Questioning Everything: My Off-Label Learnings Between Health System and Health Plan

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Disclosures

Current:

Oncology Medical Outcomes Director

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Former:

Clinical Utilization and Intelligence Manager

Kaiser Permanente

Experiences and examples in this presentation are drawn from this role

Learning

- Discern gaps in compendia guidelines and opportunities to enhance guideline concordant care
- Determine best value-based assessment tools for use in formulary decisions and clinical practice
- Illustrate the benefits of a fully integrated delivery model

What are current gaps and best practices when instituting NCCN guideline-concordant care?

A. Guidelines only draw evidence from phase 3 trials so we can widely adopt them.

B. Guidelines are consensus based, containing both high and low-quality choices. We need to consider confirmation biases and healthcare costs to the patient.

C. Guidelines consider therapy costs as the most important factor when selecting treatment so we can selectively adopt them.

D. Guidelines do not use clinical evidence at all so it’s best to not adopt them.

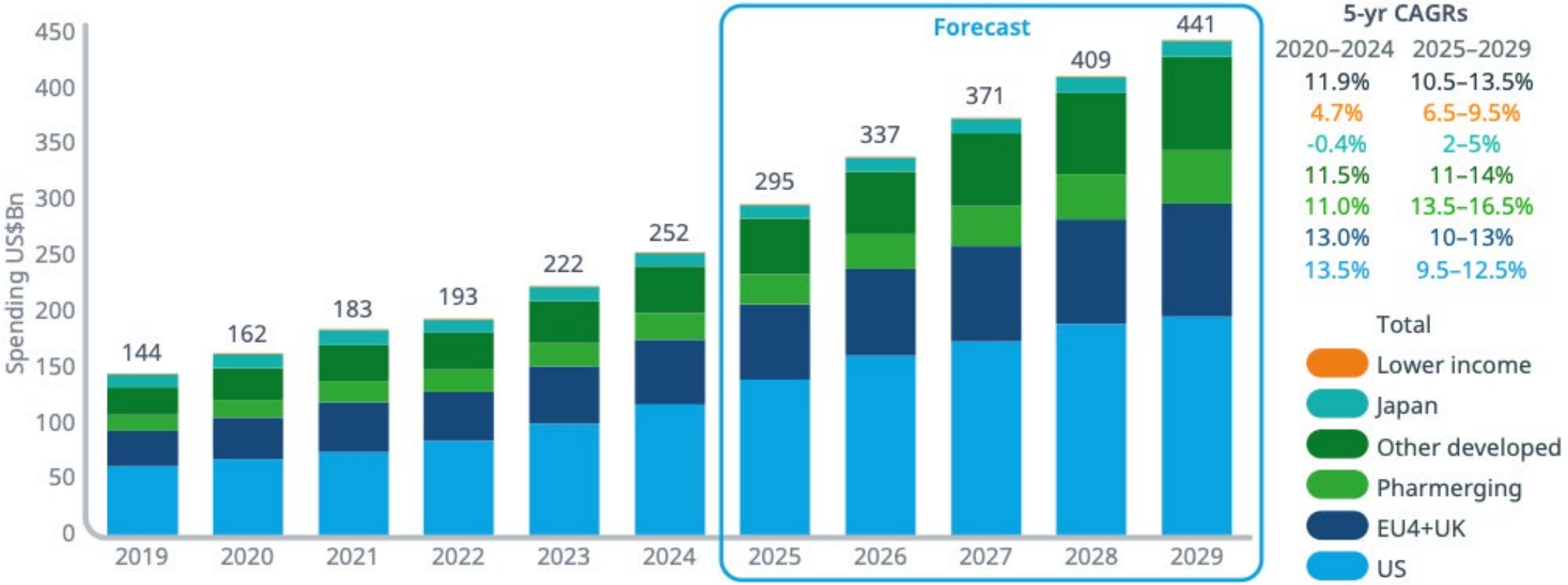
What are advantages to using ASCO value-based framework for formulary decisions?

A. It is an objective, non-weighted scoring system and not based on treatment intent
B. It equally prioritizes clinical benefit and toxicity for all lines of treatment
C. It prioritizes toxicities above other factors.
D. It considers factors such as clinical benefit, toxicity, drug cost, and treatment intent on a weighted scoring system.

How do fully integrated delivery networks (IDNs) approach cancer care differently than traditional academic healthcare systems?

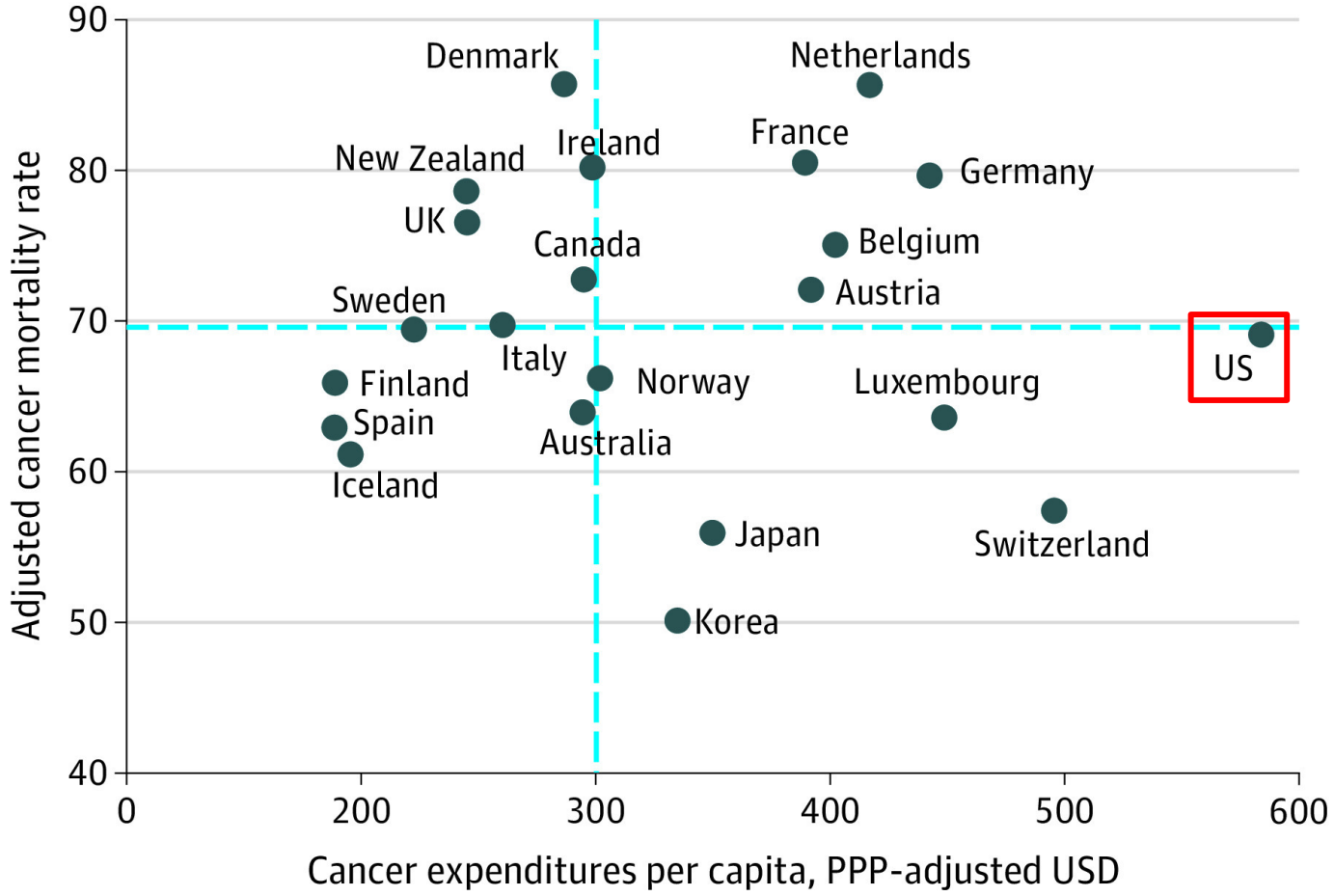
A. IDNs have both providers and payors determine practice and coverage decisions collaboratively so overall healthcare profits and costs are shared
B. IDNs do not own hospital buildings
C. Providers are owned by the health plan so they must follow the insurance team's edicts
D. Providers own the health plan so they can prescribe anything without thinking about cost

The US is 46% of global oncology spending



*Pharmerging countries are defined as those with lower than $30,000 per capita GDP PPP and 5-year forecast growth of the total pharmaceutical market of >$1Bn.
CAGR: Compound Annual Growth Rate

IQVIA Institute for Human Data Science. Global Oncology Trends 2025: Adopting New Therapies as Modalities Shift and Expenditures Rise, May 2025.



