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Patients need better treatments, not just more of the same

Drug regulation and development must be aligned with clear public health goals

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A well functioning drug development system, including legislation to generate innovative treatments that target unmet needs of patients, is an important means of improving public health. Given the complexity of drug development, the number of resources involved, and the economic implications for both the pharmaceutical industry and healthcare systems, debate is ongoing about how to optimise outcomes. One approach is to use a drug not only for one disease (the first approved indication) but also, where possible, for other diseases (supplemental indications).

The linked study by Vokinger and colleagues (doi:10.1136/bmj-2022-074166) on the added therapeutic value of first versus supplemental indications of drugs in the US and Europe reports the disappointing results of current drug development efforts.[1] Less than half of approved first indications of new drugs add value over existing treatments. Supplemental indications add even less: approvals for second and third indications were 35% and 45% less likely, respectively, to add value compared with the first approvals. This study confirms previous research on the limited or unclear added value of new drugs.[2-5]

Regulatory approval is too often equated with superiority over existing treatments.[6] The fact that new does not necessarily mean better needs to be clearly communicated to both patients and clinicians. Clinicians have a duty to provide appropriate information to patients to inform decision making that reflects patient values and preferences.[7,8] In addition, pricing decisions should consider the extent of any value added by new approved indications.

No HTA in the USA

Vokinger and colleagues' findings are based on value ratings from European health technology assessment (HTA) bodies. The lack of systematic health technology assessment in the US is an important knowledge gap for decision making in the US healthcare system. Some attempts have been made to close this gap, such as the value framework for cancer treatments developed by the American Society of Clinical Oncology.[9] However, this framework covers only one aspect of healthcare—why the US has not adopted HTA more widely is difficult to understand, as it is an important tool for improving the efficiency of healthcare.

Although these authors' findings are sobering, they are not at odds with the current legislation on drug approvals. Neither US nor European regulators require proof of added value over existing treatments for the approval of a new drug, only a positive benefit-risk ratio. Some authors have suggested that the requirements for approval should be amended to include added value,[10] but others have argued that new treatments without added value are still an important addition to patient care, as they allow drug selection according to the preferences of individual patients. For example, patients may benefit from having a range of drugs to choose from, as they might tolerate specific side effects better than others and thus consider certain treatments less burdensome.

However, even if new drugs with similar benefits are considered a useful addition to the therapeutic armamentarium, no reason exists to incentivise their development and approval. To promote real clinical innovation, incentives should specifically reward the development of drugs with proven added value for patients. For example, appropriately designed comparative studies showing clear added value relative to the standard of care could be a prerequisite for expedited approval or prolonged market exclusivity.

From a pharmaceutical company's point of view, pursuing the less risky development of drugs for supplemental indications or "me-too" drugs with cheaper drug development programmes is rational.[2] If current pharmaceutical legislation leads to such an approach, we need to change course to achieve the ultimate goal of improving patient care.

The study by Vokinger and colleagues shows once again that a detailed evaluation of the actual outcomes of pharmaceutical legislation is needed to understand the consequences of current policies and to develop evidence based adjustments targeted towards defined public health goals. The system's current performance does not meet the expectations of patients and the public, clinicians, or policy makers. Having experienced the potential of a coordinated drug development effort during the covid-19 pandemic, we should seek to align current legislation on drug development more closely with defined public health goals.

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1 Vokinger KN, Glaus CEG, Kesselheim AS, Serra-Burriel M, Ross JS, Hwang TJ. Therapeutic value of first versus supplemental indications of drugs in US and Europe (2011-20): retrospective cohort study. *BMJ* 2023;382:e074166.

2 Fojo T, Mailankody S, Lo A. Unintended consequences of expensive cancer therapeutics—the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity: the John Conley Lecture. *JAMA Otolaryngol Head Neck Surg* 2014;140:-36. doi: 10.1001/jamaoto.2014.1570. pmid: 25068501

3 Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. *BMJ* 2017;359:. doi: 10.1136/bmj.j4530. pmid: 28978555

4 Wieseler B, McGauran N, Kaiser T. New drugs: where did we go wrong and what can we do better?*BMJ* 2019;366:. doi: 10.1136/bmj.l4340. pmid: 31292109

5 Rodwin MA, Mancini J, Duran S, etal. The use of 'added benefit' to determine the price of new anti-cancer drugs in France, 2004-2017. *Eur J Cancer* 2021;145:-8. doi: 10.1016/j.ejca.2020.11.031. pmid: 33412466

6 Krishnamurti T, Woloshin S, Schwartz LM, Fischhoff B. A Randomized Trial Testing US Food and Drug Administration "Breakthrough" Language. *JAMA Intern Med* 2015;175:-8. doi: 10.1001/jamainternmed.2015.5355. pmid: 26390245

7 Dangoor A, Joffe J, Januszewski A, Mansi J, Cunningham D, Selby P17 other authors and members of the Association of Cancer Physicians, UK. The Association of Cancer Physicians responds to "Cancer drugs, survival, and ethics". *BMJ* 2016;355:. doi: 10.1136/bmj.i6487. pmid: 27920029

8 Darrow JJ, Dhruva SS, Redberg RF. Changing FDA Approval Standards: Ethical Implications for Patient Consent. *J Gen Intern Med* 2021;36:-4. doi: 10.1007/s11606-021-06762-0. pmid: 33834346

9 Schnipper LE, Davidson NE, Wollins DS, etalAmerican Society of Clinical Oncology. American Society of Clinical Oncology Statement: A Conceptual Framework to Assess the Value of Cancer Treatment Options. *J Clin Oncol* 2015;33:-77. doi: 10.1200/JCO.2015.61.6706. pmid: 26101248

10 Garattini S, Bertele' V. How can we regulate medicines better?*BMJ* 2007;335:-5. doi: 10.1136/bmj.39281.615706.94. pmid: 17947785