INTRODUCTION

In the UK around 3,800 children, teenagers and young adults are diagnosed with cancer each year, that’s 73 every week. Considerable improvements in treatments mean that more than eight in 10 children and young people with cancer now survive for five years or more, compared with just three in 10 in the late 1960s. In fact, around three in four will now survive their cancer for ten years or more. However, there are many different types of cancers that affect children and young people, and we know that for some types survival rates are still far too low – we need to continue to make progress to save more lives across all types of cancers in children and young people.

Children’s cancers are biologically very different from adult cancers. Cancer is generally a disease of the elderly since it takes time to build up multiple genetic mistakes that can turn a healthy cell into a cancer cell. Approximately 75% of teenage and young adult tumours are similar to childhood cancer tumours and cancers in these age groups often have much less genetic complexity; many are associated with only one or two genetic mistakes implying a fundamental difference in how they develop. Finding out what causes childhood and teenage cancers is crucial to figuring out how to diagnose them earlier and develop better treatments.

Due to the diversity and uniqueness of cancers in these age groups, we need more research to build our understanding and find better, kinder treatments. CRUK are committed to accelerating progress in children, teenager and young adult cancer as part of our research strategy launched in 2014. Earlier this year, we launched CRUK Kids & Teens; a new campaign to raise money for research into cancers affecting children, teenagers and young adults. We are committed to increasing our focus on children’s, teen’s and young adult’s research – our ambition is to double the amount we spend in this area over the next 5-10 years, to accelerate progress finding new cures and kinder treatments.

In order to do this, we need more high quality research proposals. That’s why we set up an expert steering group of leading researchers to help us organise a workshop aimed at identifying current challenges, opportunities and ideas for new high quality research proposals. We convened 80 researchers, clinicians and parents to discuss key research themes, identified in advance by the steering group.
THE WORKSHOP

The aim of the workshop was for the research community to agree priority areas for research and identify barriers and opportunities, and to start to develop integrated cohesive proposals that will have a transformative impact on the way the research is conducted for children and young people with cancer.

The following six themes were discussed: early phase trials and stratified medicine, evidence-based medicine, surgery, radiotherapy, data and long-term consequences of treatment. Other key themes arose throughout the discussions such as early diagnosis and prevention.

EARLY PHASE TRIALS AND STRATIFIED MEDICINE

Lead: Darren Hargrave, Great Ormond Street Hospital

Establishing a National Paediatric Precision Medicine programme in the UK is an exciting prospect, which could improve identification of new predispositions, diagnostic classification, treatment stratification and the study of tumour evolution. The opportunities identified include:

- all children and TYAs with cancer having a full molecular characterisation of their tumour (DNA, proteomics and transcriptome) at diagnosis and relapse
- developing high quality tumour banks to underpin research studies (including collecting samples on a longitudinal basis where possible)
- developing better infrastructure and regional networks to enable high quality sample collection across all treatment centres in the UK
- creating a relapse registry and being able to link this information to information about the biology of the patient's tumour and the treatment they have received
- lobbying for better access to drugs, by engaging strongly with academia, charities and parents/patients
- developing more novel combination studies and matched therapies for precision medicine in collaboration with academic and commercial partners
- learning from other rare metabolic diseases – could we replicate the systematic way they do research?
- building capacity in those trained in genomics

EVIDENCE-BASED MEDICINE

Lead: Pam Kearns, CRUK Clinical Trials Unit - University of Birmingham

A review of the UKCRN trials database and NCRI portfolio maps provide an overview of trials relevant to children and the TYA age group. There are currently 534 clinical studies which are relevant to TYA and 39 for paediatrics, extending from observational studies to experimental medicine trials and randomised phase III trials.

Across the UK, there are 15 cancer CTUs that form the NCRI CTU group, many of which have portfolios that include trials relevant to TYA. The UK is uniquely positioned, in having a CRUK core-funded Clinical Trials Unit for cancer trials designated for delivering the portfolio of trials approved by the NCRI Children’s Cancer and Leukaemia Clinical Studies Group. The CRCTU’s current trial portfolio for children and teenagers includes 12 trials open to recruitment (9 late phase/3 early phase), 11 trials in set up (7 late phase/4 early phase) and 1 programme of systematic reviews in CNS tumours evaluating the evidence base for their currently available treatment modalities.

In spite of this apparent wealth of clinical research activity, there remain major challenges in ensuring timely delivery of clinical trials and ensuring equitable access across all age groups and all geographic regions. Trials for cancers affecting children and TYA frequently target small patient populations due to the rarity of individual cancer types or stratified sub-groups. Investment in novel ways of reducing trial development times, increasing access and recruitment and building the capacity of trialists and infrastructure will help to improve outcomes for children and young people with cancer.
The opportunities identified include:

- Carrying out systematic reviews to rigorously evaluate the research evidence we have to inform clinical care and identify areas where more evidence is needed
- Facilitating the community consulting, collaborating and moving forward on areas such as:
  - Identifying research gaps
  - Prioritisation of research questions to be addressed in clinical trials
  - Designing trials more innovatively to answer research questions efficiently
  - Build the clinical trials infrastructure and capacity to enable efficient trial development, set up and delivery
  - Increase patient involvement in trial design to improve trial feasibility and inform the acceptability of more innovative trial designs
  - Increasing recruitment to trials – especially exploring why TYA are under-represented in trials compared with children; for example by opening more ‘TYA appropriate’ centres and establishing best practice to help recruitment and support families
  - to continue developing new treatments that are kinder, with lower toxicity as well as being more effective
  - to embed biology into clinical trials to inform the development and best use of novel treatments
  - building capacity in the workforce by developing the clinical trialists and leaders of the future (e.g. through training programmes for early career researchers with a strong mentoring component)

**SURGERY**

*Lead: Paul Losty, University of Liverpool*

The important role of surgery in the treatment of many cancers in childhood and teenagers was acknowledged. Facilitating greater engagement of paediatric oncology surgeons in clinical research will stimulate new ideas towards creating surgically led clinical trials research addressing important surgical questions pertinent to cancer in these age groups and promoting translational research to improve childhood cancer.

