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Q&A

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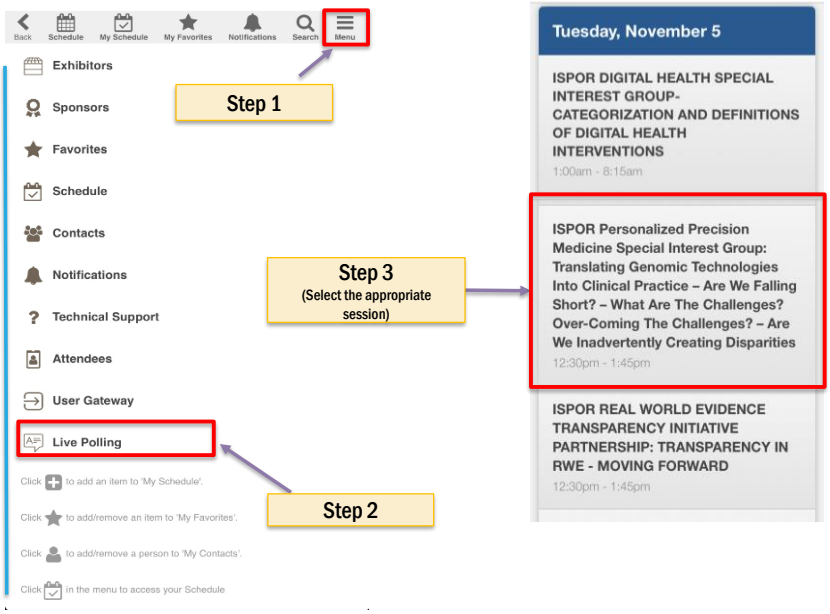

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ISPOR
Improving healthcare decisions

Translating Genomic Technologies into Clinical Practice
Are We Falling Short?
What Are the Challenges?
Over-coming the Challenges?
Are We Inadvertently Creating Disparities ...

ISPOR PERSONALIZED PRECISION MEDICINE SPECIAL INTEREST GROUP

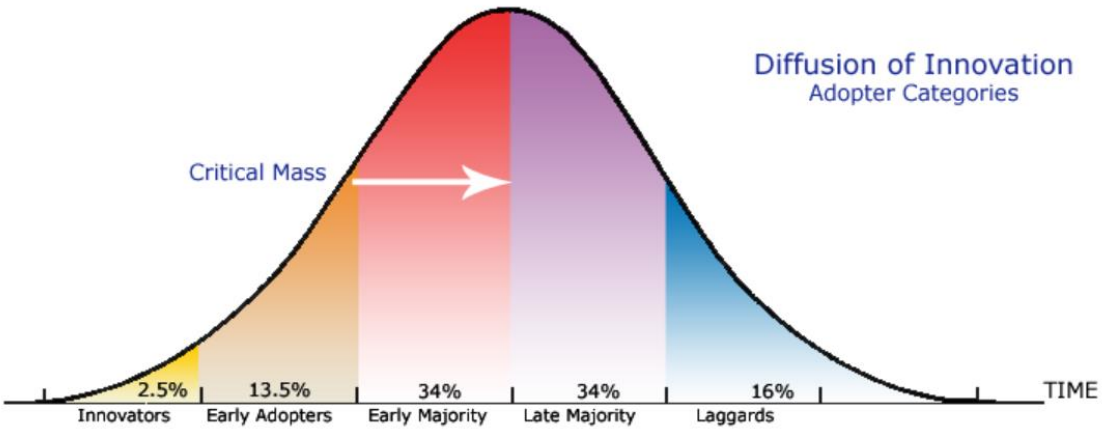
Tuesday, November 5, 2019 12:30 – 13:45

SECTION

1

Emily S. Reese, PhD, MPH,
Director, Translational Research,
Levine Cancer Institute,
Atrium Health,
Charlotte, NC, USA

Diffusion of Innovation



4 Image obtained from: Kaminski, J. (Spring 2011).Diffusion of Innovation Theory Canadian Journal of Nursing Informatics, 6(2). Theory in Nursing Informatics Column. http://cjni.net/journal/?p=1444

Innovation Characteristics

- Relative Advantage – perceived notion that an innovation is better than previous innovation
- Compatibility – an innovation's consistency with an individual's values, experiences, and needs
- Complexity – how difficult to comprehend and use an innovation
- Trialability – ability to use an innovation on a probationary basis
- Observability – the degree to which others can observe the results of an innovation

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Innovation Characteristics

~ Relative Advantage – pe … previous innovation

~ Compatibility – an innov … experiences, and needs

X Complexity – how difficu …

X Trialability – ability to us …

X Observability – the degr … innovation

Q: Do genomic technologies and advanced therapies fit any of these characteristics?