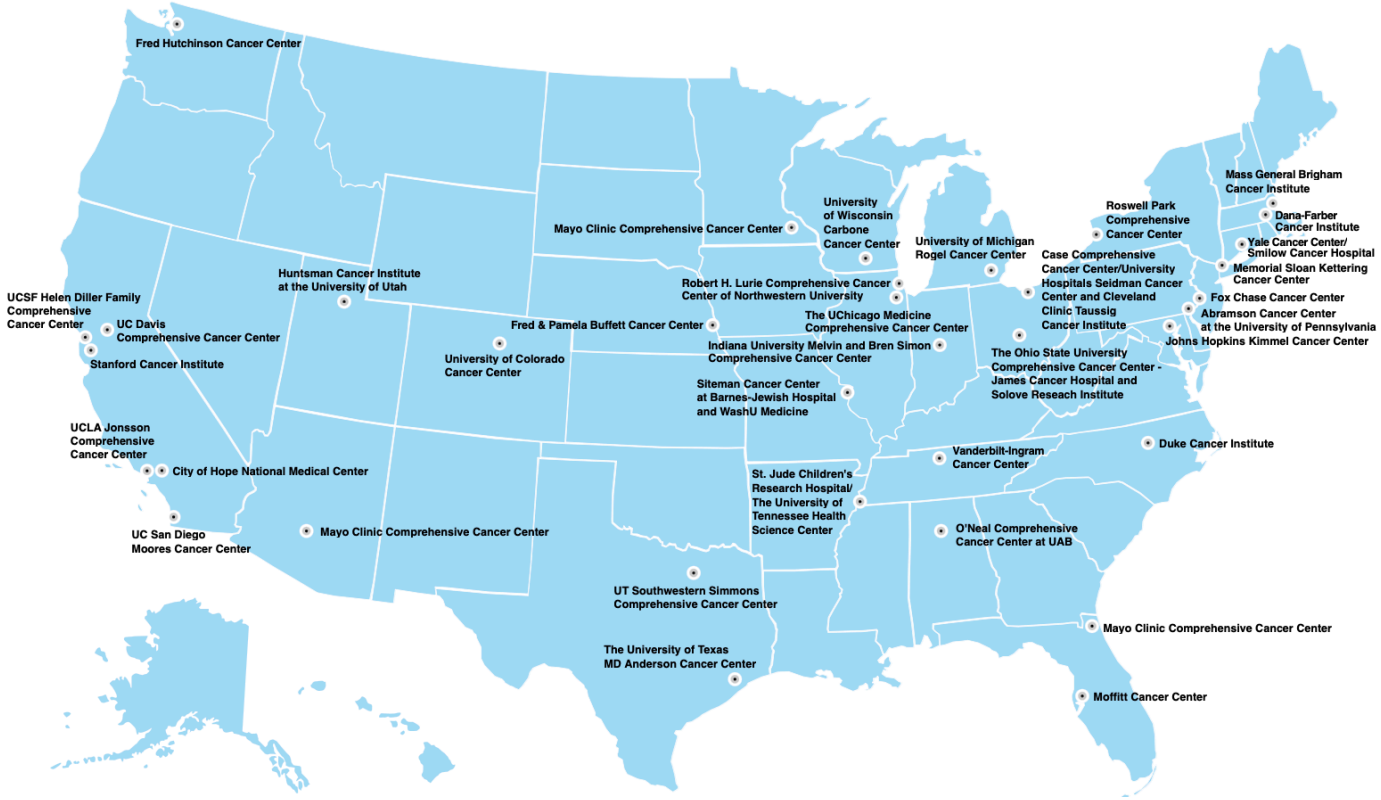
Adjusted cancer mortality rate (per 100,000)
PPP: Purchase Price Parity (normalize cost of goods)

Cancer Mortality vs. Spend per Capita

Chow RD, Bradley EH, Gross CP. Comparison of Cancer-Related Spending and Mortality Rates in the US vs 21 High-Income Countries. *JAMA Health Forum*. 2022;3(5):e221229. Published 2022 May 27. doi:10.1001/jamahealthforum.2022.1229

National Comprehensive Cancer Network (NCCN)

- Mission: “To define and advance quality, effective, equitable, and accessible cancer care […]”
- Payors rely on these guidelines for formulary decisions, prior authorization, and reimbursement



A History of NCCN. Cancer History Project. Published 2023. Accessed May 31, 2026. https://cancerhistoryproject.com/tcl-archive/20120113-3/
About. NCCN. Accessed May 31, 2026. https://www.nccn.org/home/about

When the National Comprehensive Cancer Network (NCCN) was formed in the early 1990s by five academic cancer centers, what was the *primary* driver behind its creation?

A. Developing evidence-based clinical practice guidelines for community oncologists
B. Securing managed care contracts to protect cancer centers from the threat of capitation under “Clinton-era” health reform
C. Creating a drug compendium for Medicare off-label coverage determinations
D. Building a national oncology outcomes database to demonstrate superior survival

A Brief History of the NCCN

THE ORIGIN (1992–1994)

- In the 1990s, Clinton administration ushered in a type of managed care
- Buzz words: “capitation” and “oncology carve-outs”
    - Threatened to steer patients to lower-cost community providers
- Five founders: MSKCC, MD Anderson, Fred Hutch, Fox Chase, City of Hope
- Three goals: payer contracting (the driver), clinical guidelines, and outcomes measurement

1995 First guidelines unveiled — breast, colon, prostate, lung, leukemia, pediatric (51% of all cancers)

1996 First 7 NCCN Guidelines published; first Annual Conference

1997 Outcomes Database launches; first supportive care guideline (antiemetics)

2008 CMS recognizes the NCCN Compendium for off-label drug coverage

2012 55 guidelines covering 97% of malignancies; major payors base coverage on NCCN

From Payer Threat to Practice Standard

https://cancerhistoryproject.com/tcl-archive/20120113-3/

THE CANCER LETTER

Vol. 22 No. 11
March 15, 1996

Price $265 Per Year US
$285 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Centers Network Releases "Version 1.0" Of Clinical Guidelines For Eight Cancers

Ft. Lauderdale, FL—A group of researchers and administrators at 13 major cancer centers spent more than 18 months compiling clinical guidelines for the treatment of cancer.

For the centers that comprise the National Comprehensive Cancer Network, the guidelines are no small matter. Ultimately, they are expected to offer an approach to pricing and measurement of outcomes.

