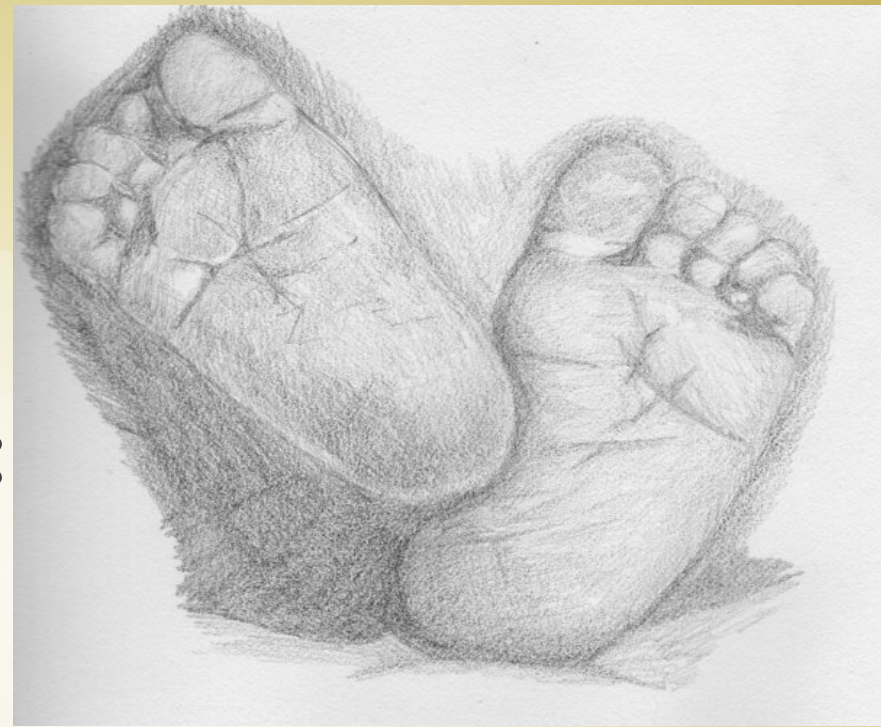


The Next Phase of Newborn Screening : Whole Genome Sequencing?



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Outline



- Introduction
- Views on newborn screening using genome sequencing
- ELSI issues
- Policy developments and needs

Introduction

- WGS already used in different fields, including in the newborn population

- Clinic → Rapid WGS for Genetic Disease Diagnostic in Neonatal Intensive Care Units (2012)



- Research → e.g. BabySeq™- Exploring Genome Sequencing of Newborns /Brigham and Women's Hospital (BWH)



WGS in Newborn Screening Program?



- Though controversial, many believe that once WGS is sufficiently robust and affordable, all newborns will have their genomes sequenced at birth (PHG Foundation, *Next Steps in the Sequences*, (2011) at 56)
- Francis Collins states that: “[...] as we learn more about effective interventions for genetic risk factors, and recognize that interventions early in life provide significant advantages, it will become more and more compelling to determine this information at birth”
F.S. Collins, *The Language of Life: DNA and the Revolution in Personalized Medicine*. New York: Harper Perennial (2010)
- Dondorp, De Wert, *The "Thousand-dollar Genome" : An Ethical Exploration*, (2013) 21 *European Journal of Human Genetics*. S6-S26

Parents' interest in whole-genome sequencing of newborns

Aaron J. Goldenberg, PhD, MPH¹, Daniel S. Dodson, MS², Matthew M. Davis, MD, MAPP²⁻⁴
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Purpose: The aim of this study was to assess parents' interest in whole-genome sequencing for newborns.

Methods: We conducted a survey of a nationally representative sample of 1,539 parents about their interest in whole-genome sequencing of newborns. Participants were randomly presented with one of two scenarios that differed in the venue of testing: one offered whole-genome sequencing through a state newborn screening program, whereas the other offered whole-genome sequencing in a pediatrician's office.

