Can Value-Based Care Exist Without Value-Based Research?

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Today’s speakers

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Agenda

1. **Defining value in healthcare**
2. **Assessing traditional clinical trials**
3. **Changing the paradigm**
4. **Selecting the optimal trial design and regulatory approach**
5. **Embracing value-based research**

Defining value in healthcare

What is value?

- Definitions of value
  - The monetary worth of something
  - The importance or usefulness of something
  - Principles or standards of behavior
- Value is relative
  - What is important to me, may not be important to you

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

DECEMBER 23, 2010

What Is Value in Health Care?

Michael E. Porter, Ph.D.

In any field, improving performance and accountability depends on having a shared goal that unites the interests and activities of all stakeholders. In health care, however, stakeholders have myriad, often conflicting goals, including access to services, profitability, high quality, cost containment, safety, convenience, patient-centeredness, and satisfaction. Lack of clarity about goals has led to divergent approaches, gaming of the system, and slow progress in performance improvement.

Achieving high value for patients must become the overarching goal of health care delivery, with value defined as the health outcomes achieved per dollar spent.[1] This goal is what matters for patients and unites the interests of all actors in the system. If value improves, patients, payers, providers, and suppliers can all benefit while the economic sustainability of the health care system increases.

Value — neither an abstract ideal nor a code word for cost reduction — should define the framework for performance improvement in health care. Rigorous, disciplined measurement and improvement of value is the best way to drive system progress. Yet value in health care remains largely unmeasured and misunderstood.

Value should always be defined around the customer, and in a well-functioning health care system, the creation of value for patients should determine the rewards for all other actors in the system. Since value depends on results, not inputs, value in health care is measured by the outcomes achieved, not the volume of services delivered, and shifting focus from volume to value is a central challenge. Nor is value measured by the process of care used; process measurement and improvement are important tactics but are no substitutes for measuring outcomes and costs.

Since value is defined as outcomes relative to costs, it encompasses efficiency. Cost reduction without regard to the outcomes achieved is dangerous and self-defeating, leading to false "savings" and potentially limiting effective care.

Outcomes, the numerator of the value equation, are inherently condition-specific and multidimensional. For any medical condition, no single outcome captures the results of care. Cost, the equation's denominator, refers to the total costs of the full cycle of care for the patient's medical condition, not the cost of individual services. To reduce cost, the best approach is often to spend more on some services to reduce the need for others.

N ENGL J MED 363;26 NEJM.ORG DECEMBER 23, 2010 2477

Source:
https://www.nejm.org/doi/full/10.1056/nejmp1011024

Value in the eyes of the stakeholder

Payer perspectives:
- Controlling providers' reimbursement and patients' out-of-pocket costs through benefit policies
- Encouraging the use of clinical pathways to reduce variation and control costs

Manufacturer perspectives:
- Bringing innovative drugs to market
- Seeking successful sales of current products to fund new drug developments

Patient perspectives:
- Receiving the best available cure
- Maintaining quality of life
- Minimizing financial impact
- Considering other factors: religion, culture, family, etc.

Provider (institutional) perspectives:
- Obtaining the best clinical outcomes for patients
- Weighing financial impact to patients
- Balancing between workload and patient benefits

