Policy Context for Cancer Medicines Forum

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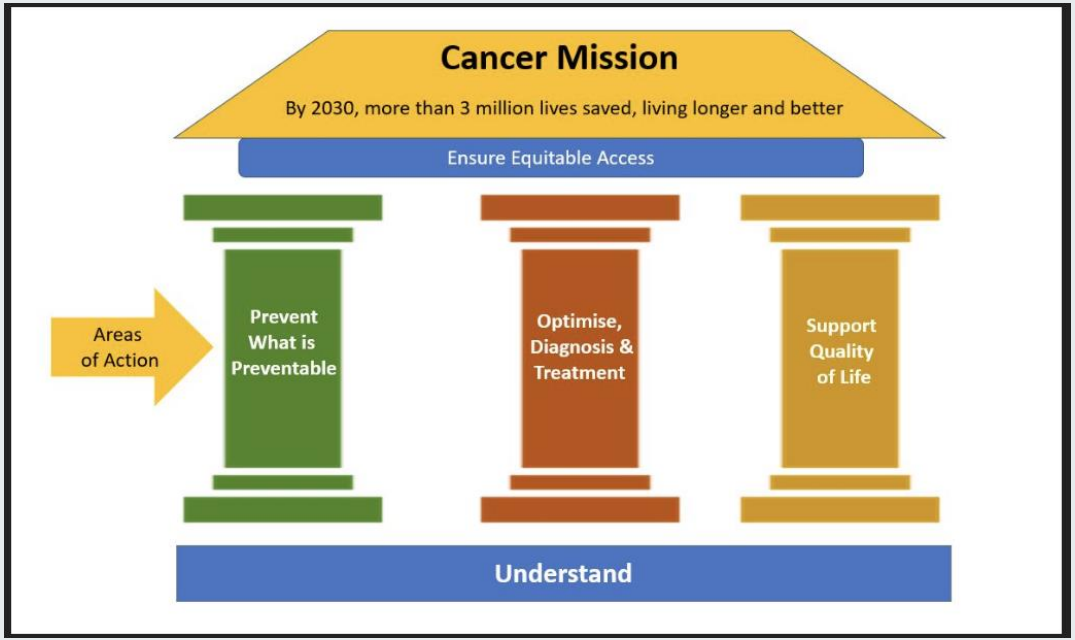
Good to be back in Europe

