

COMMENT

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Advancing the human right to health in cancer care through drug repurposing strategies

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Abstract

This perspective critically evaluates the global potential of drug repurposing strategies in oncology to advance health equity and sustainable innovation. Drug repurposing, especially with off-patent medications, offers significant advantages, including reduced costs, shortened timelines for clinical implementation, and enhanced approval success rates compared to new drug development. Herein, we advocate for leveraging of repurposing as a scientifically sound and ethically responsible strategy, while acknowledging the implementation barriers in low- and middle-income countries (LMICs) due to global systemic inequities. Fostering equitable investment in research and infrastructure worldwide is essential to realizing the full potential of this approach. We also identify specific barriers to drug repurposing, including limited funding for clinical trials, inadequate support for investigator-led trials, and the lack of commercial incentives due to non-patented drug utilization. To overcome these barriers, we propose enhanced funding mechanisms, robust advocacy, targeted education initiatives, and policy prioritization for repurposing studies. Case examples illustrate the clinical potential of drug repurposing in reducing metastatic progression and improving survival outcomes. Overall, this perspective underscores drug repurposing as a viable and impactful strategy to advance both innovation and the human right to health in cancer care for all populations. By fostering a collaborative interdisciplinary effort, the benefits of this approach can pave a way for a more equitable and sustainable future in cancer care.

Keywords Drug repurposing, Oncology treatment, Cancer research funding, Policy advocacy, Global health

Introduction

Repurposing medicines in oncology is a strategy of using off-patent non-cancer medicines for oncological treatment (“hard repurposing”) or adding new cancer indications to established cancer medicines (“soft repurposing”) [1]. As recently suggested by the WHO policy brief, and shortly exemplified below, drug repurposing in oncology is an “underrated champion of sustainable innovation” [1].

Here we briefly outline the advantages of drug repurposing in oncological treatment, primarily the off-patent generic medicines, and assert it can advance the fundamental human right to health through two key elements:

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(i) reducing the costs of treatment development and increasing the likelihood of approval, and (ii) promoting global health equity by reducing disparities in access and in systemic barriers to care. This is a perspective article informed by existing policy literature, academic literature, and cased-based illustrations. This perspective does not provide a systematic review but highlights illustrative examples and policy-relevant trends. Below, we expand on each of these elements:

Reducing costs of treatment development and improving approval success rates

In general, it would appear that drug repurposing is less risky and less demanding medically and economically, less time-consuming, thus increasing chances of treatment approval and reducing costs (Table 1) [2]. Specifically, oncology drugs examined in phase I have the lowest chance of receiving the Food and Drug Administration (FDA) approval, estimated at a 3–6% rate [3, 4]. It is still unclear whether repurposing strategies in oncology can result in a higher chance of receiving approval, but the following support this hypothesis. Existing drugs already approved for different indications often require less pre-clinical safety and efficacy evidence and can bypass phase I clinical trials, saving millions of dollars and years of research [1, 5]. Also, 25% of repurposed compounds enter the market after phase II clinical trials, and 65% after phase III clinical trials, compared with 10% and 50%, respectively for new compounds [6]. This allows repurposed medicines to reach clinical use more rapidly and at more affordable costs.

Promoting global health equity by reducing disparities in access, research investments, and treatment outcomes

Massive disparities in cancer care exist both between and within countries [7]. Specifically, although various health initiatives, such as the decrease in smoking rates, have reduced cancer risk in high-income countries (HICs), such initiatives have often not been implemented in low- and middle-income countries (LMICs). To achieve true equity, policies must undertake active programs to narrow such disparities among different populations [7]. Additionally, disparities are also reflected among patients recruited to randomized controlled trials (RCTs). A

Table 1 Comparison of development costs and timelines between new drug and drug repurposing [2]. Drug repurposing strategies are associated with reduced development time and costs

Development strategy	Estimated cost (USD)	Time to approval
New drug development	\$2–3 billion	13–15 years
Drug repurposing	\$0.3 billion	6.5 years

These are general estimations; actual timelines and costs vary widely depending on region, indication, trial phase, and regulatory context

systematic review based on a cohort study of all 694 phase III RCTs published from 2014 to 2017 found that 92% of trials were conducted in HICs versus 8% in LMICs, markedly deviating from the global burden of disease and its population-specific characteristics [8]. In contrast to the 92% vs. 8% distribution, RCTs from LMICs often identify more effective therapies in terms of clinical benefit (ESMO-MCBS grades) and have larger effect sizes, yet they face inadequate funding and diminished publication impact [8]. To achieve equity in cancer care and improve overall clinical impact and treatment generalizability, policies must ensure that research in HICs and LMICs is supported equitably to disease burden and adequately conducted and reported.

