NATIONAL ACADEMIES Sciences Engineering Medicine

WELCOME

Committee on Strategies to Better Align Investments in Innovations for Therapeutic Development with Disease Burden and Unmet Needs: Report Release Webinar

July 15th, 2025

11:00 am – 12:00 pm ET

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Aligning Investments in Therapeutic Development with Therapeutic Need

Closing the Gap

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JULY 2025

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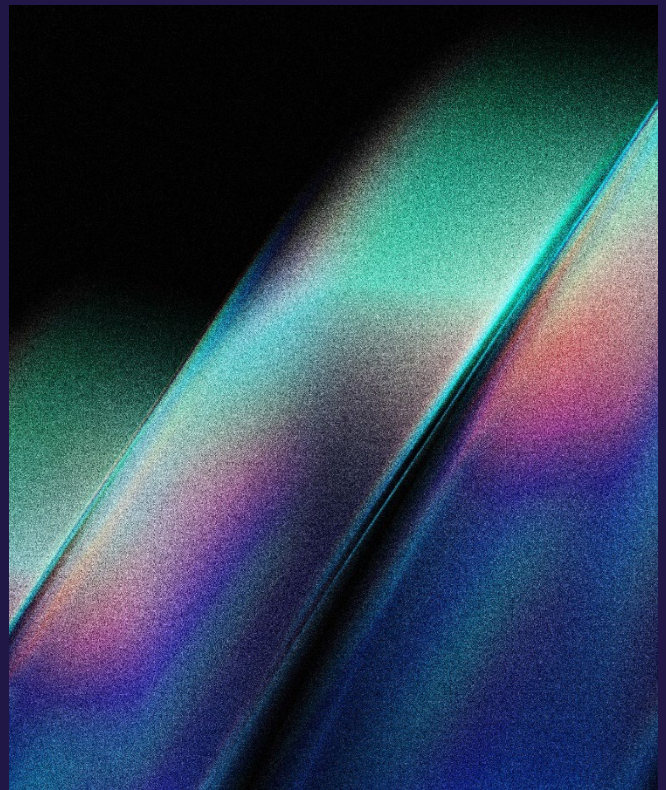
Background



01

U.S. lacks a strategic approach to research priority setting

- U.S. market has seen substantial therapeutic developments that improve care
- Therapeutic development requires investment of capital, time, and personnel
- It is unclear whether R&D investments are being made where they can provide the most benefit

Decisions regarding investments in therapeutic innovations are complex and involve multiple actors

- Drug development cycle involves many actors, including
  - National Institutes of Health
  - Food and Drug Administration
  - Insurers (CMS)
  - Pharmaceutical companies
  - Venture capital
  - Nonprofits
- Actors have different priorities that influence their investment decisions
- These priorities may or may not align with addressing unmet need
- Private sector investment decisions are often based on return on investment
- Value judgments may influence decisions

Statement of task and committee approach

Gates Ventures and Peterson Center on Healthcare asked the National Academies to:

- Describe the current disease burden in the U.S.
- Characterize the degree and patterns of mismatch between U.S. disease burden and innovation in therapeutic development
- Describe the challenges in better aligning innovations in therapeutic development with disease burden and unmet needs
- Propose strategies to better align public and private investments in innovations in therapeutic development with disease burden and unmet needs

The committee focused the scope of their work:

  - U.S. context
  - Therapeutics prioritized while recognizing influence of diagnostics
  - Consideration of market access
  - Baseline premise that maintaining U.S. leadership in innovation is valuable

Committee, fellows & staff

Donald M. Berwick (*Co-Chair*), Institute for Healthcare Improvement

Ellen MacKenzie (*Co-Chair*), Johns Hopkins University Bloomberg School of Public Health

