Pricing Tolerance & the Evolution of Cell Therapy Costs of Care

Richard T Maziarz MD

Professor of Medicine

Oregon Health & Science University

Chair, ASTCT Value & Health Economics Interest Group

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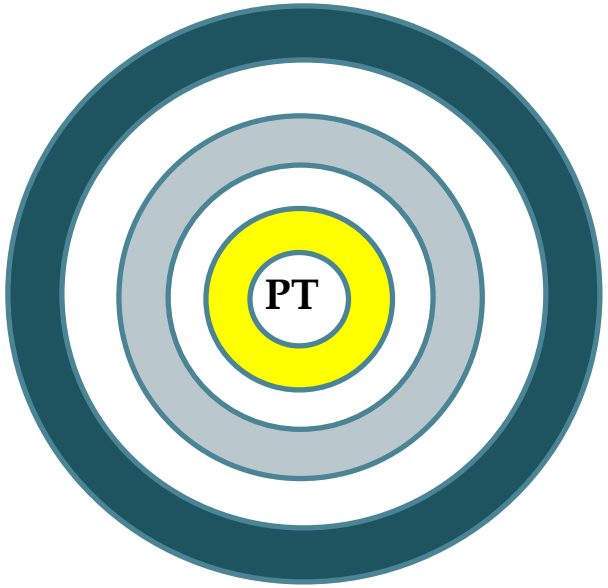
- ASTCT, Chair of Value & Health Economics Interest Group

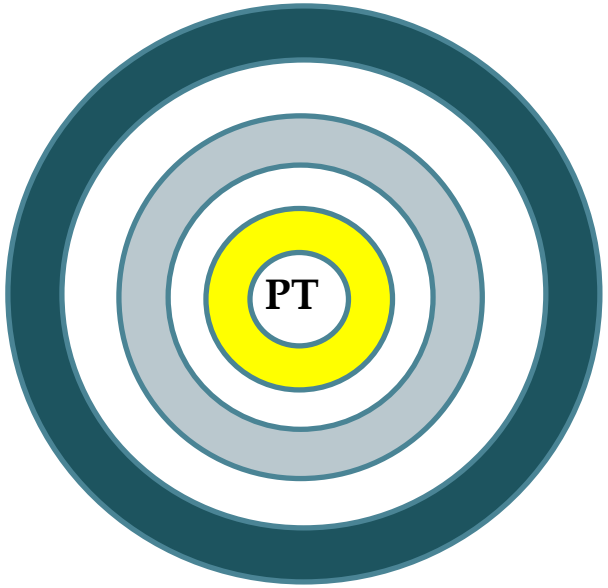
Provider Principles

- Primary goal is the direct delivery of care to patients
- The patient is the center of our attention.

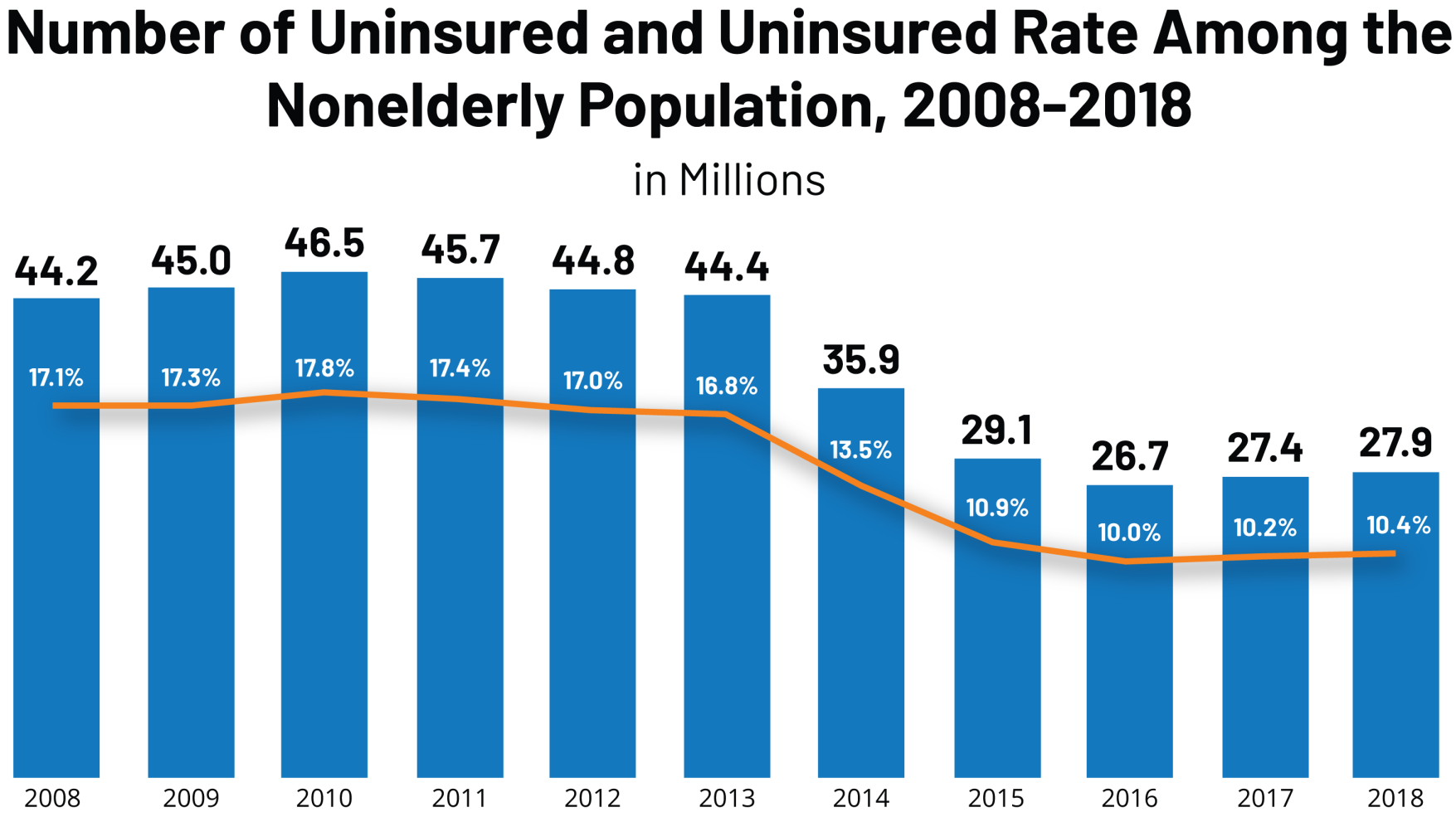


Provider Principles & Realities

- Primary goal is the direct delivery of care to patients
- The patient is the center of our attention.
- Recognition that delivery of care : generally based on contractual agreements of coverage, whether governmental or private payer



Pre & Post HCA:
Estimated Health Insurance Coverage, Tolbert, Kaiser Found., 2020