Furthermore, screening and early detection in cancer, which are key to treatment success, are more widely adopted and advanced in developed countries [9]. Most cancer treatments, including repurposed drugs, commonly do not cure cancer, but reduce its recurrence and do so more effectively in earlier stages [10] and with better outcomes [11]. Prioritizing early detection through screening in LMICs without simultaneously ensuring accessible and sustainable treatment options may strain already limited resources. Cancer control programs should be developed and implemented with context-specific goals, incorporating interventions that are tailored to the medical and cultural needs of the local populations, as well as to their economic capabilities [12].

Within the broader context, drug repurposing offers a globally relevant strategy to improve cancer treatment delivery, not as a substitute for innovation in LMICs, but as a complementary tool across all settings. Its cost-effectiveness makes it particularly attractive where resources are constrained, but its clinical potential holds equal value in high-income health systems. Implementing repurposing strategies, including through RCTs in LMICs, can promote more representative evidence and help align global cancer care efforts with the actual distribution of disease burden.

Key examples of treatments based on repurposed drugs in cancer

Generic non-oncology drugs, which hold the potential for “hard repurposing”, are often multi-target drugs [13] rather than interacting with a specific cancer-related molecule (e.g., PDL1 inhibitor). Their potential benefits are now better recognized and align with the understanding that the hallmarks of cancer are numerous and are regulated by multiple pathways [13]. One notable example of repurposed drugs that have already been adopted in cancer care is thalidomide, which was originally marketed as a sedative and a treatment for morning sickness in pregnant women [1, 14]. However, it was withdrawn in the early 1960s after being linked to severe developmental

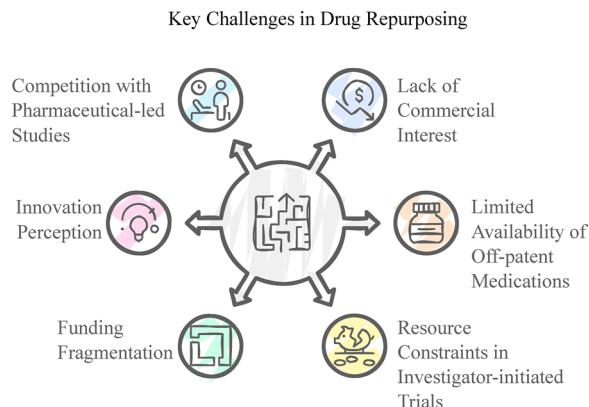


Fig. 1 Key challenges to advancing drug repurposing in oncology. Key barriers include lack of commercial incentives, competition with pharmaceutical-led studies, and fragmented funding, all of which disproportionately affect investigator-led trials and low-resource settings.

defects in children of pregnant women. Despite its teratogenic effects in the 1990s, scientists began exploring its anti-angiogenic properties. After extensive clinical trials, thalidomide was approved by the FDA in 2006 and authorized by the European Union in 2008 as part of a combination treatment for multiple myeloma [1, 14].

Additionally, inflammation and stress have now been acknowledged as hallmarks of cancer and cancer progression [15–17]. Today, clinical evidence is accumulating on a treatment regimen based on off-patent repurposed medicines that limit beta-adrenergic and prostaglandin stress-inflammatory signalling, namely propranolol, a non-selective beta antagonist, with or without etodolac, a semi-selective COX-2 inhibitor [18–21]. RCTs conducted in breast and colorectal cancer patients treated with these drugs during the immediate perioperative period, indicate improvements in tumor biomarkers of metastasis, including EMT, GATA, and STAT transcriptional activity [18, 19, 21]. This research was based on a robust and large body of evidence from pre-clinical studies [15, 22–25] and aligns with improved 5-year disease-free-survival evident in the colorectal RCT, although this latter study was not powered for this outcome [20].

A comprehensive list of repurposed drugs in oncology is well summarized in the WHO policy brief [1]. Overall, investment in these and additional repurposing cost-effective treatments could contribute to the sustainability of oncology care by reducing the number of cancer cases that progress to advanced metastatic disease, which require costly and complex therapies.

Challenges to repurposing: free market failure or policy gaps?

