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Ethics watch

NEXT-GENERATION SEQUENCING: DOES THE NEXT GENERATION STILL HAVE A RIGHT TO AN OPEN FUTURE?

Next-generation sequencing (NGS) is expected to lead to a new era in paediatric research and diagnosis. Whole-exome and whole-genome sequencing are now increasingly used to diagnose intellectual disability, developmental delay and autosomal and X-linked recessive conditions in children. Routine whole-exome and whole-genome sequencing are on the horizon[1,2]. NGS is a powerful diagnostic tool but brings with it a deluge of genetic information, including genetic data that are solicited and unsolicited, validated and non-validated, highly and poorly predictive and more or less probabilistic[3]. One of the most urgent ethical challenges is therefore whether to disclose such genetic risk information to parents of children undergoing NGS, particularly for conditions that do not have immediate consequences for the health of the child.

Until recently, the internationally widely endorsed view has been that minors should be tested only for early-onset disorders in which treatment or preventive options exist "until the child has the capacity to make the choice"[4]. Two leading ethical principles underlie this consensus. First, the beneficence-based 'best interest' standard, which urges physicians to test for clinically relevant and actionable genetic variants. Second, the 'right to an open future' principle, which urges physicians not to test for adult-onset disorders and carrier status. Disclosure of this type of genetic information could infringe on a child's anticipatory autonomy right: to have one's future's options kept open until one is capable of making one's own decisions[5]; this also concerns the possible obtainment of genetic information.

Is this ethical framework still suitable in an era in which the scope of genetic testing is the whole genome? There is a growing list of examples in which NGS studies offer parents the option of disclosure of their child's predisposition to adult-onset disease and carrier status[6–8]. In addition, commentators have recently adopted the position that parents should have the option to decide whether they want to receive results that reveal a child's predisposition to adult-onset disease for which no treatment or prevention exists, such as Parkinson's disease[7]. They argue that parents are usually granted the authority to make health-care decisions that they believe are in the best interests of their own families and that a restrictive approach is not realistic in the near future, when it may be less expensive to 'run the whole genome' rather than to sequence particular genes[8]. These opinions are in line with the so-called 'life prospects' principle[9]. Endorsement of this family-centred principle will result in a different approach regarding paediatric NGS than the child-centred 'right to an open future' principle.

Is this the direction we should aim at? Clearly, the scope and significance of genetic risk information generated by NGS has changed considerably, but it is not immediately clear why the 'right to an open future' principle should be abandoned. The child's future autonomy rights can still be taken into account by, for example, designing prudent disclosure policies. The analysis of sequencing results can still be targeted by, for example, using filters to analyse only selected parts of the genome[8]. The moral question we should therefore focus on is how broad or targeted the interpretation of sequencing results should be. We previously proposed a qualified disclosure policy for the return of genetic results to adults, for which a choice between certain 'packages' of genetic information would be offered[10]. The standard default package would contain life-saving information and data of immediate clinical utility that entail a substantial health problem. The results should be analytically valid, actionable and accurate. Additional packages could be opted into, including, for example, data with differing levels of clinical utility and different types of significance (such as reproductive significance, personal or recreational significance or ancestry). A similar approach could be applied to paediatric testing. As long as the child cannot make his or her own decisions, only the default package and possibly also data of reproductive significance would be eligible for disclosure. The additional packages would be offered when the child has reached maturity.

Clearly, these are only the general outlines of a possible paediatric NGS disclosure policy. Further interdisciplinary discussion is urgently needed to discuss questions such as what to do if one finds a genetic variant of relevance to the parents' own health. Also, if we disclose only immediately relevant data but accept the possibility that the child claims the information as an adult, then either retesting should be offered or systems should be put in place to store children's genomic data in biobanks. How would this be organized, for example, with regard to newly found variants? Is there any moral obligation to reinterpret the data? Would biobanks be allowed to use this information for scientific research? Empirical studies are also necessary to evaluate proposed disclosure policies and to investigate the preferences of parents and children.

To conclude, although the scope and significance of genetic risk information generated by NGS have changed considerably, the leading ethical principles, in our opinion, have not. A difference in degree does not always constitute a difference in kind.

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