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Health Care Analysis (2021) 29:249–261
https://doi.org/10.1007/s10728-020-00425-7

ORIGINAL ARTICLE

'We Should View Him as an Individual': The Role of the Child's Future Autonomy in Shared Decision-Making About Unsolicited Findings in Pediatric Exome Sequencing

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Accepted: 10 December 2020 / Published online: 2 January 2021

Abstract

In debates about genetic testing of children, as well as about disclosing unsolicited findings (UFs) of pediatric exome sequencing, respect for future autonomy should be regarded as a *prima facie* consideration for not taking steps that would entail denying the future adult the opportunity to decide for herself about what to know about her own genome. While the argument can be overridden when other, morally more weighty considerations are at stake, whether this is the case can only be determined in concrete cases. Importantly, when children grow into adolescents, respect for future autonomy will have to give way to respecting their emerging autonomy. When pediatric exome sequencing is done for complex conditions not involving developmental delay, respect for the child's future or emerging autonomy should be a primary consideration for those charged with deciding on behalf of the child. Building on what Emanuel and Emanuel have termed the 'deliberative model' of shared decision making, we argue that if parents fail to give these considerations their due, professionals should actively invite them to do so. Taking a directive stance may be needed in order to make sure that the future or emerging autonomy of the child are duly considered in the decision-making process, but also to help the parents and themselves to shape their respective roles as responsible care-givers.

Keywords Pediatrics · Clinical sequencing · Unsollicited findings · Future autonomy · Shared decision making · Ethics

Introduction

The introduction of exome sequencing as a diagnostic tool in clinical pediatrics has proven beneficial in that it allows finding a diagnosis for children with complex genetic disorders that would otherwise have remained unexplained. This saves

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parents and children the burdens of a further 'Diagnostic Odyssey' [11] and may help them with a more adequate prognosis and possibly also with options for treatment and care. At the same time, there is much debate about how best to deal with the challenges of this powerful technology, given its potential for findings unrelated to the diagnostic question [4]. In this paper, we refer to these as 'unsolicited findings' (UFs).[1] In pediatric exome sequencing, UFs are beneficial when revealing a variant clearly predictive of a childhood-onset disorder that allows for timely treatment or prevention. However, UFs may also show the child to be at a significant risk for later onset disease, including disorders for which no treatment or prevention are available. An important challenge, both for interpretation and counseling, is that apart from clinically relevant UFs (genetic variants classified as either 'pathogenic' or 'likely pathogenic'), sequencing may also reveal so-called Variants of Uncertain Significance (VUS): genetic variants for whose role in disease there is (presently) insufficient or conflicting data [31]. In view of the wide range of possible UFs and their complexity, difficult questions arise with how strategies for return of results, but also pretest information and counseling, should be shaped so as to enable both professionals and parents to fulfill the moral responsibilities that come with their respective roles as (medical) caregivers and representatives of the child.

In earlier papers we have reported the results of two consecutive interview studies with parents of children undergoing clinical exome sequencing in an academic hospital in the Netherlands. The first study was with parents of children (ages < 1–17) having such testing for conditions involving developmental delay (DD conditions) [16], the second with parents of children (ages 1–15) having sequencing for other complex conditions. In the latter study, all children were either expected to develop into competent adults, or well on the way already to reaching that stage in their development (non-DD conditions) [37]. All interviews were held shortly after the parents (where applicable together with the adolescent) had given consent to clinical exome sequencing for their child. In the interviews, we explored the parents' preferences for receiving or not receiving predefined categories of UFs that had been explained to them during pretest counseling.

