Precision Medicine Advisors
Advancing genomic and precision medicine through education

A practical approach to precision medicine education

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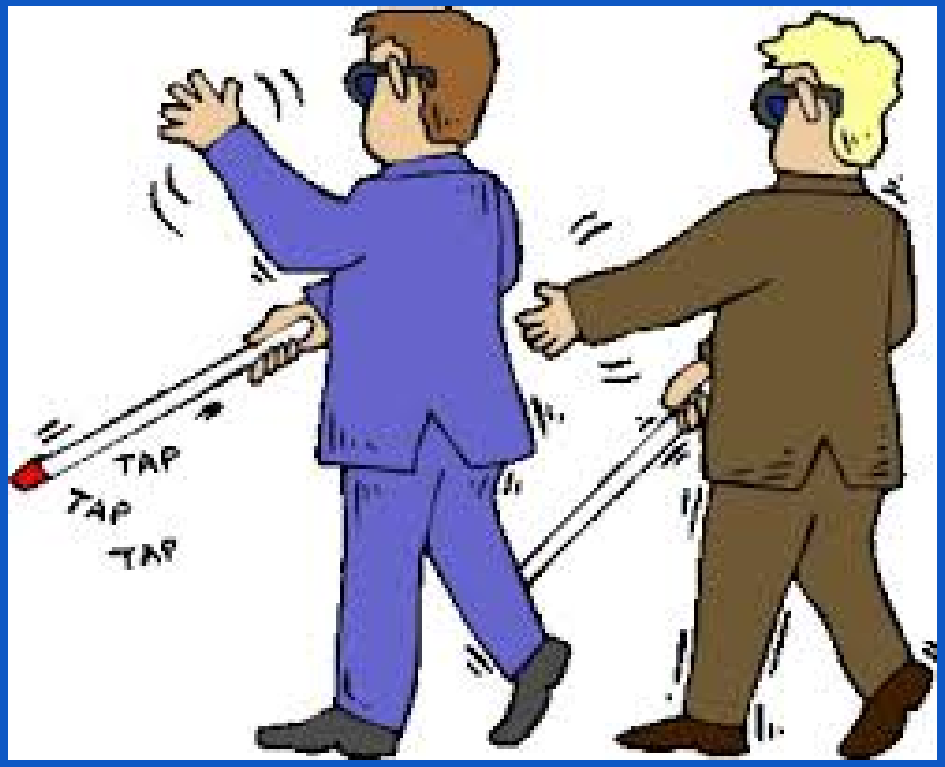
Characteristics of health care providers hindering uptake of precision medicine

- Lack of awareness
- Skepticism
- Lack of confidence

Supporting evidence, root causes, solutions

Health care providers are unaware



"It is very unclear to me that this should be even in the top 25 topics in primary care. I see the value in oncology and advancing knowledge but what else?"

It’s not my problem

“The good news is that it’s not my problem.”

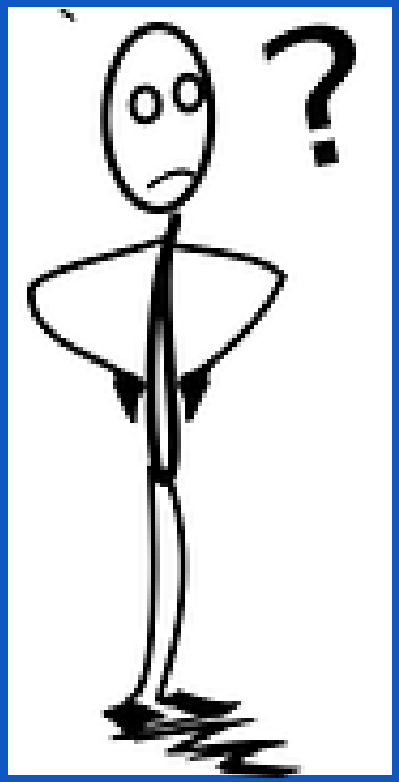
Historically, genomic medicine has been confined to medical geneticists and genetic counselors

Recommendation

17.3 **Evaluation, genetic counseling, and genetic testing of cardiomyopathy patients are complex processes. Referral to centers expert in genetic evaluation and family-based management should be considered. (Strength of Evidence = B)**

3500 genetic counselors
1/245 physicians

Is precision medicine a primary care issue?