Thus, it would have seemed reasonable for NCCN to regard the guidelines as proprietary documents, shielding them from the prying eyes

GM Corp. To Reimburse Marrow Transplants For Breast Cancer
. . . Page 5

CLINICAL DECISION SUPPORT

NCCN Guidelines

Weighing the strengths and limitations of the field's most widely used oncology framework

Advantages

- ✓ Market leader in oncology care
- ✓ Built on broad expert consensus
- ✓ Timely, frequent updates
- ✓ Free to access

Disadvantages

- — Complex to navigate
- — No transparency on level of evidence
- — Potential conflicts of interest
- — No financial / cost consideration

Cliff ERS, Rome RS, Kesselheim AS, Rome BN. National Comprehensive Cancer Network Guideline Recommendations of Cancer Drugs With Accelerated Approval. *JAMA Netw Open*. 2023;6(11):e2343285. Published 2023 Nov 1. doi:10.1001/jamanetworkopen.2023.43285

Figure 1. National Comprehensive Cancer Network (NCCN) Category of Evidence Ratings Stratified by US Food and Drug Administration (FDA) Approval Status

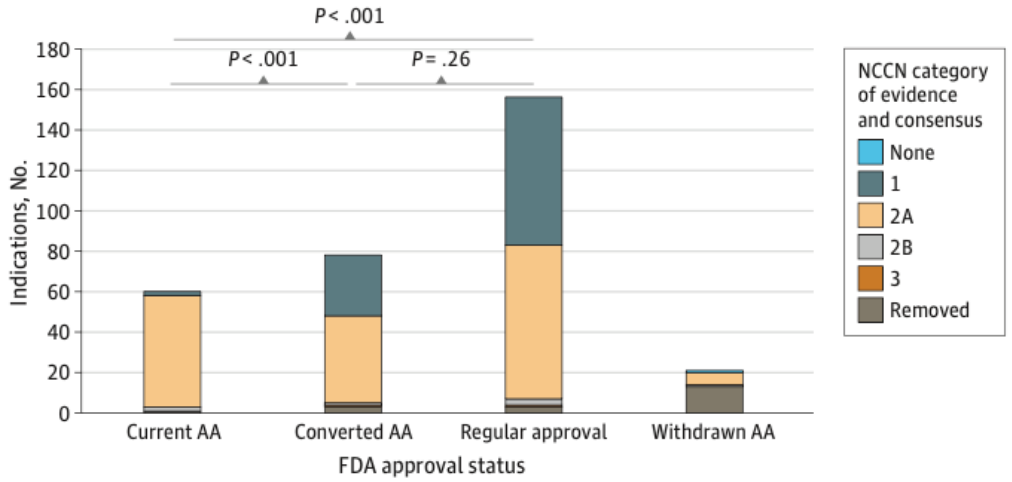
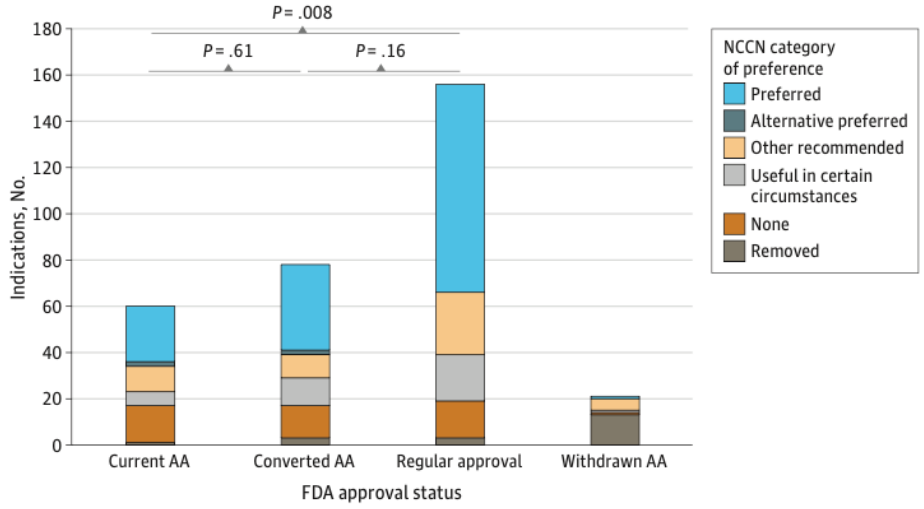


Figure 2. National Comprehensive Cancer Network (NCCN) Category of Preference Ratings Stratified by US Food and Drug Administration (FDA) Approval Status



33% of 315 indications were assigned Category 1

- Accelerated approval were less frequently assigned category 1 evidence and were less often listed as preferred treatment options vs. regular approval
- Among the 21 withdrawn accelerated approval indications, 8 (40%) remained in the NCCN guidelines, with most having level 2A evidence ratings

Cliff ERS, Rome RS, Kesselheim AS, Rome BN. National Comprehensive Cancer Network Guideline Recommendations of Cancer Drugs With Accelerated Approval. *JAMA Netw Open*. 2023;6(11):e2343285. Published 2023 Nov 1. doi:10.1001/jamanetworkopen.2023.43285

NCCN Category 2A Category 2B Off-Label Off-Guidelines

"Most accelerated and regular approval drugs had low-quality evidence ratings but high levels of consensus among NCCN panelists"

- Category 2A: lower-level evidence, 85%+ support use
- Category 2B: lower-level evidence, 50-84% support use

- 2024 Systematic Review of Off-Label & Off-Guidelines in 165,000 US patients
  - 20% Off-Label & 5% Off-Guidelines
  - Lower PS, Later Line, Academic Hospital were associated factors
  - Ex: Nivo+Ipi in SCLC

Cliff ERS, Rome RS, Kesselheim AS, Rome BN. National Comprehensive Cancer Network Guideline Recommendations of Cancer Drugs With Accelerated Approval. *JAMA Netw Open*. 2023;6(11):e2343285. Published 2023 Nov 1. doi:10.1001/jamanetworkopen.2023.43285

NCCN Payer Relations. https://www.nccn.org/business-policy/business/payer-relations

Liu R, Wang L, Rizzo S, et al. Systematic analysis of off-label and off-guideline cancer therapy usage in a real-world cohort of 165,912 US patients. *Cell Rep Med*. 2024;5(3):101444. doi:10.1016/j.xcrm.2024.101444

CLINICAL DECISION SUPPORT

NCCN Guidelines

Creating best practices from disadvantages!

Disadvantages

- Complex to navigate
- No transparency on level of evidence
- Potential conflicts of interest
- No financial / cost consideration

DO YOUR RESEARCH

- ✓ Assess the underlying reference
- ✓ Critically appraise
  - ✓ Confounding factors
  - ✓ Immortal Time Bias
  - ✓ Confirmation Bias
- ✓ Discuss/Debate with colleagues
- ✓ Consider both direct and indirect costs to patient

Cliff ERS, Rome RS, Kesselheim AS, Rome BN. National Comprehensive Cancer Network Guideline Recommendations of Cancer Drugs With Accelerated Approval. *JAMA Netw Open*. 2023;6(11):e2343285. Published 2023 Nov 1. doi:10.1001/jamanetworkopen.2023.43285

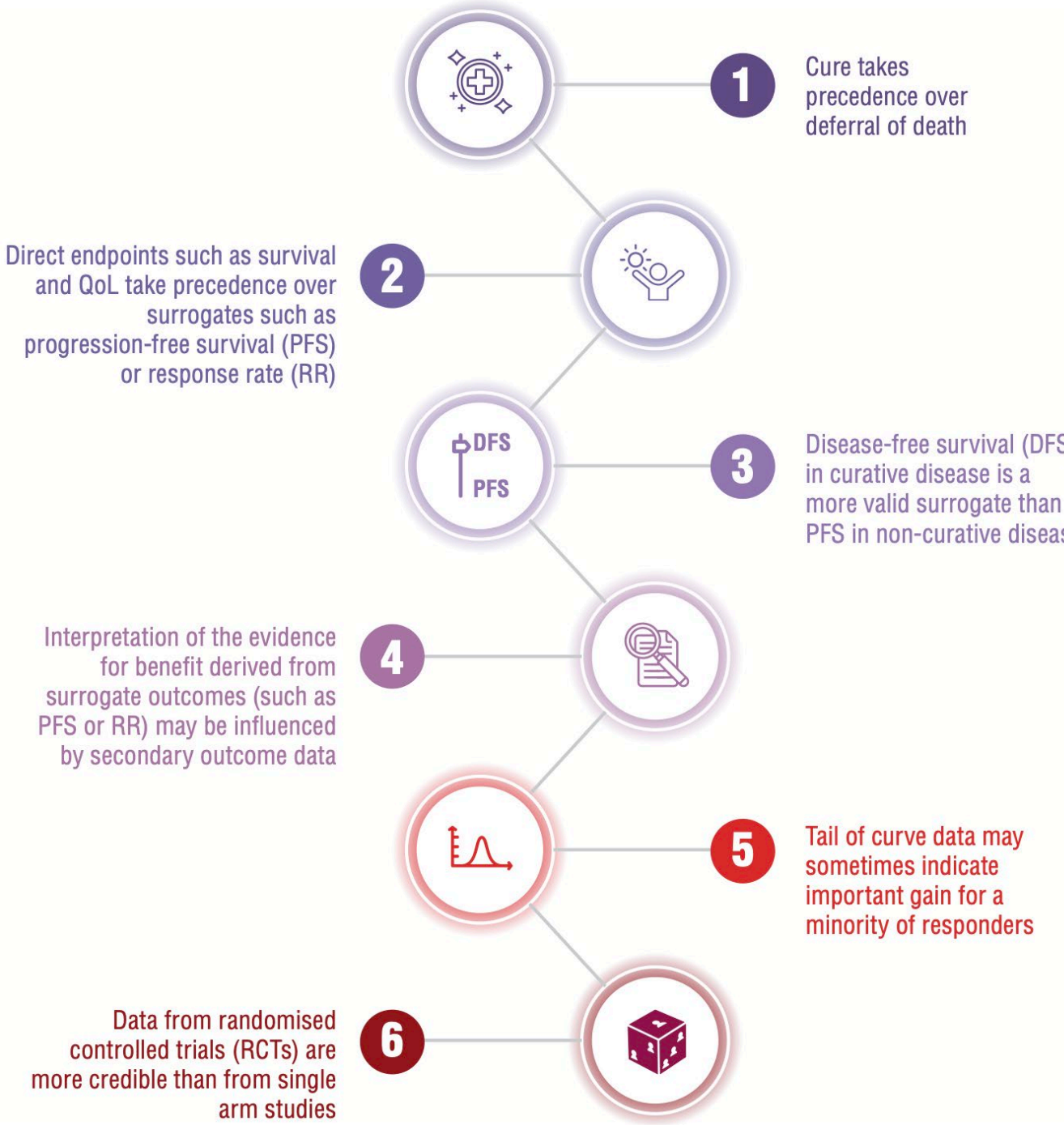
ESMO-MCBS (Magnitude of Benefit Scale)

