

Title: Toward a definition of pharmaceutical innovation

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Abstract

Despite current debate on ways to promote innovation in the pharmaceutical sector, there is little clarity about what constitutes a pharmaceutical innovation, and therefore potential confusion about what should be pursued, protected and encouraged through policy and clinical practice. We provide a brief review of the definition of innovation, drawing on clinical, economic and business literature, and offer a new conceptual framework for classifying pharmaceutical innovations. Innovation is the application of ideas in ways that effectively address previously unmet needs. A distinction can then therefore be drawn between “pharmaceutical innovations” and “commercial innovations.” Pharmaceutical innovations must effectively address previously unmet health care needs. New medicines that utilize novel mechanisms to replicate outcomes achievable through other means—while potentially important to market competition—do not constitute innovations. Commercial innovations need only generate new profit opportunities; these may or may not be the result of desired pharmaceutical innovations. We conclude that policy should aim to align incentives such that commercial innovations from R&D activities are necessarily those that effectively address previously unmet health care needs.

Toward a definition of pharmaceutical innovation

Ongoing debates in pharmaceutical sector about intellectual property,^{1,2} pricing and reimbursement,^{3,4} and public research investments⁵ have a common denominator: the pursuit of innovation. Yet there is little clarity about what constitutes a true pharmaceutical innovation, creating confusion about what should be encouraged through health policy and clinical practice. In an era of increasing drug development costs,⁶ and continued disparity between burden of illness and drug research and development,^{7,8} conceptual clarity may help policy makers and practitioners evaluate, adopt and procure products in ways that appropriately recognize and encourage truly valued pharmaceutical innovation.

Pharmaceutical Innovation

Describing a product as innovative implies that it has properties worthy of recognition and reward. This may explain why manufacturers regularly apply the term to new pharmaceuticals.⁹ It is also why a clear definition of pharmaceutical innovation is required: so that policy and practice recognize the societal value of new pharmaceutical technologies.

Notions of value depend on perspective. Commercial value, for example, is generally assessed from the perspective of firm profitability. Profits, in turn, can provide incentive to produce value for consumers and society. In markets for everyday commodities consumer value is generally related to preferences over the characteristics of goods and services. In a health care context, consumer preferences are central to determining the relative value of different health outcomes. However, it is the *health outcomes* themselves that give pharmaceuticals societal value. As health care inputs, pharmaceutical products *per se* are of no intrinsic value to patients or to society. Pharmaceuticals are licensed for sale based on whether they safely and efficaciously address a health care need, not because patients might have preferences over their shape, colour, taste or brand. To the extent that characteristics like shape, colour, taste or brand improve health outcomes—perhaps by increased adherence to prescribed treatment—it remains the health outcomes that generate value for society. Product characteristics are not unlike surrogate endpoints for clinical trials insofar as they are only of value to the extent that they predict clinical or “hard” endpoints.^{10,11}

