Professionally Responsible Disclosure of Genomic Sequencing Results in Pediatric Practice

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abstract

Genomic sequencing is being rapidly introduced into pediatric clinical practice. The results of sequencing are distinctive for their complexity and subsequent challenges of interpretation for generalist and specialist pediatricians, parents, and patients. Pediatricians therefore need to prepare for the professionally responsible disclosure of sequencing results to parents and patients and guidance of parents and patients in the interpretation and use of these results, including managing uncertain data. This article provides an ethical framework to guide and evaluate the professionally responsible disclosure of the results of genomic sequencing in pediatric practice. The ethical framework comprises 3 core concepts of pediatric ethics: the best interests of the child standard, parental surrogate decision-making, and pediatric assent. When recommending sequencing, pediatricians should explain the nature of the proposed test, its scope and complexity, the categories of results, and the concept of a secondary or incidental finding. Pediatricians should obtain the informed permission of parents and the assent of mature adolescents about the scope of sequencing to be performed and the return of results.

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Genomic sequencing, including whole exome sequencing of the coding regions of the human genome and whole genome sequencing of the entire human genome, is being rapidly introduced into pediatric clinical practice.¹ Like most new forms of laboratory testing and imaging that preceded it in the history of medicine, sequencing will first affect clinical practice by providing new diagnostic and risk assessment information and later by leading to improved and even new forms of treatment. For example, sequencing is already being used to provide a diagnosis for children with undiagnosed rare diseases, especially neurodevelopmental disorders. In some cases, these diagnoses lead to improved clinical management (eg, refinement of the search for associated features and

changes in health surveillance).² The results of genomic sequencing are distinctive for their complexity and subsequent challenges of interpretation for generalist and specialist pediatricians, parents, and patients.

Pediatricians therefore need to prepare for the professionally responsible disclosure of sequencing results to parents and patients and guidance of parents and patients in the interpretation and use of these results, including managing uncertain data. Appealing to 3 core concepts of pediatric ethics (the best interests of the child standard,³ parental surrogate decision-making, and pediatric assent³) this article provides an ethical framework to guide the professionally responsible disclosure of the results of genomic sequencing in pediatric practice.

METHODS

With the impending introduction of sequencing into pediatric clinical practice, pediatricians need to ask: What ought pediatricians disclose about the results of genomic sequencing to parents and patients? What ought to be the role of parents and patients in this process? Normative ethics addresses and aims to answer these “ought” questions by using the tools of ethical analysis (getting clear on clinically relevant ethical concepts) and argument (identifying those concepts’ implications for clinical practice).⁴

We begin with a description of the scope of categories of sequencing results. We then deploy the first tool of ethical reasoning, explication of 3 key concepts of pediatric ethics: the best interests standard, parental surrogate decision-making, and pediatric assent. Next we deploy the second tool of ethical reasoning, argument, to identify the implications of these 3 concepts for the disclosure of results of genomic sequencing in pediatric clinical practice. We aim to identify (a) the professional responsibilities of generalist and specialist pediatricians to disclose sequencing results to parents and patients in clinical practice and (b) the roles and responsibilities of parents and mature adolescents regarding whether and how to use these results in patient care.

Scope of Sequencing Results

Genomic sequencing laboratories vary in how they organize their reports of results. Despite this variation in format, the results of sequencing can be grouped into 6 convenient clinical categories: diagnosis, risk assessment for future health, combined diagnosis and risk assessment, reproductive risk assessment, variants of unknown clinical significance, and pharmacogenomics.

Diagnosis

Genomic sequencing in pediatric practice will expand the scope and precision of pediatricians’ diagnostic clinical judgments about the patient’s condition by explaining the child’s condition in terms of disease caused by highly penetrant alleles (high probability of producing clinical manifestations in individuals carrying the genetic risk allele), although phenotype may be difficult to predict (variable expressivity). Some of these diseases will be partially or completely ameliorable with appropriate medical interventions, whereas others will not be. Their outcomes will range from potentially reversible to potentially serious, far-reaching, and irreversible.

Risk Assessment for the Patient’s Future Health

Genomic sequencing, by identifying abnormal alleles known or suspected to be associated with an increased risk of disease, adds complexity to existing approaches to risk assessment. The penetrance of genes associated with these conditions will vary, from incompletely (only some patients are affected) to fully penetrant (all patients are affected). Some of these diseases will be partially or completely preventable with appropriate medical interventions, whereas others will not be. These diseases will also vary by age of onset, including early onset (during childhood) or later onset (during adult years), a distinction that will sometimes be difficult to make with precision.