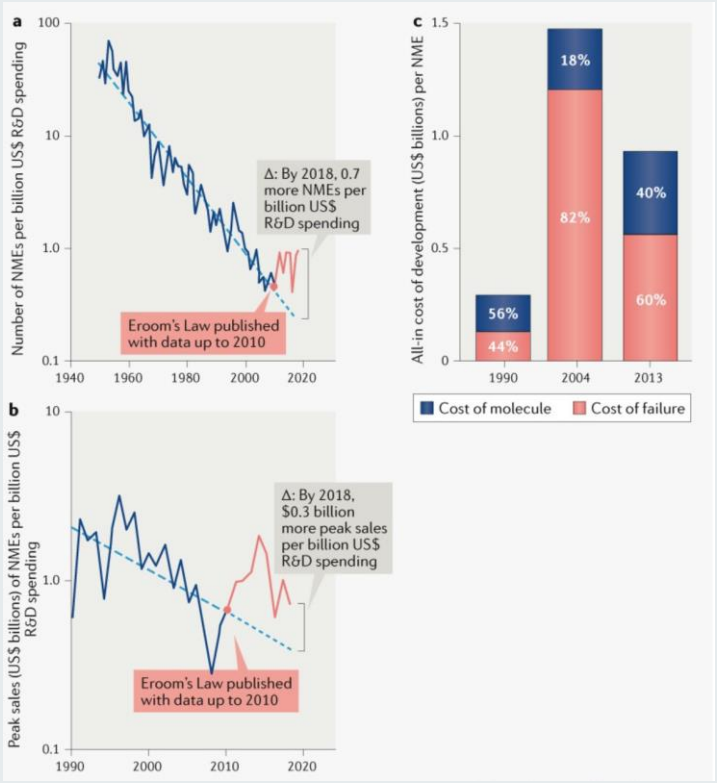
Foreground

Evolution of European policy

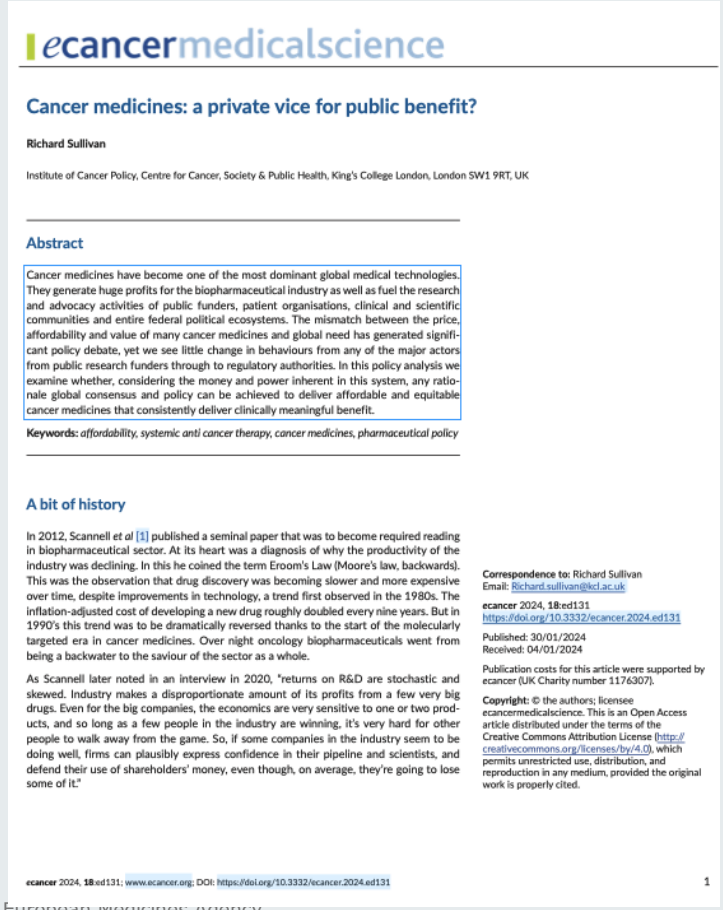


Kanavos P, Sullivan R, Lewison G, Schurer W, Eckhouse S, Vlachopioti Z (2010) The Role of Funding and Policies on Innovation in Cancer Drug Development ***ecancer*** **4** 164

Evolution of Biopharmaceutical policy



Breaking Eroom's Law. **Nature Reviews Drug Discovery** 2020 19, 833-834



ecancermedicalscience

Cancer medicines: a private vice for public benefit?

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Abstract

Cancer medicines have become one of the most dominant global medical technologies. They generate huge profits for the biopharmaceutical industry as well as fuel the research and advocacy activities of public funders, patient organisations, clinical and scientific communities and entire federal political ecosystems. The mismatch between the price, affordability and value of many cancer medicines and global need has generated significant policy debate, yet we see little change in behaviours from any of the major actors from public research funders through to regulatory authorities. In this policy analysis we examine whether, considering the money and power inherent in this system, any rationale global consensus and policy can be achieved to deliver affordable and equitable cancer medicines that consistently deliver clinically meaningful benefit.

Keywords: *affordability, systemic anti cancer therapy, cancer medicines, pharmaceutical policy*

A bit of history

In 2012, Scannell *et al* [1] published a seminal paper that was to become required reading in biopharmaceutical sector. At its heart was a diagnosis of why the productivity of the industry was declining. In this he coined the term Eroom's Law (Moore's law, backwards). This was the observation that drug discovery was becoming slower and more expensive over time, despite improvements in technology, a trend first observed in the 1980s. The inflation-adjusted cost of developing a new drug roughly doubled every nine years. But in 1990's this trend was to be dramatically reversed thanks to the start of the molecularly targeted era in cancer medicines. Over night oncology biopharmaceuticals went from being a backwater to the saviour of the sector as a whole.

As Scannell later noted in an interview in 2020, "returns on R&D are stochastic and skewed. Industry makes a disproportionate amount of its profits from a few very big drugs. Even for the big companies, the economics are very sensitive to one or two products, and so long as a few people in the industry are winning, it's very hard for other people to walk away from the game. So, if some companies in the industry seem to be doing well, firms can plausibly express confidence in their pipeline and scientists, and defend their use of shareholders' money, even though, on average, they're going to lose some of it."

