GIVING MORE YOUNG PEOPLE WITH CANCER THE OPPORTUNITY TO TAKE PART IN CLINICAL TRIALS

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SUMMARY

Teenage Cancer Trust believes that if we all work together, from patients and their families, to clinicians to regulators, pharmaceutical industry and those funding and conducting research, more teenagers and young adults with cancer would have the opportunity to take part in clinical trials.

We’ve spent time talking to patients, parents, doctors, regulators, funders of research, the pharmaceutical industry and MPs. We thank everyone involved for taking the time to discuss the issues and for their constructive input which has led to the production of this paper. The aim of this paper is to put down the issues as we now understand them in one place; this is not to exert any ownership on this issue but is to support a constructive discussion and realise improvements for young people with cancer and their families.

Clinical trials are conducted to explore the safety, efficacy and benefit/risk of new cancer treatments. With more research and trials we build up the evidence base so that we can be sure of the benefits of new medicines and understand the risks. And we need to do this in a way that is focused on the best interest of those young people with cancer.

Improved access to clinical trials is a direct way to improve patient experience, outcomes and ultimately survival for teenagers and young adults with cancer now and in the future. Yet we know that young people with cancer have very low levels of participation in trials, latest figures show only around 30% of teenagers aged 15-19 and 14% of young people aged 20-24 enter trials for common cancer types in children and young people compared with 50-70% of children.

Through our discussions we have heard about barriers in the system that need to change:

- Stop the practice of applying arbitrary age restrictions to trials that exclude young people
- Stop waivers to regulation that exclude young people without scientific justification
- Create long-term flexibility to allow access to young cancer patients moving between children’s and adult services
- Increase investment in research into the rarer cancers found in teenage and young adult patients
- Speed up research and trials whilst not sacrificing focus on safety and the balance of benefit to risk
- Facilitate European and International cooperation so trials can attract the numbers needed
- Improve communication about trials so young people can make informed choices

We believe now is the time for action, and that the UK is in the best position to lead the way for improved access to clinical trials for young people with cancer who have the rest of their lives to benefit from these treatments.

The success of the UK’s life sciences strategy in recent years has put us centre stage for research. We believe the actions outlined in this paper will build on our strong reputation and directly improve the lives of young people with cancer. Some of these are really small changes, changes that could be done in moments, like adding links to the UK clinical trials gateway or the National Cancer Research Institute’s trials maps, and Cancer Research UK’s ‘Cancer Help’ pages which list trials in cancer, to patient organisation’s websites. Others will take longer, but many of them simply build on what is already in ‘the system’.
INTRODUCTION

Lack of access to clinical trials is an issue that Teenage Cancer Trust has been aware of for some time. Whilst there have been improvements over recent years, we continue to hear from young people and their families about experiences where they have been excluded from trials.

Recently these issues have been publicly highlighted by Chloe Drury and her mother, Debbie Binner. Chloe was excluded from a trial because of her age, and since then Debbie has challenged the systems that created and allowed this exclusion.

Teenage Cancer Trust is the only UK charity dedicated to improving the quality of life and chances of survival for young people with cancer aged between 13 and 24. We fund and build specialist units within NHS hospitals and educate young people about cancer, empowering them to take control of their health. We want to make sure every young person with cancer has access to the best possible care and professional support.

As Chloe and Debbie, and many other young people and families know, getting access to new treatments and protocols designed for cancer in young people is the most direct way to improve the future survival for young people with cancer. We have seen this with improvements in survival where new treatments have been developed, and conversely the lack of improvements where they haven't been developed:

- Leukaemia survival rates, whilst still low, have improved by 15% over the last 30 years \(^1\)
- A children's clinical trial for Acute Lymphoblastic Leukaemia (ALL) which was adapted to include patients up to 24 showed a 25% increase in 5 year survival \(^2\)
- Historically, accrual rates are particularly low in bone cancers and Central Nervous System (CNS) tumours \(^3\) which are also the two types of cancer where five year survival rates have the biggest proportional impact on 5 year survival for teenagers and young adults with cancer \(^4\)

The Rt Hon Paul Burstow MP, Debbie Binner’s local MP, raised these concerns at the highest level of Government. Paul wrote several times to the Parliamentary Under-Secretary of State for Health to obtain clarification on policy around access to clinical trials for young people with cancer. He went on to host two parliamentary summit meetings, in July 2013 and a follow up summit in January 2014. These meetings brought together the experts and those leading change in one place to discuss the issues and find solutions.

