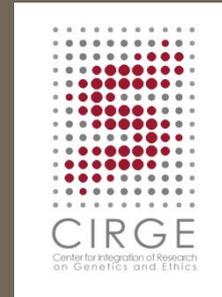


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## Incidental Findings in Genomics:

Ethical frameworks  
and practical  
challenges

# Ethical and policy frameworks

- Ethical frameworks
  - Principles: risk benefit calculus, autonomy
  - Responsibilities: duties and relationships
  - Contexts: research, clinical, public health
- Policy frameworks & drivers
  - Values in translation
  - Diagnostic technology assessment
    - Evidence-based vs. technological imperative
  - Data privacy, ownership and management
    - Open source vs. commercial interests

# Consensus on ethical framework in genetic testing

- Best interest of patient
- Reporting only information for which there is evidence of benefit
- Benefit outweighs risks
- Respecting right to know
- Respecting right not to know

# Consensus on ethical framework

- **Wilson & Jungner (1968)** *Principles and Practice of Screening for Disease.*
- **IOM (1994)** *Assessing Genetic Risks: Implications for Health and Social Policy*
- **ASHG (1995)** *Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents*
- **NIH Task Force on Genetic Testing (1997)** *Promoting Safe and Effective Genetic Testing in the United States*
- **AAP (2000)** *Newborn Screening: A Blueprint for the Future*
- **ACMG (2012)** *Points to Consider in the Clinical Application of Genomic Sequencing*
- **AAP/ACMG (2013)** *Ethical and Policy Issues in Genetic Testing and Screening of Children*

# Ethical shift

- **ACMG 2005** *Newborn Screening: Toward a Uniform Screening Panel and System*
  - Benefit to family and society
- **Alexander & van Dyck 2006** *A vision of the future of newborn screening*
  - *Pediatrics* 117: S350-S354
  - Changing “the dogma that it is appropriate to screen only for conditions for which effective treatment already exists needs to be changed, by **broadening the concept of benefit** from screening for the child to include the family.”

# Ethical shift

- "...depends on developing a new screening technology that contains costs by **screening for virtually all target conditions** with **one test system.**"

# Ethical shift

- Best interest of family
- De-emphasizing autonomy
- **ACMG 2013** *Recommendations for Incidental Findings in Clinical Exome and Genome Sequencing*

# Recommendations

- To actively search for specified mutations in specified
- To not offer the patient a preference about receiving results
- To not limit reporting by age

# Arguments

- Clinicians and laboratory personnel have fiduciary duty to prevent harm
- Amount of genetic counseling needed to discuss unrelated conditions “overwhelming”
- Masking analysis would be “unwieldy” and places an “unrealistic burden” upon laboratories
- Patients have the right to decline clinical sequencing

# Arguments

- Respect for parental decision-making about children's health
- Parents of children undergoing sequencing do not have "ready access" to sequencing in order to obtain personal risk information

# Analogies

- Analogy to physician examining cardiac and respiratory function in a patient complaining of digestive problems
- Analogy to radiologist reporting on abnormal findings not indicated in primary reason for scan

# Caveat

- “The Working Group acknowledged that there was insufficient evidence about benefits, risks and costs of disclosing incidental findings to make evidence-based recommendations.”

# Factors in assessing risk and benefit

- Virtually no assurance of analytical validity
  - FDA and NIST developing standards
  - Wide variety of platforms with differing results
- Difficult to assess clinical validity
  - Inter-lab variability in interpreting pathogenicity
  - Interpretation limited by access to data - proprietary databases
    - Regardless of patentability
  - Testing low risk populations - low PPV

# Factors in assessing risk and benefit

- Interpretation is resource-intensive and costly
  - Incidental findings a misnomer in genomics
    - In research because it is exploratory
    - In clinical setting because raw data must actively be interpreted, by groups with broad expertise
  - Some findings require extensive follow-up to interpret including gathering other samples and conducting studies

# Factors in assessing risk and benefit

- Follow up care is costly and must be included in cost benefit and cost effectiveness calculus
- Opportunity costs
- Costs of discrimination, eg insurance

# Conclusions

- Decisions about the limits of or obligations to report incidental findings should be based on established ethical principles and evidence
- Technology has changed but ethical principles per se have not
- Evidence about harms, benefits lacking