ReDefining LEADERSHIP

CONFERENCE | CONGRÈS

THE 60th ANNUAL CANADIAN REINSURANCE CONFERENCE

60 Anniversary

Genetic Testing in Insurance: A Medical View

David Moss FIA
SVP, Swiss Re Canada

Florian Rechfeld PhD
Medical Biochemist, L&H R&D, Swiss Re

Loraine Oman-Ganes MD, FRCPC
Chief Medical Director, Sun Life Financial

ReDefining LEADERSHIP

CRD CONFERENCE | CONGRÈS

THE 60th ANNUAL CANADIAN REINSURANCE CONFERENCE

60 CRD Anniversary

Leadership: Scanning the Horizon

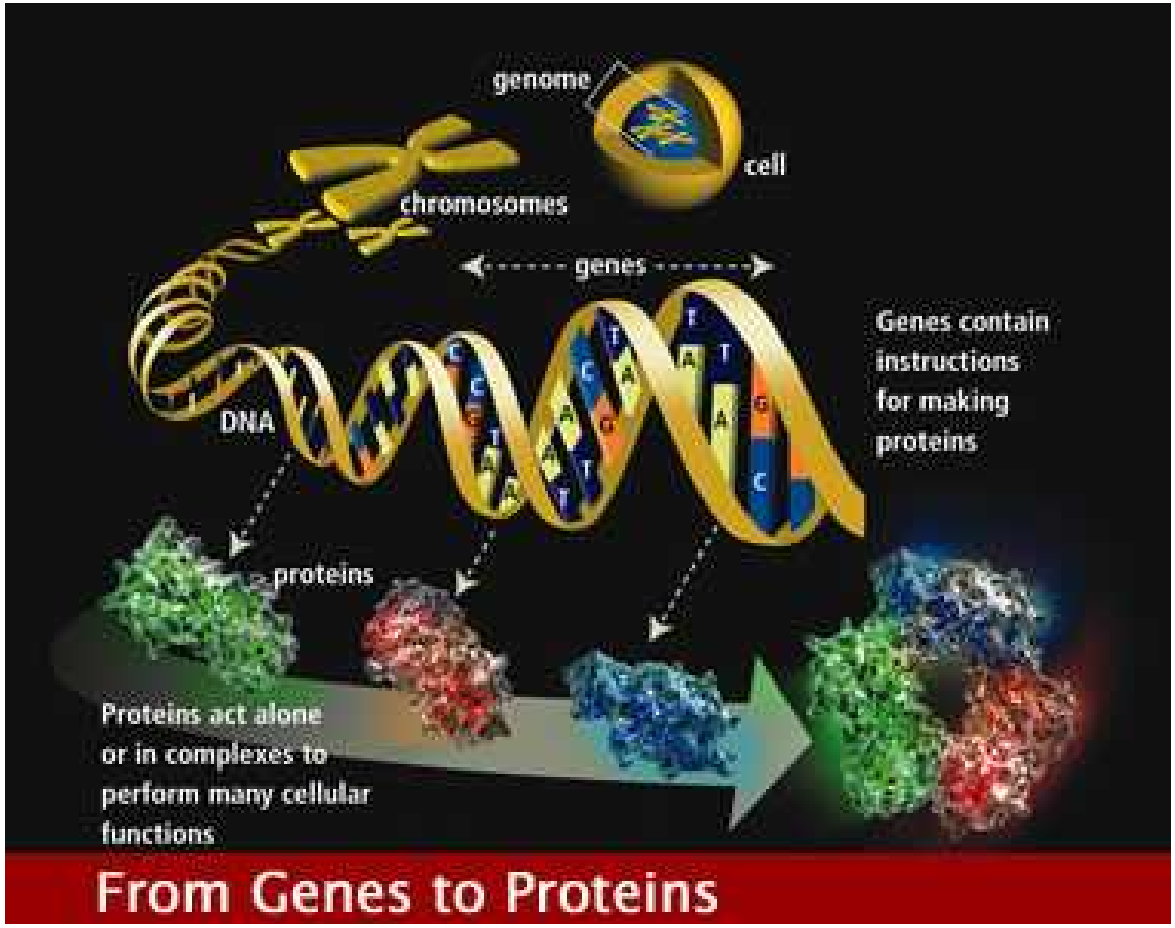
http://www.bbc.co.uk/sn/tvradio/programmes/horizon/broadband/tx/alone/

Agenda

- Advances in the landscape of genetic testing
- Clinical genetic testing, DTC-testing and insurance exposure
- Regulations on the use of genetic data in private life insurance
- What is a Genetic Test?
- Family History: It's Importance
- Transforming Challenges into Opportunities:
  - Precision Medicine
  - Pharmacogenomics
  - High Cost Drugs

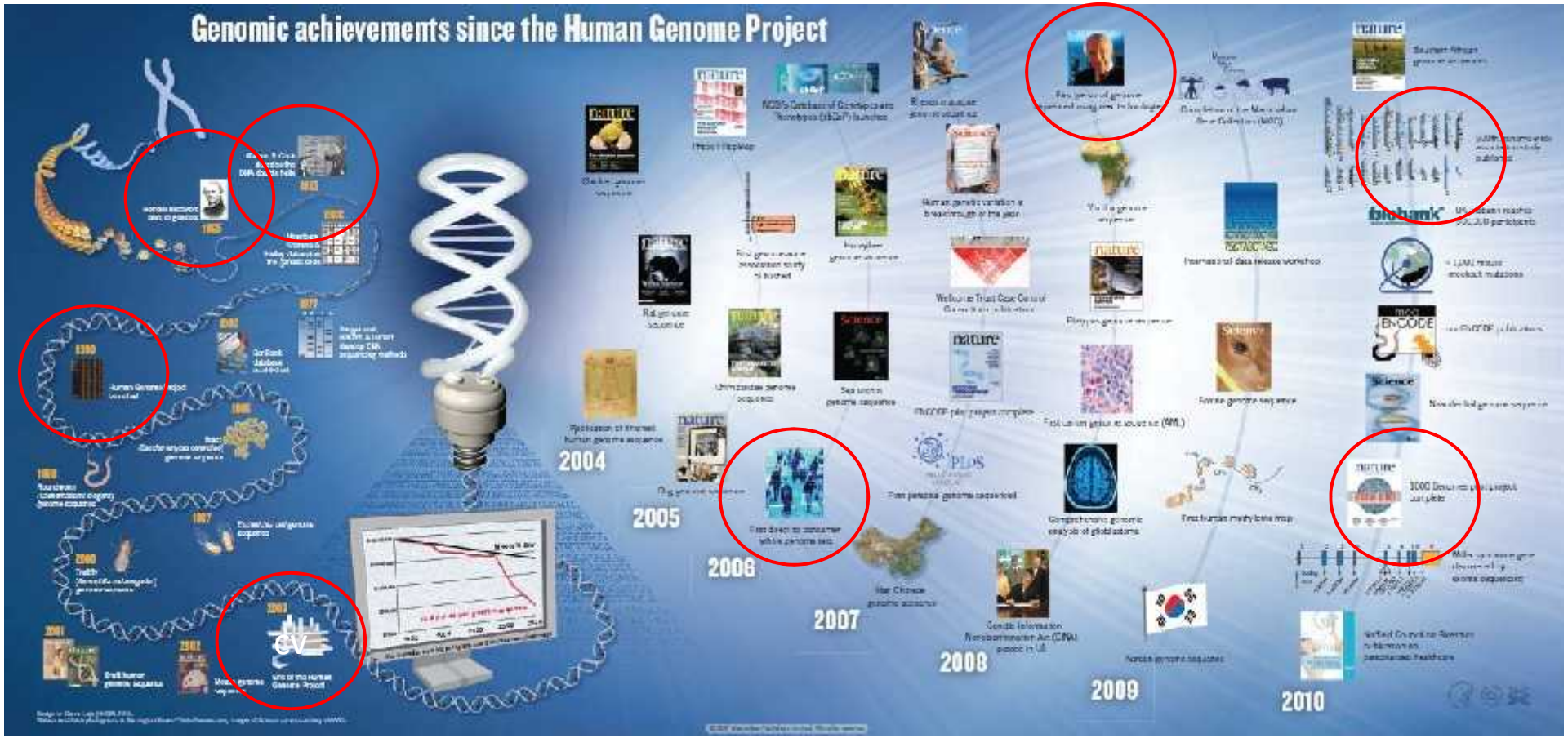
Advances in the landscape of genetic testing