An interesting difference between parental views in the two studies (for DD vs. non-DD conditions), concerned the role of the argument that the future adult should not be deprived of the opportunity to make her own decisions about what to know about her genome. In the DD group, where it was often highly questionable whether the child would ever grow into a competent adult, some parents opted to decline receiving UFs (other than for conditions actionable in childhood), precisely because

[1] Findings unrelated to the reason for testing occur in all branches of medicine. They are often called 'incidental findings' (IFs). However, 'incidental' might suggest that such findings are rare, which is certainly not the case in clinical genomics. For this reason, the European Society of Human Genetics (ESHG) regards 'unsolicited findings' (UFs) as the more appropriate term in this context. [39] Conceptually, UFs (or IF)s are to be distinguished from so-called 'Secondary findings' (SFs). Although the latter also refer to results unrelated to the original reason for testing, SFs are actively sought for, whereas UFs are not. [30] It should be noted that both with regard to UFs and SFs, there is a risk of overdiagnosis, resulting from the fact that current predictivity data for the variants in question derive from evidence generated in affected families, whereas UFs or SFs are found in unaffected individuals [38].

they wanted to protect the child's future autonomy, whereas we did not find such reasoning (at least not explicitly) in the non-DD interviews, where there was no reason not to expect the child to become an autonomous person.

These findings are interesting, firstly, because they are counterintuitive. One would have expected parents of children with a clear potential to grow into competent adults to be more inclined to regard their child's future autonomy as a morally relevant consideration, than parents of children without a similar potential. However, our findings seem to suggest the opposite. We will present an hypothesis as to how this might be explained later in this paper.

A second reason why these findings are interesting is that the moral argument of respect for the child's future autonomy has received quite some attention in debates about the ethics of genetic testing. As we will discuss below, the strong emphasis on the importance of this argument in earlier debates has more recently given way to a tendency towards questioning its relevance. If the arguments behind this shift are valid, then what to say about parents attributing moral weight to their child's future autonomy, whether realistically expected or not? Do these parents make a mistake in their moral reasoning? By contrast, if the meant shift is not based on valid arguments, then perhaps the silence of other parents on this score may reveal a lack of sensitivity for what should have been an important consideration for them?

In the two main sections of this paper, we will do the following. We will first make the case for the claim that relevant differences between the earlier debate about predictive testing and the current one about reporting UFs do not detract from the continued importance of respect for future autonomy as a prima facie consideration limiting what information the parents are morally entitled to obtain about their child's genome. In the second main section, we discuss the implications of this view for counseling parents in the context of shared-decision making about disclosure of UFs in pediatric exome sequencing. Here we argue that in this context a deliberative model is most appropriate, in which professionals need not refrain when necessary from inviting the parents to consider what follows from their responsibility for their child, including with regard to respecting the child's future (or emerging) autonomy.

The Role of the Child's Future Autonomy in Debates About Genetic Testing

The debate about disclosure of UFs following pediatric exome sequencing connects with an earlier, and still ongoing, debate about predictive genetic testing of children in families at a known high risk of a genetic disorder [7, 29]. This earlier debate led to a broad consensus, that children who are too young to be able to decide about this themselves should not be tested for later onset disorders, except for conditions where options for treatment or prevention are available that must be initiated already during childhood [5, 6, 12, 42].[2]

[2] For an early dissenting voice see the contribution to this debate by Stephen Robertson and Julian Savulescu in their 2001 Bioethics paper [32].

Arguments for this position are of two kinds, welfare based and moral rights based. Relevant welfare-based arguments reflect concerns about how the burdens of risk status information may affect the parent–child relationship and overshadow the child's psychosocial development. For instance, it is argued that since many adults in families affected by a later onset condition prefer not to be tested themselves, precisely because they fear that the psychosocial implications might on balance be negative, we should think twice about testing young children for such conditions [13]. The moral rights based argument holds that predictive genetic testing of children for later onset disorders fails to respect the child's future autonomy, as the autonomous person that she will grow into will be deprived of the option of deciding for herself about whether or not to know her at risk status for the relevant condition. Moreover, the fact that others have prior disposition of this information would amount to an infringement of her informational privacy. This line of argument refers to the central importance that in modern liberal societies is given to the principle of respect for persons as the autonomous authors of their own lives and to the subsequent acknowledgement of self-determination and privacy as important moral rights. Here it is argued that this should have consequences for how we think about testing children for later onset disorders. As the child will grow into a person with these same rights, her future ability to carry these out should not be "sabotaged" by allowing her parents to have her tested [18].