Pre HCA: “insurance” ≠ access to care

- Pre-existing conditions: 2 years (e.g. transplantation benefits)
- Lifetime maximums: $1-2 million
- Procedural maximums: $250,000 adjudicated claims

- Patients would often expend benefits and on next “open election season” opt in to a different payer to renew health care benefits

HSCT: Growth in Cost & Volume→ Greater scrutiny of utilization & outcomes

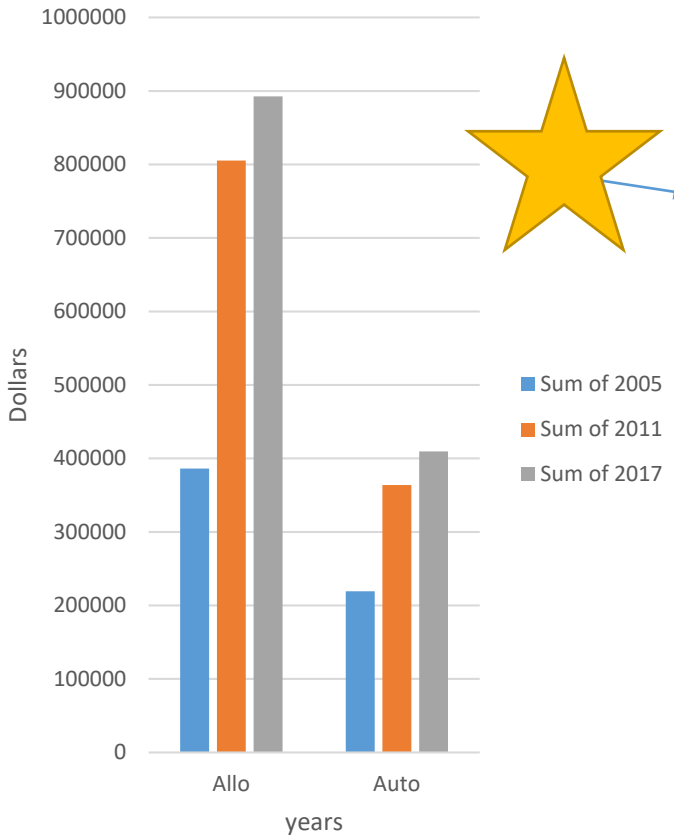


Table 1. Commonly performed procedures with the most rapidly increasing hospital inpatient costs, 2004–2007

Principal procedure category	Total costs (2007)	Total hospital stays (2007)	Percentage change	
			Total costs (2004–2007)	Total hospital stays (2004–2007)
Bone marrow transplant	$1,282,645,000	15,100	84.9%	51.3%
Open prostatectomy	$1,032,016,000	88,500	68.6%	40.8%
Aortic resection; replacement or anastomosis	$1,872,908,000	61,600	38.5%	31.9%
Cancer chemotherapy	$2,616,504,000	187,400	33.2%	14.2%
Spinal fusion	$8,863,922,000	350,700	29.5%	15.6%
Lobectomy or pneumonectomy	$1,757,748,000	81,400	29.2%	24.9%
Incision and drainage, skin and subcutaneous tissue	$1,108,187,000	158,600	28.6%	31.5%
Arthroplasty knee	$9,217,740,000	605,200	27.5%	25.7%
Nephrotomy and nephrostomy	$682,609,000	38,600	25.3%	11.7%
Mastectomy	$660,173,000	70,100	23.8%	3.6%
Total for top 10 procedures**	**$29,094,452,000**	**1,657,100**	**32.3%**	**22.2%**

*2004 costs were adjusted to 2007 dollars using the overall Consumer Price Index.
Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 2004 and 2007.

- **2005-17:** 132% increase in **billed charges** (allo)*
  - $892,700 in 2017
  - 7,659 total allo transplants

2009 – BMT had highest percentage growth in costs of any hospital procedure (AHRQ HCUP)

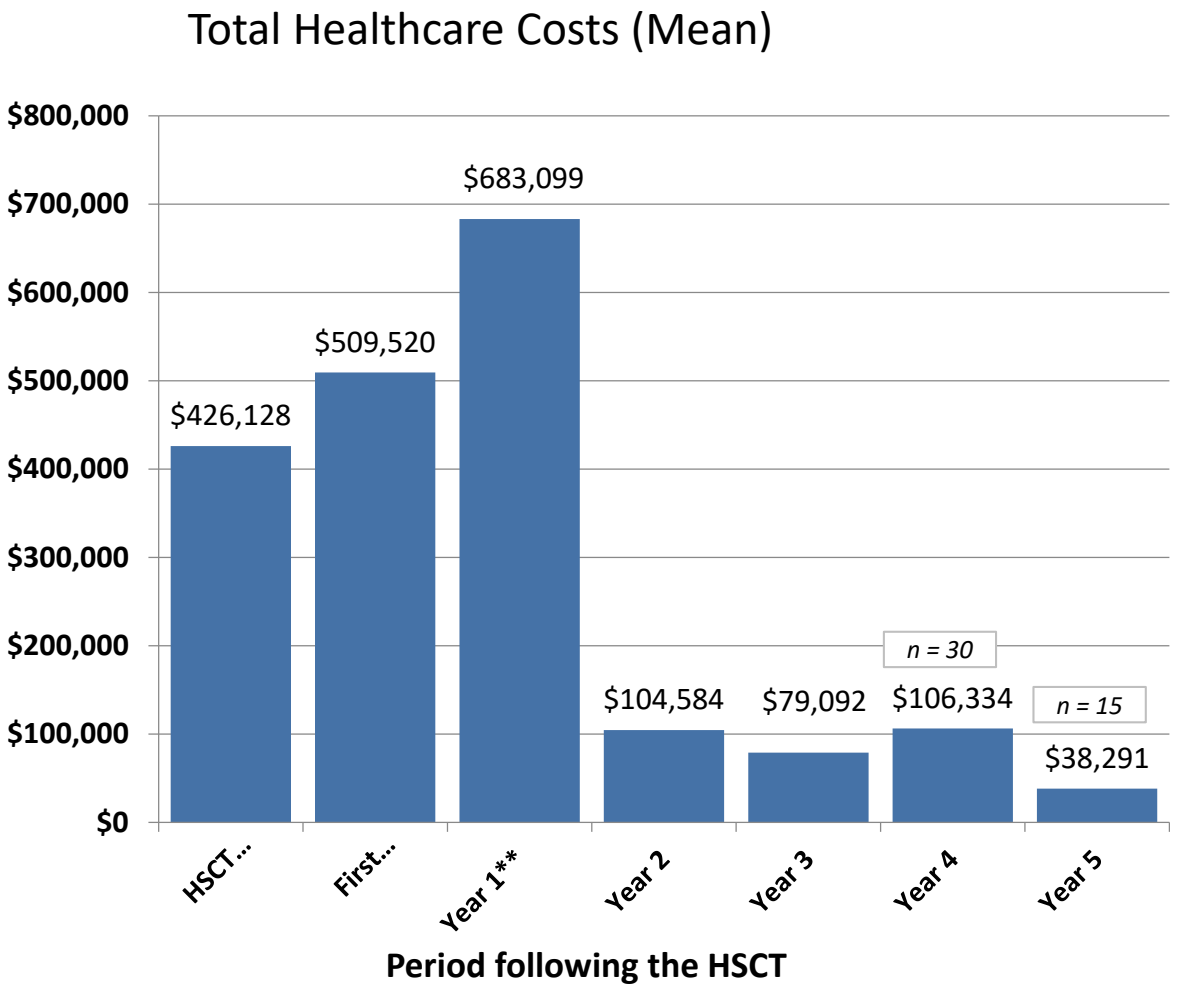
2017: Estimated 16,536 Transplants per year in U.S.

