

Post Implementation Data Collection & Monitoring

Public Health Assessment of Genetic Tests for Screening & Prevention

September 27, 2004

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Public health assessment of genetic testing

Evidence-based evaluation needed at two key points:

- Transition from research to clinical practice
- Post-implementation period
 - Demonstrate acceptable performance in practice
 - Assess implementation success and public health impact

Data collection and monitoring in the post-implementation period

- Confirm or update performance estimates
- Assess public health impact – including quality, acceptability, utilization, and access
- Document implementation issues
- Assess fit with healthcare delivery systems
- Resolve gaps in knowledge

Monitoring genetic testing



- We know very little about genetic testing in the United States
- Minimal assessment of genetic testing in clinical or public health practice setting
 - Who is being tested?
 - Who is ordering testing?
 - Why?
 - Where is testing being done?
 - What methods / technologies are used?

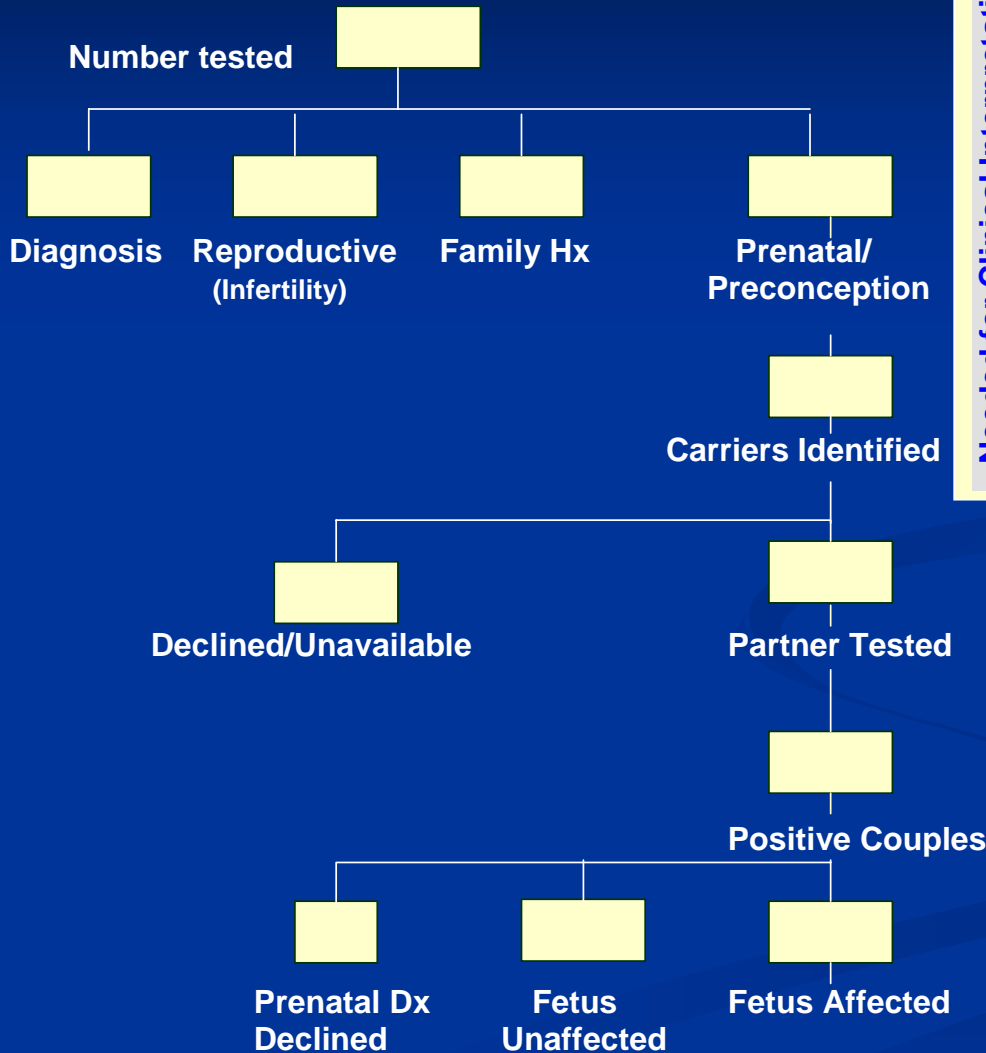
Long-term monitoring can answer questions like:

- Are providers & patients properly educated?
Satisfied with the process?
- Is the quality of laboratory service adequate?
 - Are labs able to obtain needed information?
 - Is the panel of mutations appropriate?
 - Is the test being offered appropriately?
 - How are laboratory test results being reported?
- Are performance expectations and pilot trial results being confirmed?
- Are there problems with implementation?

Long-term monitoring can answer questions like:

- What actions are being taken? Are they appropriate?
- Is there a discernable impact on outcomes?
- Are there issues with reimbursement? Access?
- Are safeguards in place to deal with ethical, legal and social issues?
 - Have additional ELSI been identified?
- Are program costs acceptable?
- Should the process or guidelines be modified?
Discontinued?

Prenatal CF screening via carrier testing



Needed for Clinical Interpretation

Needed to Demonstrate Clinical Validity & Utility in Practice

Collecting Long-term Monitoring Information: Experience of Three CFTR Laboratories

Data Collected	Strom et al, 2001		
	Clinigene	FBR	
All CFTR Tests	20,103	3,324	4,260
Screening Tests	Unk	3,298	4,260
Carriers Identified	Unk	132	153
Carrier Rate (uncorr)	Unk	1 in 25	1 in 28
Partners Tested	Unk	55*	153
Positive Couples	Unk	3*	7
Prenatal Diagnosis	Unk	Unk	6
Fetus Affected	Unk	Unk	3

* Known to be under-ascertained

Cystic fibrosis carrier testing

- ACOG/ACMG did not address evaluation
- No group charged with coordinating data collection
 - Laboratories → expense, time, increasing difficulty & no CLIA requirement
 - Providers/payers lack access through claims data
- Anecdotal reports on implementation issues
 - Access to & understanding of guidelines
 - Problems with patient information & result reporting
 - Small number of labs routinely reported 5T
 - **Difficult to quantify problems**
- Addressing performance in practice
 - Proficiency testing
 - Reports on mutation frequencies

ACMG Carrier Screening Work Group

- 2001 recommended panel of mutations & variants
 - Grody WW et al. Laboratory standards and guidelines for population-based cystic fibrosis carrier screening.
 - Mutation should be present in at least 0.1% of CF patient chromosomes
- 2002 review initiated
 - Information collected by laboratories
 - > 400,000 individuals tested
 - CF Foundation patient mutation database
 - 42,737 CF patient chromosomes
 - Reports of provider experience

ACMG Work Group Questions

Has the observed frequency of any CF mutations changed significantly since 1999?

- Any mutation with prevalence $<0.1\%$ should be removed from screening panel → **1078delT removed**
- Future decisions based on benefits & costs of incremental gain in performance
 - 6 mutations at frequencies 0.1-0.17% → + 0.77%
 - Weigh against potential increase in error rate & adaptability of current methods / platforms → **No additions at this time**
 - Local demographics may suggest need to add ethnic-specific mutations

Watson MS et al. Cystic Fibrosis (CF) Couple Carrier Screening: 2004 Revision of ACMG's Mutation Panel. *Genetics in Medicine*, in press.