While reflected in professional guidelines until around the turn of the century [2, 22], a loosening of the consensus regarding not testing children for later onset disorders is reflected in more recent statements. These still hold that predictive genetic testing for such conditions is best deferred until adulthood, but allow for more flexibility when responding to parental requests [3, 9]. The argument given for this shift is that concerns about possible harm have not materialized: "studies to date suggest that most children and families manage this type of predictive information without significant adverse impacts" [8]. It has also been argued that for children in high risk families, genetic testing may in fact be beneficial as it puts an end to uncertainty [41]. In case of an unfavorable outcome this would allow open communication with the child on the level of its understanding. At a young age, children are found to be able to incorporate far-reaching information in their developing identity, also depending on the quality of parental support [40]. However, the call for more flexibility has been questioned on two counts. Firstly, it is uncertain whether the more optimistic view of the impact of risk status information also applies to findings pertaining to serious later onset disorders for which there is a lack of adequate treatment options, such as Huntington's Disease [40]. By no longer clearly rejecting the testing of children for such conditions, the adapted statements are "disappointingly open to professional weakness", as one commentator has put it [14]. Secondly, as welfare-based concerns are only one strand of argument behind the classical consensus, the call for greater flexibility in dealing with parental requests has been criticized as too readily abandoning considerations pertaining to the child's future autonomy [10]. We agree with this: even if fears about adverse effects of telling children that they are at risk for a later onset disorder may have been exaggerated, the 'future autonomy' argument remains an important separate reason for not testing children who are expected to grow into an autonomous person.

Disclosing UFs from Pediatric Exome Sequencing: Relevant Differences with the Predictive Testing Debate

The debate about disclosing UFs of pediatric exome sequencing differs in two morally relevant respects from the earlier debate about predictive genetic testing of children in at risk families [19, 26, 36]. A first difference concerns the interests of family members. Whereas in the predictive testing context, testing the child for the specific disorder haunting its family will normally not lead to unanticipated genetic information about other persons, UFs may have precisely that effect. Child-centred (including autonomy-based) arguments for non-disclosure may thus conflict with family-centred arguments for disclosure. A second difference with predictive genetic testing of children in at-risk families is that whereas not testing (in that context) does not deprive the child of the option of testing as an adult, not-disclosing UFs involving later onset disorders may have precisely that effect, given that the future adult will have no reason to suspect being at risk for the relevant disorder. Of course, this is especially important where concerning later onset disorders for which timely treatment or prevention would be possible. By depriving the future adult of information that she might have taken as a reason for seeking timely medical help, non-disclosure of such UFs would seem difficult to justify in the light both of the child's best interest and of her future autonomy. Unless, of course, the information can be safeguarded and kept available in a way that gives the future adult the option of choosing to learn its contents.

Given these differences with the traditional predictive testing debate, it will in this context (disclosure decisions regarding UFs of pediatric exome sequencing) more often be the case that the 'future autonomy' argument has to give way to competing moral considerations pertaining to the interests either of the child itself, or of its close family members. Here we can only agree with the criticism, leveled in a recent review, of the way in which the notion of 'the child's right to an open future' has sometimes been used to turn the 'future autonomy' argument into a moral trump card that would not even allow considering any competing arguments [23]. However, even in this more complex context, it is in our view important to recognize that the moral rights based nature of the 'future autonomy' argument stands in the way of reducing it to a further welfare consideration. Respecting the child as the moral agent that he or she will become is essentially different from seeing her only as one of several stakeholders at the receiving end of an approach aimed at maximizing the welfare yield of pediatric genetic testing.

