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Introduction to Comparative Effectiveness and Patient-Centered Outcomes Research

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Overview

Session 1

- **Definitions**
- **Rationale**
- **Principles**

Session 2

- **Basic methods**

CER: Comparative Effectiveness Research

PCOR: Patient-Centered Outcomes Research

RWE: Real-World Evidence

Comparative Effectiveness Research (CER)

- Patient Centered Outcomes Research Institute (2010) pcori.org
- Aim: to inform healthcare decisions by providing evidence on the benefits and harms of different alternatives
- CER compares the effectiveness of two or more interventions or approaches to health care, examining their risks and benefits
- CER findings assist clinicians, patients, and other stakeholders in making informed decisions that improve health care
- It can both validate a particular intervention and identify which treatments best meet a certain population's needs

Difference between **efficacy** & **effectiveness**

Efficacy vs Effectiveness

Efficacy

Performance of an intervention under ideal circumstances

CAN it work?

Effectiveness

Performance of an intervention in the ‘real-world’, in the community

DOES it work?

Community Effectiveness

Efficacy x

Access x

Appropriate diagnosis x

Appropriate/actual prescription x

Adherence to treatment

Community Effectiveness

	Efficacy	Access	Dx	Rx	Adherence	**EFFECTIVENESS**
Intervention A	**48%**	80%	85%	85%	70%	**19%**

Community Effectiveness

	Efficacy	Access	Dx	Rx	Adherence	**EFFECTIVENESS**
Intervention A	**48%**	80%	85%	85%	70%	**19%**
New Intervention	**60%**	80%	85%	85%	70%	**24%**

Community Effectiveness

	Efficacy	Access	Dx	Rx	Adherence	**EFFECTIVENESS**
Intervention A	**48%**	80%	85%	85%	70%	**19%**
New Intervention	**60%**	80%	85%	85%	70%	**24%**
Intervention A + change in other factors	**48%**	90%	90%	90%	80%	**28%**

Comparative Effectiveness Research and Real-World Evidence

Effectiveness: what happens in the "real world" vs. in a highly controlled study environment

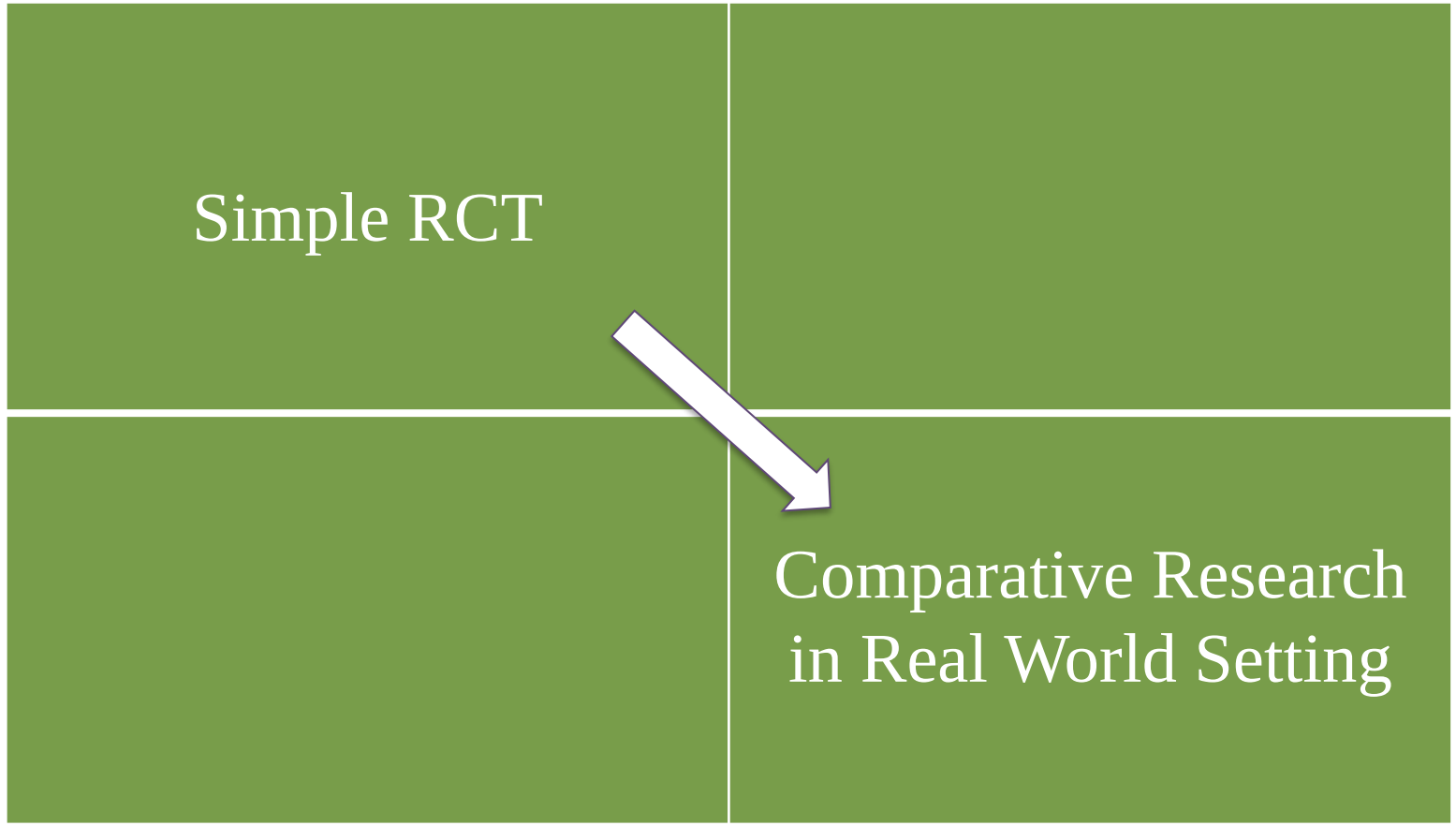
RWE: Real-world evidence

Comparative: New interventions developed at exponential rates, impossible to have trials with head-to-head comparisons