Genomics 101: DNA, Genes and Genomes



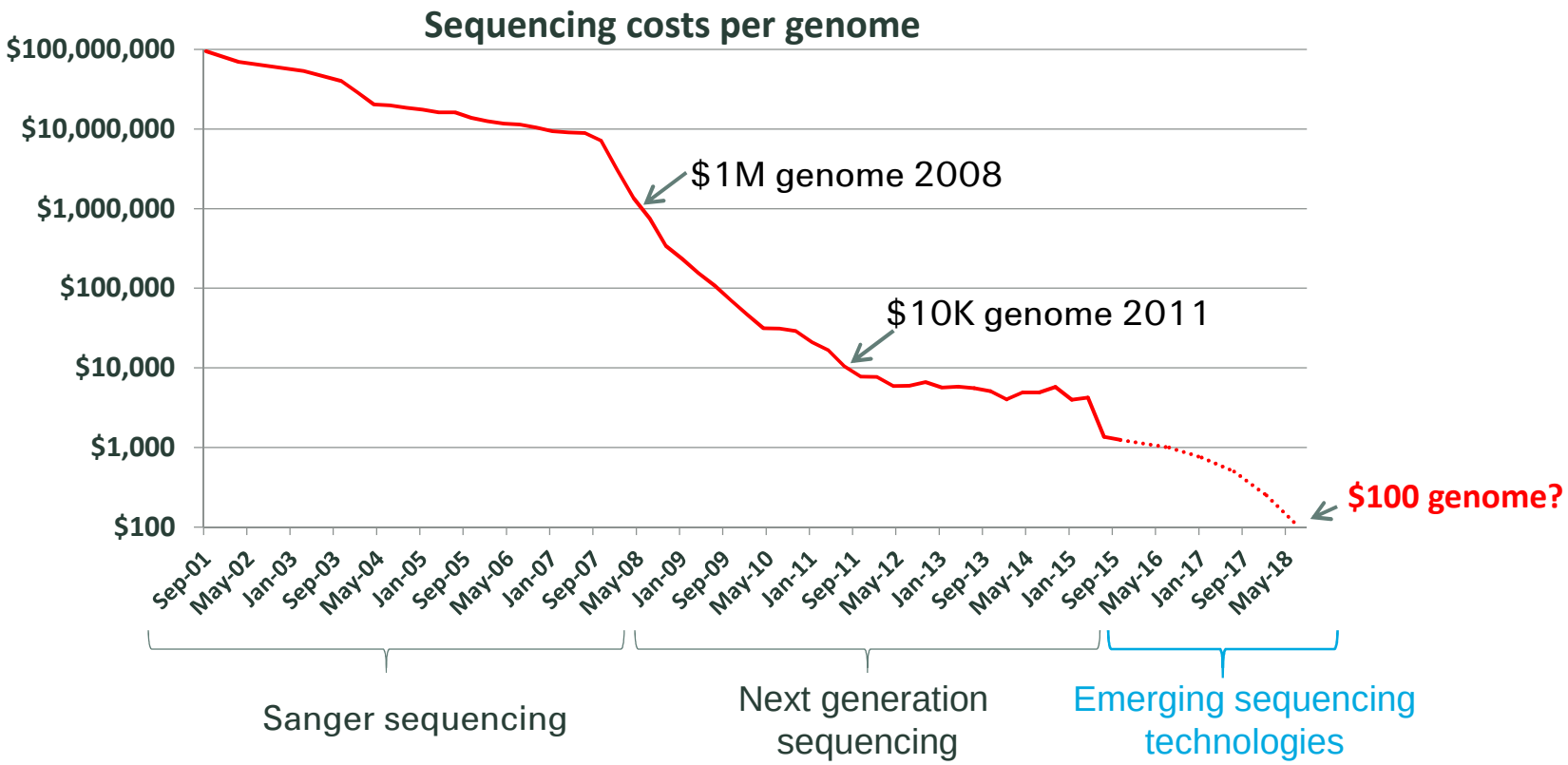
Source: http://www.voidspace.org.uk/technology/genome/1.shtml

Genetic information and technology have grown exponentially over the last decades



Source: Nature 470, 204–213, 2011

Full genome sequencing becomes affordable



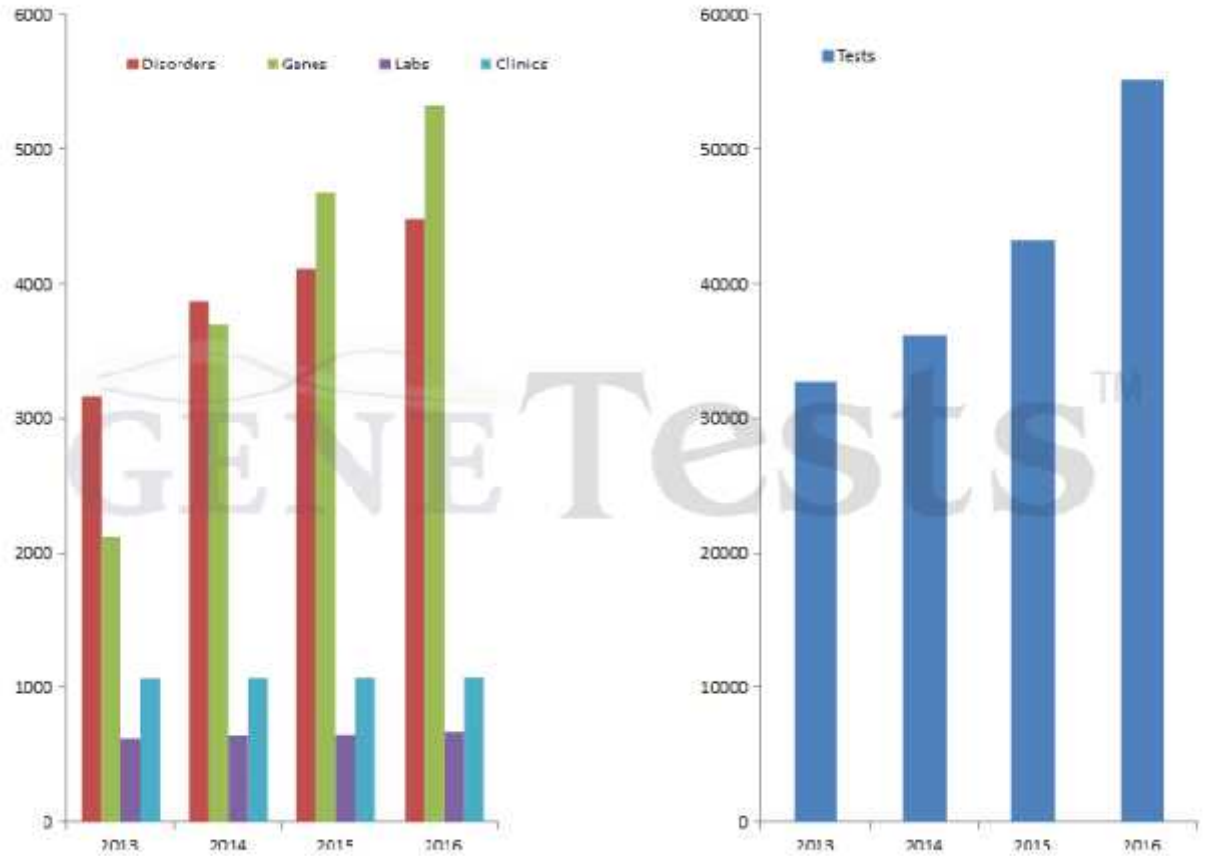
Plummeting genome sequencing costs and advances in human genetics increases the availability for different types of genetic testing.

Source: NIH National Human Genome Research Institute http://www.genome.gov/sequencingcosts/

Rapid increase in genetic test development for diseases

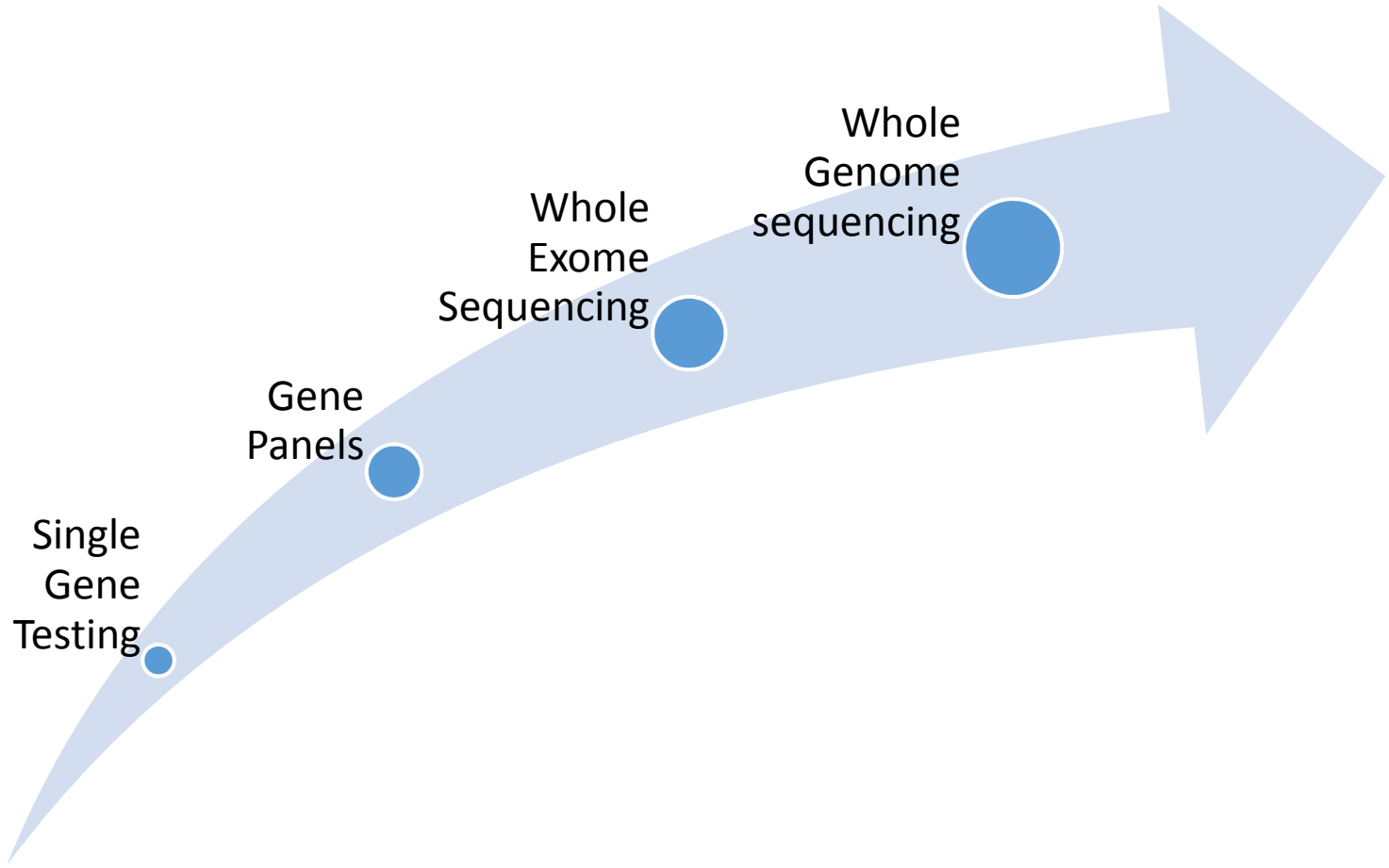
March 21, 2016

- 55,887 Tests
- 4,537 Disorders
- 5,367 Genes
- 679 Laboratories
- 1,067 Clinics



Source: https://www.genetests.org/

Evolution of genetic testing technologies



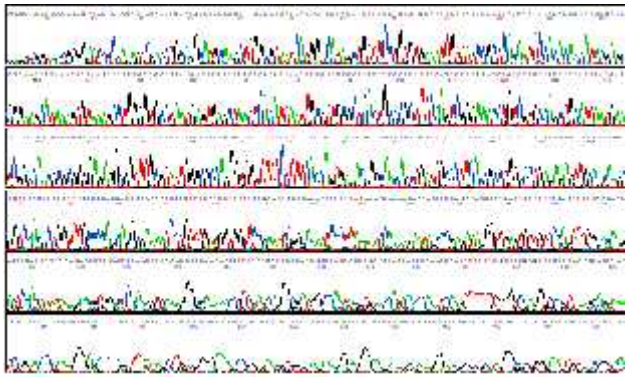
Worldwide large Genome Research Projects

- UK 10K Project (since 2010; UK):
  - Sequencing 10,000 UK individuals for analysis of low-frequency and rare genetic changes in human disease.
- The 100,000 Genomes Project (since 2013; UK):
  - Sequencing 100,000 UK patients with rare diseases and their families and patients with cancer.
- Precision Medicine Initiative (announced 2015, enrollment 2016; US)
  - Sequencing 1,000,000 US individuals to advance personalized medicine in all areas of health.
- Beijing Genomics Institute 3 Million Genomes project (announced 2014)
  - Sequencing 1 million people, 1 million microorganisms,1 million plants and animals.

