

# The Pipeline Problem: Non-Alignment of Innovation, Incentive and Access

- **Innovation:** drug and vaccine R&D and the manufacture of resulting products
- **Incentive:** financial returns adequate to sustain production and new R&D and attract investment
- **Access:** the impact of price and health care infrastructure on the ability of populations to use medical products

## More Definitions: Types of Diseases

- **Type I:** frequently afflict people everywhere (e.g., cancer)
- **Type II:** strike in diverse regions but far more often in less developed countries (e.g., TB)
- **Type III:** encountered almost exclusively in less developed countries (e.g., filariasis)

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- Incremental advances favored by lower risk, lower cost, higher profits

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- Sales fueled by marketing and advertising, not always based on correct medical indications
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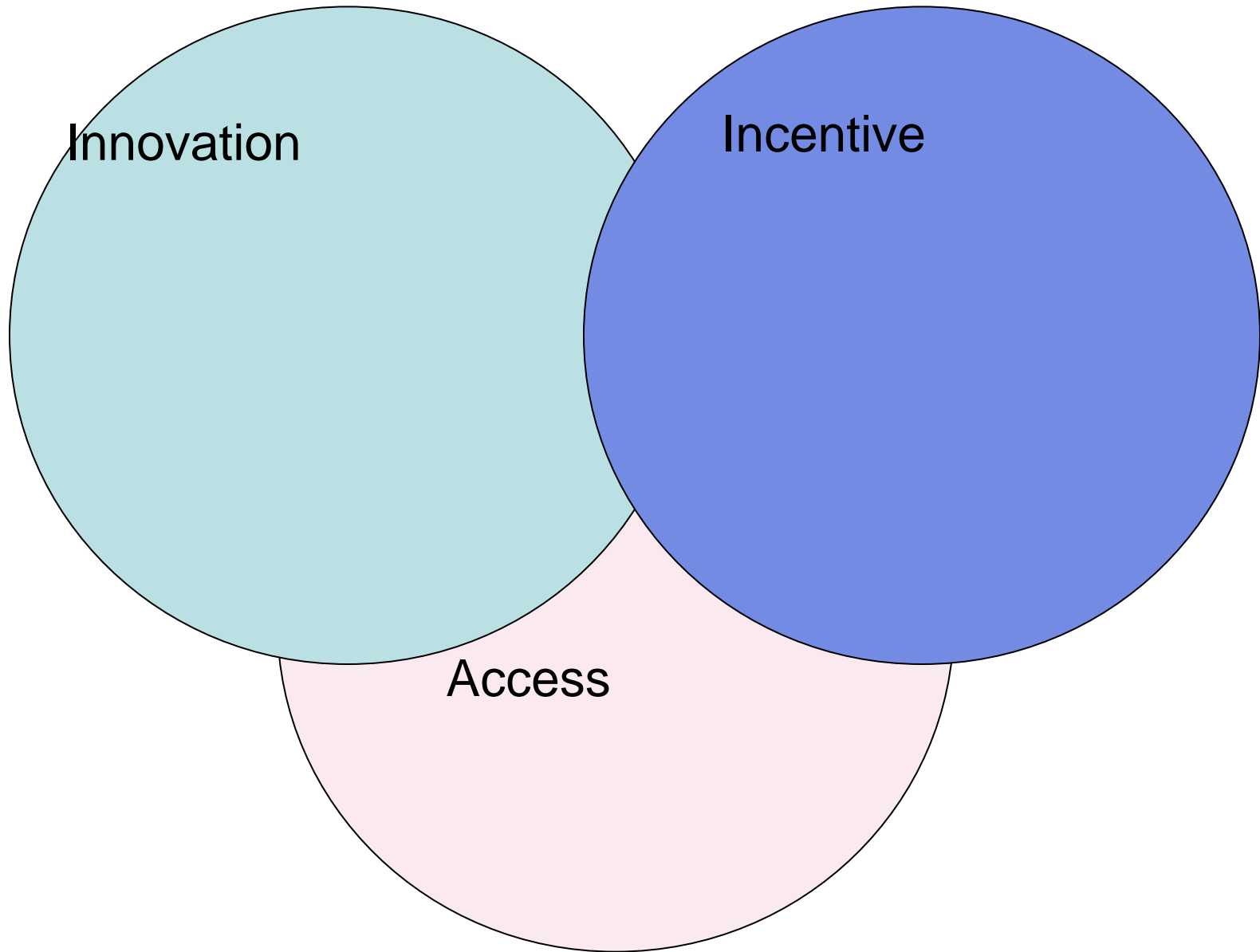
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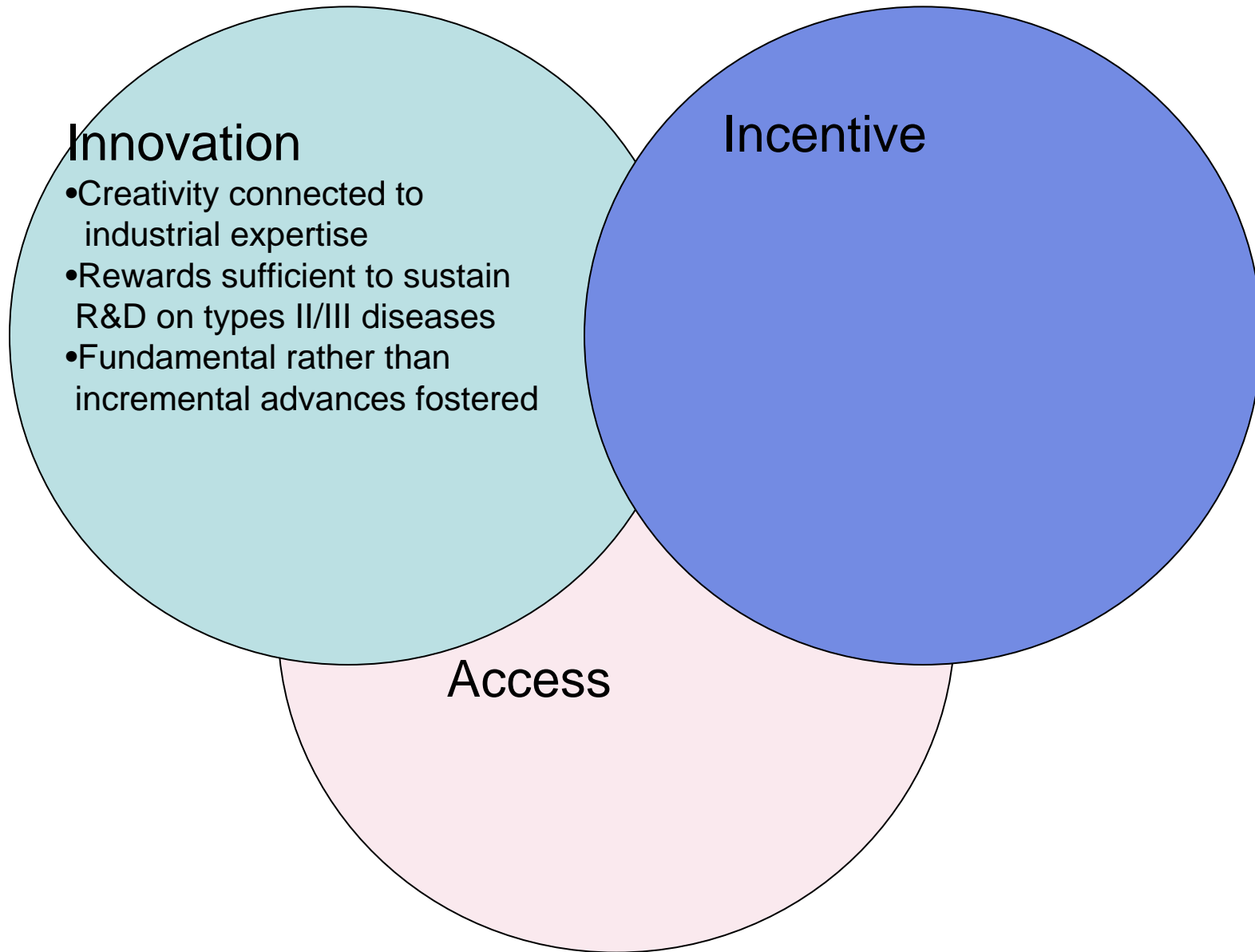
## Access

- Price blocks access of most people to most drugs
- Post-marketing impact rarely studied

