Drug Coverage Evidence and Policy Options

Emerging Therapies Workgroup

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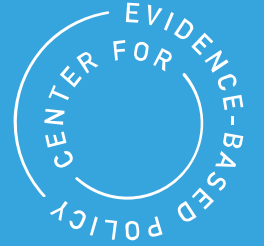


Overview

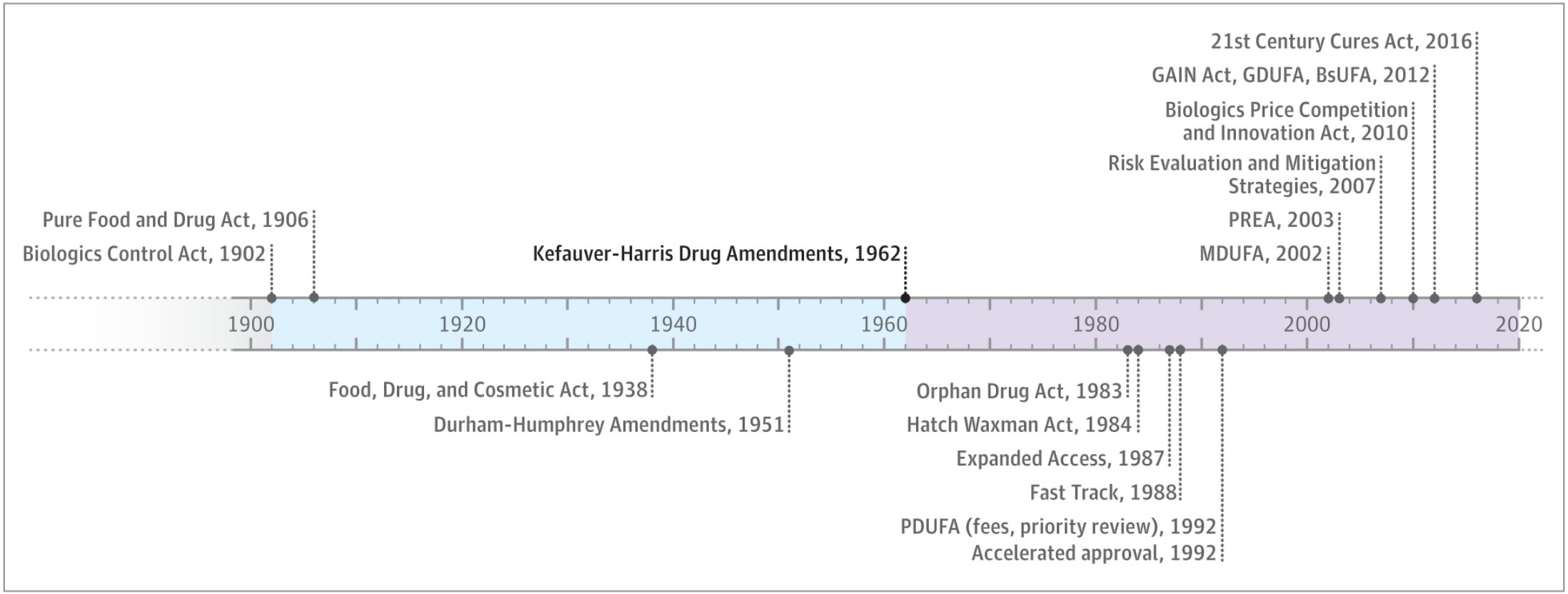
- Review the relationship between pharmaceuticals and Medicaid
- Understand the hierarchy of evidence to support coverage decisions
- Explore what states can do when there is little evidence
- Discuss best pathways forward for Washington