This paper is the result of those summit meetings and discussions with young people, parents, patient representatives and experts from across the spectrum of those involved in clinical trials. It is not a technical paper but for those interested to find out more about the issues we touch on please consult the references. It is also not a systematic review of the evidence, instead we have drawn on the publications that we were made aware of, key publications used by experts in their presentations for the summit meetings and those highlighted to us through discussion with them.

We thank everyone involved for taking the time to discuss the issues and for their constructive input, but their involvement does not imply their personal or organisational endorsement of the recommendations we make.

We know that clinical trials for young people with cancer are part of a much larger landscape of research and development, regulation, reimbursement and adoption of medicines, but we focus on the issues as we see them for young people with cancer. It also sets out what we are asking people to do, whether they work in a cancer unit, a regulator’s office, or in a pharmaceutical company, to give more young people with cancer the opportunity to take part in clinical trials now, and more research and clinical trials in the future.
Clinical trials are one part of the development process for new medicines. There are different phases of cancer trials for patients; from early phase trials (Phase I) which only provide an initial view, to Phase II trials where drug activity is evaluated and Phase III where a new treatment is tested against an existing standard of care and efficacy is measured. Increasingly an early phase trial will encompass Phase I and II elements.

Conducting clinical research takes years, and it can take around 12.5 years to bring a new medication from initial development to the regulators for them to consider the safety, efficacy and overall benefit/risk of a new treatment and decide whether to license the new medicine for wider use with patients or not. An overview is provided in figure 1. In many UK centres treating teenagers and young adults with cancer, participation in a clinical trial is seen as part of standard treatment.

Many new treatments will be investigated first in adults before being investigated for younger age groups, in order to explore safety before children and teenagers are exposed to the new treatment. This allows regulatory authorities to make evidence based decisions on the impact and safety of new treatments and allows clinicians to make informed choices about their effectiveness versus standards of care. Experts have also highlighted that sometimes we need flexibility; for example prescribing outside of trials.

The history of medicines regulation begins from tragedies such as the use of Thalidomide, so regulation is driven by a need to protect the public. An underlying requirement of clinical research, whether conducted by commercial or academic organisations, is to generate robust data; this informs decisions on the benefit/risk of a new medicine made by regulators at a population level and later, by clinicians at an individual level. Regulation is not static, and experts tell us that the regulators are open to discussions about accelerating approvals safely.

### FIGURE 1: OVERVIEW OF CLINICAL RESEARCH TO BRING A NEW MEDICINE TO LICENSING

<table>
<thead>
<tr>
<th>4.5 years</th>
<th>5.5 years</th>
<th>7 years</th>
<th>8.5 years</th>
<th>11 years</th>
<th>12.5 years</th>
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<tr>
<td>Pre Discovery</td>
<td>Drug Discovery</td>
<td>Pre-clinical testing</td>
<td>Phase I clinical trials</td>
<td>Phase II clinical trial</td>
<td>Phase III clinical trial</td>
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<tr>
<td>Scientists work to understand the disease</td>
<td>Target molecules are identified to target disease</td>
<td>Safety &amp; efficacy explored in computer models and animals</td>
<td>20-100 volunteers - for cancer trials these are cancer patients</td>
<td>Safety &amp; efficacy explored in 100 to 500 patients with the disease</td>
<td>Safety, efficacy and benefit/risk explored in 1,000 to 5,000 patients</td>
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The UK has an impressive record for research in the life sciences and was recently crowned the cancer clinical trials capital of the world. There have been efforts to maintain a focus on life sciences research, including basic research and clinical trials. Efforts have also included both rare diseases and cancer (and the two overlap – there are many cancers that are less common such as those in young people). Figure 2 below provides an overview of some of the key initiatives over recent years at the UK level. It also sets out recent events at the European level too – because improving research and clinical trials in teenage and young adult cancers is not just a national issue but also a European, and even global, one too.
Figure 2 highlights the complex landscape for research and clinical trials and also the efforts being made to improve the landscape: from encouraging patients and families to ask about current research in the Ok to Ask Campaign, to efforts to improve regulation in new Clinical Trials Regulation at the European level. There are also novel approaches that explore safety and efficacy of new treatments that may be faster.