Reduces bias in data interpretation and analysis and enhance critical appraisal of clinical trials

Reduces hype

Provides robust validation with strict adherence to standards for “accountability for reasonableness”

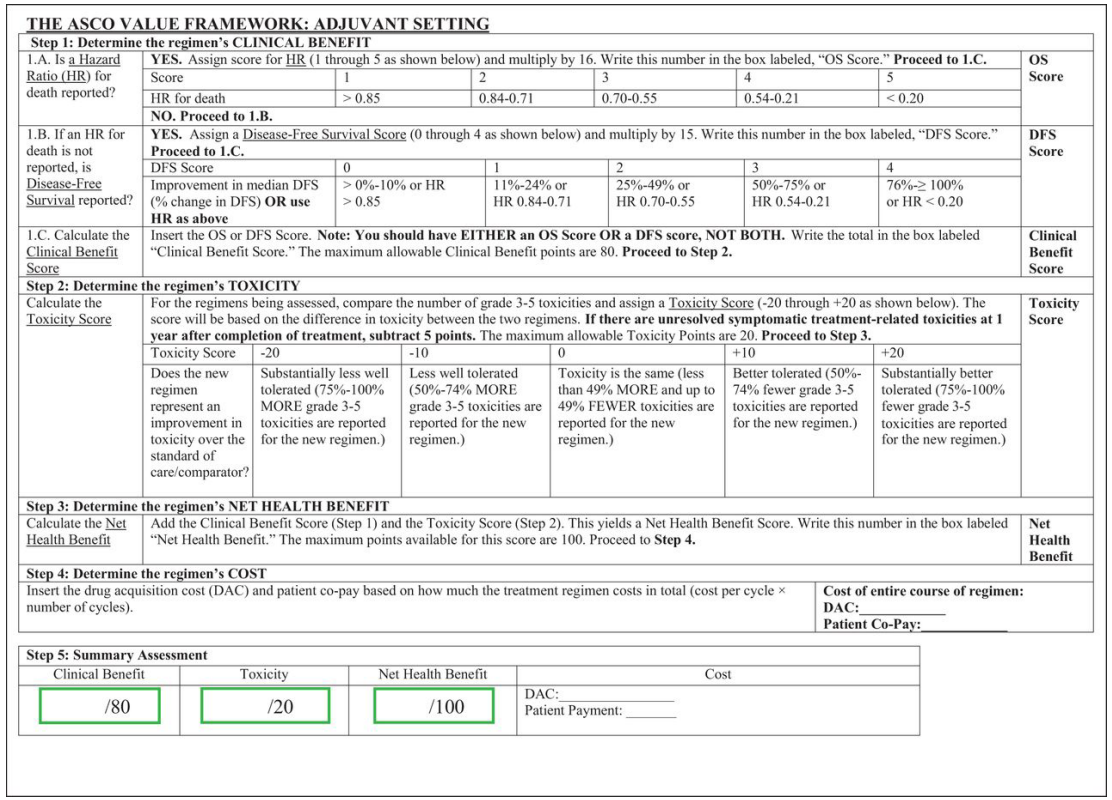
Provides reliable and fair evaluation of benefit to assist in cancer planning, value-based priority-setting and impact-oriented resource allocation decisions



Understanding ESMO-MCBS? Accessed June 30, 2026. https://dam.esmo.org/image/upload/v1765891590/ESMO-MCBS-Booklet_oohqcy.pdf

ASCO Value-based Framework

- A value-based decision support tool for providers and patients to assess:
  - Clinical benefit
  - Toxicity
- Objective, weighted scoring system by treatment intent
  - Net health benefit (NHB)
- Drug Cost



THE ASCO VALUE FRAMEWORK: ADJUVANT SETTING

Step 1: Determine the regimen's CLINICAL BENEFIT

1.A. Is a Hazard Ratio (HR) for death reported?	**YES.** Assign score for HR (1 through 5 as shown below) and multiply by 16. Write this number in the box labeled, "OS Score." **Proceed to 1.C.**					**OS Score**
	Score	1	2	3	4	5
	HR for death	> 0.85	0.84-0.71	0.70-0.55	0.54-0.21	< 0.20
	NO. Proceed to 1.B.					
1.B. If an HR for death is not reported, is Disease-Free Survival reported?	**YES.** Assign a Disease-Free Survival Score (0 through 4 as shown below) and multiply by 15. Write this number in the box labeled, "DFS Score." **Proceed to 1.C.**					**DFS Score**
	DFS Score	0	1	2	3	4
	Improvement in median DFS (% change in DFS) **OR use HR as above**	> 0%-10% or HR > 0.85	11%-24% or HR 0.84-0.71	25%-49% or HR 0.70-0.55	50%-75% or HR 0.54-0.21	76%-≥ 100% or HR < 0.20
1.C. Calculate the Clinical Benefit Score	Insert the OS or DFS Score. **Note: You should have EITHER an OS Score OR a DFS score, NOT BOTH.** Write the total in the box labeled "Clinical Benefit Score." The maximum allowable Clinical Benefit points are 80. **Proceed to Step 2.**					**Clinical Benefit Score**

Step 2: Determine the regimen's TOXICITY

Calculate the Toxicity Score	For the regimens being assessed, compare the number of grade 3-5 toxicities and assign a Toxicity Score (-20 through +20 as shown below). The score will be based on the difference in toxicity between the two regimens. **If there are unresolved symptomatic treatment-related toxicities at 1 year after completion of treatment, subtract 5 points.** The maximum allowable Toxicity Points are 20. **Proceed to Step 3.**					**Toxicity Score**
	Toxicity Score	-20	-10	0	+10	+20
	Does the new regimen represent an improvement in toxicity over the standard of care/comparator?	Substantially less well tolerated (75%-100% MORE grade 3-5 toxicities are reported for the new regimen.)	Less well tolerated (50%-74% MORE grade 3-5 toxicities are reported for the new regimen.)	Toxicity is the same (less than 49% MORE and up to 49% FEWER toxicities are reported for the new regimen.)	Better tolerated (50%-74% fewer grade 3-5 toxicities are reported for the new regimen.)	Substantially better tolerated (75%-100% fewer grade 3-5 toxicities are reported for the new regimen.)

