Pivoting Clinical Trials into a New and Evolving World

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Agenda

“Current” State of Affairs

What are the problems?

What are the solutions?

The Bad News

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We're losers

JAMA Network™

Patient Enrollment for Cardiovascular Clinical Trials in the United States

Research Letter

February 12, 2025

Patient Enrollment for Cardiovascular Clinical Trials in the United States

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» Author Affiliations | Article Information

JAMA Cardiol. 2025;10(3):298-300. doi:10.1001/jamacardio.2024.5537

Table 2. Site-Specific Enrollment Characteristics for Trials Reporting Patient-per-Site Data

	Patients enrolled			No. (%)		
					Sites enrolling <10 patients	
Trial	Total No.	US, No. (%)	Total sites, No.	US sites	Overall	US[a]
Total	89 172	17 705 (19.9)	4388	1133 (25.8)	2014 (45.8)	659 (58.1)
ISCHEMIA-CKD	777	159 (20.5)	118	36 (30.5)	95 (80.5)	31 (86.1)
COP-AF	3209	355 (11.1)	45	8 (17.8)	12 (26.7)	3 (37.5)
THEMIS	19 220	2266 (11.8)	1297	307 (23.7)	668 (51.5)	228 (74.3)
ILUMIEN IV: OPTIMAL PCI	2487	909 (36.6)	80	35 (43.8)	23 (28.7)	14 (40.0)
PARADISE-MI	5702	454 (8.0)	494	82 (16.6)	284 (57.5)	73 (89.0)
REPRIEVE	7769	3787 (48.7)	145	100 (69.0)	23 (15.9)	18 (18.0)
SELECT	17 604	3652 (20.7)	804	201 (25.0)	220 (27.4)	58 (28.9)
ISCHEMIA	5179	853 (16.5)	319	109 (34.2)	207 (64.9)	88 (80.7)
AEGIS-II	18 219	1993 (10.9)	899	196 (21.8)	450 (50.1)	138 (70.4)
TWILIGHT	9006	3277 (36.4)	187	59 (31.6)	32 (17.1)	8 (13.6)

Clinical Trial Humility

- North America:
  - Most sites: 1377 sites [31.4%]
  - Lowest median enrollment (8.0 patients/site)
- South America,
  - Fewest sites: 329 sites [7.5%]
  - Highest patients per site (24.8 patients/site)
- Eastern Europe
  - Highest median per-site enrollment (16.0 patients/site)

- Author's Conclusion:
- … Notably, the United States had the **most sites** but enrolled **significantly fewer patients**.

- These trends suggest **underlying legal, regulatory, and cost-related barriers**, highlighting the need for improved clinical trial infrastructure

JAMA Cardiol. 2025;10(3):298-300. doi:10.1001/jamacardio.2024.5537

WE have created a Gordian Knot for Research

- Administrative Challenges
- Complex Study Designs
- Logistical Difficulties
- Trust in Science
- Financial Misalignment
- Extensive Compliance & Monitoring Requirements
- Misaligned or Wrong Infrastructure
- Policy and Regulatory Barriers
- Patient Barriers
- Inadequate Knowledge of Clinical Research

Image Created by DALL-E/ OPEN-AI

So a question…
have you stepped into the roles of others?

Changing Times (overnight?)

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Absolutely Yes!

And No! Trends > 10 years

U.S. BUREAU OF LABOR STATISTICS

Monthly Labor Review

ARTICLE

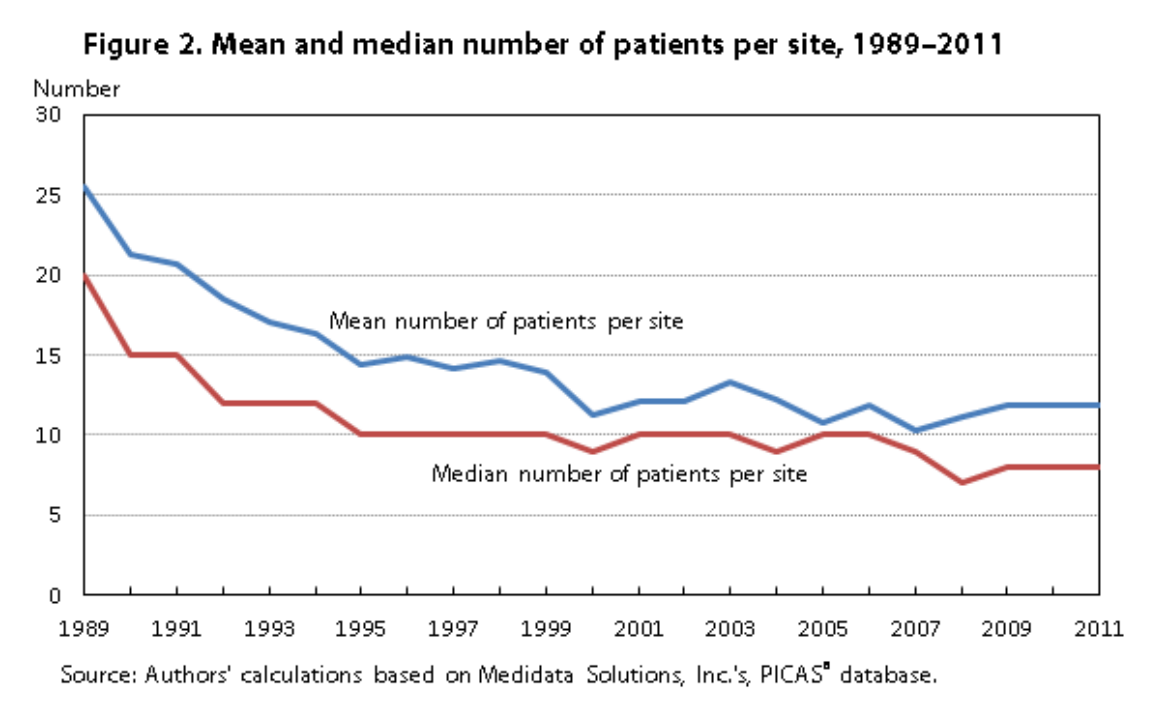
JUNE 2014

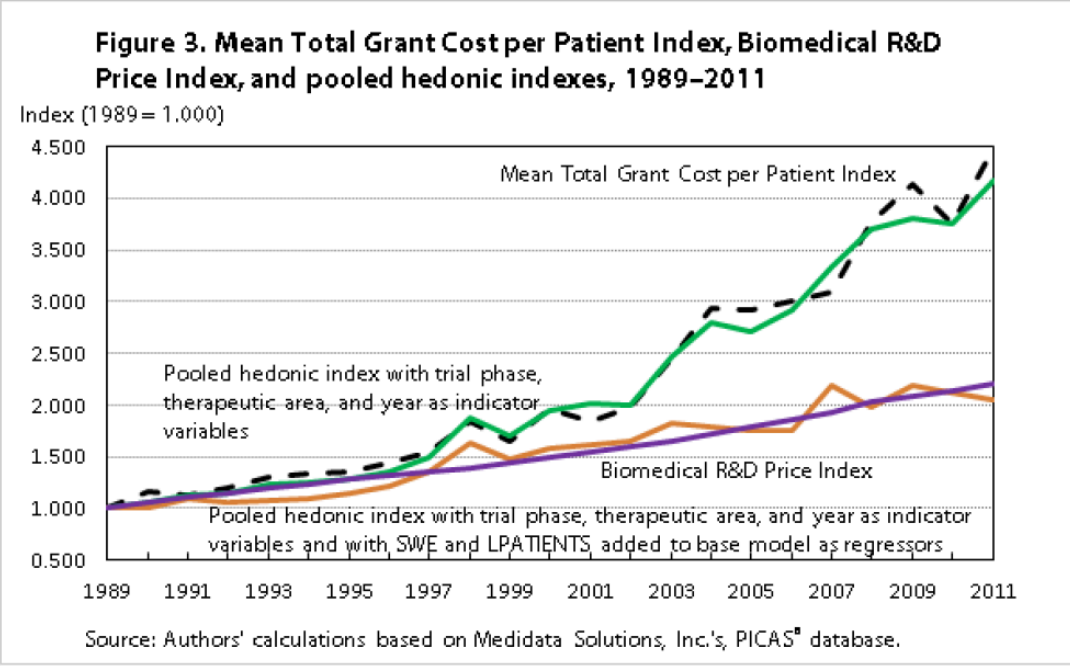
Price indexes for clinical trial research: a feasibility study

A study using a large sample of agreements between sponsors of clinical trials and clinical investigators produces estimated hedonic price indexes for clinical trial research, an important component of biomedical research and development. Measured as total grant cost per patient, nominal prices grew by a factor of 4.5 between 1989 and 2011, while the U.S. National Institutes of Health Biomedical R&D Price Index, the only published source of information on trends in pricing in the biomedical research-and-development sector, rose only slightly more than twofold. After

Berndt E, Cockburn I. Monthly Labor Review, June 2014

Higher costs, lower productivity

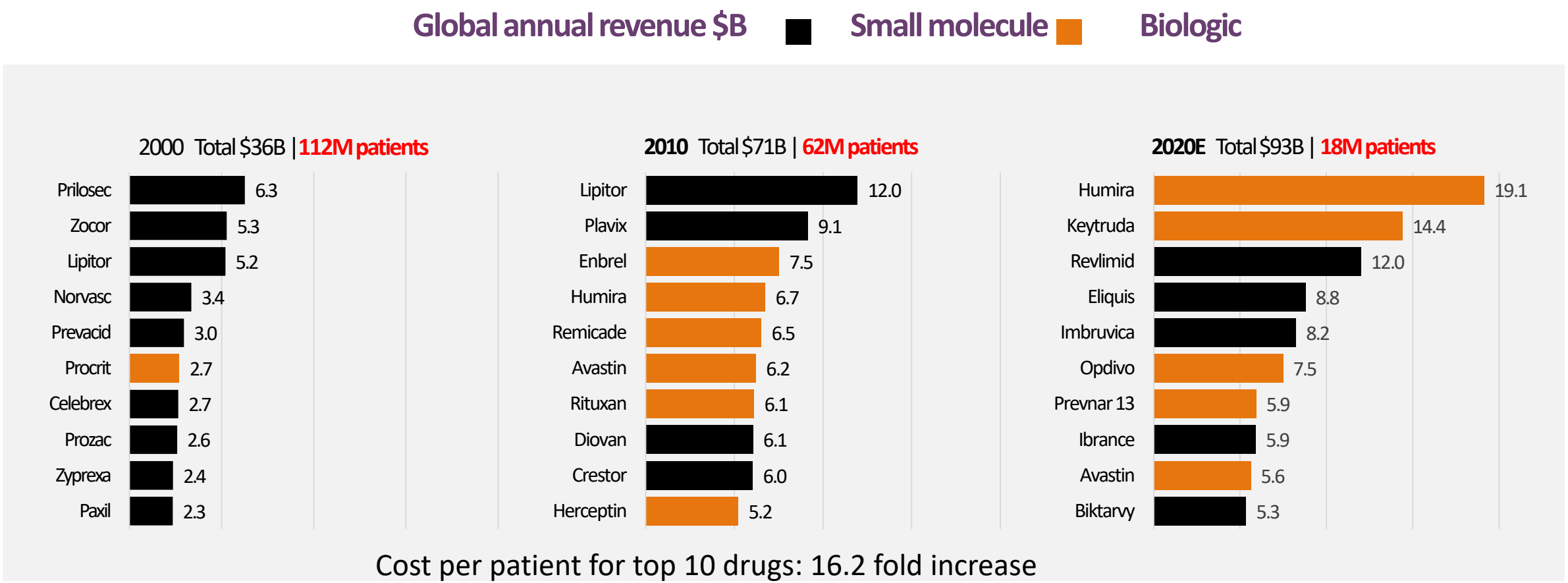




Berndt E, Cockburn I. Monthly Labor Review, June 2014

Simple incentives?