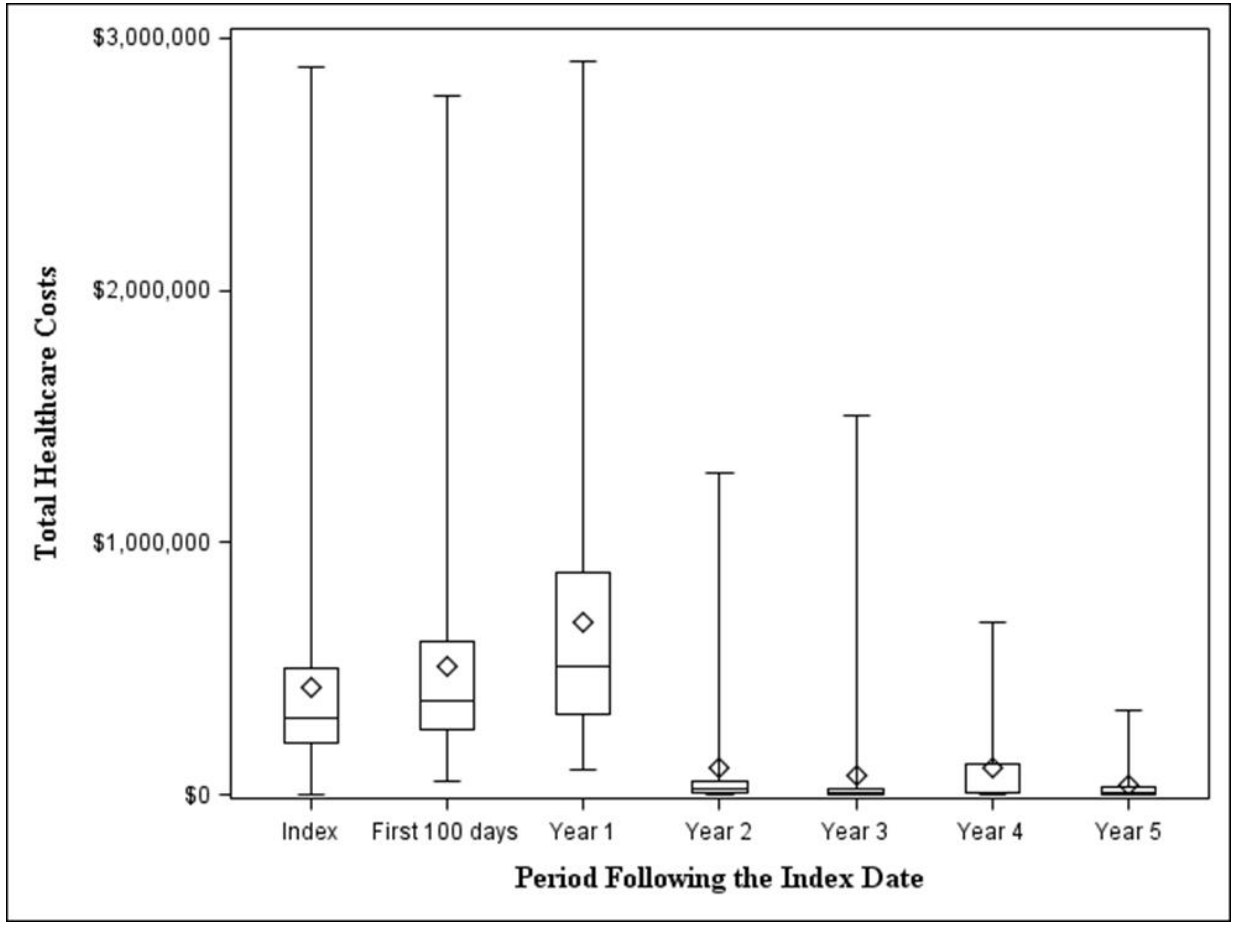
- **~$6.8 & $3.6 billion for allo & autoHCT** (charges)

*Data courtesy of Milliman Cost of Transplant Reports, 2005-2018

Five Year Direct Cost of Pediatric Patients with Acute Lymphoblastic Leukemia Undergoing Allogeneic Stem Cell Transplantation: an Analysis from US Payers' Perspective, Maziarz et al, 2016

Impact of outliers

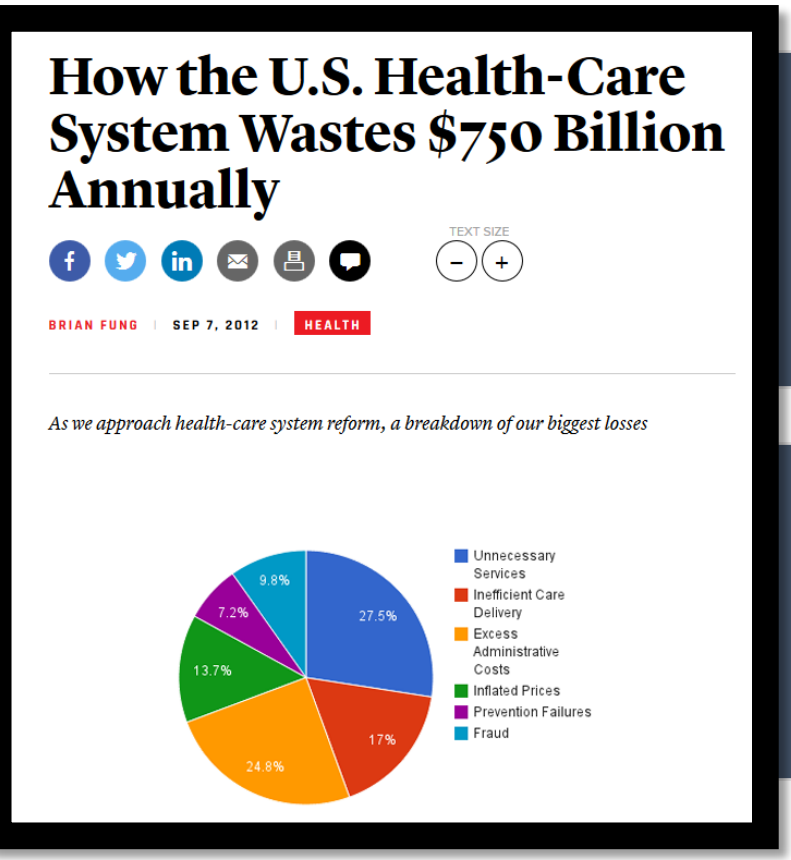




- High variation in healthcare costs across individual patients; a small proportion of patients account for the majority of the total costs, Maziarz et al, 2016