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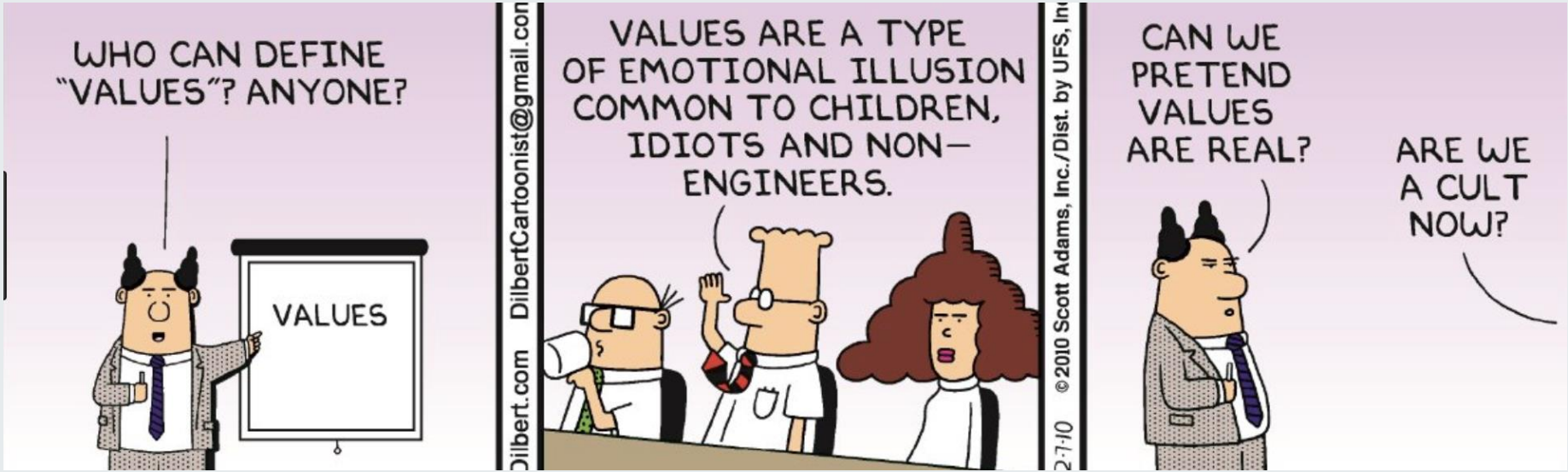
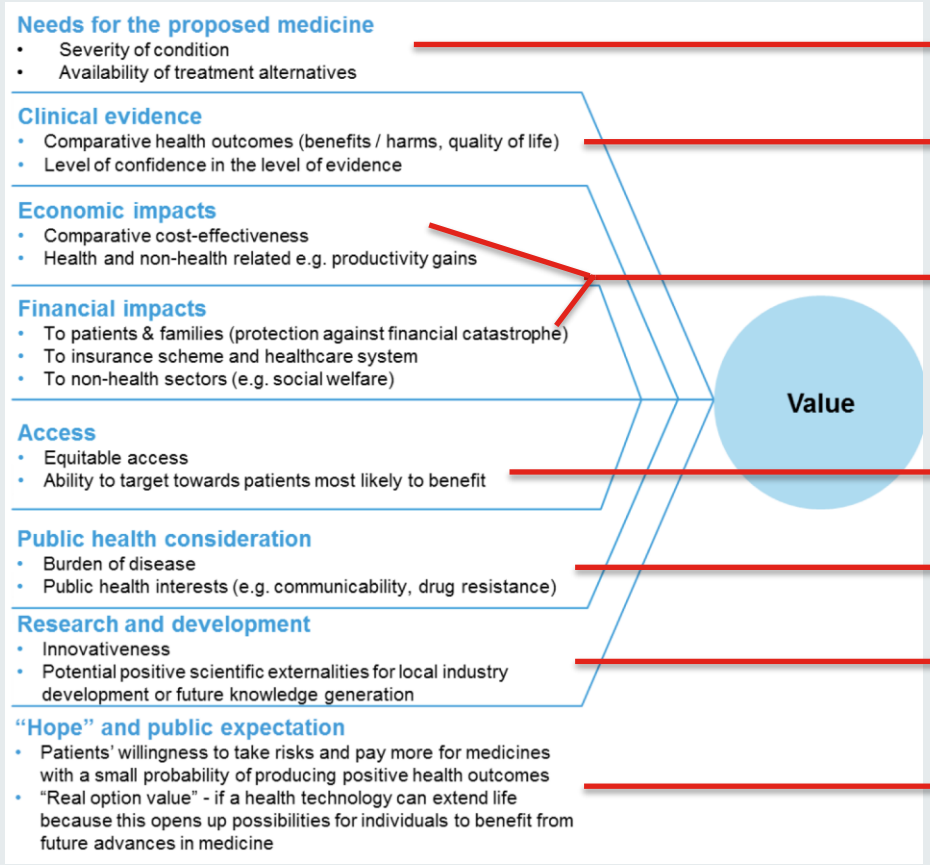
Evolution of policy(s) directed towards ‘value’



Pignatti, F., Wilking, U., Postmus, D. *et al*. The value of anticancer drugs — a regulatory view. ***Nat Rev Clin Oncol*** 2022 **19**, 207–215

Can optimization strategies provide better ‘value’?