Cancer patients have benefited from research and clinical trials of new cancer treatments. Survival rates are increasing for many cancer types, with five-year survival rates now over 80% for cancers of the breast, prostate and testis.9 Young people with cancer have seen improvements too: since the mid-1970s the death rate from teenage and young adult cancer in the UK has halved and now more than 80% of teenagers and young adults diagnosed with cancer in the UK survive for at least 5 years.10 However, this statistic hides significant variation in survival between different types of cancers found in teenagers and young adults. Survival rates are important, however, they do not tell us how young people are living and so we must also continue to develop therapies which improve quality of life without compromising survival.

The UK’s research landscape is considered to be impressive within the European Union, particularly recruitment to children’s cancer trials. So the starting point for our work is to build on the successes to date and ask everyone to keep up the effort especially for teenagers and young adults, who have their whole lives ahead of them to benefit from better treatments.

**FIGURE 2: KEY INITIATIVES ON RESEARCH AND CLINICAL TRIALS IN THE UK AND EUROPE, 2011 – 2014**

Sources: See appendix 1

- UK STRATEGY FOR LIFE SCIENCES - £130m for stratified medicine
- Web based UK Clinical Trials Gateway
- Patients to be approached about research studies

- UK LIFE STRATEGY FOR LIFE SCIENCES - PROGRESS
  - DNA mapping for cancer patients & those with rare diseases

- SELECT COMMITTEE INQUIRY INTO CLINICAL TRIALS
  - Interest in barriers to conducting clinical trials in UK and Europe

- EXPERIMENTAL CANCER MEDICINE NETWORK
  - Launched Teenagers and Young Adults Strategy

- UK STRATEGY FOR RARE DISEASES
  - Covers the role of research including:
    - Health Research Authority to continue efforts to streamline research
    - Coordination of research through work of Office for Strategic Coordination of Health Research

- OK TO ASK CAMPAIGN
  - To encourage patients/families to ask about research

- EUCLINICAL TRIALS GATEWAY LAUNCHED
  - A resource on UK trials

- UK STRATEGY FOR RARE DISEASES
  - Covers the role of research including:
    - Health Research Authority to continue efforts to streamline research
    - Coordination of research through work of Office for Strategic Coordination of Health Research

- SELECT COMMITTEE INQUIRY INTO CLINICAL TRIALS REPORTED
  - Biggest barrier to trials in the UK are the numerous governance approvals

- OK TO ASK CAMPAIGN
  - To encourage patients/families to ask about research

- HEALTH RESEARCH AUTHORITY ASSESSMENT AND APPROVAL
  - Single approval alongside Research Ethics Committee opinion

- EARLY ACCESS TO MEDICINES SCHEME AT THE MEDICAL AND HEALTHCARE REGULATORY PRODUCTS AGENCY
  - Companies can apply for Promising Innovation Medicine Designation and Early Access to Medicine Designation before formal licensing

- NICE STANDARDS ON CARE FOR CHILDREN AND YOUNG PEOPLE WITH CANCER
  - All children and young people should have the opportunity to take part in relevant clinical trials

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We want the future to be even brighter for teenagers and young adults with cancer. That means:

- More opportunities to take part in clinical trials now
- More research and clinical trials in the future
WHY DO YOUNG PEOPLE WITH CANCER NEED MORE OPPORTUNITIES TO TAKE PART IN CLINICAL TRIALS?

Every day in the UK, around seven young people aged between 13 and 24 are diagnosed with cancer. Overall though, cancer is relatively rare in teenagers and young adults: cancers in these age groups account for less than 1% of cancers at all ages. The impact of a cancer can be devastating, with cancer being the most common cause of death by disease in teenagers and young adults.

The type of cancers seen in teenagers and young adults tend to be different to the cancers seen in children and adults, as shown in figures 3 and 4, although there are still cases of cancer that are often seen as ‘adult’ such as bowel cancer.