Combined Diagnosis and Risk Assessment

It has recently been suggested that the association between genes and health status can be “promiscuous.”⁵ That is, the relationship between genotype and phenotype will often not be straightforward, sorting readily into either diagnosis or risk assessment because early disease manifestations may be present but

not recognized by the patient. For present purposes, this means that the distinction between diagnosis and risk assessment may become blurred: some genomic sequencing results may be classified as diagnostic when the patient is already symptomatic but as risk assessment when the patient is not yet symptomatic.

Reproductive Risk Assessment

Sequencing may also provide reproductive risk assessment by identifying increased risk of disease or disability in future children of the patient, the patient’s parents, and other family members. Diseases in this category may be preventable or nonpreventable, incompletely or fully penetrant, of early and later onset. Their outcomes will range from potentially preventable to potentially serious, far-reaching, and irreversible.

Genes and Variants of Unknown Clinical Significance

In addition to variants of known or highly likely clinical significance, genomic analysis will identify variants that are likely damaging in genes that have not previously been implicated in human disease. Genomic analysis will also identify variants of unknown clinical significance, for example, previously unreported missense alleles in genes known to be associated with disease. The genes in which variants of unknown significance are identified may be related or unrelated to the indication for which the sequencing was ordered. Laboratories differ in their interpretations of genes of uncertain significance and variants of uncertain significance.⁶ Efforts are underway to standardize interpretation of genetic variants through new guidelines from the American College of Medical Genetics and Genomics and through sharing of data across laboratories in ClinVar.⁷ Individual laboratories determine which variants are initially reported. Whether variants are reinterpreted over time is not yet standardized, and

whether the professional responsibility for initiating variant reinterpretation should rest with the laboratory or the ordering physicians remains unresolved.

Pharmacogenomics

A patient's genes may affect how he or she responds to pharmacotherapy. Sequencing may therefore be helpful in selecting a drug for treatment of the patient's condition, or for appropriate dosing, rather than relying on a "one size fits all" approach that pediatricians currently use on a trial-and-error basis.

Untargeted and Targeted Diagnostic and Predictive Genomic Sequencing

Targeted Diagnostic and Predictive Genomic Sequencing

In certain circumstances, sequencing will be used as a cost-effective alternative to single gene analysis to pursue a clinical diagnosis, with analysis limited to a select, predefined set of genes at the request of the ordering physician. The pediatrician's focus will therefore be on results that either establish or rule out a specified clinical diagnosis. In such cases, because the focus of analysis is limited to a small number of prespecified genes, there will be no interpretation or analysis of other genes even if the sequence data have been generated.

Untargeted Diagnostic Genomic Sequencing

In pediatric practice sequencing will often be used in the context of an existing clinical diagnosis or differential diagnosis. The pediatrician's focus will therefore be on results that either establish or rule out a specified clinical diagnosis. Given the scope of genomic sequencing described earlier, results may also include other diagnoses not previously considered in the differential diagnosis, risk assessment (s), and variants of unknown clinical significance. Like other forms of clinical analysis of wide scope such as MRI or computed tomography,

sequencing may produce "off-target" or incidental findings, now labeled as secondary findings.

Secondary or Incidental Findings of Genomic Analysis

The concept of secondary or incidental findings of sequencing applies in the context of genomic sequencing. The American College of Medical Genetics and Genomics (ACMG) has defined "incidental findings" of genomic sequencing: "Incidental (or secondary) findings, which are results that are not related to the indication for ordering the sequencing but that may nonetheless be of medical value or utility to the ordering physician and the patient"⁸ (p. 565). ACMG clarifies the meaning of "not related to the indication for ordering the sequencing" as follows: "We use 'incidental findings' in this article to indicate the results of a deliberate search for pathogenic or likely pathogenic alterations in genes that are not apparently relevant to a diagnostic indication for which the sequencing test was ordered"⁸ (p. 566). ACMG prioritizes these genes: "The Working Group prioritized disorders where preventative measures and/or treatments were available and disorders in which individuals with pathogenic mutations might be asymptomatic for long periods of time"⁸ (p. 567). In its endorsement of the nomenclature "secondary findings," ACMG does not change any of these definitions.⁹ Secondary or incidental findings include (a) diagnoses not related to the targeted use of sequencing, regardless of age of onset, that are treatable and (b) risk assessments for conditions, regardless of age of onset, for which the risk is modifiable either during childhood or during adulthood.