No

Yes

Yes

Yes

Yes

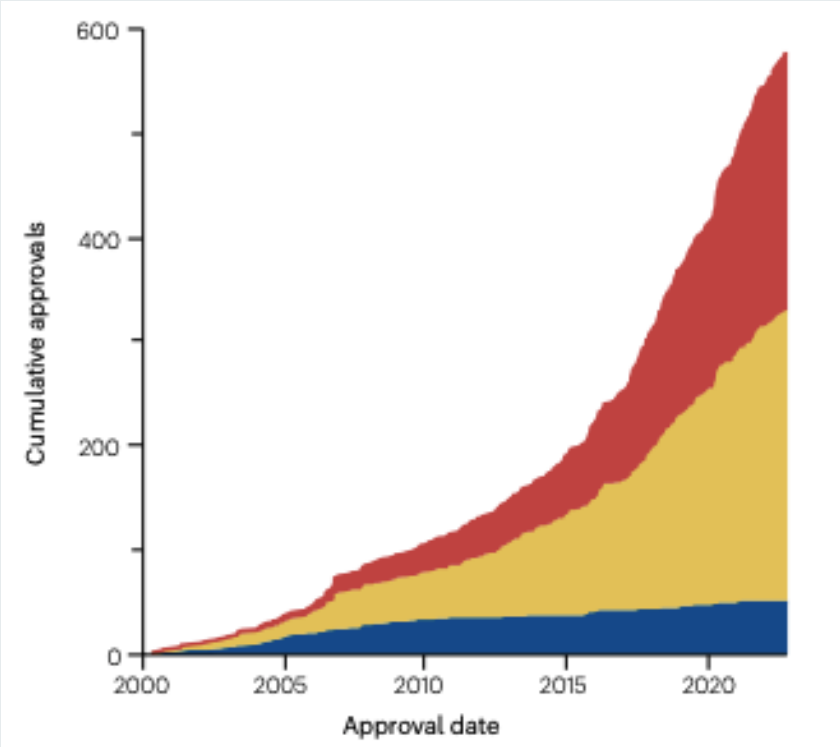
Yes

Maybe*

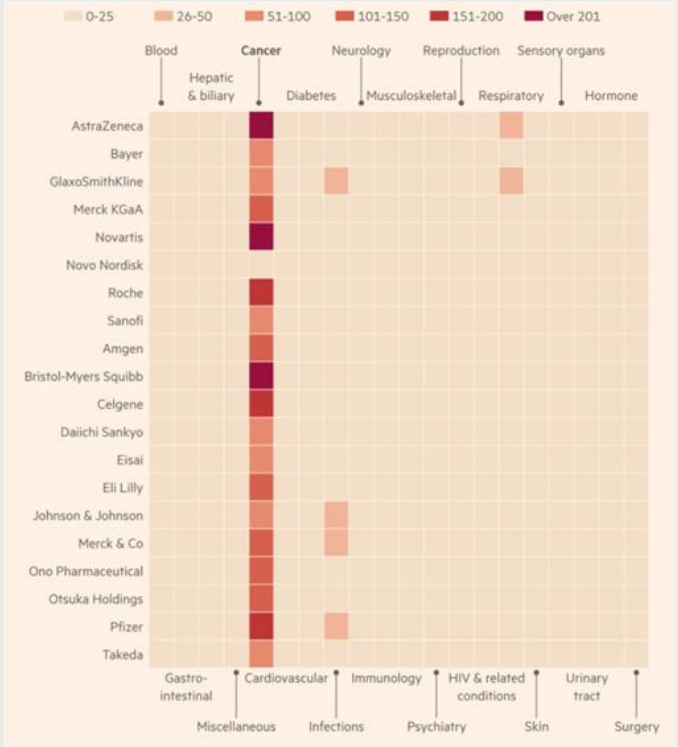
Policy Drivers

Relentless ‘innovation’

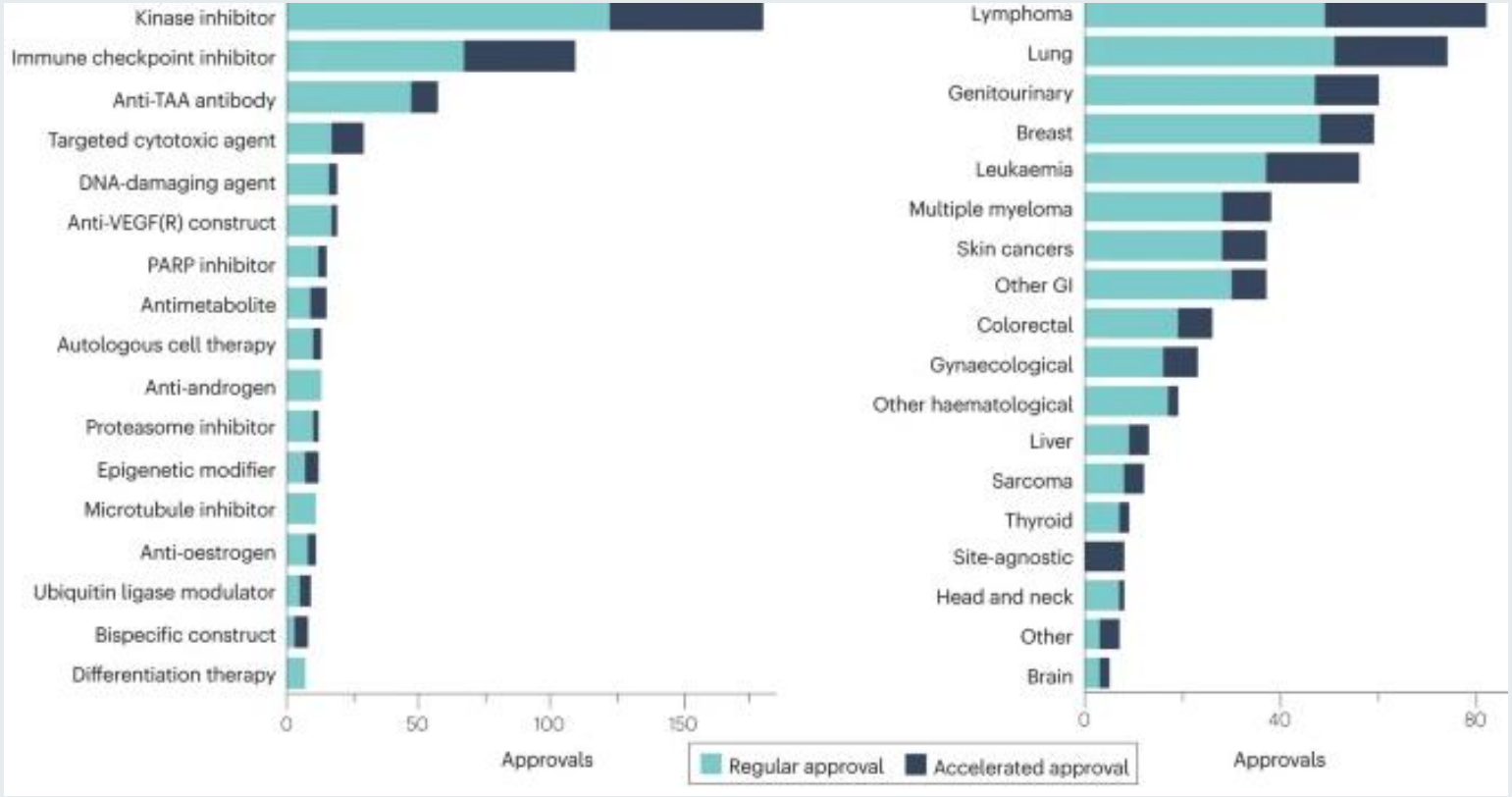
Past



Future



Greater uncertainty



Scott, E.C. *et al*. Trends in the approval of cancer therapies by the FDA in the twenty-first century. **Nat Rev Drug Discov 2023** 22, 625–640

