

NON-PHARMACEUTICAL TECHNOLOGIES IN CANCER CARE: FOR PROFIT OR FOR PATIENTS?

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Summary: Non pharmaceutical technologies (NPT) in cancer are a growing and significant burden on health system costs. This domain of technology in cancer covers a huge range of non-pharmaceutical areas from artificial intelligence, mHealth technologies, diagnostic testing platforms, imaging, radiotherapy and surgery, among others. These rapid advances are heavily driven by commercial incentives. However, for many NPT within cancer care systems we are rapidly hitting the “break-even point” when additional costs of providing new technologies with small benefit causes more harm than good by diverting resources and efforts from ensuring broad access to the interventions which are known to have large benefits.

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Rapid advance of technology in cancer research

The last two decades have witnessed an explosion of non-pharmaceutical technologies (NPT) in cancer care. These advances cover the full spectrum of domains from companion diagnostics (imaging, pathology) through to therapeutic innovations in applied surgery (robotics, minimally invasive, etc.) and radiotherapy (e.g. proton beam therapy, stereotactic body radiotherapy (SBRT)). A staggering 64% of cancer research papers from Europe in 2017 had some form of NPT at their core.¹ Meanwhile, in a recent review of the 150 most important cancer research questions, 149 concerned some form of NPT.² Research agendas driven by high income countries have led to an ecosystem which is dominated by ‘high tech’.

This, of course, is in the context of an even greater surge in pharmaceutical technologies, i.e. new cancer medicines and associated biomarkers.

The latest review of future research innovations by the Cancer Moonshot 2020 program created a top 20 list of some of the most advanced technologies.³ For example, liquid biopsies, Artificial Intelligence (AI)-coupled to imaging and radiotherapy planning, embedded sensors, as well as ‘next generation’ radiotherapy and robotics. The traditional hegemony of pharmaceuticals in the European technospace is now being challenged by precision surgery including iKnife (diagnostic surgical scalpel), nanorobotics and radical new applications of computing to cancer diagnostics (e.g. Google’s DeepMind).

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Overall, cancer NPT has become a ‘Trojan horse’ for science and technology; there are few spheres of technology that cannot be applied to cancer care.⁴ Neoliberal policies that favour the commercial sector above the public have also dictated national policy agendas.⁵ The commercial imperative has created an ecosystem where NPT innovation (typical for-profit) takes primacy. In many instances this has led to value creep whereby NPT innovations lead to incremental improvements.

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Ecosystems of NPT

The commercial determinants of NPT are being played out across three major ecosystems – diagnostic (molecular pathology), radiotherapy and radiology (including novel imaging technologies) and surgical (especially robotics but also in minimally invasive surgery). According to Statista global, NPT revenue is now over USD 380 Billion per annum, rising to a projected USD 600 Billion by 2024. On the one hand, some NPT have driven better outcomes (e.g. Intensity-modulated radiation therapy (IMRT) and Image-Guided Radiation Therapy (IGRT)); however, the benefits of these technologies are unevenly distributed within and between European Union (EU) countries and populations (particularly for the poor, older people, and ethnic minorities). Analysis of direct cancer expenditures across Europe has found, particularly in lower Human Development Index (HDI) Member States, significant over-spend on

low impact NPT, and underspend on basic, high impact ones, leading to a dangerous disconnection between cancer-expenditure and outcomes.⁶

As proposed by Woolf and Johnson, in all fields there is a “break-even point” when the additional costs of providing new technologies with small benefit may cause more harm than good by diverting resources and efforts from ensuring broad access to the interventions which are known to have large benefits.⁷ An emerging issue in all countries is the perception, misled by media hype, that the latest technologies provide some miraculous route to cure, irrespective of the clinical facts.

Da Vinci Robot: the archetype of NPT

Few technologies better represent the commercialisation of NPT than the Da Vinci Robotic Surgical System. This device, which allows surgeons sitting at a console to operate remote-controlled arms for minimally invasive surgery, was first given approval by the US Food and Drug Administration (FDA) in 2000. It had been expected that its inherent advantages, including improved visualisation of the surgical field, enhanced range of motion of the robotic arms and improved ergonomics for the surgeon, would translate into improvements in patient outcomes. However, in the case of prostate and rectal cancer, no improvements in functional or oncological outcomes have been observed. Despite the lack of clear evidence for its superiority over open and laparoscopic techniques and its higher associated costs (up to four times more expensive), it has undergone rapid adoption across Europe, even penetrating many middle income countries.⁸ It could now be considered the cornerstone of surgical treatment for prostate cancer in these countries with increasing utilisation across tumour types despite the lack of level one evidence. Studies have demonstrated that the uncoordinated adoption of new technologies in health systems has created a socioeconomic differentiation in access to cancer care.⁹

Moreover, for example, in the United Kingdom where health care is free at the point of use, the commercial drive for

centres to adopt Da Vinci led to significant bypassing of local centres by people wishing to access this novel treatment. Men who sought out this NPT were younger, fitter and more affluent.¹⁰ This provides some evidence that the European geographical variation in the availability of new “innovative” technologies within health systems, means that those patients with greater financial or physical resources are more likely to access them even across-national boundaries, creating profound inequities in access and outcomes.