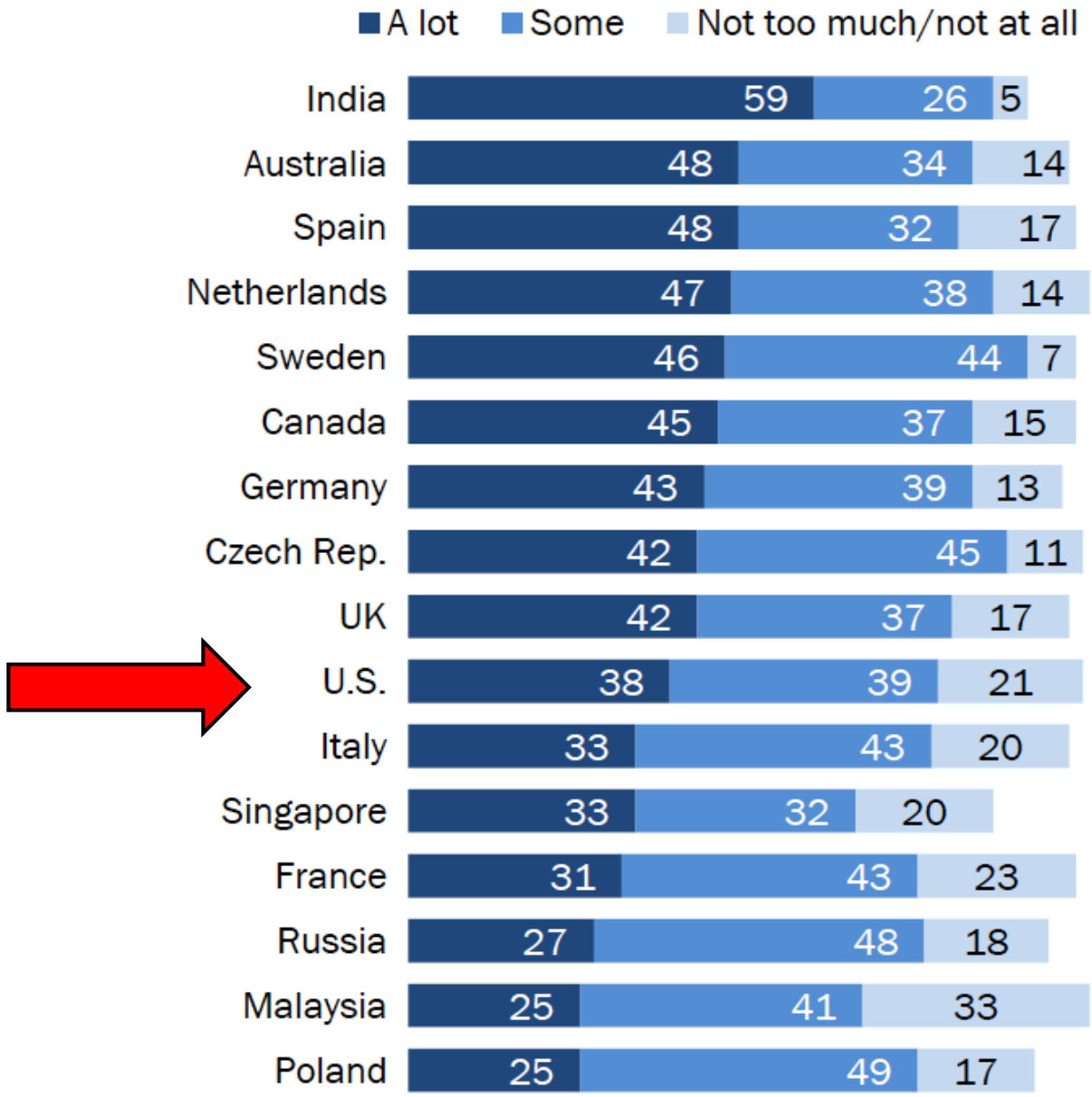
- A substantial shift over decades



Cost per patient for top 10 drugs: 16.2 fold increase

Krychtiuk KA, et al. Drug development for major chronic health conditions-aligning with growing public health needs: Proceedings from a multistakeholder think tank. *Am Heart J*. 2024;270:23-43.

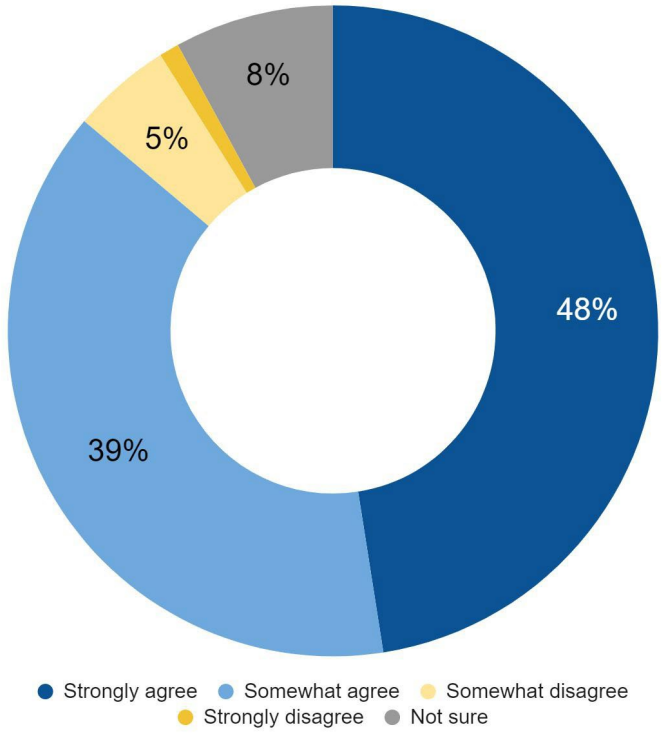
Trust in Science



Pew Research Center: International Science Survey 2019-2020; 2023

8 in 10 say clinical trials discussion should be part of routine care

Do you agree or disagree that health care professionals should discuss clinical trials with patients diagnosed with a disease as part of their standard of care?



92%
Say "Strongly or Somewhat Agree"

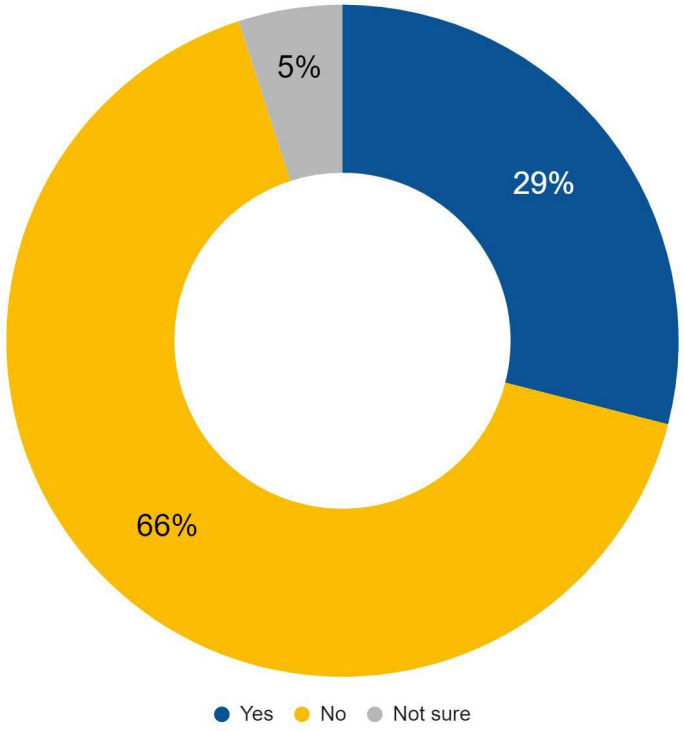
87%
Say "Strongly or Somewhat Agree"

85%
Say "Strongly or Somewhat Agree"

Source: A Research!America survey of U.S. adults conducted in partnership with the ACRO and Zogby Analytics in October 2023.

Most have not talked with their doctor about participating in health research

Has your doctor or other healthcare professional ever talked to you about opportunities to participate in any kind of medical, health, and clinical research?



Source: A Research!America survey of U.S. adults October 2023.