The opportunities identified include:

- collating information to understand current barriers to surgically-led clinical research
- developing and promoting opportunities that would attract more surgeons to participate in research; for example through fellowships with protected time for research activities
- improving pathways that enable collection of robust data on surgical outcomes to help inform current clinical care and inform the development of future surgical research questions
- engaging the surgical community to develop guidance and best practice on how to design surgery trials (e.g. standards, ethics, surgical trial methodology)

**RADIOThERAPY**

*Lead: Mark Gaze, University College London*

With technical advances in radiotherapy we should be able to improve cure rates and diminish late effects, however, further research is needed to ensure there is an evidence base to support this. The opportunities identified include:

- predicting radio-sensitivity in patients to enable safe and effective dose escalation
- collecting high quality data from patients who are on and not on clinical trials
robust evaluation of new technologies via randomised controlled trials and other studies
optimisation of radiotherapy in individual cancer types, regardless of the technology used, by attempting to answer uncertainties through randomised clinical trials and other studies
making best use of emerging diagnostic imaging to refine the use of radiotherapy
establishing international consistency and best practice in radiotherapy quality assurance across tumour types – consideration also needs to be given as to how to resource this appropriately

**DATA**

**Lead: Martin McCabe, University of Manchester**

High quality clinically relevant population-based data has the potential to transform research and improve outcomes for children and young people with cancer. A cohesive focus on improving collection of high quality data for research purposes that is cost effective and accurate was identified as a key opportunity. This will require:

- the clinical and research communities working together to determine what data items should be routinely collected and in what formats
- the collection of high quality baseline clinical data
- enabling of two-way flow of data between clinical care and research (e.g. linking NHS records with molecular information (prognostic and diagnostic data) and consideration of how to react to novel data – translate new data into benefits for patients)
- collection of follow-up data for all patients at all stages of their cancer journey, especially primary treatment
- ensuring high data quality across the age spectrum from infancy to young adulthood
- lobbying for policy change around access to data, and determine the role of patient advocates
- development of new research methodologies to enable long term studies (e.g. approaches to consent for studies that will take place over a long time period and may involve multiple interactions with research participants, designing novel population-based outcome studies involving biomarkers and developing predictive measures of survival)

**LONG-TERM CONSEQUENCES OF TREATMENT**

**Lead: Helen Jenkinson, Birmingham Children’s Hospital NHS Foundation Trust**

We need to improve our understanding of long term impact of cancer therapy on the physical and psychological well being of the patient. We need to better understand the individual genetic mechanisms that lead to, or protect from, treatment toxicity. The opportunities identified include:

- collecting high quality outcomes data on childhood and TYA cancer patients over the long term and thinking about mechanism for achieving this (e.g. role of GPs, use of social media, etc)
- the community collaborating to identify priority areas for research studies, suggestions included:
  - second malignancies
  - psychological and patient factors
  - late mortality and the role of:
    - disordered immune function
    - cellular senescence and its effect on premature aging and frailty
    - disorders of glucose metabolism and cardiovascular health
- developing novel cost effective ways to enable long-term survivorship studies – this would include how to create a UK survivorship platform to enable this and how to engage with research participants over the long term (e.g. use of social media, etc)
SUMMARY AND NEXT STEPS

The workshop provided an opportunity for a wide variety of stakeholders to come together to discuss new ideas and identify areas in which groups may collaborate to develop research proposals. Some of the areas identified are not research questions per se, but are key components of the broader landscape that will be required to enable research to be delivered. These include areas such as infrastructure to support high quality longitudinal data collection and the adoption and roll out of new technologies in the NHS (e.g. molecular diagnostics).

We will drive forward the vision to improve survival for children, teenagers and young adults via a number of routes: through supporting the best research, through new funding mechanisms and through our policy activity. In terms of policy for example, considerable progress has been made in tobacco control, including legislation to ban smoking in cars carrying children and to introduce standardised packaging for cigarettes.

We will continue to lobby government, carry out policy activities and support interventions that support children and young people having healthier life styles. The independent Cancer Taskforce, chaired by Harpal Kumar, have published a strategy for 2015-2020¹, which recommends a "strong focus on children" for research into interventions to improve awareness, encourage healthy behaviours and improvements in cancer treatment and long-term effects.

In September 2015, CRUK held an Innovation Workshop on Cancer Prevention in Early Years, bringing together a multidisciplinary group to brainstorm novel approaches to tackling cancer prevention in children and young adults. Four exciting new feasibility projects were funded across a range of topics including obesity, physical activity and human papilloma virus vaccination.

CRUK provides a number of response mode funding streams that support research across the spectrum from laboratory based science through to clinical and population studies. More information about these funding streams can be found here. Importantly, CRUK also provide a number of schemes to support researchers at different stages in their career. All of these schemes would welcome research proposals in the area of childhood, teenage and young adult cancers and CRUK staff would be happy to provide further advice and guidance on the types of awards that are available. We actively encourage the community to come together, via NCRI Clinical Study Groups and other appropriate fora, to develop high quality proposals for submission. CRUK will continue to work with other organisations in this space and are also exploring ways to work together more broadly.