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Where Are We with Adoption of Personalized Medicine and Advanced Therapies?

- Mapping of the human genome “completed” in April 2003
- Newborn screening and single gene tests
- Label changes, black boxes, approvals
  - clopidogrel and *CYP2C19*; abacavir and *HLA-B*5701*
- Predictive risk tests are familiar to the general public
  - Focus in breast, ovarian, colon cancers (e.g., the “Angelina effect”)
- Treatment response indicators (e.g., PD-1, PDl-1, MSI, TMB/TML)
- CAR-T procedures in some medical centers

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How can we ensure adaption of these technologies is fair and equitable to all people?

- Potentially first thoughts are in the domains of
  - Implementing the technology
  - Paying for the technology
  - Accessing the technology
  - Understanding preferences for the technology
  - General knowledge of the new technology

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Moderator:

Emily S. Reese, PhD, MPH, Director, Translational Research, Levine Cancer Institute, Atrium Health, Charlotte, NC, USA

Speakers:

Gavin Outteridge, MA, Managing Director – Europe, AESARA, London, UK

Eline van Overbeeke, PhD researcher, IMI PREFER project, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven - University of Leuven, Antwerp, Belgium

Jan Geissler, MBA, Chair, ISPOR Patient Representatives Roundtable – Europe, Co-founder, Acute Leukemia Advocates Network and CML Advocates Network, Switzerland, Germany

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Levine Cancer Institute

- Housed within an academic community-based healthcare system
- More than 25 individual facilities in North and South Carolina in US
  - ≥ 15,000 cancer cases each year
    - ~50% thoracic or lung cases
    - ~75% of thoracic of lung cases are advanced or metastatic disease
- Advanced Therapies Integration - ~ 20 CAR-T cases
- Genetic/Genomic Integration
  - Systematically processed care via section-specific pathways for treatment, consults, genomic/genetic test ordering, etc.
  - Active immunologic, molecular, and pharmacogenetics cores
    - PGx: reflexive *CYP2C19* testing for voriconazole and *DPYD* testing for 5 FU
  - Weekly consultative molecular tumor board
    - NGS: no reflexive testing

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- Nearly 1,300 NGS tests ordered from June 2015 to September 2017

