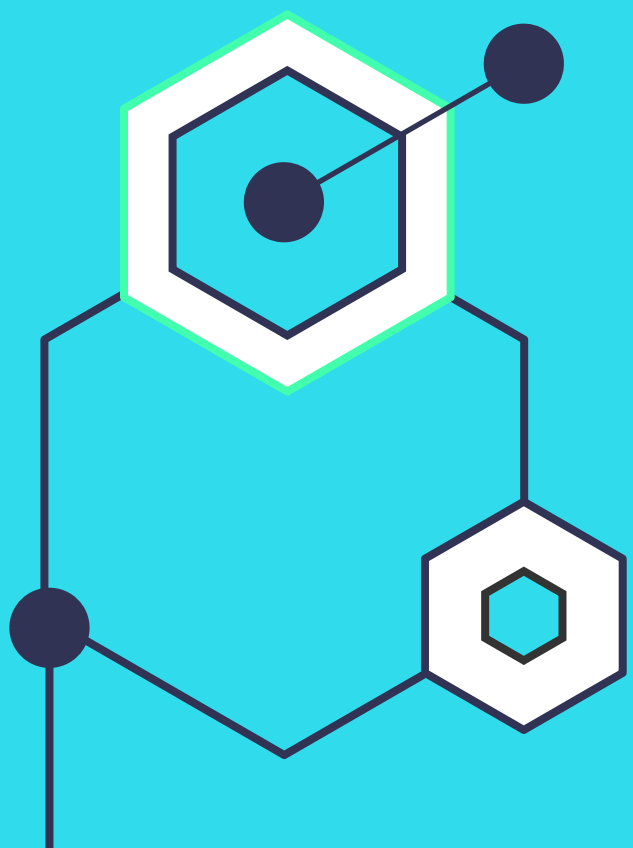
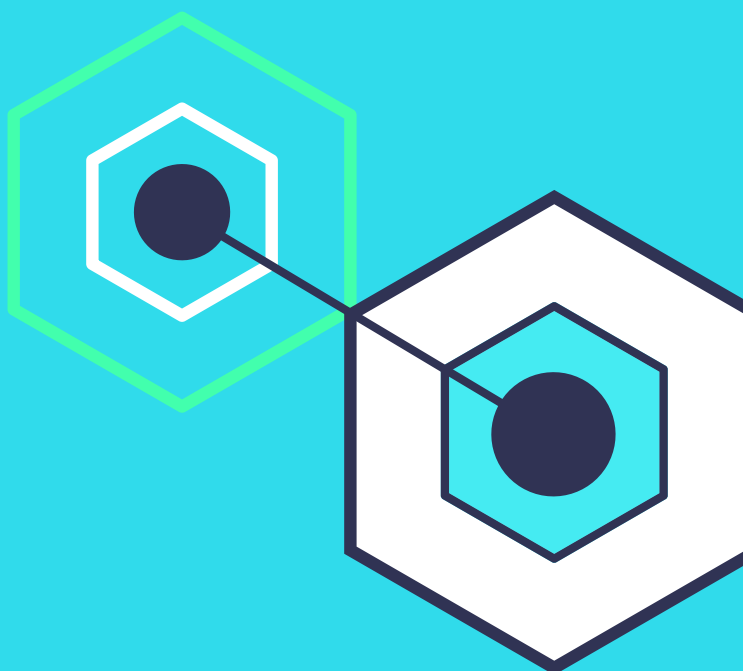
MILKEN INSTITUTE

Strengthening the Biomedical Innovation Ecosystem

A Scorecard for System Assessment

ESTHER KROFAH, SUSAN GUTHRIE, ALISHA SUD, ANNA DEGARMO





ABOUT THE MILKEN INSTITUTE

The Milken Institute is a nonprofit, nonpartisan think tank.

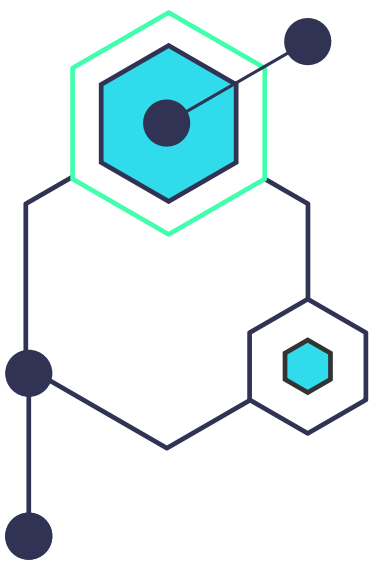
We catalyze practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. We leverage the expertise and insight gained through research and the convening of top experts, innovators, and influencers from different backgrounds and competing viewpoints to construct programs and policy initiatives.

Our goal is to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

ABOUT FASTERCURES

FasterCures, a center of the Milken Institute, is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.

CONTENTS



BACKGROUND

As patients, we often evaluate our interactions within the "system" of biomedical innovation with a simple question: "Did it work for me?" This evaluation considers many issues, including whether the best treatments are accessible and available, how they are delivered, and how they align with our identity, circumstances, and values to achieve the best possible health outcomes. However, of the myriad rankings that currently exist to measure health innovation, none can answer this fundamental question—which became even more pertinent as the COVID-19 pandemic underscored the longstanding health disparities in this country.

Recognizing this inadequacy, FasterCures, a Center of the Milken Institute, spent the past two years conducting research, convening experts, and developing a comprehensive framework to evaluate whether or not the biomedical innovation ecosystem is working for patients and society. Ideally, policymakers and other stakeholders will use the framework to identify and fix misaligned incentives, systemic barriers and gaps, and inefficiencies—and then evaluate the impact of implemented changes. Ultimately, we hope this framework can help evolve the biomedical innovation and care delivery ecosystem to work better for patients.

As a first step, FasterCures, in collaboration with RAND Europe, conducted an in-depth literature review to identify existing frameworks and, based on this research, proposed a strawman set of **domains and corresponding metrics** that encapsulate the key criteria necessary for a healthy and productive biomedical innovation ecosystem. FasterCures then convened a workshop with biomedical ecosystem stakeholders to vet and finalize seven proposed domains: **(1) capacity, (2) market environment, (3) collaboration and transparency, (4) efficiency, (5) patient centricity, (6) innovation and productivity, and (7) equitable access and use.**

Drawing on this research and stakeholder input, FasterCures built a visual tool to evaluate the health-care innovation ecosystem, which we refer to as a "dashboard." To reach this step, FasterCures created four domain-specific working groups tasked with finalizing the definition and rationale for each domain and identifying, modifying existing, or creating corresponding metrics. Because this work began in mid-2018, before the COVID-19 pandemic, we reconvened the broader project working group in June 2021 to ensure that the metrics within each domain held up given the new, added layer of complexity to the biomedical innovation ecosystem. The working group reached a consensus that they did.

We envision that these metrics will be refined through frequent use and ultimately integrated into performance assessments of the biomedical innovation ecosystem and global frameworks.

METHODS

PHASE 1: IDENTIFYING EXISTING FRAMEWORKS THROUGH LITERATURE REVIEW

FasterCures and RAND Europe conducted a targeted literature review to capture and summarize the existing literature regarding metrics and frameworks to assess the biomedical innovation ecosystem. To facilitate this work, we separated the "biomedical innovation ecosystem" into five topics to guide searches, assist in consultation with experts, and identify gaps in the literature: academic research, translation, private-sector research, regulation, and patient access.