Pharmaceuticals and Medicaid

Background

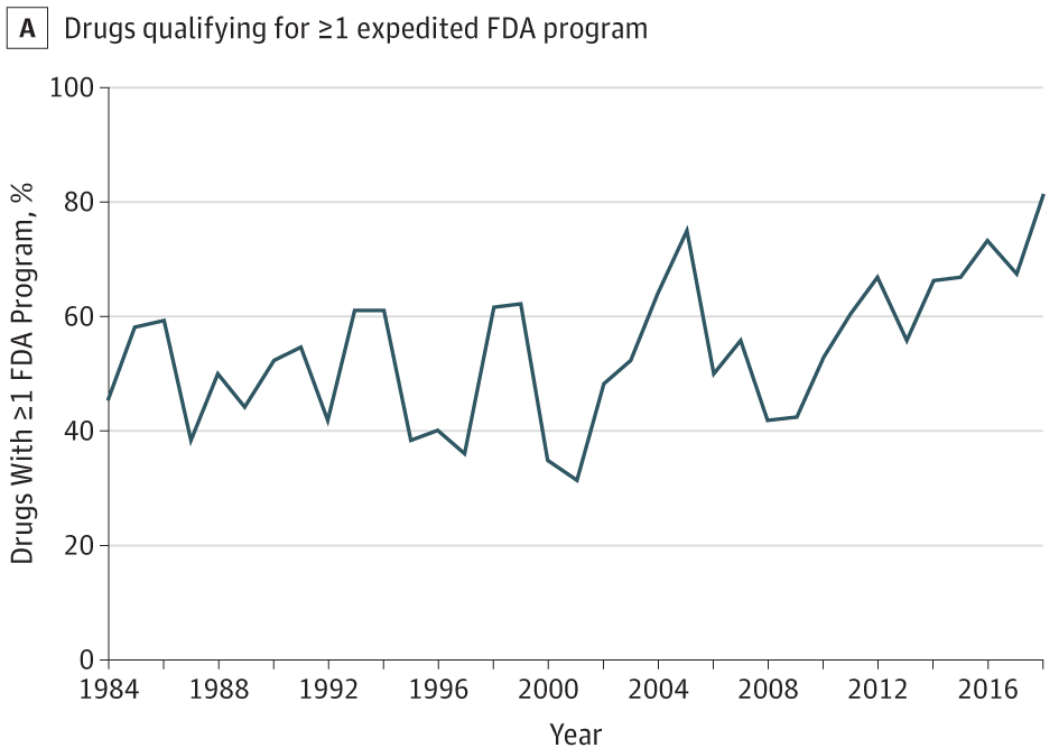
- Prescription drugs--fastest growing component in U.S. healthcare spending
- Directly resulting from influx of high cost specialty drugs and genetic therapies onto the marketplace
- Treating serious and complex disease states
  - Cancers
  - Blood Disorders (Sickle Cell Anemia, Hemophilia)
  - Hepatitis C
  - Genetic neurological disorders (Spinal Muscular Atrophy, Duchenne Muscular Dystrophy)

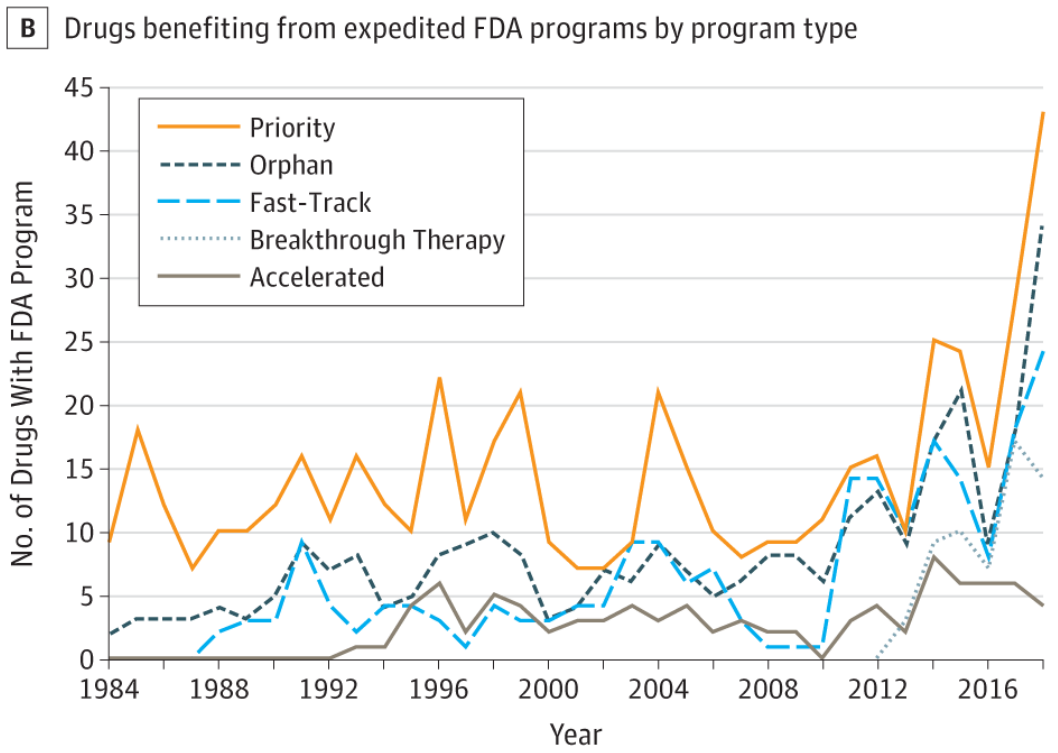
Evidence and New Drugs: Faster Approvals, Weaker Proof