Compare available alternatives with respect to:

- **Value: Benefits vs. Harms/Costs**
- **Applicability to different populations**
- **Feasibility**

Two Dimensions to CER: Effectiveness & Comparisons



Efficacy

Effectiveness

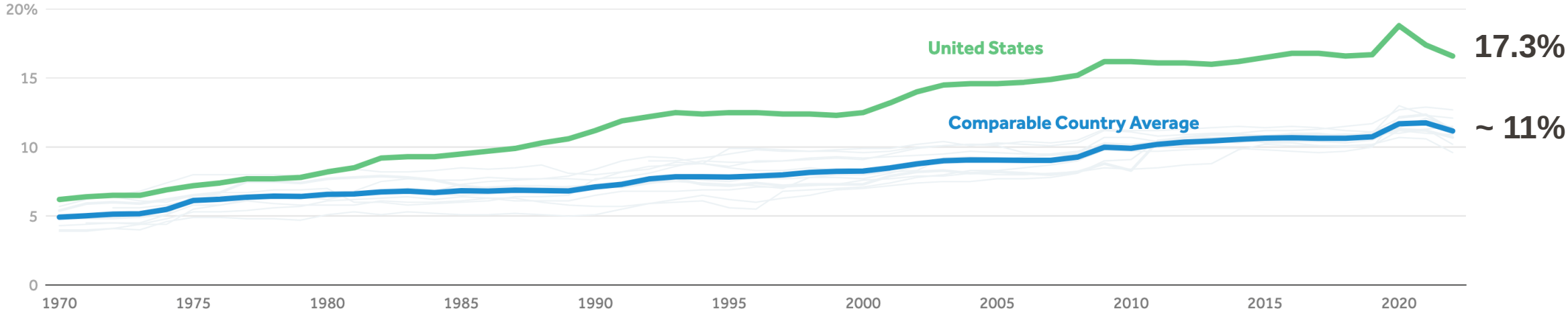
Placebo
Single drug comparator

Real-world comparisons or usual care

Bird’s Eye View

Health spending as a share of GDP in the U.S. declined in 2022 as growth in the economy outpaced health spending growth

Health expenditures as percent of GDP, 1970-2022



Notes: Data from 2022 for Australia, Belgium, France, Japan, Switzerland, and the U.S. are estimated. Data from 2022 for Austria, Canada, Germany, the Netherlands, Sweden and the United Kingdom are provisional. Data for Australia is unavailable in 1970. Data for France from before 1990 is not available. Data from Germany prior to 1992 refers to West Germany. Data for Germany is not available for 1991. Data for the Netherlands is unavailable in 1970 and 1971.

Source: KFF analysis of OECD data • Get the data • PNG

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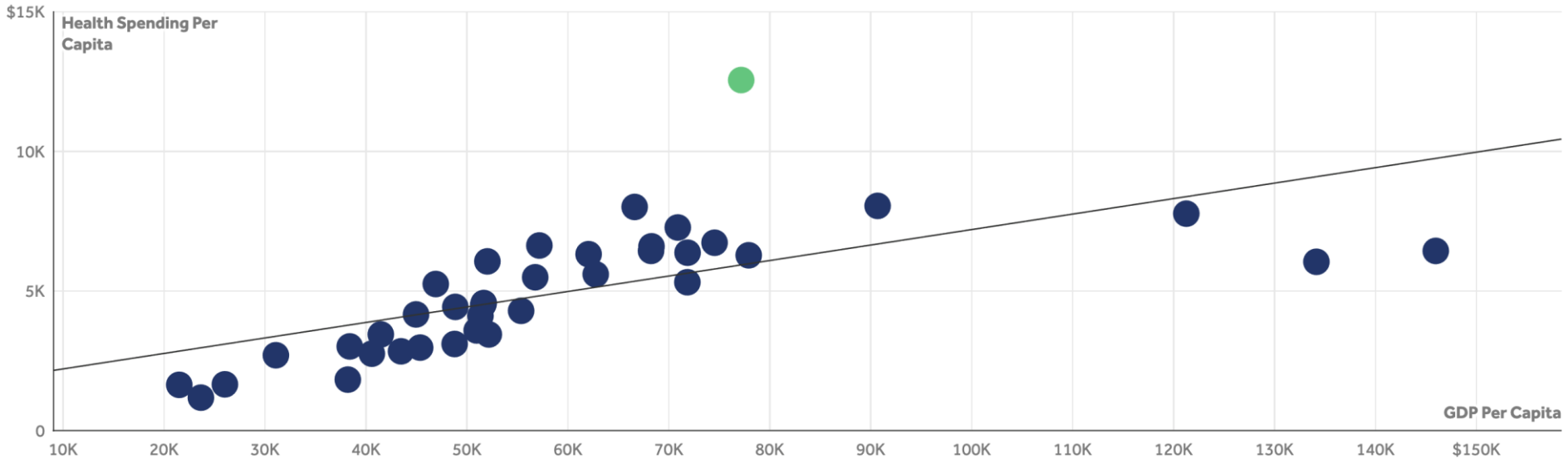
Health System Tracker

Relative to the size of its economy, the U.S. spends a greater amount on health care than other high-income nations

GDP per capita USA # 8

GDP per capita and health consumption spending per capita, U.S. dollars, 2022 (current prices and PPP adjusted)



Notes: Health spending per capita for Czech Republic, Denmark, France, and the Slovak Republic are estimated. For all other countries except the United States, health spending per capita is provisional. Health consumption does not include investments in structures, equipment, or research.