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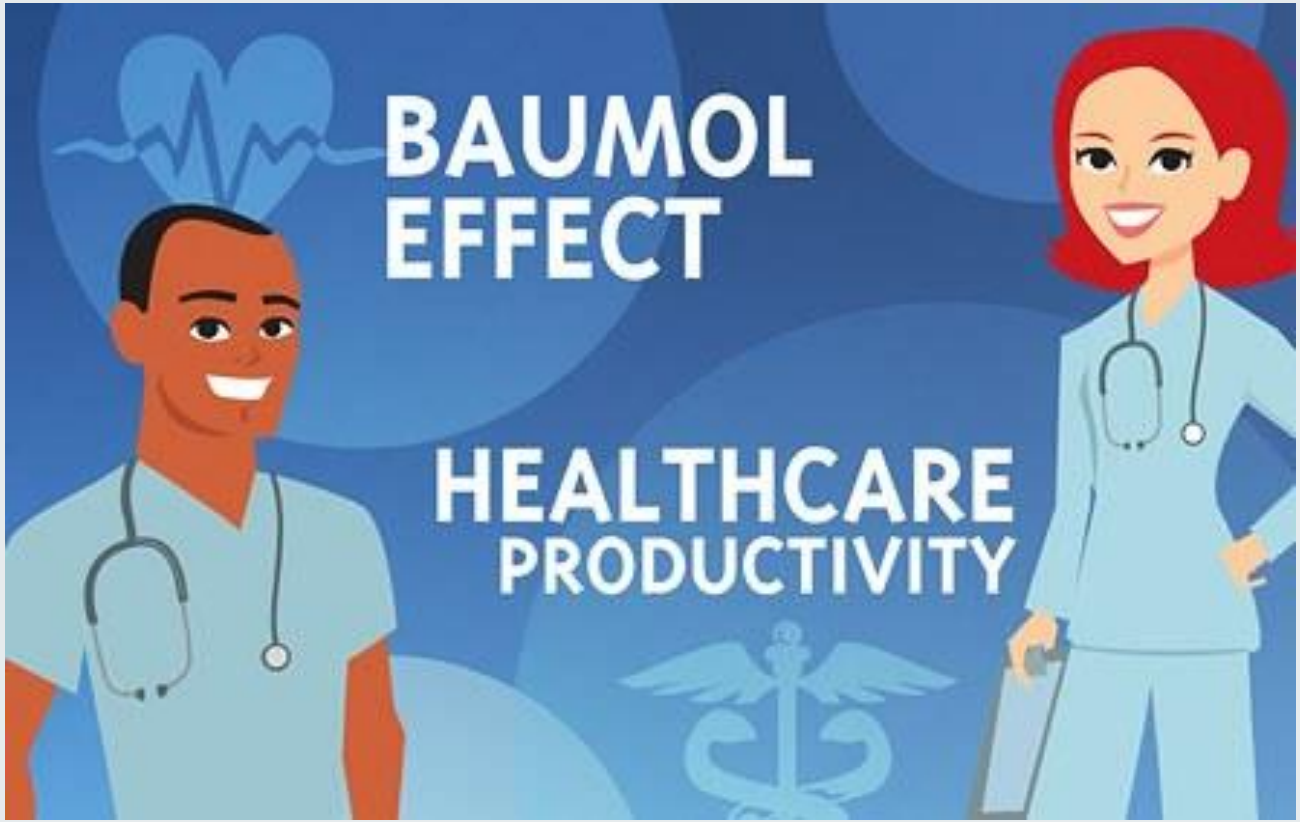
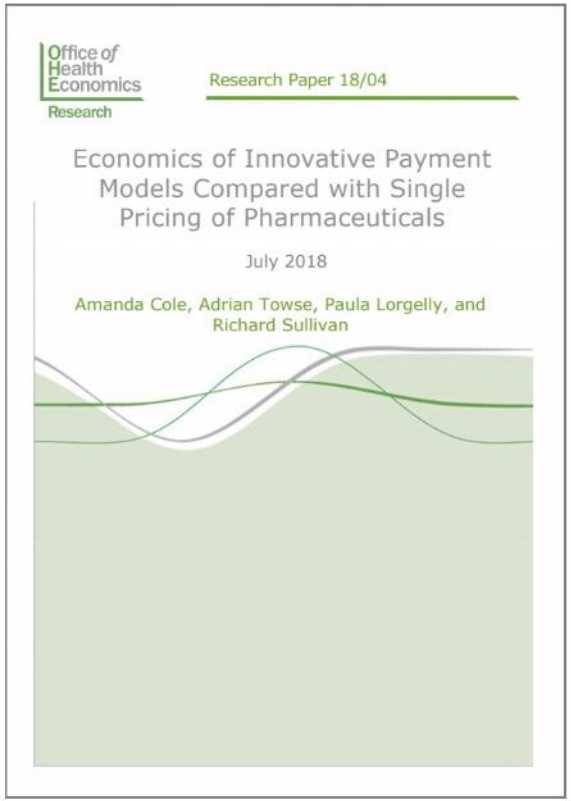
Affordability



The Cost Disease: why computors get cheaper and healthcare doesn't. William Baumol, 2012.