Step 3: Determine the regimen's NET HEALTH BENEFIT

Calculate the Net Health Benefit	Add the Clinical Benefit Score (Step 1) and the Toxicity Score (Step 2). This yields a Net Health Benefit Score. Write this number in the box labeled "Net Health Benefit." The maximum points available for this score are 100. Proceed to **Step 4.**	**Net Health Benefit**

Step 4: Determine the regimen's COST

Insert the drug acquisition cost (DAC) and patient co-pay based on how much the treatment regimen costs in total (cost per cycle × number of cycles).	**Cost of entire course of regimen:** **DAC:**_____ **Patient Co-Pay:**_____

Step 5: Summary Assessment

Clinical Benefit	Toxicity	Net Health Benefit	Cost
/80	/20	/100	DAC:_____ Patient Payment: _____

Measure	Score/Result
Clinical benefit score (maximum, 180 points)	
Improvement ([12.3 − 10.3]/10.3 = 19%)	
OS score (1 × 16)	16
Toxicity score (maximum, 20 points)	
Carboplatin plus paclitaxel (control)	15 (grade 3 to 5)
Bevacizumab, carboplatin, and paclitaxel	22 (grade 3 to 5)
Toxicity score ([22 − 15]/15 = 46%)	0
Bonus points (maximum, 30 points)	
Palliation	0
Treatment-free interval	0
Total bonus points	0
Net health benefit (maximum, 130 points)	16
Drug cost (monthly)	
Drug acquisition cost	$11,907.87
Patient copay	Calculated per patient

Abbreviation: OS, overall survival.

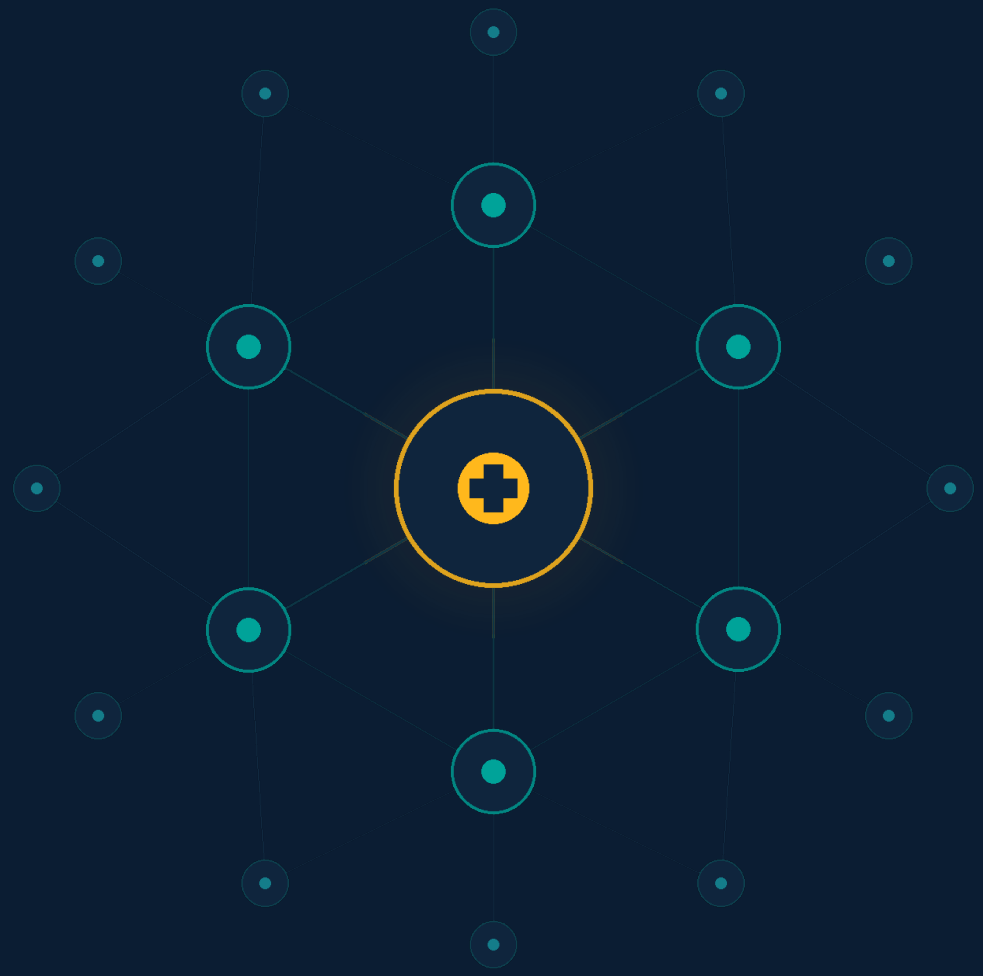
Schnipper LE, Davidson NE, Wollins DS, et al. American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options. *Journal of Clinical Oncology*. 2015;33(23):2563-2577. doi:https://doi.org/10.1200/jco.2015.61.6706

KAISER PERMANENTE®

Provide high-quality, affordable health care services and to improve the health of our members and the communities we serve.

What is an Integrated Delivery Network (IDN)?

An Integrated Delivery Network (IDN) is an organization that owns and operates a network of healthcare facilities, designed to improve quality of care, efficiency, and cost by providing a wide variety of coordinated care services under one system.



FACILITIES WITHIN AN IDN

- Hospitals
- Health Clinics
- Imaging Centers
- Physician Groups
- Ambulatory Surgery Centers
- Pharmacies

WHY IDNs MATTER

Coordinated Care
Shared information and resources across all facilities in the network

Reduced Leakage
Patients' needs met in-network, preventing revenue loss

Purchasing Power
Leverage market influence for competitive supply chain pricing

https://www.definitivehc.com/resources/glossary/integrated-delivery-network

Levels of IDN Integration

Integrated Delivery Networks | From Regional Hospital Systems to Full Strategic Integration

SYSTEM II

Horizontal Integration

Regional or national multi-hospital systems. Primarily owns and manages hospitals with some additional care facilities.

Government | State-owned | Investor-owned

EXAMPLE

NYC Health + Hospitals

12 hospital locations, FQHCs, physician groups, imaging centers

SYSTEM III

Vertical Integration

Cradle-to-grave healthcare services. Wide variety of care facilities sharing information and resources equally across the system.

Academic | Catholic | Community

EXAMPLE

HCA Healthcare

214 hospital locations, physician groups, urgent care, imaging, home health, SNFs

SYSTEM IV

Strategic Integration

Vertically integrated with exceptional strategy and organization. Centralized admin, purchasing, and distribution aligned across all facilities.

Centralized | Aligned | Coordinated

EXAMPLE

Kaiser Permanente

43 hospital locations, ASCs, hospices, imaging, retail clinics, urgent care

INCREASING INTEGRATION →

https://www.definitivehc.com/resources/glossary/integrated-delivery-network

Top 10 U.S. Health Systems by Annual Revenue

Becker's Hospital Review | FY 2025 Data

#1 HEALTH SYSTEM

Kaiser Permanente

$127.7B

Annual Revenue (FY 2025)

1.7×	larger than #2 (HCA)
12.9M	members served
#1	integrated delivery model

Source: Becker's Hospital Review, April 2026 | Most results for 12 months ending Dec. 31, 2025

How we work

"Our model puts the patient, the doctor, the hospital, the employer, and the insurance company all on the same side of the ledger. They all benefit by the patient remaining well."