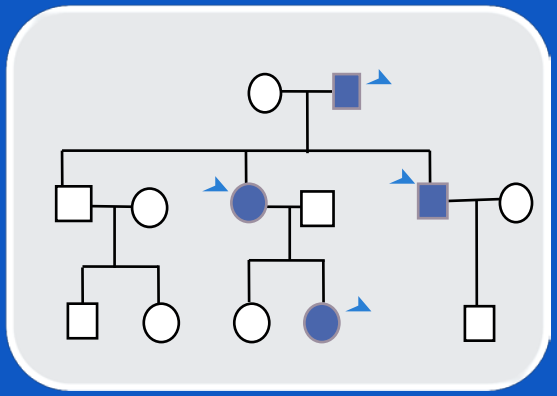


Precision medicine in primary care

Diagnostic sequencing

Pharmacogenomics

Predisposition testing

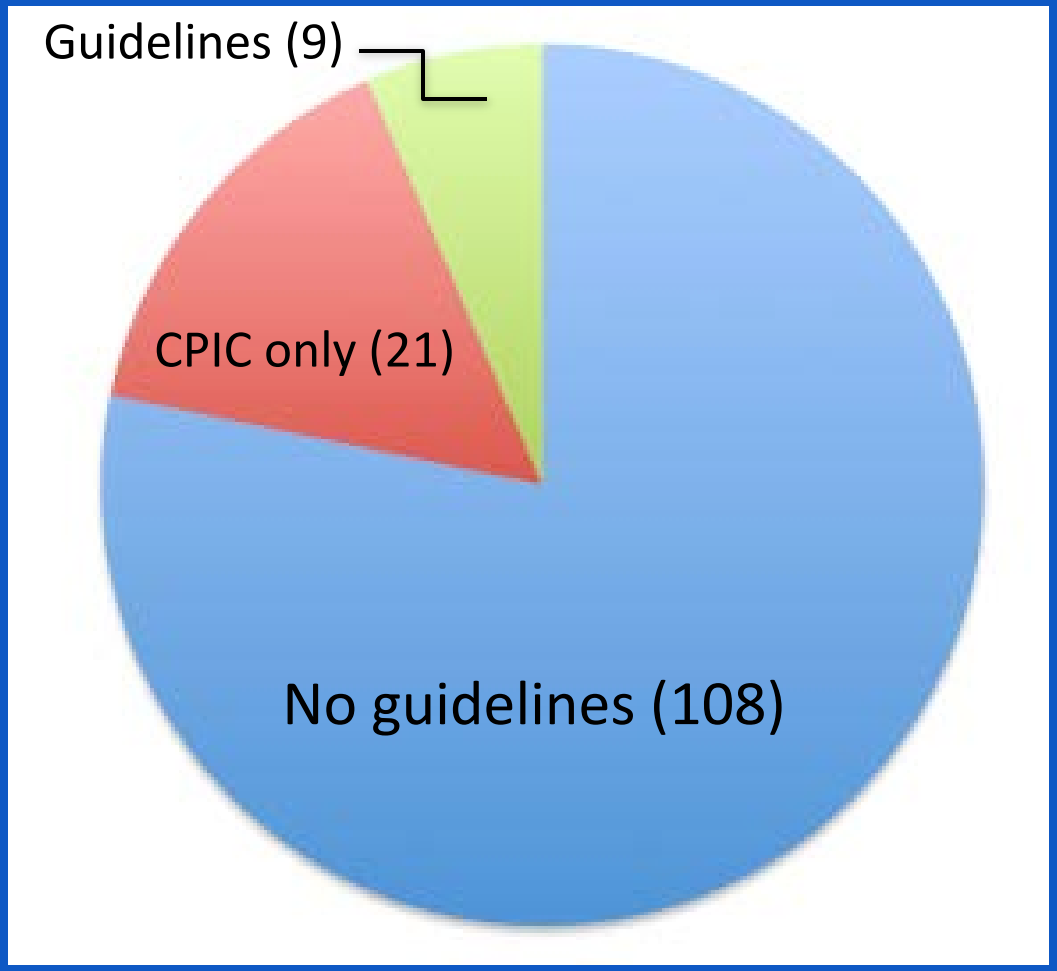


Consumer genomics

Health care providers are skeptical

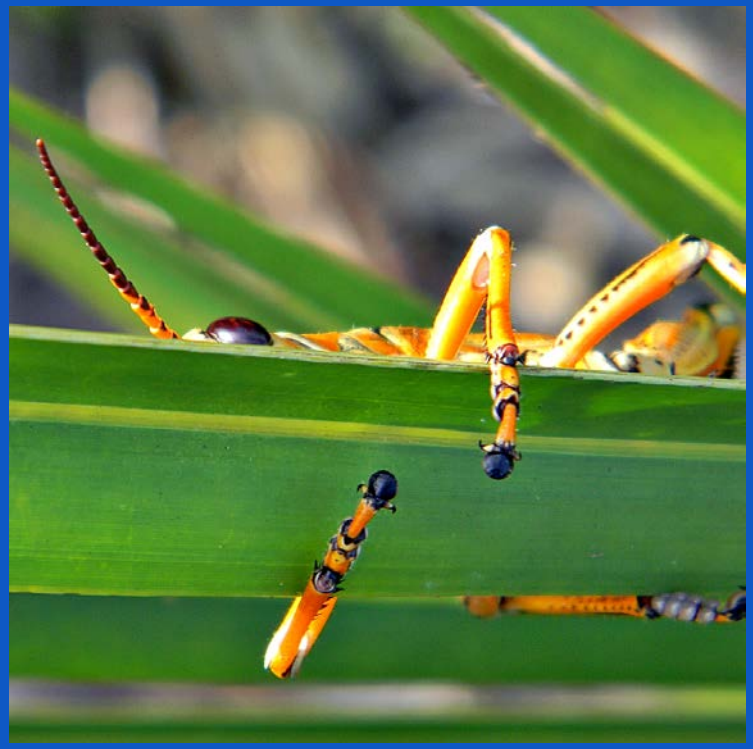
“I don't (and shouldn't) adopt any new technology test or therapy until patient centered improvements in outcomes are demonstrated and until that RCT data is available, I am going to tune this out.”

138 drugs with PGx in label



Adapted from: Community Pharmacist Pharmacogenetics Network Rxpgx.com

Health care providers lack confidence



Surveys show lack of knowledge and skills

Reasons for lack of self-confidence

- Lack of appropriate training in genomic medicine

Medical school

Narrowly focused content
Mostly taught in first year

CME

Limited opportunities for practicing health care providers to learn

- Lack of clinical experience with genomic tools

13% of 10,000 physicians had ordered a PGx test in the past 6 months

Stanek et al. 2012

UCSF Coursera Genomic and Precision Medicine, Spring 2014

UCSF University of California San Francisco

Genomic and Precision Medicine

A critical, unbiased introduction to using new genomic tools for diagnosing and managing disease.

Coursera GPM overview

- Designed for health care providers
- Seven 1-hour lectures + brief assessment
- 14.00 AMA PRA Category 1 CME credits (requires final grade of 70% or above)
- Modular – allows one to skip over sections based on competence