The most common use case

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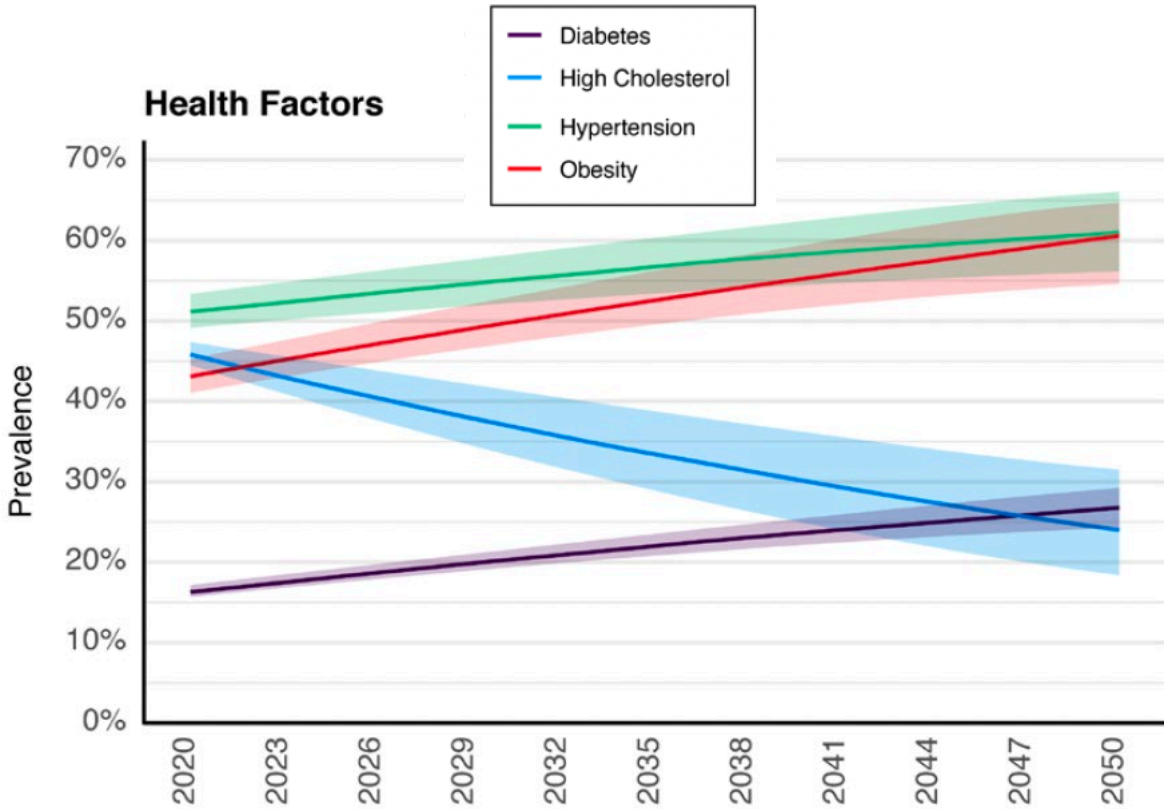
Gloomy Forecast for 2050…

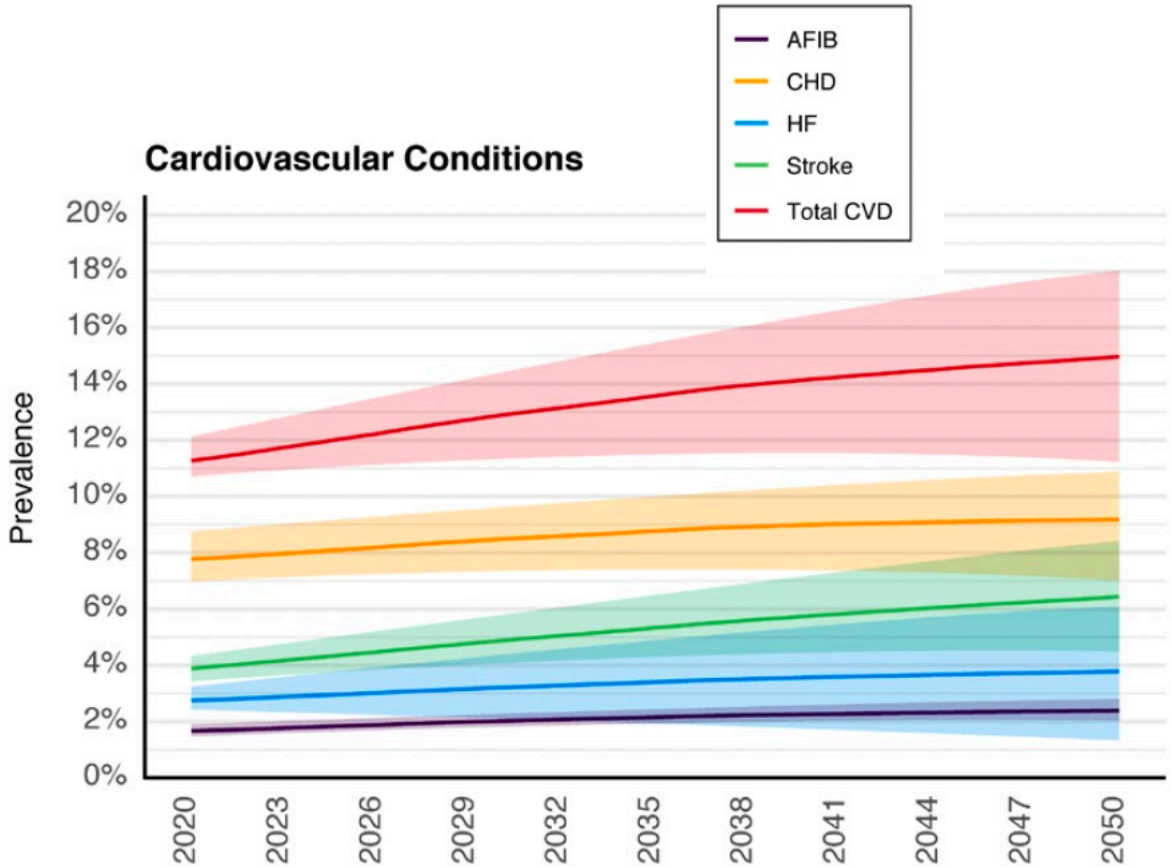
AHA PRESIDENTIAL ADVISORY

Forecasting the Burden of Cardiovascular Disease and Stroke in the United States Through 2050—Prevalence of Risk Factors and Disease: A Presidential Advisory From the American Heart Association

Karen E. Joynt Maddox, MD, MPH, FAHA, Chair; Mitchell S.V. Elkind, MD, MS, FAHA; Hugo J. Aparicio, MD, MPH; Yvonne Commodore-Mensah, PhD, MHS, BSN, RN, FAHA; Sarah D. de Ferranti, MD, MPH, FAHA; William N. Dowd, BA; Adrian F. Hernandez, MD, MHS, FAHA; Olga Khavjou, MA; Erin D. Michos, MD, MHS, FAHA; Latha Palaniappan, MD, MS, FAHA; Joanne Penko, MS, MPH; Remy Poudel, MS, MPH, CPH; Véronique L. Roger, MD, MPH; Dhruv S. Kazi, MD, MSc, MS, FAHA, Vice Chair; on behalf of the American Heart Association

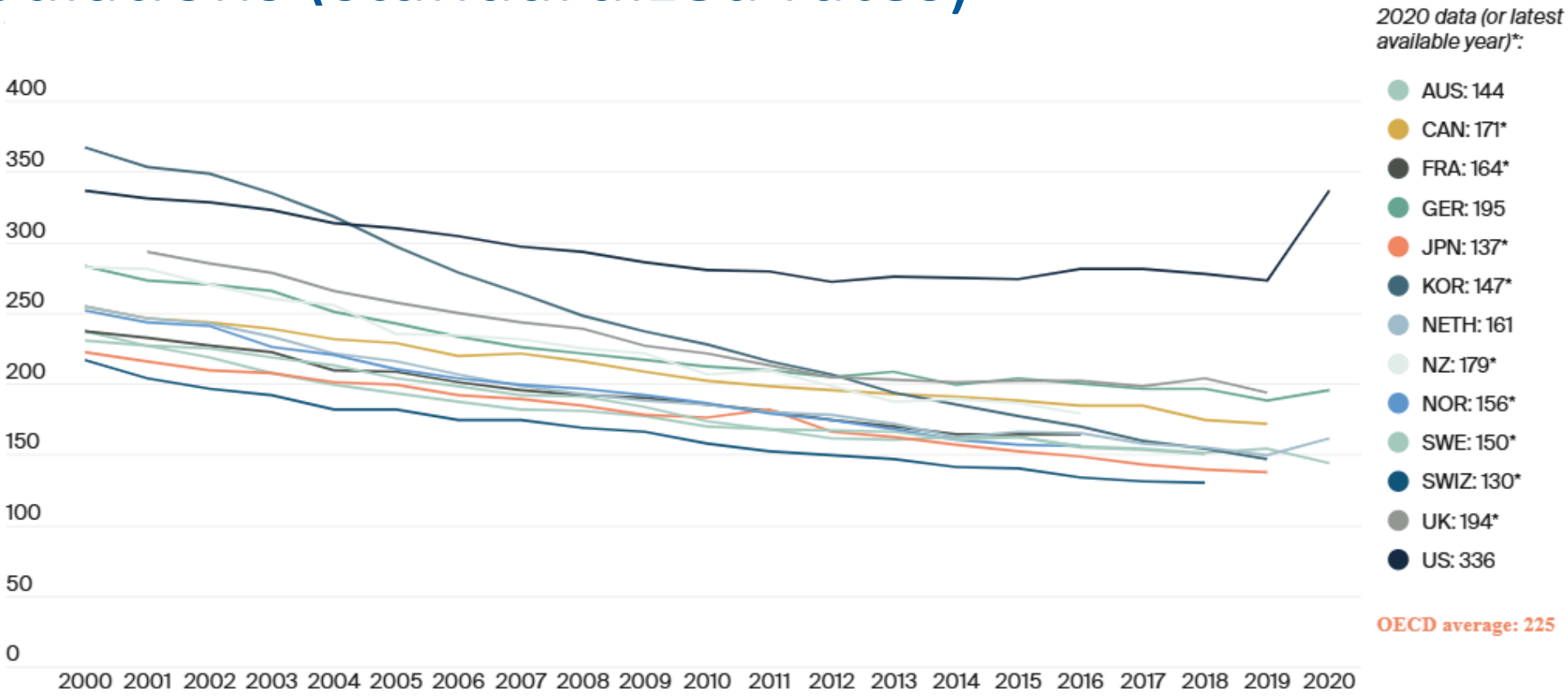
Gloomy Forecast for 2050





Joynt Maddox KE, et al. Forecasting the Burden of Cardiovascular Disease and Stroke in the United States Through 2050-Prevalence of Risk Factors and Disease. Circulation. 2024;150(4):e65-e88..