Certainly, despite the clear advantages of repurposing, there are several “non-scientific challenges” that researchers face, as acknowledged by the FDA and the NIH [26], particularly with repurposing of generic

medicines (Fig. 1, created using Napkin AI tool). These challenges include:

Lack of commercial interest to conduct RCTs to test repurposed drugs

Given minimal expected future financial profit from non-patented drugs, the return on investment (ROI) for developing a treatment regimen based on repurposed generic medicines in cancer is expected to be low compared with new patented products. Pharmaceutical industries, which often play a crucial role in funding clinical trials, tend to prioritize investments with potential for exclusive market rights. Consequently, RCTs to test repurposed medicines are mainly investigator-initiated trials led by academic researchers, rather than being industry-sponsored [27].

Limited availability of generic medicines

Many repurposed drugs are not available in national health systems due to lack of regulatory approval, and this challenge is particularly acute in LMICs. A recent analysis across 54 LMICs found that the availability of generic medicines in public sectors ranged from 37.8 to 68.3%, lower than in HIC and far below WHO's recommended availability target of 80% [28]. This “local” limited availability threatens global equity and reinforces geographic disparities in treatment access and health outcomes.

Resource constraints and patient recruitment

In general, patient recruitment is considered a significant barrier in RCTs, as less than 5% of adult cancer patients participate in clinical trials [29]. Beyond this initial obstacle, investigator-initiated trials are believed to be more disadvantaged compared with industry-sponsored trials, due to limited financial resources that cause hardship in RCTs' marketing, smaller research teams, and less advanced administrative infrastructure. Additionally, the administrative and regulatory burden in clinical trials can be heavier for academic individuals and institutions, with their limited experience and resources [30].

Limited and fragmented funding

The distribution of global funding for cancer research between 2016 and 2020 indicates a focus on early-stage pre-clinical research, rather than on clinical trials [31]. Pre-clinical research received 73.5% of the funding across these 5 years (\$18 billion), while phase I-IV clinical trials collectively received only a 7.4% (\$1.8 billion). Moreover, while there are numerous small proof-of-concept studies (i.e. phase I or II) to test the activity and safety of repurposed medicines in new therapeutic indications, there is an unmet need for larger RCTs to confirm promising outcomes from such repurposing studies [31]. Large phase III RCTs are expensive, time-consuming

and labour-intensive, and limited and fragmented funding remains one of the critical barriers for initiating and completing such studies [27]. Additionally, recent cohort studies suggest that contemporary oncology RCTs are almost exclusively funded by the pharmaceutical industry (57% in 1995–2004, 78% in 2005–2009, and 89% in 2010–2020), raising concerns about potential biases in research priorities [32].

Definition of innovation in funding options

Funding options for clinical trials of repurposed treatment are at a clear disadvantage, due to a traditional perception that repurposing is not as innovative scientifically as testing new drugs and thus should not have high funding priority [27]. However, research suggest that repurposing strategies can be highly innovative. It involves novel applications of existing knowledge, offering new therapeutic options for diseases with limited treatments. It can be efficient in reducing development time and costs and often involves cross-disciplinary collaborations. These factors highlight the scientific and practical innovation inherent in drug repurposing, although not intuitively recognized as such.

Mismatch between trial demand and availability of patients

In recent years, the number of oncology RCTs has increased [33], with the proportion of RCTs published in major journals rising from 11% of overall publications in 2010 to 44% in 2020 [32]. The concern that there may be more clinical trials waiting to be conducted in oncology than available patients to be recruited for these trials has been discussed within the scientific and medical communities. The growing number of trials and the increasing costs of cancer care are factors that may contribute to intense competition among RCTs for patient recruitment. Notably, financially stronger entities, such as pharmaceutical companies that test new patented drugs, have transparent and apparent advantages in this competitive environment.

Strategic actions to advance drug repurposing

To fulfil the potential of repurposing generic medicines, the following is suggested:

Safeguard policy to prevent patent abuse

The promise of repurposed treatments in cancer care can be undermined by the exploitation of secondary patents. Through strategies like evergreening, meaning filing new patents on minor modifications to existing compounds, or combining therapies, pharmaceutical companies can extend market exclusivity and maintain monopoly pricing, even when the original molecule is off-patent [34]. One example is the

thalidomide-lenalidomide-pomalidomide sequence, where secondary patents enabled sustained high prices and limited access [35]. Such practices pose a significant threat to the equity goals of drug repurposing. As outlined by Strohbehn et al. (2021), key policy safeguards should be considered, including stricter patentability standards and improved transparency [34].

