

The Need for Open Access Publications in Commercial Clinical Genetic Workflows



A 501(c)(3) nonprofit humanitarian organization

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ROADMAP



Intro:

1. *Commercial clinical genetics overview.*

Open vs restricted access impact:

2. *Restricted access can hurt genetics patients.*

Publishing FROM commercial laboratories:

3. *CGI is working towards encouraging open access data publishing FROM commercial labs by using commercial forces.*

ROADMAP



Intro:

1. *Commercial clinical genetics overview.*

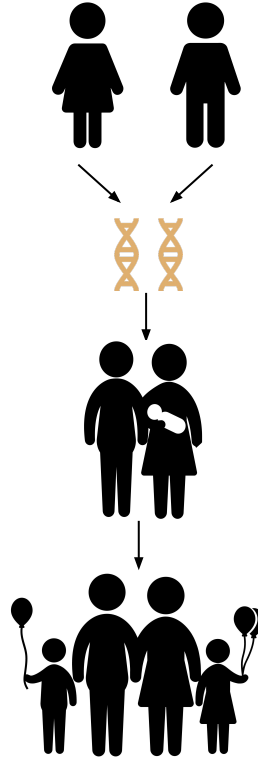
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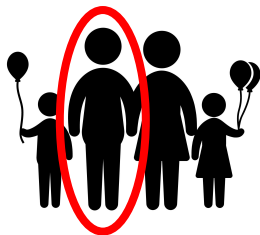
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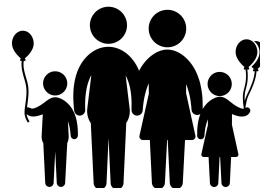
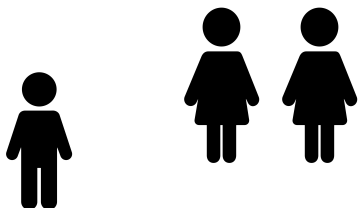
GENETICS - BLAME YOUR PARENTS!



GENETIC DISEASE IS COMMON



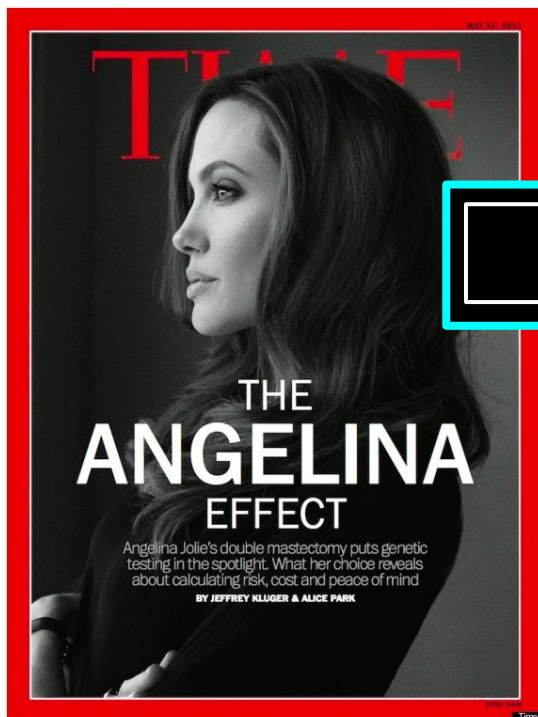
2 in every 25 people
have a genetic disease