U.S. leads world in avoidable deaths per 100,00 populations (standardized rates)

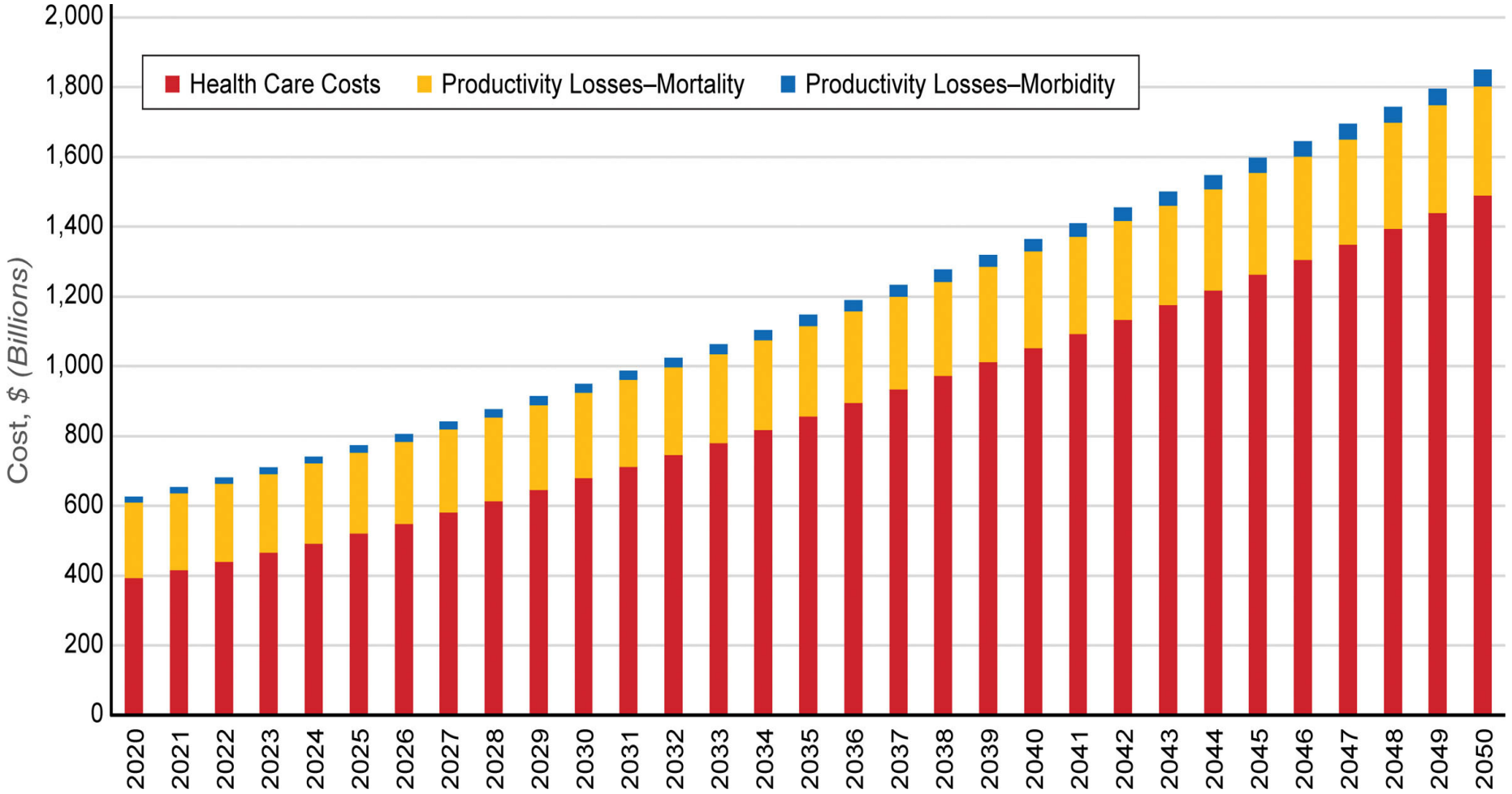


Notes: Rates reflect age-standardized rates. Avoidable mortality includes deaths which are preventable and treatable. * 2019 data for CAN, JPN, KOR, and UK; 2018 data for SWE and SWIZ; 2016 data for FRA, NZ, and NOR.

Data: OECD Health Statistics 2022.

Source: Munira Z. Gunja, Evan D. Gumas, and Reginald D. Williams II, *U.S. Health Care from a Global Perspective, 2022: Accelerating Spending, Worsening Outcomes* (Commonwealth Fund, Jan. 2023). https://doi.org/10.26099/8ejy-yc74

Gloomy Forecast for 2050: Tripling Costs



Kazi DS, et al. Forecasting the Economic Burden of Cardiovascular Disease and Stroke in the United States Through 2050. Circulation. 2024;150(4):e89-e101.

Let's consider heart disease: Challenges vs. Opportunities

>13 million with heart disease

>800,000 heart attacks/year

- If 2%-4% of eligible participate in clinical trials
- ~ 250-500,000 participants in a national, coordinated platform
- Why doesn't that happen?

What would it take to a platform in the US of ~1 million or so across 100 centers?

Diagnostic Tests/Biology

Pragmatic Trials

Efficacy Trials

Real World Evidence

The industry perspective of a new research paradigm

Healthcare expenses account for ~28% of U.S. Federal budget

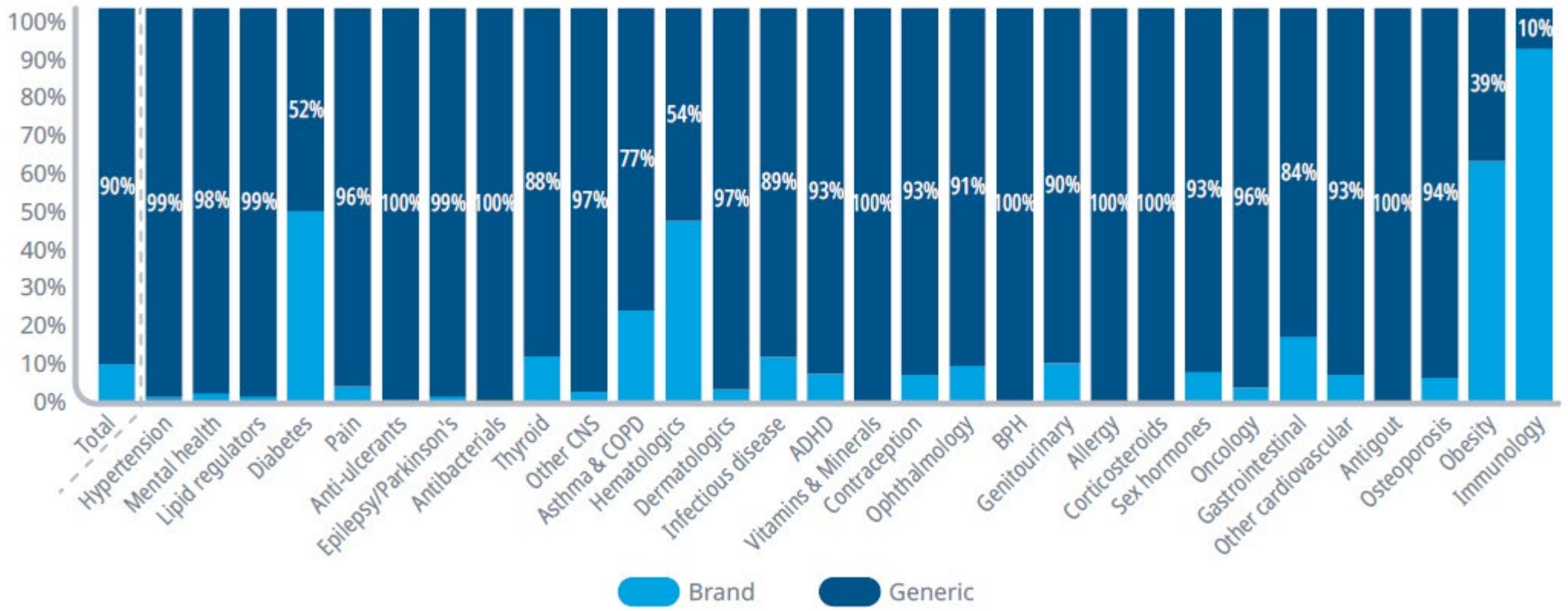
Country	Life expectancy ▲	Health spending, per capita
United States	**78.4**	**$13,432**
Germany	80.6	$8,441
United Kingdom	81.1	$6,023
Austria	81.6	$7,811
Canada	81.7	$7,013
Netherlands	82.0	$7,737
Belgium	82.5	$7,380
Comparable Country Average	**82.5**	**$7,393**
Australia	83.1	$6,931
France	83.1	$7,136
Sweden	83.4	$7,522
Japan	84.1	$5,640
Switzerland	84.2	$9,688

Notes: Health spending per capita data represent health consumption spending per capita. Comparable countries include: Australia, Austria, Belgium, Canada, France, Germany, Japan, the Netherlands, Sweden, Switzerland, and the U.K. 2023 U.K. life expectancy data is only for England and Wales. See Methods section of "How does U.S. life expectancy compare to other countries?"

From Peterson KFF Health System Tracker "how does U.S. life expectancy compare to other countries, 2025

Share of adjusted prescriptions by product type in 2024

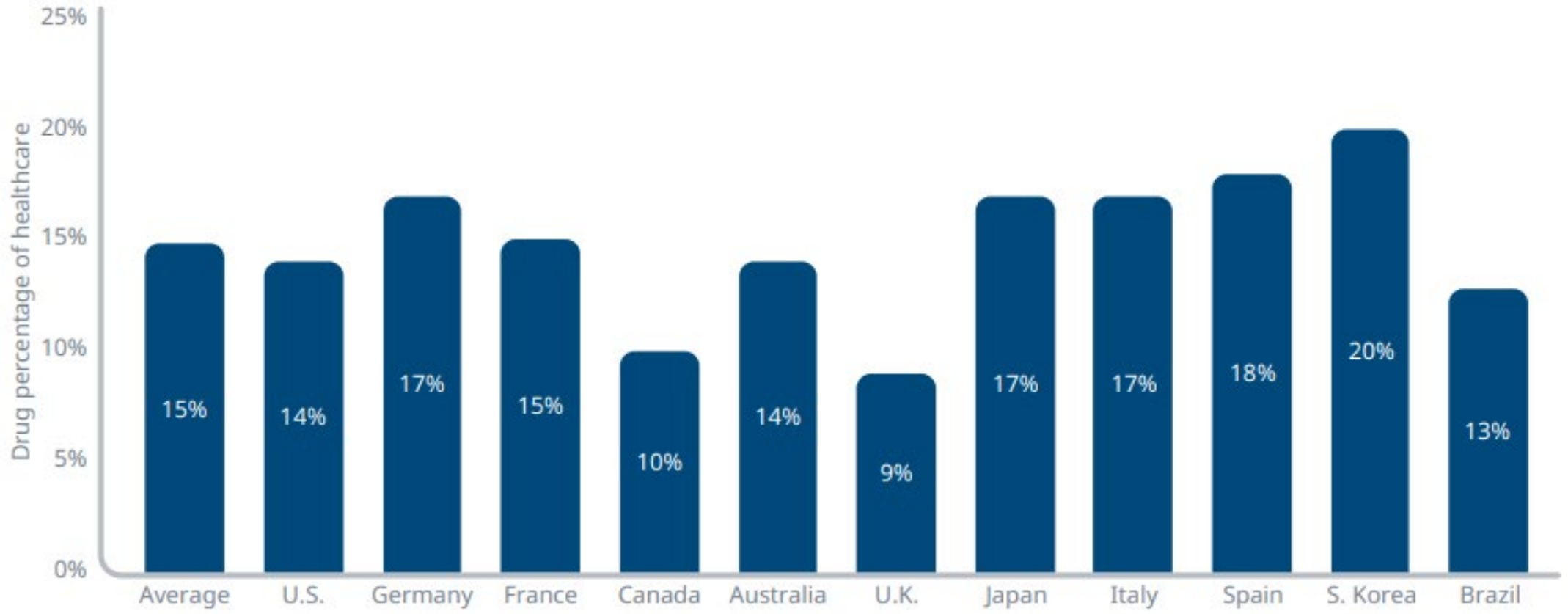
90% of prescriptions are generic with exception of immunology, obesity, and diabetes



Source: IQVIA National Prescription Audit, Dec 2024.