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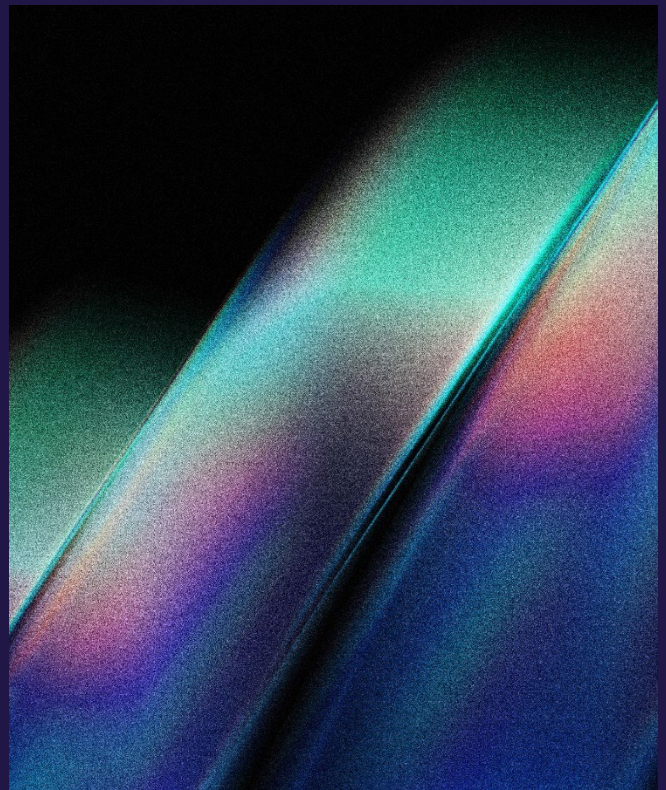
Defining Disease Burden & Unmet Need



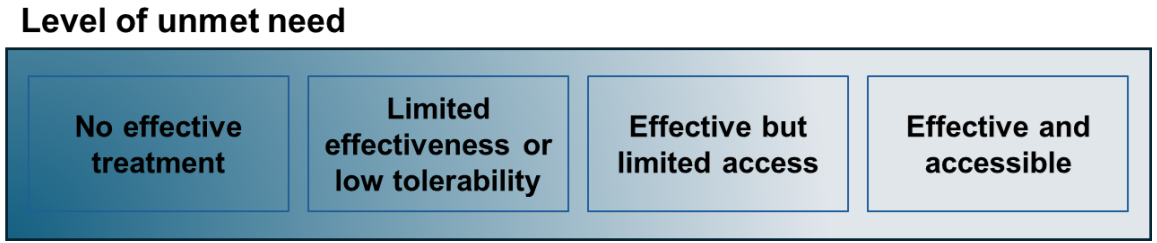
02

Measuring disease burden is complex and unstandardized

- Disease burden encompasses frequency, duration, and severity of disease
- Multiple measures of disease burden on society have been developed
  - Disability-adjusted life-years
  - Quality-adjusted life-years
  - Health-related quality of life
- Measures of disease burden on individuals can help contextualize lived experience
  - May be particularly useful for estimating the burden of rare diseases
- There is no single method for measuring disease burden

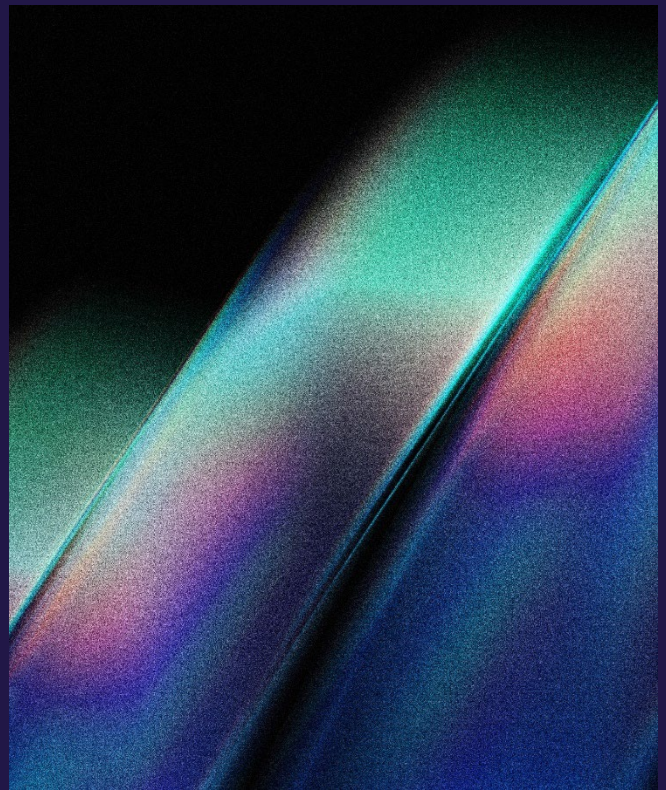
Unmet need exists on a continuum

- Unmet need may refer to various scenarios in which a patient population lacks adequate treatment to effectively manage their condition



