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The "Right Not to Know" in the Genomic Era: Time to Break From Tradition?

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The target article by Clayton and colleagues (2014) helpfully lays out the differences between two recent sets of genetic testing guidelines, referred to as the "AAP/ACMG" (American Academy of Pediatrics [AAP] and American College of Medical Genetics and Genomics [ACMG] 2013; Ross et al. 2013) and "ACMG ES/GS" (exome sequencing/genome sequencing) (Green et al. 2013; Incidental findings 2013) statements. These statements differ markedly in their respective positions on the testing of children for adult-onset disorders that cannot be treated during childhood. While AAP/ACMG generally discourages such testing, ACMG ES/GS requires analysis of some gene variants that could predict adult-onset disorders in children.

This difference reflects a dramatic shift in the priority granted to a person's "right not to know" genetic information. ACMG ES/GS explicitly acknowledges that its support for generating genetic results for adult-onset conditions in children is a departure from previous recommendations. Its authors argue that the interests of other parties, including the child's parents, must be taken into account: "To mask or withhold the incidental finding is to state that the child's right not-to-know supersedes the parent's opportunity to discover a life-threatening risk factor" (Green et al. 2013, 572; Incidental findings 2013). This stance has been met with significant criticism; some argue that the ACMG ES/GS recommendations contradict ethical clinical practice by failing to preserve a child's future choice about genetic results (Allyse and Michie 2013; Wolf, Annas, and Elias 2013), and others argue that these recommendations are also problematic from the parents' perspective, impinging on their right to refuse information and even lifesaving treatments based on that information (Burke et al. 2013).

Are these critiques valid, or is the "right not to know" an anachronistic concept in the genomic era? The current formulation of a right not to know emerged in relation to the ability to test for a small number of devastating genetic conditions with distinctive features. The introduction of large-scale sequencing in the clinical setting prompts us to consider the

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extent to which the right not to know paradigm still holds true, given the dramatically expanded scope and diversity of information that is likely to be generated.

THE "RIGHT NOT TO KNOW" PARADIGM

In the context of genetic testing, the "right not to know" refers to the idea that adults should be permitted to control whether they receive genetic information—particularly information about the risk of future illness—and that their desire not to know certain kinds of information should be respected. The justifications offered for a right not to know are twofold, grounded in respect for decisional autonomy and/or an interest in protecting individuals from receiving unwanted and potentially harmful information. An adult's right not to know genetic information has implications for children; testing a child preempts the option for that child not to learn the information as a future autonomous adult. Some (ourselves included) have argued that respect for a child's emerging autonomy provides a justification for deferring genetic testing until adulthood, unless there is a compelling medical indication to test sooner (AAP and ACMG 2013; Abdul-Karim et al. 2013; Ross et al. 2013).

Defenders of a right not to know often point to empirical data on the uptake of predictive genetic testing, with Huntington's disease (HD) serving as the paradigmatic case (Hayden 2003; Tibben 2007). That up to 80% of adults with a family history of HD refuse genetic testing (Creighton et al. 2003; Robins Wahlin 2007; Tassicker et al. 2009) is commonly cited as evidence that many reasonable, autonomous adults choose not to know genetic information of this nature. The inevitable neurological features of HD and lack of effective interventions make it a compelling case for a right not to know, but also perhaps an idiosyncratic example. A positive HD genetic test result changes an at-risk individual's chance of developing HD from 50% to 100%, which, although removing uncertainty, creates a substantial psychological burden without offsetting clinical benefits.

The genetic counseling and testing paradigm that has emerged from the experience with HD, which entails significant effort and resources, has been applied to predictive genetic testing for other adult-onset conditions like hereditary breast cancer (BRCA) and Alzheimer's disease (AD) (Hayden 2003). Although there is growing evidence that predictive testing for BRCA mutations can be beneficial (Nelson et al. 2013)—perhaps less so for AD (Howard and Filley 2009)—concern for psychosocial harms has led to an emphasis on developing robust counseling consent processes that permit adults to make informed decisions about testing (Howard and Filley 2009; Nelson et al. 2013; Van Oostrom and Tibben 2004).

The right not to know paradigm is invoked in the genetic research setting, particularly when the information in question is incidental or secondary to the condition under study. Participant preferences about receiving genetic test results in the future may be solicited prospectively via "checkboxes" on consent documents (Hull et al. 2004), using language such as the following: "If a genetic condition is identified that may have potentially important health and treatment implications for me, I agree to allow [name of study/ investigator] to notify me and with my permission to notify my physician" (Levy et al. 2010). Using checkboxes in consent forms is a fairly common but imperfect method to

safeguard the right not to know genetic research results, given the necessarily broad framing of result categories and the fact that a checkbox cannot stand in for robust pretest counseling.