Paradigm shifts in modern clinical medicine

Millennia ago
"**Macroscopic**" med.

Centuries ago
"**Microscopic**" med.



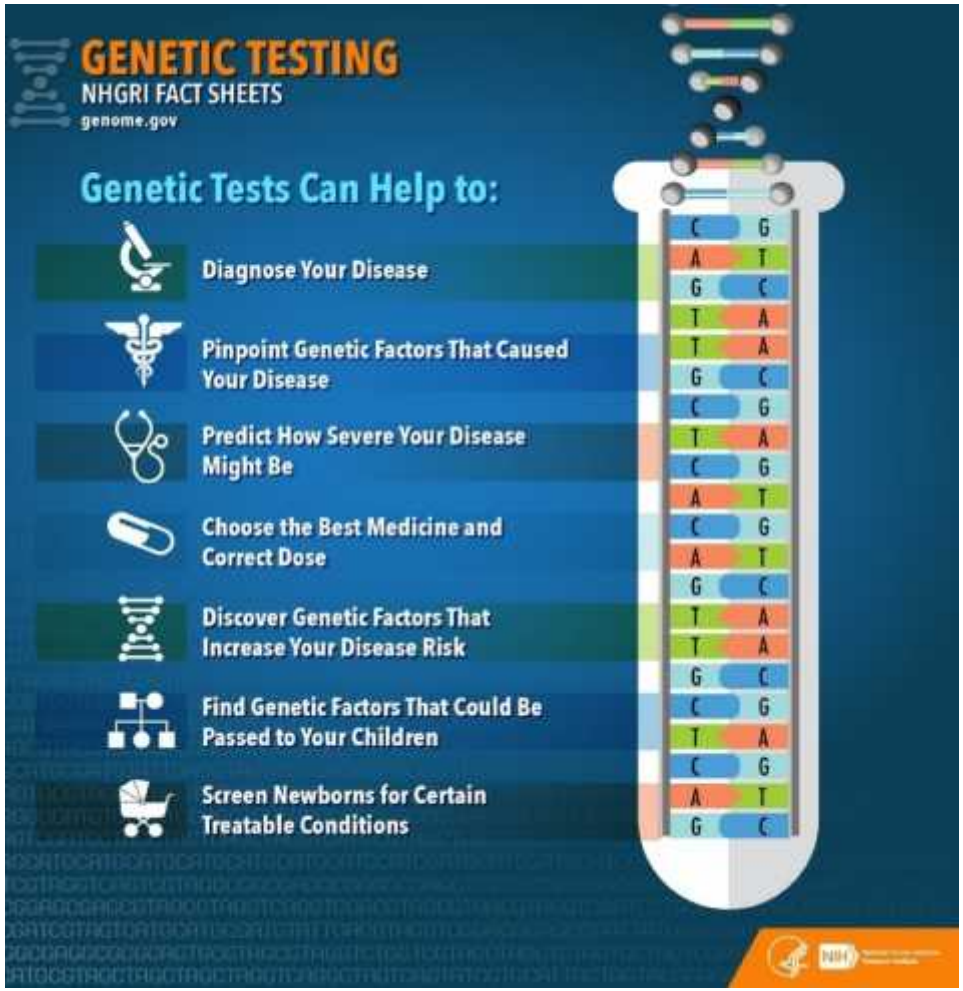
Last decade
"**Molecular**" medicine

Genetic testing is the key to personalized medicine which aims at better diagnosis, prevention and effective treatment of disease

Clinical genetic testing, DTC - testing and insurance exposure

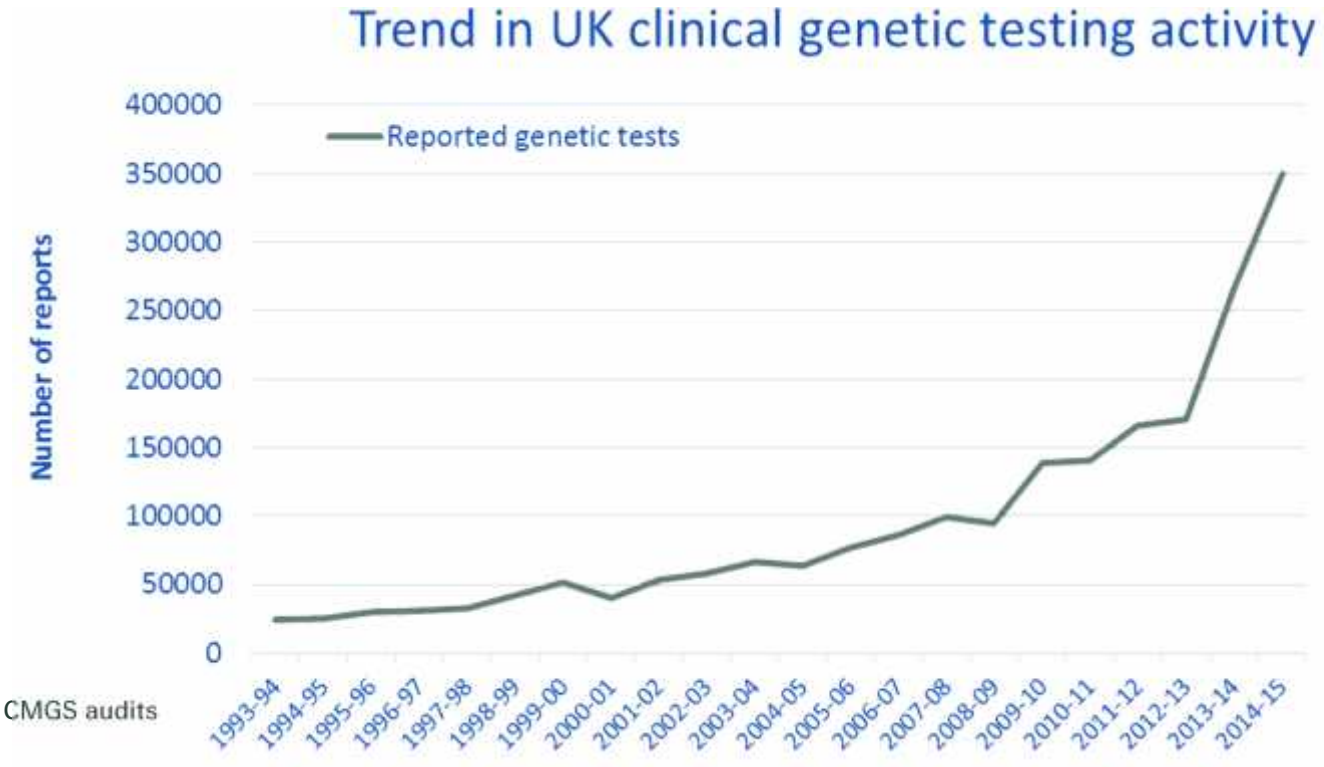
Types and use of different genetic tests

1. Diagnostic testing
2. Pharmacogenomic testing
3. Predictive/presymptomatic testing
4. Carrier testing
5. Newborn screening
6. Prenatal testing
7. Preimplantation testing
8. Research testing



Source: http://www.genome.gov/19516567

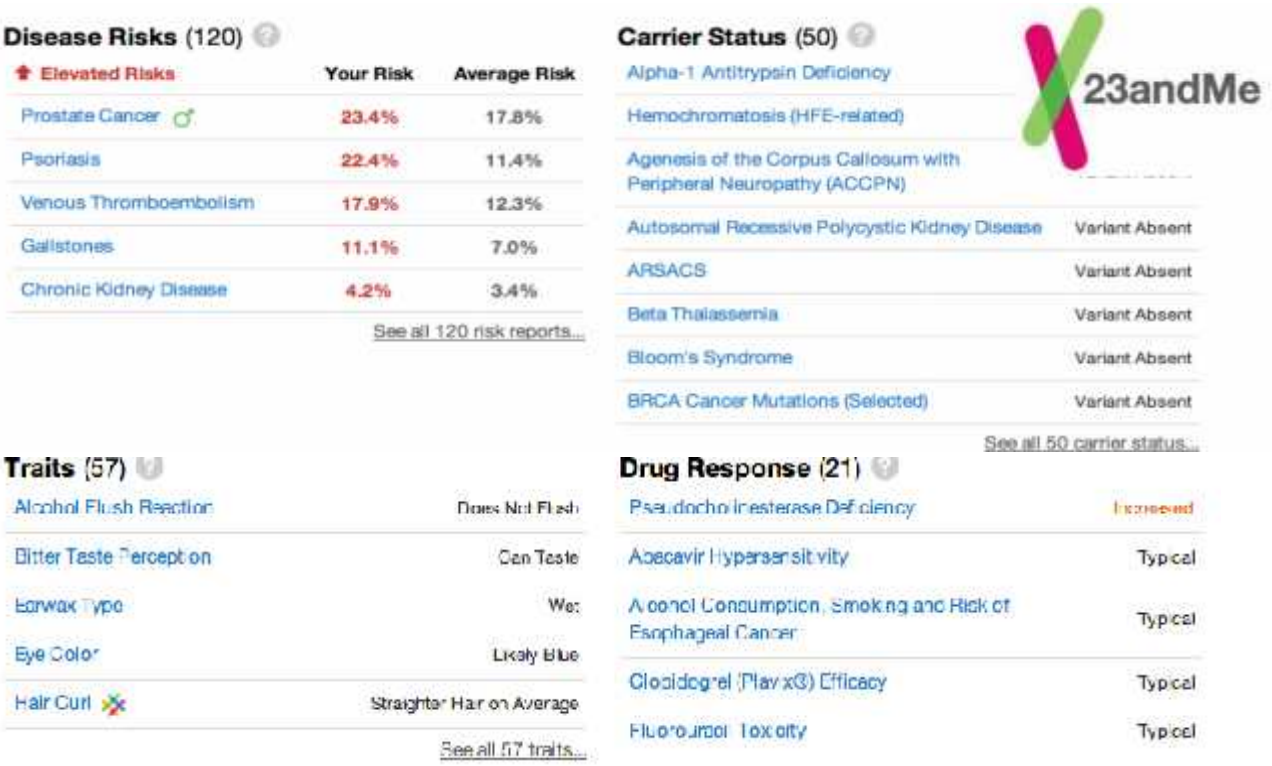
Genetic testing in the clinical practice grows rapidly