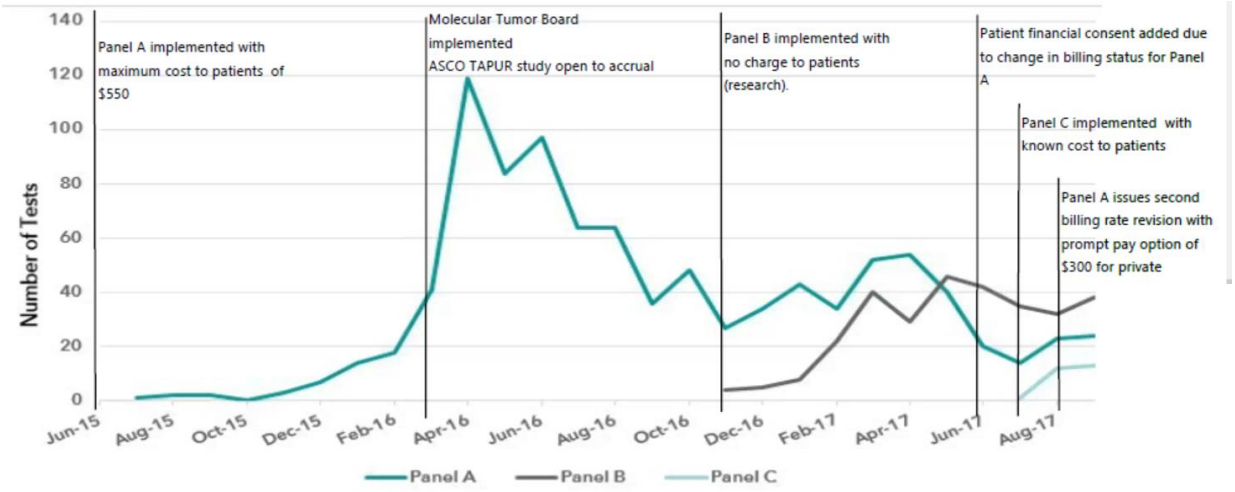

Figure 1. Genomic Test Volume Ordered at LCI, 01 June 2015-30 September 2017

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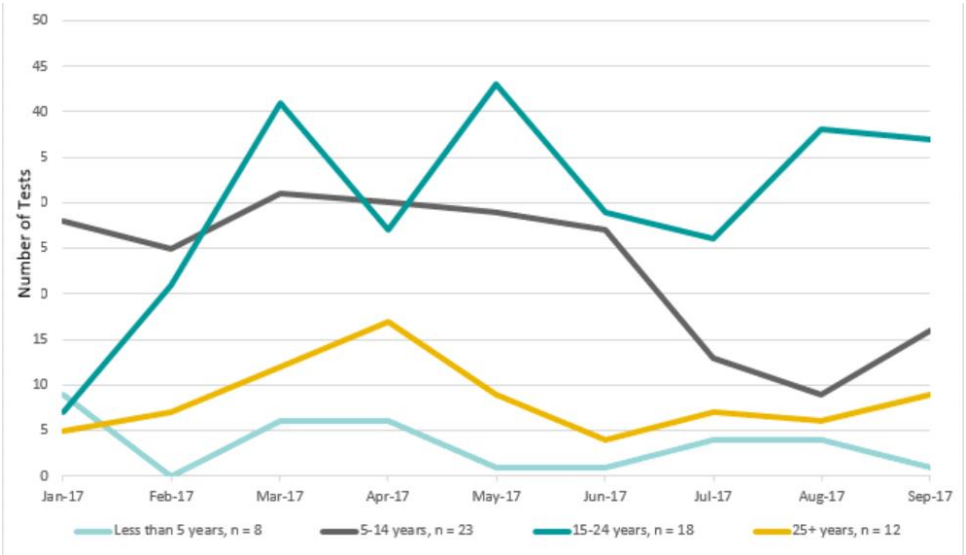
- NGS test accession by years of ordering physician experience



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Lessons learned (so far…)

- Challenges for implementation are pervasive
- Genomic and advanced therapy clinical implementation need continuous process evaluation for successful integration
- All parties impacted by test must be involved
  - Clinicians – physicians, advanced practitioners, nursing, clinical pharmacists, genetic counselors
  - Administrative/Support – Financial counselors, social workers, coding/billing
  - Researchers
  - Patients

SECTION

2

Gavin Outteridge, MA,
Managing Director – Europe,
AESARA,
London, UK

Mortality rates in a range of cancer indications have declined over the past 30 years, with Precision Medicine playing a part

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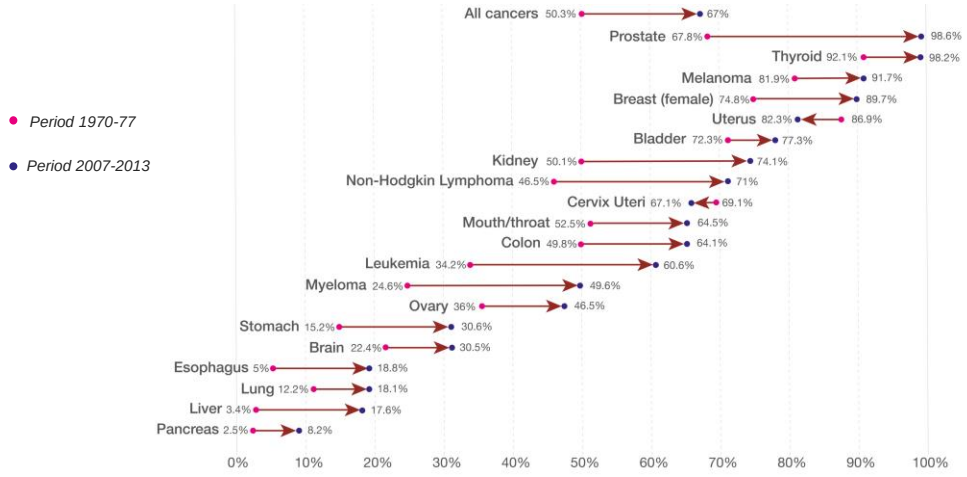
Five-year cancer survival rates in the USA