Source: Darrow, et al. FDA Approval and Regulation of Pharmaceuticals, 1983-2018
JAMA. 2020;323(2):164-176. doi:10.1001/jama.2019.20288

Expetited FDA Approvals





Source: Darrow, et al. FDA Approval and Regulation of Pharmaceuticals, 1983-2018
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What is the Problem?

- Over 80% of new drugs benefit from at least 1 such program
- The proportion of approvals supported by at least 2 pivotal trials decreased from 80% in 1995-97 to 53% in 2015-17, while average trial size did not change[1]
- Overall, drugs are approved based on fewer and earlier stage trials, that may not be RCTs, blinded, controlled or based on outcomes that matter to patients[1]
- FDA required postapproval studies are often not done at all (35%) and most continue to use surrogate outcomes (66-92%), with only 5% demonstrating superior efficacy over comparators[2]

1. Darrow JJ, et al. FDA Approval and Regulation of Pharmaceuticals, 1983-2018. JAMA 2020;323(2):164-176.
2. Pease AM, et al. Postapproval studies of drugs initially approved by the FDA on the basis of limited evidence: systematic review. BMJ 2017;357:j1680.

A Cautionary Tale: Accelerated Approval of 17α Hydroxyprogesterone Caproate (17P) (Makena)

- From 2003-2011, 17P exclusively available as a compounded product
- FDA approval of Makena via the Accelerated Approval Pathway, based on 1 RCT using a surrogate outcome, with methodological limitations
- FDA required a 2nd confirmatory RCT which was finally begun in 2009
- Manufacturer granted 7 years of exclusivity under the Orphan Drug Act
- AMAG Pharmaceuticals had $1.2 Billion in revenue from Makena between purchase in 2014 and entry of generics in 2018
- The confirmatory RCT did not find improvements in gestational age, preterm birth, or perinatal mortality
- Advisory Committee recommended FDA withdraw approval of Makena for preventing preterm birth in October, 2019 . . . still awaiting a final FDA decision . . .

Godlewski BJ, et al. Obstet Gynecol 2020;135:1207-13.

Complicating Issue for States--
The Medicaid Drug Rebate Program

- Congress enacted MDRP in 1990
- MDRP created the construct of a voluntary rebate agreement between the drug manufacturer and HHS
  - If manufacturer enters into a rebate agreement, they are **assured coverage** of their drugs by Medicaid and Medicare
  - Voluntary, but **all** states participate
- Rebate agreement also ensures that CMS and the states:
  - Receive a rebate on a drug's price – set in statute
  - Do not pay more than a brand name drug's "Best Price" in the U.S. market

Medicaid Drug Rebate Program

- State management tools are limited under the MDRP
  - States are required to cover a drug if a federal rebate agreement exists
  - States can negotiate supplemental state rebates; typically confidential
  - States cannot use closed formularies, although preferred drug lists are allowed; and prescription limits are regulated
  - States can use prior authorization criteria with the PDL

