Previous research by Lemke et al. suggests that clinical genetics professionals may be more conservative in their disclosure recommendations for parents of patients compared to what they would like disclosed about their own child [Lemke et al., 2013]. In the present study, we wished to concentrate on the respondents as parents (or hypothetical parents), not as medical experts. Furthermore, all focus group participants were instructed to respond as realistically as possible, and the moderator occasionally reminded participants that the researchers were not interested in what the participants thought parents in general should or should not do, but in how the participants thought they themselves would act in a given situation. Responses based on personal experience and what was judged to be personally meaningful were encouraged over hypothetical views [Rabiee, 2004]. In the current study, all responses about secondary variant disclosure were of course unavoidably hypothetical as none of the participants had direct experience with receiving secondary variants regarding themselves or their children. In addition, the two student groups could only respond as hypothetical parents. To offset this, participants were encouraged to respond as personally as possible, and to reflect on and discuss what they would do as (grand-) parents in the context of their specific (grand-) children. The parents were asked what they personally would like to be told; those without children were asked what they thought they would like to be told if they were parents; and the grandparents were asked what they thought their children should be told about their grandchildren.

2. Methods

The aim of the focus group discussions was to provide a broad sketch of concerns and ideas around the communication of secondary variants from next-generation sequencing technologies involving children. Ethics committee approval was sought and obtained from the medical ethics committee of the University Hospitals Leuven (study number S54646). Recruitment was conducted through designating one or two contact people per target population. We aimed for between five and eight participants per group [Hydén and Bülow, 2003; Kitzinger, 1995]. A range of stakeholders was recruited (Table 1): participants with (grand-) children of various ages and those without children; participants involved professionally with genetics and those who were not;