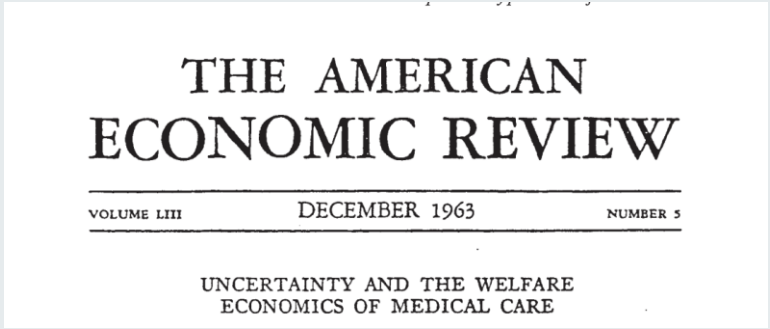
More complex patients, and more complex care[1]

Higher public expectations, exponential increase in all cancer technologies, and less fiscal headroom

But less and less focus on 'implementation' / optimization gap

[1]Lythgoe MP, *et al*. Development and economic trends in anticancer drugs licensed in the UK from 2015 to 2019. **Drug Discov Today**. 2021 26:301-307

Clinical asymmetry



THE AMERICAN
ECONOMIC REVIEW

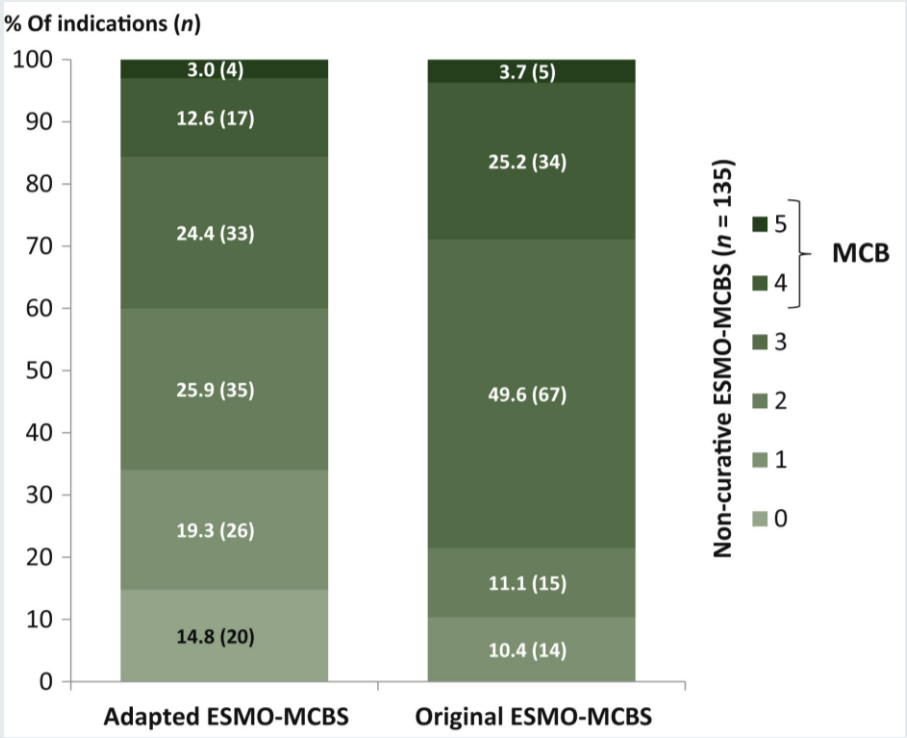
VOLUME LIII DECEMBER 1963 NUMBER 5

UNCERTAINTY AND THE WELFARE
ECONOMICS OF MEDICAL CARE

- many drugs, with a similar mechanism of action (“me-too”), concentrated in few tumor types, are mainly approved based on surrogate end-points

- many drugs with the same, or a very similar mechanism of action, are approved for the same indication without a direct head-to-head comparison

Falcone R, *et al*. Oncologic Drugs Approval in Europe for Solid Tumors: Overview of the Last 6 Years. **Cancers (Basel).** 2022 Feb 11;14(4):889



Two ways of looking at data –

1. Drugs '*don't clinically work*'!

1. They do but specific clinical context has not been established (optimization) – especially true for grade 3

Grössmann N,. Twelve years of European cancer drug approval-a systematic investigation of the 'magnitude of clinical benefit'. **ESMO Open**. 2021 6(3):100166

The research policy landscape

Shifting Research Funding Policy

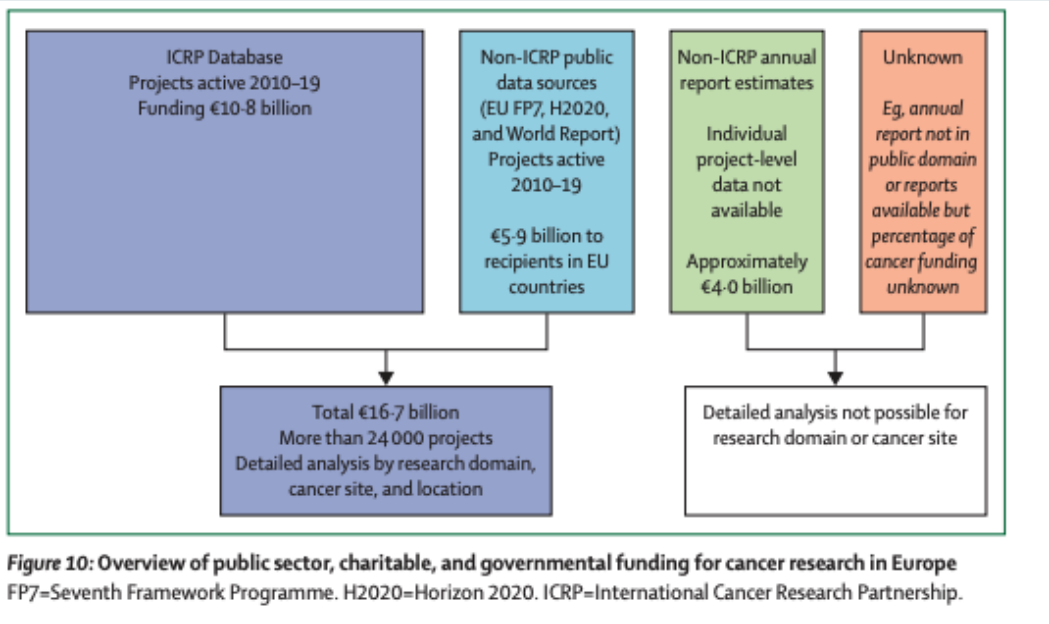


Figure 10: **Overview of public sector, charitable, and governmental funding for cancer research in Europe**
FP7=Seventh Framework Programme. H2020=Horizon 2020. ICRP=International Cancer Research Partnership.