We identified four good-quality reviews covering frameworks and metrics in the evaluation of academic biomedical and health research (see References). We initially focused our analysis on these four sources and then turned to specific reference papers where salient details were available. Further, to ensure adequate coverage of the literature on research integrity and research waste, we reviewed the series of papers in the *Lancet* on research waste and the 10th-anniversary commentary on progress by Glasziou and Chalmers (2018).

We found that the existing literature primarily focuses on the measurement of public- and charitably-funded research and development (R&D) and neglects broader components of the biomedical innovation ecosystem, regulatory systems, translational research, interactions between public and private research, and patient access to treatment.

Finally, we subjected the five topics to additional, targeted searches in specific databases (e.g., Google Scholar, PubMed), complemented by a review of relevant grey literature. A list of relevant search terms for each area and a description of screening, extraction, and analysis processes are provided in Appendix A.

PHASE 2: STAKEHOLDER ENGAGEMENT

Based on the literature review, FasterCures developed a strawman set of domains that provide a framework to assess the biomedical innovation system's performance for patient and societal benefit. Domains represent broad elements or characteristics of a high-functioning system that apply across all of the organizations and sectors within the system.

FasterCures then invited stakeholders engaged in product R&D to attend a workshop to review the strawman set and then decide on a final set of framework domains. Participants represented patient organizations, drug and medical device developers, regulatory agencies, basic science research, translational research, and the government. During the workshop, participants (1) discussed the comprehensiveness and accuracy of the strawmen set of framework domains, (2) crafted definitions of each domain

and the rationale for inclusion, (3) considered the role and importance of each domain within the ecosystem, and (4) specified the hoped-for actions that would result from measuring performance in each domain, toward achieving FasterCures' vision.

DEVELOPING A SET OF DOMAINS

STRAWMAN SET OF DOMAINS

The biomedical innovation ecosystem is complex and multifaceted. Many models of the ecosystem, or elements of it, are characterized linearly. Although this approach can inform understanding of processes within the ecosystem, a systems-led approach, which accounts for the multiple and complex interactions between actors and within the system, may better characterize and assist assessment of the health and development of the overall biomedical innovation ecosystem. Drawing on our 2019 literature review with RAND Europe of existing indicators and metrics for the biomedical innovation ecosystem and the domains in which they fall, we developed an initial strawman set of domains for discussion (see Appendix B, Figure B1). We also relied on the following sources to help us understand the collaborative, coordinated, and competitive nature of biomedical innovation originating in basic and translational research: the "Navigating the Ecosystem of Translational Sciences (NETS)" model, developed by the Genetic Alliance in 2013, and the "Drug Discovery, Development, and Deployment Map (4DM)" model, developed by the National Institutes of Health (NIH) in 2017.

The strawman domains represented a comprehensive set of elements or characteristics to which specific performance measures could be assigned. We chose broad domains that would:

- apply across every organization, step, and component of the innovation biomedical ecosystem;
- represent characteristics of a biomedical ecosystem that are important for optimal operation to benefit patients (e.g., patient-centeredness and transparency), as well as of any high-functioning system (e.g., efficiency);
- cover all aspects of performance important to patient-centered assessment; and
- remain commensurate with the scope of new medical product development.

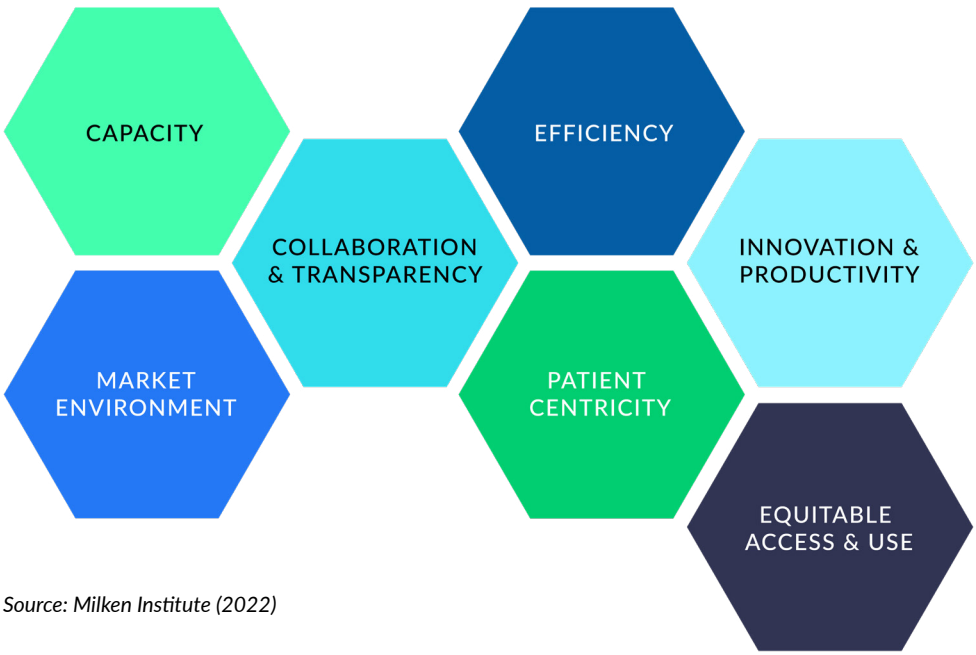
We avoided domains that apply specifically to the performance of parts of the broader health-care system (e.g., health-care delivery). We intended to create a framework that focuses on the critical elements of system performance from a patient benefit lens.

For the full set of strawman domains and examples of the types of measures and issues captured in these domains, see Appendix B.

FINAL SET OF DOMAINS

During a half-day workshop, FasterCures received a range of feedback on the strawman. Some stakeholders commented that the domains could be considered cross-cutting and therefore not warrant its own category. Stakeholders did not identify any missing domains. Figure 1 shows the domain set based on this feedback.

Figure 1. FasterCures' Final Consensus Domain Set



Source: Milken Institute (2022)

These domains encapsulate the key criteria necessary for a healthy and productive biomedical innovation ecosystem and provide a framework to assess the ecosystem through a social benefit lens. The stakeholder-generated definitions/rationales for each are described below.

DOMAIN 1: CAPACITY

A biomedical innovation ecosystem's capacity allows for sustainability and creativity through sufficient resources, including adequate and well-directed funding and a trained, diverse workforce to ensure a variation of thought to drive innovation. Capacity is a primary factor in driving innovation—without funding, a workforce, and training for the workforce, work cannot be done. Capacity encapsulates a blend of resources that address system-wide gaps that might otherwise not be addressed by individual stakeholders. It also includes investing in under-resourced areas that are critical to efficiency in biomedical innovation.

DOMAIN 2: MARKET ENVIRONMENT

A healthy market environment for biomedical innovation is fueled by diverse capital sources—such as those with different time horizons and risk profiles, including venture capital, private funding, and philanthropy—that drive R&D of new products for patients. It includes financial incentives and reimbursement policies, and while a healthy market environment is important for driving innovation, it will not always be present. For example, a fluctuating market can impact the productivity, resources, and timeline during an innovation's pre-discovery phases. Current events may also drive demand in the market, as demonstrated by the COVID-19 pandemic and influx of aid toward R&D in that area.