~7000 patients tested
everyday in the USA



GENETIC TESTING IS NOW MAINSTREAM



May 27, 2013

BRCA1



December 24, 2012

Cystic fibrosis

CLINICAL GENETICS PROCESS FLOW



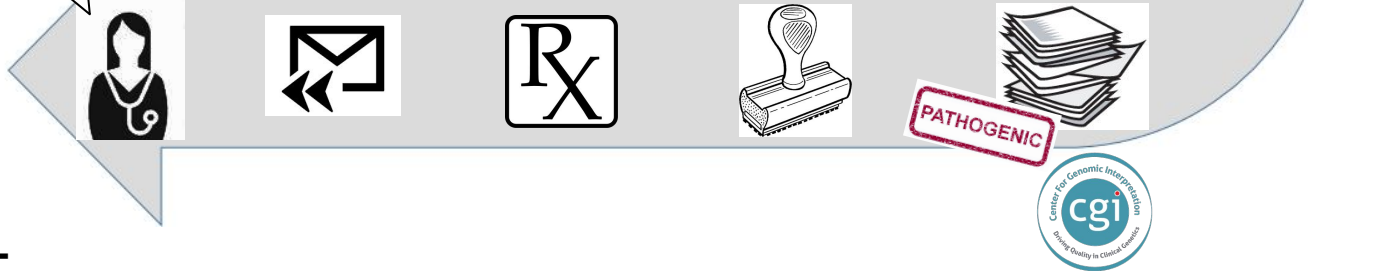
(Case level data is siloed)



PATIENT



PATIENT



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CLINICAL GENETICS: WHERE RESEARCH IS STILL TRANSLATED DIRECTLY INTO MEDICAL PRACTICE



Five Classifications:

- Pathogenic**
- Likely Pathogenic**
- Variant of Uncertain Significance
- Likely Benign**
- Benign**

RESEARCH LITERATURE IS RIDDLED WITH ERROR

“The *literature is riddled with false claims of pathogenicities* from researchers who have not done a good job of interpretation.”

Heidi Rehm, PhD FACMG, Harvard Medical School
17 August 2016, **Wall Street Journal**

“As many as *30 percent of mutations associated with disease aren't*. We're going to have to do *a lot of cleanup work*.”

Michael Ackerman, MD PhD, Mayo Clinic
31 Oct 2016, **STAT**

CLINICAL GENETIC ERRORS IMPACT THOUSANDS OF FAMILIES EACH YEAR



FALSE POSITIVE genetic tests erroneously send
>100,000
individuals into the US medical system EACH YEAR
(1 every 5 minutes) for unnecessary:



- Pregnancy termination



- Organ and tissue removal



- Traumatic therapies

CLINICAL GENETIC ERRORS IMPACT THOUSANDS OF FAMILIES EACH YEAR



Genetic diagnostic **ERRORS** cost at least **ONE BILLION DOLLARS** directly to the US medical system EACH YEAR as a result of unnecessary:



- Pregnancy termination



- Organ and tissue removal

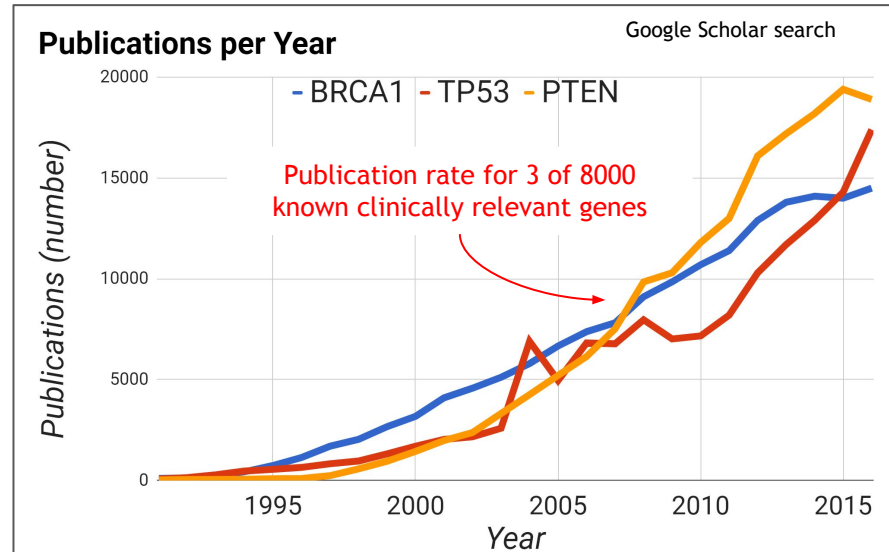


- Traumatic therapies

CLEAN UP REQUIRED

“As many as **30 percent** of mutations associated with disease aren’t.
We’re going to have to do a lot of cleanup work.”

