in genomic research," but "these recommendations [are] for the situation in which a clinician orders exome or genome sequencing for a specific clinical indication. In this circumstance, a laboratory report *will be* returned to that clinician" (my emphasis). It is hard to understand why there should be less debate about returning incidental findings in clinical practice than in research, given the uncertainties discussed above. Clinical practice should require a more rigorous debate, and it should be performed before recommendations that "may be introduced as evidence of the standard of care"[2] are promulgated. Truncating debate will have as serious consequences for society as truncating sequences may have for individuals. The ACMG should rescind these recommendations and proceed more cautiously.

DISCLOSURE

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Paternalism and the ACMG recommendations on genomic incidental findings: patients seen but not heard

To the Editor: Incidental findings that may arise in whole-exome or whole-genome sequencing pose significant challenges for clinical care. The American College of Medical Genetics and Genomics' (ACMG's) recent article, "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing," establishes routine analysis of pathogenic variants of a list of disease-associated genetic loci as a standard of practice when clinical whole-genome sequencing is done for any reason except prenatal testing.[1] The findings are to be reported to the ordering physician for disclosure to the patient (or if a child, to his/her parents). This recommendation reverses current practice that supports the patient's right to choose not to be informed of incidental genetic information.

The year-long consensus process used to develop the recommendations involved extensive discussions among an ACMG Working Group, review by an independent group of experts, and approval by the ACMG Board of Directors. The individuals involved are all well-qualified representatives of the medical, clinical laboratory, and genetic counseling communities. Conspicuously absent from the ACMG process, however, are the voices of patients and families who might need whole-exome or -genome sequencing to diagnose a serious medical condition. This is a concern because a key ethical principle in devising effective and practical clinical recommendations is that they are fair, which means that all individuals affected by the recommendations should contribute to their development.

Ethical concerns underpin clinical genetics but are compressed in these recommendations in which the professionals' fiduciary duty trumps patient autonomy: "Clinicians and laboratory personnel have a fiduciary duty to prevent harm by warning patients and their families about certain incidental findings and that this principle supersedes concerns about autonomy, just as it does elsewhere in medical practice."[1] The physician–patient relationship is based on trust and responsibility, but it is not an ethical principle, nor is it a fixed concept. The traditionally paternalistic model of medicine, underpinned by values and assumptions about passive patient and authoritative physician roles, is increasingly criticized by patients, advocacy groups, health policy makers, and many physicians. Notions of trust and the fiduciary relationship are shifting as medical practice engages patients, offers transparency of information, and encourages more patient responsibility for the choices made.

We also question the ACMG Working Group's contention that routine disclosure of the results of a set of genetic analyses that is actively sought in every case is no different from reporting the incidental discovery of an unexpected disease manifestation in other clinical contexts. When physicians perform a complete medical history and physical examination or carefully review the entire field revealed by an imaging study, they are looking for signs of disease that is already present in a particular patient. By contrast, the ACMG recommendations require looking for mutations that predict diseases that have not yet occurred in each patient who is tested.

The ACMG Working Group acknowledges that their recommendations are not evidence based: adequate evidence regarding the best way to return genomic incidental findings does not yet exist. Nevertheless, the evidence that is available—some of which was neglected in the recommendations—should be considered before endorsing disclosure to patients regardless of their preferences. Many people choose not to learn about

mutations they may carry that predict serious and medically actionable disease. For example, only 43% of 2,646 female first-degree relatives of patients with known *BRCA1/2* mutations in one study chose to be tested.[2]

In a qualitative study,[3] we explored patient, public, and professional views of disclosing genomic incidental findings. Patients and public groups emphasized patient choice while acknowledging difficulties around decision making. They emphasized having "the power" to choose disclosure or not, and that patients no longer accept medical paternalism. They also recognized practical difficulties of uncertain data interpretation and the difficulty of effective communication of extensive data to patients. However, our study participants emphasized that such challenges do not pose insurmountable barriers to patient choice. They suggested information be communicated to patients in novel and user-friendly computer-based formats that emphasize actively engaged and responsible patients and facilitate patient choice.

Another key concern prompted by the ACMG recommendations is the notion of coercive consent to testing and disclosure for vulnerable patients desperate to find the cause of a serious disorder. Although the recommendations claim that people can opt out, this is unlikely to be presented as a freely available choice in most instances. Some patients who prefer nondisclosure may decline whole-genome sequencing even though by doing so they lose the opportunity to end their diagnostic odyssey.

Rather than establish disclosure of a list of secondary genomic results regardless of patient preferences as a standard of care, it is important to consider patient perspectives and to understand what disclosure might mean in an individual's life context beyond the clinic. At every stage from "bench to bedside," the ACMG recommendations neglect patient viewpoints, and in doing so fail to provide patient-centered care, which is recognized as good practice in the rest of medicine. The recommendations, therefore, demonstrate an unfortunate kind of genetic exceptionalism.

We need to ask, "what are the barriers to informed choice?" We need more evidence and to draw fully on the evidence that we already have. Consensus among experts alone is not sufficient; recommendations that consider the patients' perspective will be more ethical and ultimately more effective. The paradox is that these recommendations at the cutting edge of medical practice are grounded in the past. By contrast, we call for the patient voice to be part of the decision-making process and for studies of patient concerns and perspectives to be incorporated into the evidence base for clinical genomics practice. We believe that these recommendations should be withdrawn and revised, taking into account existing research on patient concerns about genomic incidental findings as well as the results of direct consultations with genetic disease patients and their families. Further studies of patient perspectives and decision making in this context should also be encouraged.

DISCLOSURE

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Response to Townsend et al.

To the Editor: I appreciate Townsend et al.'s thoughtful response ("Paternalism and the ACMG Recommendations on Genomic Incidental Findings: Patients Seen But Not Heard"[1]) to the "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing."[2] The crux of their objection to the recommendations is that the input of consumers (or patients) was not sought as part of the process and that the recommendation that laboratories return results of specific incidental findings violates patient autonomy.

I am concerned that much of the discussion about the recommendations has been couched in terms such as "paternalism," "patient autonomy," "genetic exceptionalism," etc. I worry that these words tend to polarize arguments, making things seem more black and white than I think they are.

The key point that influenced the thinking of the working group, speaking from my own perspective as a member of the working group, is that the laboratory that interprets the sequencing and generates the report is not in a position to judge whether the person whose genome is sequenced should or should not be privy to results that could have life or death implications. We believe that this is the job of the clinician who has ordered the sequencing, who can take into account the perspectives and needs of his or her individual patient.

The analogy of reporting incidental findings from radiological studies is frequently cited in the context of the American College of Medical Genetics and Genomics recommendations.[2] It is an imperfect analogy; incidental findings sometimes jump out at the radiologist and may be difficult to consciously ignore. I have not heard arguments, however, that reporting such incidental findings in radiology violates patient autonomy and suspect that consenting all patients in advance who are about to have X-rays or other radiological studies would be viewed as impractical. Townsend et al.[1] make the point that incidental