Source: KFF analysis of OECD data • Get the data • PNG

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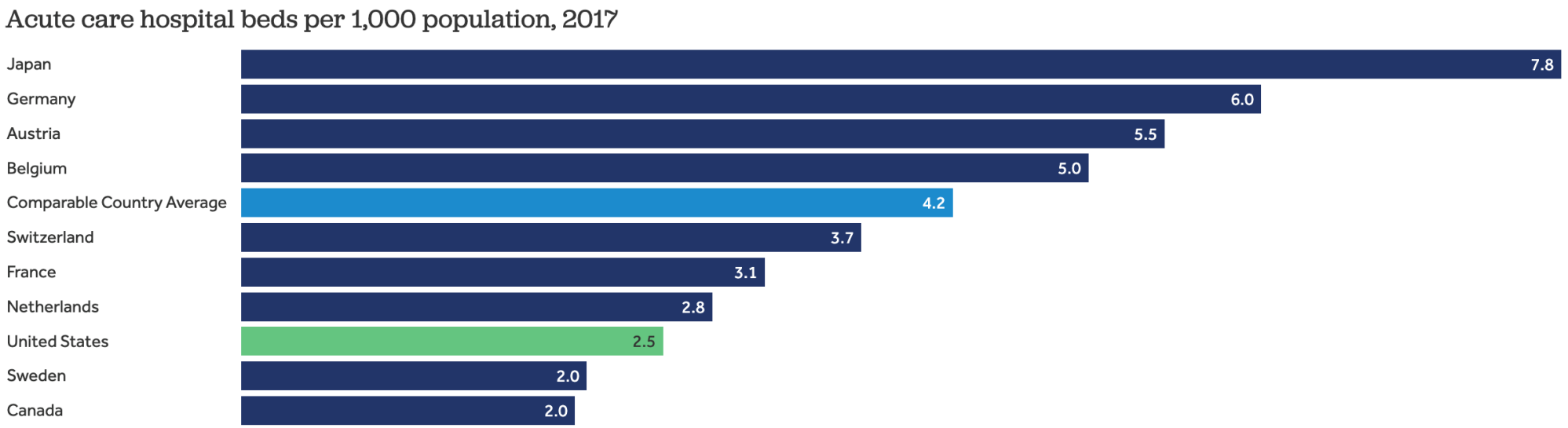
The U.S. has fewer acute care hospital beds per capita than many comparably wealthy countries



Source: Kaiser Family Foundation Analysis of OECD Data • Get the data • PNG

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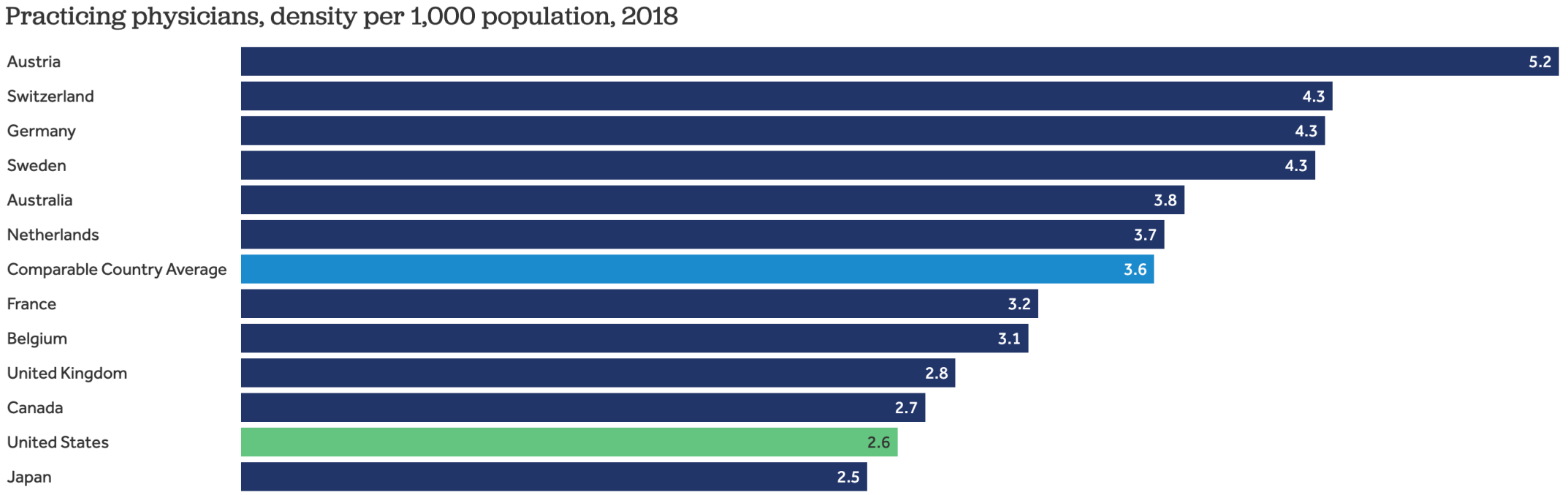
Health System Tracker

There are fewer physicians per capita in the U.S. than there are in most comparable countries



Notes: Data for Sweden is from 2017.

Source: Kaiser Family Foundation Analysis of OECD Data • Get the data • PNG

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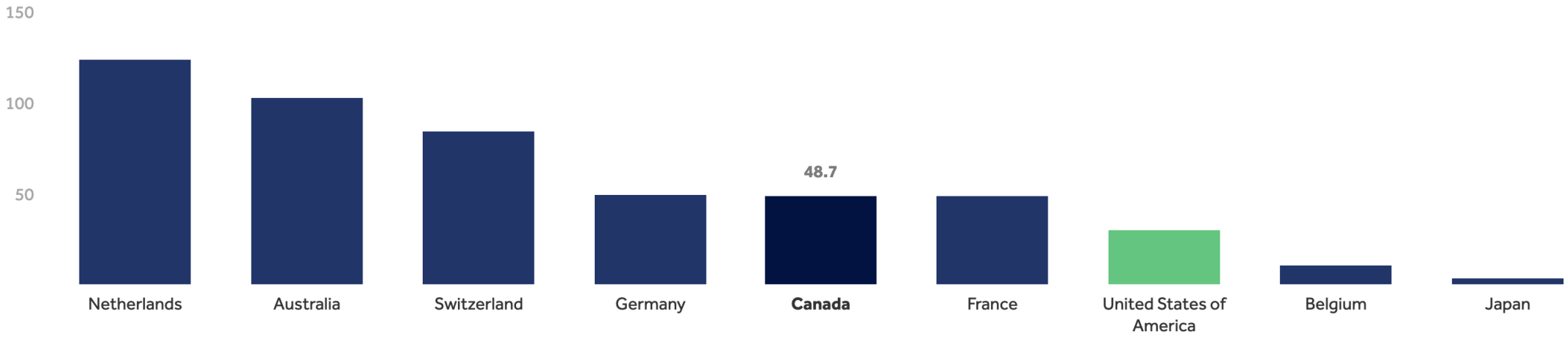
Health System Tracker