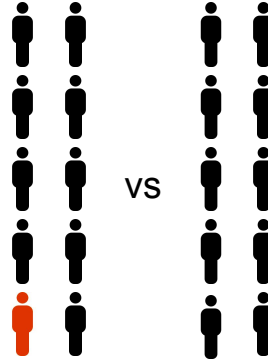
Michael Ackerman, MD PhD, Mayo Clinic
31 Oct 2016, STAT



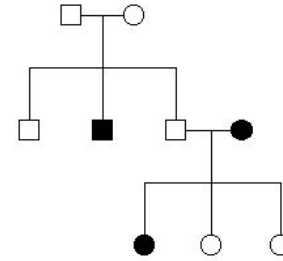
CLEAN UP: ASKING THE HARD QUESTIONS



Is the experimental design correct? Is the organism relevant?



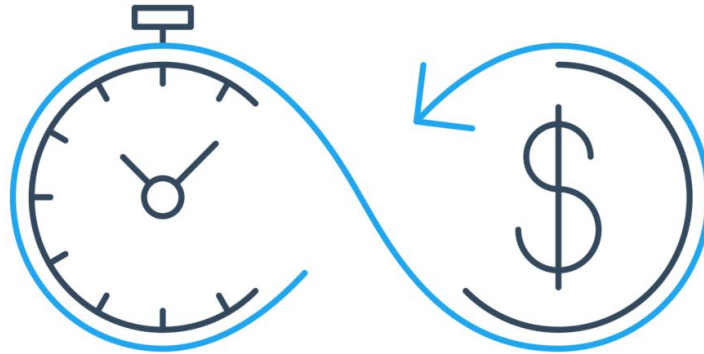
Are the statistics sufficient?



Are the relations strong enough?

Majority of research conclusions are insufficient for clinical application

COMMERCIAL LAB SCIENTISTS IN “PRODUCTION”