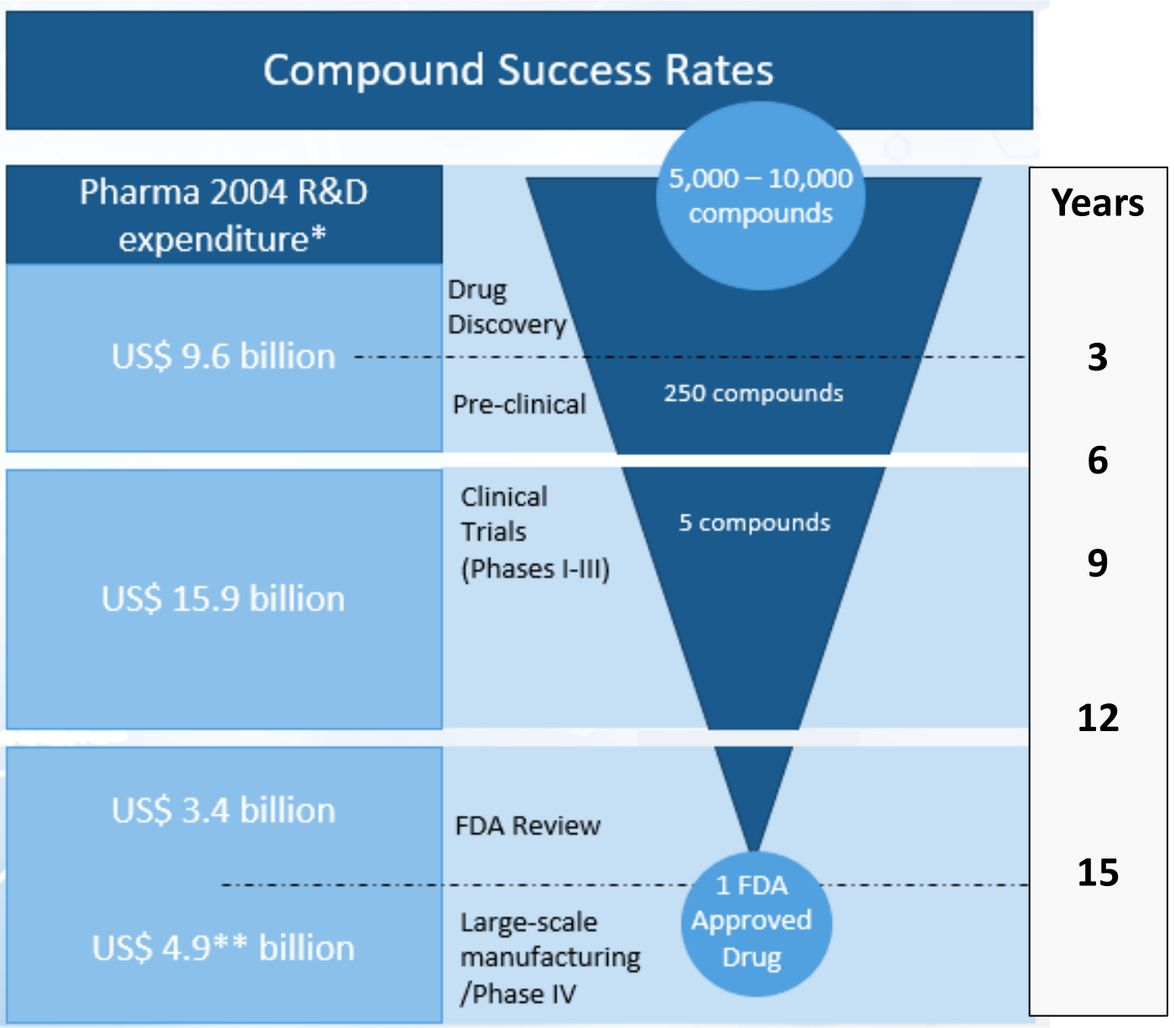
Source: https://pubmed.ncbi.nlm.nih.gov/30659123/