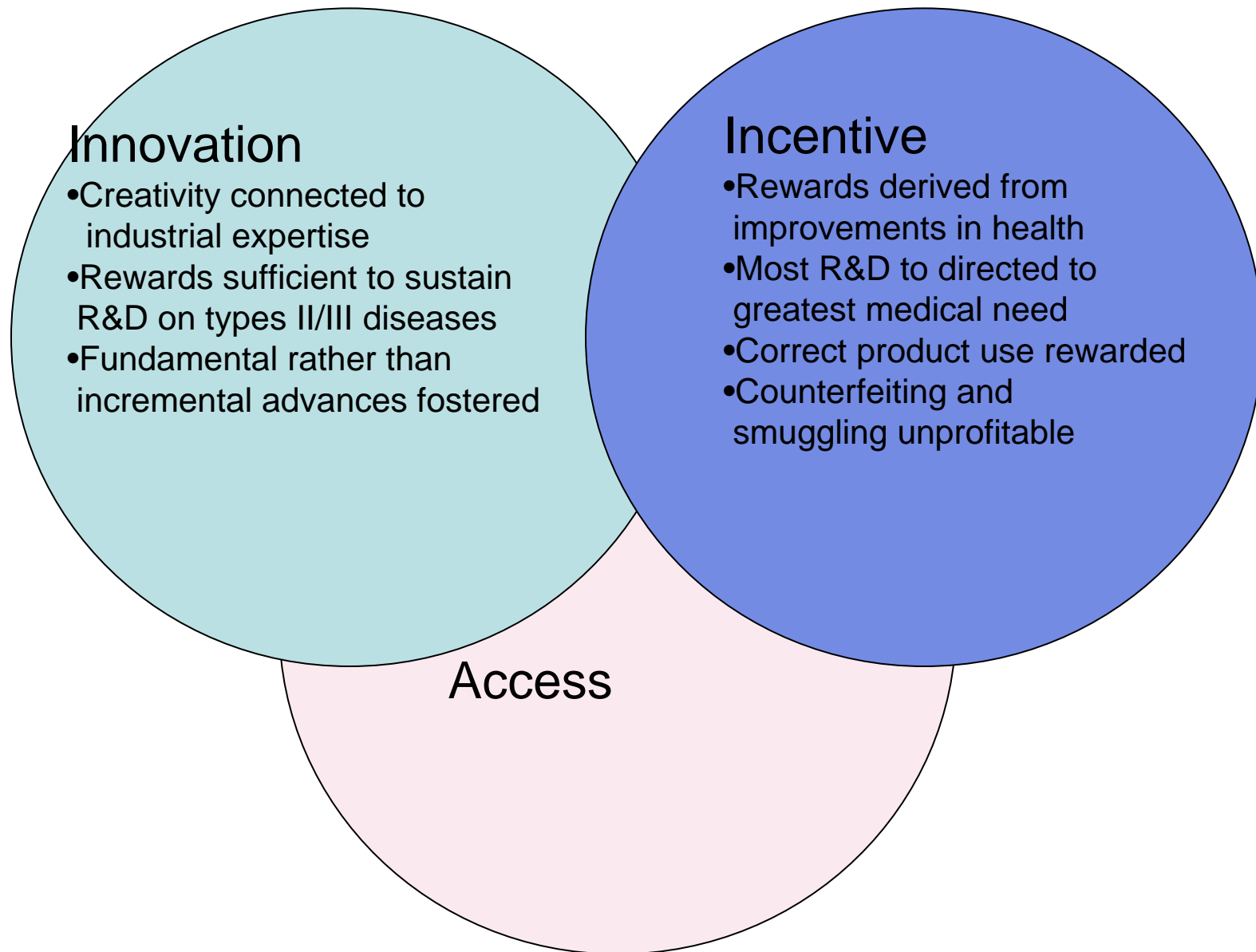
# Aligning Innovation, Incentive and Access