The U.S. has fewer psychologists and psychiatrists working in mental health than most comparable countries

Number of professionals working in mental health per 100,000 population, 2016

Psychologists | Psychiatrists | Social workers | Nurses



Source: Kaiser Family Foundation analysis of WHO Global Health Observatory • Get the data • PNG

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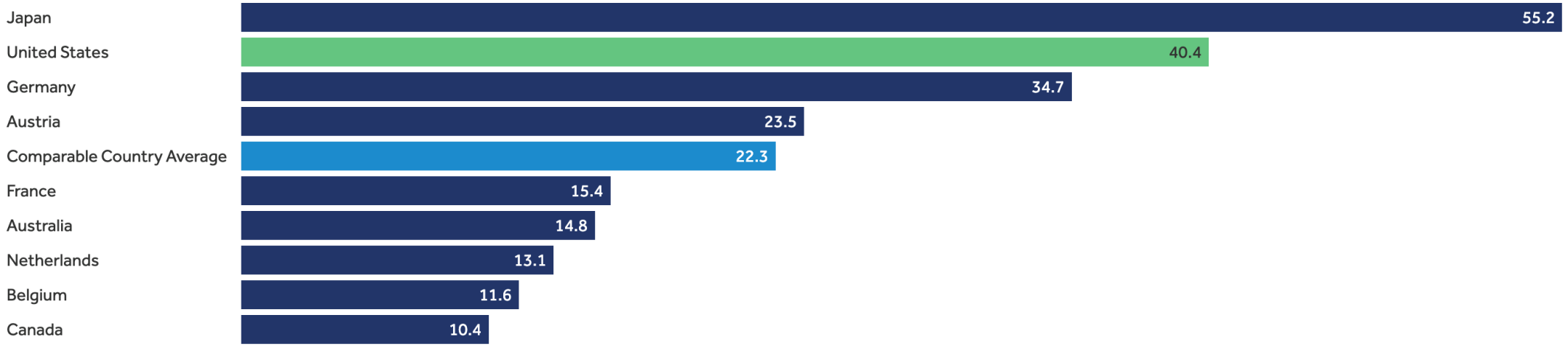
On average, the U.S. has around two times as many MRI machines per capita than comparable countries

Magnetic Resonance Imaging (MRI) units per million population, 2019



Notes: Data for Austria and the Netherlands are from 2018. Data for Germany and Japan are from 2017.

Source: Kaiser Family Foundation Analysis of OECD Data • Get the data • PNG

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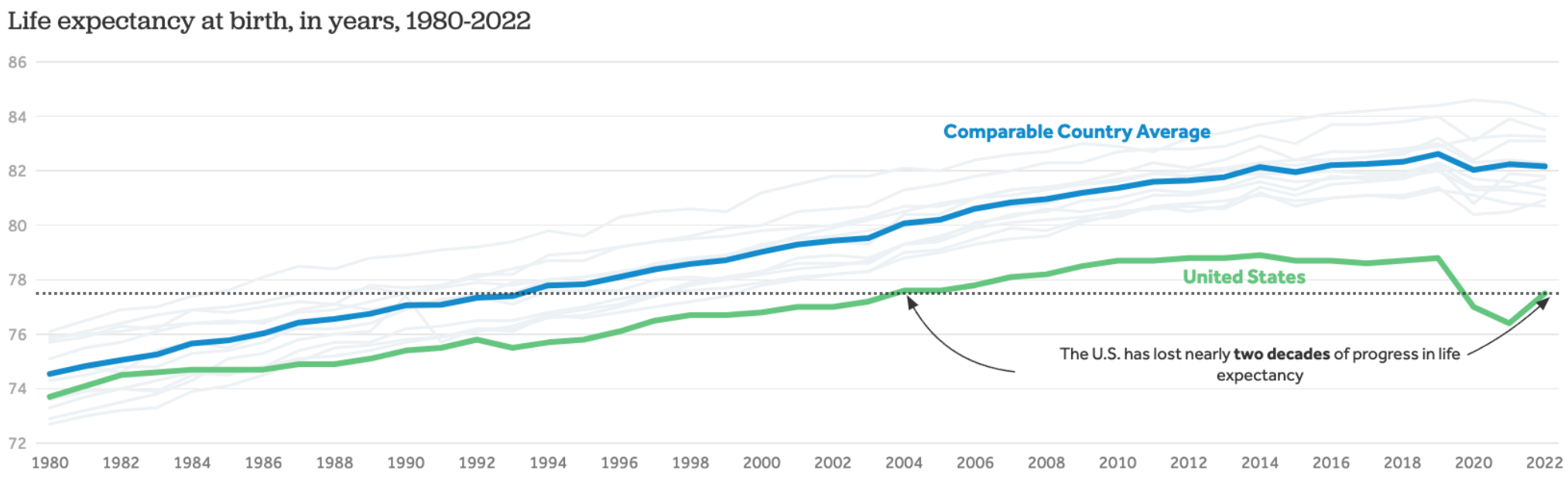
Health System Tracker

Life Expectancy at Birth



Notes: Comparable countries include Australia, Austria, Belgium, Canada, France, Germany, Japan, the Netherlands, Sweden, Switzerland, and the U.K. See Methods section of "How does U.S. life expectancy compare to other countries?"