A clear instance of what we mean here is the recommendation of the American College of Medical Genetics and Genomics (ACMG) to use pediatric exome sequencing as an opportunity to screen for 'secondary findings' unrelated to the initial indication, including for later-onset disorders [1, 25, 27]. The arguments given are the health interests of the child's family members as well as the importance of not leaving the future adult unaware of important health information. In our view, however, there is a significant difference between acknowledging that these considerations can be relevant for decision-making about disclosing UFs in individual cases, and regarding them as grounds for actively screening children's genomic data for later onset conditions [33]. With welfare as the only moral currency, any

remaining concerns about autonomy easily lose out against the far more pressing health interests (not just of the child, but also of her close relatives) potentially served by the proposed search for secondary findings [15].

The Moral Importance of Respect for Future and Emerging Autonomy

Given the moral importance of the child's future autonomy, we think it should be taken seriously as a *prima facie* argument that requires separate consideration in each of these contexts and debates. Whereas in the light of this, testing (or screening) young children for later onset disorders would seem difficult to justify, disclosing UFs revealing the child to be at risk for such conditions may or may not be justified, depending on the relative weight of case-specific considerations including respect for the child's future autonomy. However, in both contexts, it is important to note that the case for safeguarding future autonomy can only be made with respect to those who will become, but are not yet themselves, fully autonomous persons. Where the child turns into an adolescent and becomes a mature minor, respect for autonomy must take the form of respecting her the emerging, no longer future, autonomy [29]. Here, the challenge facing parents and professionals is to determine whether the adolescent child's capacity to make well-considered decisions about her own life is sufficiently robust for making this shift [17].

Shared Decision-Making About Disclosure of UFs in Pediatric Exome Sequencing

In our earlier interview studies with parents of children undergoing clinical exome sequencing either for DD [16] or non-DD [37], we discussed their preferences for receiving or not receiving predefined categories of UFs against the background of our centre's default disclosure policy for these categories. Parents told us that this had the effect of eliciting critical reflection on the issues at stake in those choices. This fits the ideal of shared decision-making, where the role of the professional is not just to provide information, but also to support deliberation [20]. Especially in contexts involving complex choices between options that are not fully determined by strictly medical considerations, shared decision making is increasingly regarded as the ethically preferred approach to enabling truly informed decision making and consent [28]. This is also in line with the recent call to liberate the practice of genetic counseling from the spell of a narrowly understood ideal of non-directiveness, which leaves it ill-equipped to really help patients navigate the complicities of the choices they face in clinical genomics [35].

Two Models of Shared Decision-Making

However, as Emanuel and Emanuel have explained in their well-known paper on models of the doctor-patient relationship, shared decision-making can mean different things [21]. In what they call the 'interpretive model', counseling is aimed at

supporting the patient in finding out what decision is most in line with her personal values and ideals. Following this model, shared decision-making is still non-directive in the fundamental sense of not going beyond an exploration of what would follow from the values of the patient herself. For instance: given a choice between treatment options that are both in the range of the professional standard, but with different profiles in terms of aspects that individual patients may value differently (think of the choice between having mastectomy or breast saving surgery for breast cancer), all that counts is helping patients to arrive at decisions that are really theirs. By contrast, in the 'deliberative model', the professional has a moral stake in the matter of which she tries to persuade her patient: "(t)he physician's objectives include suggesting why certain health related values are more worthy and should be aspired to" [21].