DOMAIN 3: COLLABORATION & TRANSPARENCY

Collaboration and transparency promote greater openness throughout the biomedical innovation ecosystem, allow patients to make better-informed decisions, reduce wasted R&D time and effort, and make it easier to identify challenges and modify the system as needed. Collaborations may be measured by the number and effectiveness of public-private partnerships and the relationships that patients and patient groups have with the biomedical ecosystem. Data sharing and transparency are essential to ensuring that efforts are not duplicated, minimizing waste and inefficiency. The elimination of wasted time and actions, and the increased sharing of data, can be powerful in accelerating the speed of innovation.

DOMAIN 4: EFFICIENCY

A productive biomedical innovation ecosystem is efficient. It allows for increased speed, improved quality, and/or the reduced cost of innovations. Measuring efficiency in innovation is essential to making a learning system possible and justifies needed changes in the system. It can be measured through process markers (e.g., the reduction in time from the first clinical trial in humans to marketing application submission, a decrease in a product's overall development time, the increased speed of regulatory review), system innovation (e.g., improved approaches and the numbers and quality of new processes), and the increased sharing of learnings (e.g., in measuring the introduction of new knowledge into other system areas, the existence and effectiveness of feedback loops). Efficiency should focus on improving the processes that influence system learning and should acknowledge that efficiency is irrelevant when quality and safety are forfeited.

DOMAIN 5: PATIENT CENTRICITY

The involvement and agency of patients in the biomedical innovation ecosystem are essential to ensuring that innovation truly addresses patient needs, preferences, and health. A patient-centric biomedical ecosystem is empowered to achieve greater patient engagement and produces a more inclusive and diverse distribution of benefits. Patient participation must be measured when evaluating patient centricity. It could include the range of outreach activities, the level of patient input in R&D, the number of product development/research projects meaningfully and continually engaging patients, the level of patient input in regulatory decision-making, and the number of decisions made with patient input considered. Further, the incorporation of patient-provided data (e.g., patient preferences, patient experience data, patient-reported outcomes) in R&D is essential to ensuring that products and regulatory decisions are patient-focused.

DOMAIN 6: INNOVATION & PRODUCTIVITY

Innovation and productivity in the biomedical ecosystem ensure that a critical volume of quality product candidates come out of every stage of the R&D process and a diversity of effort is used to improve the odds of innovative discoveries. Metrics within this domain may focus on research productivity (e.g., the quality of outputs that include publications, the development of new research tools and resources) and product development productivity (e.g., the number and quality of products being developed and meeting patients' needs). It could also track drug candidates in development; new products approved, rejected, or withdrawn; the number of drug shortages; and products shelved for nonclinical reasons. The combination of such factors provides a perspective on where innovation may be lacking and where opportunities for productivity to advance may exist.

DOMAIN 7: EQUITABLE ACCESS & USE

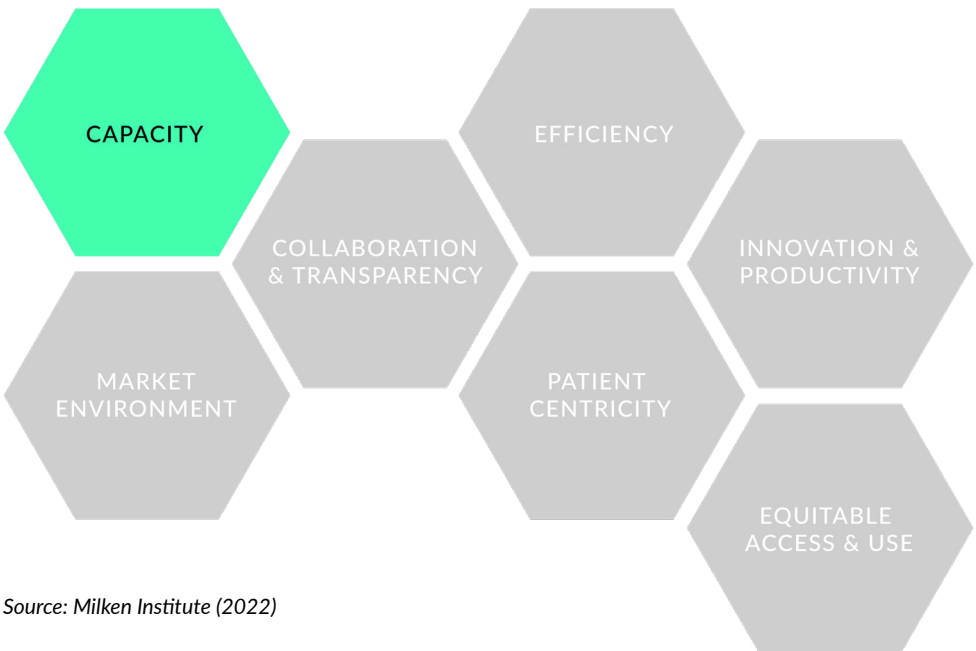
The objective of biomedical innovation is to develop products that are available to and can be used by patients when they need them. Equitable access and use ensure that innovations reach the appropriate audiences when and where needed. Metrics assessing access can include the percentage of met need, equitable access to products, the number of patients without access to a product (e.g., due to reasons such as cost, geography, and distribution/allocation issues), the expansion in the number of patients treated, and the delay in access to new products in developing countries versus developed countries. The equity component seeks to ensure that all population groups (racial, ethnic, socioeconomic, and geographic) can access and thus use a needed product. Additional metrics could include the adoption and overall uptake of a product and the circumstances under which a product was adopted.

DEVELOPING A DASHBOARD

To translate the framework into a dashboard of measures, we tasked our domain-specific working groups with finalizing the definition and rationale for each domain and identifying, modifying existing, or creating a set of sub-domains and metrics for each domain. In addition, we considered the impact of the COVID-19 pandemic on the framework because the pandemic has accelerated changes in the biomedical innovation ecosystem that may influence how we think about the framework domains and identify appropriate metrics.

We envision that the performance dashboard presented below will be refined through use. For example, in partnership with the RAND Europe, FasterCures conducted an initial study of the domains and measures in oncology. We are considering other use cases focusing on specific disease states as well as existing challenges in biomedical innovation. A fuller list of metrics for each domain and sub-domain are included in Appendix C. These measures are not exhaustive; further evaluation will be needed to determine whether each measure fits within the broader framework.

DOMAIN: CAPACITY



Source: Milken Institute (2022)

DEFINITION

A biomedical innovation ecosystem's capacity allows for sustainability and creativity through sufficient resources, including sufficient and well-directed funding and a trained, diverse workforce to ensure a diversity of thought to drive innovation. Capacity is a primary factor in driving innovation—without funding, a workforce, and training for the workforce, work cannot be done. Capacity encapsulates a blend of resources that address system-wide gaps that might otherwise not be addressed by individual stakeholders. It also includes investing in under-resourced areas that are critical to efficiency in biomedical innovation.