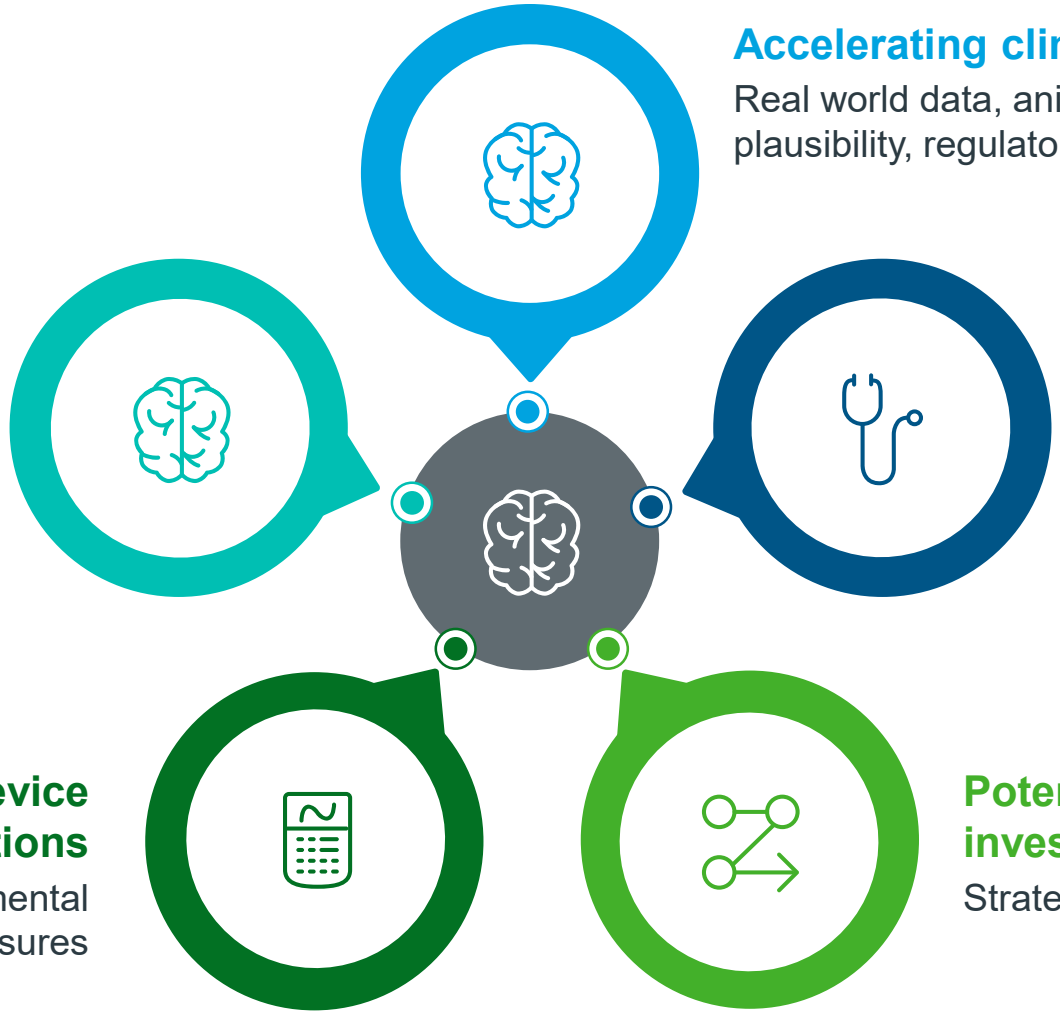
From: IQVIA Institute Global Trends in R&D 2025

Percentage of healthcare expenditures due to net drug expense in 2018



Source: IQVIA Institute for Human Data Science, Sep 2021; See Methodology in Appendix

Emerging clinical research themes



Accelerating clinical development

Real world data, animal testing, scientific plausibility, regulatory efficiency, AI

Prevention and chronic treatments

Rebalance episodic or acute care vs. Prevention or chronic

Clinically meaningful outcomes

Greater emphasis on ”hard” endpoints, optimized comparators, long-term outcomes

Non-pharma/device interventions

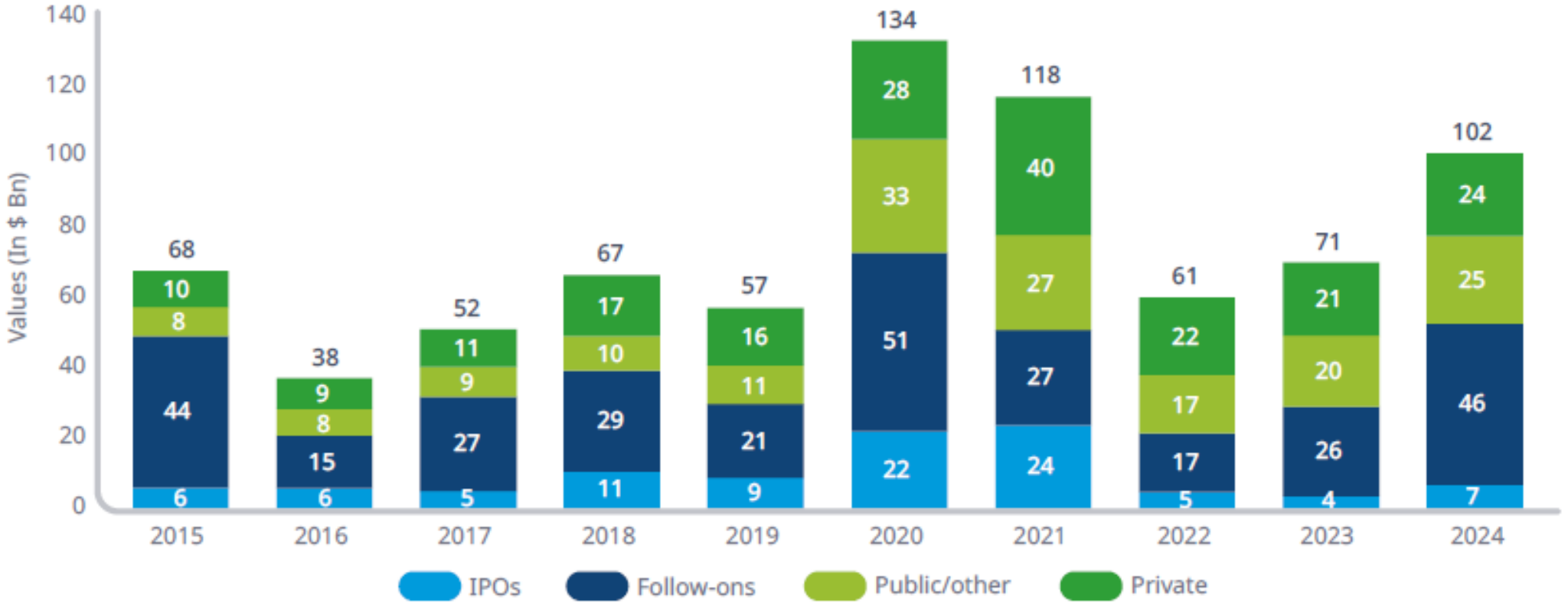
Food, microbiome, environmental exposures

Potential increase in research investment

Strategy-focused research

Context of industry-sponsored clinical research

Biopharma funding levels increasing, with emphasis on later-phase assets

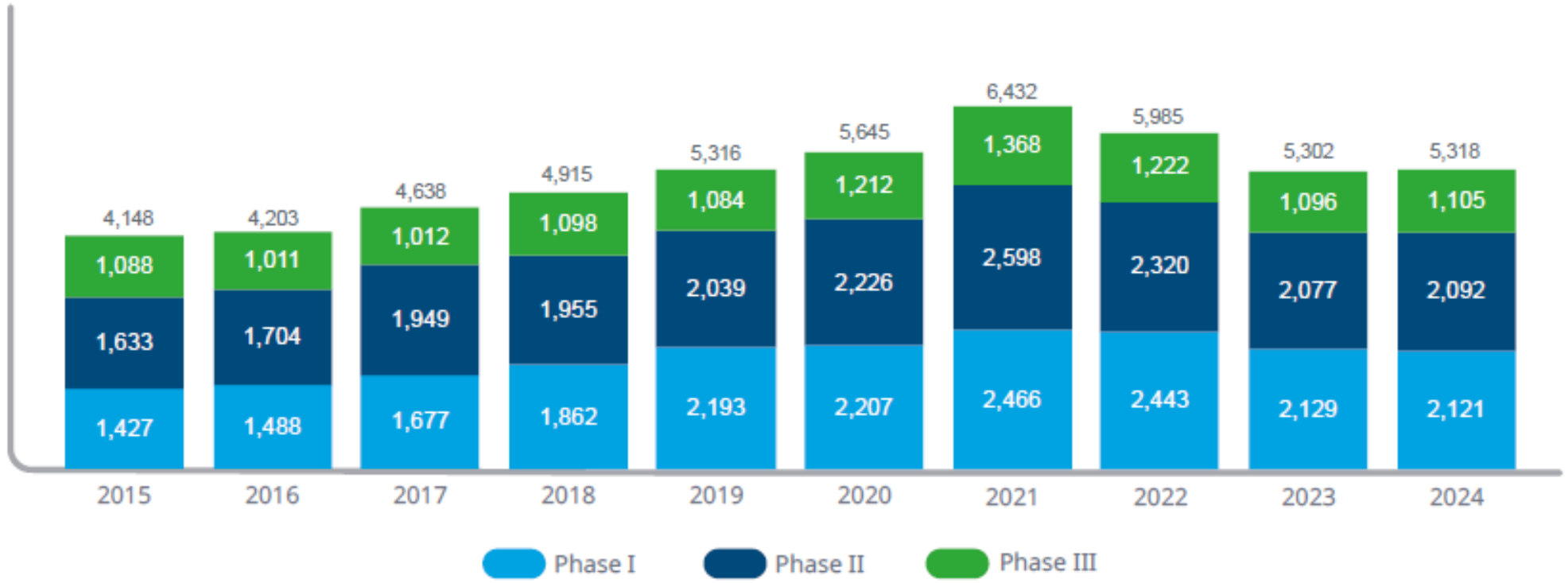


Source: BioWorld, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Trends in industry-sponsored research