European Groundshot – Addressing Cancer Research Challenges **Lancet Oncology** 2023: 24: e11-56

1. Insufficient to just do more RWE/RWD – **what matters is the quality of the studies** - 293 RWD studies, dominated by prostate cancer (29%) – no high-quality studies (78% 'low')[1]
2. Dose optimization (e.g. Project Optimus) **is just one strand**[2]
3. Research funding organizations policy is **too directed** towards discovery science / 'standard' drug development[3]

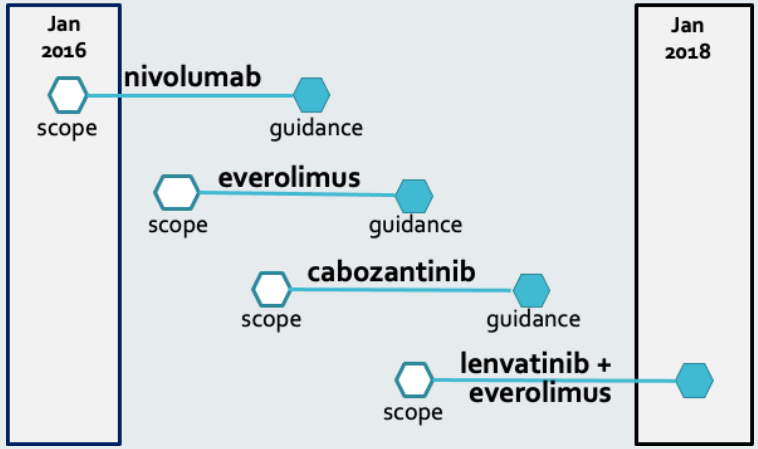
[1]Boyle JM, *et al*. Real-world outcomes associated with new cancer medicines approved by the Food and Drug Administration and European Medicines Agency: A retrospective cohort study. **EJC**. 2021 155:136-144.

[2]Moon H. FDA initiatives to support dose optimization in oncology drug development: the less may be the better. **Transl Clin Pharmacol.** 2022 Jun;30(2):71-74.

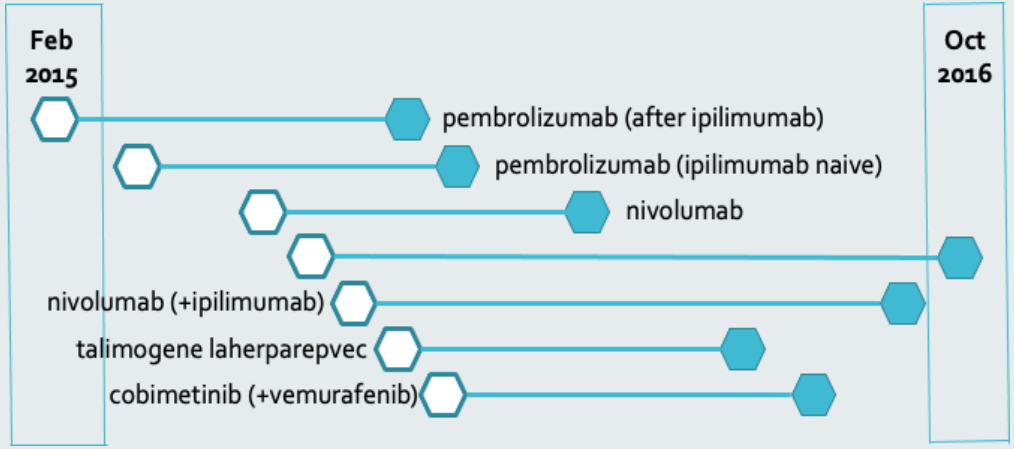
[3]Begum M, Lewison G, Lawler M, Sullivan R. Mapping the European cancer research landscape: An evidence base for national and Pan-European research and funding. **Eur J Cancer.** 2018 100:75-84

Research policy that links to HTA

2nd Line RCC



Malignant Melanoma



HTA bodies such as NICE increasingly dealing with **clustering of Rx**..
..plus.....