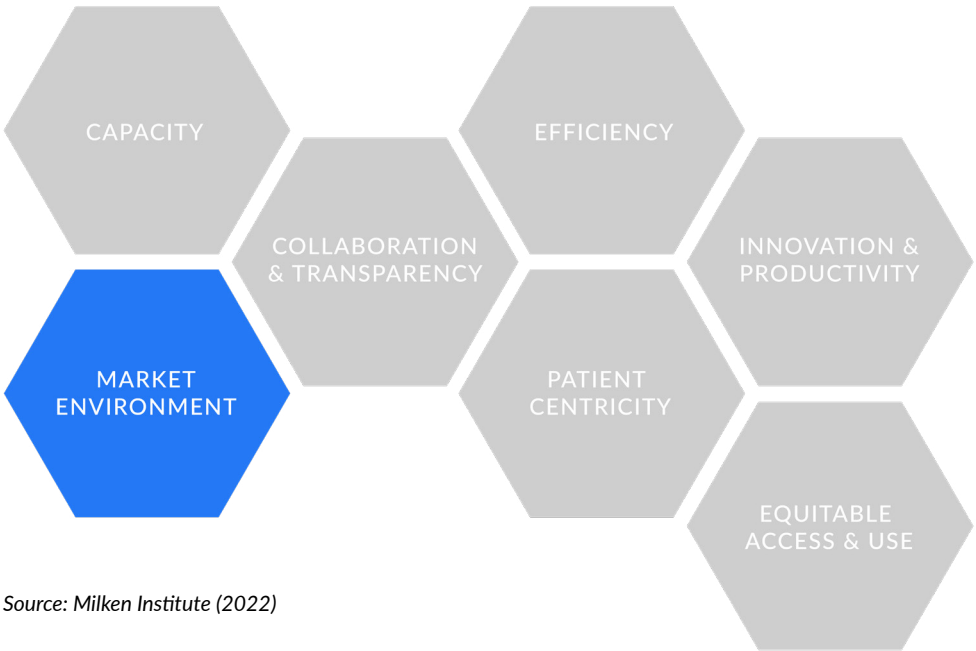
SUB-DOMAINS

- Quality of scientific research
- Scientific research culture
- Capacity of biomedical workforce
- Strength of biomedical infrastructure
- Strength of biomedical funding/research investment

EXAMPLE METRICS

- Percentage of research findings resulting in enhancement of existing resources and expertise
- Number of new institutes or centers as a result of research
- Number of new entrants in biomedical research workforce
- Percentage of biomedical research workforce shortages
- Career outcomes for biomedical researchers and trained students

DOMAIN: MARKET ENVIRONMENT



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DEFINITION

A healthy market environment for biomedical innovation is fueled by diverse capital sources—such as those with different time horizons and risk profiles, and venture capital, private funding, and philanthropy—that drive R&D of new products for patients. It includes financial incentives and reimbursement policies, and while a healthy market environment is important for driving innovation, it will not always be present. For example, market flux can be an impending factor during the pre-discovery phases of an innovation. Current events may also drive demand in the market, as demonstrated by the COVID-19 pandemic and flux of aid towards R&D in that area.

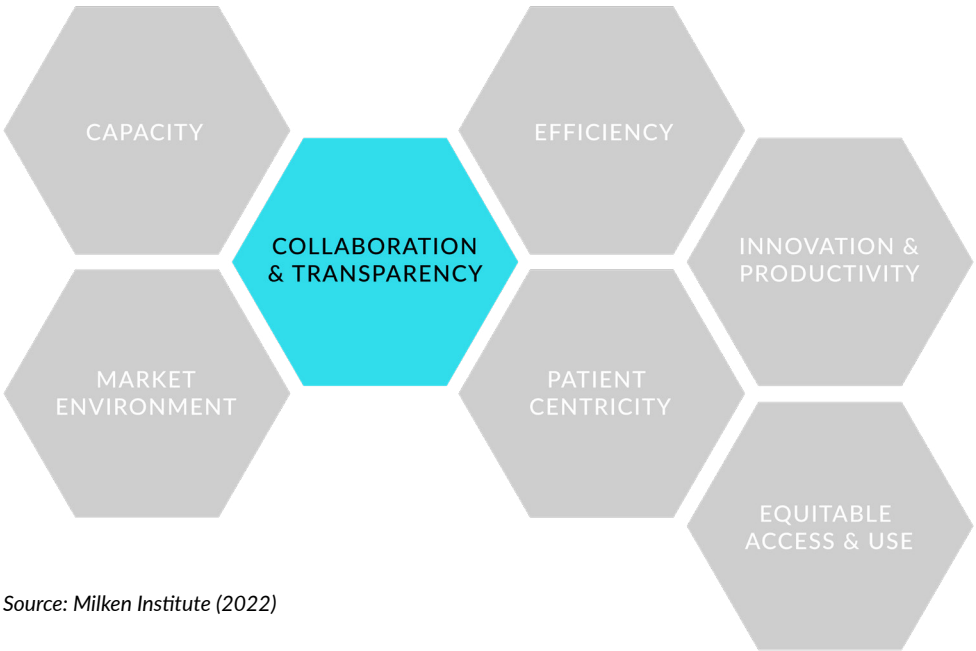
SUB-DOMAINS

- Activity of the policy and regulatory environment
- Strength of reimbursement policies
- Pace of biomedical research and development
- Market size and costs
- Innovative capacity and activity
- Scope of market networks

EXAMPLE METRICS

- Number of active biomedical research policy and regulation measures
- Number of changes to biomedical research legislation
- Number of new molecular entity approvals
- Number of new biologic approvals
- Number of drugs approved through accelerated regulatory pathways

DOMAIN: COLLABORATION & TRANSPARENCY



Source: Milken Institute (2022)

DEFINITION

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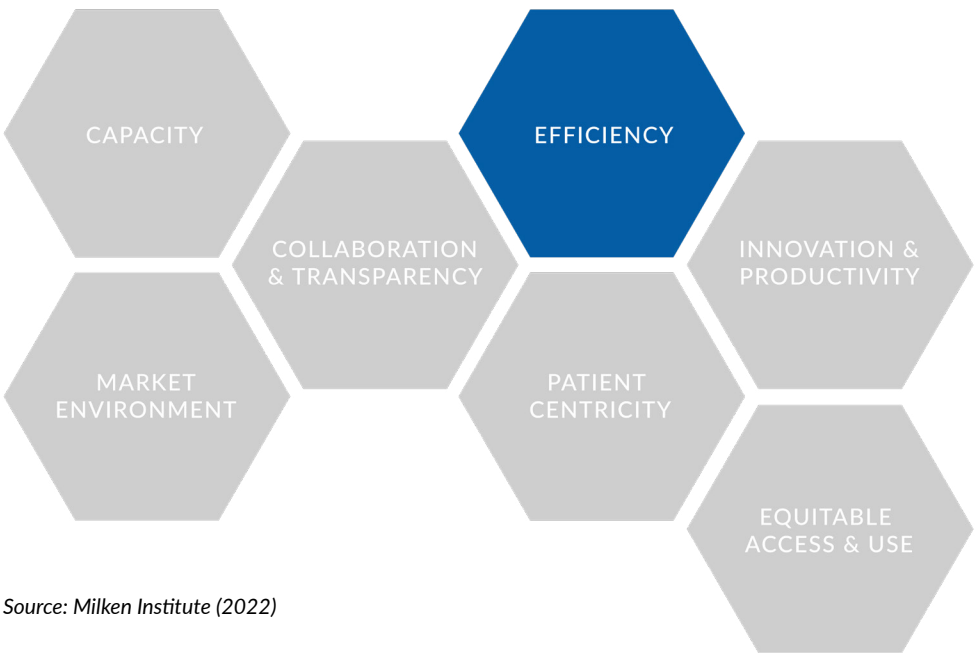
SUB-DOMAINS