Return to pre-COVID volume of clinical trial starts

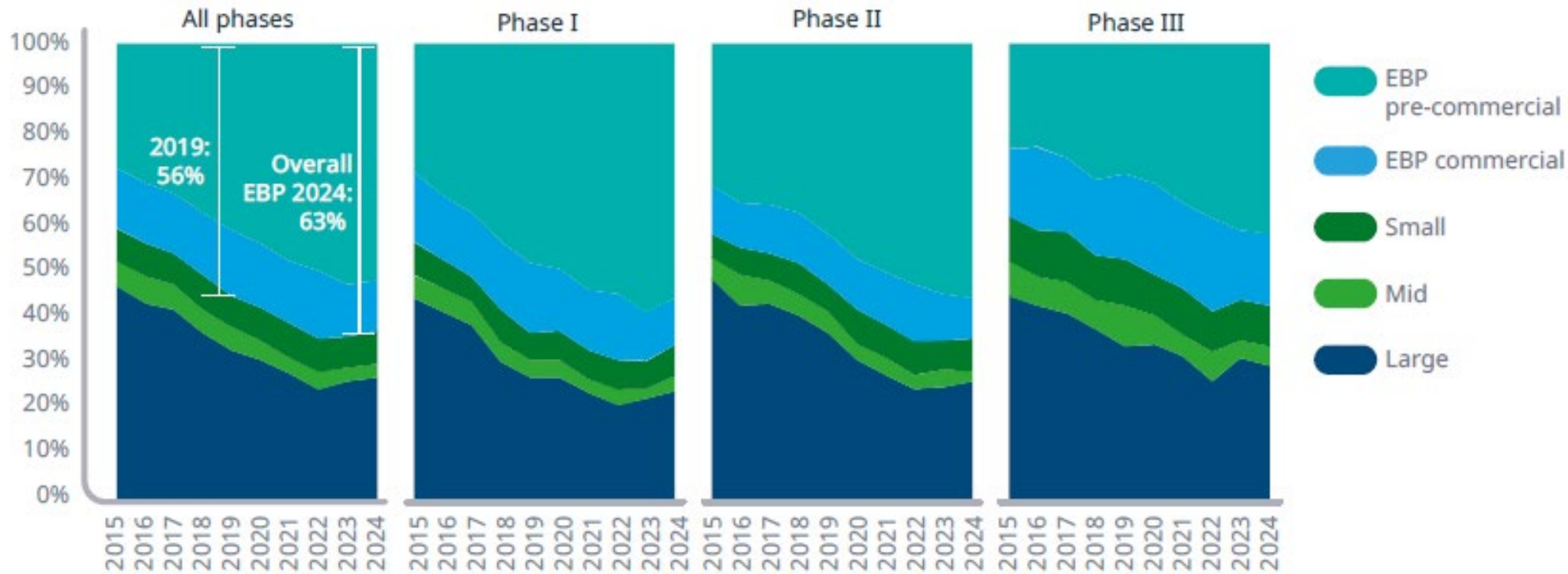


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Characteristics of sponsors initiating clinical trials

Increasing proportion of studies initiated by emerging bio-pharma (EBP) sponsors

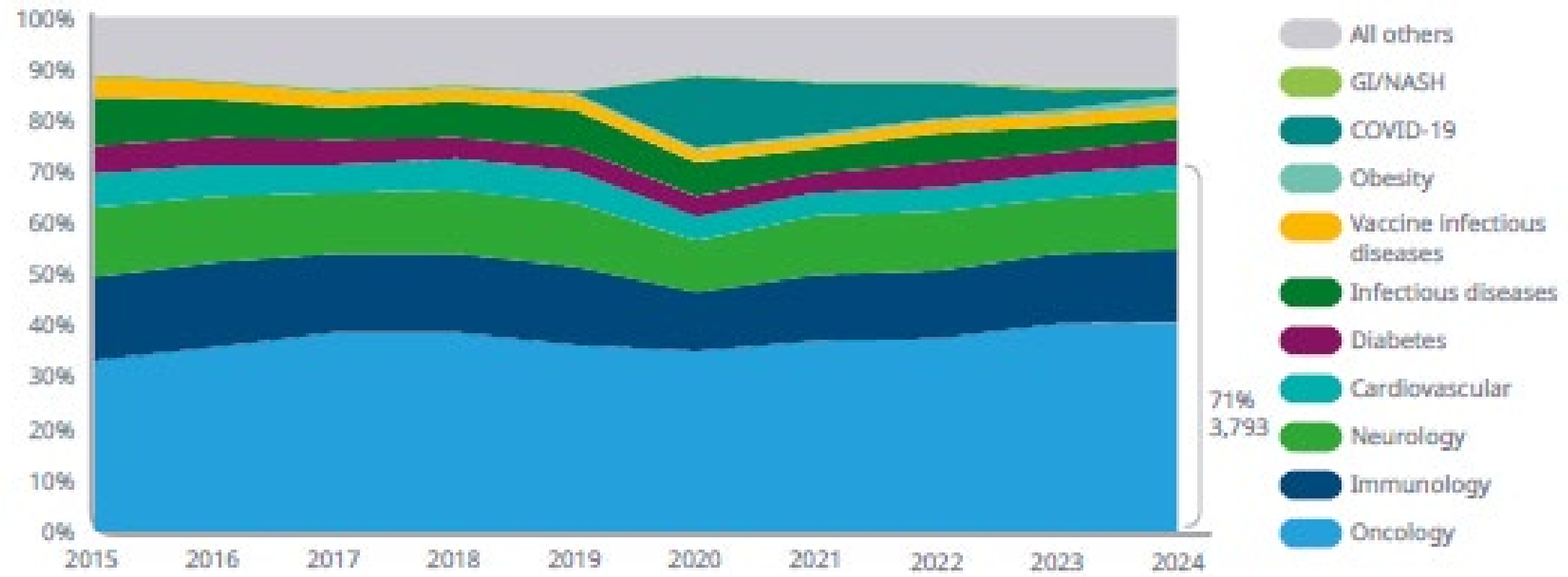


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Therapeutic area of industry-sponsored trials

Top four areas account for 71% of all trials, while weight loss trial starts increased 77% vs. 2023

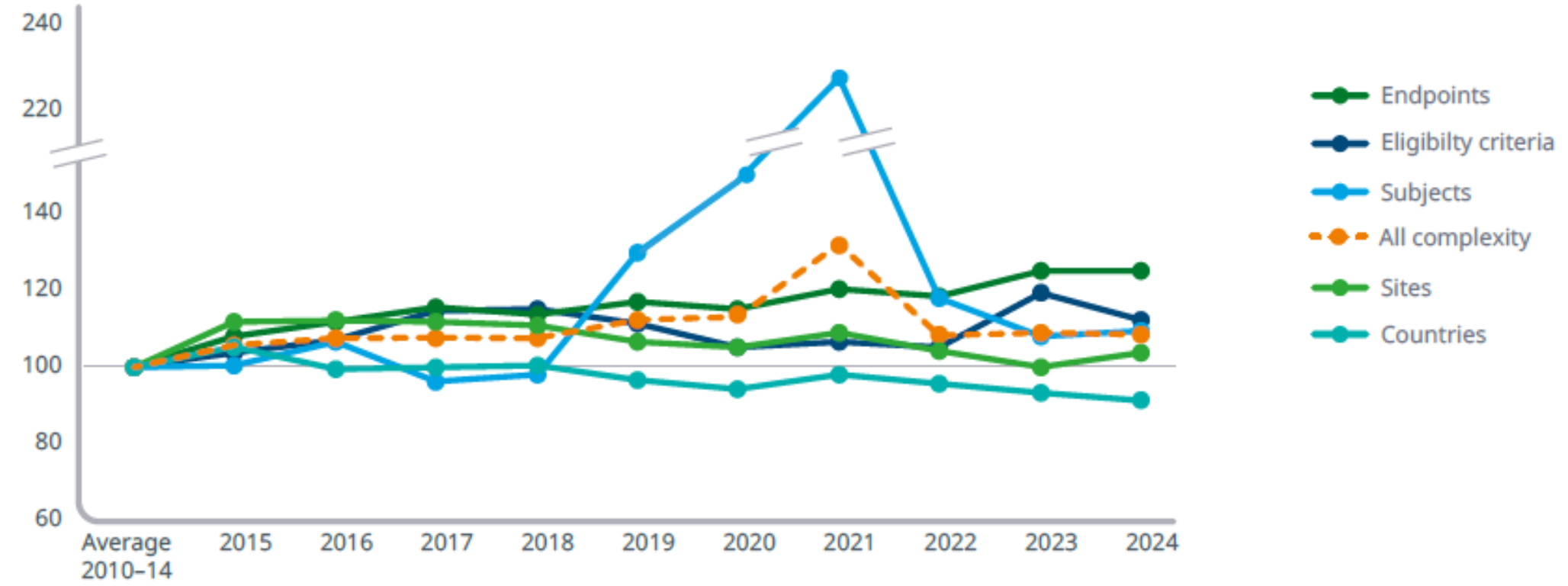


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Complexity of clinical trials

While overall measures of complexity has increased modestly, sites have experienced greater increase