Source: CMGS audits

Advances in the understanding of human genetics increases the availability and uptake of genetic testing in the clinical practice.

Growing Direct-to-consumer (DTC) genetic testing market: Accuracy, Validity and Utility



Disease Risks (120)

Elevated Risks	Your Risk	Average Risk
Prostate Cancer	23.4%	17.8%
Psoriasis	22.4%	11.4%
Venous Thromboembolism	17.9%	12.3%
Gallstones	11.1%	7.0%
Chronic Kidney Disease	4.2%	3.4%

See all 120 risk reports...

Carrier Status (50)

Alpha-1 Antitrypsin Deficiency	
Hemochromatosis (HFE-related)	
Agenesis of the Corpus Callosum with Peripheral Neuropathy (ACCPN)	
Autosomal Recessive Polycystic Kidney Disease	Variant Absent
ARSACS	Variant Absent
Beta Thalassemia	Variant Absent
Bloom's Syndrome	Variant Absent
BRCA Cancer Mutations (Selected)	Variant Absent

See all 50 carrier status...

23andMe

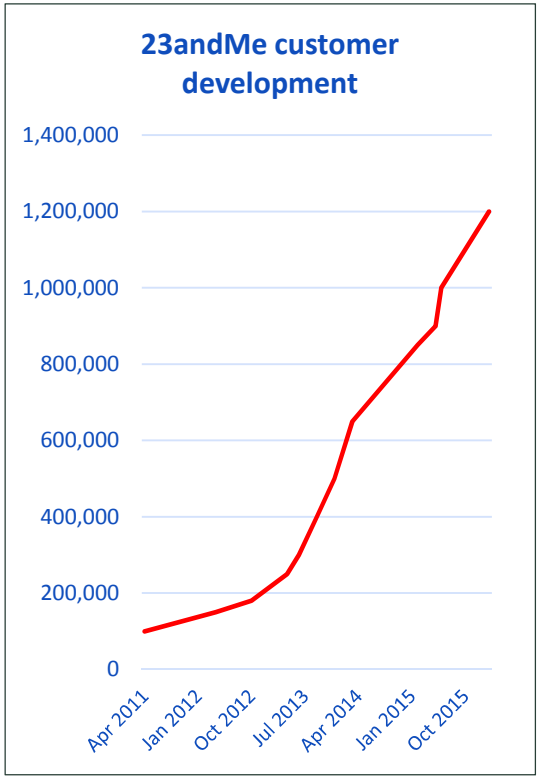
Traits (57)

Alcohol Flush Reaction	Does Not Flush
Bitter Taste Perception	Can Taste
Earwax Type	Wet
Eye Color	Likely Blue
Hair Curl	Straighter Hair on Average

See all 57 traits...

Drug Response (21)

Pseudocholinesterase Deficiency	Increased
Abacavir Hypersensitivity	Typical
Alcohol Consumption, Smoking and Risk of Esophageal Cancer	Typical
Clopidogrel (Plavix®) Efficacy	Typical
Fluorouracil Toxicity	Typical



- **November 2013: FDA notifies 23andMe to stop offering health-related genetic reports in the US pending completion of the agency's regulatory review processes**
- **December 2014: 23andMe launched slimmed-down version in UK and Canada**
- **October 2015: 23andMe relaunched restricted health testing in the US market**

Genetic test definitions: Diagnostic vs. Predictive genetic test

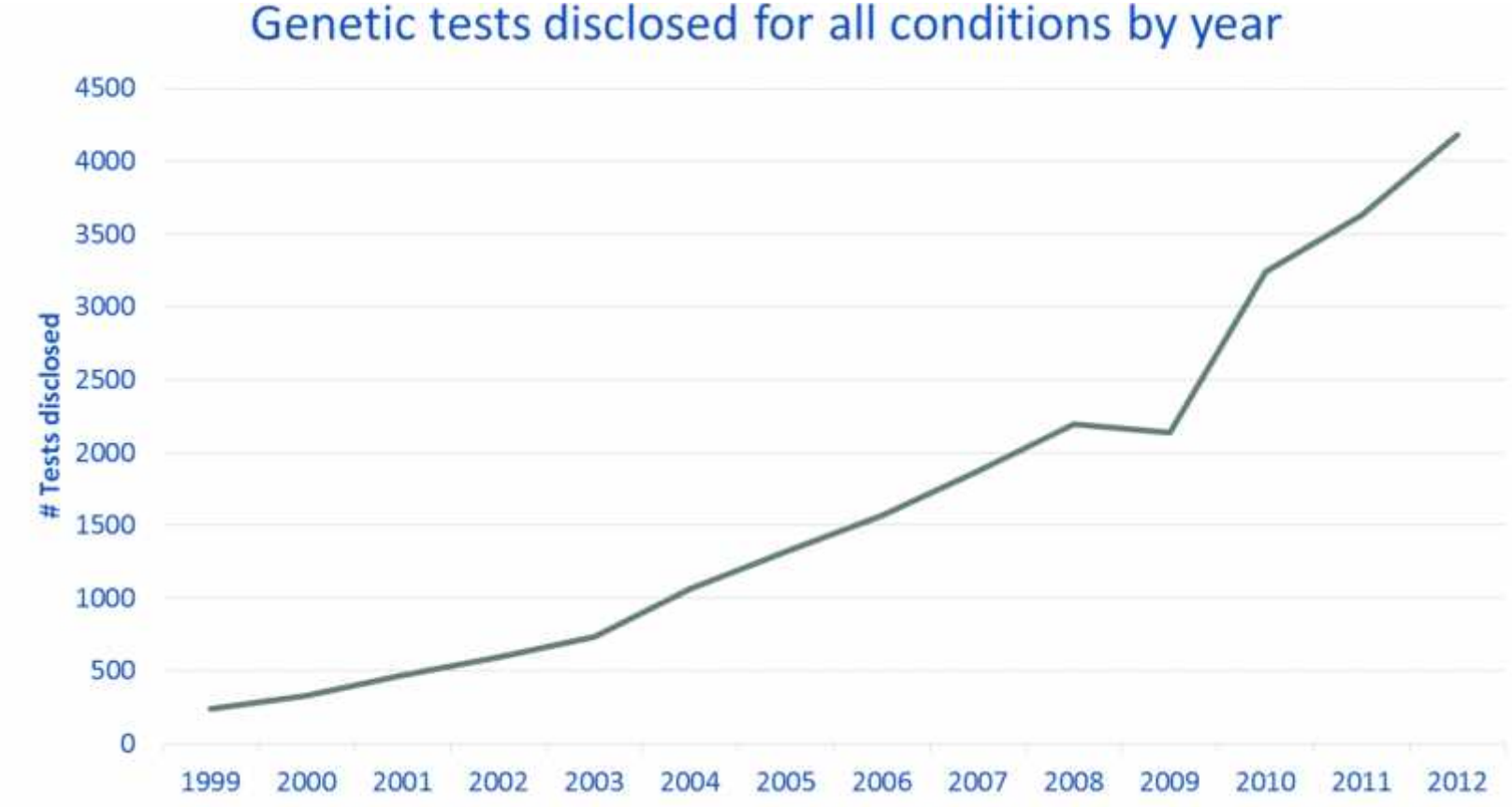
Diagnostic genetic test

- To confirm or rule out a known or suspected genetic disorder in a **symptomatic** individual.
- **Generally no restrictions** on the use of diagnostic tests in insurance underwriting.