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Roser and Ritchie (2018) Cancer. Available at: https://ourworldindata.org/cancer (Accessed November 1 2018)

Precision Medicine's promise to payers: the potential to improve outcomes without increasing healthcare costs

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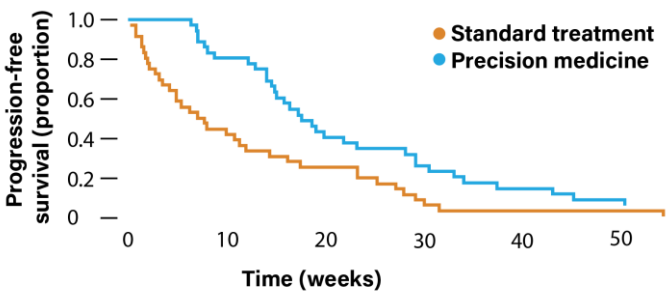

Cost Outcome	Precision Medicine Mean ($)	Standard Treatment Mean ($)	P
Total costs per patient	91,790	40,782	.002
Total drug costs per patient	59,259	20,189	<.001
Cost per patient per progression-free survival week	4,665	5,000	.126

P < 0.01 considered to be significant

Longer progression-free survival enabled additional costs of precision medicine to be spread over a longer period of time

Intermountain Healthcare *Healing for Life*

Stanford SCHOOL OF MEDICINE

Duke University School of Medicine

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Haslem DS, Van Norman SB, Fulde G. A Retrospective Analysis of Precision Medicine Outcomes in Patients With Advanced Cancer Reveals Improved Progression-Free Survival Without Increased Health Care Costs. J Oncol Pract. 2017 Feb;13(2):e108-e119.

Despite this promise, payers are generally skeptical when the term “Precision Medicine” is deployed

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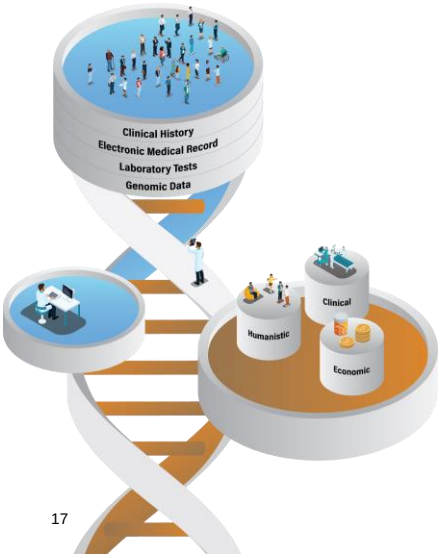

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“Precision medicine is a very marketing term. I got 4 newsletters on it in the last 2 weeks and there are lots of meetings on it, driven by industry.”

Medical Director and Health Economics advisor to major private health insurer

“Precision medicine is an ISPOR word. I never here about precision medicine except at ISPOR.”

Health economics professor and HTA Advisor to NICE and SMC

“Opportunity for manufacturer for higher price and more likely to have best supportive care as comparator. Challenge is non-quantifiable improvement based on evidence provided. Precision medicine has attracted some negative connotations. Pay for evidence not for promises.”

Health economics professor and member of arbitration board

Populations throughout society can experience disparities, leading to lower outcomes and higher costs

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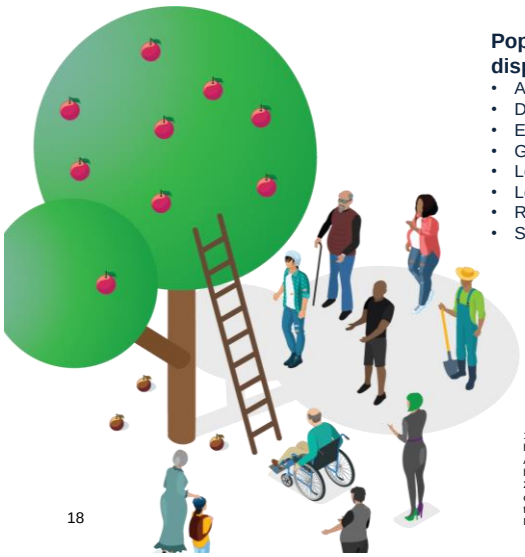