- Unmet need can persist after treatments are developed for multiple reasons
  - Adverse effects/ poor tolerability
  - Modest effectiveness
  - Effectiveness limited to certain subpopulations
  - Technology and infrastructure limitations

Identifying & Diagnosing Misalignment

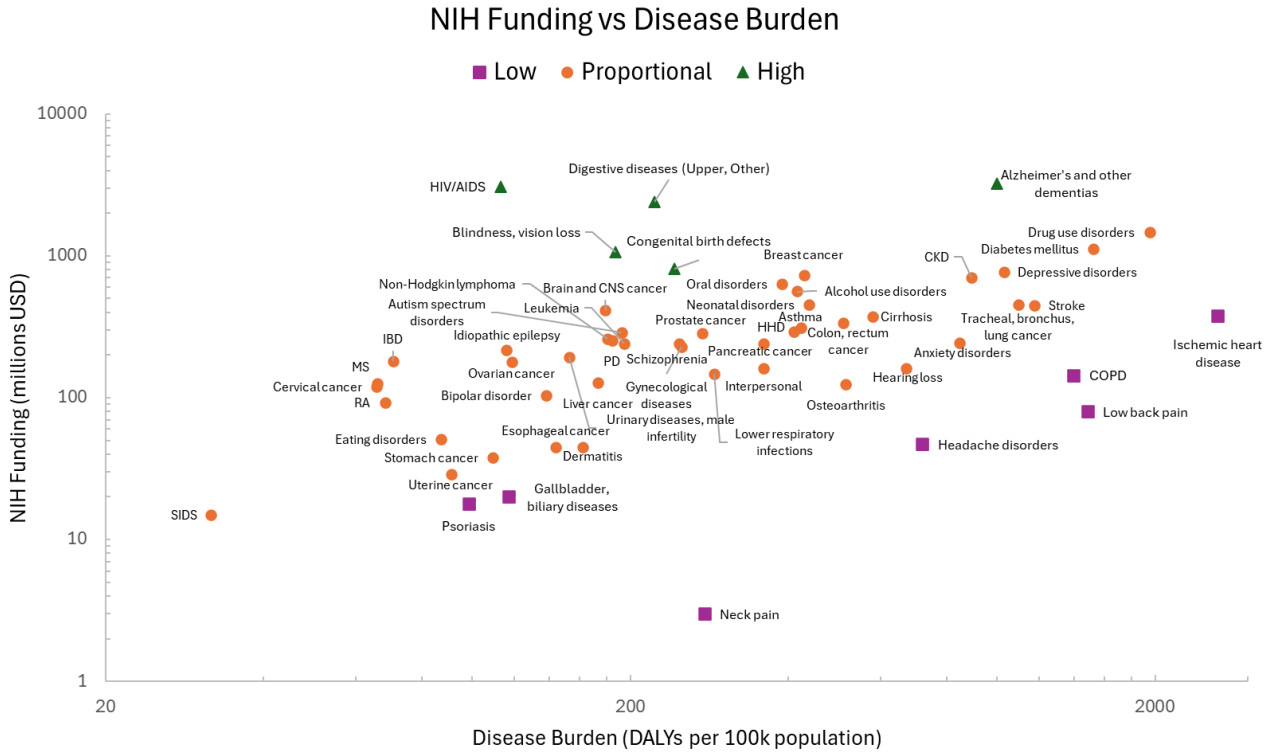


03

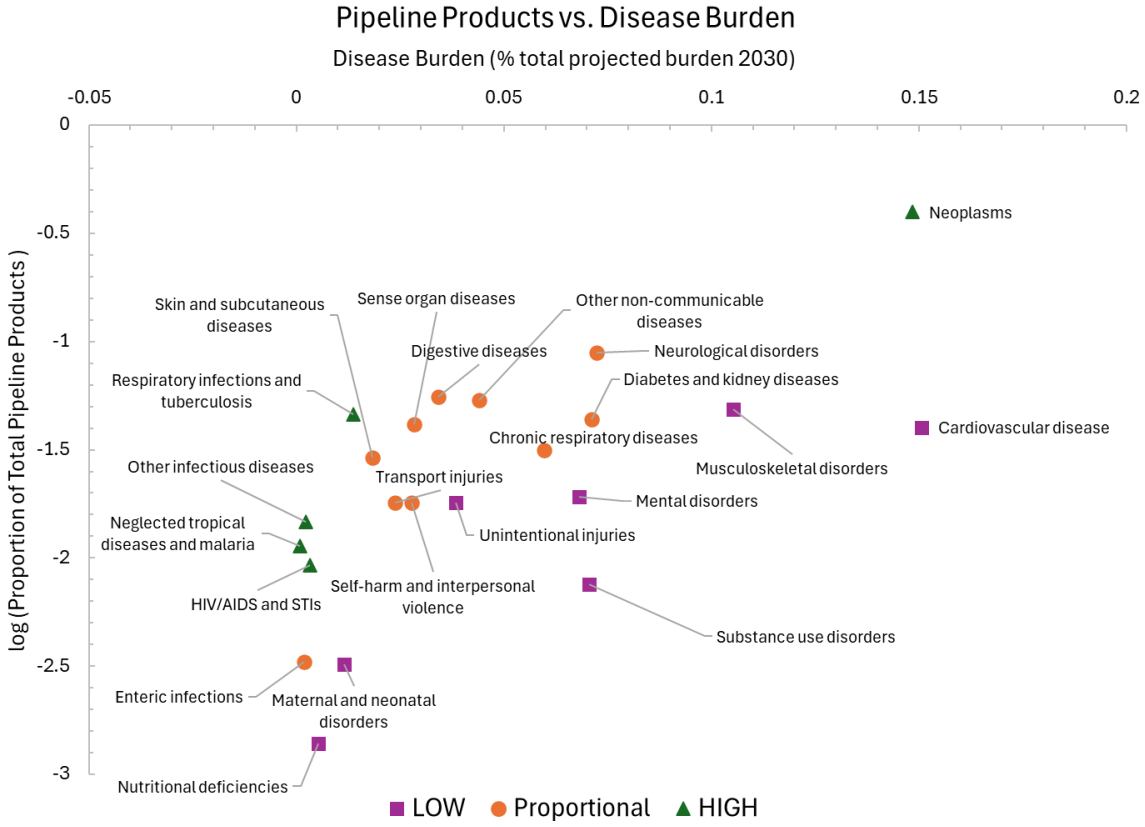
Data limitations complicate a full accounting of misalignment

- Categories used to measure funding and disease burden are inconsistent
- Early-stage investments may have broad benefits for multiple disease areas
- Available metrics are imperfect measures of disease burden
- A multitude of agencies contribute to public funding of biomedical research
- Data on private funding levels are unavailable
- Inability to compare between public and private investments

NIH funding is broadly aligned with disease burden, with some exceptions



Private investment in therapeutic development is difficult to track



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Congress should establish and fund an interagency consortium charged with tracking and assessing unmet therapeutic need associated with U.S. disease burden and current investments in innovation, with a critical focus on identifying areas of mismatch and reducing health disparities. The consortium should be led by a relevant unit of the Department of Health and Human Services (HHS) as determined by the Secretary of HHS.