Results: Overall interest in having future newborns undergo whole-genome sequencing was generally high among parents. If whole-genome sequencing were offered through a state's newborn-screening program, 74% of parents were either definitely or somewhat interested

in utilizing this technology. If offered in a pediatrician's office, 70% of parents were either definitely or somewhat interested. Parents in both groups most frequently identified test accuracy and the ability to prevent a child from developing a disease as "very important" in making a decision to have a newborn's whole genome sequenced.

Conclusion: These data may help health departments and children's health-care providers anticipate parents' level of interest in genomic screening for newborns. As whole-genome sequencing is integrated into clinical and public health services, these findings may inform the development of educational strategies and outreach messages for parents.

Genet Med advance online publication 6 June 2013

Key Words: newborn screening; parents; whole-genome sequencing

Public Views on Participating in NBS Using Genome Sequencing

Y. Bombard et al., 2013 (submitted):

- "Our results suggest that integrating WG/ES into NBS in an untargeted fashion might reduce public participation in NBS as well as the moral authority that NBS programs rely upon to ensure population benefits"
- Public is committed to participating in NBS programs that identify known and treatable disorders
- Public willingness was reduced for untargeted WG/ES compared to traditional targeted NBS technologies

Overview of the issues



Review in Advance first posted online on July 15, 2013. (Changes may still occur before final publication online and in print.)

Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice

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Ethical Issues with Newborn Screening in the Genomics Era

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Overview of the issues

Wade, Tarini, Wilfond, Growing Up in the Genomic Era, Annu. Rev. Genomics Hum. Genet. (2013) 14:23.1-23.21

Table 2 Health information that can be detected by pediatric whole-genome sequencing (P-WGS)