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Populations experiencing disparities may include:[1-2]

- Age (e.g., elderly and young adults)
- Disabilities
- Education (e.g., illiteracy)
- Gender (e.g., women)
- Location (e.g., inner city and rural)
- Low income/lack insurance
- Race/ethnicity
- Sexual orientation

Barriers to access[3-4]

- Limited access to health insurance or a healthcare system
- Limited healthcare awareness and education
- Limited access to earlier detection, leading to identification of disease in later stages
- Limited access to innovative treatments[5]

Barriers to clinical trial involvement[6]

- Minority care at underserved healthcare facilities do not have the resources to conduct clinical trials
- Patients are unaware of eligibility for clinical trials
- Patients lack personal resources to enroll in clinical trials
- Perceived mistrust of research limits minority enrollment

1 Orgera K, Artiga S. Disparities in health and health care: five key questions and answers. Kaiser Family Foundation. 2018. Available at http://files.kff.org/attachment/Issue-Brief-Disparities-in-Health-and-Health-Care-Five-Key-Questions-and-Answers (Accessed January 16, 2019). 2 Agency for Healthcare Research and Quality (AHRQ). 2017 National healthcare quality and disparitites report. Available at: https://www.ahrq.gov/research/findings/nhqrdr/nhqdr17/index.html (Accessed January 17, 2019). 3 Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2019. CA Cancer J Clin. 2019 Jan;69(1):7-34. 4 Rhoads KF, Patel MI, Ma Y, Schmidt LA. How do integrated health care systems address racial and ethnic disparities in colon cancer? J Clin Oncol. 2015 Mar 10;33(8):854-60. 5 Ailawadhi S, Frank RD, Advani P. Racial disparity in utilization of therapeutic modalities among multiple myeloma patients: a SEER-medicare analysis. Cancer Med. 2017 Dec;6(12):2876-2885. 6 Hamel LM, Penner LA, Albrecht TL, et al. Barriers to clinical trial enrollment in racial and ethnic minority patients with cancer. Cancer Control. 2016 Oct;23(4):327-337.

While tax-payer funded national health services are designed to be equitable…

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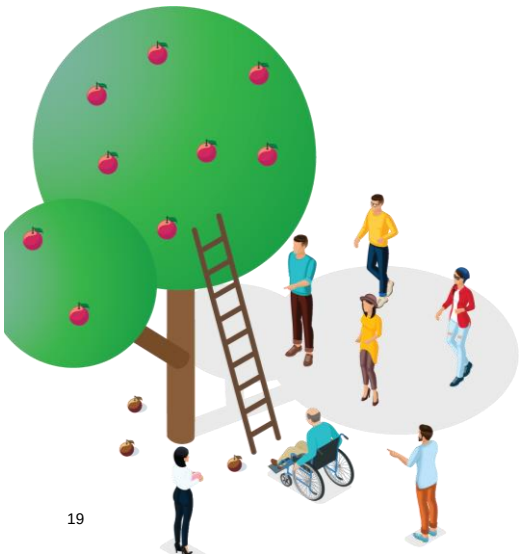

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"Part of NICE process… does genetic disposition effect certain groups? NHS is designed for everyone to pay in and everyone gets equal access… don't currently see link."

Health economics professor and HTA Advisor to NICE and SMC

"Not a major problem in the German system."

Health economics professor and member of arbitration board

…when pressed, payers can readily identify access disparities

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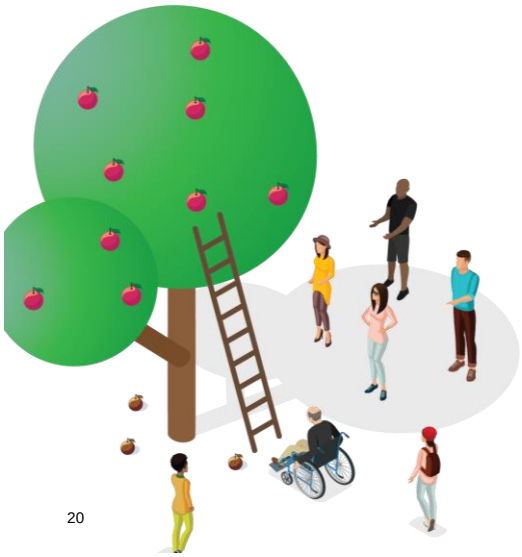

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"The primary disparity is economic. Very difficult to get to the first appointment.