RECOMMENDATION 1

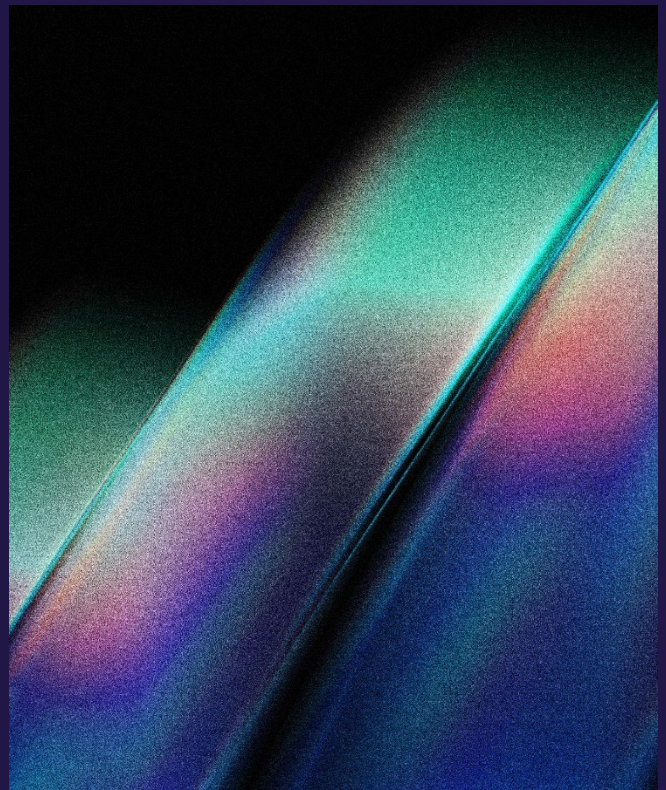
Limitations in scientific knowledge and capabilities can impede innovation

- A poor understanding of disease pathophysiology and associated molecular targets can limit development
  - Artificial intelligence and platform technologies could advance understanding of disease mechanisms and accelerate treatment development
- A high degree of heterogeneity within a disease can also stall innovation
  - Diagnostics that can identify likely treatment responders could minimize uncertainty and promote treatment innovation
- Challenges measuring outcomes, including lack of biomarkers, can make therapeutic development more complex
  - Timely development and validation of novel endpoints could facilitate development and approval of innovative drugs

Misaligned economic incentives can produce misalignments in innovation

- Net present value and return on investment drive for-profit investment decisions
- Lengthy trials increase development costs and can discourage development
- The scientific complexity of certain populations increases the cost of development
- Trials with both small and large patient populations can discourage investment
- Low reimbursement rates can discourage development of drugs with a large share of Medicaid enrollees
- The U.S. reimbursement structure limits willingness to develop one-time curative therapies and drugs for low-probability, high-impact scenarios

Strategies to Improve Alignment



04

Public investment steers research priorities

- NIH is the largest funder of biomedical research in the world
- Basic research discoveries funded by NIH enable the private sector to develop therapeutic innovations
- Private funders often rely on evidence generated through publicly-funded research to de-risk their investments in later stage research
- Investment decisions at NIH affect research priorities of other downstream actors
- Neither NIH or Congress explicitly consider unmet need in funding decisions

Funders of biomedical research should consider disease burden and unmet need when setting research priorities and directing funding.

RECOMMENDATION 2

Key questions can inform research priority setting

- What is the burden of disease based on occurrence and impact?
  - How is it measured?
- What is the level and type of unmet need?
- What is the current level of investment, and does it address the level of burden and unmet need?
- What are the barriers or challenge to innovation for this therapeutic area?
- What are potential strategies to spur innovation?

Public-private partnerships can promote innovation through cost and risk sharing

- PPPs enable collaborations that combine scientific capabilities with practical expertise
- Distributing risks across multiple partners can encourage investments in high-risk, high-reward technologies
- Agency-affiliated nonprofit foundations are well-suited to facilitate the establishment of PPPs
- PPPs could address unmet need by developing industry's shelved assets, but visibility of these assets is limited

U.S. federal scientific agencies with congressionally authorized nonprofit organizations associated, such as the Foundation for the NIH, CDC Foundation, Reagan-Udall Foundation, and Henry M. Jackson Foundation for the Advancement of Military Medicine, should increase the use of their nonprofits in order to focus on building PPPs in areas of mismatch between unmet need (encompassing both therapeutics and diagnostics) and innovation.