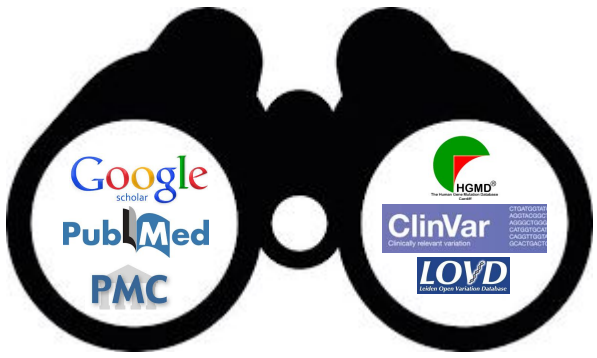
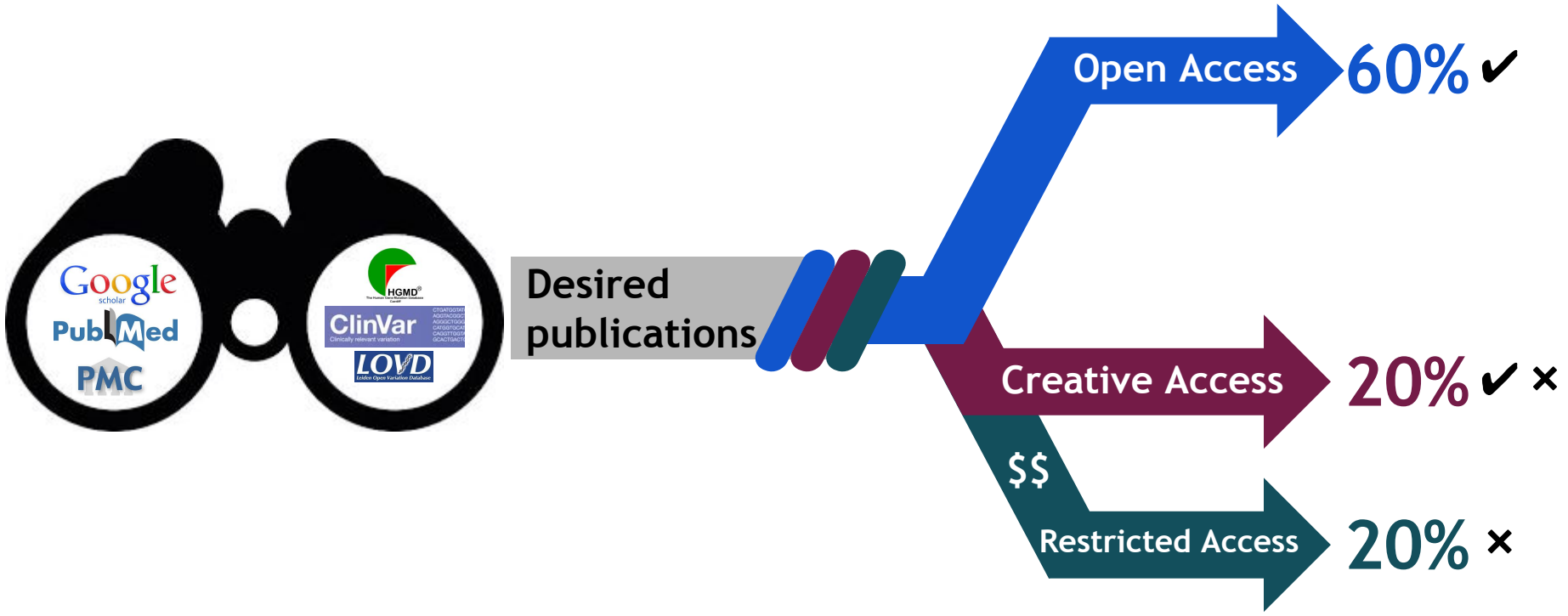


90% of scientists cannot easily access the literature they need.

(Source: Reprints Desk, <http://info.reprintsdesk.com>)

Laboratory turn-around-time and profitability requirements cap literature review efforts.

MANY CLINICAL VARIANT SCIENTISTS RELY ON ABSTRACTS ONLY FOR RESTRICTED ACCESS ARTICLES



TITLES & ABSTRACTS VS. FULL CONTENT



Generic example of a genetic variant report publication:

Title & Abstract:



AUTHOR LIST:

Respected scientists at top institutions

TITLE:

“XYZ is the most deadly genetic variant in human history”

ABSTRACT:

We did a lot of awesome science and **PROVED** that XYZ is really, really bad and is going to kill any person that carries it, like, tomorrow.