When discussing these models, Emanuel and Emanuel show how they play out in the one-to-one clinical relationship between doctors and competent adult patients. Whereas in that context, the 'deliberative model' may well invite the criticism of amounting to a subtle form of paternalism [34], things are different where concerning shared-decision making with parents or other representatives of an incompetent patient. In this context, it is the 'interpretive' model of shared decision-making that seems to fall short, because it would require the professional to step back from her very responsibility to serve the best interest of her patient.[3]

As pediatric professionals and parents have overlapping responsibilities with regard to the child, a shared decision, in the sense of one that both parties can agree with, will quite naturally and without much debate or disagreement be arrived at in most cases, especially where regarding decisions with direct consequences for the child's health. In the context of our discussion, an instance of this is the strong parental support, found in both our empirical studies, for the policy to always disclose UFs pertaining to actionable childhood onset disorders. Where regarding UFs in other categories, there was more divergence, with parents often also disagreeing with proposed policy standpoints. Clearly, this did not reflect a failure on the part of the parents to appreciate their responsibility towards their child. In fact, we found that in all their reasoning about what to decide about UFs, parents very much took the perspective of how the information would be relevant for carrying out their role-related responsibility as primary caregivers [37]. However, following the deliberative model of shared decision-making, professionals may in this setting still feel duty bound to question any resulting choices that they think are not in the child's best interest.

[3] In their paper, Emanuel and Emanuel discuss two further models: the 'informative' and the 'paternalistic' model of the clinical relationship. In the former of these two, the professional limits herself to providing factual information, leaving it entirely to the patient to come to a decision; in the latter, the professional already knows what the best decision should be, and encourages the patient to consent to it. As there is no trace of shared decision making worth the name in either of these two models on the extremes of the 4-model spectrum, they are not relevant for our discussion.

The Child's Future Autonomy as a Consideration in Parents' Reasoning

In our interviews with parents of children having clinical exome sequencing for other reasons than developmental delay (non-DD group) we observed a strongly shared view that any information that might in whatever way be relevant for the health and wellbeing of their child in the course of its further life, should be for them as parents to control. Among these parents, we found this line of reasoning not only with regard to information about non-actionable childhood disorders, where parents felt they needed the information in order to be able to best take care of a child still dependent on them, but also where concerning carrier status of autosomal recessive disorders and later onset conditions [37].

With regard to later onset disorders allowing for timely treatment or prevention later in life, the reasoning was not only that the information might otherwise be lost, but very much also that it was up to them as parents to decide how and at what age to tell the child about its being at risk for the relevant condition. Whereas with regard to non-actionable later onset disorders several parents thought that without options for treatment or prevention such information was only burdensome and should not be revealed, others thought differently. They either emphasized the possibility of medical progress leading to a timely cure, or stressed the non-medical utility of information about what to expect for one's future health. Here again, the basic pattern of reasoning was that as parents they needed to be put in control of any information with a potential utility for the health or wellbeing of their child, either presently or in the future: "if someone (the hospital) knows something about one of us, then it must also be known to us" [37].

Those with adolescent children in this group were of course aware that their children were growing into competence. For instance, as one mother said: "If at some point they are in puberty you also grow towards the fact that they become adults. And that they make their own choices" [37]. However, none of the parents of pre-adolescent children in this group explicitly referred to their child's future autonomy as a consideration limiting parental rights to information about later onset conditions. By contrast, in the DD group some parents explicitly made this argument. Our hypothesis is that for the latter parents, the hope that their child would grow into an autonomous person, even against all odds, was reflected in a felt need to at least consider this an open possibility. This meant that as parents they were reluctant to make certain decisions that they regarded as belonging to the prerogative of their child as a future adult: "It's just, at least I feel that right now, even though he's still really young, we should view him as an individual, like 'hey, that's your call'" [16]. That we did not encounter this specific argument with parents of pre-adolescent children in the non-DD group, may indicate that for these parents considerations regarding the future autonomy of their child did not naturally emerge as a prominent element of the choices they were asked to reflect upon.

The Child's Future Autonomy as a Consideration for Shared Decision-Making

In this paper we have argued that the child's future autonomy should be taken seriously by all stakeholders as a *prima facie* argument in debates about disclosure of UFs. We have also argued that in this setting, what we have referred to as the

'deliberative model' of shared decision making is best capable of doing justice to the overlapping role-related responsibilities of professionals and parents. As we have explained, this entails that professionals should not refrain from bringing in their own moral perspective insofar as this reflects their understanding of their professional responsibility for the best interests of their incompetent patient.