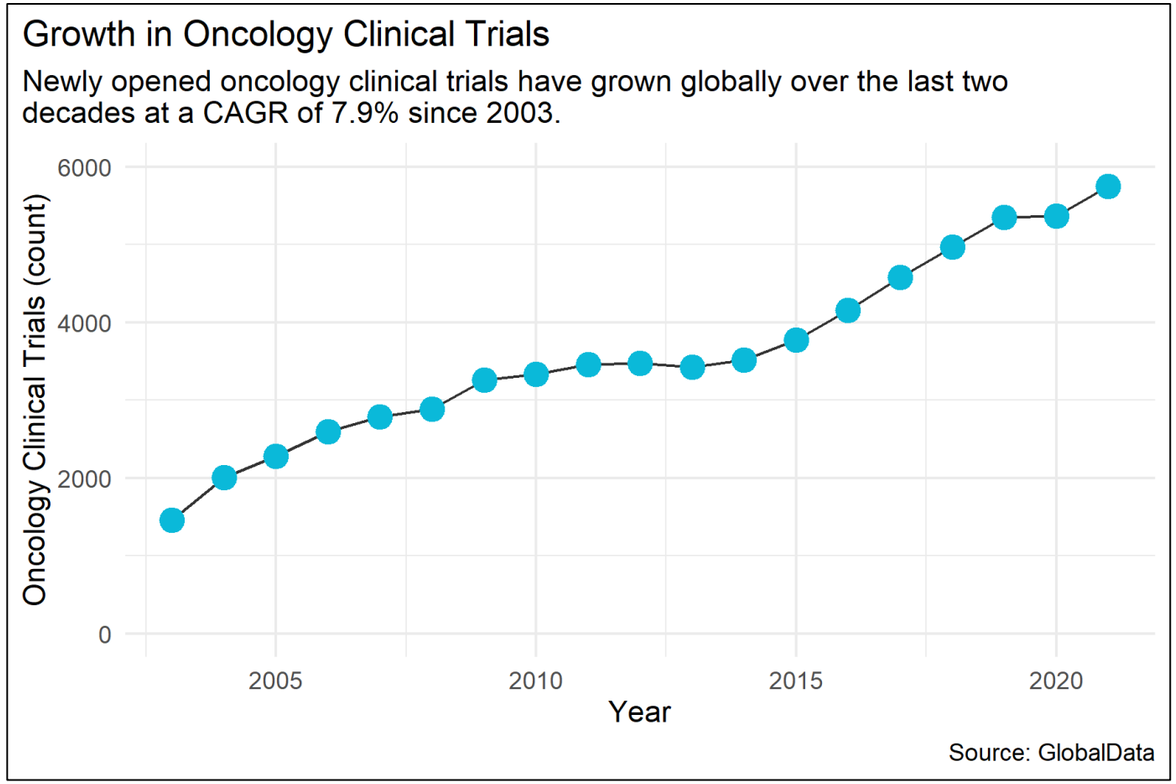
Polling question

- What is more valuable?
  - Increasing life span
  - Increasing life quality

Assessing traditional clinical trials

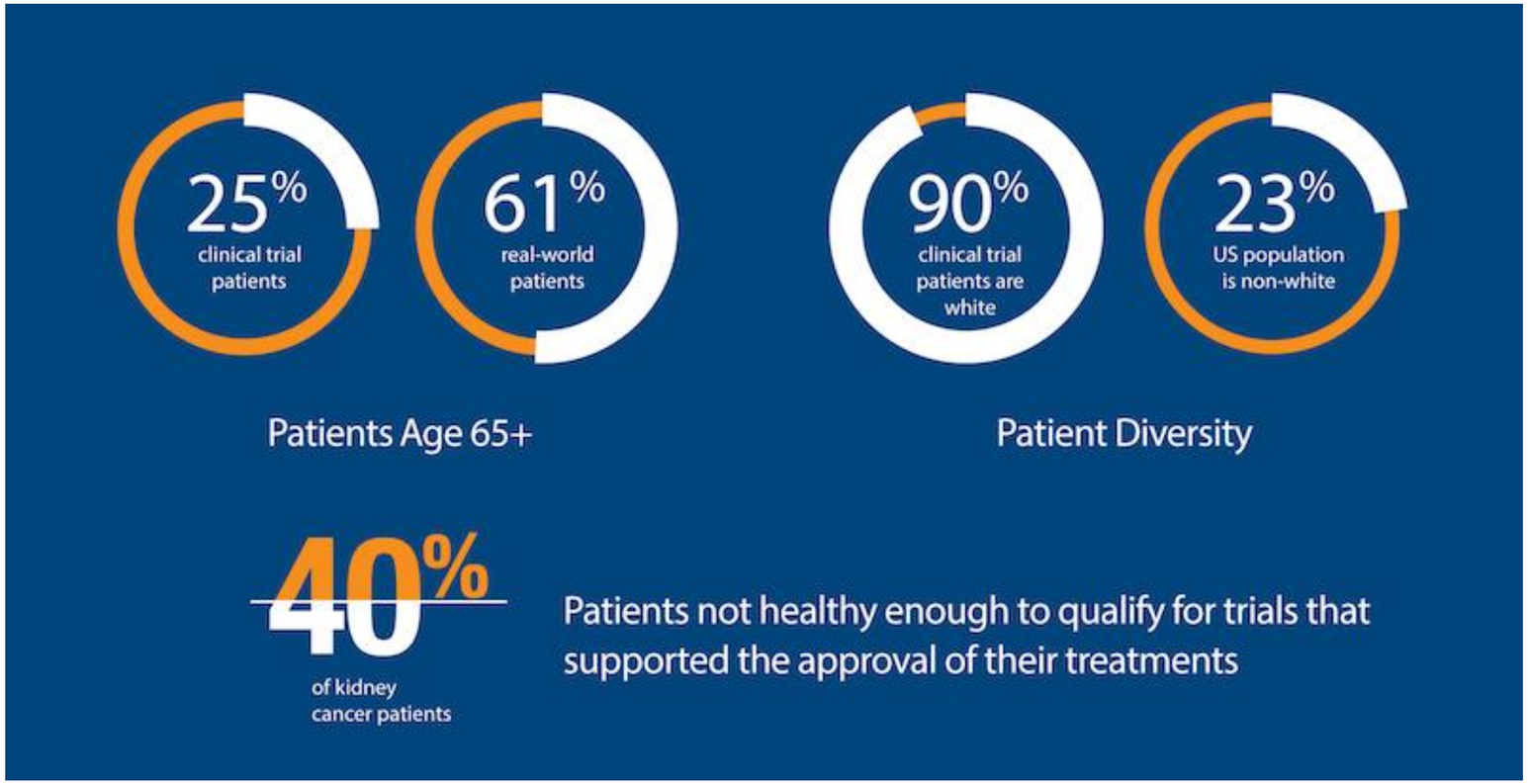
Are traditional RCT's valuable?





Source: https://www.pharmafocusasia.com/strategy/drug-development-challenges

Statistically significant but clinically meaningless



All clinical decisions today are based on those who participated in clinical trials, **only 3% of the population**

Source: ASCO Cancer-LINQ.

Polling question

- What is more valuable?
  - Statistical significance
  - Clinical significance
  - Patient-centricity

Changing the paradigm

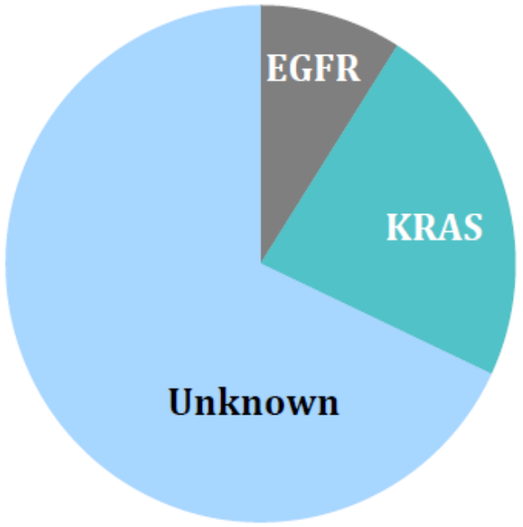
What is the paradigm?