Categories of Waste

American Society for Quality (ASQ) = *"Healthcare services that do not add value or improve patient outcomes"*



How the U.S. Health-Care System Wastes $750 Billion Annually

TEXT SIZE

BRIAN FUNG | SEP 7, 2012 | HEALTH

As we approach health-care system reform, a breakdown of our biggest losses

Failures of Care Delivery

Adverse Events, HAIs, Misdiagnosis

Failures of Care Coordination

Readmission, Decline in Functional Status

Overtreatment

Defensive medicine, provider preference, futile care

Administrative Complexity

Unstandardized forms and procedures

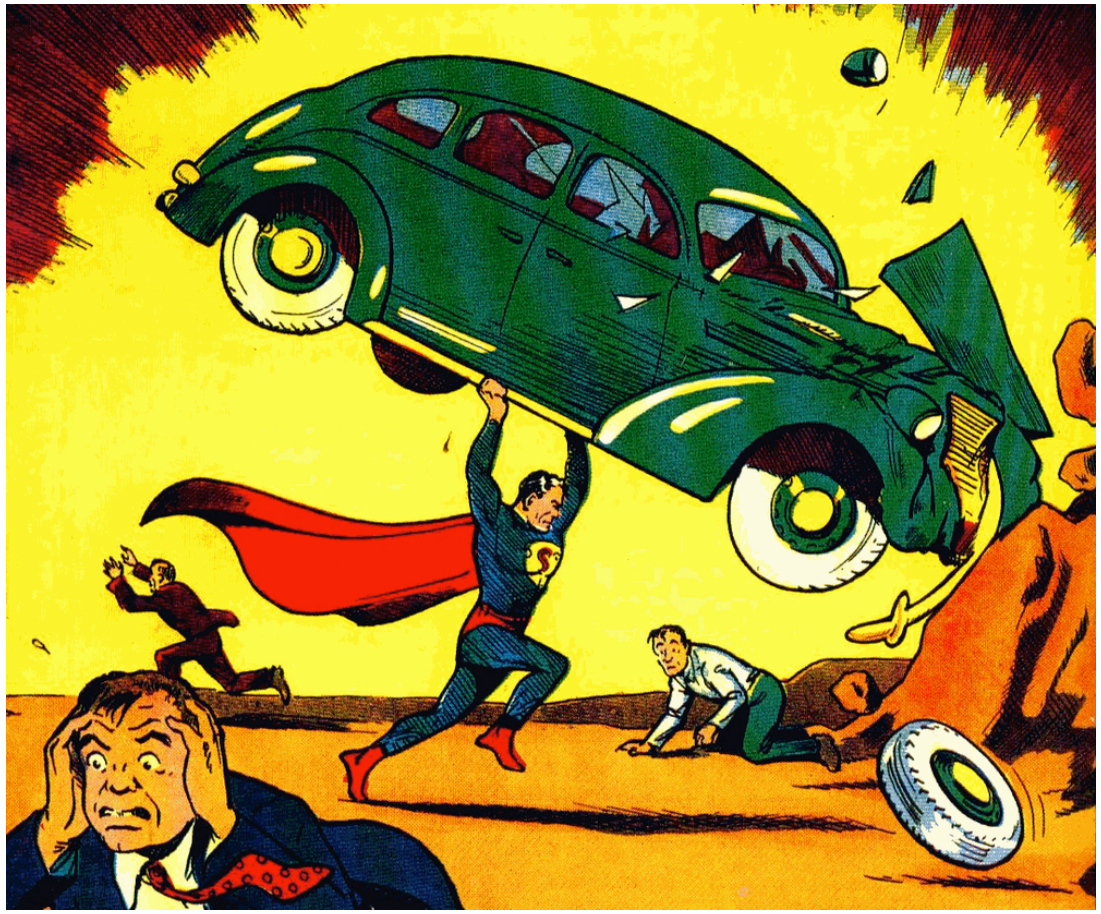
Pricing Failures Above market value for no reason

Rx 169B

Fraud and Abuse

Health Affairs (2012)

Cell Therapy:
CAR T makes headlines



The NICE CAR T-cell review exercise

- NICE conducted a ‘mock appraisal’ of a hypothetical regenerative medicine product CAR (chimeric antigen receptor) T-cell therapy for treating B-cell acute lymphoblastic leukaemia (NICE, 2016; Hettle et al., 2016)

Benefits and Costs of the two TPPs	TPP1: Bridge to stem cell transplant	TPP2: Curative intent
Assumed individual patient level incremental QALY gain	7.46	10.07
Assumed price (acquisition cost)	£356,100	£528,660

NICE, 2016. *Exploring the assessment and appraisal of regenerative medicines and cell therapy products*. London: National Institute of Health and Care Excellence.
Hettle, R., Corbett, M., Hinde, S., Hodgson, R., Jones-Diette, J., Woolacott, N., Palmer, S., 2016. *Exploring the assessment and appraisal of regenerative medicines and cell therapy products*. CRD/CHE University of York.

The Institute for Clinical and Economic Review (ICER) created a new drug assessment program with the goal of changing how drugs are priced and evaluated, Steven Pearson, MD, MSc, FRCP, founder and president of ICER.

What are the goals of the ICER's new drug assessment program?

"From our perspective, **the current landscape for how drugs are priced and evaluated, especially at or near the time of FDA approval, has really been broken**. In some ways it's been a black box, but what we do know is that there has not been any consistent way for the discussions about effectiveness and value to be woven into the way that drugs are covered and priced at the beginning.

There's still a lot to do, also, with drugs that have been on the market for a long time, when the evidence of their effectiveness or their price changes rapidly. But our new program is meant to "ramp up" the focus, primarily in the short term, on emerging, significant drugs at or near the time of their approval. And our goal is to provide reports that can be used by insurers, by doctors' groups, by policy makers, and by patients, to try to get a much clearer view of the comparative effectiveness and value of these drugs.

With that information we now include what we call a value-based price benchmark. And that, too, is meant to send a signal that, if we wish to do a better job of pricing drugs according to the added benefits that they bring to patients, we want to provide a marker to kind of trigger the right discussions, negotiations, and policies that will focus on value."

ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures

A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines

Table 2. Proposed Integration of Level of Value Into Clinical Guideline Recommendations*

Level of Value
High value: better outcomes at lower cost or ICER <$50,000 per QALY gained
Intermediate value: $50,000 to <$150,000 per QALY gained
Low value: ≥$150,000 per QALY gained
Uncertain value: value examined but data are insufficient to draw a conclusion because of no studies, low-quality studies, conflicting studies, or prior studies that are no longer relevant
Not assessed: value not assessed by the writing committee

Proposed abbreviations for each value recommendation:

Level of Value: H to indicate high value I, intermediate value; L, low value; U, uncertain value; and NA, value not assessed

*Figures used in this table are based on U.S. GDP data from 2012 and were obtained from WHO-CHOICE Cost-Effectiveness Thresholds (24).

GDP indicates gross domestic product; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; and WHO-CHOICE, World Health Organization Choosing Interventions that are Cost Effective.

Source: Anderson et al., 2015

"QALY is the coin of the realm in cost-effectiveness analysis
Combines length of survival and health-related quality of life

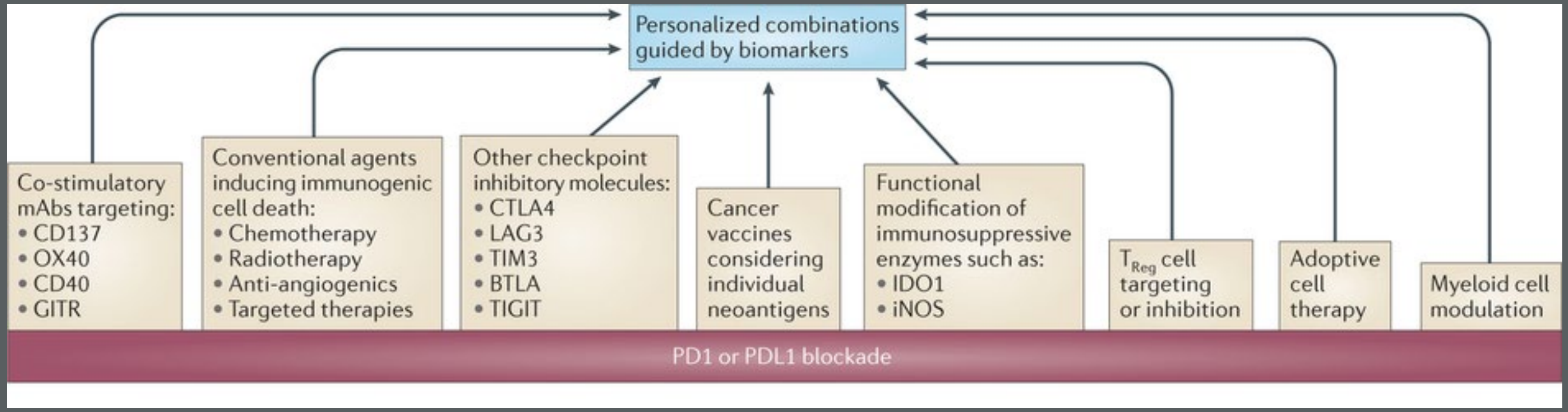
Discounting: for a patient, health gained in the future is worth < health gained today"

ICER Base-Case Incremental Results: CAR T

B-ALL/BLBCL	Incr Costs	Incr LYs	Incr QALYs	Incr CE Ratio per LY	Incr CE Ratio/QALY
Tisagenlecleucel					
vs. Clofarabine	$329,498	7.91	7.18	$41,642	$45,871
Axicabtagene Ciloleucel					
vs. Chemotherapy	$462,043	4.12	3.40	$112,168	$136,078

Base-case payment for tisagenlecleucel assumes payment only for responders at one month. Base-case payment for axicabtagene ciloleucel assumes payment at infusion.
CE: cost-effectiveness, LY: life year, QALY: quality-adjusted life year

How to improve on outcomes? Potential trial candidates



There is an internal message: CAR T does not cure all!!!!!

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ICER April 2021, Myeloma CAR T:

Treatment of PFS Gained	Comparator	Cost per QALY Gained	Cost per evLYG	Cost per Life Year Gained	Cost per Month
Ide-cel	CAR-T Comparator	$247,000	217,000	$194,000	$27,000
Cilta-cel (prelim)*	CAR-T Comparator	$110,000	$96,000	$85,000	$13,000

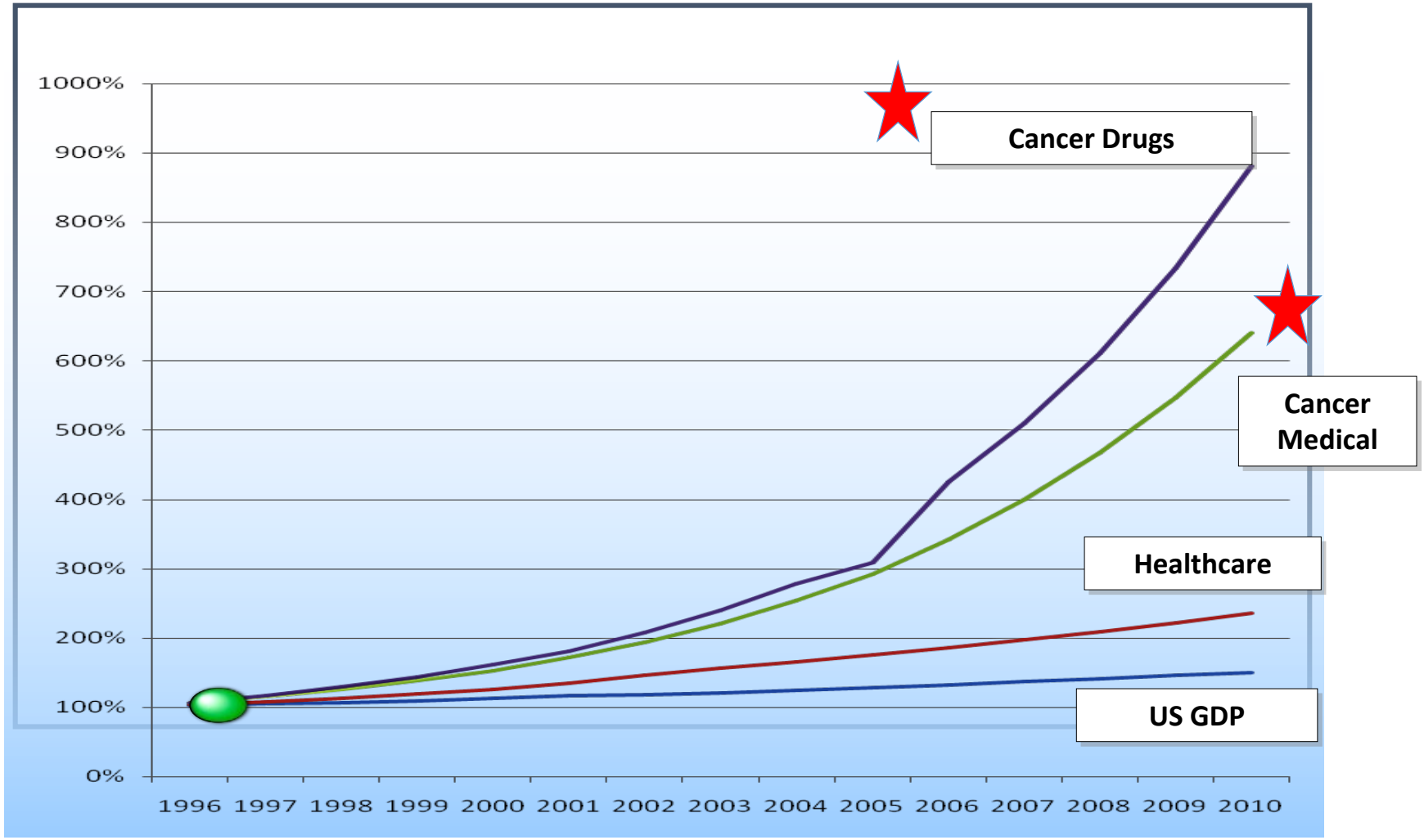
- evLYG: equal-value of life years gained, QALY: quality-adjusted life year, LY: life years *Using placeholder price for cilta-cel

