Improvement in child cancer survival rates threatened by lack of new drug development

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Remarkable improvements in survival from childhood cancer have taken place in high- income countries over the past 50 years, but further progress is being threatened by increasingly strict research regulations and insufficient development of new drugs, according to a major new *Lancet Oncology* Series on improving cancer care for children and young people.

"In high-income countries, we have nearly reached optimisation of present anticancer treatments", says Series leader Professor Kathy Pritchard-Jones from the Institute of Child Health, University College London, UK. "New regulatory approval and research strategies are urgently needed to speed the development of new, effective, and safer treatments for children with cancer if we are to continue to improve the cure rate, reduce toxicity compared to existing treatments, and minimise side effects in later life."*

Although more children and young people in high-income countries are surviving cancer than ever before, cancer remains the leading cause of death from disease in children aged 1 to 15 years, and more than 5000 children still lose their lives to cancer every year in these regions.

Increased participation in international, collaborative clinical trials has successfully raised survival from 30% to 80% over the last half century. "But an increasingly complex and strict regulatory environment for clinical research and data sharing is limiting children's access to early-phase clinical trials and delaying the development of new drugs"*,

explains co-leader Richard Sullivan, professor of cancer policy and global health at King's College London and King's Health Partners Integrated Cancer Centre. "For example, the implementation of the EU Clinical Trials Directive, in 2004, has almost quadrupled costs, led to substantial delays, and even the discontinuation of trials."*

Other factors leading to longer clinical development include: the complex nature of the biology underlying childhood cancers; the difficulty of identifying targets suitable for drug treatment; a lack of long-term sustainable funding for research and development, particularly outside the USA; and little economic incentive for pharmaceutical companies to develop anticancer drugs adapted for children.

To fast track the most relevant and new medicines for childhood cancers will require a renewed focus on the potential role of adult cancer drugs in children as well as newer methods and clinical trial design that aim to more rapidly predict the optimal (ie, effective and safe) dose.

In recent years, it has been industry that has driven the clinical trials in children to meet regulatory requirements rather than the paediatric oncology expert community who understand the clinical unmet needs of children and young people with cancer, write the authors. "The trend in the past few years for industry to drive the development of clinical research plans contrasts with the need for broad research and development partnerships that can deal with complex biology and drug development."

"Fostering open collaborations with many groups from industry, regulatory bodies, academia, governments, and patient advocacy will be crucial to speeding up drug development", says co-author Professor Gilles Vassal from the Institut Gustave Roussy, Paris-Sud University, France. "The key is precompetitive collaboration that benefits all stakeholders, ensuring broad access to the results."*

According to Professor Pritchard-Jones, "new biology-driven approaches are needed, but this will only be achieved through increased international cooperation in clinical trials and sharing of research tissue samples and data. This is necessary as these diseases are already rare, and dividing patients into increasingly smaller biological subgroups might amount to just a handful of trial participants a year in each country." *

She adds, "The introduction of drugs that are less toxic and more targeted than those currently used necessitates a partnership between clinical and translational researchers, the pharmaceutical industry, drug regulators, and patients and their families. This therapeutic alliance will ensure that efforts are focused on the unmet clinical needs of young people with cancer."

As well as drug development challenges, more needs to be done to address the long-term consequences of cancer treatment. Estimates suggest that one in 1000 adults in high-income countries are survivors of childhood cancer, and 40% of these survivors experience adverse effects throughout life.

"These are serious issues that can have a real impact on a person's quality of life", says Sullivan, "It is essential that academic programmes and trial investigators ensure better follow-up of survivors to appropriately address the complications childhood cancer survivors may experience in later life."*

The authors conclude by calling on every country to develop a national cancer plan that recognises the unique demographic and care needs of young people with cancer, adding that, "If policy makers continue to fail to pay attention to this issue then in 10 years…the infrastructure will not be in place to deal with what will have become the most common disease-related cause of death in childhood."

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