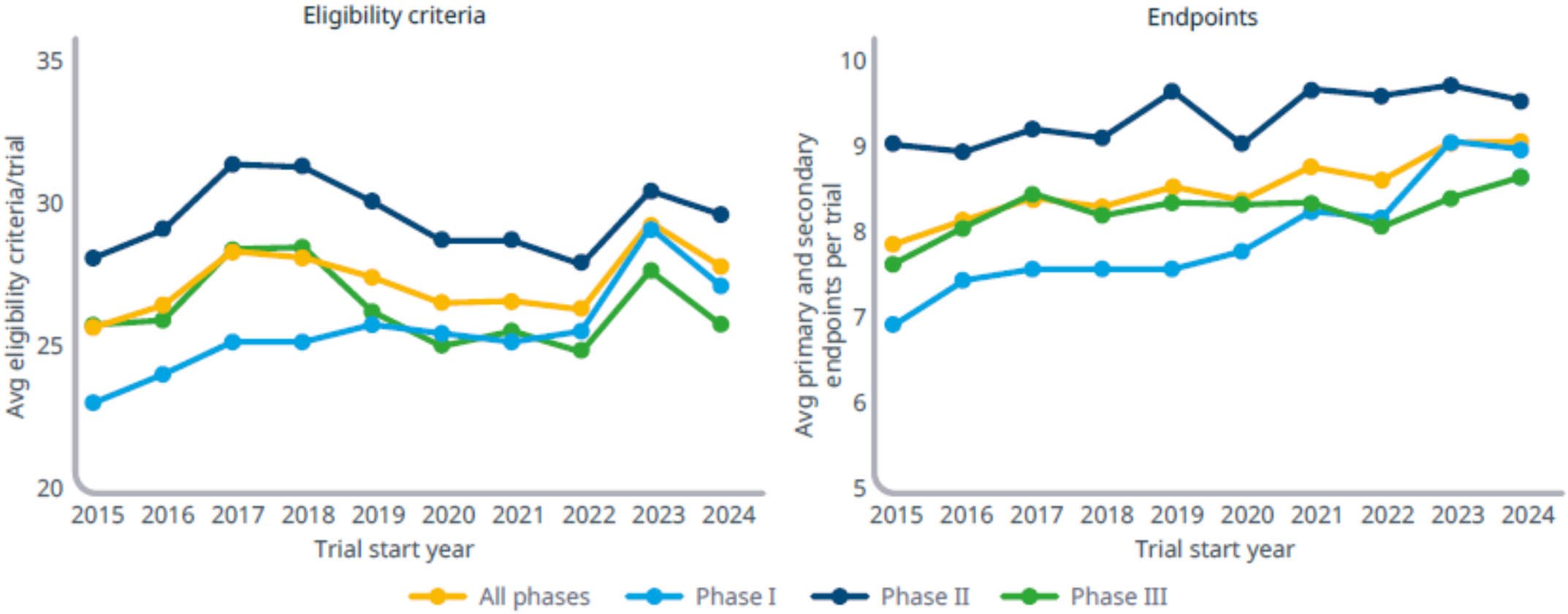


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Complexity of clinical trials experienced by sites

Increase in complexity experienced by sites has increased in all phases, especially Phase 1