**Figure 3: The Five Most Commonly Diagnosed Cancers in Females – Average Percentages and Numbers of New Cases, by Age, UK, 2009-2011**

**Figure 4: The Five Most Commonly Diagnosed Cancers in Males – Average Percentages and Numbers of New Cases, by Age, UK, 2009-2011**

Source: Cancer Research UK, Cancer Incidence by age, [Accessed 13 Apr 2014]
These differences mean that young people need research and clinical trials that are tailored to the cancers that affect them, and they need this urgently.

Many trials exist which are relevant to young people but do not allow them to enter due to restrictive age entry criteria. Chloe’s story (in the box below) demonstrates how age can be used to restrict entry into trials and the impact this can have for young people with cancer and their families. Chloe’s is one experience that illustrates why young people with cancer need more opportunities to access clinical trials. But that one story is supported by the absence of trials in some teenage and young people’s cancers.

**CHLOE’S STORY**

Chloe was diagnosed with Ewing Sarcoma. Her mother, Debbie Binner, tells their story: “Chloe was blocked from entering a clinical trial for a new investigational drug when she was 17 and nine months. The entry criteria for the trial was 18 years. There was no clinical reason why the entry criteria was 18 years. At nine stone, Chloe was an adult weight. The only thing that would change in her body in the time before her 18th birthday was her cancer. At this point we had run out of all other options and we were told this drug ‘may’ work. We kicked, screamed and begged to be allowed on this trial. Doctors agreed we should have been allowed on it, the chief executive of Teenage Cancer Trust intervened personally. Her hospital, The Royal Marsden, wanted Chloe to go on the trial; so did University College London Hospital. But the door remained tightly closed and Chloe was not allowed on. Chloe died. Many other young people with same illness are also dying. We must change things.”

The good news is that there are trials for some teenagers and young adults. Considerable improvements in recruitment to cancer clinical trials for teenagers and young adults have been observed over the past six years in England, Scotland and Wales. There’s been a 13% rise in 15-19 year old cancer patients taking part in clinical trials between 2005 and 2010 (from 24 to 37 per cent), and a five per cent rise in 20-24 year olds (from 13 to 18 per cent) has been noted in cancer types common in young people: leukaemia, lymphoma, male germ cell, brain and central nervous system cancers, bone and soft tissue sarcomas. xiv

The increased recruitment is due to increases in availability and access to trials for young people with cancer, increased awareness of healthcare professionals, patients and the public about research, and importantly the opening of trials with broader age limits that allow older teenagers and young adults to enter trials. xiv

Young cancer patients aged 16-25 in England who had chemotherapy between February and June 2013 were more likely to say that they had been spoken to about taking part in clinical trials than other age-groups (56% of those aged 16-25, see figure 5 below). Even more want to know about research studies, with 68% of teenagers and young adults at Teenage Cancer Trust’s Find Your Sense of Tumour UK Conference in 2013 agreeing that they should be told about all research studies so that they can decide. The decision to participate is facilitated by the delivery of age-appropriate information given by skilled staff.
That means it is inherently feasible to conduct clinical trials for teenage and young adult cancers and information about trials is already being shared with young people. We want to see the participation rates continue to rise substantially in the future. It’s hard to set an exact ‘target’ for clinical trial participation, and we wouldn’t want to, when it is a personal choice for the teenager or young adult to take, with the support of their family and clinical team. But if we could see rates near to those of children, at between 50-70% participation in clinical trials that would be a fantastic achievement.

We also need to increase research activity into teenage and young adult cancers, and correspondingly, we need more clinical trials too. This needs to take account of why young people get cancer, how we can prevent cancer in young people, how we can improve the care of young people, how we can help young people return to as healthy a life as possible after a cancer diagnosis, how we can appropriately classify their tumour, and the potential of genetics, mode of action of new treatments and stratified medicines. This is an exciting and promising area where researchers are exploring which treatments work for which patients in different cancers. 

Dispelling the ‘human guineapig’ fears surrounding clinical trials and providing accurate information to young people empowers them to make informed choices and so is also very important. If we are successful in increasing the number of trials available, we need to make sure that young people are prepared to take part in these studies.