Predictive genetic test

- Offered to **asymptomatic** individuals with a family history of a genetic disorder to **predict future risk of disease.**
- Disclosure obligation and use of predictive genetic test results in insurance underwriting **vary by market practice and legislation.**

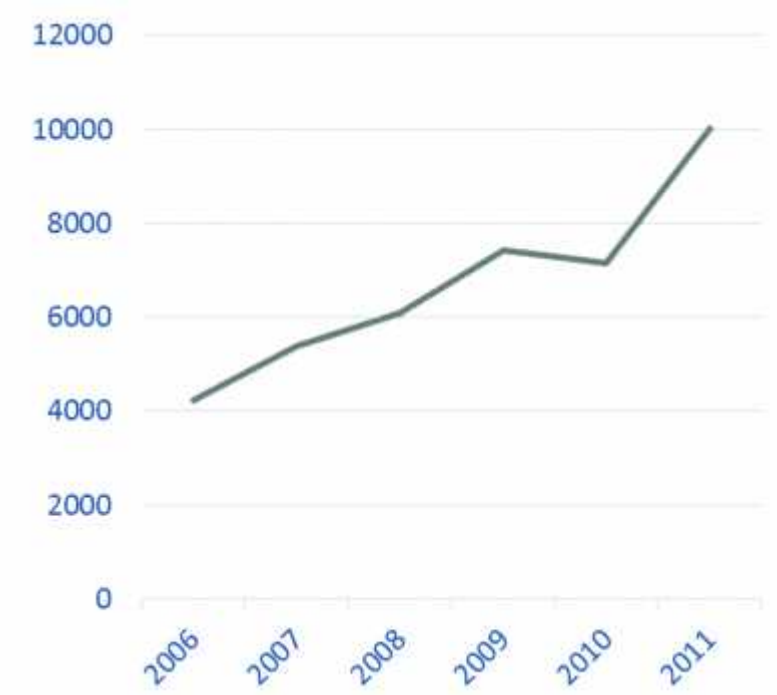
A steady increase of genetic tests results disclosed to the UK life insurance industry can be observed



Source: Swiss Re

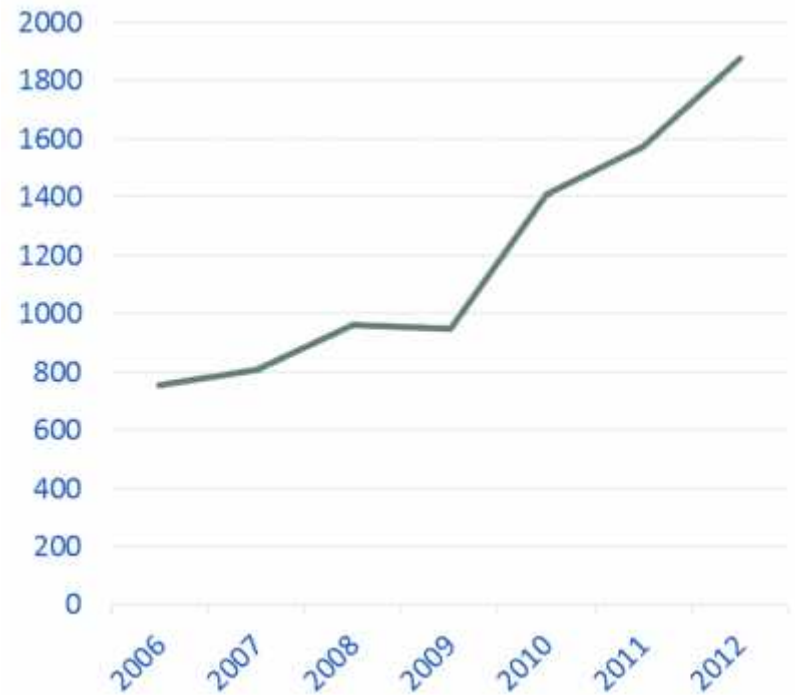
Predictive genetic tests performed in the clinical practice and disclosed to UK life insurers

19% annual growth rate of predictive genetic tests performed in clinical practice



Source: CMGS Audit Reports

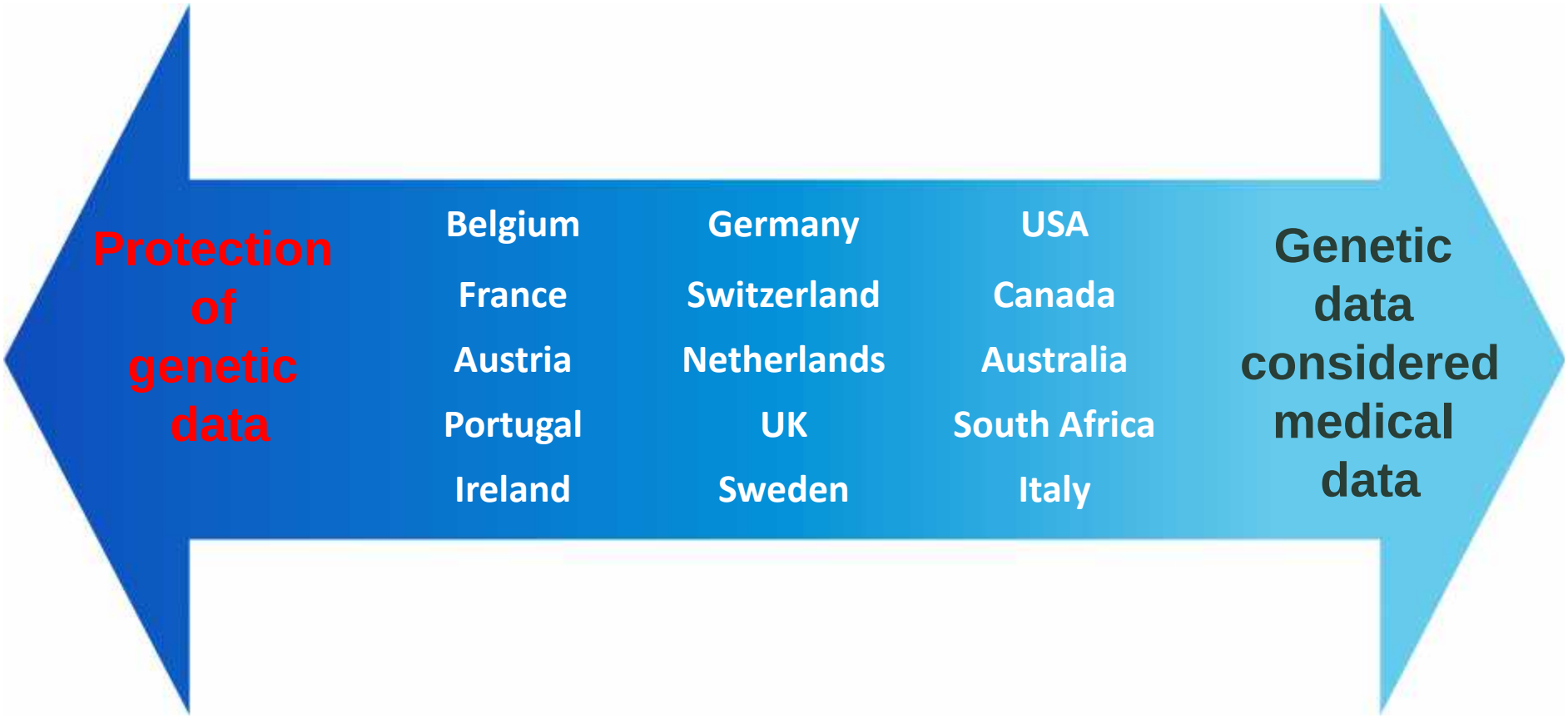
16% annual growth rate of predictive genetic test results disclosed to UK insurers



Source: Swiss Re

Regulations on the use of genetic data in private life insurance

Insurers are faced with various levels of restriction on use of genetic data in different countries



Legislative regulations range from voluntary moratoria, legislation to strict outright bans and approaches continue to evolve.

Regulations on the request and use of predictive genetic tests in insurance underwriting in different markets

Limitations	Level	Countries and limits (life cover/annuity)
No request/use of predictive genetic test results	Ban	Austria, Belgium, France, Ireland, Portugal
	Moratorium	Finland, Greece
No request/use of predictive genetic test results up to certain insured sum/annuity	Law	Germany < EUR 300 000 / 30 000 Switzerland < CHF 400 000 / 40 000 Netherlands < EUR 250 000
	Moratorium	UK < GBP 500 000 / 300 000 (CI) Sweden < EUR 140 000 / 19 000
Minor restrictions with general anti-discrimination and data protection laws		Czech Rep., Italy, Spain,
Data protection/Privacy laws (minor restrictions in US by state laws)		**Canada, USA**

Private insurers do not require or initiate genetic testing to be done in order to obtain insurance cover!

- Restricions on request/use of family history information at UW stage in Belgium, Finland, Netherlands*, Norway, Portugal, Sweden**

* limited by amount and cause, ** limited by amount

CLHIA Industry Code: Genetic Testing Information for Insurance Underwriting

- April 23, 2015: Canadian Life and Health Insurance Association Industry Code on Genetic Testing:
  - Insurers will not require an applicant to undergo a genetic test.
  - Insurers will not ask for the results of genetic test done as part of a research project where the results are not shared with the applicant.
  - Insurers may use or request the results of an existing genetic test for the purposes of classifying risk.
  - Insurers will use genetic testing information for the applicant's benefit where it offsets information available from other sources.
  - A dispute resolution system will be established to address complaints related to underwriting decisions involving genetic test results

Regulatory approaches in Canada?

- Oct. 17, 2013
  - Senate Bill S-201 (Formerly S-218): An Act to prohibit and prevent genetic discrimination seeking to prohibit the requirement of genetic testing and the disclosure of genetic testing results as a condition for insurance underwriting.
- July 10, 2014
  - Office of the Privacy Commissioner statement asking life and health insurers to refrain from requesting access to existing genetic test results for insurance underwriting purposes.
- Feb. 19, 2015
  - Senate Bill S-201 Final report from Standing Senate Committee on Human Rights. All sections that would have had a negative impact on insurance companies removed.

The debate over use of genetic testing information in insurance underwriting will remain and Canadian insurers are on the verge of being legislated against!

What is a Genetic Test?

Everything's Genetic…

There is a genetic contribution to all aspects of health and disease

Genetic Exceptionalism

Genetic Tests relevant to Insurers
are Medical Tests

Some insurance applicants who are at increased risk for genetic/hereditary conditions apply for insurance before they have genetic testing.

Traditional Lens of a Genetic Test: Rare, Single Gene Conditions

Time.com
May 27, 2013

Question

What were the clues which may have led to Angelina's BRCA1 test?