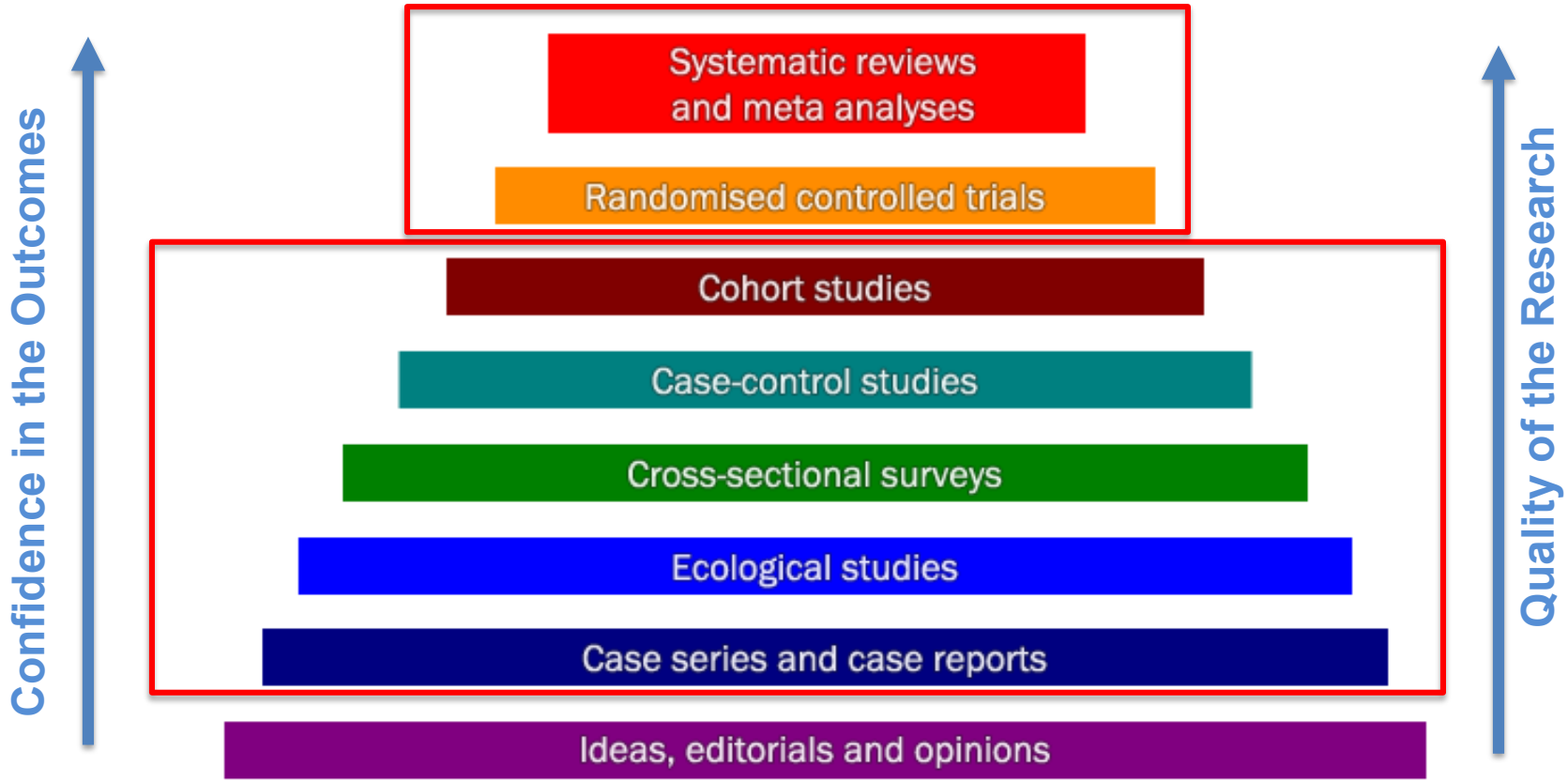
…**but in the end, the states will have to pay** – regardless of price, or effectiveness