There is a big public health focus on children but poor adults are the worst served."

Medical Director and Health Economics advisor to major private health insurer

"Depends on disease…Rare disease network is not as good… difficult for a patient to get the proper diagnosis… there is room for improvement. Precision medicine requires highly specialized experts, so there is some disparity for rural patients and poor suburbs and less educated."

Oncologist and HTA advisor

"In the German system [there is] No discussion about disparate populations… only health literacy… educational issue for migrants."

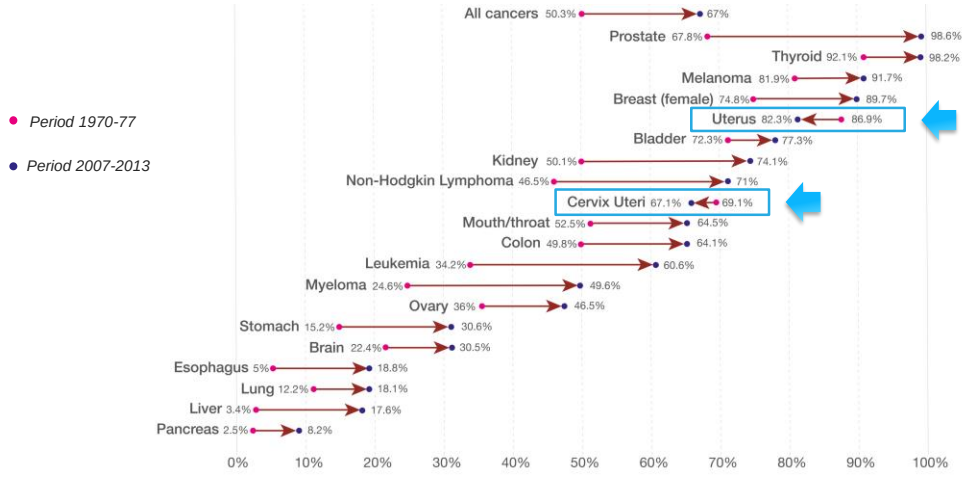
Health economics professor and member of arbitration board

"Complex genomic profile that leads to a range of treatment requires high levels of expertise and it is just not at every hospital... disparity if can't get to the expertise."

Professor and Advisor to PBAC

Precision Medicine has contributed to improved outcomes over the last 30 years but benefits may not be equal throughout society

Five-year cancer survival rates in the USA



Roser and Ritchie (2018) Cancer. Available at: https://ourworldindata.org/cancer (Accessed November 1 2018)

SECTION

3

Eline van Overbeeke,
PhD researcher, IMI PREFER project,
Department of Pharmaceutical and Pharmacological Sciences,
KU Leuven - University of Leuven, Antwerp, Belgium

SECTION

4

Jan Geissler, MBA
Chair, ISPOR Patient Representatives Roundtable – Europe
Co-founder, Acute Leukemia Advocates Network and CML Advocates Network, Switzerland, Germany

Genomic testing may lead us into targeted, personalized, curative medicine

Genomic testing and models help on:

- **Timely diagnosis**
- **Prevent progression and death** through early diagnosis and detection of relapse
- **Avoid exposure to ineffective treatment:** apply only treatments that are likely to work
- **Better risk stratification:** identify high risk patients to treat effectively, while avoiding to jeopardize quality of life too early with overtreatment of low risk patients

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Example Chronic Myeloid Leukemia: 15-20 years of experience with molecular testing and sequencing

- **Molecular testing** has been an inherent component of any CML treatment and follow-up since TKIs were introduced in 2001
- **Sequencing** has guided 2nd line therapy choice already over the past 15 years
- **Stopping treatment in remission** is possible for about 25% of CML patients - assumed they can get access to frequent high-quality PCR testing, which is not the case for many patients
- **Genomics** will hopefully guide the way from chronification to cure

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New therapeutic approaches, tailored to individual biology and patients' preferences, is exactly what we want