Predictive Genomic Sequencing

In pediatric practice, genomic sequencing may also be used in a less-targeted way, for example, in patients without a phenotypic or

family-history indication. For example, sequencing may in the future be used to supplement conventional newborn screening or as tools to inform preventive health measures. When there is no "diagnostic indication for which the sequencing test was ordered,"⁸ (p. 566) the concept of a secondary or incidental finding may have no or only limited application to less-targeted sequencing. There are currently no recommendations for the use of sequencing in children without a phenotypic or family-history indication.

ETHICAL FRAMEWORK

The proposed ethical framework comprises 3 core concepts of pediatric ethics: the best interests of the child standard, parental surrogate decision-making, and pediatric assent.

The Best Interests of the Child Standard

This ethical concept was endorsed as a core concept in pediatric ethics by the American Academy of Pediatrics in 1995. In endorsing this component of parental decision-making, the "Academy acknowledges that this standard of decision-making does not always prove easy to define"³ (p. 315). Ross has elaborated the variability in the expression and application of this concept.¹⁰ There is also international support for the best interests of the child standard in pediatric research ethics.¹¹ Both pediatricians and parents have beneficence-based prima facie obligations (Box 1) to protect the health-related interests of the child who is a patient.

The best interests of the child standard should be understood in the larger context of the best-interests standard in medical ethics and bioethics.¹² This beneficence-based (Box 1) standard "permits complex judgments about what, on balance, is likely to be best for an individual in light of available options"¹² (p. 535).

A judgment sorts items of interest into relevant categories, in this case, the ethical categories of acceptable, questionable, and unacceptable clinical management of children. The pediatrician making the judgment should focus on the individual, in this case, the child who is a patient. To maintain this focus and prevent unjustifiably sacrificing the interests of the child for the interests of others, the child's health-related interests should be identified independently of the child's relationship to others. As a result, the "available options" are those that are clinically salient, that is, reliably expected to protect the life and health of the pediatric patient.

Clinically comprehensive judgments about what is in the pediatric patient's interest should be biopsychosocial¹³ judgments. Forms of diagnostic or clinical management that protect the life of the child are judged to be in the pediatric patient's interest from a biomedical perspective.¹² This is because life is a necessary condition for biopsychosocial health. The psychosocial components of health¹² are judged to be in the pediatric patient's interest from both a clinical and a family perspective. One invokes the best interests of the child standard in 1 of 2 ways. The first is as an ideal: a goal worth striving to achieve, knowing that one usually falls short of doing so. The second is as a norm or ethical standard that generates prima facie obligations to meet the requirements of the norm.¹² To prevent confusion and lack of clinical application, the best-interests of the child standard in pediatrics requires that one be precise and distinguish the implications of the standard as a norm from implications of the standard as an ideal. In this article, this standard is treated as a norm that creates prima facie ethical obligations that should be fulfilled in clinical practice.

The major implication of this pediatric ethical standard as a norm

for the role and responsibilities of parents in pediatric decision-making is that it creates an ethical obligation that constrains parental authority in pediatric decision-making. In pediatric ethics, the primary ethical relationship between parents and children who are patients is that of the role-related prima facie, beneficence-based ethical obligation to protect and promote the health-related interests of the child who is a patient. This is not a unique feature of pediatric ethics: by their very nature ethical obligations constrain the exercise of decision-making authority and rights. The unique feature of pediatric ethics is that parents are not sovereign over their children and therefore give permission, rather than consent, for clinical management.³ Parental pediatric decision-making is an informed permission process.³ This implication was also endorsed by the American Academy of Pediatrics in 1995: "Practitioners should seek the informed permission of parents before medical interventions (except in emergencies when parents cannot be contacted)"³ (p. 315). The pediatrician's role includes empowering parents to give permission by providing them with clinically salient information about their child's condition, including the clinical justification for genomic sequencing, its broad scope and complexity, and the distinctions among diagnosis, risk assessment, and variants of unknown clinical significance.