**FIGURE 5: PERCENTAGE OF RESPONDENTS BY AGE WHO HAD BEEN SPOKEN TO ABOUT TAKING PART IN A CLINICAL TRIAL, FEBRUARY TO JUNE 2013**

Source: Data provided by Quality Health from the Chemotherapy Patient Experience Survey 2013
**WHAT DIFFERENCE WILL MORE OPPORTUNITIES FOR YOUNG PEOPLE WITH CANCER TO TAKE PART IN CLINICAL TRIALS MAKE?**

Increasing the opportunities to take part in clinical trials and increasing the level of research and clinical trials in the future, will make a real difference to young people with cancer and their families, and their clinical teams.

**IMPROVED EVIDENCE BASE**

In the near term, it will mean an improved evidence base to inform choice of treatment. It will help clinicians make more informed decisions about dosing and the incidence and nature of side effects as there will be a more robust evidence base than using data from off-label prescribing alone.

**IMPROVED UNDERSTANDING OF CANCER IN YOUNG PEOPLE**

In the medium term, it will open up new avenues to explore the biology of teenage and young adult cancers, and elucidating which treatments might work for different cancers. We can’t know for sure if this will be a small or big change, but we must be open to exploring it. And this has the potential to improve both quality of life for young people with cancer, and their survival.

**IMPROVED ENGAGEMENT**

It will also help individuals and their families make more informed decisions with their clinical team, too. This means young people with cancer have more say over their lives and options.

**IMPROVED SURVIVAL AND QUALITY OF LIFE**

We can show that entering young people into cancer trials designed for them does improve survival, one example is a children’s clinical trial for Acute Lymphoblastic Leukaemia (ALL) adapted to include patients up to 24, showed a 25% increase in 5 year survival.\(^{xvi}\)

**POTENTIAL CHALLENGES**

We can’t ignore the wider pressures on the research environment and on the NHS too, particularly the financial challenges. Recruitment of young people to trials takes time and additional resource in an environment where both are constrained.

But teenagers and young adults have the potential to benefit for the whole of their lives if we can get them the treatments that will manage or cure their cancer. Even better if those treatments are improved and optimised to reduce the impact of side effects that can range from amputation, early menopause and infertility, incontinence, scarring... to name a few.

We also believe that giving more young people opportunities to access clinical trials will support the achievement of good practice and the NHS England Constitution (see box).

<table>
<thead>
<tr>
<th>NICE Quality Standard ‘Children and Young People with Cancer’ (QS55), 2014</th>
<th>The NHS Constitution</th>
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<tr>
<td>This includes Quality Statement 2: Access to clinical trials, stating that: “Children and young people (aged 0–24 years) with cancer should be offered the opportunity to take part in clinical trials if they are eligible”</td>
<td>This includes the NHS commitment to: “inform you of research studies in which you may be eligible to participate”</td>
</tr>
<tr>
<td>The rationale is that involvement in trials has made an important contribution to improved childhood cancer survival rates.</td>
<td>Source: NHS, The NHS Constitution, 2013</td>
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<td>Source: NICE, Quality Standard for Children and Young People with Cancer, 2014</td>
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WHY DON'T TEENAGERS AND YOUNG ADULTS WITH CANCER GET THE SAME OPPORTUNITIES TO ENTER TRIALS AS CHILDREN AND ADULTS DO?

It’s complicated. We’ve been talking to young people with cancer, their families and a range of experts and the reasons that there are fewer clinical trials and fewer opportunities to enter clinical trials for teenage and young adult cancers stem from the interaction of a number of factors:

• **Age restrictions** have traditionally been included in trial protocols. Even if aged 17 years 364 days, if the trial inclusion criteria is set at age 18 then those under 18 cannot participate. This seems to be a convention that has evolved over time; a culture rather than driven by a clinical rationale. Inclusion criteria are needed to help ensure that conclusions can be drawn from trials with confidence, however, there is no scientific rationale for using 18 as a lower age limit and this can be lowered.

• Setting up trials can be more complicated because young people fall between traditional age-based services such as paediatrics and adult services. It can take longer to set up and recruit when multiple clinicians and sites need to be involved in recruitment and participation in trials. It can take extra effort to recruit children when clinicians primarily focus on adults and vice versa.

