Perspectives on Existing Genetic Variation Resources—Clinician Perspectives

Howard P. Levy, MD, PhD
Johns Hopkins University

Characterizing and Displaying Genetic Variants for Clinical Action Workshop

Gaithersburg, MD
December 1, 2011

Disclosures

- Medco Health Solutions:
  Pharmacogenetics consultation
- Co-editor-in-chief, GeneFacts

Email Survey

- IRB approval: none
- Informed consent: minimal
- Subjects: academic 1^{o} care clinicians
  - Clinician educators
  - Clinician researchers
- Recruitment : 7 hours on 11/30/11

Questions

1. What resource(s) do (or would) you turn to if you want more information about the significance or management of a genetic variation?

2. What would the ideal resource provide?

Results: What Resource?

	Educators N=10	Researchers N=6	All N=16	
UpToDate	5 [HHH]	3	8	8 Internet (primary care)
Consultant/Specialist	4	1	5	5 Person
Google	3*	1	4	6 Internet (general)
Wikipedia	2		2	
Pubmed/Google Scholar	2	1	3	6 1^{o} Lit & Guidelines
Guideline, EGAPP		2	2	
Cochrane		1	1	
NIH	2*		2	9 Internet (specialty)
OMIM	2 (-1)** [HH]		2 (-1)	
GeneTest/GeneReviews	2**		2	
GeneFacts	2**		2	
Specialty Disease Site	1		1	
No answer	1		1	

Results: What Resource? (n=16)

- *Google: 1 searches “NIH + {mutation}”
- *NIH: 1 is the above Google search
  1 “NIH polymorphism database”
- **GeneFacts, GeneReviews: the other 2 GeneFacts co-editors-in-chief
- **OMIM: 1 GeneFacts eic uses;
  1 GeneFacts eic specifically doesn’t use
- HHH: 3 found UpToDate hard to use;
  2 found OMIM hard to use

Clinicians' Preferred Information Sources

Most Preferred:

- Internet
- CD-ROM
- Textbooks
- Consultant/Specialist
- Seminars/Meetings

Least Preferred:

- Lectures
- Journals
- Guidelines

Burke W *et al*. *Genet Med* 2006; 8:109.