State Situation and Needs

- New high-cost therapies are increasing
- State budgets are finite – 49 states have balanced budget requirements
- Trade offs are real
- States need better tools to provide access while managing costs

Evidence Hierarchy

The Evidence Hierarchy



The Evidence Hierarchy

The New Evidence Pyramid

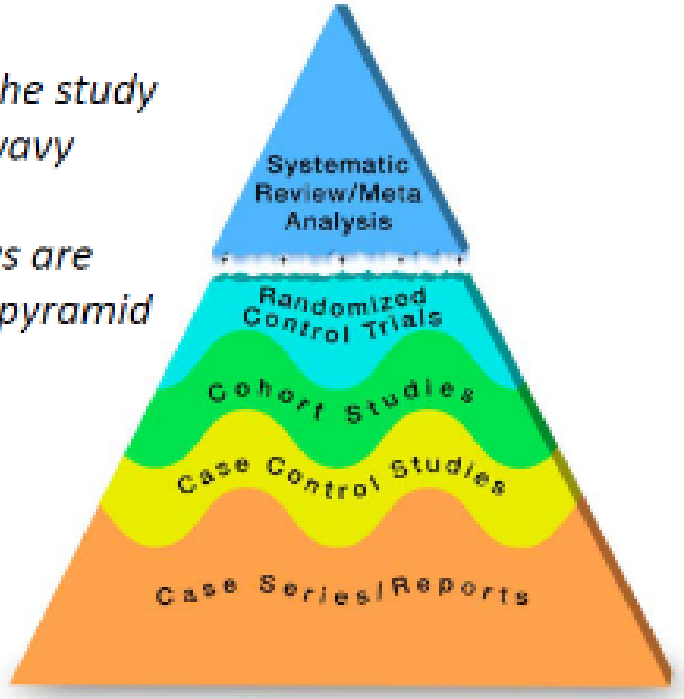
(*The Evidence Trapezoid*)

The traditional pyramid

(1) Lines separating the study designs become wavy (GRADE)

(2) Systematic reviews are 'chopped off' the pyramid

Revising the pyramid



Source: Murad, M H, Asi, N, Alsawas, M, & Alahdab, F. New evidence pyramid. *Evidence Based Medicine*. 2016. 21(4);125-127. *http://dx.doi.org/10.1136/ebmed-2016-110447*

What happens when interventions come into practice without sufficient evidence?

- 17P for recurrent preterm labor
  - Lots and lots of wasted money
- Stockpiling oseltamivir
  - Wasted money, false security
- Antiarrhythmics after MI
  - Excess death, wasted money, false security
- Rofecoxib (Vioxx) for osteoarthritis
  - Excess MI deaths for a condition that is not fatal
- Hydroxychloroquine & chloroquine for COVID-19
  - Data still accumulating, excess deaths and wasted money
  - FDA revoked emergency authorization on June 15, 2020

So, what's a state to do when evidence is poor?

- Cover for FDA indications and get best rebate possible
- Base medical necessity on characteristics of study population and inclusion or exclusion criteria from available studies
- Conditional continuation coverage
- Negotiate price based on volume or exclusivity
- Negotiate price based on outcomes
- Require data for coverage with subsequent tailoring of coverage criteria

- Or maybe just print money?
  - And is it only about cost anyway?

Coverage with Evidence Development

Coverage with Evidence Development (CED)

- CMS issued guidance November 2014
  - https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=27
  - *"While CMS has embraced an evidence-based medicine coverage paradigm, CMS is increasingly challenged to respond to requests for coverage of certain items and services when we find that the expectations of interested parties are disproportionate to the existing evidence base. At the same time, we believe that CMS should support evidence development for certain innovative technologies that are likely to show benefit for the Medicare population, but where the available evidence base does not provide a sufficiently persuasive basis for coverage outside the context of a clinical study, which may be the case for new technologies, or for existing technologies for which the evidence is incomplete."*
  - Does not apply to self-administered treatment (Medicare Part A and B only)
  - Routine costs of care are covered in both experimental and control arms of studies
  - Cost of the interventions themselves are covered by the study sponsor