- Findings suggest CAR-T therapies provide clinical benefit in terms of gains in QALYs and LYs over current treatment options
- Ide-cel meets commonly cited cost-effectiveness thresholds with discounts of > 37% (from current announced market price)
- Preliminary evidence on cilta-cel meets commonly cited thresholds given limited evidence

Value Frameworks:
The Roadmap TO THE FUTURE

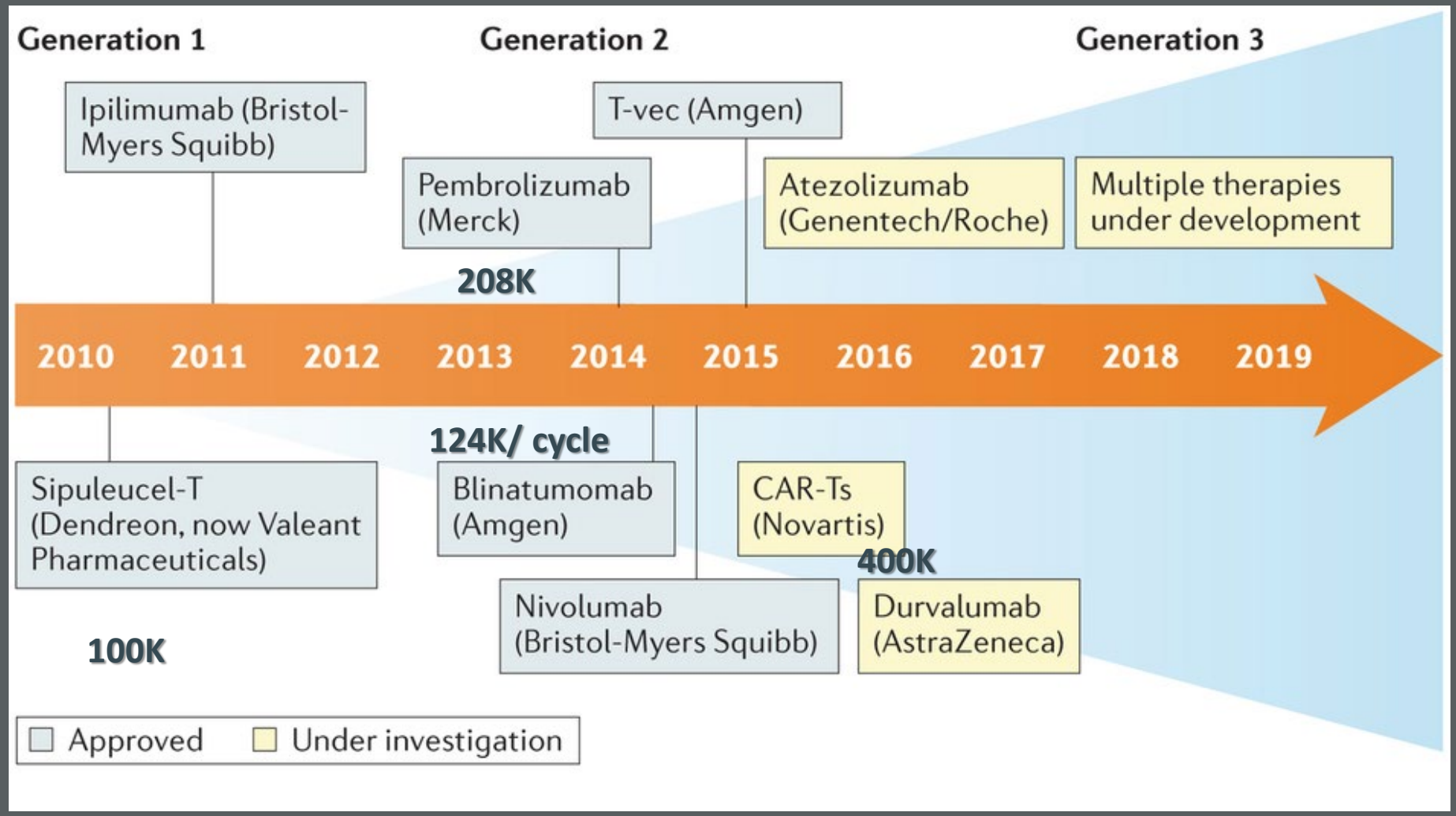
- Current value-based frameworks for cancer therapy: can CAR-T fit?
- Most prior assessments for R/R disease → measurement of PFS and OS. CAR-T has the outcomes paradox of mixing cure and Progressive R/R disease
- Vision for a learning value-based healthcare finance system

Cancer care costs rising faster than overall healthcare:
Cancer costs account for approximately 5% of US health care spending



Source: Blue Cross Blue Shield Association

Pipeline of Cancer Immunotherapies-Commercialization



Axel Hoos, Nature Reviews Drug Discovery (2016) doi:10.1038/nrd.2015.35

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Specifically, we see cell and gene landscape rapid growth

- Fewer than 10 cell and gene therapies currently approved and in use, but with another 10+ expected annually in 2021 and beyond
- 1,000+ clinical trials for cell and gene therapies underway in the U.S. (asgct.careboxhealth.com)
- 24+ conditions on the near-term pipeline and constantly changing
- Number of manufacturers in cell and gene therapy market growing exponentially including big player
- Constantly shifting market

Forecast (2021-2022 Pipeline)

Blood Disorders

- Hemophilia B (gene)
- Hemophilia A (gene)
- Transfusion dependent β-thalassemia (gene)