A. Her mother had ovarian cancer in her 50's

B. She read about BRCA testing in a magazine

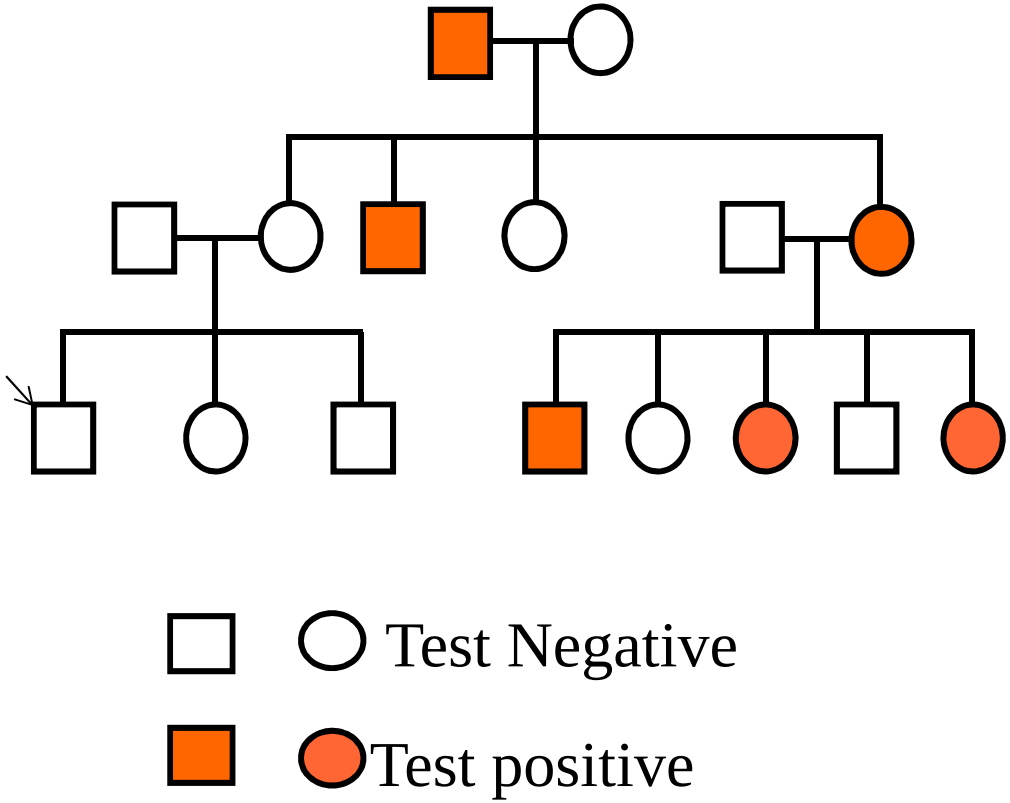
C. She had a family history of breast and ovarian cancer

D. A and C

The Importance of Family History

Does it suggest Autosomal Dominant Inheritance?

- Search for “large buckets” of Risk: Does the pattern suggest a hereditary condition?
- Most of the Family History reflects “common disease”: genetic and environmental causes



The Family History is Self-Reported

familyhistory.hhs.gov

Test ideally starts with an Affected Family Member

…informative results become a reference point for others who may wish testing

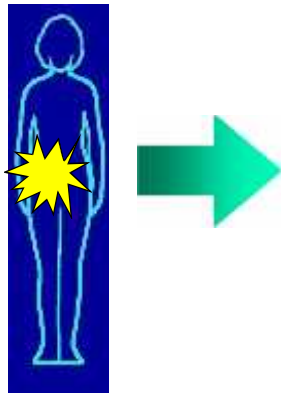
All Cancer is Genetic:
Cancer Arises From Gene Mutations

Germline mutations

(hereditary: 10%)

Parent Child

Mutation in egg or sperm



All cells in offspring have the mutation

-Present in egg or sperm
-Pass from one generation to next
-Cause hereditary cancer syndromes

Somatic mutations

(common: 90%)

Somatic mutation (in tissue where cancer forms:
ie. breast)
Accumulate with AGE

-Occur in nongermline tissues
-Are not passed from one generation to next

Source: ASCO

Into the Future: Projecting Risk

Favorable

- Risk can be mitigated
- Management effective
- Evidence of ongoing compliance
- Access to specialist care
- Evidence-based care
- Few organs at risk
- Non- progressive disease

Unfavorable

- Risk cannot be mitigated
- Management: limited efficacy
- Non-compliant or inconsistent compliance
- Limited access to care
- Medical care not evidence-based
- Multi-system risk
- Progressive/Degenerative disease

Genetic Tests are Voluntary!

- Prenatal- includes preimplantation diagnosis
- Newborn Screening (exception to Consent requirement)
- Single gene disorders testing (over 2700 tests; over 7,000 conditions)
- Genomic and Epigenomic tests
- Pediatric vs Adult onset and testing
- Variability!
  - In clinical expression
  - In genetic basis … of the same disease
- Traditional vs Direct to Consumer (DTC)
- Research vs Clinical Practice
- Consent, Disclosure, Family Implications

Genetic Counseling Involves Families and a Process of Pre- and Post Test Counseling

- Referral/visit for genetic counseling does not necessarily mean that the client
- 1. attended the appointment or
- 2. had genetic testing

- Test may be declined due to perception of insurance impact.

Image source: ASCO

You May Not Need to obtain the Genetic Test Result…

- Will having the genetic test result add any value to the Risk assessment?

A. 35 yo female; states she tested positive for the BRCA1 “gene”…

B. 2 year old male; identified to have an abnormal newborn screen result for cystic fibrosis. His doctor says he does not have CF.

Testing Expands from Single Genes to Panels of Genes

CancerNext is a next generation sequencing (NGS) panel that simultaneously analyzes 32 genes associated with increased risk for breast, ovarian, colorectal, uterine, and other cancers.

Print

Quick Links to Relevant Resources

http://www.ambrygen.com/tests/cancernext

Genetic Testing which is no longer based on Family History: will identify numerous individuals testing positive- prior to onset of clinical features of disease

CDC Features

Data & Statistics

Diseases & Conditions −

Genetic Testing for Hereditary Colorectal Cancer

Emergency Preparedness & Response

Environmental Health

CDC > CDC Features > Diseases & Conditions

Genetic Testing for Hereditary Colorectal Cancer

Recommend Tweet Share

The EGAPP Working Group recommends that everyone with a new diagnosis of colorectal cancer (regardless of age or family health history) be offered genetic testing for Lynch syndrome. If you have colorectal cancer, getting tested for Lynch syndrome can help your family members find out if they are at risk and, if so, take steps to lower their risk.

Transforming Challenges Into Opportunities

1. Precision Medicine is a current reality
2. Genetic Tests Refine Diagnosis, Prognosis, and Treatment of common diseases
3. Genetics is the Foundation of Drug Discovery
4. The Access Challenge:
   - What medical options will we cover?
   - How will we pay for it?
5. Be Anticipatory: The Future

Single Gene Disorders
and
Complex Traits (Common Diseases)

How Useful Is Whole Genome Sequencing to Predict Disease?

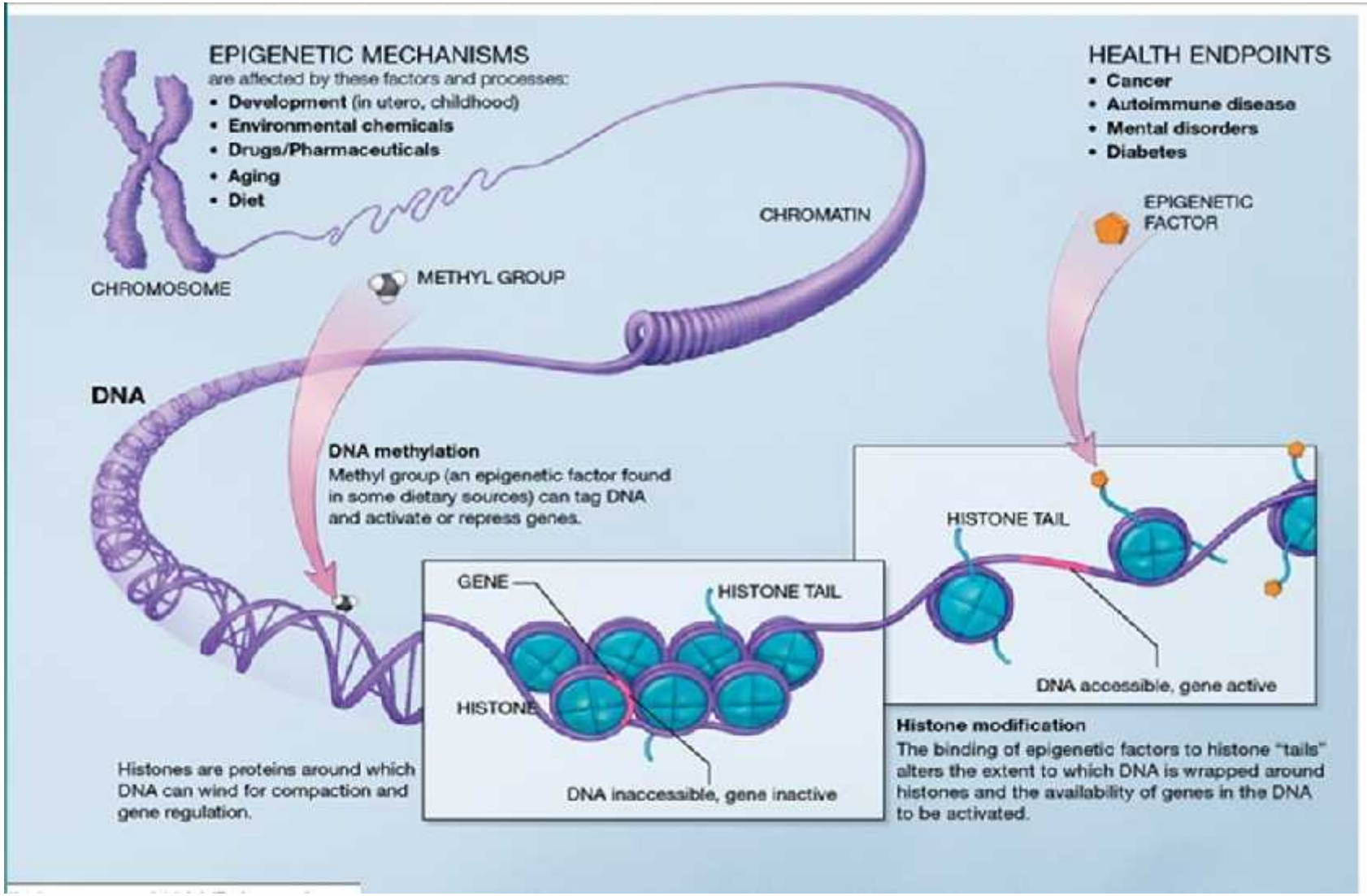
Few diseases have strong enough genetic components to make sequencing a solid way to assess individual risk

By Katherine Harmon | April 2, 2012

A $1,000 genome sequence is close to being available. What will your sequence tell you about your actual risk for certain diseases?