- Key stakeholder collaboration
- Communication and public engagement
- Strength of data and information sharing
- Patient engagement
- Policy engagement
- Publication, citation, and reference

EXAMPLE METRICS

- Number/level/quality of partnerships among academia, industry, government, patient/disease advocacy groups, and other key stakeholders
- Number and range of dissemination and outreach activities
- Metadata from research data are shared with other parties
- Number/percentage of patients enrolled in clinical trials
- Number/percentage of citations/references of research findings in policy documents/guidelines/legislation

DOMAIN: EFFICIENCY



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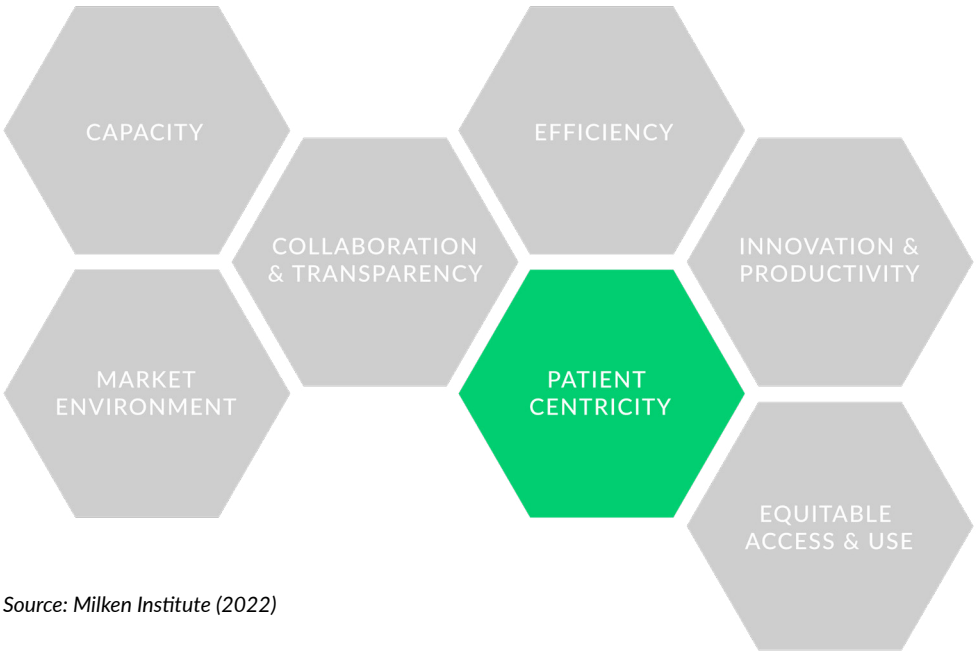
SUB-DOMAINS

- Process markers
- System innovation
- Sharing of learnings
- Time efficiency in biomedical research and development

EXAMPLE METRICS

- Reduction in time from first trial in humans to marketing application submission
- Overall development time
- Regulatory review timeline
- Average time for new drugs to pass through trial stages
- Introducing new knowledge into other system areas
- Number of new drugs brought to market (per billion US dollars of R&D spending)

DOMAIN: PATIENT CENTRICITY



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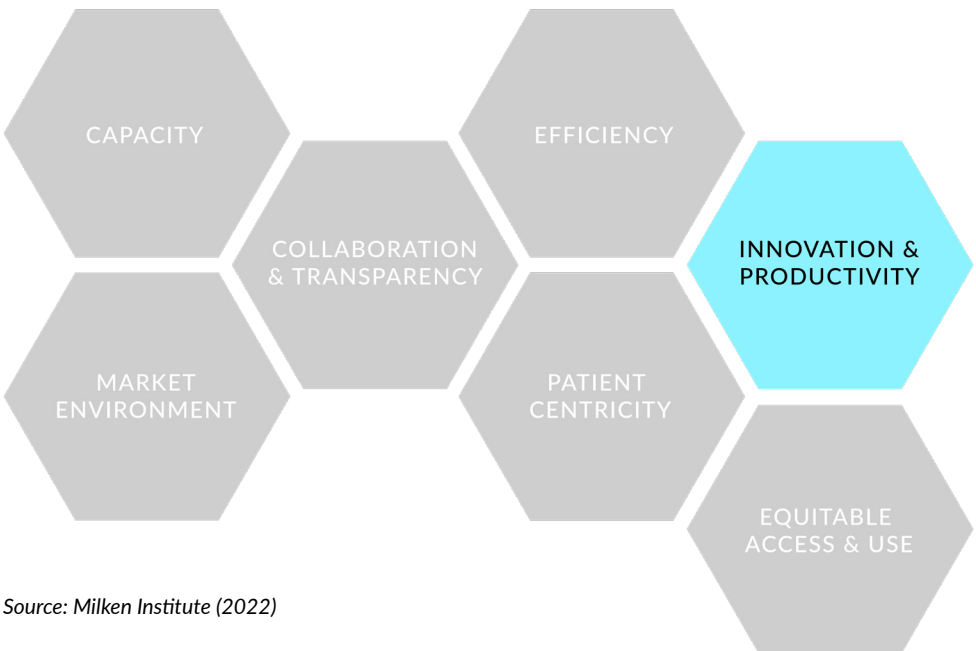
SUB-DOMAINS

- Communication and public engagement
- Patient input
- Patient preference
- Patient representativeness
- Patient outcomes
- Patient engagement infrastructure and training

EXAMPLE METRICS

- Number activities that include meaningful participation of patients or members of the public as appropriate
- Number of meetings/check-ins with patients
- Patient input during protocol/design phase
- Patient Reported Experience Measures (PREMs)
- What was the value of this patient-centric program–both quantitative and qualitative?

DOMAIN: INNOVATION & PRODUCTIVITY



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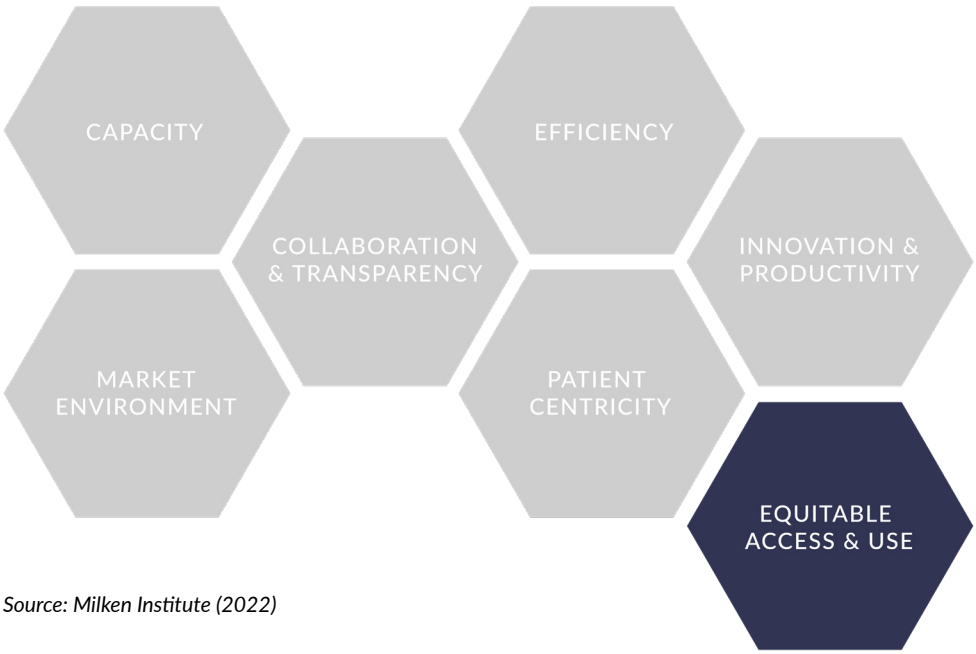
SUB-DOMAINS