Source: KFF analysis of CDC, OECD, Australian Bureau of Statistics, Japanese Ministry of Health, Labour, and Welfare, Statistics Canada, and U.K. Office for National Statistics data • Get the data • PNG

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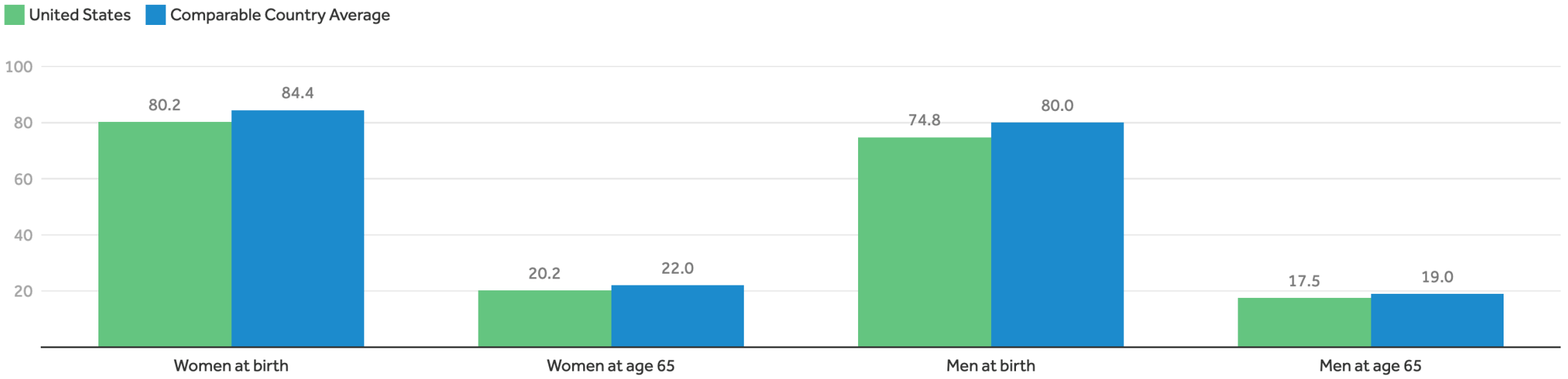
Life expectancy at given age, in years, 2022



Notes: In the chart above, comparable countries include Australia, Austria, Belgium, Canada, France, Germany, Japan, the Netherlands, Sweden, Switzerland, and the U.K. See Methods section of "How does U.S. life expectancy compare to other countries?"

Source: KFF analysis of data from national health and statistics departments. See Methods section of "How does U.S. life expectancy compare to other countries?" for all sources • Get the data • PNG

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Life expectancy and per capita healthcare spending (PPP adjusted), 2022

Country	Life expectancy ▲	Health spending, per capita PPP adjusted
United States	**77.5**	**$12,555**
Germany	80.7	$8,011
United Kingdom	80.9	$5,493
Austria	81.1	$7,275
Canada	81.3	$6,319
Netherlands	81.7	$6,729
Belgium	81.8	$6,600
Comparable Country Average	**82.2**	**$6,651**
France	82.3	$6,630
Sweden	83.1	$6,438
Australia	83.3	$6,372
Switzerland	83.5	$8,049
Japan	84.1	$5,251

Notes: Comparable countries include: Australia, Austria, Belgium, Canada, France, Germany, Japan, the Netherlands, Sweden, Switzerland, and the U.K. See Methods section of "How does U.S. life expectancy compare to other countries?"

Source: KFF analysis of CDC, OECD, Australian Bureau of Statistics, Japanese Ministry of Health, Labour, and Welfare, Statistics Canada, and U.K. Office of National Statistics data • Get the data • PNG

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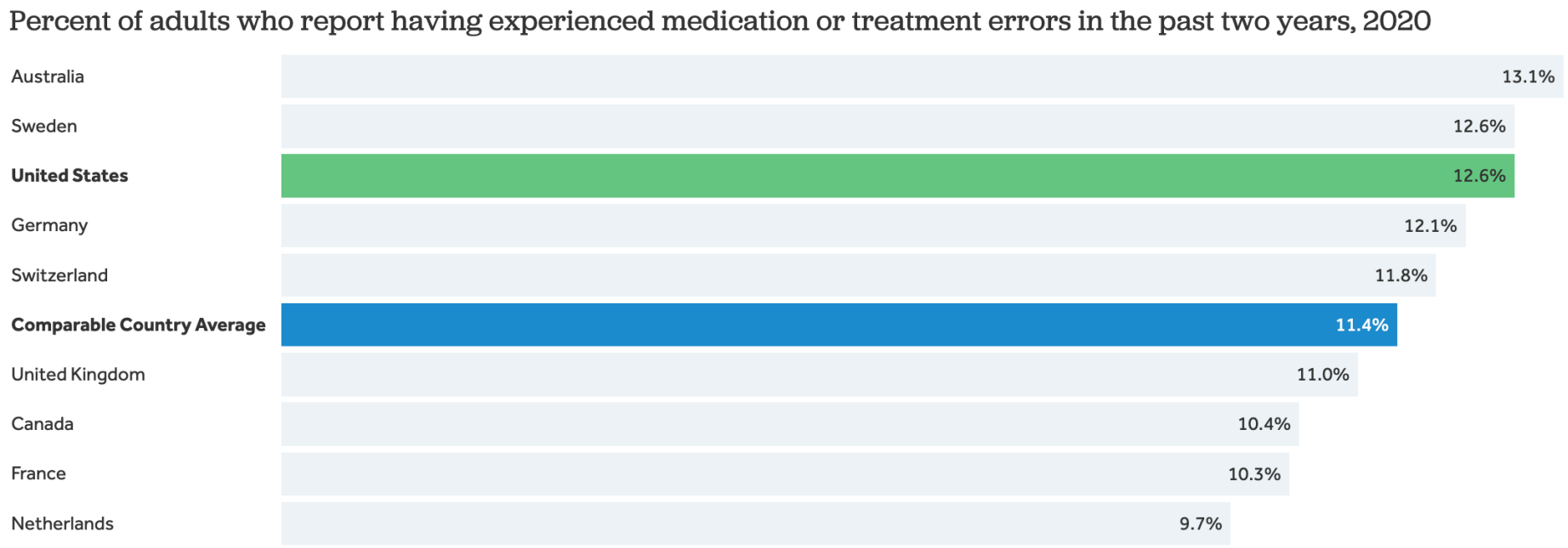
The U.S. has higher rates of reported medication and treatment errors than most comparable countries



Note: Share responding that in the past 2 years, they had been given the wrong medication or wrong dose by a doctor, nurse, hospital or pharmacist, or if there a time they thought a medical mistake was made in their treatment.

