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Looking for Trouble and Finding It

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We agree with Lázaro-Muñoz and colleagues that patient preferences matter. Clinicians should strive to elicit and respect those preferences. We take issue, however, with how the authors apply this precept to “preventive genomic screening” (PGS). We believe their argument is flawed by the failure to distinguish screening from other medical care, or to acknowledge clinicians' responsibility to weigh the potential for benefit and harm in determining what healthcare choices to offer.

Against The Paternalism Versus Individualism Framing

The authors frame the central ethical tension in PGS as a conflict between paternalism and individualism. In part they do so because they take their definition of paternalism from the 2013 policy statement of the American College of Genetics and Genomics (ACMG) on pursuit of additional findings when genomic sequencing is done (Green et al. 2013). That statement proposed that clinicians have a duty to look for, and inform patients of, “risks of potentially preventable harm … even if these risks were not part of the clinical purpose for ordering genomic sequencing, and their examination was not explicitly consented by patients.” The authors contrast this position with the “individualistic counterpoint,” grounded in respect for patient autonomy, which argues for patient control and choice in healthcare decision-making. Lázaro-Muñoz et al. are of course right to characterize the 2013 ACMG statement as an instance of paternalistic overreach; the recommendation to proceed with additional analysis in the absence of consent was widely rejected as inconsistent with the ethical and legal duties of clinicians (Burke et al. 2013), and was subsequently reversed (ACMG Board of Directors 2015).

However, framing the debate as a case of paternalism versus individualism sets up a false choice between two dysfunctional extremes: either the clinician makes decisions without involving the patient, or the clinician provides technical information and leaves the patient to decide. Neither of these is a good model of patient care, as is borne out by the growing body of work around patient engagement.

Clinicians deeply respected by their peers emphasize the importance of establishing a shared understanding with their patients about the goals of care (Schenck and Churchill 2012); and patients testify to the importance of a dual agency between patient and clinician in medical decision-making (Churchill et al. 2013). Indeed, “patient choice” can turn into patient abandonment if a therapeutic alliance of this kind is not established (Woolf et al. 2005).

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The question raised by PGS is not about the competing claims of paternalistic advice and patient autonomy, but rather about how healthcare choices should be formulated and offered. When a patient brings a health problem to a clinician, we expect the clinician to offer appropriate healthcare, taking into account the efficacy and potential harms of different therapeutic approaches. Patient choices are not open-ended, but rather are a matter of deciding among the available options. The competent provider thus has two tasks: (1) to identify what can realistically be achieved with available technology, and (2) to help the patient determine how available options may best be deployed to meet the patient's goals and preferences. Patients may sometimes request particular treatments, and their preferences should always be taken seriously; but if the request is for care that is unrelated to the problem or unlikely to work (e.g., antibiotic treatment for a viral infection), the clinician has a duty to recommend against it. This duty stems from the reality that all medical interventions (even tests to assess risk) have the potential to cause harm. It is therefore a foundational principle of clinical practice that interventions should be offered only when there is a likelihood of benefit commensurate with foreseeable risks. This consideration has particular importance for screening.

The Offer of Pgs Is Premature

PGS, as Lázaro-Muñoz and colleagues note, is an exercise in “looking for trouble.” This is an apt description of all medical screening, which seeks to identify actionable health problems in the absence of clinical signs or symptoms. In the case of PGS, screening would consist of looking for genetic disease (or risk for disease) in the absence of personal or family history pointing to the disease. The authors acknowledge that a public health rationale is lacking for PGS. They suggest that this point bolsters their preference for a menu-based approach to testing; but we would argue that in the absence of a public health rationale, PGS should not be offered.

All screening, including PGS, must be justified by evidence of net benefit at the population level, because screening by its very nature exposes many people to potential harm in order to benefit the few who are identified with actionable findings. As with other screening tests, the potential harms of PGS relate to false positives, ambiguous results, and overdiagnosis, that is, the diagnosis of a condition that was destined to remain asymptomatic or could have been treated when symptoms occurred (Grimes and Schulz 2002). Each of these outcomes has the potential to generate medical work-up, distract health providers from more important concerns, increase healthcare costs, and expose patients to unnecessary risks of medical intervention (Grimes and Schulz 2002). There is ample reason to be concerned about such outcomes with PGS: the current technical performance of genomic sequencing (Dewey et al. 2014), and our limited knowledge about the penetrance of most genetic disorders, indicate that PGS will generate problematic findings in many patients – likely far more than would receive true positive results.

Genomic screening in some form may ultimately have the potential to provide public health benefit (Prince et al. 2014). For example, an argument has recently been mounted for population-based *BRCA1/2* screening (King et al. 2014). A few other conditions on the ACMG list (e.g. malignant hyperthermia, Lynch syndrome, Multiple Endocrine Neoplasia

Type 2) might also be suitable for population screening, if we had evidence that a screening protocol could minimize false or ambiguous findings. Investigation would also need to compare PGS to other available screening methods. For example, familial hypercholesterolemia, another condition on the ACMG list, can be identified via genomic analysis; but this approach is unlikely to outperform lipid studies as a general screening strategy. In short, there is reason to pursue research to assess PGS as a means to identify actionable genetic conditions, but our current evidence base – which lacks any systematic population-based studies to correlate sequencing results with health outcomes – is woefully inadequate to support screening. Hence, it would be irresponsible for a health provider to offer PGS at this time.

Role of Patient Choice

Lázaro-Muñoz and colleagues propose that some patients might want to pursue genomic sequencing because of personal or family history disease. But this would not constitute screening; instead it would represent healthcare to address a presenting complaint, arguably the core function of medical practice. Rather than asking patients to select from a menu of options, this process is best approached as a discussion between the patient and provider, possibly augmented by physical or other examinations, culminating in testing (or other work-up) that has the potential to benefit the patient. As with all medical care, the patient's preferences should determine what course is pursued among the available options.

Patient choice has the same significance when screening recommendations are made. If rigorous research eventually establishes a legitimate public health rationale for PGS, it should be offered just as colon cancer screening or other established screening tests are offered. Clinicians should explain the rationale for such screening (including the scope of potential benefits and harms) and answer any questions the patient has. And of course, the patient is always free to refuse. This approach brings beneficence and respect for persons into harmony, rather than opposition; and would give PGS its proper place in the context of patient care.

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