What patients want:

- Timely diagnosis
- The right treatment for the right patient at the right time
- Avoiding over-treatment, under-treatment and ineffective treatment
- Well-tolerable, curative therapies for **every** patient in need

Current therapeutic, diagnostic and computational advances allow us to:

- Understand the biology of diseases
- Understand the unique characteristics of each patient
- Understand patients' preferences

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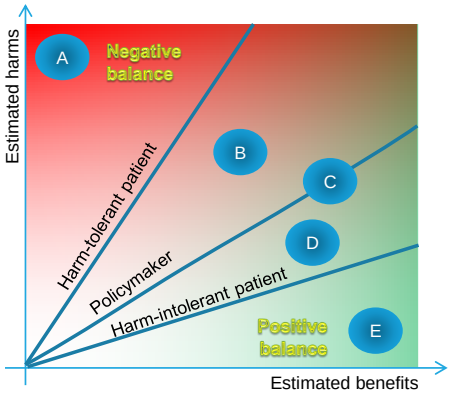
Does it really count what patients want? Each stakeholder has its agenda and risk attitude

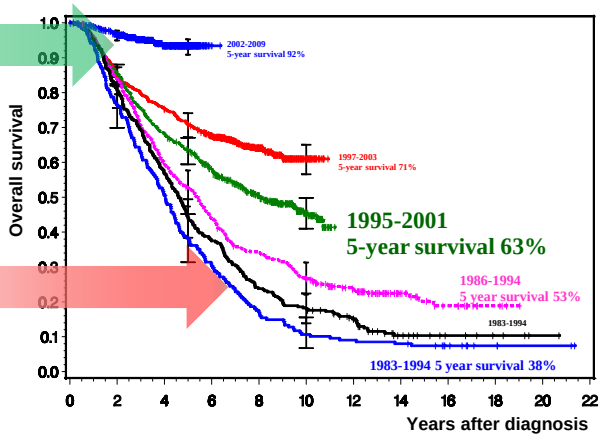
- **Physicians** → best clinical outcomes, keeping a customer
- **Regulators** → safety, efficacy, market authorisation
- **Payers** → societal goals: budgets, cost-effectiveness, health care sustainability
- **Industry** → return on invest, shareholder value
- **Researchers** → research questions, study design, high-tier publications
- **Patients** → personal goals: living a good life as long as possible (but that depends)



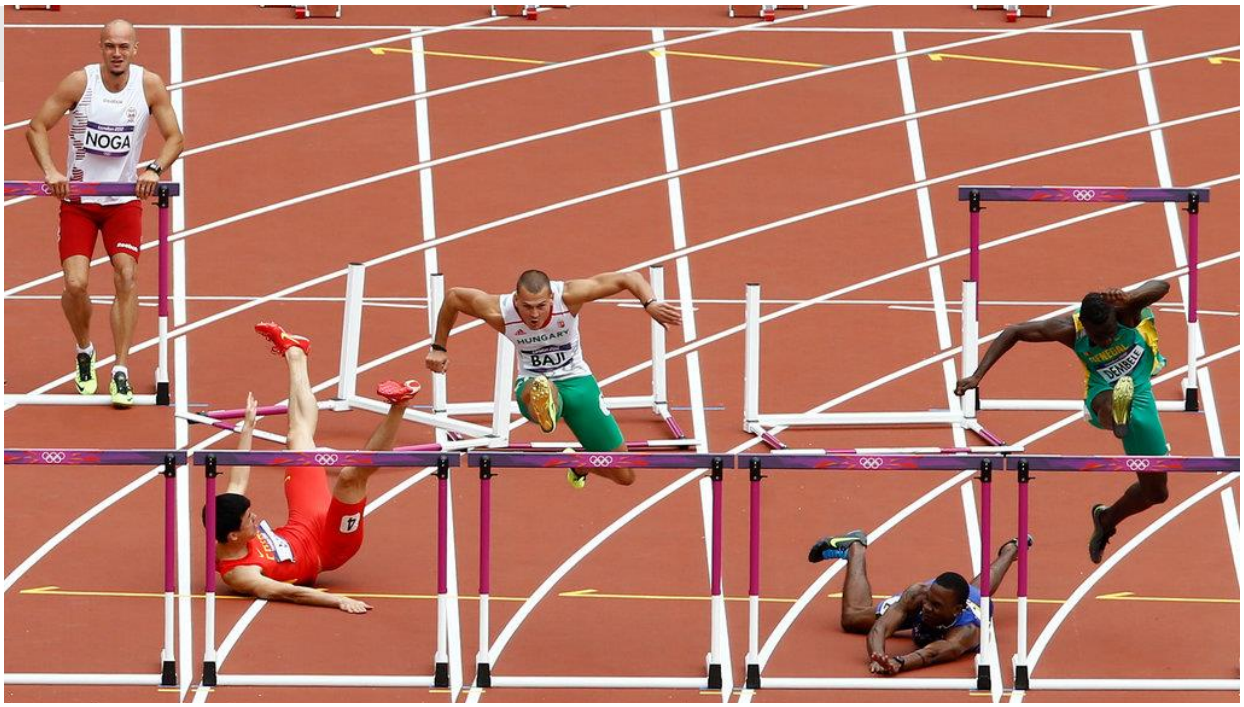
If personalized medicine holds its promise, it's all about *access* to diagnostics and treatment