Cancer

- Follicular lymphoma (CAR-T expanded indications)
- Multiple myeloma (CAR-T)
- Bladder cancer (gene)
- Epstein-Barr virus-associated post-transplant lymphoproliferative disease (CTL)
- Cervical cancer (TIL)
- Metastatic melanoma (TIL)
- Marginal zone lymphoma (CAR-T expanded indications)
- Diffuse large B-cell lymphoma (CAR-T)
- Acute lymphoblastic leukemia (CAR-T)
- Synovial sarcoma (TCR T-Cell)

Ocular Disorders

- Choroideremia (gene)
- Leber hereditary optic neuropathy (gene)
- Wet & dry age-related macular degeneration (gene/cell)

Metabolic Disorders

- Cerebral adrenoleukodystrophy (gene)
- Mucopolysaccharidosis type III (gene)

Neurodegenerative

- Aromatic L-amino acid decarboxylase (AADC) deficiency (gene)
- Spinal muscular atrophy (expanded indications-gene)

Skin Disorders

- Recessive dystrophic epidermolysis bullosa (gene)
- Scleroderma (gene)

Inherited Immunodeficiencies

- Wiskott-Aldrich syndrome (gene)
- Leukocyte adhesion deficiency type I (gene)

Spinal Muscular Atrophy

The UK’s National Health Service just approved a drug that costs nearly $2.5 million a dose

PUBLISHED MON, MAR 8 2021 9:33 AM EST

KEY POINTS

•The innovative gene therapy, called Zolgensma, has a reported list price of £1.79 million ($2.48 million) per dose.
•That makes it the most expensive drug in the world, NHS England said in a statement Monday.

- Zolgensma, which is manufactured by Novartis Gene Therapies has been shown in studies to help babies reach milestones such as breathing without a ventilator, sitting up on their own, and crawling and walking after a single infusion treatment.
- The latest data suggests that Zolgensma can provide rapid and sustained improvement in motor function for young children with type 1 SMA and prolong their lives.
- As many as 80 babies and young children a year could potentially benefit from the gene therapy, the NHS stated.

Pricing

- Not linked to FDA approval in US
- Not the same in other countries
- Fiduciary responsibility of industry
  - Shareholders, not patients
- Recapturing costs of R & D
- Cost of drug development is exaggerated & ROI often far exceeds costs of goods & manufacture, Prasad, JAMA Int Med Sept 2017

CAR T expense: Drug (not Care)

ALL

Tisagenlecleucel

$475,000

US Market: 100s

DLBCL

~~Axicabtagene Ciloleucel~~
Tisagenlecleucel

$373,000

Axi-cel $399,000

- **Lisocabtagene maraleucel**

$410,300

1000s

Mantle Cell

Brexucabtagene autoleucel

~~$373,000~~
$399,000

100s (?)

Follicular NHL

Axicabtagene Ciloleucel

~~$373,000~~
$399,000

1000s

Myeloma

Idecabtagene vicleucuel

$419,500

1000s

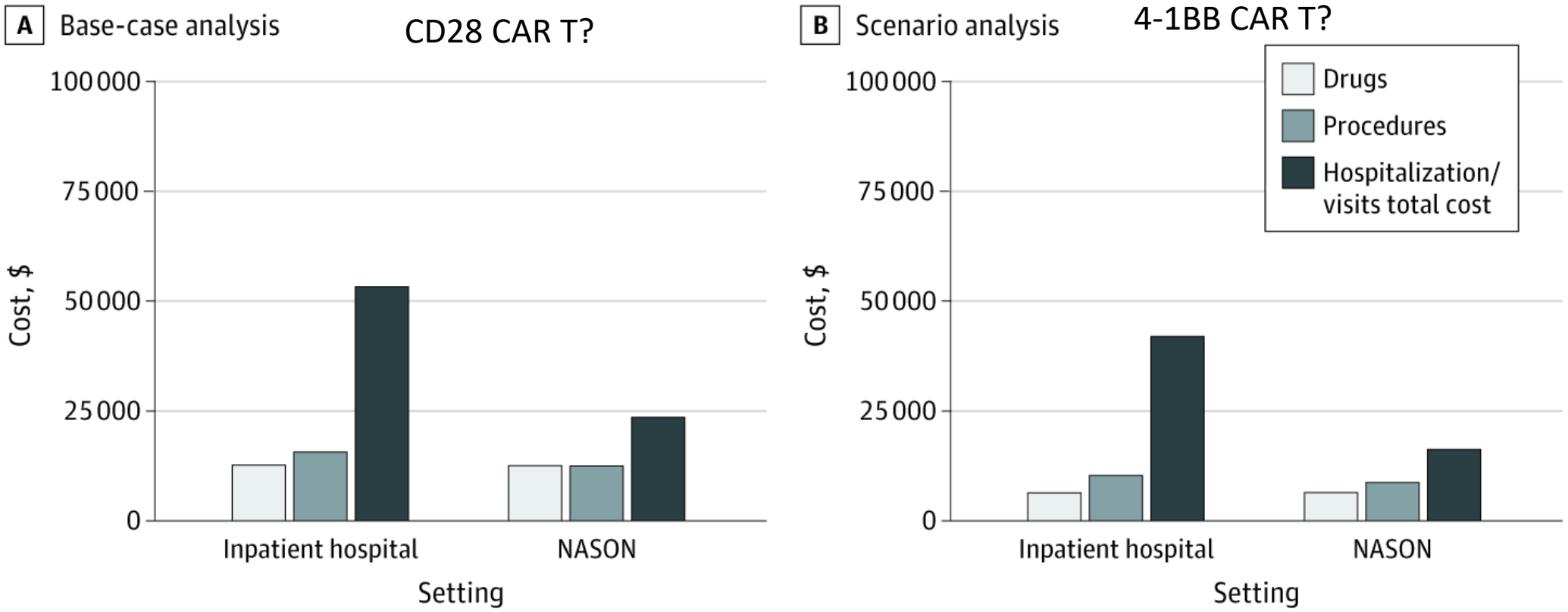
JAMA Network™ From: **Economic Evaluation of Chimeric Antigen Receptor T-Cell Therapy by Site of Care Among Patients With Relapsed or Refractory Large B-Cell Lymphoma**

JAMA Netw Open. 2020;3(4):e202072. doi:10.1001/jamanetworkopen.2020.2072

What does the Model not Reveal?

CD28 CAR T?

4-1BB CAR T?



Base-Case and Scenario Analyses

A, In this analysis, 97.5% of patients had an adverse event. Costs in the inpatient hospital setting were $12 561 for drugs, $15 690 for procedures, and $53 360 for hospitalization and office visits, for a total cost of $81 611. Costs in the nonacademic specialty oncology network (NASON) setting were $12 561 for drugs, $12 537 for procedures, and $23 526 for hospitalization and office visits, for a total cost of $48 624. The total cost difference between the inpatient hospital and NASON settings was $32 987, reflecting a 40.4% cost reduction. The chimeric antigen receptor (CAR) T-cell acquisition cost, assumed to be $373 000, was excluded from the total costs. All costs are in US dollars.