• There’s a need for appropriate information to inform decisions to take part in trials, provided in an appropriate setting with access to knowledgeable clinicians and specialist research nursing staff who can answer questions that patients and their families may have. There are concerns that when these are not in place that some may choose not to take part, however if the decision not to take part is fully informed then those decisions must always be respected.

The cancers experienced by young people also have features, shared with other diseases that are rare or affect children, which influence the number of clinical trials undertaken:

• The number of teenagers and young adults with each individual cancer can be small and often the cancers found in young people are rare. This means there’s a greater need for international trials to achieve sample sizes where safety, efficacy and quality can be explored meaningfully. That is just harder: more people are inevitably involved including patients, parents, clinicians, research ethics committees and so on. And that also means it costs more and can take more time to set up and run trials.

• Whilst not all research and clinical trials are conducted by the commercial pharmaceutical industry, they play a vital role in researching and developing new medicines. Their commercial set up can mean that there are more profitable targets outside of rare cancers. Rare cancers, which overlap with many teenage and young adult cancers, generally receive less research attention and funding than the more common cancers (although leukaemia research bucks this trend). There are incentives to encourage products that treat rare diseases through European Regulation introduced in 2000.

• When there are no licensed medicines to treat a teenage and young adult cancer, a clinician can take the responsibility of prescribing a medicine licensed for another indication (for example, a medicine licensed to treat the same cancer in an adult). This is known as off label prescribing. This might be an option for that patient and we support clinical freedom to explore this, with appropriate consent. But this off label prescribing means that there is often less evidence (such as dosing, side effects etc) and can also mean that the commercial incentives are lower than they might otherwise be because the medicine is paid for without the need for the developer to obtain a license with the time and expense this incurs. This is why it’s desirable to find ways of increasing the numbers of licensed medicines through clinical trials.

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1 Please also see Orme, LM, Thomas, D and Walker, DA, Adaptation of a conceptual model of barriers and promoters to trials for adolescents and young adults with cancer (AUAC) in Australia, Poster Teenage Cancer Trust Conference 2008 for a fuller discussion of a wider set of issues. Although this is focused on Australia we believe many of the same issues apply here in the UK.
• It can be difficult to achieve the right balance of collaboration and competition in research in the rarer diseases and in rarer cancers as there are commercial interests to consider. It can also be difficult to collaborate across borders but this is increasingly recognised as being needed.\textsuperscript{ix}

• Regulation of clinical research is in place to help balance safety and risk. But that regulation also needs to be balanced: to ensure that it is not stifling research\textsuperscript{x}. Things are changing, as the new European Clinical Trials Regulation has been approved and we now need to work on pragmatic implementation.

• Regulation of new drugs is also in place to help balance safety and risk and there are regulations intended to encourage paediatric trials\textsuperscript{3}. But the intention of the regulations has not been delivered in practice\textsuperscript{xii}. For example, the need for investigation in children has been waived for some new medicines. There have been examples of where this has been the case because of a focus on the disease which may not occur in children, rather than a focus on the mechanism of action which could mean that the new medicine under investigation for an adult cancer could have potential relevance to a different cancer seen in children, teenagers or young adults. Indeed regulators have acknowledged the wider problem of drug development in paediatric oncology\textsuperscript{xii} and actions are currently being considered both at a European and national level.

• European regulations only apply to Europe\textsuperscript{4}. Research and development can start outside of Europe, and that can mean that clinical trial criteria are set before trials start in Europe and the UK.

Participation by young people with cancer is lower than that seen in children, and that may be related to simple practicalities like how to find out about relevant trials even where trials exist, an issue the National Cancer Research Institute is trying to address through developing portfolio maps. Many patients will rely on their oncologist to tell them about trials. We’ve heard that there may not always be a culture of referring patients to other oncologists who are running trials, so sometimes it relies on the young person or their parent proactively trying to find out about trials. That can mean searching on the internet, talking to other patients and parents, and that also means that the information is not necessarily easy to find nor available in a way that is easy to interpret for the individual.

As a result of a lack of proper information and/or preconceived ideas about what clinical trials are, some young people express fear about taking part in research studies. Improving communication about clinical research itself via teenage and young adult cancer specialist staff on our units, via websites and other social media, as well as ensuring patients are routinely made aware of individual studies that may benefit them is an immediate priority.