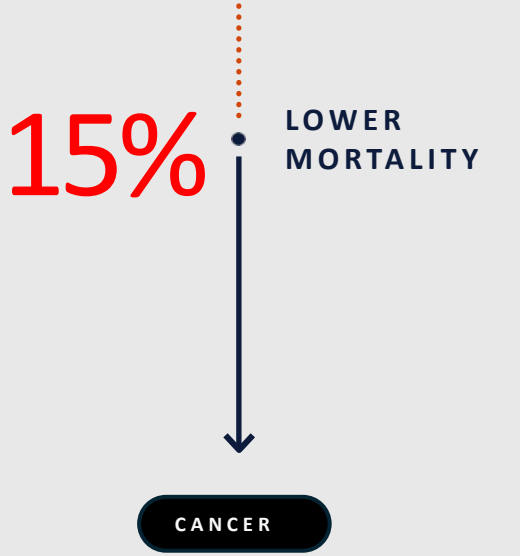
Sydney R. Garfield, MD
Kaiser Permanente Founding Physician, April 4, 1975

12.9M
MEMBERS

600+
MEDICAL OFFICES

40+
HOSPITALS

10
STATES

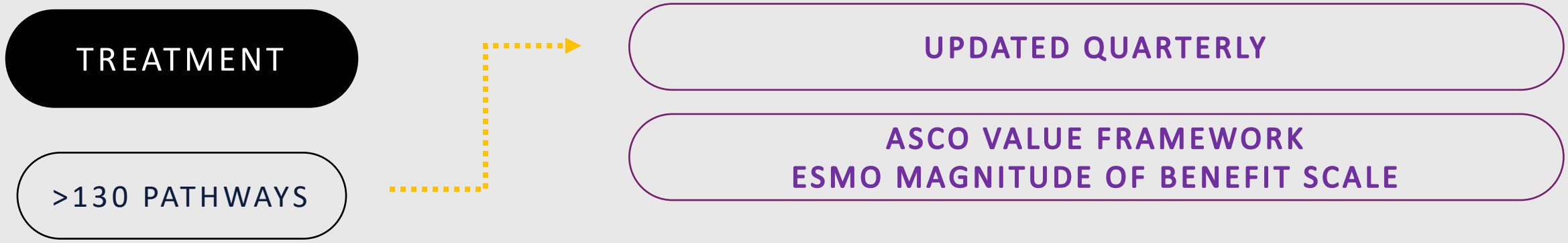


Member retention that's nearly double the industry average

KAISER PERMANENTE®

Cancer Care Reimagined

We treat one type of cancer – Yours.



https://international.kaiserpermanente.org/blog/2021/04/01/cancer-care-reimagined/

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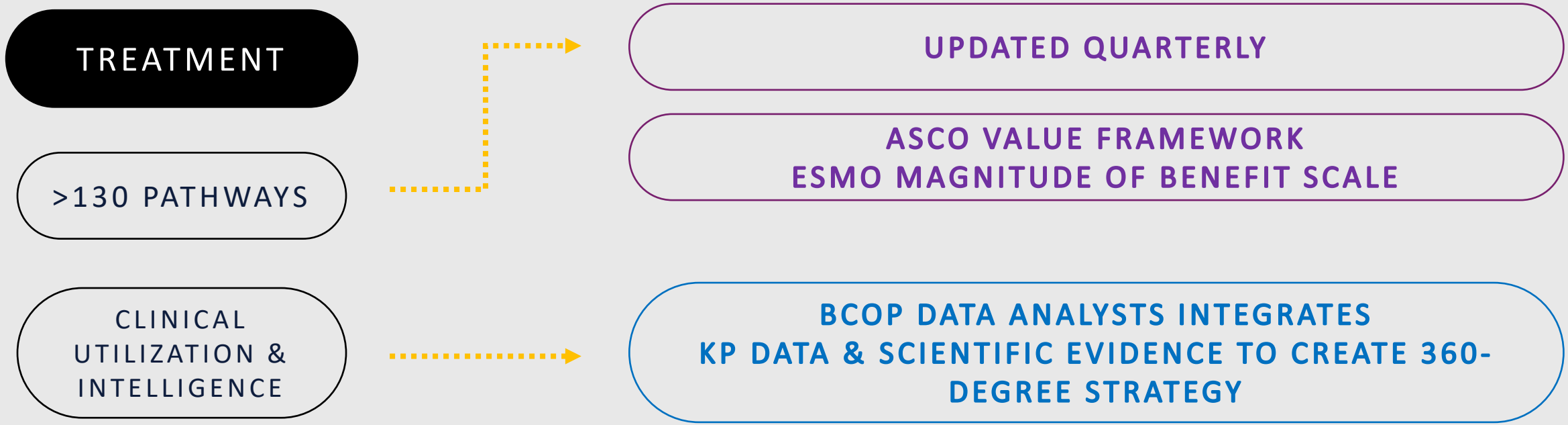
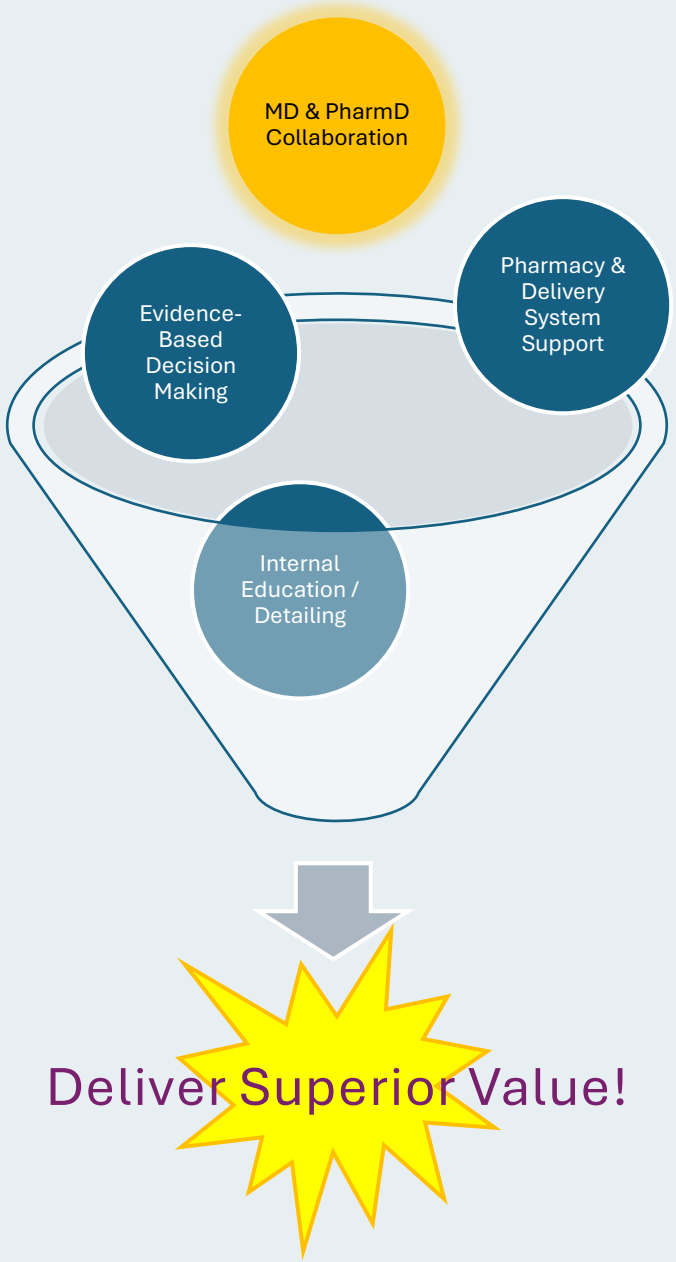
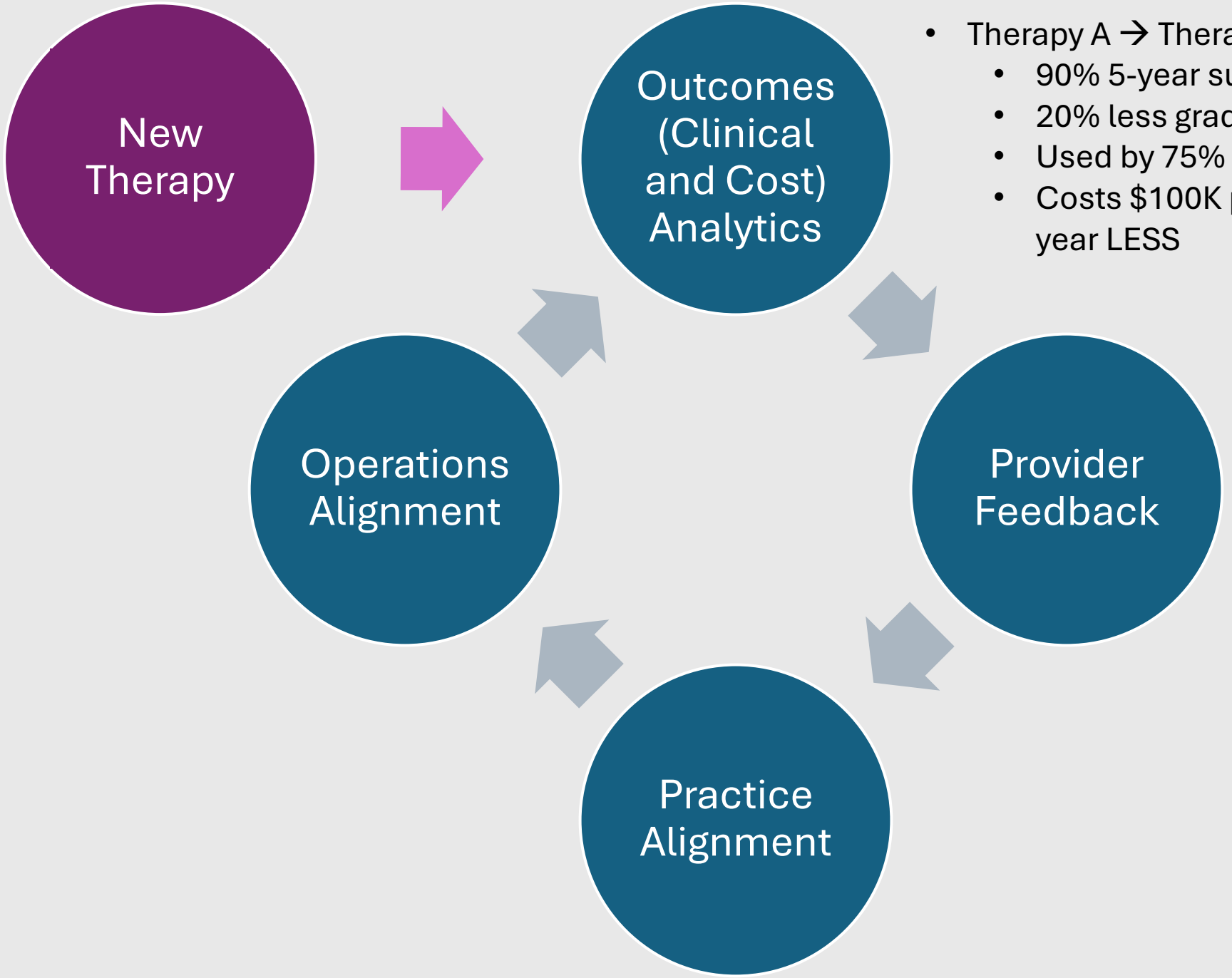