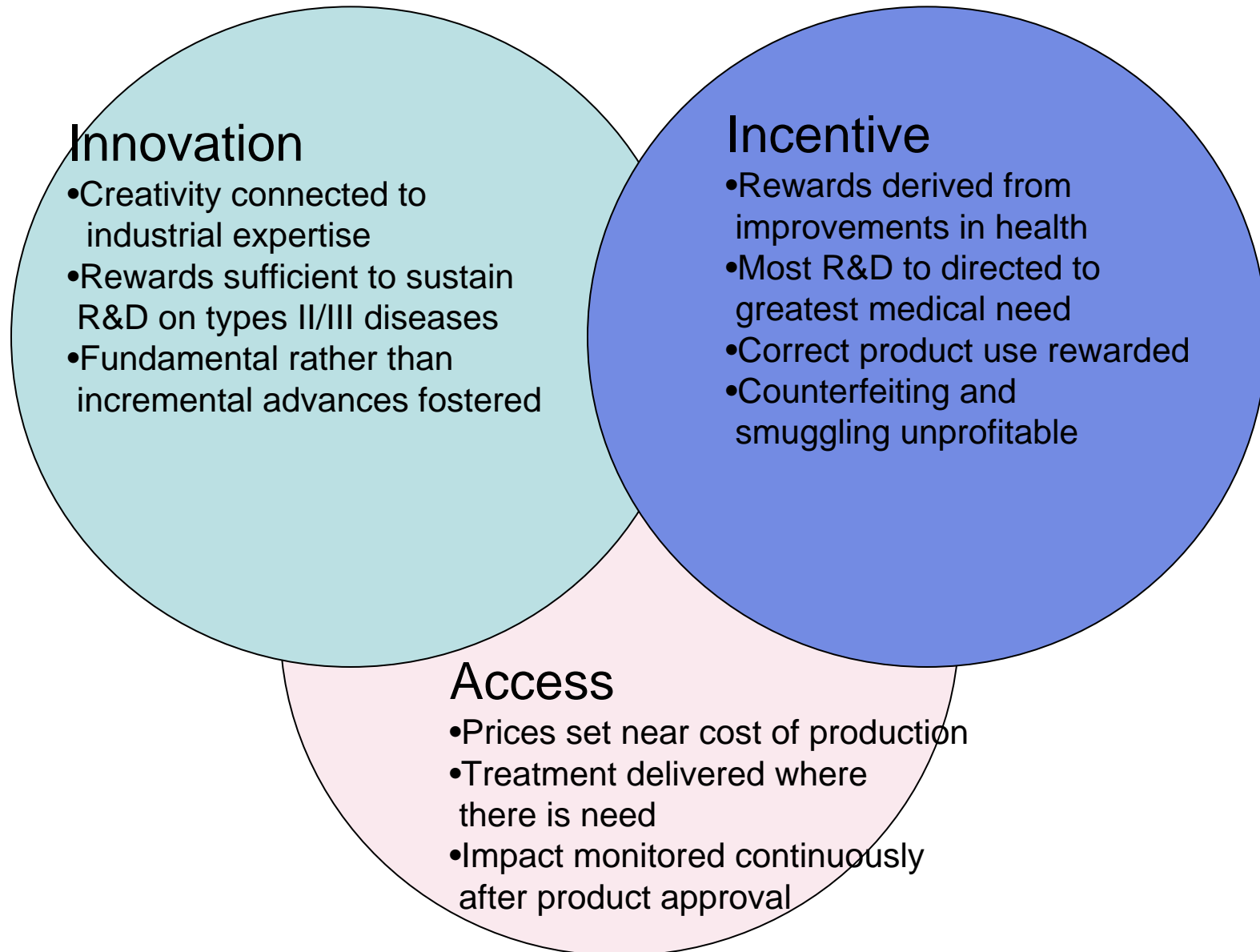
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# Recently Proposed Solutions to the Pipeline Problem

Proposal	Shortcomings
Companies donate drugs (eg Merck: Ivermectin)	1, 2, 3, 4
Companies donate IP rights (eg Moore/WMC: Merck, BMS, biotech to PPP)	1, 2, 3
Universities donate IP rights (eg Yale to OneWorld Health)	1, 2, 3
Companies set up R&D units for type II/III diseases (eg GSK Tres Cantos; AstraZeneca Bangalore; NITDR Singapore; (J&J, Otsuka, Bayer internally)	1, 3, 5
US government doubles support for biomedical research, devotes the increment to drug R&D with the patents placed in the public domain: Free Market Drug Act (Rep. D. Kucinich)	1, 6
Government and philanthropy fund medicinal chemists in academia to promote type II/III disease drug R&D (eg NIH, Sandler at UCSF)	1, 3, 5, 7