Source: Unpublished data from 2020 Commonwealth Fund International Health Policy Survey • Get the data • PNG

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Post-operative complications — such as pulmonary embolism or deep vein thrombosis — are more common in the U.S. than most peer countries

Crude rate per 100,000 hospital discharges for post-operative pulmonary embolism and deep vein thrombosis after hip or knee surgery, ages 15 and older, 2018

Note: Data is unlinked.

Source: KFF analysis of OECD data • Get the data • PNG

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How Do we Do with Cancer?

Original Investigation

May 27, 2022

Comparison of Cancer-Related Spending and Mortality Rates in the US vs 21 High-Income Countries

Ryan D. Chow, PhD[1]; Elizabeth H. Bradley, PhD[2]; Cary P. Gross, MD[3,4]

» Author Affiliations | Article Information

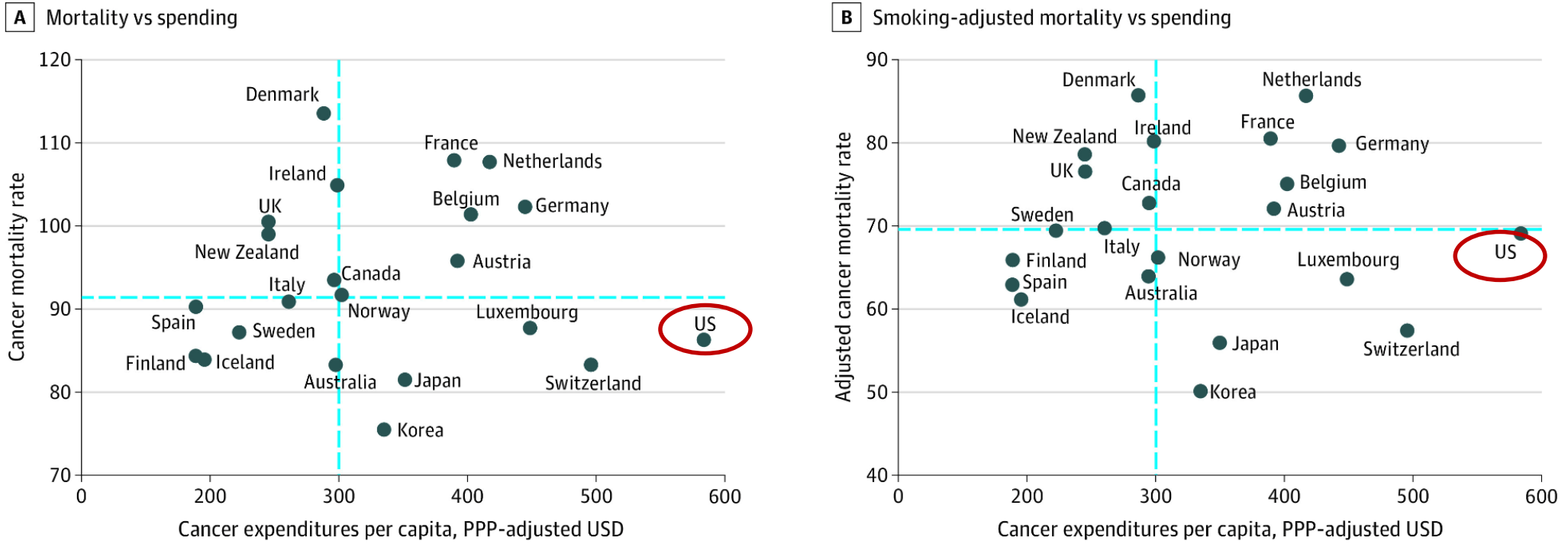
JAMA Health Forum. 2022;3(5):e221229. doi:10.1001/jamahealthforum.2022.1229

Key Points

Question Is spending on cancer care associated with lower cancer mortality rates?

Findings In this cross-sectional study of 22 high-income countries, national cancer care expenditures in 2020 were not associated with age-standardized cancer mortality rates. Although the US had the highest per capita spending on cancer care, after adjustment for smoking, the US cancer mortality rate was comparable with that of the median high-income country.

Meaning Results of this cross-sectional study suggest that understanding how countries outside the US achieve lower cancer mortality rates with lower spending may prove useful to future researchers, clinicians, and policy makers seeking to best serve their populations.



Association Between National Cancer Expenditures Adjusted for PPP (Purchasing Power Parity) and Cancer Mortality

Cancer care expenditures adjusted for economywide PPP in relation to total cancer mortality rates (deaths per 100 000 standard population). Dashed lines indicate the median. A, Unadjusted cancer mortality compared with PPP-adjusted cancer care expenditures. B, Cancer mortality compared with PPP-adjusted cancer care expenditures, after adjustment for smoking rates.

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 May 27;3(5):e221229. doi: 10.1001/jamahealthforum.2022.1229. PMID: 35977250; PMCID: PMC9142870.

Better Bang for Our Buck with Outcomes that Consider Patient Well-being and Preferences

Why do we need Comparative Effectiveness Research (CER)?

