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Vital Role of Clinical Research in Delivering The 10-Year Cancer Plan

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The ambition of the UK government's 10-year cancer plan consultation document to transform cancer outcomes is highly welcome (1). This consultation must reflect on the extraordinary role played by the UK research community in responding to COVID-19, a response enabled by clinical research delivery infrastructure embedded within the NHS, which allowed rapid clinical evaluation of novel treatments and vaccines to save and transform lives. This unique national research delivery capability is the legacy of over two decades of national clinical research networks, with co-operation between government agencies, charitable funders and many others. It started in cancer with the inception of the National Cancer Research Network and Institute (NCRN and NCRI) in 2001, and with the NIHR Clinical Research Network (CRN), now extends across all of health and social care. Cancer outcomes have been radically improved during this time, but further gains will require reinvigoration and realignment of our research capability at multiple levels, starting with our workforce.

Research workforce

Driving large-scale research programmes requires significant clinical leadership, time and resources. The NCRI Research Groups, and NIHR CRN Cancer Specialty Oversight Groups are an established network of expert clinicians, scientists, and consumers, ready to advise on key priorities and develop research proposals addressing them; while both the NIHR and Royal Colleges have initiatives to train and enthuse tomorrow's investigators and innovators. However, urgent attention is needed to maintain momentum, and support existing consultants, who, in the post-pandemic climate of a severely overstretched cancer workforce, face unprecedented service demands; time for research is scarce. National leaders applauding COVID-19 research programmes demand that research becomes integral with NHS service delivery (2, 3). To achieve this, research time must be embedded within consultant job plans. Furthermore, releasing highly trained staff to lead research requires funding to backfill service

commitments. Clinical academic excellence must be valued and fairly-rewarded, to avoid demoralisation and clinicians disengaging from research.

Prevention and Early Detection

'Screening, Prevention and Early Detection' (SPED) has perhaps the greatest potential to reduce our population's cancer mortality. Rapidly evolving SPED technologies need critical evaluation through robust, large-scale prospective trials. National clinical initiatives such as Targeted Lung Health Checks, Rapid Diagnostic Centres (RDCs) and Community Diagnostic Hubs (CDHs) are ideal platforms for such endeavours, exemplified by NIHR portfolio lung screening and biomarker research. Multi-cancer early detection tests such as the Galleri programme of studies supported by NHSE and NIHR are particularly attractive, but require rigorous analysis of many aspects of implementation, beyond simply assay performance (4). The UK's research infrastructure is uniquely capable of rapidly recruiting large numbers of at-risk individuals across wide geographical and cultural strata.

However, SPED research is predominantly a community endeavour, conducted outside acute hospital oncology and surgery departments, so requires new infrastructure distinct from existing resources, which instead focus primarily on patients already diagnosed with cancer. Stretched primary care services are poorly equipped to embrace research expansion critical for SPED to flourish. This needs careful consideration and better resourcing, as well as primary and secondary care experts collaborating on optimal use of finite resources. In particular, this needs systematic expansion of research infrastructure supporting screening, RDC and CDH networks, which should be mandated to host research as a matter of course.

Innovation

Modern cancer drugs, which have transformed survival for some cancers, largely stem from laboratory discoveries associated with cancer biology, with effective partnership between academia and Life Sciences Industries. In the UK, much of this early phase research has been led by our Experimental Cancer Medicine Centre (ECMC) Network, which must be sustained and expanded if we are to retain the strong Pharma relationships that currently exist, given international competition. NHS genomics services are developing apace, offering many benefits for Precision Medicine; however, our full research potential is often constrained by

manpower, equipment and commissioning arrangements which are significant barriers to attaining our full research capability. The current NHS genomics focus is necessarily on comparatively few genetic alterations associated with approved targeted cancer medicines - generation of far more extensive genetic information to signpost patients to trials of novel therapies must be developed and made readily accessible in real-time through initiatives such as Our Future Health (5).