Parental Surrogate Decision-Making in the Informed Permission Process

In the informed permission process parents act as surrogate decision-makers for patients who are not legally able to provide consent (Box 1). For older children capable of pediatric assent (see next section), in addition to the best interests of the child, the child's wishes should also guide and may constrain parental surrogate decision-making. This

approach will help to meet the standards of both substituted judgment (Box 1) and best interests (Box 1). Infants and younger children are not able to express stable values and preferences. As an ethical norm, the best interests standard alone should guide parental surrogate decision-making for such children in the informed permission process (Box 1).

Pediatric Assent

Pediatric assent calls for more than the child's simple agreement or disagreement with a plan of clinical management. Pediatric assent (Box 1) in its general meaning calls for more: the developmentally appropriate involvement of children in the decision-making process. In our judgment, pediatric assent regarding genomic sequencing applies mainly to adolescent pediatric patients, especially those who are capable of adultlike decision-making. The more adultlike the older pediatric patient's decision-making process, such as that exhibited by many adolescents with chronic conditions, the more authority pediatricians should ethically accord the patient. Legal authority remains with parents unless otherwise provided for by law. This means that pediatricians should be willing to advocate for the patient's preferences about genomic sequencing and return of results when in the pediatrician's clinical judgment the patient demonstrates adultlike decision-making.

IMPLICATIONS FOR CLINICAL PEDIATRIC GENOMIC SEQUENCING

We first identify the pediatrician's prima facie ethical obligations and then the parents' and patient's roles and responsibilities.

The Pediatrician's Prima Facie Ethical Obligations in the Informed Permission Process

All parents and patients capable of pediatric assent should be informed about the 6 categories of the results

of genomic sequencing. Results from 3 categories should be recommended: diagnosis, risk assessment for future health, and pharmacogenomics (Table 1). Parents and patients should also be informed about a current limitation of reports from genome laboratories, that is, variation in which genes and variants of unknown clinical significance are included in the report sent to the requesting pediatrician. The concept of secondary or incidental findings and their role in targeted and less-targeted genomic sequencing should be explained. Pediatricians should be alert to the cognitive demands that comprehending the nature of genomic sequencing and its results places on parents and children capable of assent. The pediatrician has a *prima facie* ethical obligation to recommend genomic sequencing

TABLE 1 Categories of Genomic Sequencing Results Ethically Obligatory to Disclose and Therefore Recommend to Parents

- Diagnoses, regardless of whether they are treatable. The latter is ethically significant because a fundamental aspect of protecting and promoting the child's interests is classifying the patient's condition, an especially important consideration in cases of a "diagnostic odyssey." Genomic sequencing may bring such an odyssey to its end, which prevents further unnecessary workup of the patient, with its attendant biopsychosocial¹⁰ risks for both the patient and his or her parents/responsible caregivers.
- Risk assessment for future health: early-onset conditions, diseases, or disabilities the risk of which is modifiable. This is especially the case when the condition, disease, or disability is serious and far-reaching in its outcomes for the patient and potentially irreversible if preventive measures are not deployed.
- Risk assessment for future health: later-onset conditions, diseases, or disabilities the risk of which is modifiable during childhood. The child's long-term health interests are protected and promoted by efforts to prevent adult-onset conditions, diseases, or disabilities for which effective prevention can begin during childhood. Such early preventive efforts may help establish long-lasting habits of self-care and seeking appropriate medical surveillance.
- Pharmacogenomic results with immediate clinical application.
- Incidental or secondary findings of life-threatening conditions.

when its results are reliably expected to protect and promote the patient's health-related interests by confirming or ruling out a diagnosis or by refining a differential diagnosis.

As an ethical norm, the best interests of the child standard creates a *prima facie*, beneficence-based ethical obligation of the pediatrician to seek and disclose diagnostic and risk assessment results of both early-onset condition and later-onset conditions when the risk is modifiable during childhood. (Table 1) The pediatrician should recommend disclosure of these 2 categories of results. Disclosure, with appropriate discussion of inherent uncertainty, should extend to variants of unknown clinical significance identified in genes that are related to the indication for sequencing. In contrast, variants of unknown clinical significance in genes that are unrelated to the indication for sequencing need not be disclosed. To manage the challenges of later reanalysis of results, some have proposed storing these results with a link to the patient's record¹⁴ so that it can be more easily accessed if future investigation converts results to the clinically significant categories of diagnosis or risk assessment.