Examples of Medicare CED Treatment Decisions

- Currently there are 23 CED treatments being studied:
  - Allogenic hematopoietic stem cell transplants (for multiple conditions)
  - Autologous platelet-rich plasma for non-healing wounds
  - Off-label use of drugs for colorectal cancer (irinotecan, cetuximab, and bevacizumab)
  - Pharmacogenomic testing for warfarin response
  - Vagus nerve stimulation for treatment resistant depression
- CED can be discontinued if more definitive evidence is gathered
  - Positron emission tomography for some solid tumors approved (brain, cervical, ovarian, pancreatic, small cell lung, and testicular cancers)
  - Issued 2004 and coverage without CED determined in 2009

Private Insurance and CED

- Generally slow to join the effort
- WISDOM breast cancer screening trial in California is an exception
  - Important comparative effectiveness question
  - Compares age-based vs. risk-based screening for women > 40 y.o.
  - Aims to enroll 100,000 women
  - UCSF investigators and Blue Shield of California key leaders, 2014
  - PCORI funding in 2015
  - Due to complete in 2023

Is CED an Option for Medicaid?

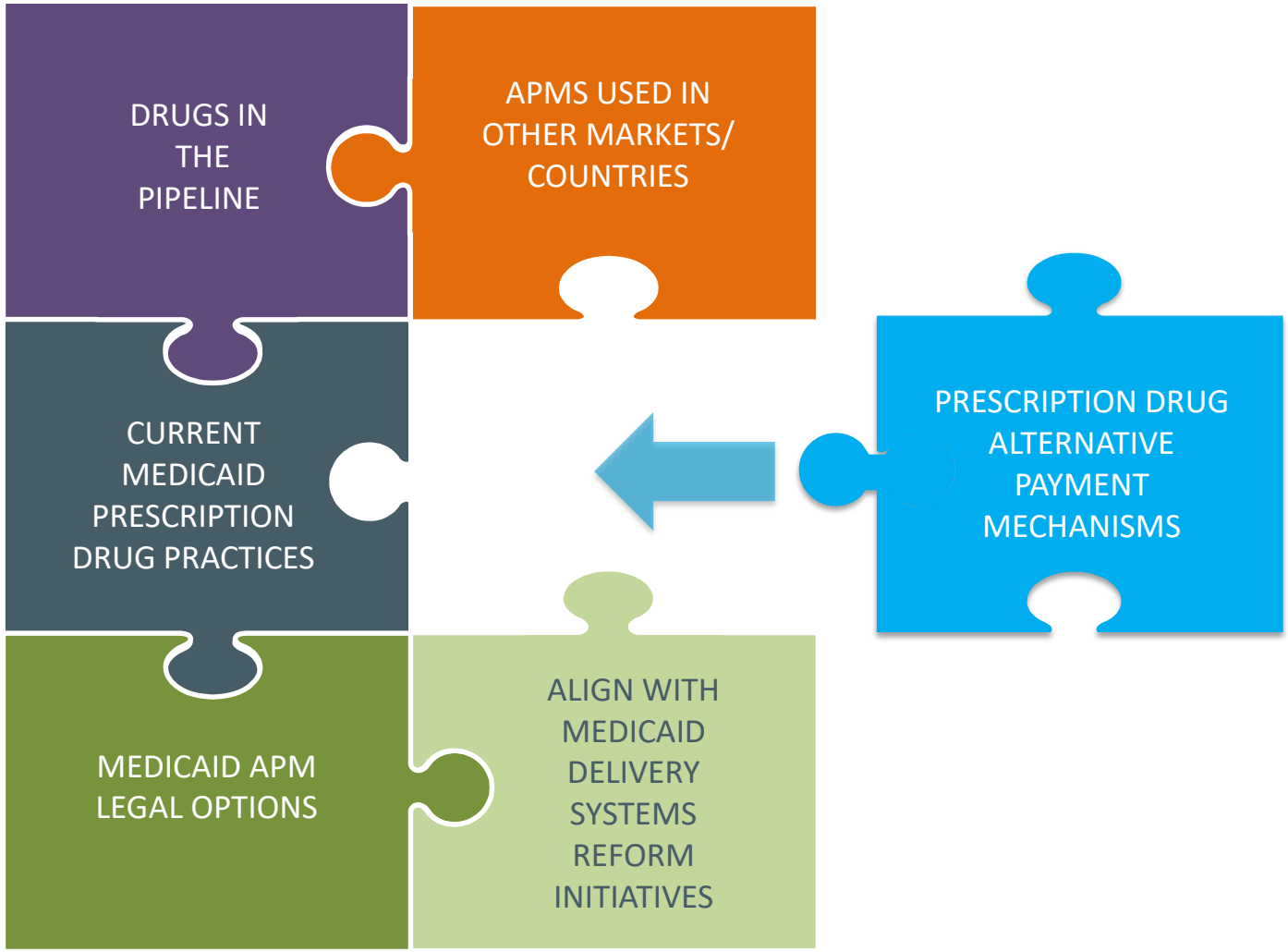
- States can allow participation in trials, paying for routine costs of care
  - Washington does this via an appeal mechanism
- Participate in evidence development while covering treatment
  - May help fill in evidence gaps
  - State data collaborations can help gather data faster
  - Requires a fair amount of coordination and effort
  - Academic partners may be valuable
  - Probably worth it, but states will assume costs of projects to gather information which has not been provided in the FDA approval process

