Assessing Genomic Sequencing Information for Health Care Decision Making: A Workshop

Developing Guidelines

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Genetic testing

- Assays designed to provide a definitive diagnosis
- Criteria for testing include
  - Positive screening results
  - Family history
  - Ethnicity/race (genetic predisposition or carrier status)
  - Physical and other clinical stigmata

Why do clinical genetic testing?

- Diagnosis of a genetic condition
- Identify genetic predisposition to illness
- Test for carrier status for a specific disorder
- Prenatal testing
- Testing for identity
- Testing for status of a specific illness (usually related to malignancy)

Genetic testing for rare disorders

- Thousands of genetic disorders, most of them are rare and unique disorders
- 50% of clinical genetics cases are without diagnoses
- Chromosomal microarray increased diagnostic yield by approximately 10-15%
- Next Generation sequencing may increase yield by another 25%

Next Generation Whole exome sequencing (WES)

- Diagnosis of extremely rare and possibly unique genetic disorders
- Costly
- Tedious
  - Technical aspects are straightforward
  - Bioinformatic resources
  - Analysis of data is time consuming

Ethical and Policy Issues in Genetic Testing and Screening of Children

COMMITTEE ON BIOETHICS, COMMITTEE ON GENETICS, THE AMERICAN COLLEGE OF MEDICAL GENETICS, GENOMICS SOCIAL, ETHICAL and LEGAL ISSUES COMMITTEE

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Technical report: ethical and policy issues in genetic testing and screening of children

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General recommendations

- Decisions about genetic testing of children should be driven by the *best interest of the child*
- Respect *autonomy*
- Genetic and genomic testing should be offered in the context of genetic counseling

Parents should be informed about

- Potential benefits
- Potential risks
- Possibility of no diagnosis being made
- Possibility of a diagnosis being made for a condition with no known treatment
- Identification of possible variants of unknown significance
- Possible identification of misattributed parentage

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Ethical principles
Beneficence

- Positive outcome from making a diagnosis
- Potential opportunities for treatments and interventions
- Often gives resolution to families as to etiology
- The end of the diagnostic odyssey

Nonmaleficence

- Interpretation and management of variants of unknown significance
- Diagnosis with no known intervention
- Impact of unanticipated results on patient and family
  - Additional testing and screening
  - Diagnosis of adult onset disease in minors
- Testing may be done for the convenience (or curiosity) of the healthcare provider.

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Autonomy

- Informed consent and assent
- Parents, guardians, and competent children should receive comprehensive genetic counseling prior to deciding whether they wish to have testing
- They should have the right to refuse testing or portions of testing
  - Prenatal testing for single gene disorder
  - Whole exome sequencing

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Justice

- Obligation to treat all people equally, fairly, and impartially
- Should WES be denied for all patients whose parents who are looking for a diagnosis but wish not to have information regarding unanticipated or incidental findings
- Is it appropriate to withhold results of certain disorders (Alzheimer disease) if results can impact life choices?

Genetic testing is expensive

- Chromosome analysis - $900
- Microarray - $3000
- Single gene sequencing - $600-$4000
- Whole exome sequence - $8000-$12,000

Developing Guidelines

1 in 4 families struggled with medical bills

Bloomberg News

One in four U.S. families struggled to pay medical bills in 2012, and 1 in 10 said they had costs they couldn't pay at all, according to a new government survey.

The survey from the National Center for Health Statistics at the U.S. Centers for Disease Control and Prevention also found the lack of health insurance increased the burden of medical debt.

Major provisions of the 2010 Patient Protection and Affordable Care Act take effect this year as the Obama administration seeks to extend health care coverage to most of the nation's 48 million uninsured. The law may help lessen some of the financial burdens of medical care, said Karen Pollitz, a fellow at the Kaiser Family Foundation and lead author of a separate study on medical debt published Jan. 7.

"Unpaid medical bills is the number one reason why families declare personal bankruptcy," Pollitz said. "It causes people to lose equity in their homes, to endanger their retirement and their kid's college education. It will destroy a family financially."

Besides bringing coverage to the previously uninsured, the Affordable Care Act requires that health plans remove annual dollar limits on covered benefits, meaning patients will no longer face huge bills after reaching their coverage limit.

Health coverage alone can't prevent medical debt. Among families in which all members were insured, 21 percent had difficulty paying medical bills, the survey found.

The Affordable Care Act marks the largest U.S. expansion of medical insurance in more than 40 years. The law created government-run insurance exchanges where Americans can buy private health plans with the help of federal tax credits. It also expanded eligibility in some state-run Medicaid programs for the poor.

The Kaiser Family Foundation study found that 70 percent of people reporting problems with medical debt already were insured. Cost-sharing was the leading contributor to the debt, as typical out-of-pocket costs were higher for health bills than the amount of cash most households had available.

Insurers, trying to lower premiums on the government-run exchanges, have raised co-pays and deductibles to compensate.

Deductibles for some policies can reach $6,350 for a single person and $12,700 per family, according to a November survey by HealthPocket Inc. of seven states, including California and Ohio. ■

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Discrepancies in healthcare coverage in the United States

- Third party payors determine what genetic tests are covered
- Many families are faced with huge co-payments and deductibles and co-payments
- Third party payors often do not cover genetic testing
- Their protocols for which genetic conditions are covered are often dated and randomly determined

Challenges to guideline development

- Next Generation genetic testing is complex
  - It generates a great deal of data
  - Interpretation is difficult and challenging
- Informed consent is essential and cannot be obtained without genetic counseling

Challenges to guideline development

- Who should be able to order Next Generation genetic testing?
  - Medical geneticists
  - Neurologists
  - Developmental pediatricians
  - Neonatologists
  - Pediatricians
  - Family practitioners
- Who should be responsible for genetic counseling?

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Disclosure

- Results disclosure to family
  - Ideally should address disclosure issues prior to genetic testing
- Who owns the results
  - Genetic information belongs to the child being tested
  - Encourage parents or guardians to inform their child of the test results at an appropriate age

Challenges to guideline development

- There is an insufficient number of genetic counselors to meet the future needs of advancing clinical testing technology
- Medical genetics residency programs need to enhance training in genetic counseling
- Need to expand genetics and genomics curriculum in medical schools and residency programs to address the influx of genetic/genomic technology into healthcare

Challenges to guideline development

- Next Generation genetic testing is hampered by insufficient data from normal individuals to assist with clinical data interpretation
- Even if a diagnosis is made, what is the likelihood that there will be an available intervention?

Clinical Practice Guidelines

- No member of the Committees had any conflict of interest
- The representation for the AAP and the ACMG was multidisciplinary and balanced with regard to specialty and institution
  - All involved members reviewed and critiqued the reports
  - External review was performed by the Boards of both AAP and ACMG and the reports were reviewed by several AAP committees

Clinical Practice Guidelines

- The recommendations were made available by the AAP online as a freely available policy statement published in *Pediatrics*
- The Technical Report with full explanation of recommendations was made available by the ACMG and published in *Genetics in Medicine*

Genetic and genomic testing

- Diagnostic testing is a one time event
- Genetic testing has implications for the patient and other family members
- Diagnosis of a genetic disorder may not change outcome or prognosis

Genetic diagnostic testing in children

- Use same criteria for testing as other medical diagnostic evaluations
- Inform parents of benefits and risks of testing
- Get permission for testing from parents
- Need to consider cost of testing
- Genetic testing should always be accompanied by genetic counseling