https://international.kaiserpermanente.org/blog/2021/04/01/cancer-care-reimagined/

BCOP Data Analysts

- **Dedicated Pharmacy Specialists**
  - Coding/Data Analytics
  - Generate KP RWE datasets
  - Validate therapy and sequencing outcomes
- **Provider Collaboration**
  - Partnership promoting quality and equitable patient-centered care
- **Evidence-Based Decision Making**
  - Initiatives are based on clinical and scientific evidence
- **Longitudinal Care Delivery**
  - Align systems to oncology utilization management goals





- Therapy A → Therapy B (vs. Therapy A+B):
  - 90% 5-year survival
  - 20% less grade 3+ ADEs (that matter)
  - Used by 75% of prescribers
  - Costs $100K per treated patient per year LESS

Cancer Care Reimagined

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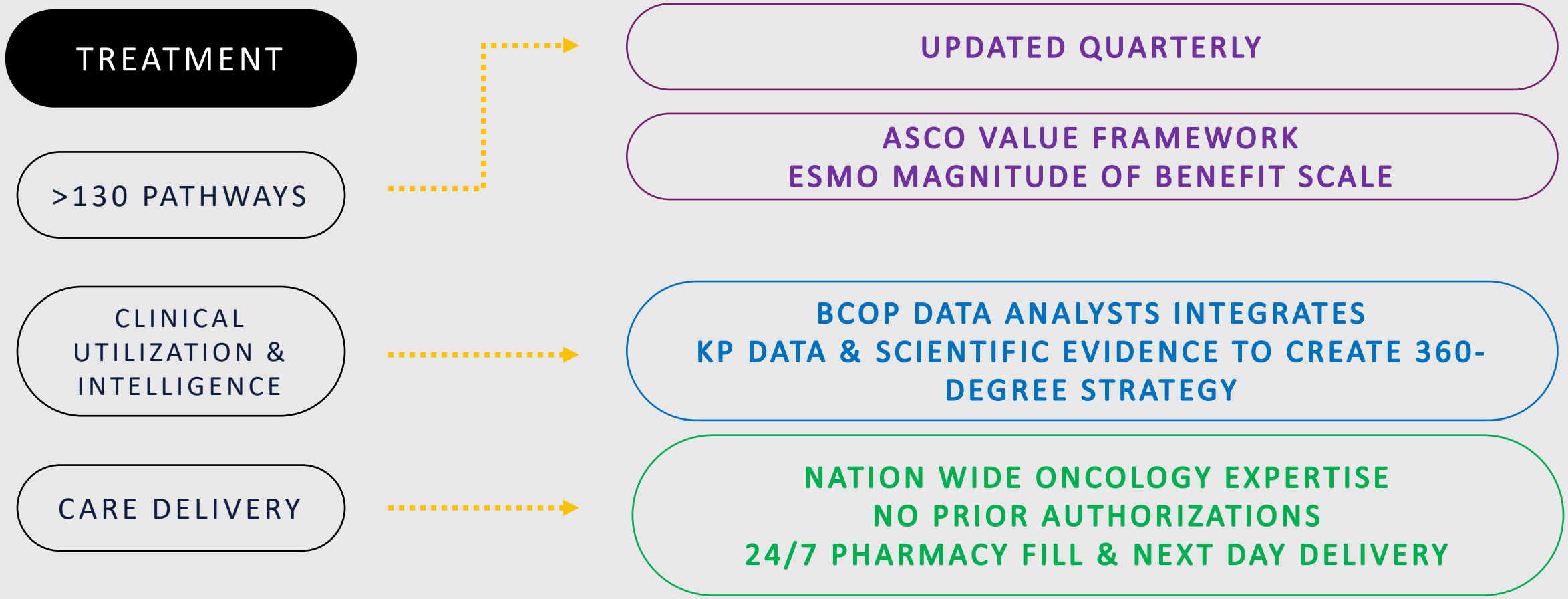


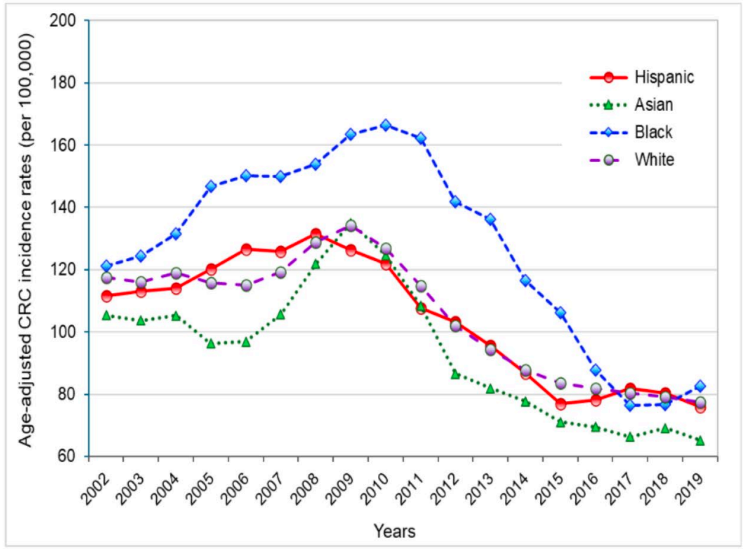
https://international.kaiserpermanente.org/blog/2021/04/01/cancer-care-reimagined/