The implications of the best interests of the child standard for disclosure of risk assessment for adult-onset conditions, the preventive management of which can be safely postponed to adult years, are less clear. Such results have no bearing on parental responsibility to protect and promote the child's health-related interests in preadolescent years. Disclosure of such risk assessment results may be useful to some adolescents and parents as they prepare for the assumption of adult responsibility. We suggest that this should be decided by mature adolescents and their parents (Table 2).

TABLE 2 Categories of Genomic Sequencing Results That May Be Disclosed at the Discretion of Parents and Mature Adolescents

- Risk assessment for future health: later-onset conditions, diseases, or disabilities the risk of which is modifiable only during adulthood. The child's long-term health interests as an adult can be protected and promoted by efforts to prevent adult-onset conditions, diseases, or disabilities for which effective prevention can begin during adulthood. Alternately, parents and mature adolescents may elect to receive these results at the time of sequencing.
- Incidental or secondary findings of non-life-threatening conditions.

If a child is found to have a mutation for a dominant condition, a parent may have the same mutation. When trio sequencing is performed, it is ethically appropriate to offer the affected parent the results directly. When sequencing is performed only on the child, providing the parent with the child's result could be life-saving for the parent or other relatives. For example, the identification in a child of a pathogenic mutation predicted to cause hereditary breast and ovarian cancer or cardiomyopathy¹⁵ could allow a parent also carrying that mutation to receive important preventive care. In that case, the pediatrician should recommend that the parents seek testing as appropriate. If results confirm that the parent carries the mutation, decision-making should include a plan to manage what, if anything, will be shared with the patient.

Pediatric assent creates a *prima facie*, autonomy-based ethical obligation to provide adolescent patients, ideally before they become sexually active, with reproductive risk assessment results and help them interpret their clinical significance. This is required by the pediatrician's existing professional responsibility to support voluntary, informed, and responsible decisions by sexually active patients about engaging in sexual intercourse.

For some of the ethical obligations described here, pediatricians may

find themselves unable to fulfill them as a result of inadequate training. In such cases, the pediatrician has a strict ethical obligation to refer the patient and parents to a professional colleague capable of fulfilling the obligation in question.

Parents' Role and Responsibilities

Parents may have reasonable views about the implications of the best interests standard in its psychosocial dimensions for their child's clinical care and well-being that differ from those of the child's pediatrician for non-life-threatening conditions. In such cases, parents may appeal to values and beliefs that are not exclusively health-related when they more broadly conceptualize their child's best interests. As a consequence, parents may reach an informed and considered judgment about the benefits and risks of receiving or not receiving results of genomic sequencing about non-life-threatening conditions that differ from the *prima facie* ethical obligations of pediatricians, as described above. Given the uncertainty of long-term psychological and social outcomes of genomic sequencing, parental judgments about psychosocial benefits and harms of such sequencing results typically will have as much authority as those of the pediatrician. The pediatrician could claim controlling authority about judgments about a patient's genomic health-related interests and therefore the clinical application of the best interests standard only by engaging in equation of health-related interests of the child to biomedical interests, which is known as biomedical reductionism.

Biomedical reductionism is not permitted by the biopsychosocial concept of health and comprehensive beneficence-based clinical judgment and therefore lacks intellectual and ethical authority. The alternative to biomedical reductionism is shared intellectual and ethical authority

between pediatricians and parents about the interpretation of the best interests standard in its psychosocial dimensions and the scope of results that should be provided to parents. It follows that parents are ethically free to refuse the recommended scope of disclosure of results described here. Put another way, parents do not violate a *prima facie*, beneficence-based obligation to their child should they authorize only the return of diagnostically related results of genomic sequencing and refuse disclosure of risk assessment or of secondary or incidental findings of non-life-threatening conditions (Table 2). They should be informed of the biomedical risks of doing so: a lost opportunity to obtain clinically significant information about diagnoses and risk assessments. If, after becoming aware of these biomedical risks and having made a considered judgment about their child's overall health-related and other interests, parents elect for a scope of disclosure limited to diagnosis of their child's condition, they are ethically free to do so.