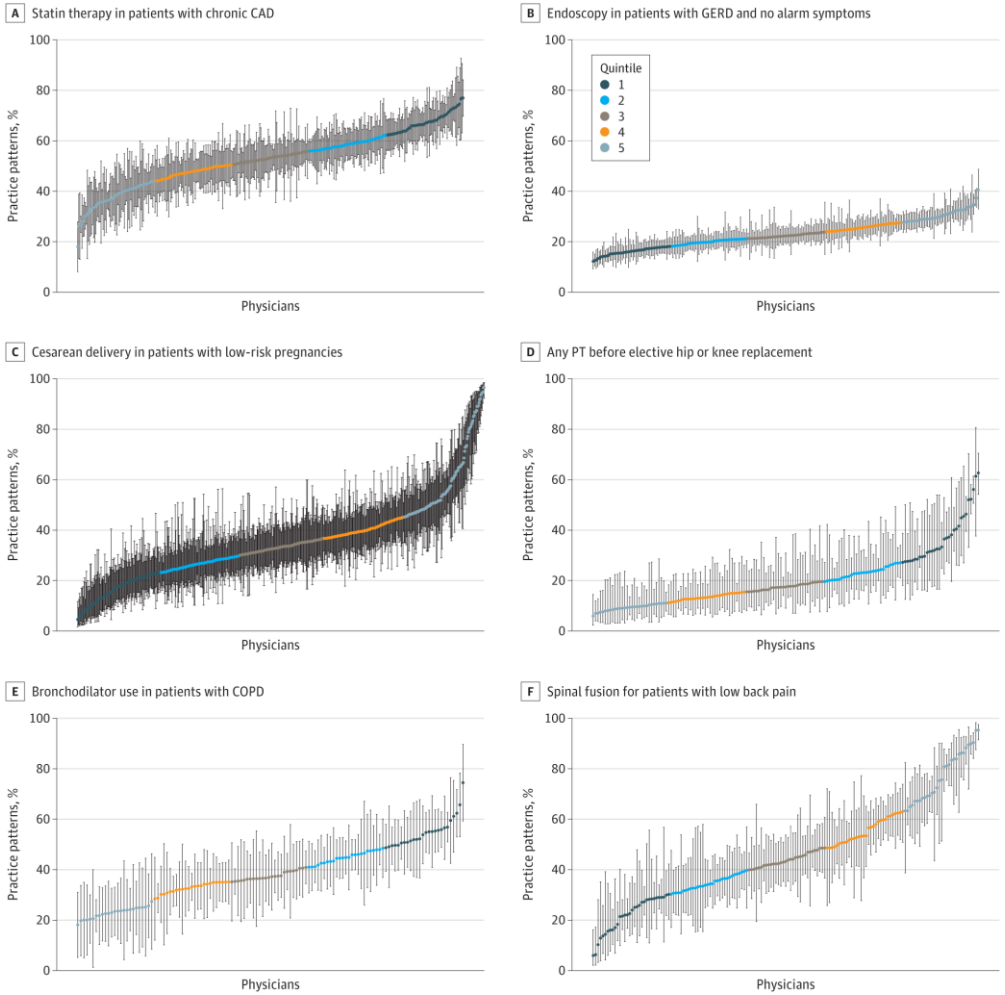
- Lack of evidence on “head-to-head” comparisons of alternative interventions
- Too many interventions to compare
- Inappropriate health care technologies use (i.e., over-use, under-use, and improper use)
- Large variations in management
- Best comparison is ‘standard of care’
- Inconsistent, insufficient ability to conduct subgroup analyses
- Increasing health care costs (elephant in the room)
- Development and implementation of Clinical Practice Guidelines

Adapted from: Agency for Healthcare Research and Quality. http://effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1/

JAMA Network™

From: **Physician Practice Pattern Variations in Common Clinical Scenarios Within 5 US Metropolitan Areas**

JAMA Health Forum. 2022;3(1):e214698. doi:10.1001/jamahealthforum.2021.4698



5 metropolitan areas
>8700 physicians from different specialties

Physician-Level Variations in Practice Patterns Across 6 Clinical Scenarios in the South Central Metropolitan Statistical Area

Quintile 1 (dark blue) represents, on average, more appropriate care, and quintile 5 denotes less appropriate care on average.

Statin therapy in patients with chronic coronary artery disease (CAD) (A), endoscopy in patients with gastroesophageal reflux disease (GERD) and no alarm symptoms (B), caesarean delivery in patients with low-risk pregnancies (C), any physical therapy (PT) prior to elective hip or knee replacement (D), use of bronchodilator in patients with chronic obstructive pulmonary disease (COPD) (E), and spinal fusion for patients with low back pain (F).

Each physician is denoted by a data point and vertical 95% CI.

Multiple Alternatives for Treatment
Example: Rheumatoid Arthritis

Disease-Modifying Antirheumatic Drugs (DMARDs)

Corticosteroids	Conventional Synthetic csDMARDs	Biologic bDMARD	Targeted synthetic tsDMARDs (JAK inhibitors)
	Methotrexate	TNF inhibitors (5)	Tofacitinib
	Leflunomide	IL6 inhibitors (2)	Baricitinib
	Hydroxychloroquine	CTLA4 agonists (1)	Upadacitinib
	Sulfasalazine	CD20 inhibitors (1)	

- Some of these agents can be used in combination
- There will never be a trial that compares head-to head all single agents and combinations
- Risks and benefits may vary across populations (e.g. young vs old)
- Other methods needed to assess comparative effectiveness

Patient Centered Outcomes Research (PCOR)

Outcomes that matter to people

PCOR helps people make informed health care decisions and allows their voice to be heard in assessing the value of health care options

Answers patient-focused questions:

- Given my personal characteristics, conditions and preferences, what should I expect will happen to me?
- What are my options and what are the benefits and harms of those options?
- What can I do to improve the outcomes that are most important to me?
- How can the health care system improve my chances of achieving the outcomes I prefer?