- Strength of sharing ecosystem
- Innovative and evidence-based decisions
- Innovative partnerships
- R&D productivity
- Returns on investment and human health

EXAMPLE METRICS

- Application focus rather than constriction of ownership
- Shift in pipelines toward innovative and differentiated mechanisms, exploiting new pathways and targets
- Percentage of research spend or number of investments made with venture or other equity partners
- Success rates in clinical development
- Return on R&D investment
- Human health return per dollar of R&D investment

DOMAIN: EQUITABLE ACCESS & USE



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SUB-DOMAINS

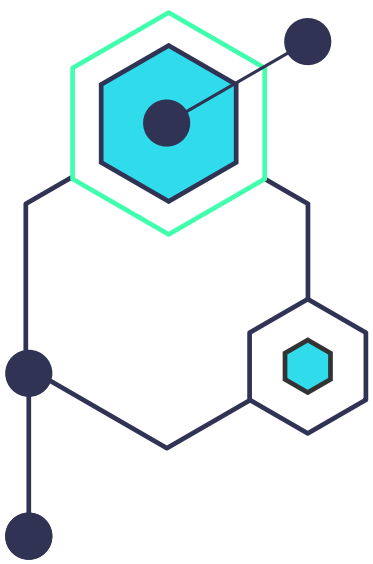
- Percentage of unmet need gap closed
- Equitable access to products
- Number of patients without access to product
- Expansion of patient population treated
- Access to R&I

EXAMPLE METRICS

- Access to clinical trials
- Number of lives touched
- Narrowing of health/health-care disparities
- Reduced cost of treatment
- Mortality rates

CONCLUSION

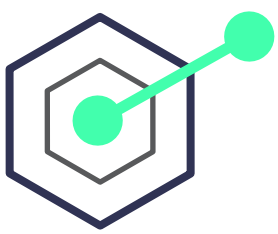
As outlined in this report, traditional metrics linked to biomedical innovation do not fully characterize the innovation process or its impact on health outcomes and patient needs. We believe that the global biomedical innovation system can do better for patients. By developing a comprehensive framework that enables evaluation of the whole ecosystem through a societal benefit lens and implementing a performance dashboard, we aim to optimize and re-align the system to do just that. Ultimately, we would like to see this work and the framework used to correct misalignment of incentives, identify bottlenecks, and drive policy change across the whole biomedical innovation ecosystem to ensure a learning biomedical ecosystem that improves health outcomes for all.



APPENDIX A

SEARCH STRATEGY

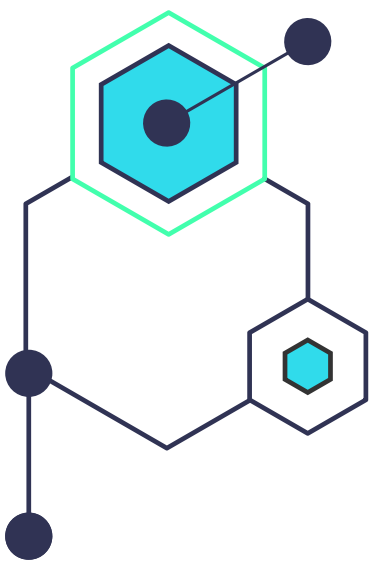
Issue Area	Relevant Search Terms
Translational research	((knowledge OR research) AND translation AND health) OR ((translational research) AND (indicators OR metrics OR measurement OR assessment))
Regulatory environment	Biomedical AND (innovat* OR treatment OR device) AND (regulat* OR legal OR law OR barrier OR challenge) (conceptual[All Fields] AND framework[All Fields] AND 'biomedical' [All Fields]) AND ('regulation' [All Fields]))
Private investment and public-private collaboration	Biomed* AND innov* AND (private* OR indust* OR pharma) Biomed* AND innovati* AND public AND private
Patient access to treatment[1]	(biomedical OR medical) AND ((new OR innov* OR pioneer*) AND (treatment OR device OR drug OR intervention OR procedure) AND (patient OR market OR cost OR price OR equity OR afford*)) AND (framework OR metric OR (access AND (evaluat* OR assess*)))
Ecosystem	Biomed* AND innov* AND (ecosystem OR system) OR incentive Biomed* AND innov* AND (ecosystem OR system) AND (framework OR metric* OR indicat*)



1. *Supplemented by targeted searches by author name for known experts—notably Peter Groeneveld and Janet Woodcock. Also supplemented by publications identified by experts at interview.*

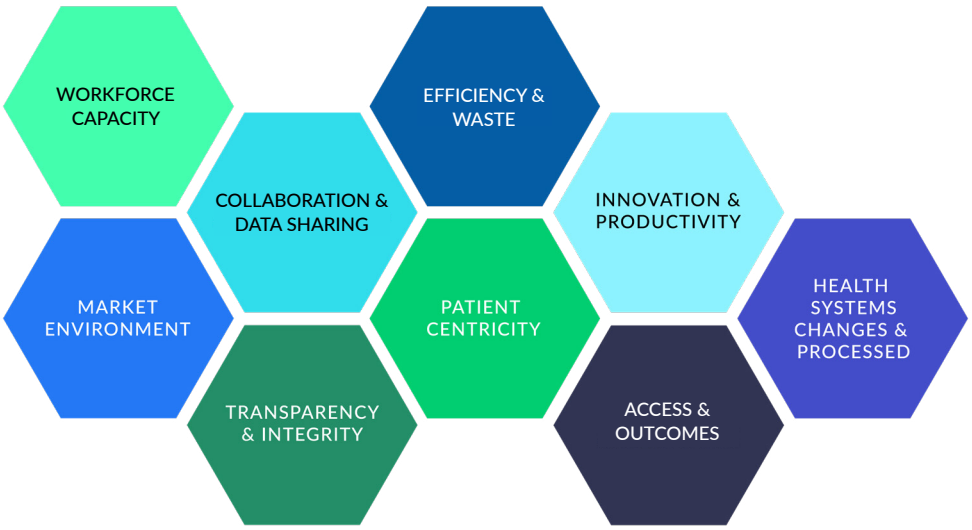
SCREENING, EXTRACTION, AND ANALYSIS

- **Screening:** Typically, we screened the first 100 papers by relevance for each search and identified those most relevant to the aim of this review—particularly those articulating specific indicators or metrics that have been used or proposed or those discussing frameworks and conceptualizations regarding the biomedical innovation ecosystem or its components. We prioritized papers based on year of publication (with priority given to more recent publications, e.g., in the past 10 years) and geographical location (with priority given to the US and comparable research and innovation systems). We accepted only publications in English. Following an initial screening based on title and abstract, we reviewed the full texts of relevant papers.
- **Extraction:** RAND Europe's research team recorded data about each reviewed paper, including general information about the publication, the key study questions addressed, and the evidence presented about the issue under analysis (e.g., regulatory environment, ecosystem, etc.).
- **Analysis:** We mapped the relevant evidence against initial study questions to identify the main findings of relevance. We then synthesized the evidence in this paper using a narrative synthesis approach.