The NIHR portfolio currently contains over 1300 cancer studies, with more than 800 actively recruiting. The burden on multiple elements of the NHS to undertake this research activity is not insignificant. Our resources are finite, so we need a manageable portfolio, but with sufficient breadth and variety to ensure all can benefit from state-of-the art interventions. We must propagate the successes of the Urgent Public Health COVID-19 studies and generate efficiencies in both study set-up and study design (e.g. platform studies) if we are to become more cost-effective with our time and manpower. The new national Patient Recruitment Centres are generating successes by adopting single approval and costing processes that need adopting throughout all NHS trusts. Regulatory and research governance processes, so risk-averse that they restrict even access to anonymised patient data, require urgent revitalisation and risk-proportionate approaches.

Changing Practice

Demand for access to new treatments is fierce, generating significant risk of new treatment adoption based on limited early positive data, not borne out in subsequent phase III trials. The UK's robust evidence-based approach to evaluating new innovations gives an important opportunity to work with commercial partners to address health economic endpoints and prioritise cost-effective interventions. Our new proton beam radiotherapy centres, combining traditional randomised trials and thorough 'Commission through Evaluation', is already generating data likely to be internationally practice-changing. Learning from this approach - bringing healthcare providers closer to our research community - and applying it to other expensive healthcare technologies, could become a key UK strength. Evidence-based practice in surgery for example, has grown rapidly in recent years, and remains a key treatment modality for many patients with cancer. Implementation of new surgical technologies and/or devices needs well governed processes if we are to avoid harm and adverse outcomes (6).

Above all, we are mindful that significant inequalities in access to routine health services and research participation were exacerbated by the COVID-19 pandemic. Cancer patients in England deserve equitable access to clinical trial participation, evidenced transparently by NIHR and NHSE data collection systems. The NIHR 'Be Part of Research' platform has huge potential to signpost patients and clinicians to clinical trials in real-time, but needs significant development to be truly impactful. 'Best Research for Best Health: The Next Chapter' expects research to improve outcomes for diverse and underserved communities, addressing at-risk populations and promoting equity of access (2).

Routinely collected 'real-world' health data must revolutionise research data curation. Despite impressive UK national datasets and IT capability, data remain disproportionately difficult to access. Flagship digital policy documents such as those of The Health Foundation (5) and Goldacre Review (7), should be scrutinised for research opportunities, and recommendations implemented. The 10-year cancer plan must include investment in technologies to facilitate research within all service as well as digital environments, with focus on keeping patients closer to home, using virtual interaction tools, remote consultations and e-consent platforms.

Optimisation

UK cancer research has a strong track record in designing and delivering academically led studies investigating treatment de-escalation, reducing the burden of treatment on individual patients physically, emotionally and financially, as well as on the healthcare system, whilst maintaining best outcomes (8-10). Such trials save healthcare resources and are globally relevant. Yet, few countries can deliver such trials, rarely prioritised by Pharma. This depends on a strong programme of NIHR- and NCRI-led research, underwritten by co-ordinated support from regulators, research funders and cancer care commissioners. This unique strength of UK academia could be the focus of a specific HTA programme supported with NIHR and NHS funding.

Much academic research developed in direct partnership with patient and public involvement includes important patient-centred outcomes focussing on quality, as much as quantity, of life. Our strong research programmes addressing end-of-life care, and long-term survivorship

issues are unique strengths affording great potential for the UK to be world-leading in these challenging areas of cancer care.

Summary

Healthcare innovation and technological advances depend upon vital research infrastructure and translational research community resource. It is imperative to prioritise and properly resource all aspects of cancer research capacity, from bench to bedside, if we are to make significant gains on cancer outcomes in the next decade. We call on the UK government and oncology research community to draw on these views to ensure a 'research-embedded' 10-year cancer plan.

Contribution

All authors contributed to conceptualisation and writing of the original draft and editing/review. RL/PC/JW oversaw content of the final manuscript and decision to publish.

Conflict of Interest Statement and Role of Funding Source

All authors have secondment roles within the NIHR CRN as National Specialty Leads or in an advisory capacity to the NCRI. Authors were not precluded from accessing the content of the comment. No original data was necessary to the creation of this manuscript, which derives from the views of previous meetings and correspondence between the group as well as co-creation electronically. All authors accept responsibility for publication.

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