Syllabus

Week 1: Human genomics

Week 2: Prenatal carrier testing and newborn screening

Week 3: The use of NGS for solving diagnostic dilemmas

Week 4: Methods of association

Week 5: Predictive tests for common, complex diseases

Week 6: Pharmacogenomic testing

Week 7: Tumor profiling

Students

Spring 2014

13,178
total learners joined

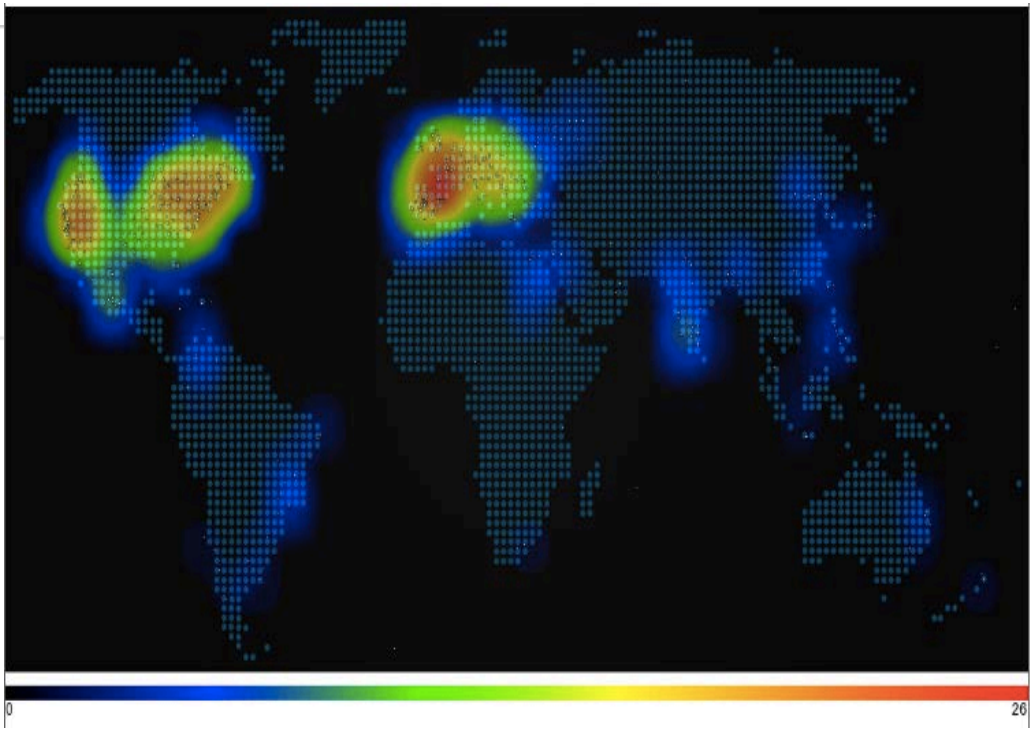
195
with Signature Track

Committed to complete – 2,840

Committed to audit – 3,095

Uncommitted – 1,948

Values extrapolated based on responses from 7,124 learners.



From survey (n=470): 65 countries (37% from US), 118 involved in patient care

Students

Spring 2015

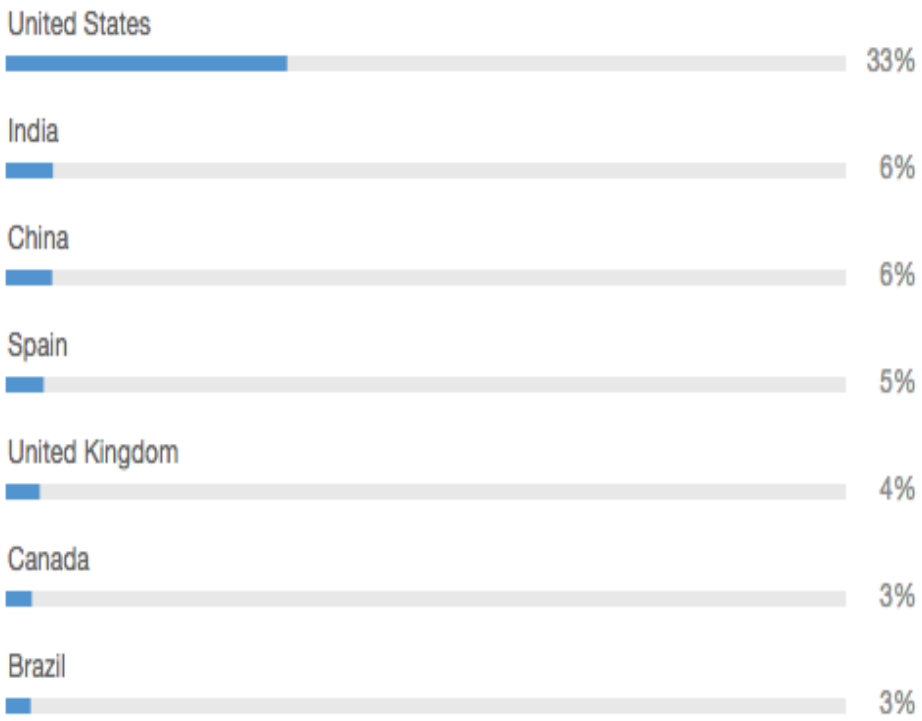
7,663
total learners joined

175
with Signature Track

- Formally affiliated with your institution — 61
- Familiar with your institution — 2,121
- Heard of your institution — 2,707
- Not heard of your institution — 566

Institutional brand awareness values are extrapolated based on responses from 270 learners.