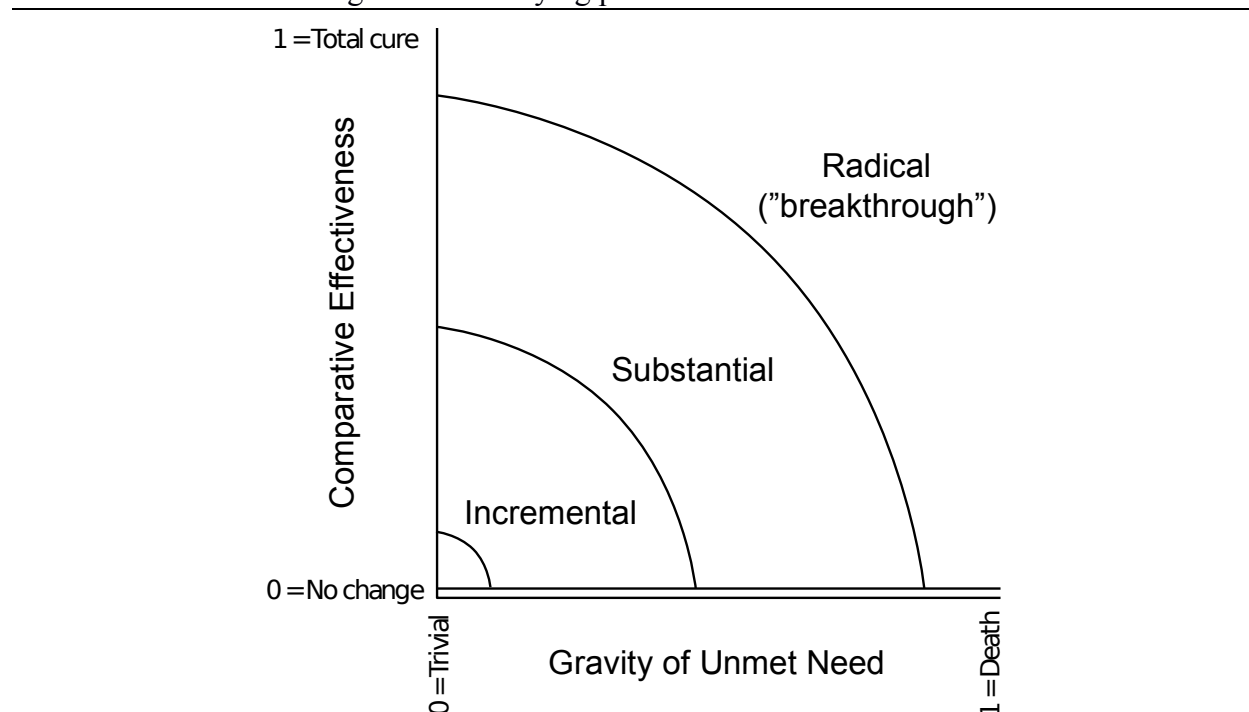
Placing the societal value of pharmaceuticals exclusively in the context of health production implies that, while concepts of novelty and innovation are often associated,¹² product novelty alone will not constitute pharmaceutical innovation. New chemical structures or mechanisms of action do not necessarily generate new health outcomes.^{13,14} To be a pharmaceutical innovation requires some level of effectiveness. Yet, effectiveness also falls short of defining pharmaceutical innovation when considered in isolation. A generic drug, for example, may be effective—and may therefore provide some value (e.g., price savings) to patients and society—but it would hardly be considered an innovation. Thus, neither novelty nor effectiveness alone is enough to qualify as pharmaceutical innovation. Even the combination of novelty *and* effectiveness is not enough.

Pharmaceutical innovation requires novelty *of* effectiveness. Pharmaceutical innovations generate value by making new health outcomes possible. A drug can therefore only be considered a pharmaceutical innovation to the extent that it actually meets otherwise unmet or inadequately met health care needs. The extent to which a drug achieves this depends on its effectiveness relative to technologies prevailing when it is introduced. For example, cimetidine, the prototypical histamine₂-receptor antagonist (H₂RA), was considered a pharmaceutical innovation when introduced in 1977 because it addressed a previously inadequately met need.¹⁵ The notion of innovation is time-limited because of competition and technological change. Neither cimetidine nor other H₂RAs would be considered innovations today because the outcomes they generate have been established, replicated, and even surpassed.

Replicating outcomes obtainable with existing treatments is important for economic competition and efficiency but is not innovation. However, surpassing previous levels of performance, or matching previous levels of output more efficiently, would be considered innovation. Again, consider advances in gastroenterology: the first proton pump inhibitor (PPI), omeprazole, introduced in 1989, was an innovation because, relative to H₂RAs, it met a given need with greater efficacy. PPIs have since become the mainstay of treatment for acid-related gastrointestinal disease in adults and, without detracting from the value of the outcomes they generate, would no longer be considered innovations.