- **Phase I: Is the treatment safe?**
  - Assessed in a small group of people to evaluate optimal dosage, safety, and identify common side effects
- **Phase II: Does the treatment work?**
  - Administered to a larger group of patients to verify optimal dose (if necessary), assess efficacy, and further evaluate safety
- **Phase III: Is the treatment better than placebo or standard of care?**
  - Administered to a large group of patients to confirm efficacy, monitor side effects, compare it to commonly used treatments (or placebo), and collect information that will allow safe use
- **Phase IV: What else do we need to know to establish risk/benefit balance?**
  - Postmarketing studies to provide additional information about risks, benefits, and best use

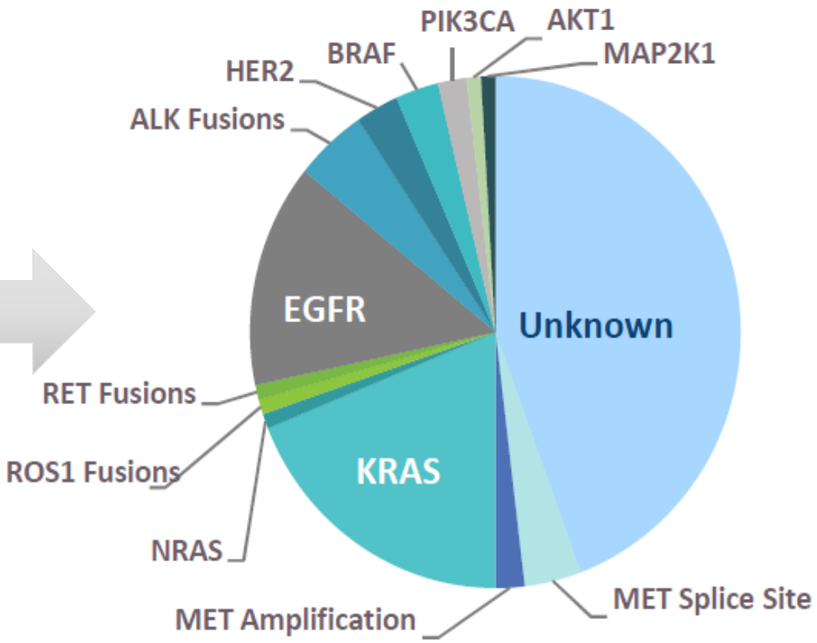
Sources:
What Are the Different Types of Clinical Research? https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research
Types and Phases of Clinical Trials: https://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/what-you-need-to-know/phases-of-clinical-trials.html

Precision medicine leading to paradigm shift in the classification of lung cancer

2004

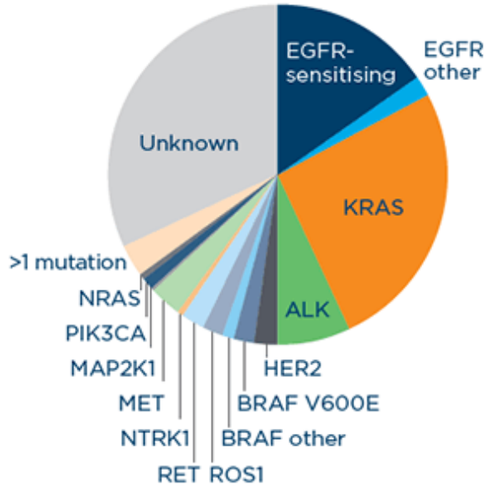


2015



2019

DRIVER MUTATIONS IN LUNG ADENOCARCINOMA



Driver mutations in lung adenocarcinoma	
EGFR-sensitizing	15%
EGFR other	2%
KRAS	25%
ALK	7%
HER2	2%
BRAF V600E	2%
BRAF other	1%
ROS1	2%
RET	2%
NTRK1	0–5%
MET	3%
MAP2K1	0–5%
PIK3CA	1%
NRAS	0–5%
>1 mutation	3%
Unknown	31%

Source: Pao W and Hutchinson KE. *Nat Med*. 2012;18(3):349-351. 2. Lovely C, Horn L, Pao W. *My Cancer Genome*. 2018.