SMARTEN Project

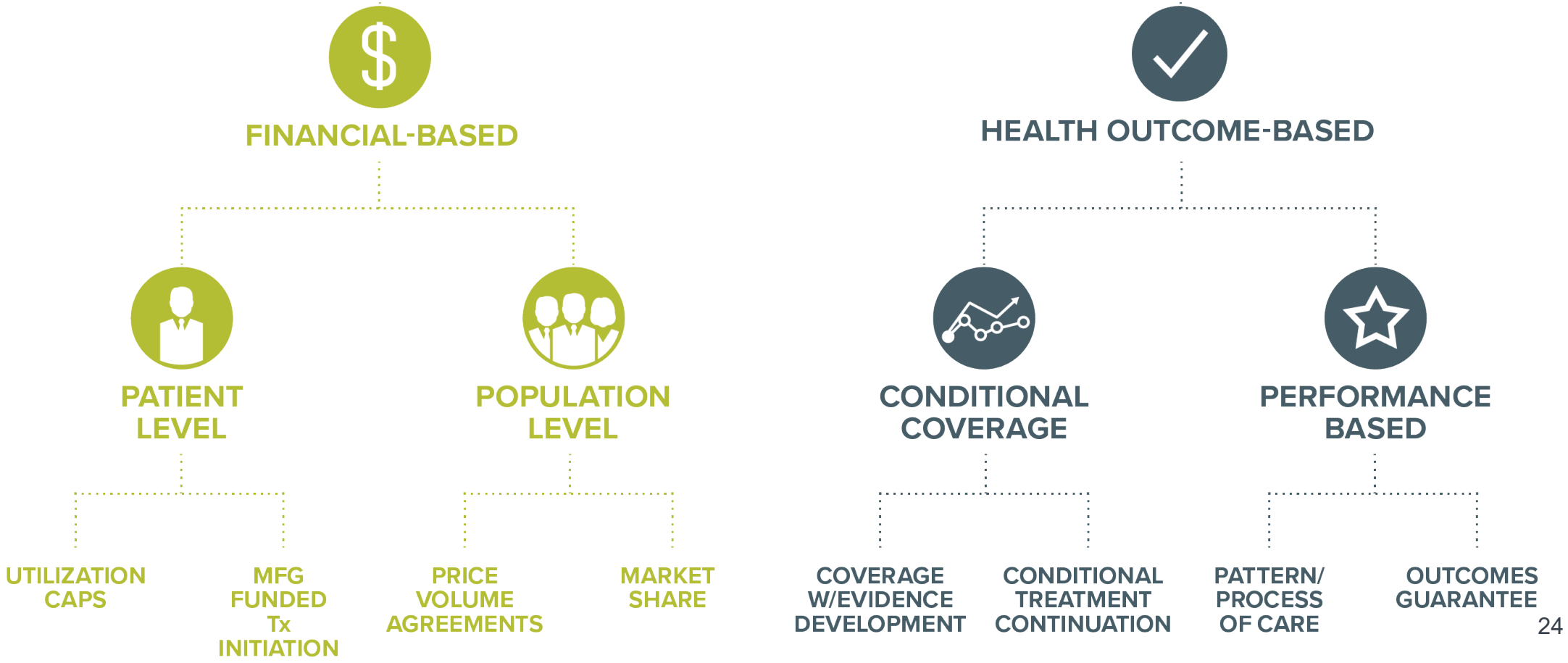
- The Spinal Muscular Atrophy Research: The Effectiveness of Nusinersen (SMARTEN) project
- Jointly funded by the DERP and MED projects at CEBP
- 7 participating states
- Population
  - Children with SMA types 1 or 2 not enrolled in a trial
- Outcomes
  - Mortality
  - Need for permanent ventilation (i.e., 16 hours or more/day)
  - Motor function
- Additional data on sex, dates of birth and diagnosis, use of PT and other care
- 30 month study, due to complete 2021