RECOMMENDATION 3

FDA administers multiple programs that address unmet needs

Efforts to Encourage Investment to Address Unmet Need	Efforts to Address Broad Scientific Challenges	Programs to Facilitate & Expedite Development & Review to Address Unmet Need
• The Orphan Drug Act • Patent term extensions • Priority review vouchers • Best Pharmaceuticals for Children Act	• Pediatric study requirements • Accelerating Rare Disease Cures program • Rare Disease Innovation Hub • START & RDEA pilot programs • Leader 3D • Rare Neurodegenerative Diseases Task Force	• Fast track • Breakthrough designation • Priority review • Split real time application review pilot • Real-time oncology review • Accelerated approval • FDA flexibility

FDA exercises regulatory flexibility to improve access to treatments, but occasionally overextends

Formal mechanism – accelerated approval

- Rather than established clinical endpoints, accelerated approval relies on surrogate endpoints, which may be unvalidated
- Confirmatory studies are required, but challenges with their timeliness and impact are prompting reforms

Informal mechanisms

- FDA frequently approves drugs outside of the accelerated approval pathway that have less evidence or certainty of effectiveness
- May lead to unresolved uncertainty in the drug's effectiveness or value

To maintain the appropriateness of FDA programs that expedite the development and review of therapies in areas of unmet need, including the accelerated approval program, the FDA should generously use its authority to impose post-market study requirements, ensure that required post-market studies are appropriately designed to confirm clinical benefit, and strictly enforce post-market study requirements.

RECOMMENDATION 6

To ensure that regulatory flexibility is exercised in a manner that promotes the approval of drugs that are both safe and effective, FDA should uphold strong regulatory approval standards. When FDA exercises flexibility, whether through accelerated approval or outside that pathway, the agency should require rigorous, timely confirmatory studies.

RECOMMENDATION 7

Congress should authorize a significant expansion of Food and Drug Administration (FDA) staffing and consistent resources to support the implementation of Recommendations 6 and 7, and especially to ensure that FDA has sufficient resources to monitor and enforce requirements for postmarketing surveillance and drug evaluation research.

RECOMMENDATION 8

Aligning reimbursement with product value would incentivize innovation for unmet needs

- Other countries limit drug spending by tying reimbursement to added value of the drug
- Value-based reimbursement could guide R&D investment toward products that address unmet need
- The IRA gives CMS authority to negotiate prices for several drugs
  - Unmet need is a factor that can be considered in negotiations
- The New Technology Add-on Payment program is another mechanism for CMS to incentivize development of products that address unmet need
- CMS currently has limited authority to connect reimbursement with societal value

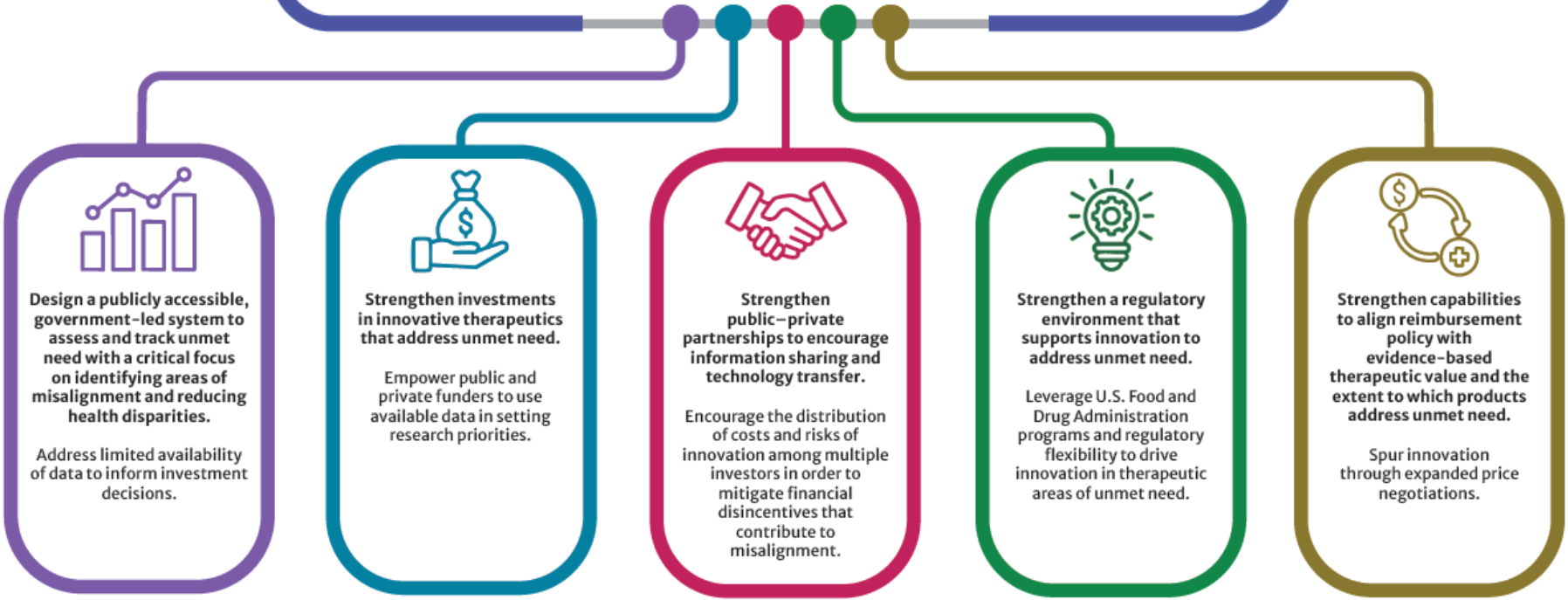
Congress should reform the statutory framework that regulates public reimbursement for novel drugs to better align reimbursement rates with evidence of clinical benefit as compared with existing therapeutic alternatives, if any.