Country



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Pre-course survey

24. Have you ever ordered a genomic test of any kind for a patient?

#	Answer	Bar	Response	%
1	Frequently, including diverse diseases and/or risk factors.		16	15%
2	Yes, but only standard screening such as newborn screening, standard prenatal screening, or carrier screening recommended by ACOG or ACMG.		7	7%
3	Occasionally.		15	14%
4	Rarely.		20	19%
5	Never.		47	45%
	Total		105	

25. How often has a patient initiated a request for a specific genetic test by name?

#	Answer	Bar	Response	%
1	Frequently		7	7%
2	Occasionally		14	14%
3	Rarely		30	29%
4	Never		52	50%
	Total		103	

26. How often has a patient presented genetic results to you for interpretation that you did not order?

#	Answer	Bar	Response	%
1	Frequently		5	5%
2	Occasionally		11	11%
3	Rarely		32	31%
4	Never		56	54%
	Total		104	

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Student forum - problem solving

Why the current Whole genome sequencing can not reliably detect trinucleotide repeat or large deletions?

↑ 1 ↓ · flag

Hi,
It could possibly be because of the limitation in the allignment of the reads . Though there is a reference sequence available you cant be sure enough of the positions of trinucleotide repeats . In case of larger deletions, I think if the deletion if matches some other position in the genome, it can at times show negative for deletions which would be is a false negative.

↑ 0 ↓ · flag

+ Comment

If you have a trinucleotide repeat (CAGCAGCAG...) that goes on for longer than any one sequence read, you can't tell how long that triplet repeat section really is. If the read is 99bp and it's all CAGCAGCAG..., you know that there are at least 33 copies of the (CAG) but you can't tell the difference between a genome with 33 copies and a genome with 133 copies. You can only tell how long a repeat span is if you can sequence into the unique areas on either side of it. This is something that will become less of as sequencing technology improves and reads get longer.

My silly example with words in place of nucleotides. You can only "read" 5 words at a time:

Reference genome - Genomics is very very interesting. (Easy, the whole thing's in one read)
variant 1 - Genomics is very very very interesting. (Easy, you can get a read that covers 'is' through 'interesting')
variant 2 - Genomics is very very very very interesting. (Impossible, now you can't get a read that has unique words on each end)
variant 3 - Genomics is very very very very very very very interesting. (Same situation as variant 2, but now you could get a read that has no unique words at all.)

Assessments – built in research

The following is an opinion question to encourage discussion and thought on the intersection of ethics and genetics. There is no right answer and it will have no effect on your grade.

You work for an organization that provides whole-exome sequencing analysis and interpretation. A variant classified as a "variant of unknown significance" in TP53 (often referred to as p53) was detected in a child and his 19-year-old father who underwent testing for an unrelated suspected genetic syndrome. Because the significance was unknown, this variant was not reported. Five years later, a paper is published describing this precise variant as causative of Li-Fraumeni syndrome, a disorder with high risk of several types of cancer for which aggressive screening is recommended. The physician who ordered the test retired four years ago and is no longer in contact with the family, and the family's address provided on the initial test is also no longer up-to-date. Which option most closely reflects your opinion as to the organization's obligation to locate the family and alert them to their high risk for cancer and recommended screening precautions?

	First attempt	Last attempt
The organization is obligated to locate and notify this family at any cost.	266	265
The organization is obligated to find and notify the patient's health care provider, but does not need to find the family itself.	390	396
The organization is obligated to provide information on its website for patients who receive test results to check back frequently for updates on the status of variants.	602	588
The organization has no obligation to contact this family, and the family has the responsibility for following up on their own test.	92	93

