Discussions about outcomes of genomic medicine center on the construct of utility. Callahan et al \(^1\) reported findings from a systematic review of the literature on genomic medicine, which they define as genome or exome sequencing and associated care, for critically ill infants. Through a careful dissection of the ways in which genomic medicine utility has been prospectively measured, the review provides insight into how investigators have conceptualized and assessed utility in a specific, policy-relevant clinical context. Callahan and colleagues \(^1\) found that nearly all the prospective studies included in their review reported evidence on utility according to their classification categories, indicating widespread acknowledgment of the importance of the outcome. However, they found considerable heterogeneity in terminology, domains measured, reporting transparency, and approaches to data collection among 21 included studies, indicating a lack of consensus on utility assessment in genomic medicine.

**From Individual Patients to Populations**

In more than a decade since genomic sequencing was first used for a patient diagnosis, clinical applications of this technology have rapidly increased. Successful early applications resulting in patient diagnoses and changes in care trajectories were primarily communicated through case reports. \(^2\) Larger numbers of patients now have genetic sequencing performed as part of research cohorts and clinical care, allowing calculations of the average effect of the intervention; however, the influence of compelling individual patient stories on outcomes reporting remains. The case report tradition is reflected in the findings of Callahan and colleagues \(^1\) in 2 ways: investigators’ choice to highlight “exemplary cases of utility” within larger patient cohorts and the reporting of outcomes using study-specific, investigator-developed processes to assess utility. Given the potential for large, life-changing impacts for some patients, case reports are undoubtedly important to humanize data sets. However, a commitment to tailored assessment of individual patient outcomes is perhaps a reason why standardization of a utility metric has lagged. Disproportionate highlighting of certain cases indicates the tension between a focus on individual patient care in clinical medicine and a focus on population-level outcomes more common in the public health sciences. As genomic sequencing applications have scaled up, so should the approach to assessing effectiveness. Standardization of outcome measurement to examine population-level effects does not detract from genomic sequencing success stories for individual patients; rather, it supports their generation by informing evidence-based application of this technology.

**Utility According to Whom?**

One of the key impediments to consistent measurement of utility is the definition of it. The American College of Medical Genetics and Genomics defines utility to include health, psychological, and economic outcomes for patients, families, and health systems. \(^3\) This definition does not lend itself to a single methodological approach to assessment. Broad understandings of utility have led to numerous operationalizations, with distinct types of utility reflecting various ways in which effects of genomic medicine might be categorized. Effects of knowing genomic information that manifest outside health care, known as personal utility, have traditionally fallen within the scope of research on
the ethical, legal, and social implications of genomics in the US. Research on personal utility centers patient and family perspectives on broad benefits and harms, often using qualitative methods. In contrast, clinical utility, which is the focus of the analysis by Callahan et al,¹ is usually assessed based on clinicians’ perceptions of the effect of genomic sequencing on prognostication and care. Neither personal utility nor clinical utility alone tells the full story of the effects of genomic medicine. However, a valid and reliable measure of clinical utility may be fit-for-purpose, such as being a primary outcome in effectiveness trials.

From a health system perspective, the association of genomic sequencing with length of stay in costly neonatal intensive care units and with downstream health care utilization have been important considerations for short-term economic value.⁴ Associations of expected longer-term effects of genomic medicine with quality-adjusted life-years among critically ill infants have been modeled.⁵ Although there are numerous methodological challenges associated with conducting such analyses, evaluation of effects on length of stay and quality-adjusted life-years is not necessarily inconsistent with the goal of genomic medicine, as Callahan and colleagues¹ imply, even if consideration of these outcomes is not what drives clinicians’ decisions about patient care. Benchmark data on the effect of genomic medicine on health care utilization and health outcomes in various clinical contexts can inform efficient implementation. Data on these outcomes can also affect access to genomic services through influencing insurance coverage decisions.⁶ Although length of stay and quality-adjusted life-years do not directly measure the value of knowing information or broader conceptualizations of benefits and harms to patients and families outside health, they do allow systematic assessment of the effects of genetically informed care that provides important evidence to decision makers and that can complement other measures.

**Toward Standardized Measures**

As genomic medicine is increasingly implemented in clinical care, valid and reliable measures of key end points that can be collected in clinical settings are needed to inform clinical guidelines and coverage policy. State Medicaid programs are beginning to cover the cost of rapid genome sequencing for critically ill infants, and federal legislation to support broader increases in access to genomic services for infants and children has been introduced.⁶ Collection of effectiveness data should be standardized and scalable because consistency and transparency of outcomes assessment will be integral to demonstrating the effects of these policies.

One path toward a more broadly accepted set of genomic medicine outcomes is to use consensus methods to develop a core outcome set for effectiveness trials in a given patient population and clinical care setting, such as newborns and infants in intensive care units. Rigorous assessment should extend to patient-reported outcomes, avoiding assumptions on the part of clinicians about how families are affected. Instruments to assess parents’ perceptions of the utility of genomic medicine are being developed and should be considered alongside clinical metrics.⁷ Continued efforts to establish methods to appropriately capture the full value of genomic medicine by integrating aspects of personal and clinical utility to avoid either underinvestment or overinvestment are warranted.

Callahan and colleagues¹ assert that the goal of genomic medicine is to benefit patients and families. Strengthening the rigor with which utility is measured is ultimately in service of that goal. If genomic medicine’s critical application is for infants in intensive care,⁸ genomic medicine’s critical outcome—utility—must be carefully measured. Development of methods to assess utility for acutely ill infants may serve as the foundation for evaluation of genomic medicine in other clinical contexts. Consistently applied measures ultimately benefit patients though development of a more robust evidence base, facilitation of a systematic analysis of which patients are most likely to benefit, and standardization of implementation according to best practices to ensure genomic medicine is applied in an equitable manner.
REFERENCES