Dedicated mechanisms to fund repurposing efforts

To address fundamental questions in oncology that are of low priority for the pharmaceutical industry, dedicated funding mechanisms are essential to ensure that cancer research targets medically-important questions and interventions, rather than financially profitable approaches [32]. One suggestion is employing a modest \$1 surcharge on the sale of each generic medicine in order to fund studies of repurposing. Given the huge volume of generic prescriptions, this would generate almost \$6 billion annually in the US alone [6]. Another option is to dedicate a specific portion of non-profit funding to clinical studies of repurposing, thereby accelerating the development of new therapeutic options. Collaborations among governments, non-profit funders, and private industry, such as public-private partnerships, could support large scale implementation.

Ensure regulatory availability

Availability must be addressed alongside affordability. Many off-patent potential repurposed drugs remain unavailable, specifically in LMICs due to lack of regulatory approval or absence from national formularies [28]. Coordinated efforts are needed to streamline approvals, support local registration, and promote the inclusion of evidence-based repurposed drugs in essential medicines lists.

Advocacy for repurposing research

A collaborative policy advocacy effort between patient advocacy groups, academic institutions, healthcare professionals, government agencies and policymakers, and non-profit organizations and foundations, can jointly influence funding priorities of non-profit and for-profit organization toward dedicating funds for repurposing studies. This effort should also promote regionally led research that evaluates the safety and efficacy of repurposed drugs across genetically and culturally diverse populations, particularly those underrepresented in clinical trials. Institution such as the Africa Centres for Disease Control and Prevention can play a key role in leading such efforts, ensuring that repurposed treatments are fit for purpose and contextually relevant. For example, LMIC-led efforts, such as the use of aspirin for colorectal cancer prevention in India, demonstrate the

potential of repurposing strategies to be both evidence-generating and contextually relevant [36].

Education and awareness campaigns to highlight the value of repurposing trials

This could include the development of position papers and fact sheets, the organization of workshops and webinars to share case studies and success stories, and the creation of platforms to reach a broader audience of healthcare professionals. Local initiatives, similar to the Anticancer platform, which provides a database of non-cancer drugs that have shown some evidence of anticancer activity, and the 2-day workshop led by the FDA and the NIH, could serve as models and key components of this effort.

Conclusions and hopes

Drug repurposing can offer more affordable treatment options, that often can have well-established safety profiles and reduced burden to patients, while potentially yielding meaningful clinical benefits across diverse settings. Today, experimental and retrospective data exist [18, 20, 21, 37, 38], which highlight the need for RCT-based conclusive clinical evidence. Repurposing strategies based on specific off-patent medicines may be both life-saving, as well as paving the way to make oncology care more sustainable and accessible globally.

This review is not questioning the importance of investments in developing new drugs, but rather raises questions of sustainability for patients and society, and emphasizes the unexploited potential of using existing off-patent medicines due to non-medical considerations. Importantly, we do not present drug repurposing as a “low-cost alternative” exclusive to low-resource settings, but rather as a globally relevant, right-based strategy that can complement innovation, advance equity, and promote sustainable access to effective care for all populations. This perspective also challenges profit-driven pharmaceutical industry priorities by advocating for research that is aligned with population needs, not just profit.

We urge non-profit and for-profit organizations to support drug repurposing strategies in oncology, prioritize funding for these trials, and minimize recruitment and economic barriers for such studies. While this perspective does not address technical implementation mechanisms in depth, we call on regulatory, procurement, and access experts to engage with the urgent need for collaborative pathways that can translate repurposing opportunities into equitable global impact. Importantly, we acknowledge that repurposed treatments should not be assumed effective in all contexts. Their evaluation must include diverse populations to ensure they are truly fit for purpose and contribute meaningfully to equitable

cancer care worldwide. A few existing repurposed medicines have already shown promising outcomes, offering complementary, pragmatic, and accessible strategies to improve patient outcomes and enhance the overall cost-effectiveness of cancer care.

Abbreviations

FDA	Food and Drug Administration
HIC	High-Income Country
LMIC	Low-and Middle-Income Country
RCT	Randomized Controlled Trial
ESMO-MCBS	European Society for Medical Oncology-Magnitude of Clinical Benefit Scale
ROI	Return on Investment

Author contributions

N.S contributed to conceptualization and manuscript drafting. M.S performed critical reviews and contributed to editing the manuscript. N.M contributed to conceptualization and manuscript review. S.B.E supervised the work and contributed to conceptualization and drafting the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval

Not applicable.

Competing interests

The authors declare no competing interests.

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