Many companies advertise a laundry list of disease risks associated with your genes. But your genome is unlikely to reveal

EPIGENETICS: Your DNA is Not your Destiny



"Opting out"
of obtaining Actionable Incidental Results from Genome Sequencing

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACMG NEWS

Media Contact: ACMG Media Relations
kbeal@acmg.net

ACMG Updates Recommendation on "Opt Out" for Genome Sequencing Return of Results

Bethesda, MD - April 1, 2014| There has been significant discussion surrounding the initial ACMG recommendations for the return of results from genome-scale sequencing issued in March of 2013. The ACMG Board of Directors has listened carefully to the members' views and appreciates the many forums in which divergent and valuable opinions have been expressed. The positions of ACMG members regarding the issues raised by the recommendations have been assessed through a variety of mechanisms, including direct feedback, participation by Board members in numerous forums exploring these issues, informal conversations, published

Feb 2, 2015

Is Your DNA Clock Running Fast? You May Die Sooner Than Later

University of Edinburgh researchers find that the difference between actual age and DNA methylation age is predictive of all-cause mortality in later life. [©Ilaronova/Fotolia]

Precision Medicine is a Current Reality

- January 30, 2015: President Obama's Precision Medicine Initiative: $215 M
- Precision Medicine=Personalized, Individualized
- Based on Genomics: Analyze genomes of 1 million Americans
  - Also:
    - Electronic Health Record (HER) Data
    - Medical Device Data
    - Epigenomic Data
- Goal: Customize health care:
  - Diagnosis
  - Prognosis
  - Treatment
- Current focus: Cancer
- Goal: expand to all diseases

Cancer is a disease of DNA…
"Our means of defining cancer by what tissue it arose in is going to go by the boards pretty soon"

Francis Collins- WSJ November 8, 2013

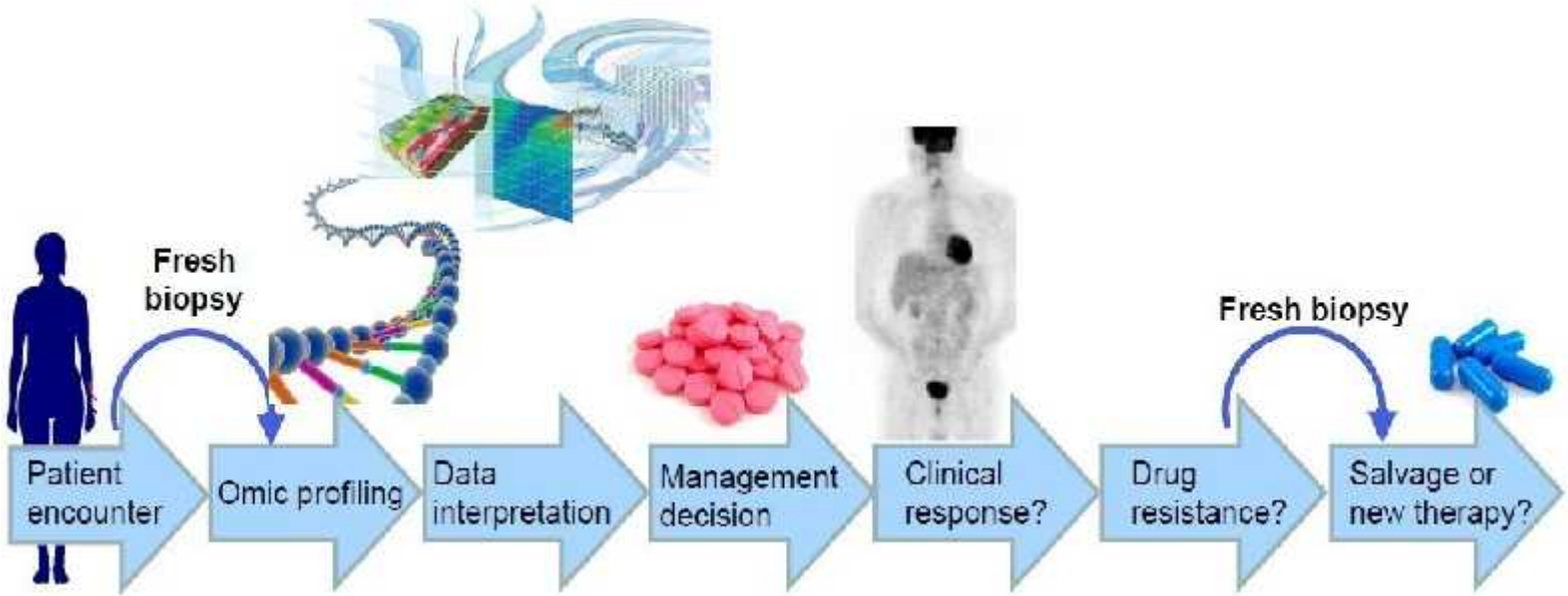
Cancer Staging

Key Points

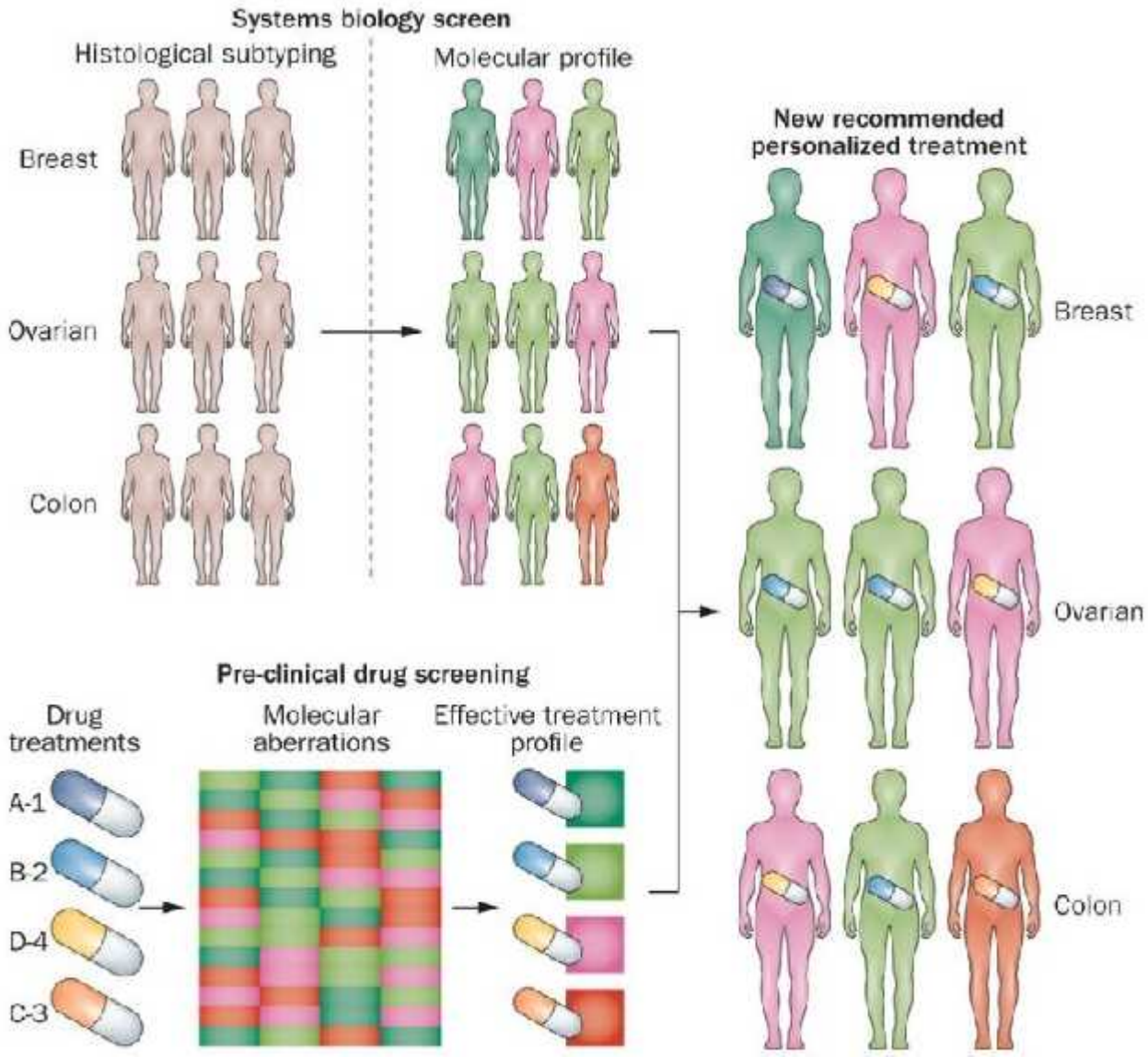
- Staging describes the extent or severity of a person's cancer. Knowing the stage of disease helps the doctor plan treatment and estimate the person's prognosis.
- Staging systems for cancer have evolved over time and continue to change as scientists learn more about cancer.
- The TNM staging system is based on the size and/or extent (reach) of the primary tumor (T), whether cancer cells have spread to nearby (regional) lymph nodes (N), and whether metastasis (M), or the spread of the cancer to other parts of the body, has occurred.
- Physical exams, imaging procedures, laboratory tests, pathology reports, and surgical reports provide information to determine the stage of a cancer.

http://www.cancer.gov/cancertopics/diagnosis-staging/staging/staging-fact-sheet

The Engine of Precision Cancer Medicine



The molecular "footprint" of cancer guides treatment



Werner, H. et al. Nature Reviews Clinical Oncology 11, 167-176 (2014)

The Search for “Exceptional Responders”

HEALTH

Finding Clues in Genes of ‘Exceptional Responders’

By GINA KOLATA OCT. 8, 2014

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NAOMI WATTS

Grace Silva has a horrible form of thyroid cancer that is considered untreatable — usually, patients are sent to a hospice and die within months of learning they have the disease. But she is still alive four years after her diagnosis. She is what cancer doctors call an exceptional responder: someone who defies all expectations by responding dramatically to a drug tried not with a real rationale but more out of a doctor's desperate urge to do something.