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\textsuperscript{2} The number of clinical trials conducted in Europe between 2007 to 2011 fell by 25%. Source: European Commission, Fostering EU’s attractiveness in clinical research: Commission proposes to revamp rules on trials with medicines, 17th July 2012

\textsuperscript{3} Since 2007, those developing new medicines have to submit a Paediatric Investigation Plan (PIP). The aim is to ensure that new medicines with potential benefit for young people include a trial for them. Where a marketing authorisation application includes the results of all studies conducted in compliance with an agreed paediatric investigation plan, the holder of the patent or supplementary protection certificate is entitled to a six-month extension. There is also provision for a one-year extension of the period of marketing protection for a medicinal product, on the grounds that a new paediatric indication brings a significant clinical benefit in comparison with existing therapies. Sources: European Medicines Agency, Paediatric Regulation and MHRA, Report of the Expert Group on innovation in the regulation of healthcare, September 2013

\textsuperscript{4} For example, the National Cancer Research Institute (NCRI) analysis of the International Cancer Research Partnership (ICRP) data set found that of a total of US$3.1 billion of research spend in 2008, US$163.5 million (3.2%) had an identifiable association with children’s cancer. Of this US$163.5 million, 2/3rds was from funders in the USA. Source: NCRI, Funding of children’s cancer research, 2008 data from the International Cancer Research Partnership Portfolio, January 2014
WE’RE NOT ALONE IN BELIEVING THAT THERE IS A PROBLEM

Cancer Research UK say:

“Survival is significantly lower in teenagers and young adults (TYAs) than in children for several cancer types. Factors relating to diagnosis, different treatment protocols and low levels of participation in clinical trials may explain some of the differences.”

Professor Kathy Pritchard-Jones from the UCL Institute of Child Health (ICH) says:

“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.”

And positive changes are already happening.

**Cancer Research UK funding applications – challenging arbitrary age restrictions**

Since June 2013, CRUK’s Cancer Clinical Trials Awards and Advisory Committee now asks for the specific justification for both upper and lower age limits.

Their funding applications also state that: **“Please note that if a lower age limit for studies involving adults is deemed essential it should normally be set at 16 rather than 18 years. Low incidence of patients aged 16 and 17 is not sufficient reason alone for selecting a lower age criterion of 18 years.”**

This reflects the consensus that there is no good scientific, ethical, regulatory or consent reasons for any trial to have a lower age limit of 18.

**National Cancer Research Institute (NCRI) Teenage and Young Adult Clinical Studies Group (TYA CSG) proposed a checkpoint system – encouraging investigators to question age restrictions and consider value in teenage and young adult cancers.**

The NCRI TYA CSG suggest that investigators in trials consider two checkpoints. The first checks whether age eligibility criteria are needed, the second prompts consideration of whether the agent could be valuable in a teenage and young adult priority cancer such as bone or soft tissue sarcoma.

**Health Research Authority Assessment and Approval – streamlining approvals and speeding up research set up times.**

This will provide a single approval for research in the NHS alongside the independent Research Ethics Committee opinion. This will mean that decisions at the local site will be made on local capacity and capability alone. This will provide “authoritative assurance to NHS organisations about the suitability, compliance and quality of research proposals”.

This will be rolled out over time, with completion expected by the end of 2015.
**WHAT CAN WE DO NOW TO GIVE YOUNG PEOPLE WITH CANCER MORE OPPORTUNITIES TO TAKE PART IN CLINICAL TRIALS?**

We believe there’s a lot that we can do, which builds on recent initiatives, such as the NICE Quality Standard and National Cancer Research Institute TYA CSG initiatives. We would like the following groups to:

Table 1: Actions needed by stakeholder group to increase and improve access to clinical trials for young people with cancer.