Access to treatment AND molecular testing

Access to no treatment AND/OR no molecular testing



Source: German CML Study Group



Are genomic testing and advanced therapies the next step towards personalized medicine for everyone, or are we creating the next wave of **supermodel medicine:**

lovely to look at, very costly, accessible only to a few, of no real value to many?

Courtesy of Richard Sullivan, King's College (2018)
Photo 1: unknown male model, Creative Commons Zero License (CC0), source
Photo 2: Photograph by Designecologist, Creative Commons Zero license (CCO), source

Access issues to genomic technologies may increase inequalities of access to innovative cancer care

What if patients can't access a potentially effective treatment just because patients can't access the test for the biomarker

- because the center **can't provide** it?
- because the treating physician **can't deal with it**?
- because the patient's coverage doesn't **reimburse** it? (e.g. lower GDP countries) and the patient can't afford it?

Access to quality molecular testing or mutation testing is an issue for many CML patients today, … **not to speak of genomic testing or gene/cell therapies for the whole cancer patient community!**

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How do we make it work?

Taking shared decisions in the era of genomics

- Increased demand on direct to consumer genomic testing demonstrates there is **unmet need by patients**
- **With appropriate information and counseling**, patients will deal with probabilistic measure of certainty on diagnosis or prognosis
- Information should be made available **in appropriate time and in a language that patients understand**
  - Can this be done in the average 8.1 minutes counseling time?
- **Patient organizations** can help with patient communication, and training physicians how to get this right

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Physicians (also) need tools, education and time for dealing with genomics

- **More education** – Genomic counseling should become part of HCP's education, supported by physician guides for clinicians, and educational tools to support patients
- **Better decision support tools** – Infrastructure for processing and interpreting genomic data in daily clinical practice should not just be the privilege of the top-notch centers
- **Better regulation** – Large heterogeneity in the way European countries have regulated genetic testing (medical supervision, genetic counselling and informed consent), incl. direct to consumer testing

Legislation of direct-to-consumer genetic testing in Europe: a fragmented regulatory landscape. Kalokairnou, J Community Genet (2018)

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Conclusion

- Moving from organ-based oncology to genomics-based personalized medicine **will become the norm (for those who can afford)**
- **Patients see great potential in genomics** if results translate into clinically relevant actions.But be sure you know the preferences of the individual patient!
- **Challenges**: genetic counselling, informed consent, regulatory heterogeneity, affordability, … they should be tackled jointly
- **Advanced therapies should not become supermodel medicine:** access to genomic testing and treatment may become/remain a key barrier to access to effective innovative treatment – we can learn from CML

Jan Geissler <jan@patvocates.net>

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Poll: What best describes your current role?

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Poll: What do you think are the main 3 challenges in translating genomic technologies (e.g., genomic testing and gene therapies) into clinical practice?

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Poll: Do you think these challenges you selected in question 2 could/are creating disparities in implementing genomic technologies?

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Post-Question

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Poll: After this presentation do you believe there are challenges that could/are creating disparities in implementing genomic technologies?

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Pre/Post Comparison: Do you think these challenges you selected in question 2 could/are creating disparities in implementing genomic technologies?

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