# Recently Proposed Solutions to the Pipeline Problem

Proposal	Shortcomings
Governments pay for more drug R&D in government, academia or drug companies if recipients will forego monopoly; costs met from mandated contributions by individuals or employers or by governments via international treaty (Hubbard, Love)	1, 2, 7
Public private partnerships (philanthropically funded) use contracts to manage drug development mostly in biotech or pharma	1, 3, 7
Tax incentives favor R&D for high medical need and can be invested or traded (Nathan, Goldberg)	2, 5
Extend Orphan Drug Act to cover type II/III diseases (fast track approval, 7 year extended market exclusivity, 50% tax credit on clinical trials)	2, 5, 11
Wild card patent extension (IDSA)	4, 5, 6, 12
Advance purchase commitments (Kremer, Glennerster)	1, 4, 9, 10, 13
Tiered pricing	2, 3, 6, 8, 9

# Recently Proposed Solutions to the Pipeline Problem

Proposal	Shortcomings
Price controls	2, 3, 4, 9, 10
International pooled purchasing consortia	1, 2, 3
Compulsory licensing	2, 3, 4, 8
Obligatory choice of protecting patents in either rich or poor countries, but not both (Lanjouw)	2, 3, 5, 8
Buyout pricing or prize system (government provides patent holder its profit) (Abramowicz)	1, 4, 9, 10
Patent buyouts at auction (Kremer)	1, 4, 9, 10
Reward global disease burden reduction from a government fund (Pogge, Hollis)	initially 3; 10
Conduct some R&D in not-for-profit drug companies with for-profit distribution that bring together academics, government, pharma and NGOs (Nathan)	3

# Proposed Solutions: Shortcomings

1. Limited coverage of disease or limited participation by innovators or companies (eg: companies donate drugs)
2. No incentive for R&D for types II/III diseases , or for distribution in less developed countries (eg: extend Orphan Drug Act)
3. Not economically self-sustaining (eg: pharma sets up units for types II/III diseases)
4. No incentive to improve, market or distribute products (eg: prize system)
5. Does not address problem of access (eg: wild card patent extension)
6. Politically objectionable (eg: tiered pricing)
7. Does not incorporate requisite expertise at one or another stage of drug development (eg: governments fund academia for drug R&D)
8. Incentivizes counterfeiting of drugs, backflow of drugs from low- to high-price markets, or travel of patients from high- to low-price markets (eg: tiered pricing)
9. Lets government choose which drugs to promote (eg: advanced purchase commitments)
10. Requires difficult-to-obtain information (eg: prize system)
11. Has led to extraordinarily high prices without attracting large firms (Orphan Drug Act)
12. Only attracts firms holding lucrative patents; increases costs for other drugs (eg: wild card patent extension)
13. Disincentivizes participation through risk of not winning the race to meet specifications (eg: advance purchase commitments)

# How Can We Best Evaluate Such Proposals?

- No one proposal solves the pipeline problem.
- We should ask: Which changes are feasible? What minimum combination of feasible changes will align innovation, incentive and access?
- Feasibility does not mean that which requires the least in thought, work, change or cost.
- Feasibility means: improving the lot of all major stakeholders (patients, citizens, governments, producers),
- with net costs to governments and philanthropies not much larger than the sums they already spend on the research, development and purchase of health care products.

# A Combined Approach for Fundamental, Feasible Change

- Establish a patent track that provides financial reward in proportion to medical benefit, alongside the traditional system
- Establish open access drug companies alongside and within traditional companies

# Alternative Uses of Medical Patents

(Thomas Pogge, Aidan Hollis)

## Track I

- ***Purpose: create and enforce monopoly***
- Monopoly allows prices far above production costs
- Profits cover costs, reward innovation and incent R&D
- R&D addresses wants of wealthy consumers
- Marketing warrants resources comparable to those for R&D

## Track II

- ***Purpose: earn credit for utility***
- Governments reward products for their contribution to reducing global burden of disease (rewards can outlast patents)
- Incentivizes fundamental advances for diseases that are serious and widespread
- Incentivizes sales near cost and royalty-free licenses to in-country makers
- Incentivizes improvement of health care infrastructure and monitoring
- Recoups some of cost through reduced government outlay for drug purchase and reimbursement
- Sustains industry growth through increased targets and markets
- Improves global health