Hitting the ‘break-even point’ in NPT

It is increasingly clear that we have hit a break-even point in commercially driven research in cancer where effective innovation is less important than improving the fidelity with which all these technologies are delivered, i.e. the extent to which European health systems provide equity in access to the interventions they need, precisely when they need them.¹¹ We still fail to either provide access to NPTs that we know improve outcomes for patients or with the required quality assurance. In this regard it is idealistic to expect private industry to retain a public health perspective, when other priorities influence their resource allocation decisions. The commercial sector is accountable only to its shareholders and investors. Fundamentally, it is European governments that are responsible for putting in place the mechanisms, including health technology assessment processes that cover both pharmaceutical and NPT, to reward NPT that delivers clinically meaningful benefit at a fair price. Markets respond to externalities, and it is our view that the failure to deliver cancer NPT with significant value is a shared problem, with the bar for market entry set so low that capital funding for research and development of low value NPT is too easy to obtain.

The failure of the private sector to drive up the value offering for NPT for cancer is reinforced by weak federal governance mechanisms and a public European research funding environment that myopically focuses on innovation with little consideration for implementation, services and systems research for NPT.

Whilst guidelines have been created to improve the rigour of evidence collection, particularly for medical devices prior to implementation, a major factor influencing the type of study performed is the regulatory requirements of different health technologies prior to regulatory approval. Regulatory approval for a new medical device or technology requires clinical data, and a demonstration of its safety, prior to putting the device on the market. By comparison, systemic therapies need to go through the complex process of demonstrating superior efficacy compared to current standards of care.^{11 12} This in part explains the paucity of randomised controlled trials for medical devices.^{13 14} For example, only 5% of all research outputs in radiotherapy relate to clinical trials. However, the recent Cumberledge review highlighted the devastating impact of integrating drugs and devices without careful and robust evaluation of the impact on patients with respect to safety and health benefit. Unfortunately, the design of studies used for evaluation of new technologies are often lacking in rigour yet may form the basis for clinical implementation with retrospective single-centre case series (a low evidence standard) still dominating the literature.¹⁴

“allowed evidence-based medicine in cancer to be hijacked by using technologies with marginal effectiveness but maximum cost

Part of the explanation for hitting the break-even point now is that the business models at the heart of the European innovation systems – profits without prosperity as Lazonick describes it¹⁵ –

Box 1: Policy interventions to reduce inequalities in access to affordable and necessary cancer technologies

1. Build a culture of funding effective and affordable technologies: this is around re-orientation of public funding for research that builds orphan technology domains e.g. automation in radiotherapy workflows, virtual reality enhanced surgical training, mHealth and self-management referral systems. But this needs to come with building momentum in key NPT domains, e.g. pathology and surgery, as well as creating a policy dialogue that such approaches are not ‘second class’ technology and medicine.
2. Coupled to cultural re-engineering, there is a need to hold NPT to high levels of evidence. We need trials/well conducted studies to show NPT have benefit AND we need the magnitude of benefit to be meaningful (i.e. not trivial). This needs to be coupled to a willingness to de-implement new tech when future evidence shows it may not work as well as we once thought.
3. Audits to ensure gaps in access and quality from proven innovation are managed to maximise outcomes. With this public reporting of outcomes and benchmarking of best practice, one can identify optimum processes for delivery and support rapid knowledge transfer and uptake of high value NPT.
4. Pricing and reimbursement: a wide range of supply and demand side policies are needed to manage technologies, with a specific focus on value-based payment systems and health technology assessment programs for all technologies.
5. Public and Patient engagement: a new narrative is necessary to balance out the unrelenting personalised-medicine and ‘access to everything for everyone’ mantra. Technology is not a ‘bypass’ for better governance in the face of clinical, and systems failure, nor for the lack of human resources.

are not fit for purpose. Yet, turning this around will be profoundly difficult. As one surveys the wider cancer technology landscape, especially in the ‘new’ digital world of AI, the commercial actors have become, arguably, far more diverse and powerful. NPT in cancer has never been more profitable and AI is now the new ‘precision’ cancer medicine. However, our own clinical community must also shoulder a significant portion of both the blame and the solution. As Ioannides noted, medicine and health care are wasting societal resources because ‘we’, clinicians, have allowed evidence-based medicine in cancer to be hijacked by using technologies with marginal effectiveness but maximum cost.¹⁶

Policy interventions to manage NPT

Industrial and macroeconomic policy frame much of the impact of NPT on cancer control, and it remains an open question whether political elites and

clinical communities have the will or appetite to embrace different paradigms. This is especially so when more and more of health care is being delivered in mixed market economies with unregulated private sectors, and underinvested public systems.¹⁷ The impact of this is crystal clear; poor and unequal outcomes coupled with declining value, of which very high cost (and in many cases unnecessary) NPT constitute a substantial part of the problem. So what could and should be done?

On the one hand, in many European countries there remains a failure to ensure universal health coverage or the rational allocation of limited resources to key modalities and site-specific cancers. On the other hand, governments are engaging in *ad hoc* funding of expensive pharmaceutical technologies and/or NPT in the absence of basic radiotherapy provision or adequate surgical capacity. This is a massive political failure at

national and supra-national levels. However, to rectify these intrinsic flaws there are a number of possible policy interventions aimed broadly at reducing inequalities in access to affordable and necessary cancer technologies as well as addressing technology-induced inequalities (see Box 1).

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A short guide to cancer screening. Increase effectiveness, maximize benefits and minimize harm

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The purpose of cancer screening tests is to detect pre-cancer or early-stage cancer in asymptomatic individuals so that

timely diagnosis and early treatment can be offered, where this treatment can lead to better outcomes for some people.

The aim of a cancer screening programme is either to reduce mortality and morbidity in a population by early detection and early treatment of a cancer (for example, breast screening) or to reduce the incidence of a cancer by identifying and treating

its precursors (such as cervical and colorectal screening).

This short guide is designed to be a quick reference that contains the important ideas about cancer screening. Readers should refer to other publications for comprehensive discussion and detailed guidance on cancer screening programmes.