The proposed approach is consistent with the ethical guidance provided by ACMG, when its 2013 statement^{8,16} and 2014 update¹⁷ are considered together. In 2013, ACMG took the view that it was ethically obligatory to identify and report all clinically significant findings, including secondary or incidental findings.^{8,16} In 2014, ACMG reversed its position and added the alternative for patients or parents to opt out of identifying and reporting secondary or incidental findings.¹⁷

Patient's Role and Responsibilities

The ethical concept of pediatric assent requires that parents and pediatricians give considerable weight to the decisions of an adolescent patient who is capable of mature, adultlike decision-making. Specifically, such a pediatric patient is ethically free to refuse to learn about risk assessment or secondary or incidental findings for non-life-

threatening conditions. In addition, such a pediatric patient is ethically free to refuse to learn or to act on the results of reproductive risk assessment. This is because there is no settled view in the genetic/genomic ethics literature about whether there is a duty to learn about, or act on, increased reproductive risk for adults, much less mature adolescents.

The pediatrician should take a preventive ethics¹⁸ approach to potential disagreement between parents and the patient when the patient is capable of adultlike or sufficiently mature judgments and decision-making processes. The pediatrician should explain the concept of pediatric assent and its ethical implication: when the patient is capable of mature judgments and decisions, these should be taken seriously. The parents should be willing to listen to their child and be prepared, with the pediatrician's support, to accept their child's judgments and decisions based on them.

CONCLUSIONS

Three core concepts of pediatric ethics (the best interests of the child standard, parental surrogate decision-making, and pediatric assent) constitute an ethical framework to guide pediatricians in introducing genomic sequencing into pediatric clinical practice in a professionally responsible way. In all cases, when recommending genomic sequencing, pediatricians should explain the nature of both, their broad scope, the 6 clinical categories of their results, and the concept of a secondary or incidental finding. Within the ethically justified constraints identified in this article, pediatricians should implement the informed permissions of parents and the informed assents of mature adolescents about the scope of genomic sequencing to be performed and the return of results.

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ABBREVIATION

ACMG: American College of Medical Genetics and Genomics

BOX 1 DEFINITIONS

Beneficence

An ethical principle that obligates the pediatrician to offer, recommend, and perform clinical management that, in deliberative (evidence-based, rigorous, transparent, and accountable) clinical judgment, is reliably expected to promote the health-related interests of the child who is a patient. As a rule, beneficence-based clinical judgment, because it requires deliberative clinical judgment, is expert, not lay, clinical judgment. Clinical management that passes muster in beneficence-based clinical judgment is medically reasonable, that is, technically possible and reliably expected to result in net clinical benefit for the patient.

Best interests standard of surrogate decision-making

The surrogate should make a decision from among the medically reasonable alternatives presented by the physician for clinical management that is reliably expected to protect and promote the health-related and other interests of the patient. These interests should be understood biopsychosocially.

Deliberative clinical judgment

Diagnostic, therapeutic, and prognostic clinical judgment that is evidence based, rigorous, transparent, and accountable.

Ethical obligation

Behavior that is required on the basis of either virtues (traits of character such as professional integrity and honesty) or ethical principles (action guides such as beneficence and respect for autonomy).

Informed refusal

In response to refusal of the decision-maker (the patient or the patient's surrogate decision maker) to authorize any medically reasonable alternative, the pediatrician informs the decision maker of the clinical risks for which the patient will be at risk if the refusal is implemented and this disclosure is documented in appropriate detail in the patient's record. The decision maker should be engaged by the pediatrician to discover the decision maker's reasons and asked to reconsider, especially if any of the decision maker's reasons support a medically reasonable alternative.

Pediatric assent

Children who are patients should be routinely involved in decisions about their health care in a developmentally appropriate fashion. The more adultlike the decision-making processes of the child, the greater the ethical weight that should be given to preferences based on those processes.³

Prima facie ethical obligation

An ethical obligation that ought to be fulfilled unless there is an argument-based reason why another, conflicting obligation should be fulfilled, instead. A prima facie ethical obligation differs from an absolute ethical obligation, which cannot be justifiably overridden by any other ethical obligation or right.

Respect for autonomy

An ethical principle that obligates the pediatrician and other health care professionals to empower the parents and mature patient (a) to make an informed decision by providing the parents and mature patient with information about medically reasonable alternatives for managing the patient's condition, disease, disability, or injury and (b) to make a voluntary decision by ensuring that the parents and mature patient's decision-making processes and expression of a preference based on those processes are free of internal and external controlling influences.

Substituted judgment standard of surrogate decision-making

The surrogate should make a decision from among the medically reasonable alternatives presented by the physician for clinical management that is reliably based on the values, beliefs, and preferences of the patient.

Surrogate decision-making

Decision-making by the person authorized (under applicable law) for a patient who does not have the decisional capacity to participate in the informed consent process.

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