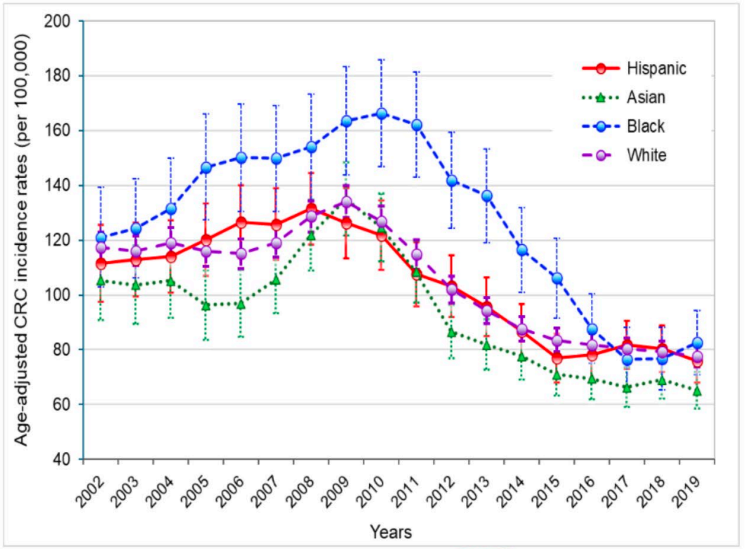
Integrated Oncology Care Architecture

One Patient. One Record. One Team.

- SCREENING
- PRIMARY CARE
- EHR
- SURGICAL COORDINATION

KEY FINDINGS





Findings consistent with prevention from pre-cancerous polyp removal. Increase in early-stage tumors, decrease in late-stage tumors

@DDWMeeting | #DDW2025

DDW2025
Digestive Disease Week®
MAY 3–6, 2025 | SAN DIEGO, CA
EXHIBIT DATES: MAY 4–6, 2025

Doubeni CA, Corley DA, Jensen CD, et al. Fecal Immunochemical Test Screening and Risk of Colorectal Cancer Death. *JAMA Netw Open.* 2024;7(7):e2423671. doi:10.1001/jamanetworkopen.2024.23671

5-Year Breast, Colorectal, and Lung Survival at KP vs. SEER (Diagnosed 2004-2013)

Pooled 5-year relative survival, KP vs. SEER (2004–2013)

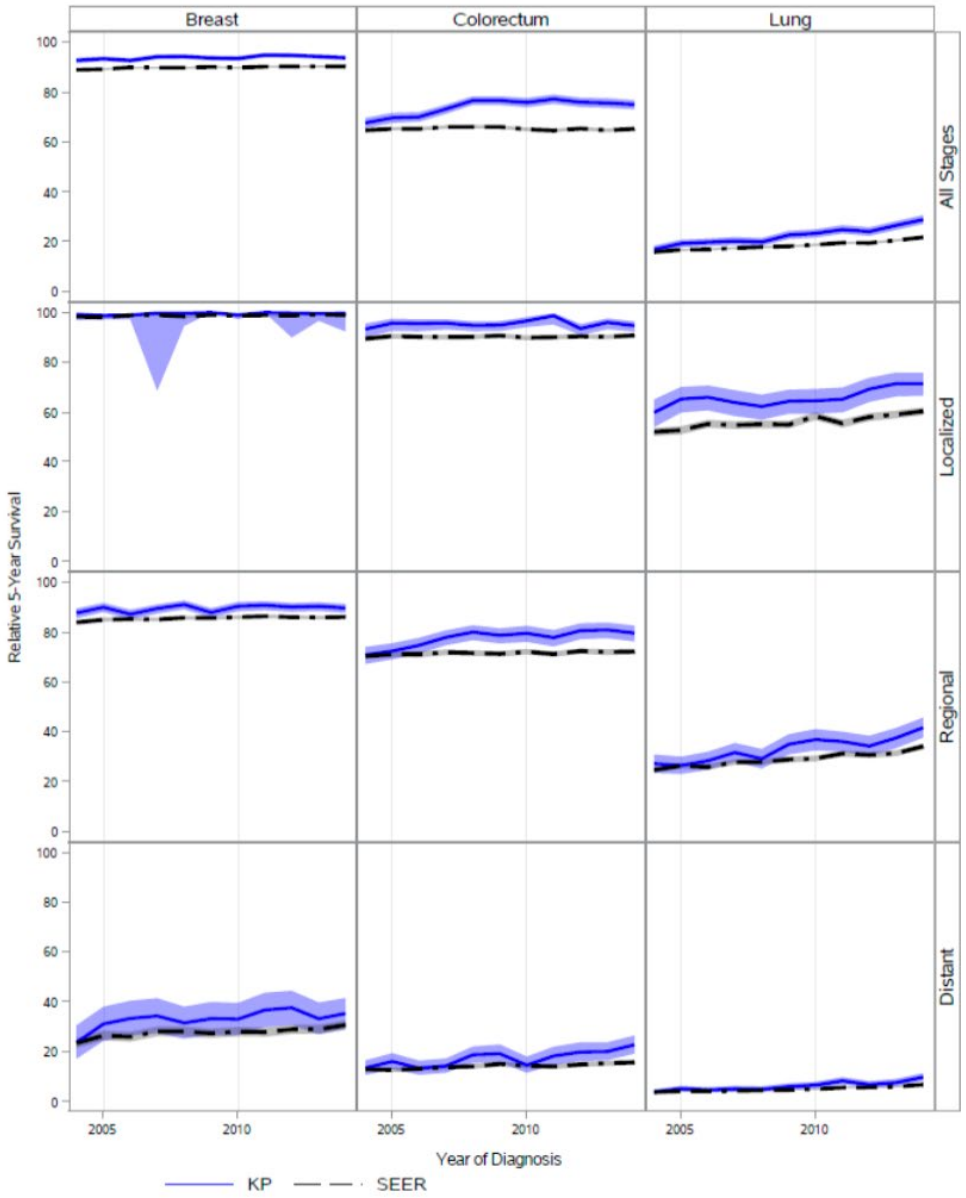
Inverse-variance weighted fixed-effect meta-analysis | All race/ethnicity, all stages, n = 10 years

Cancer site	KP (95% CI)	I² KP	SEER (95% CI)	I² SEER	Diff, pp (95% CI)
Breast	94.4 (94.1–94.7)	79%	90.0 (89.8–90.1)	82%	+4.4 (+4.1 to +4.7)
Colorectal	74.9 (74.3–75.5)	93%	65.4 (65.1–65.6)	67%	+9.5 (+8.9 to +10.1)
Lung	22.5 (22.0–23.0)	92%	18.0 (17.8–18.1)	98%	+4.5 (+4.0 to +5.1)

SE derived from published 95% CIs: SE = (upper – lower) / (2 × 1.96). Diff CI from independent SEs. I² = Cochran's Q-based heterogeneity; high values reflect temporal trends in survival improvement across the pooled decade. Source: Hahn et al., *Perm J* 2023;27:23.021, Supplemental Table 2.

Hahn EE, Ritzwoller DP, Munoz-Plaza CE, Gander J, Kushi LH, McMullen C, Oshiro C, Roblin DW, Wernli KJ, Staab J. Incidence and Survival for Patients Diagnosed With Breast, Colorectal, and Lung Cancer in an Integrated System. Perm J. 2023 Dec 15;27(4):129-135. doi: 10.7812/TPP/23.021. Epub 2023 Sep 19. PMID: 37724894; PMCID: PMC10723094.

Incidence and Survival for Patients Diagnosed With Breast, Colorectal, and Lung Cancer in an Integrated



: Five-year relative survival for breast, colorectal, and lung cancers diagnosed between January d December 31, 2013 for Kaiser Permanente members compared to Surveillance, Epidemiology, a ults (SEER) by SEER stage.**

approaches 100% for localized breast cancer (demonstrated by the Kaiser Permanente and SEER survival lines), any small variation produces a large confidence

My Learnings

- Demand higher levels of evidence – Your patients deserve it
- Using population data for a patient-level decision is tricky
- Keep confirmation bias at bay
- The Hype is Real: Newest is not always the best and that’s OK!
- How do we best begin a different type of partnership?

THANK YOU!

TIMOTHY MOK, PHARMD, BCOP, BCPS