Of course, the fact that parents of pre-adolescent children expected to become competent adults later in their lives did not bring up the moral importance of safeguarding their child's future autonomy as a consideration that might be relevant for their decision-making, need not mean that they would not acknowledge the importance of that consideration, or that they did not take it into account. However, to the extent that something morally important may be missing out in the reasoning of these parents, the upshot of our argument is that professionals should not hesitate to actively invite them to consider the future autonomy of their child in all decisions pertaining to later onset disorders or other conditions only relevant later in life. Clearly, this does not hold for parents of children undergoing clinical exome sequencing for reasons making it highly unlikely that they will indeed grow into autonomous persons. Our finding that some of those parents chose not to receive certain UFs on the basis of an unfounded hope about their child's future autonomy, raises the question whether professionals should take the opposite stance: should they try to help these parents base their decision making on more reasonable expectations about their child? As long as there is no reason for thinking that having that information would be vital for them in their role as life-long care givers of their child, the case for this would at least not be obvious. Clearly, being considered as a child who will grow into autonomy as any other, is not in itself harmful.

Any questioning by professionals of parental reasoning in the context of shared decision making is not just to make sure that the interests of the child are duly considered in the process, but also to help parents shape their role as responsible caregivers. Indeed, parents may need protecting from putting themselves in a position where they will not be able to fully serve the interests of their growing child. Specifically, the wish as parents to control all information about one's child including about how and when to disclose UFs pertaining to later onset conditions may lead to burdening the parent–child relationship by secrets that may prove difficult to manage and may also stand in the way of acknowledging the emerging autonomy of the adolescent.

The Role of 'Mirroring concerns' in Shared Decision-Making About Incompetent Patients

Finally, the proposed deliberative approach is also important from the perspective of enabling professionals to fulfill their responsibility. As we have argued, the 'interpretive model' of shared decision making falls short in precisely this respect in situations where the interests of incompetent patients (including children) are at stake. The deliberative model not only allows the professional to be directive if necessary, but a further important function is also that it enables her to reassure herself that the representatives of the patient have taken all relevant considerations into account.

This is what Gerrits et al., in the somewhat different context of decision making pertaining to the interests of future children in medically assisted reproduction, have referred to as "mirroring concerns". In an interview study performed in a Dutch fertility clinic, they found that where shared decision-making led professionals to conclude that their own moral concerns were 'mirrored', so to speak, in the reasoning and reflections of the parents-to-be, this made it easier for them to leave it to the prospective parents to make the decision [24]. We think that shared decision-making about disclosure of UFs may serve the same purpose of allowing professionals to find themselves reassured that relevant moral considerations, including the child's future or emerging autonomy, are well-understood and taken seriously by the parents.

Conclusion

The child's future autonomy should be taken seriously by all stakeholders as a *prima facie* argument in debates about disclosure of UFs of pediatric exome sequencing. Our finding that parents of pre-adolescent children expected to grow into an autonomous person did not bring up the moral importance of safeguarding their child's future autonomy may signal a need for professionals to actively invite parents to consider the possible relevance of this perspective for their decision-making. This presupposes what we have referred to as a 'deliberative model' of shared decision-making that acknowledges professionals and parents to have a joint responsibility to serve the best interest of the child.

Author Contributions All authors contributed to the design of the paper; a first draft was written by WD; IB, AT and GdW revised it for important intellectual content. All authors approved of the final version of the manuscript.

Funding This research was funded by ZonMw—the Netherlands Organization for Health Research and Development (Grant No. 70-73000-98-047).

Compliance with Ethical Standards

Conflict of interest The authors declare no conflict of interest.

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