APPENDIX B

FIGURE B1: STRAWMAN SET OF DOMAINS



Source: Milken Institute (2018)

Examples of the types of measures and issues captured in these domains are shown in the table below.

Domains	Types of Measures
Workforce capacity	**Measures of research capacity:** number and quality of researchers trained, collaboration and networking (academic and wider), career outcomes for researchers and students trained
Market environment	**Level of investment:** government spending on health research and development, funding received in different areas; Measures of pharmaceutical/other relevant industry spend on R&D **Global performance:** global sales, national origins of leading 75 global medicines, profit and revenues **Outcomes for companies:** new businesses developed and benefits for existing companies in terms of profitability, new clients, competitive advantage, efficiency, etc., percentage of sales revenues from new products/services

Domains	Types of Measures
Market environment	**Supply of biomedical innovations:** number of novel drugs approved; the number of drug shortages **Demand for biomedical innovations:** number of units sold one and three years after launch, percentage by value of national pharmaceutical market accounted for by new molecular entities (NMEs) launched within past five years
Collaboration and data sharing	**Interaction between public and private sector:** number and effectiveness of public-private partnerships, public-sector influence on innovations in drug development, industry/ institute co-publications or co-patents **Policy engagement:** interaction of researchers with policy and decision-makers through invitations, meetings, committees **Community engagement and empowerment:** number and range of dissemination and outreach activities; increased public understanding of and engagement with science and research (e.g., participation in clinical trials); more positive attitudes toward research and researchers; improved health literacy and empowerment of health-care consumers
Transparency and integrity	**Rigor:** research with appropriate design and methods (e.g., proportion of studies for which protocols and analysis plans are published at study inception) **Access:** is research fully published and accessible (e.g., the proportion of registered trials published) **Ethical oversight:** improvements in the ethical conduct of research and human subjects protection **Patient safety:** number of adverse drug events by severity, number of drug recalls, number of drug shortages prevented, number of ongoing drug shortages, number of new drug shortages

Domains	Types of Measures
Efficiency and waste	**Research and innovation process markers:** different points in the translational process can be used as markers to assess the level of progress or the time for progress between them (e.g., discovery, proof of concept, prototype development). Can also be used to measure the effectiveness and efficiency of specific elements of the process (e.g., percentage of clinical trials that fail to meet expected completion dates, or time from first screened patient to last screened patient) **Usability:** unbiased, usable research reports **Regulatory process measures:** overall time from first protocol submission to final medicines regulatory approval, the proportion of studies approved by research ethics committees without deferral, the average time from developed market authorization to approval in the global market
Patient centricity	**Relevance:** research that address questions relevant to clinicians and patients (e.g., the proportion of primary research studies that are funded based on a systematic review of existing evidence)
Innovation and productivity	**Measures of research productivity:** number and quality of outputs including but not limited to publications; new research tools and resources generated; relevance of research conducted; targeting of future research **Improved study designs and methods:** improved methods for recruitment of study participants, improved Institutional Review Board processes, improved approaches to cross-disciplinary working **Significance/level of innovations developed:** measures of efficacy and effectiveness of new interventions; the number of NME launches receiving US Food and Drug Administration (FDA) priority review (granted by the FDA to drugs offering a significant improvement); Cost-effectiveness for the consumer **New products and processes developed** (and patented, licensed, used), proportion of NMEs launched and scope of launch (internationally); venture capital access

Domains	Types of Measures
Access and outcomes	**Improvements in patient safety, quality of care, and outcomes:** e.g., patient-reported outcomes Measures (i.e., PROMs, QALY, Disability-Adjusted Life Year [DALY] measures, outcome measures by condition, mortality, and morbidity) **Equity of access:** Access to biomedical innovations by insurance type, demographic groups, and socioeconomic characteristics; share of patients recruited to global clinical research studies, by disease type and other characteristics; the number of and time to approval for generics; improved reimbursement practices and policies for providers **Population health improvements** (reflecting improvements in prevention and health promotion alongside treatment)
Health systems changes and processes	**Clinician engagement and relationships:** increased clinician engagement in research, more evidence-based practice, improved patient-clinician relationships **Clinical practice:** impact on professional training or development in health, impact on practice including efficiency/cost savings, implementation of new interventions, practice reflects evidence-based guidelines, making processes more efficient or resilient, etc. **Impact on policy:** citation of research in, or other influence on, policy documents including guidelines; resulting changes in policy and improvement in public services (including outside of health, e.g., science, technology, engineering, and mathematics education)

Source: Milken Institute (2022)

APPENDIX C

FasterCures, along with our working groups, developed a broader list of metrics to evaluate each of the seven domains and corresponding sub-domains. These measures are not exhaustive; further evaluation will be needed to determine whether each measure fits within the broader framework.

DOMAIN: CAPACITY

- Research and Its Quality
  - Percentage of research findings resulting in enhancement of existing resources and expertise
  - Number of new institutes or centers as a result of research
  - GPA of graduates
  - Number of PhD graduates and proportion completing PhD
  - Number of publications per PhD graduate
  - Number and total value of awards, repeat funding
  - Number and size of awards from major funders (e.g., NIH, Howard Hughes Medical Institute)
  - High grant application success rate
  - Researchers or staff recognized for leadership in the field
- Capacity of Biomedical Workforce
  - Number of new entrants in biomedical research workforce
  - Percentage of biomedical research workforce shortage
  - Career outcomes for biomedical researchers and trained students
- Scientific Research Culture
  - Evidence of opportunities to develop skills and knowledge through practical involvement in research activities (e.g., "learning by doing" opportunities)
  - Evidence of support for co-production of research (e.g., individuals/ organizations share ideas and knowledge development through networks and partnerships)
  - Percentage of research activity that has an impact on practice to make a difference
  - Protected time to signal the importance of research alongside practice
  - Partnered (co-invested) funding investments (name of organization, investment dollar [$] amount and percent [%] total, area of research)
  - Leveraged funding from follow-on funding

- Startup company formed as a result of the research study.
- Existence of IP policy

- Strength of Biomedical Infrastructure
  - Infrastructure (e.g., infrastructure grants, percentage of activity grants with infrastructure support)
  - Size of tech transfer office
- Strength of Biomedical Funding/Research Investment
  - Evidence of research priority-setting mechanisms to release resources to fund research that can "make a difference" (e.g., clear percentage of allocation to user-inspired, translational research)
  - Research targeting; funding calls to a release resource and signal importance of research activity
  - Use of matched funding models in large research programs
  - Funding opportunities to support "learning by doing" opportunities for individuals, to complement more formal research training
  - Venture capital (VC) money invested in startups