State Pharmacy Purchasing Alternatives

Medicaid Prescription Drug APMs: Putting the Pieces Together



ALTERNATIVE PURCHASING MODELS



Potential Drugs & Conditions for APM Development Consideration

- Hemophilia
- Hepatitis C
- Biologic Anti-inflammatories
- Oral Chemotherapy
- Atypical Antipsychotics – Long-Acting Injectables
- Multiple Sclerosis
- Spinal Muscular Atrophy (SMA)
- Duchenne Muscular Dystrophy
- Cystic Fibrosis

Frameworks for Using Evidence in Policymaking

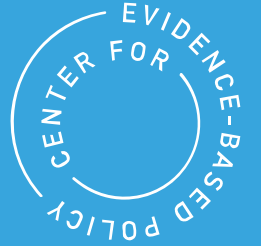
Source: Jacobs JA, Jones E, Gabella BA, Spring B, Brownson RC. Tools for Implementing an Evidence-Based Approach in Public Health Practice. Prev Chronic Dis 2012;9:110324.

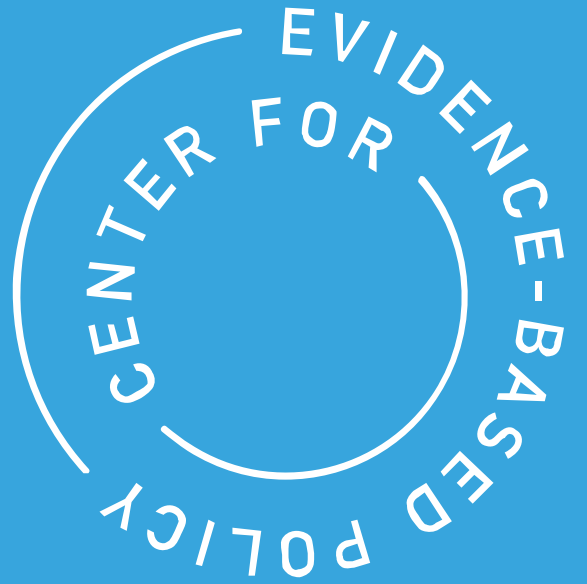
Discussion

What are the best pathways forward for Washington?

- How should the state consider evidence?
- Should the state be explicit about trade-offs?
  - Population vs. Individuals
  - Health vs. Other state priorities and needs
- Should the pathway vary by drug?
  - By condition or population?
  - By manufacturer?
  - By a price threshold?
  - By an evidence (or lack thereof) standard?

Questions?




CENTER FOR EVIDENCE-BASED POLICY