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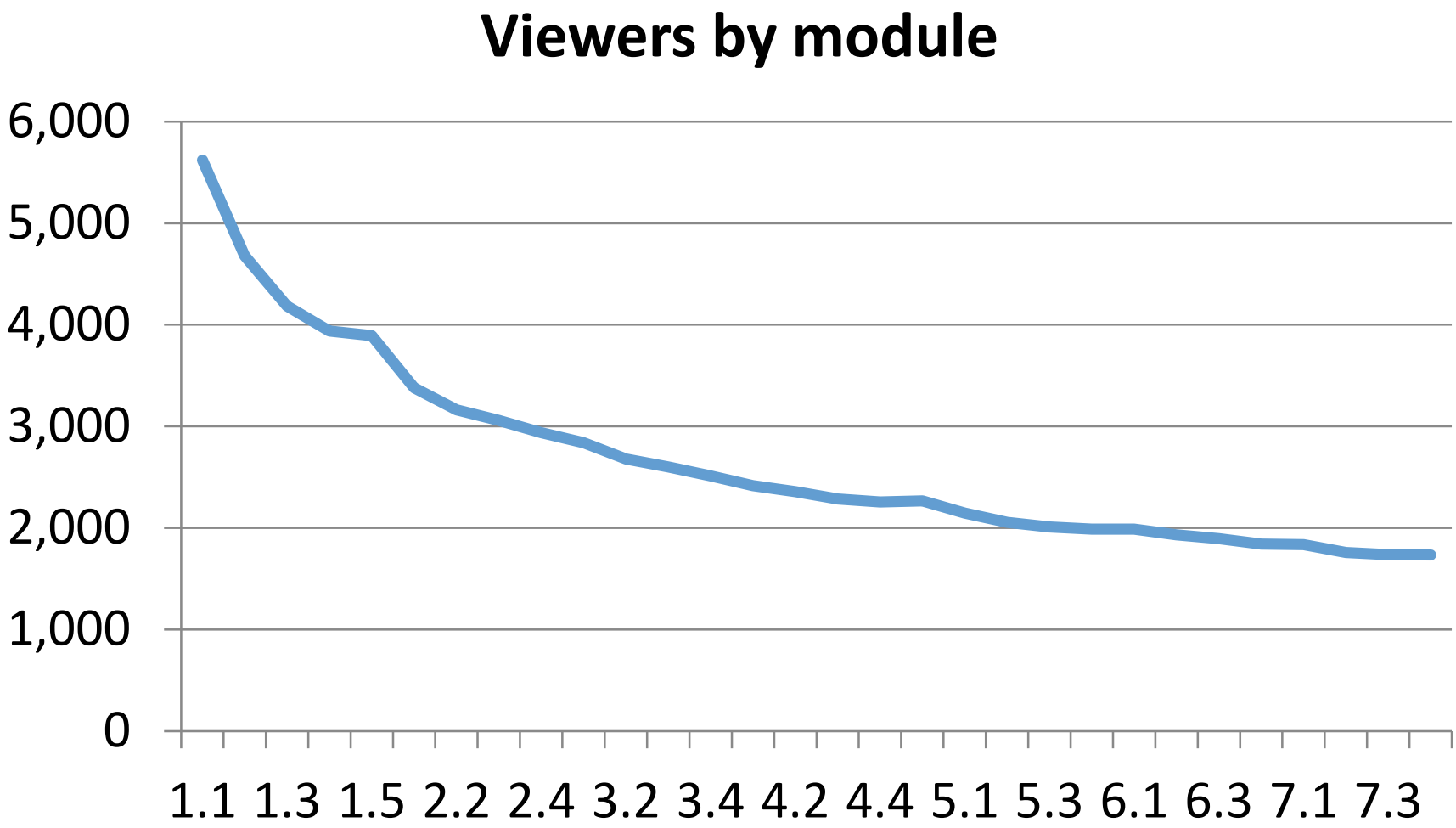
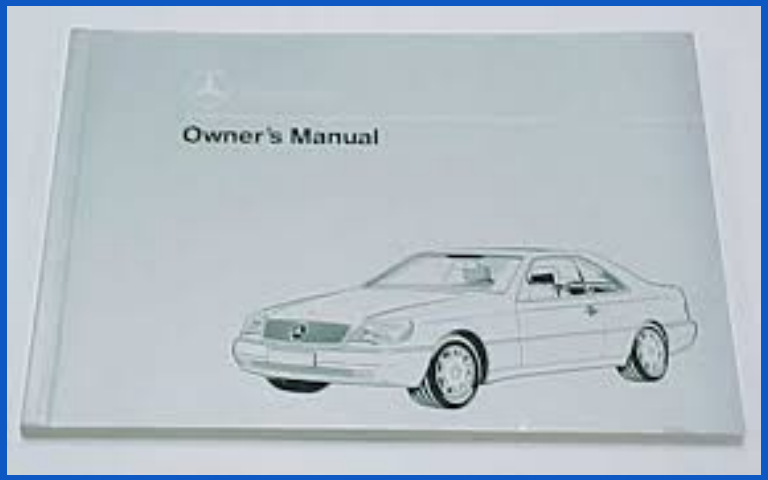
Drop off


Viewers by module
6,000
5,000
4,000
3,000
2,000
1,000
0
1.1 1.3 1.5 2.2 2.4 3.2 3.4 4.2 4.4 5.1 5.3 6.1 6.3 7.1 7.3