DOMAIN: MARKET ENVIRONMENT

- Activity of the Policy and Regulatory Environment
  - Policy decisions or changes to legislation (e.g., National Cancer Act of 1971)
  - Policy decisions or changes to regulation (e.g., Treatment Priority Review Voucher Program, Drug User Fees, etc.)
  - Number of active biomedical research policy and regulation measures
  - Number of changes to biomedical research legislation
- Pace of Biomedical Research and Development
  - Number of new biologic approvals
  - Number of new molecular entity approvals
  - Number of drugs approved through accelerated regulatory pathways
- Evidence of Support for the Protection of Patents
- Strength of Reimbursement Policies
- Strength of Health Infrastructure
- Changing Roles and/or Incentives for Health Professionals
- Consistent and Transparent Quantitative Data (e.g., disease burden, frequency, trends over time) that help define the market today and the potential market in five or ten years

- Innovative Capacity and Activity
- Scope of Market Networks

DOMAIN: COLLABORATION & TRANSPARENCY

- Key Stakeholder Collaboration
    - Number/level/quality of bilateral or multilateral partnerships; participation in networks, consortia, or other initiatives
    - Number/level/quality of collaborations with other departments/researchers within an organization
    - Number/level/quality of collaborations on grant applications and projects
    - Number/level/quality of partnerships among academia, industry, government, patient/disease advocacy groups, and other key stakeholders
    - Number/level/quality of networking activities (e.g., boards, panels, committees, meetings)
    - Number/level/quality of activities/projects involving co-production of knowledge with knowledge users
    - Number/level/quality of collaborations that continue and/or are established after completion of a research study within and/or outside the organization
    - Number of collaborators
    - Number/level/quality of co-authorship
    - Number of collaborations on grant applications and projects
    - Number/level/quality of links with clinicians
    - Number/level/quality of links with the patient and/or community-based organizations
    - Number/level/quality of materials transfer agreements granted for the transfer of tangible property generated by the research study
    - Number/level/quality of licensing agreements and licensing revenue
- Communication and Public Engagement
    - Number and range of dissemination and outreach activities
    - Number and type of knowledge exchange and/or outreach activities
    - Expert audience communication and public engagement: number of lectures, seminars/meetings/workshops, organized events)
    - Lay audience communication and public engagement (increase public understanding and engagement)
    - The health literacy of the target population is considered when developing communication strategies

- Existence of specifically tailored material for different community groups
- Assumptions and inputs used are articulated in an understandable, lay/patient-friendly way
- Activities conducted openly and assumptions, inputs, processes, and results disclosed to patients in plain language and a timely fashion
- Research investigators create a Wikipedia or other wiki entry based on the research study
- Research investigators create a YouTube video about the research study

- Strength of Data & Information Sharing
  - Metadata from research shared with other parties
  - Research data deposited into a shared repository
  - Supplemental materials deposited into a shared repository
- Policy Engagement
  - Metadata from research data shared with other parties
  - Research data deposited into a shared repository
  - Supplemental materials deposited into a shared repository
- Patient Engagement
- Publication, Citation, and Reference
  - Publication
    - Number/quality of peer-reviewed journal articles resulting from the research study
    - Quality of supplemental materials provided by research investigators
    - Average impact factor of journal articles authored or co-authored
    - Number of research output downloads
    - Number of trade publications resulting from the research study
  - Citation/Reference
    - Research study findings cited in a review
    - Research study findings cited in the meta-analysis
    - Research study findings cited in materials for patients or the public (e.g., consumer health materials)
    - Research study findings cited in teaching/educational materials
    - Research study findings cited by a funding agency
    - Number of mentions in social media

DOMAIN: EFFICIENCY

- Process Markers
  - Reduction in time between the first trial in humans to marketing application/ submission
  - Overall development time
  - Regulatory review timeline
- Regulatory review
  - Average time for new drugs to pass through trial stages
  - Number of new drugs brought to market (per billion U.S. dollars of R&D spending)
- Sharing of Learnings
  - Introducing new knowledge into other system areas
- Patient outcomes
- Time Efficiency in Biomedical Research and Development

DOMAIN: PATIENT CENTRICITY

- Communication and Public Engagement
  - Number of activities that include meaningful participation of patients or members of the public as appropriate
- Patient Input
  - Number of meetings/check-ins with patients
  - Patient input during protocol/design phase
  - Patient Reported Experience Measures (PREMs)
- Patient Preference
- Patient Representativeness
- Patient Outcomes
- Patient Engagement Infrastructure and Training

DOMAIN: INNOVATION & PRODUCTIVITY

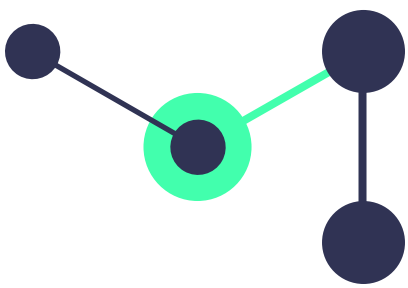
- Strength and Quality of Data Sharing
- Effectiveness of Resource Allocation
  - Shift in pipelines toward innovative and differentiated mechanisms, exploiting new pathways and targets

- Innovative and Evidence-Based Decisions
- Innovative Partnerships
    - Percentage of research spend or number of investments made with venture or other equity partners
- Research & Development Productivity
    - Number of new outputs, including new publications, research tools, resources, and knowledge
    - Measures of product development productivity (e.g., new products approved, rejected, withdrawn, number of drug shortages, products left behind)
    - Success rates in clinical development
- Returns on Investment and Human Health
    - Return on research & development investment
    - Human health return per dollar of research & development investment

DOMAIN: EQUITABLE ACCESS & USE

- Percentage of Unmet Need Gap Closed
- Equitable Access to Products
    - Number of patients without access to product
    - Number of lives touched
    - Narrowing of health/healthcare disparities
    - Reduced cost of treatment
    - Mortality rates
- Economic Impacts
    - The costs of treatment or health care have been reduced
- Biological material application generated by the research study used by health-care providers and/or consumers
- Medical device generated by the research study used by health-care providers and/or consumers
- Mobile application developed by the research study is used by health-care providers and/or consumers
- Drug generated by the research study is listed on a drug formulary list
- Drug generated by the research study is listed on the WHO Model List of Essential Medicines

- Drug generated by the research study is prescribed by health-care providers
- Drug generated by the research study is used by consumers
- Research study cited in private insurance benefit plan in support of coverage
- Research study cited in a public insurance benefit plan in support of coverage
- Numbers of lives touched
- Narrowing of health/health-care disparities
- Disparities in health and the provision of health care are reduced
- Distance patient has to travel
- Insurance coverage of patient



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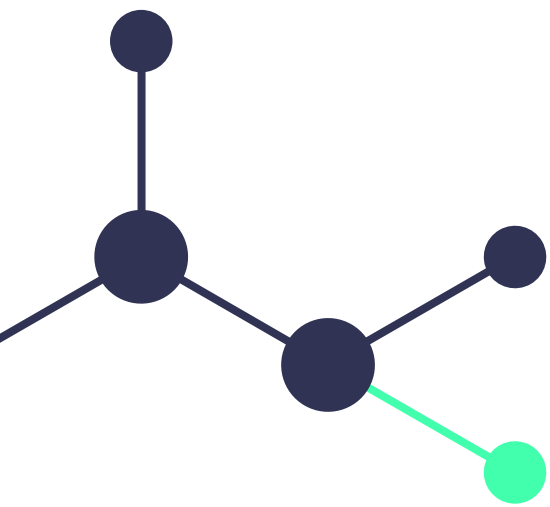

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