The annals of medicine are full of stories of exceptional responders, but until recently, they were just that: stories. Case histories that could not be generalized because there was no way to know why these patients got better when others did not.

But now, with the advent of rapid and

Grace Silva of Dartmouth, Mass., has a form of thyroid cancer that is considered untreatable, but she responded well to a drug. Kayana Szymczak for The New York Times

Pharmacogenomics: Transforming Care

the gap test
genetic assisted prescribing

ID# : PGX00001A
Test Report Date : April 29, 2014

Samantha Smith

Drug inquiry:

CLOPIDOGREL

Recommendation:

Start with normal starting dose (e.g., 75 mg/m2/d or 1.5 mg/kg/d) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow 2 weeks to reach steady state after each dose adjustment. (CPIC)

FOUND ISSUES

(See recommendations page for more info)

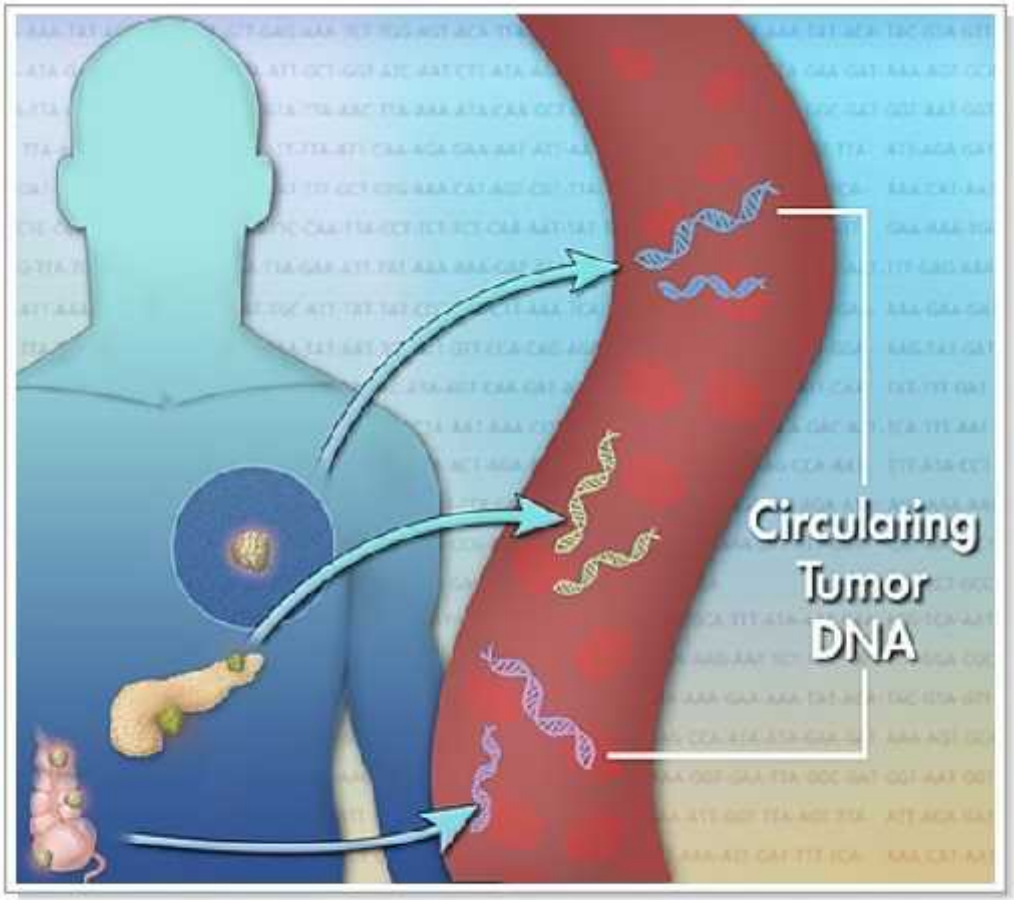
NO ISSUE FOUND
Use as directed for Samantha

CAUTION: ISSUE FOUND
Medications may not work for Samantha

URGENT: ISSUE FOUND
Medications may not work or cause serious issues for Samantha

DRUG NAMES	DRUG NAMES	DRUG NAMES
amitriptyline *(Brand name)*	amitriptyline *(Brand name)*	amitriptyline *(Brand name)*
aripiprazole *(Brand name)*	aripiprazole *(Brand name)*	aripiprazole *(Brand name)*
clomipramine *(Brand name)*	clomipramine *(Brand name)*	clomipramine *(Brand name)*
doxepin *(Brand name)*	doxepin *(Brand name)*	doxepin *(Brand name)*
flecainide *(Brand name)*	flecainide *(Brand name)*	flecainide *(Brand name)*
fluorouracil *(Brand name)*	fluorouracil *(Brand name)*	fluorouracil *(Brand name)*
hormonal contraceptives for systemic use	hormonal contraceptives for systemic use	hormonal contraceptives for systemic use

Circulating Tumor DNA (ctDNA): A New Generation of Cancer Biomarkers



Scientists have discovered that dying tumor cells release small pieces of their DNA into the bloodstream. These pieces are called cell-free circulating tumor DNA (ctDNA).

ctDNA:

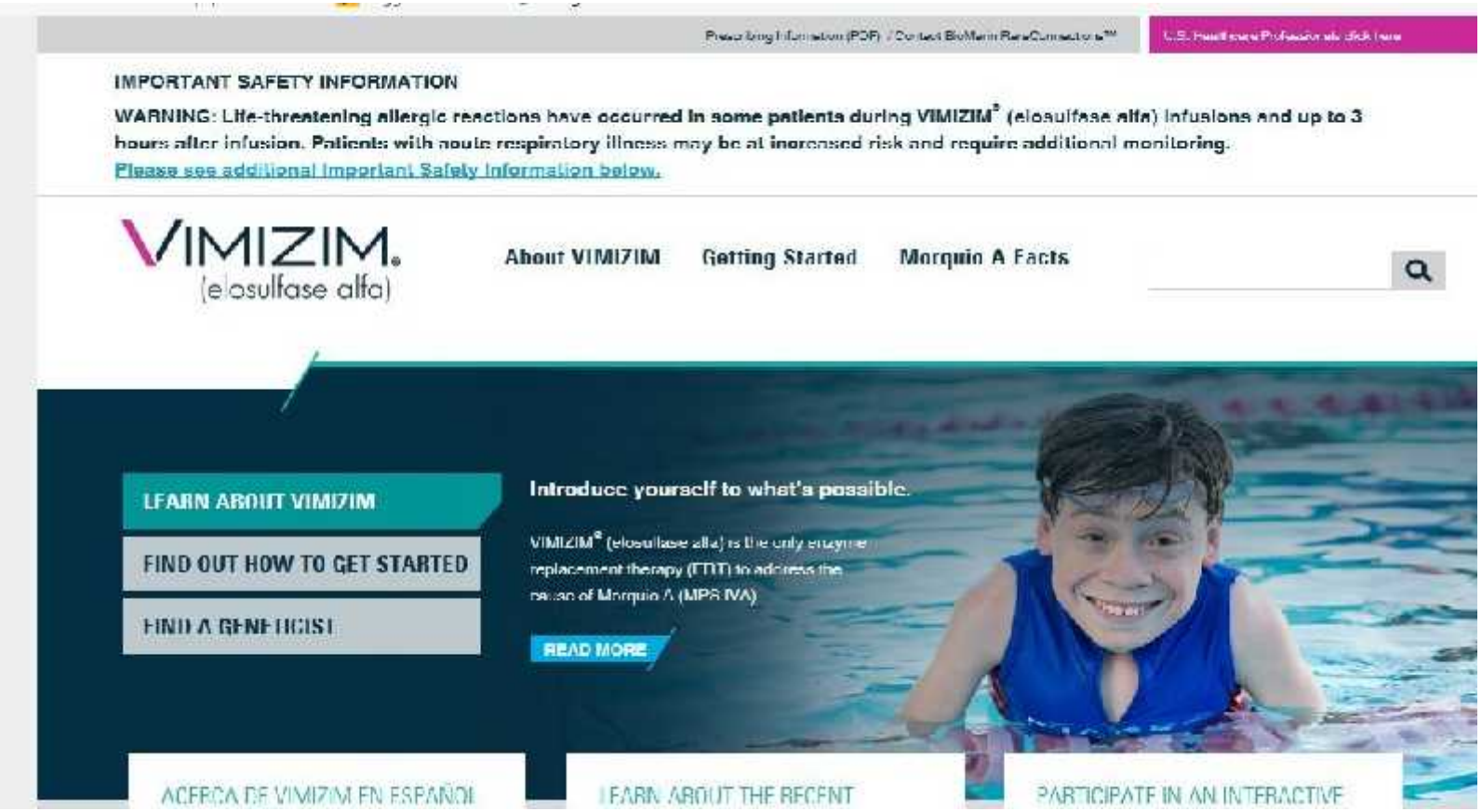
- **small pieces of DNA released into blood by dying tumor cells**
- **Detectable levels correlate with stage of cancer**
- **Screening detects and follows progression of tumor**
- **Screen for mutations pre- and post therapy; test targeted drug response and identify new mutations formed during therapy**

http://www.genome.gov/27556716

Bettegowda C. et al. Sci.Transl.Med., 6(224);ra24.2014

High Cost Drugs for Rare Diseases

Vimizim: $1 M/year



"Thinking Differently About Leadership"

1. Gather current information; Analyze it differently
2. Keep a scope on the horizon: Be Anticipatory
   - What will change in the future? (Legal, Regulatory issues)
   - How will we prepare?
3. Create collaborative solutions
   - New product innovation
   - Pooling
   - Industry/Government collaborations
   - Intra-industry collaboration
   - Big Data analysis
4. Client focus: autonomy, devices, simplicity of access
5. Navigating the Access Challenge and Ethical Issues

QUESTIONS?