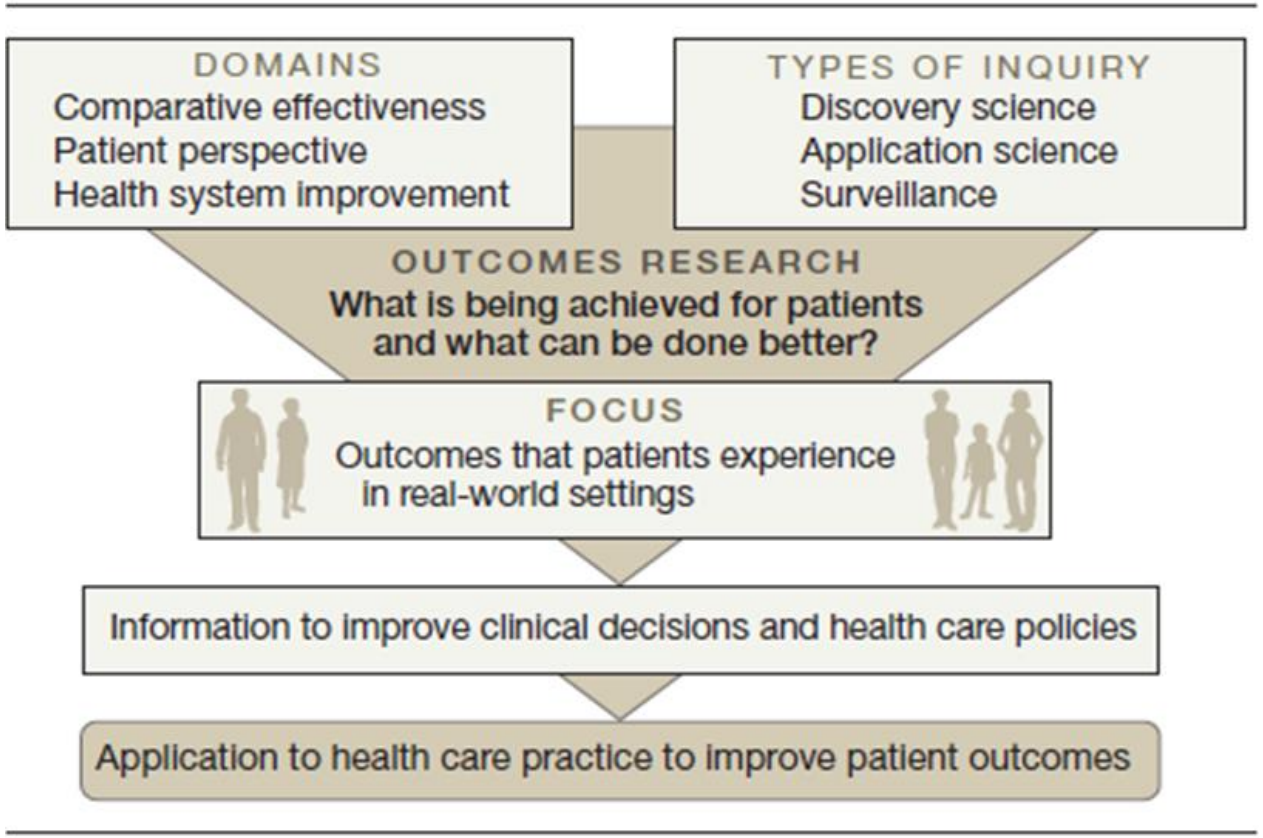
Is all CER patient-centered?

Not necessarily, in order for CER to be patient-centered, it needs to answer patient-focused research questions

To respond to patients' need, CER & PCOR:

- Assess the **benefits and harms of various alternative interventions to inform decision making**, highlighting comparisons and outcomes that matter to people
- Inclusive of an individual's preferences, focusing on outcomes that **people notice and care about**
- Incorporate a wide **variety of settings and diversity of participants** to address individual differences and **barriers to implementation and dissemination**
- Investigate optimizing outcomes while addressing **burden to individuals, resources, and other stakeholder perspectives**

CER Framework



Krumholz HM. Real-world imperative of outcomes research. JAMA 2011:306(7):754-5

PCORI Methodology Standards

- Specific recommendations for researchers that designate requirements for PCOR best practices
- Provide guidance in areas where there are either substantial deficiencies or inconsistences
  - How research question is selected, formulated, and addressed, and how the findings are reported
- Designed to promote transparency
  - How properly to communicate-in both study protocols and published reports-exactly what was planned and what was done
- Regularly updated

https://www.pcori.org/research-related-projects/about-our-research/research-methodology/pcori-methodology-standards

PCORI Methodology Standards

Guidance in 17 areas, for a total of 67 standards

Cross-Cutting Standards for Patient-Centered Comparative Clinical Effectiveness Research (CER)*

1. Formulating Research Questions
2. Patient Centeredness
3. Data Integrity and Rigorous Analyses
4. Preventing and Handling Missing Data
5. Heterogeneity of Treatment Effects (HTE)
6. Usual Care (UC) as a Comparator

Source: PCORI methodology report, November 2013

Standards for Specific Study Designs and Methods

7. Standards for Data Registries
8. Standards for Data Networks as Research-Facilitating Structures
9. Standards for Causal Inference Methods
10. Standards for Adaptive and Bayesian Trial Designs
11. Standards for Studies of Medical Tests
12. Standards for Systematic Reviews
13. Standards on Research Designs Using Clusters
14. Standards for Studies of Complex Interventions
15. Standards for Qualitative Methods
16. Standards for Mixed Methods Research
17. Standards for Individual Participant-Level Data Meta-Analysis (IPD-MA)

How to Develop a Research Question: PICOTS

- **P** Population (who)
- **I** Intervention (what are we examining)
- **C** Comparator (compared to)
- **O** Outcome (what happens)
- **T** Timing (when)
- **S** Setting (where)

PCORI Standards for Formulating Research Questions

1. Identify gaps in evidence
2. Develop a formal study protocol
3. Identify specific populations and health decisions affected by the research
4. Identify and assess participant subgroups
5. Select appropriate interventions and comparators
6. Measure outcomes that people representing the population of interest notice and care about

PCORI Standards for Patient Centeredness

1. **Engage people representing the population of interest and other relevant stakeholders in ways that are appropriate and necessary in a given research context**
2. **Identify, select, recruit, and retain study participants representative of the spectrum of the population of interest and ensure that data are collected thoroughly and systematically from all study participants**
3. **Use patient-reported outcomes when patients or people at risk of a condition are the best source of information for outcomes of interest**
4. **Support dissemination and implementation of study results**

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https://www.pcori.org/research-related-projects/about-our-research/research-methodology/pcori-methodology-standards