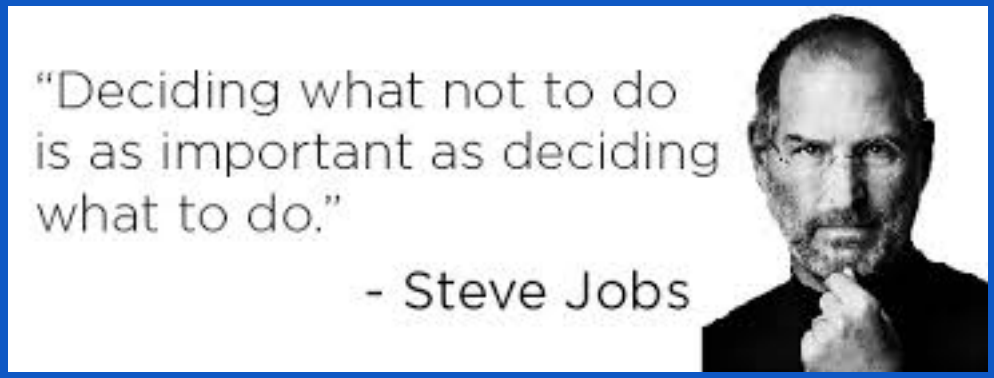
Drivers ≠ mechanics



Driving school

Guiding principles

- Structure around clinical applications of PM
- Address awareness
- Teach skills to build confidence
- Both didactic and time behind the wheel (hands-on learning)
- Brief and focused
- Convenient



Clinical applications of PM

- Rare Mendelian diseases
  - Carrier testing
  - Newborn screening
  - NGS for Idiopathic diseases
- Common Mendelian diseases
  - Hereditary cancer predisposition panels
  - Hereditary heart disease predisposition panels
- Common disease/common variants (limitations)
- Pharmacogenomics
- Tumor molecular profiling in cancer

What are the behaviors we want to change?

- Order more tests?
- Order fewer tests?
- Maximize the potential value of existing genomic information from patients

Driver's school: didactic content

- Current testing landscape
- Indications for testing
- Selecting a test
- Interpreting results
- Value of testing
- Limitations of testing

Build a library for training across institutions

Driver's school: didactic format

Considerations:

- Reach, convenience, interaction, cost

Formats:

- Online videos (on demand)
- Online videos (set period)
- Webinar
- Live (grand rounds)

Drivers school: behind the wheel

Evaluating clinical validity/utility
Where and how to order test

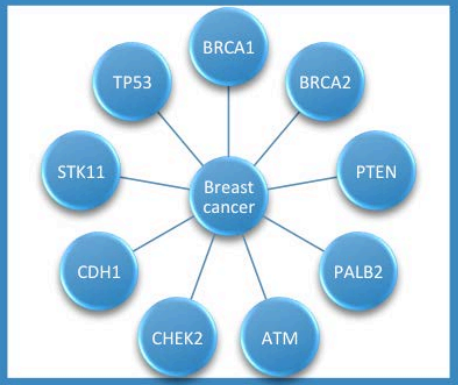
Interpreting and using results to manage patient

Explaining benefits, limitations and results to patients

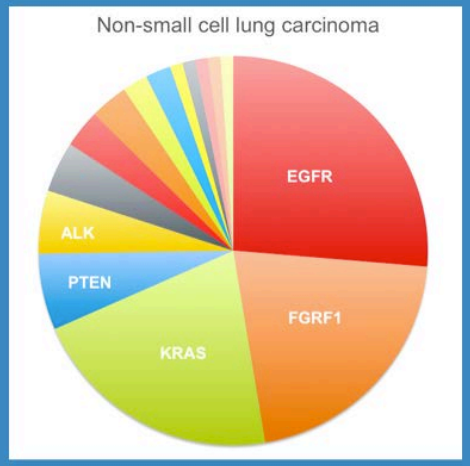
Give providers the experience of ordering, interpreting and communicating test results

Workshops

Hereditary cancer predisposition testing



Tumor Profiling in Practice



Pharmacogenomic testing to prevent adverse drug events

Convenient CME

Other pieces

Driver's license

- Certification?

Owner's manual

- Practical guide, websites, CDS

Jiffy Lube

- Genetic counselors or similar

The push and pull of precision medicine

Educating and enabling providers

Empowering consumers

Genome, from Big Science Media

www.genomemag.com

Our vision is a world in which everyone knows the power of his genome. As the most trusted source of information on personalized medicine, Big Science Media will transform the way healthcare is delivered by inspiring people to demand the care they deserve.