# Open-Access Drug Companies: Building on Public-Private Partnerships

- PPPs are experiments that provide positive precedent. The challenge is to institutionalize and improve them:
- Philanthropy lacks the means to carry society's load indefinitely.
- Each infusion of philanthropic funds into PPPs has had a short time window, drastically impacting the type of project PPPs can support.
- PPPs cover relatively few diseases and have the resources to pursue only a small fraction of routes of interest.
- Given the constraints on time and resources, PPPs are forced to patch together a layer-cake approach to drug development: academics carry out early research, usually without benefit of access to compound libraries, screening facilities or medicinal chemists; then medicinal chemists and pharmacologists take over with an unnecessarily limited number of what are likely to be suboptimal lead compounds.
- In contrast, optimal drug development requires that pharmaceutical professionals participate with discovery-oriented biologists from the outset. There is great benefit to a project of frequent personal contact among team members who have the diversity of expertise generally found only in vertically integrated pharmaceutical companies.

# Open-Access Drug Companies: Features and Goals

- Contract-based frameworks and sites for collaborations between academics and drug companies and among companies
- Funded by users and government (perhaps after a demonstration-project launch by philanthropy)
- Pharmaceutical companies are enlisted in geographic regions. Each company designates a sector of an R&D facility in which it admits approved scientists from academia and other companies to work with its own scientists.
- Participant admission and funds allocation are controlled by a site management board, appointed by and employed by the funders.
- The management board prioritizes projects that offer hope of meeting substantial medical needs that are not otherwise likely to be addressed.
- Leading examples are narrow-spectrum antibiotics for type I infections; preventive and therapeutic approaches to diseases of types II and III; and treatments designed from the outset to be used in combination, such as for infectious disease and cancer.

# Open-Access Drug Companies: Flow of Work and Funds

- Scientists apply to the management board for access to specific services on a fee for service basis, such as screening, medicinal chemistry, pharmacology, molecular modeling, or formulation science.
- The earlier the phase of the work, the greater the share the scientist covers from his/her grants or with the support of his/her employer. As a project advances, university-based projects compete for management board funds via peer review. Company-owned projects continue to pay their own costs.
- Management boards work collectively to identify redundancies and potential synergies among projects. Combination approaches are encouraged from the outset.

# Open-Access Drug Companies: Intellectual Property

- Intellectual property is assigned to inventors as defined by patent law. Pharmaceutical company employees share inventorship as their contributions warrant.
- However, by terms of the open-access contract, control over the use of intellectual property is vested with the funders, not the contractors.
- The funders register patents under track II. Profit is shared among owners of intellectual property in accord with a contractual policy that requires minimal if any negotiation by each new participant and includes procedures for dispute resolution without litigation.

# Open-Access Drug Companies: Novel Compound Collections

- A major goal is the generation and curation of novel chemical libraries likely to be rich sources for anti-infectives (and anti-neoplastics).
- These libraries feature natural products from under-explored sources, such as marine actinomycetes, plants, or as produced by recombinant bacteria using operons cloned from uncultured organisms.
- The libraries include compounds donated to promote discovery of new uses, such as drug candidates whose development has been halted and the archived precursors or analogs of existing drugs.
- Compounds that have already been patented can be donated if licensed for potential new uses via track II
- Given the urgency of antibiotic R&D, access is also provided to the for-profit sector, as recommended by Alliance for Prudent Use of Antibiotics
- Users pay an access fee to defray costs and return to the open-access system a proportion of resulting profits.
- Companies using the libraries may patent novel derivatives of the compounds in the collection, but not the open-source compounds themselves.

# Conclusions

- Using substantially the same funds that governments and philanthropies now spend on R&D and health care product delivery, it is possible to restructure working relationships among scientists, business and government so that disconnects and conflicts among innovation, incentive and access are replaced by mutual reinforcement.
- Open access drug companies can spur innovation while improving the science, widening the scope and stabilizing the funding of the PPPs.
- They can boost R&D directed toward type II/III diseases and develop new approaches to diseases of type I.
- Financial incentive can come from registering patents on track II, so that innovators are rewarded for products that reduce the burden of disease.
- Companies would then strive to maximize patient access to such products through low pricing, wide licensing and improved infrastructure.
- There are major issues: How much will governments contribute, collect reliable information on changes in burden of disease and discern which products to credit?
- These challenges are manageable, in contrast to the calamitous consequences of the present course.