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- Differences between the characteristics of the trial participants & those of the patient group
- Limited duration of trials giving rise to the need to make projections regarding future events
- Treatment effects being biased as a consequence of crossover or treatment switching

Henderson et al.
Journal of Pharmaceutical Policy and Practice (2023) 16:84
https://doi.org/10.1186/s40545-023-00590-9

Journal of Pharmaceutical Policy and Practice

RESEARCH Open Access

Delivering the precision oncology paradigm: reduced R&D costs and greater return on investment through a companion diagnostic informed precision oncology medicines approach

Raymond H. Henderson[1,2,3,4*], Declan French[3], Elaine Stewart[3], Dave Smart[3], Adam Idica[5], Sandra Redmond[4], Markus Eckstein[6], Jordan Clark[3], Richard Sullivan[7], Peter Keeling[3] and Mark Lawler[1]

Research agenda for regulatory policy

Policy Review

From the European Medicines Agency to Project Orbis: new activities and challenges to facilitate UK oncology drug approval following Brexit

Mark P Lythgoe, Jonathan Krell, Mark Bower, Ravindhi Murphy, John Marriott, Sarah P Blagden, Ajay Aggarwal, Richard Sullivan

The departure of the UK from the European Union (EU) and affiliated European regulatory bodies, including the European Medicines Agency, on Dec 31, 2020, has resulted in the Medicines and Healthcare products Regulatory Agency becoming an independent national regulator. This change has required a fundamental transformation of the UK drug regulatory landscape, creating both opportunities and challenges for future development of oncology drugs. New UK pharmaceutical policies have sought to make the UK an attractive market for drug development and regulatory review, by offering expedited review pathways coupled to strong collaborative relations with other leading international medicines regulators, outside of Europe. Oncology is a key global therapy area for both drug development and regulatory approval, and the UK Government has been keen to show regulatory innovation and international collaboration through approval of new cancer medicines. In this Policy Review, we examine the new UK regulatory frameworks, policies, and global collaborations affecting new oncology drug approvals after departure from the EU. We explore some of the challenges that might lie ahead as the UK creates new and independent regulatory review and approval processes for the next generation of cancer medicines.

Lancet Oncol 2023; 24: e150–60

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Introduction

The UK formally left the European Union (EU) on Jan 31, 2020 (Brexit). After a short transition period, ending on Dec 31, 2020, the UK withdrew from participating EU institutions, including the European Medicines Agency (EMA), leaving the Medicines and Healthcare products Regulatory Agency (MHRA) as the UK's standalone medicine and medical device regulator. The departure from the EU has necessitated major health-care reform in the UK. New government policy has consistently focused on transforming the UK into a so-called life sciences superpower, capitalising on the UK's strong science base and previous track record in delivering timely innovations (eg, COVID-19 vaccines).[1,2] A central tenet of these new policies is establishing the UK as an attractive market for new drug development by forging greater international collaboration, beyond the EU, and offering expedited regulatory review.[3] Effective and efficient medicine regulation by the MHRA is fundamental for realising this ambition, and new oncology drug approvals are at the forefront of this.

All medicine regulation in the UK had been subject to European Law since 1973. However, after the outcome of the EU membership referendum in 2016, the UK has become a designated third country (outside the EU and European Economic Community) with EU pharmaceutical law ceasing to apply, except for Northern Ireland, which under the Ireland and Northern Ireland protocol continues under EU jurisdiction.[4] To replace EU pharmaceutical law, the UK has enacted the Medicines and Medical Device (MMD) Act to regulate human medicines, veterinary medicines, and medical devices. The MMD Act has provided a crucial step towards forging an independent regulatory landscape and new pharmaceutical policies after Brexit.[5]

Decoupling of the MHRA from the EMA infrastructure has presented both great opportunities and major challenges for medicines review in the UK. A key focus of new UK pharmaceutical policy is accelerating regulatory review and drug approval. To enable these processes, the MHRA has launched multiple new assessment routes for marketing authorisation applications (MAAs) (table 1), and is fostering greater collaboration (table 2) with other international regulators (eg, Project Orbis) outside the EU to accelerate the regulatory review of new medicines, while retaining full independence in all approval decisions.[6] Expedited approval of the next generation of new cancer medicines is viewed as a key pillar of this new policy.[7,8] However, despite the rhetoric around the potential benefits that the new policy might bring to patients with cancer, major challenges in terms of ensuring appropriate access and reimbursement remain.

This Policy Review focuses on new UK medicines regulatory frameworks, global collaborations, and policies affecting new oncology drug approvals in place after the UK's departure from the EU. We explore the potential opportunities and challenges of these new frameworks for cancer medicines, as the UK creates new independent regulatory review and approval processes.

Forging greater international collaboration

One of the first steps taken by the MHRA after the end of the UK–EU transition period was to join Project Orbis[9] and commence work sharing with the ACCESS Consortium.[7,8] Both collaborations (table 2) bring together the most powerful and influential global medicine regulators (eg, the US Food and Drug Administration [FDA] and Health Canada), with the goal of evaluating new drugs concurrently to expedite multigeographical approval. Project Orbis has a remit restricted to oncology therapies, but the ACCESS Consortium review can assess

- Research agenda for different regulatory review routes
- Studies that align with different collaborative pathways
- Influence on national research strategies

Alignment with European research policy

Advantages and opportunities	Disadvantages and challenges
Benefits for patients: clinically relevant outcomes and increased personalisation	Lack of funding
Cost savings for healthcare systems	Missing methodological framework
Therapies with added clinical value are rewarded	Competition with commercial trials for recruitment
If performed before approval: early assessment of marketability	Reluctance of industry to invest due to associated business risks
Registration of new combinations and additional indications in specific subpopulations	Missing infrastructure for international and/or multi-stakeholder setting
Filling of evidence gaps left by clinical trials	Ethical issues: conflicts of interest
Improvement of HTA and payer decision-making	Legal issues: liability, change in label
Improvement of clinical decision-making	If performed before approval: delay in patient access to new therapies
Faster patient accrual	If performed after approval: recruitment difficulties
Marketing advantage for industry	If performed by industry: increase in drug prices

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Multifaceted policy challenges for CMF

Critical need for research into the second translational gap for cancer medicines

Consistent policy and political engagement is key for change