WHO WOULDN'T WANT TO KNOW LIFESAVING INFORMATION?

Although the right not to know is rooted in important foundational research on people's preferences about learning genetic information about themselves, conditions like Huntington 's disease and Alzheimer's Disease are *sui generis* because they are such devastating and unmitigatable neurological conditions. Given that next-generation sequencing technology produces a broad range of results, it is time to look beyond the limited examples on which the right not to know has been established. It seems uncontroversial to state that almost everyone would (and perhaps even should) want to know genetic information that could lead to an intervention that would prevent or mitigate serious morbidity or mortality. Although whether ACMG ES/GS included the correct 56 variants remains controversial, we support their view that genetic variants strongly associated with serious disease for which there is an effective treatment or intervention might warrant special handling that deviates from norms about the so-called right not to know (Abdul-Karim et al. 2013).

This position is supported by unpublished survey data, currently under analysis, from nearly 800 institutional review board (IRB) members and staff about their views on genetic incidental findings. When asked whether it would be acceptable for individuals to choose not to know their genetic information, an overwhelming majority (96%) endorsed the right not to know. In response to a more concrete scenario wherein a research participant has chosen not to receive any genetic results but during its analysis the research team finds information that will prevent serious disease and perhaps even save the life of the participant, when asked whether the team should disclose the finding even though the participant indicated that they did not want to receive any genetic information, only 35% said that the team should definitely respect the individual's choice not to know, and 28% said that they probably should not return the information.

These data support the proposition that while the right not to know may seem appropriate in the abstract, people's views change once they are presented with a case where a specific piece of lifesaving information is available. This suggests that conceptions of the right not to know aren't absolute, and that some people will move to the view that it is appropriate to disclose a lifesaving piece of information to people who didn't think that they wanted it. This also suggests that responses to an abstract checkbox on a consent form differ radically from responses to a conversation about an actual, concrete example.

WHY NOT JUST SOLICIT PREFERENCES?

In response to this argument, some might propose that the problem of sorting through the deluge of data that will be produced by genomic medicine should be solved by simply asking people up front, in a robust manner, what they do or don't want to know. We believe, however, that it will be extremely challenging to solicit preferences for every conceivable category of genetic variant. Furthermore, we question the validity of privileging broad, hypothetical answers to a series of checkboxes in consent forms over well-informed and

nuanced professional clinical judgments. Finally, people's views will change over time; the prospect of continuously soliciting preferences seems unwieldy and unduly burdensome.

This isn't to say that we should abandon the principle of respect for an individual's autonomous choices. Clearly, reasoned choices not to know genetic information about oneself, especially where there is no possibility of harm flowing to others, should be upheld. Although we believe that most autonomous adults would want to know lifesaving information, there will be compelling exceptions, such as for people with previously diagnosed terminal illnesses, elderly people for whom invasive medical treatment might not be indicated, or people with religious objections to certain kinds of treatments. In general, these exceptions center on cases where individuals with a valid reason why they would not want to take clinical action should be able to exercise their right not to know. But these kinds of cases should represent a clearly defined exception, rather than the basis for a broadly applied conception of the right not to know.

With the imminent adoption of genomic sequencing technologies into the practice of medicine, now is an appropriate time to reexamine the extent to which we need to preserve a robust right not to know. At a minimum, we believe there are some cases in which it might be appropriate to override a previous broadly expressed preference not to receive genetic information, and that it is not appropriate in the genomic era to solicit and document a preference not to receive genetic information via broad and oversimplified tools such as consent form checkboxes. Furthermore, there may be cases in which the benefits of disclosing predictive genetic information to a parent will override the goal of deferring a child's choice to be tested for that information until adulthood, as we've argued elsewhere (Abdul-Karim et al. 2013). While a fully developed argument against an absolute right not to know is beyond the scope of this brief commentary, we hope that we have at least given others pause before falling back on standard arguments that were born in a targeted genetic testing era. We think that the impending era of genomic medicine should prompt better research on whether the public actually thinks that an absolute right not to know exists, and if not, the contours of the cases where clinicians should be allowed to freely exercise their clinical judgment about the kinds of genetic findings that should automatically be returned.

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