Evolving approach to drug evaluation

- FDA recognizes that traditional medical product development and approval pathways may not be practical, efficient, or even feasible for some indications
- FDA has embraced multiple initiatives focused on modernizing medical product development and approval
  - Assisting with medical product development (pre-IND)
  - Alternative trial designs
  - Accelerated (and/or priority) review
  - Accelerated approval
- Where traditionally there were limited options for medical product development and approval, now there are many potential pathways

Polling question

- What is more valuable?
  - Sample size
  - Diversity
  - Access
  - Equity
  - Adherence

Selecting the optimal trial design and regulatory approach

Beyond Phase I, II, III

Type	Description	Example
Adaptive designs	A clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.	STAMPEDE simultaneously evaluated multiple treatments for prostate cancer
Complex innovative designs	Trial designs that have rarely or never been used to date to provide substantial evidence of effectiveness in new drug applications or biologics license applications (e.g.: complex adaptive, Bayesian, simulation, etc.).	2014-2016 Ebola outbreak master protocol (PREVAIL II) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
Decentralized trials	Those executed through telemedicine and mobile/local healthcare providers, using processes and technologies that differ from the traditional clinical trial model.	Pfizer's REMOTE trial in 2011 assessed tolterodine ER 4 in participants with overactive bladder
Real-world evidence (RWE)	The clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of real-world data (RWD).	Palbociclib, lutetium lu 177 dotatate, pembrolizumab, tafasitamab, etc.

Beyond Phase I, II, III

- **Potential benefits of alternative study design include:**
  - Increased efficiency: time, cost, duration of study, number of participants, etc.
  - Improved ability to quantify safety and efficacy in typical care settings
  - Easier to identify and enroll patients
  - Increased access for patients
  - More meaningful outcomes
  - Ethical considerations

Expedited review methods

Fast track - Facilitates development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need

Breakthrough therapy - Expedites development and review of drugs intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)

Rolling review - Can submit completed sections of NDA/BLA for review, rather than waiting until the application is completed before the entire application can be reviewed

Priority review - Goal to act within 6 months (vs 10 months under standard review)

Accelerated approval - Allows for earlier approval of drugs that treat serious conditions, and fill an unmet medical need, based on a surrogate endpoint

CDER uses several regulatory pathways to enhance efficiency and expedite the development and approval of novel drugs

Source: New Drug Therapy Approvals 2019. https://www.fda.gov/media/134493/download. Accessed 9/28/2020

Polling question

- What is more valuable?
  - Selecting an optimal clinical trial design
  - Selecting an optimal regulatory approach

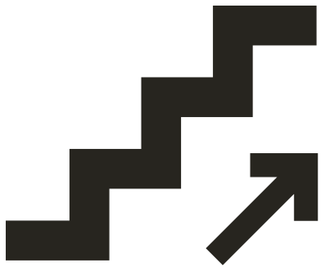
Embracing value-based research

Examples of value-based research

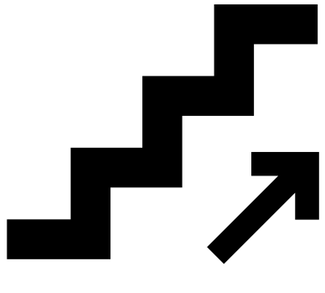
- Traditional clinical trial with patient-centric outcomes
- Semi-pragmatic trial with synthetic control arm
- All-phase (Phase I/II/III/IV) clinical trial in oncology

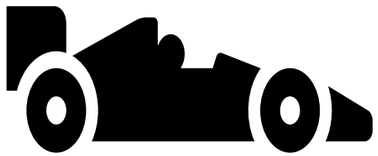
From one pathway to many customized pathways

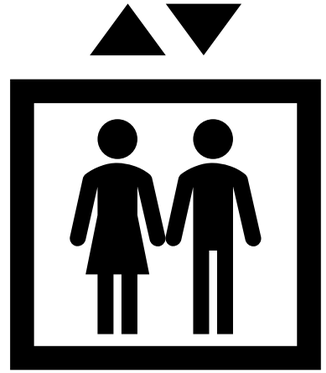
Traditional Pathway



Alternative Pathways







Polling question

- What is more valuable?
  - Reducing drug development time
  - Reducing drug development cost
  - Increasing patient access to clinical trials
  - Increasing patient representativeness in clinical trials

Questions

Thank you