A pharmaceutical innovation may be thought of as incremental, substantial, or radical according to the significance of the unmet health care need it addresses (*gravity of unmet need*) and the extent to which it improves health outcomes related to that need (*comparative effectiveness*)—see Figure 1. Gravity of the unmet need can be thought of as the gap between an ideal health status and the health status attainable for patients with a given condition using prevailing technologies. The lowest gravity of unmet need (zero) would represent conditions for which existing treatments offer a total cure or ones for which the underlying need is relatively trivial in terms of health status (e.g., male pattern baldness). The highest gravity of unmet need (one) would represent conditions for which existing treatments result in a prognosis of death or, perhaps, fates worse than death.

Figure 1: Classifying pharmaceutical innovations



Gravity of unmet need establishes the potential for pharmaceutical innovation (i.e., the maximum improvement in health status that a new drug might offer, over and above existing technologies). Actual pharmaceutical innovation depends on the drug's comparative effectiveness. Zero comparative effectiveness indicates that the drug offers no change in health status compared to existing treatments for patients affected by the given condition. The highest

value of comparative effectiveness (one) indicates that the drug entirely closes the gap between health status attainable with prevailing treatments and ideal health status. The categories of innovation in Figure 1 are drawn with a lower boarder because a medicine must offer some level of comparative health benefit to be considered an innovation, no matter how grave the condition it aims to remedy.

The greater the gravity of unmet need being addressed and/or the greater the comparative effectiveness in addressing that need, the greater the degree of pharmaceutical innovation represented by a new treatment. Radical innovations, or “breakthroughs,” would be effective treatments for conditions that would otherwise significantly reduce the quality and/or length of life, or treatments that provide major improvements over existing options in cases where the prevailing unmet needs are more moderate. Substantial innovations might offer modest improvements in health outcome for those with moderately grave unmet needs, or substantial improvements over existing treatments in cases where unmet health care needs are less serious. Finally, incremental innovations would be drugs that offer minor to moderate improvements in treatment areas where prevailing unmet needs are moderate to trivial.

New drugs to treat conditions for which existing therapies offer relatively good outcomes will have little potential for being significant pharmaceutical innovations. Variation within a drug class may generate certain therapeutic advantages but difference *per se* does not constitute innovation. For example, early and late entrants into a drug class might each be more effective or better tolerated among certain population subgroups. However, late entrants will not represent significant pharmaceutical innovation unless they are systematically superior to early ones. The value of products that produce outcomes similar to those achievable with other treatment options lies not in innovation but in the potential competition that they may bring to the marketplace — such competition would contribute to consumer and social value through reduced costs per outcome achieved.

Ultimately, it is commercial value that drives investments and activities in private sector. Firms may strive for commercial performance by developing drugs that effectively address grave, unmet health care needs. Firms may also be “commercially innovative” without generating pharmaceutical innovations, such as when a marketing campaign builds brand loyalty

for a product that does not effectively address unmet health care needs. Indeed, when Figure 1 is viewed from a societal perspective on a global or national basis, it appears that most of the commercial activity in the pharmaceutical market is focussed on product development and marketing in therapeutic areas where new products would, at best, provide incremental advances in population health. This is true not only in terms of the global divide between burden of illness and drug research and development,^{7,8} but also in terms of the share of product development, marketing, and sales in wealthy countries that is accounted for by medicines offering little or no advances over established treatment alternatives.¹⁶

Ultimately, industry is not to blame. The pharmaceutical industry's focus on activities of incremental value results from way drugs are appraised, selected, and rewarded by policy makers, practitioners and, to an increasing extent, patients. If a premium was selectively placed on true pharmaceutical innovations—effective treatments for previously unmet needs—and competition was encouraged among technologies that replicate otherwise achievable outcomes, then private investments in research and development would be stimulated in areas of greatest value to society.⁴ Thus, when assessing a pharmaceutical to determine whether, and to what extent, it is an “innovation” for the purposes of listing, prescribing or pricing decisions, the questions to ask are: does it address previously unmet or inadequately met needs; and, to what extent does it improve outcomes along those dimensions of need?

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