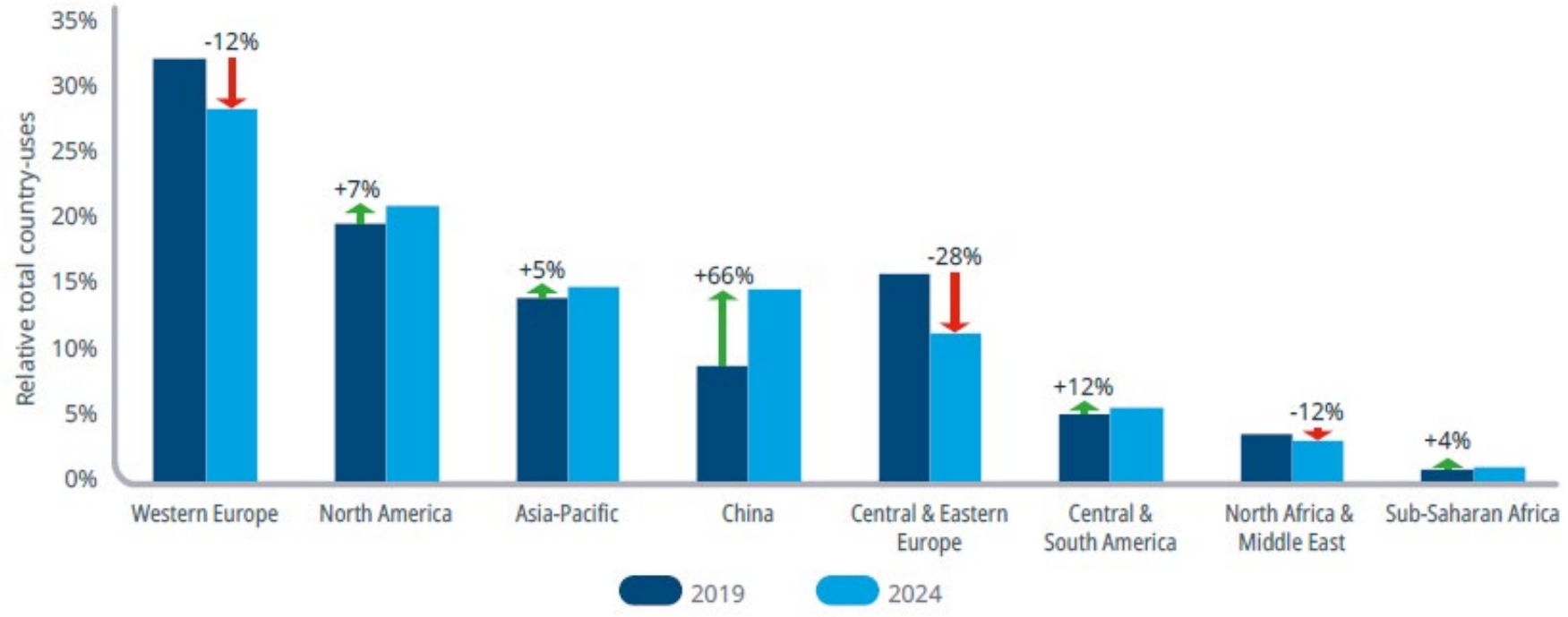


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

From: IQVIA Institute Global Trends in R&D 2025

Change in utilization of regions in interventional studies

Increasing concentration of studies in fewer countries

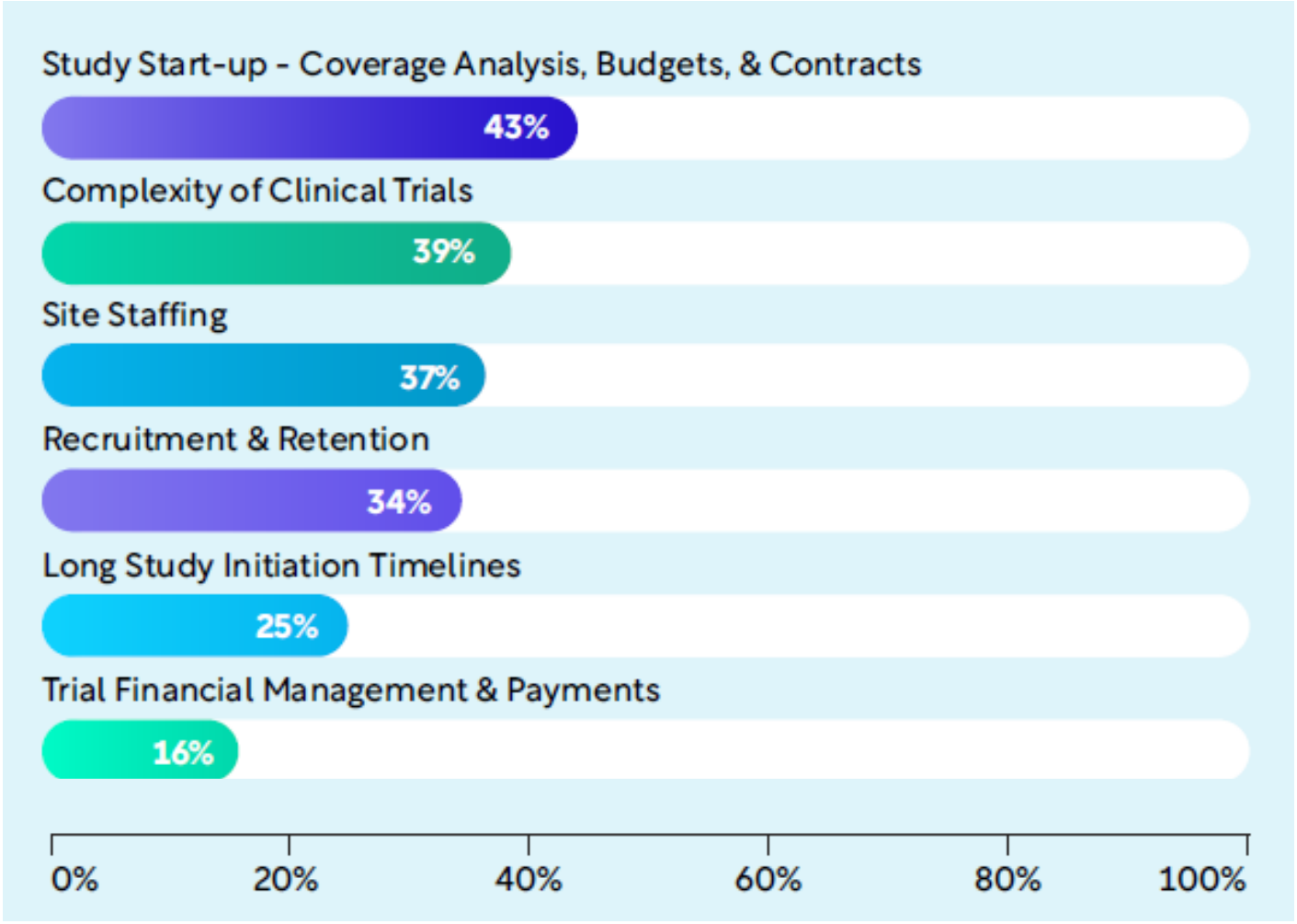


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

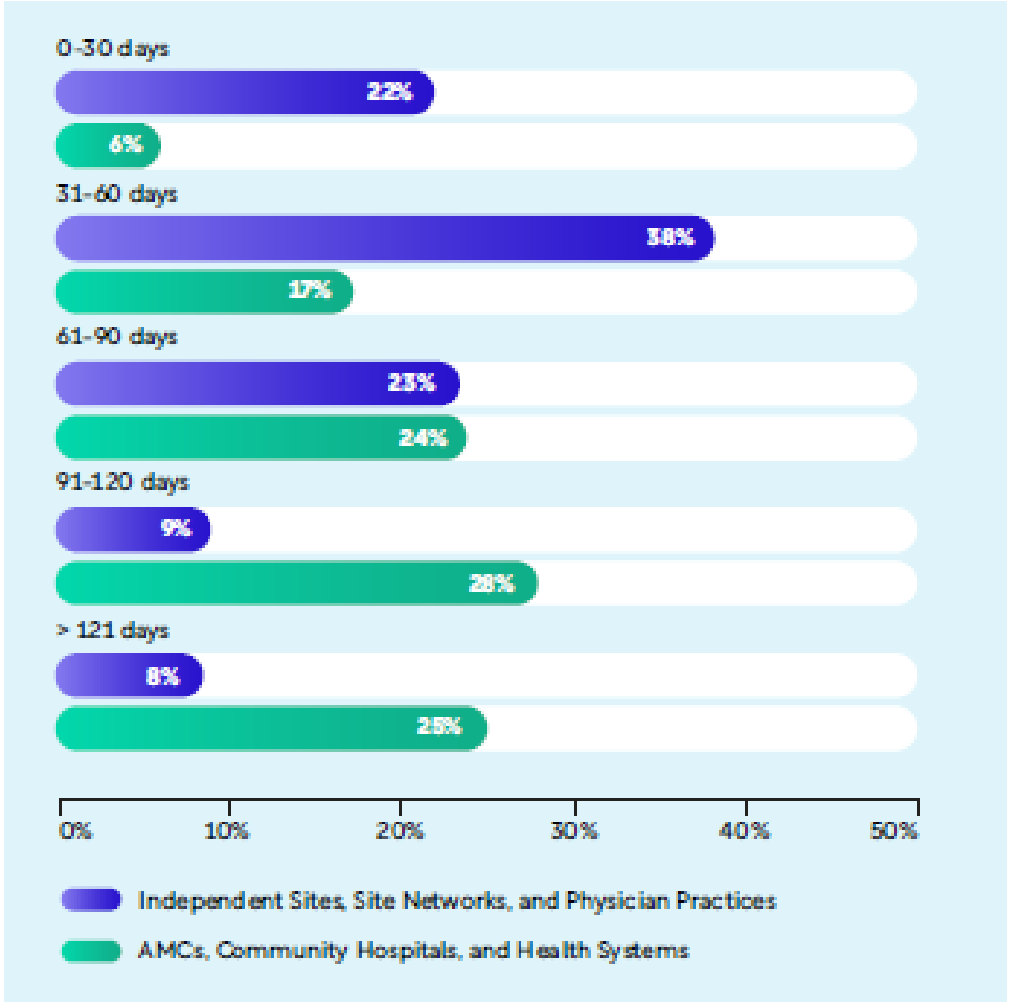
From: IQVIA Institute Global Trends in R&D 2025

Top issues impacting academic, health system, and community hospital research sites

Top issues impacting ability to conduct research

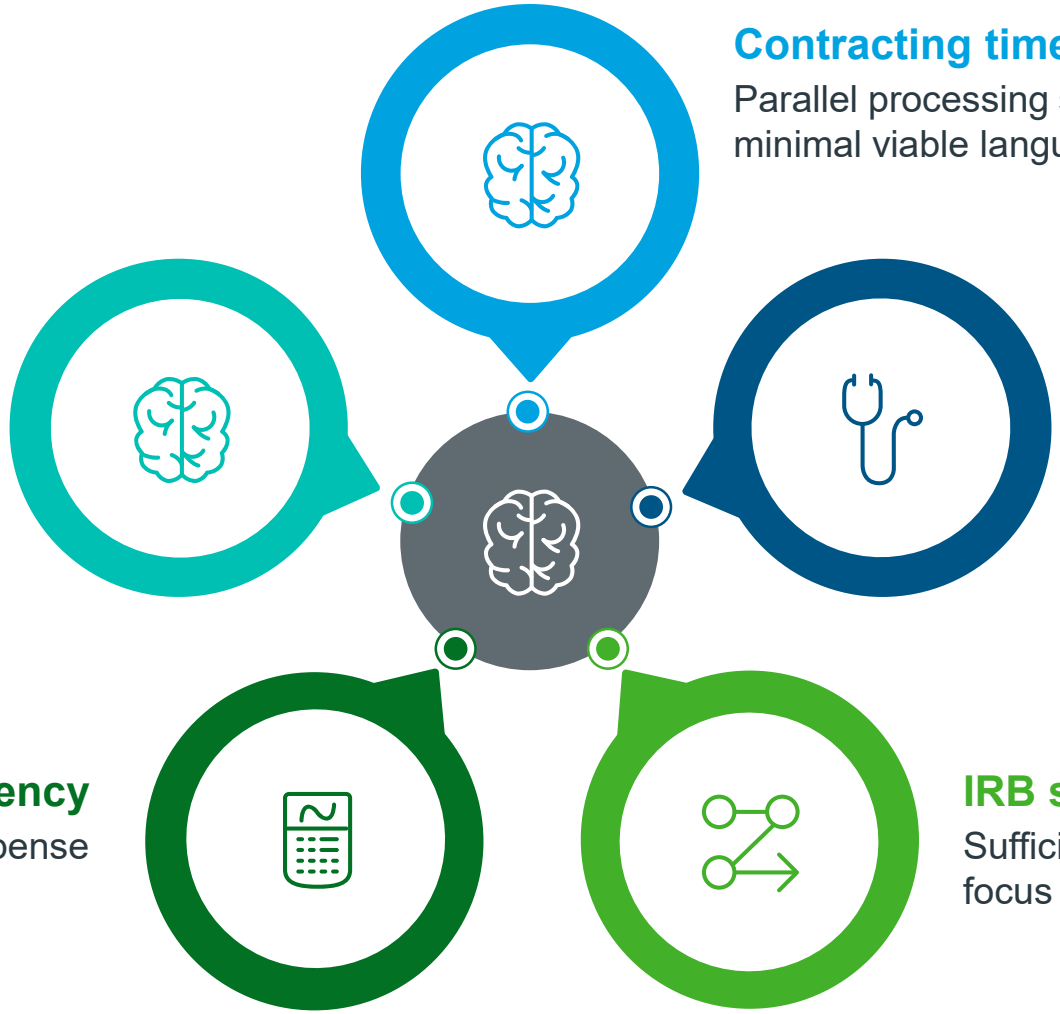


Reported start-up timelines



From: WCG Clinical 2024 Clinical Research Site Challenges Survey Report

Accelerating industry sponsored research in academic settings



Contracting timelines
Parallel processing suprior to sequential, minimal viable language and acceptance

Prioritization
Availability of Principle Investigators and incentivization

Intellectual property
Signfiicant divergence with non-academic sites

Cost and efficiency
Appropriate value for expense

IRB staffing and responsiveness
Sufficiency of expertise, availability, and focus

Summary and Discussion

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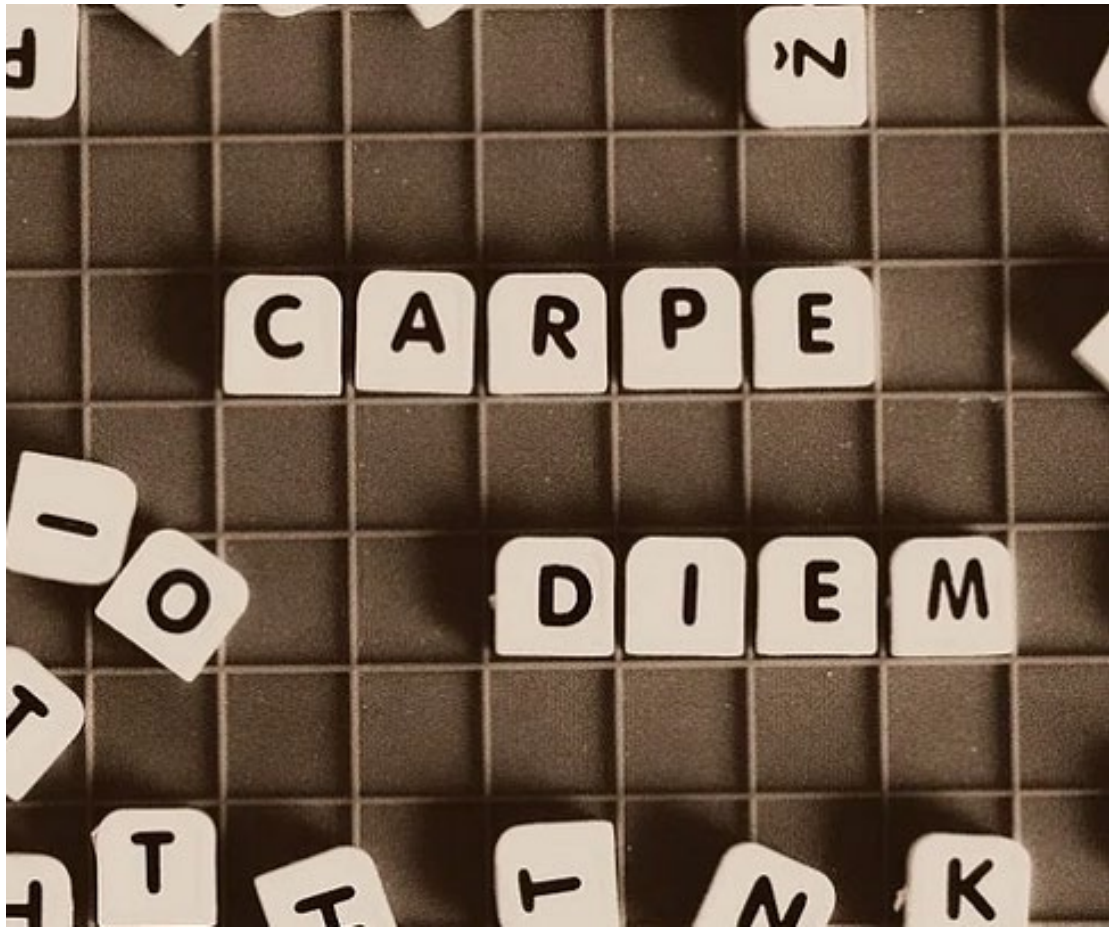
Opportunity Ahead (Right Now)

A. Grow
B. Improve efficiency
C. Expand portfolio
D. Increase taxes
E. A-C
F. All of the above



Enablers

Administration Intelligence

Collaboratives

Pay for Performance

Public Reporting

Centralization

Conclusions: “Think Differently” vs. “Do Differently”

- “The problem we're trying to solve is that there are rich teams and there are poor teams….It's an unfair game. And now we've been gutted.”
- **“We’ve got to think differently.”**
- **“Adapt or Die”**