RECOMMENDATION 9

CMS should use its existing regulatory authority to reduce the mismatch between Medicare reimbursement for a drug and that drug's ability to address unmet medical needs, including through its implementation of the drug price negotiation program and the NTAP program.

RECOMMENDATION 10

Five Strategic Goals



Design a publicly accessible, government-led system to assess and track unmet need with a critical focus on identifying areas of misalignment and reducing health disparities.

Address limited availability of data to inform investment decisions.

Strengthen investments in innovative therapeutics that address unmet need.

Empower public and private funders to use available data in setting research priorities.

Strengthen public–private partnerships to encourage information sharing and technology transfer.

Encourage the distribution of costs and risks of innovation among multiple investors in order to mitigate financial disincentives that contribute to misalignment.

Strengthen a regulatory environment that supports innovation to address unmet need.

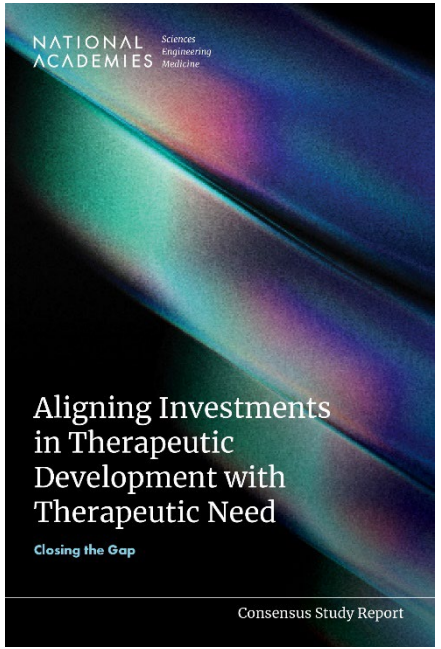
Leverage U.S. Food and Drug Administration programs and regulatory flexibility to drive innovation in therapeutic areas of unmet need.

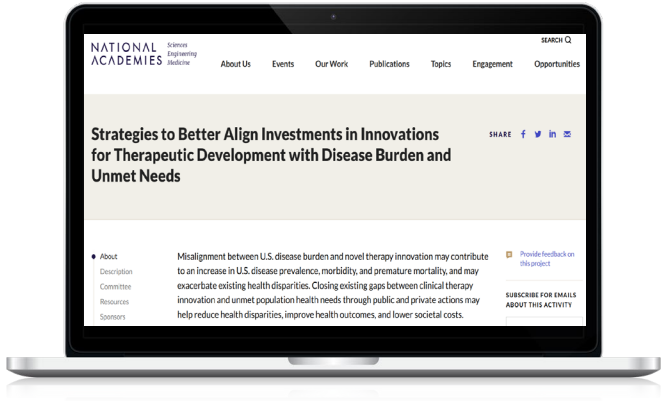
Strengthen capabilities to align reimbursement policy with evidence-based therapeutic value and the extent to which products address unmet need.

Spur innovation through expanded price negotiations.

Upcoming activities

- July 14: Public report release
- July 15: Report release webinar





Questions