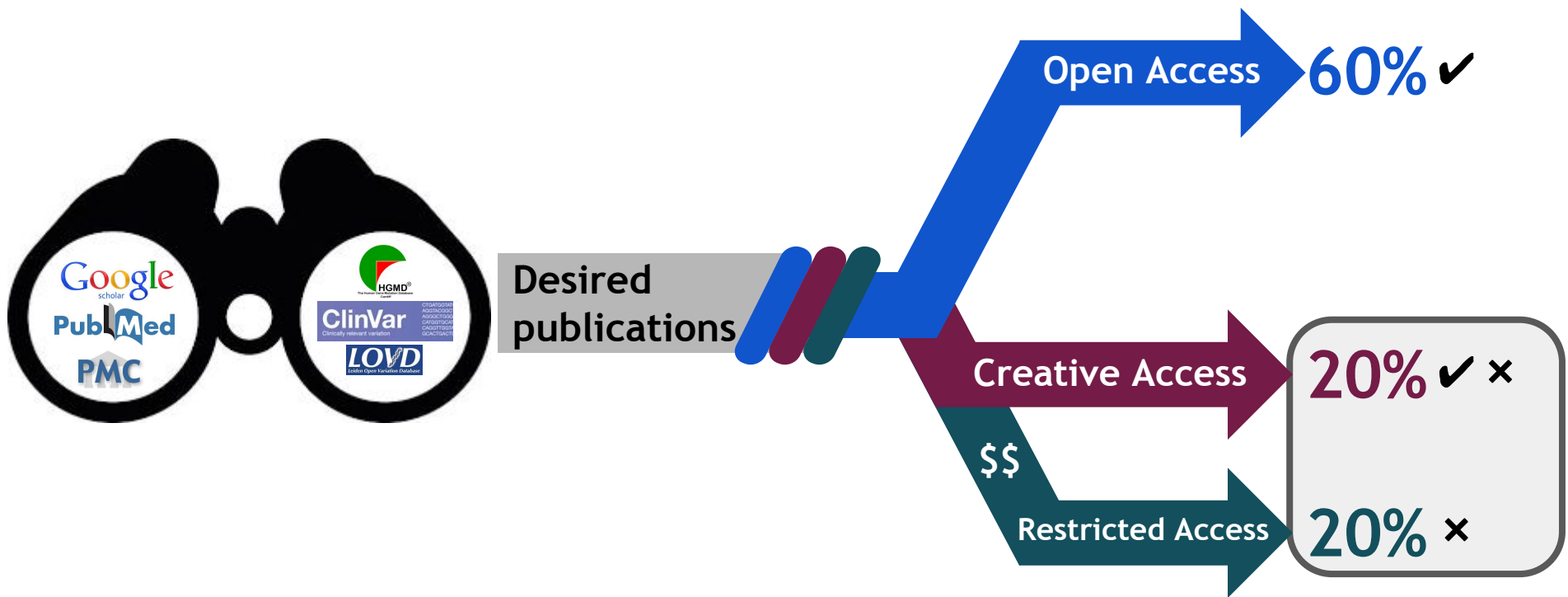
Full Content:



CRITICAL READING OF FULL ARTICLE:

- Single case report (N=1)
- Scientific conclusions were made using approaches that have not been clinically validated, with some algorithms that have already been debunked repeatedly in numerous well powered studies.

MANY CLINICAL VARIANT SCIENTISTS RELY ON ABSTRACTS ONLY FOR RESTRICTED ACCESS ARTICLES



RESTRICTED ACCESS ARTICLES CONTRIBUTES TO ERROR



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OPEN ACCESS ARTICLES SAVES & IMPROVES THE LIVES OF CLINICAL GENETICS PATIENTS



A CGI GOAL:

HIGH VOLUME COMMERCIAL
CLINICAL GENETIC DISCOVERIES



For profit companies answer to investors.

- When working with companies to encourage open access publishing of their data, we must demonstrate that data sharing will ultimately increase their profits.
 - If this isn't true, can it be made true?

CGI'S PLANS FOR HIGH THROUGHPUT OPEN ACCESS PUBLISHING FROM COMMERCIAL DATA

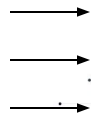
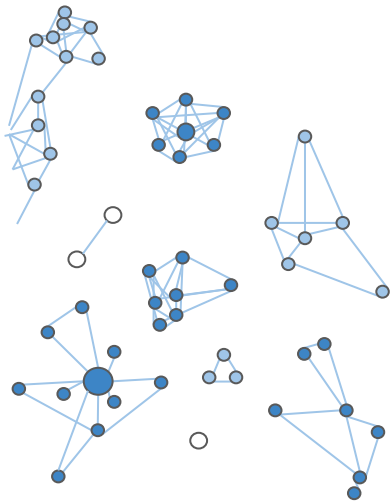


1. "Un-siloing" and curating data

2. Aggregating and analyzing data

3. Services

4. Impact



Variant Classification

Variant Reclassification

FiNDitALL™

Data Publishing

Variant FactChecker™

VUSolve™

CGI: BETTER, FASTER, CHEAPER VARIANT CLASSIFICATION AS A SERVICE



QUESTIONS?

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