B, In this analysis, 50% of patients had an adverse event. Costs in the inpatient hospital setting were $6460 for drugs, $10 313 for procedures, and $42 003 for hospitalization and office visits, for a total cost of $58 776. Costs in the NASON setting were $6460 for drugs, $8718 for procedures, and $16 304 for hospitalization and office visits, for a total cost of $31 482. The total cost difference between the inpatient hospital and NASON settings was $27 294, reflecting a 46.4% cost reduction. The CAR T-cell acquisition cost, assumed to be $373 000, was excluded from the total costs. All costs are in US dollars.

Current backlash against drug costs

- **Americans overpaying hugely for cancer drugs – Reuters:** Tue Sep 22, 2015 Several TKIs are expected to become available as generics within 5 years, as patents expire. Large-scale production could achieve treatment prices in the range of $159 to $4,022 per person a year, vs current U.S. prices of around $75,000 to over $100,000.

- **"The majority of drugs for indications with fewer than 10,000 patients in the United States are priced at or above $200,000 per year",** Yang, Chen, Bennett; JCO, Nov 2016.

- **Trump Administration Announces Historic Action to Lower Drug Prices for Americans, HHS Press Off, July 24, 2020**

- **Trump unveils plan linking drug payments to cheaper overseas prices:** Friday is also the last day that the Trump administration can release a rule that could be finalized in the 60 days before Joe Biden assumes office, Nov 20, 2020

- **Biden's drug-price goals:** Reducing the cost of prescription medications is one of Biden's top health care priorities. He supports allowing Medicare to negotiate drug prices and consumers to import medicine from abroad, February 1, 2021

- Re: private ins self funded plans, 1 Natl Payer Dir shared that a company client- "No Gene Therapy Coverage!!!"

- **The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts.** 119 Experts in Chronic Myeloid Leukemia. Blood. 2013 May 30;121(22):4439-42. doi: 10.1182/blood-2013-03-490003

- This editorial addresses the multiple factors involved in cancer drug pricing and their impact on individual patients and health care policies, and argues for the need to (1) lower the prices of cancer drugs to allow more patients to afford them and (2) maintain sound long-term health care policies.

- The doctrine of *justum pretium*, or just price, refers to the "fair value" of commodities. In deciding the relationship between price and worth (or value), it advocates that, by moral necessity, price must reflect worth.

- This doctrine may be different from the doctrine of free market economies where prices reflect "what the market bears," or what one is willing to pay for a product.

Ways that drugs are valued- impact on pricing

1. Costs to bring a drug to market and to manufacture it

2. Market value: price and units sold based on supply and demand considerations

3. Economic value: point in time and futures, intangible values

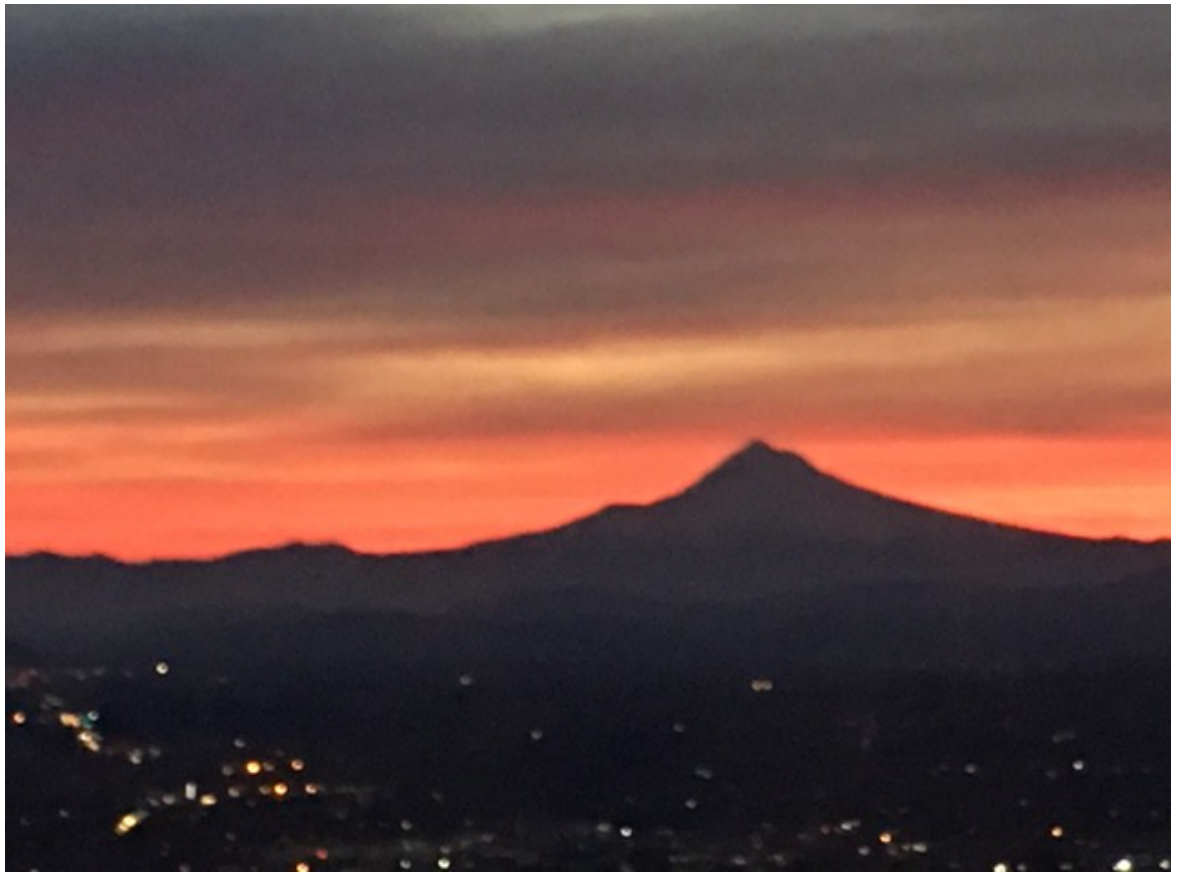
4. Remember- value is comparative. Value of a new treatment is ultimately assessed by measuring improvement in outcomes vs cost

Questions on cell and gene therapies for providers and payers

1. How to determine who to offer therapy to, what therapy to offer,
2. What coverage should look like and who should be covered
3. How to maximize value for patients
    - Where to provide care
    - How to choose treatment options
    - How to sequence care

CAR T vs Transplant: the work evolves

Thanks to all for joining



Dawn over Mt Hood near Portland, OR