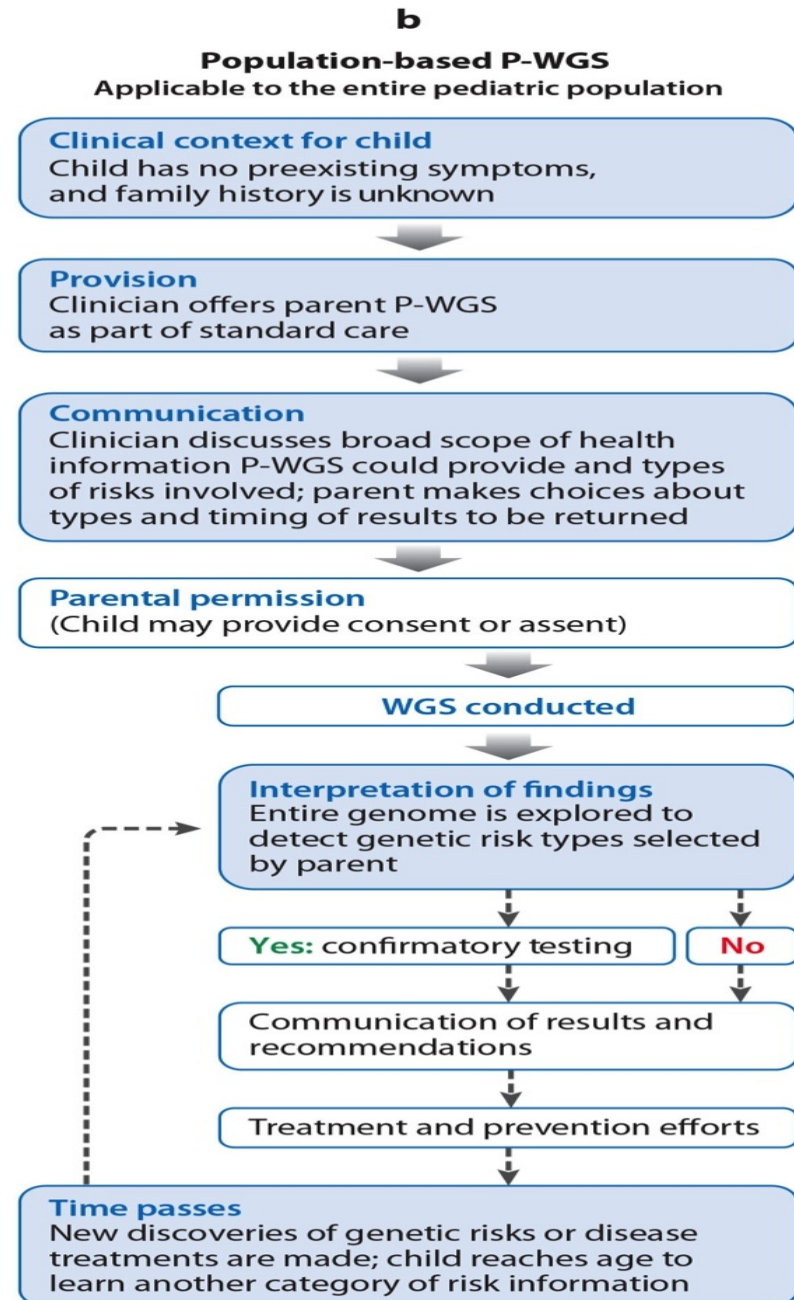
Type	Example of pediatric health use	Example(s) of challenges when detected by P-WGS
Single-gene and preventable childhood-onset condition	Testing for sickle cell disease, a part of standard newborn screening, helps prevent a range of negative childhood symptoms	A large number of false positives need to be resolved
Single-gene and nonpreventable childhood-onset condition	Early identification of Tay-Sachs disease, a fatal condition, could decrease time seeking a diagnosis	Unanticipated findings of a severe nonpreventable condition could have a particularly negative impact on parental well-being
Multi-gene and preventable childhood susceptibility	Findings of increased asthma risk could lead to earlier detection and prevention efforts	Evidence of clinical validity and recommendations for prevention are not established; a large number of people need to be treated per case prevented
Single-gene and preventable adult-onset condition	Beta blockers can be prescribed to children with Marfan syndrome to prevent cardiovascular events	Prevention recommendations need to be developed and adherence effectively supported
Single-gene and nonpreventable adult-onset condition	Huntington's disease testing could relieve uncertainty for children with a high-risk family history and could benefit those who test negative	Concerns about harms to children and unclear benefit mean that high-quality information and opportunities to decline would need to be provided
Multi-gene and preventable adult susceptibility	Knowledge of increased cardiovascular disease risk could lead to public health interventions, encouraging preventive health behaviors	There is only limited evidence of clinical validity and utility; a large number of people need to be treated per case prevented
Pharmacogenomic information	<i>TPMT</i> gene function can inform acute lymphoblastic leukemia treatment for children	Clear, evidence-based treatment recommendations need to be developed; WGS results need to be made rapidly available to prescribing clinicians
Carrier status	Knowledge of cystic fibrosis carrier status could help prepare teens for future reproductive choices	Health benefits are unclear; reproductive risk may be confused with personal health risk

WGS in NBS?

"Nonetheless, it is generally recognized that there should be a high burden of proof demonstrating the clinical utility of a population-based test, and the nonexistence of evidence supporting population-based P-WGS suggests that extensive research will need to be conducted prior to implementation"

"Population-based P-WGS is unlikely to be warranted in the near future given the need for research to resolve a host of ethical and practical considerations"

Wade, Tarini, Wilfond, Growing Up in the Genomic Era, Annu. Rev. Genomics Hum. Genet. (2013) 14:23.1-23.21



Overview of the issues

- Which information to report?
- Impact on the healthcare system
- Health professionals and parents
- Communication of results
- Treatment and follow-up
- Storage

Norsk Epidemiologi 2012; **21** (2): 163-168

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Newborn screening programmes: Emerging biobanks?

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Learning from established population-based screening programs?

E.g. of population-based screening programs:

- Antenatal screening
- Neonatal screening (storage and secondary use of DBS)
- Cancer screening (e.g. breast cancer / colon cancer)
- Carrier status screening in some at-risk populations

Some lessons?

- Involvement (e.g. parents/ community) in the decision-making process
- Education
- Respect for autonomy
- Policy / guidance needs:
 - evidence, and
 - flexibility

Conclusion



- Public health systems ("values")
- Surveillance / stratification / targeting
- Duty to follow?
- Family unit / rights
- Physician liability
- Right not to know