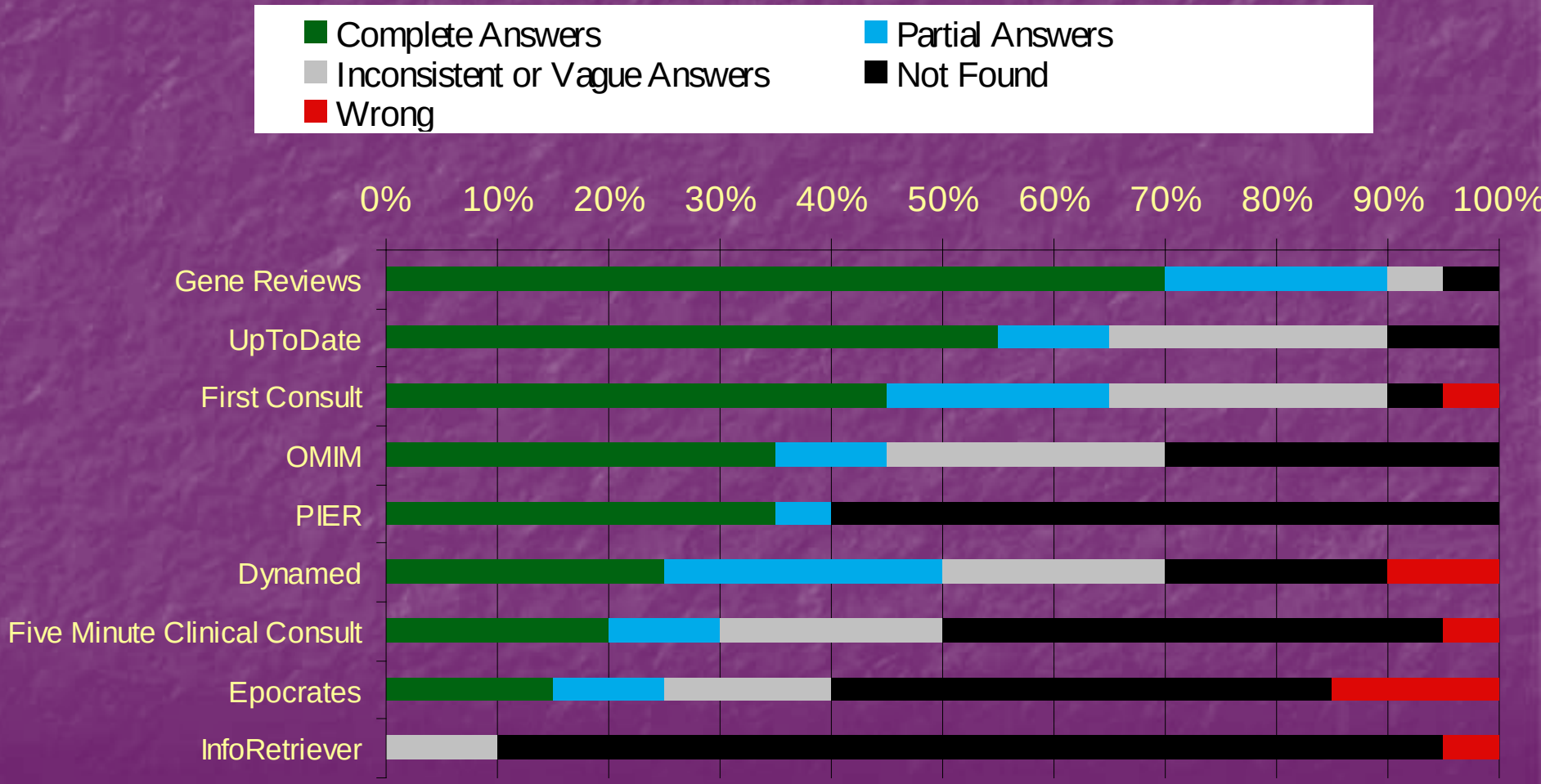
Metcalfe S *et al.*, *Genet Med* 2002;4:71

Watson EK *et al.*, *Fam Pract* 1999;16:420

Other Resources I Use

- PharmGKB
  - includes Clinical Pharmacogenetics Implementation Consortioum (CPIC) guidelines, and others
- Specialty labs
- Flockhart tables http://medicine.iupui.edu/clinpharm/ddis/
- warfarindosing.org (& similar)

Accuracy Of Databases



Levy HP *et al.*, *Genet Med* 2008; 10:659

Ideal Resource Provides? N=12

Characteristics:

- Concise, Easy to use: 3
- Fast: 2
- Accurate: 2
- Free: 1
- Educational: 1
- Something like UpToDate: 1
- Links to other resources: 1

Ideal Resource Provides? N=12

Content-1:

- Management, Clin. Significance, Implications: 4
- CDS w/in EHR: 1
- Actionability, Clin. Utility: 3
- Testing: 4

(clin. validity, who/when, methods, interpretation, cost)

Ideal Resource Provides? N=12

Content-2:

- Clinical manifestations: 3

(pathophys., phenotype, prognosis, severity, penetrance, pleiotropy)

- Frequency: 2

(especially indicate most common variants)

- Inheritance and *de novo* mutation rate: 2
- Evidence-based: 2

Clinicians Most Want:

- Accurate
- Accessible
- Clinically relevant
- Fast (< 2 minutes)

Ely JW *et al.*, *BMJ* 1999; 319:358

Ely JW *et al.*, *J Am Med Inform Assoc* 2005;12:217

Gonzalez-Gonzalez AI *et al.*, *Ann Fam Med* 2007; 5:345

Metcalfe S *et al.*, *Genet Med* 2002;4:71

Watson EK *et al.*, *Fam Pract* 1999;16:420

Zack P *et al.*, *Community Genet* 2006;9:260

Evidence-Based?

- Specialties & individuals vary
- Some very high standards (RCTs)
- Some less rigorous
- Many follow specialty society guidelines/recommendations