| European Commission | • Start planning now to monitor the impact of changes to the Clinical Trials Regulation on the number of clinical trials undertaken in Europe  
|                     | • Modify the implementation of the European Paediatric Medicine Regulation so that drug companies are not granted a waiver when a drug is registered for an adult cancer that does not occur in children or young people |
| UK Government       | • Provide funding to support implementation of data collection around clinical trial access for young people with cancer  
|                     | • Work to ensure pragmatic UK implementation of the European Clinical Trials Regulation  
|                     | • Explore scope for a single Scientific Review Board for trials across Europe to facilitate synchronised national funding approval in participating member states  
|                     | • Encourage new and innovative trial designs that are safe and have potential to speed up drug developments |
| Funders of research | • Challenge arbitrary age restrictions – just as we have seen already with Cancer Research UK  
|                     | • Encourage new and innovative trial designs that are safe and have potential to speed up drug developments |
| Pharmaceutical companies | • Demonstrate their commitment to tackling diseases that affect teenagers and young adults and cease using arbitrary age restrictions. Instead, companies should adopt National Cancer Research Institute TYA CSG checkpoints  
|                     | • Take part in the pilot for Adaptive Licensing from the European Medicines Agency, contributing to developing novel approaches to inform licensing decisions and the Early Access to Medicines Scheme (EAMS) from the Medicines and Healthcare Products Regulatory Agency (MHRA)  
|                     | • Encourage new and innovative trial designs that are safe and have potential to speed up drug developments |
| Regulators          | • Build on changes underway to make the system more flexible, whilst maintaining the focus on an acceptable balance of benefit/risk  
|                     | • Continue to encourage and request, where appropriate, a broader age range of clinical trials exploring new treatment for treating the cancers experienced by teenagers and young adults |
| **Ethics Committees** | • Reflect on the real life context for teenagers and young adults when making decisions about participation in clinical trials when considering applications  
• Reviewers of protocols should ask researchers and investigators to justify any age restrictions |
| **NHS** | • NHS England and Wales should set out a baseline of how many young people aged 16-25 are asked about taking part in a clinical trial, and monitor whether this improves over time  
• NHS England should incorporate recruitment into clinical trials into quality metrics for teenage and young adult cancer services and explore how recruitment into clinical trials can be incorporated into clinicians’ peer review  
• NHS Wales should review their current targets for clinical trials access (currently 10% across all ages) and publish data on participation by age  
• NHS Wales should actively promote and report on the National Standard for Teenagers and Young Adults with cancer which stipulates that all patients should have the opportunity to join trials  
• NHS Scotland should ensure the Cancer Champion’s remit includes improved access to clinical trials by this age group, and expand their Cancer Quality Performance Indicator on clinical trials to publish access by age  
• NHS Northern Ireland should ensure there is a ambitious target for improving clinical trials for young people with cancer in their Service Framework for Cancer, Prevention, Treatment and Care  
• Individual NHS Trusts/Boards should make quick progress in implementing and auditing the NICE Quality Standard for Children and Young People with Cancer |
| **National Institute for Health Research Cancer Network** | • Establish a central source for collecting the ages of patients recruited to all portfolio studies  
• Encourage research staff to approach young people about research  
• Develop support to train staff in consenting young people to research  
• Ensure equality in distribution of resources across common and rarer cancers |
| **National Cancer Research Institute** | • Encourage funding partners to ask investigators to justify age related restrictions on trials  
• Encourage relevant Clinical Studies Groups to consider young people in the development of their research studies  
• Encourage relevant Clinical Studies Groups to ensure young people are given the opportunity to enter studies within their portfolio |
| **Clinicians** | • Refer teenagers and young adults with cancer to Teenage Cancer Trust units wherever this is possible and is agreed with the teenagers and young adults and their families  
• Ensure that they are up to date with the NICE Quality Standard for Children and Young People with Cancer and inform teenagers and young adults and their families about appropriate trials |
**Multi-disciplinary teams (MDT)**

- Clinicians and research nursing staff should discuss patient eligibility for ongoing trials at local MDT and then take time to discuss studies with patients to enable them to make fully informed choices whether to participate in a clinical trial.

**Patient groups**

- Patient groups, just like ourselves, should raise awareness of clinical trials in teenage and young adult cancers by:
  - hosting a link to the UK Clinical Trials Gateway on our webpages
  - hosting a link to CRUK’s Cancer Help which includes details of trials ongoing in the UK
  - hosting a link to the NCRI CSG trial map
- All resources that are available on the trials ongoing in the UK should provide clearly the age criteria.

**Young people with cancer and their families**

- Where it is appropriate, ask the clinical team if there are relevant clinical trials ongoing.

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**WHAT WILL WE NEED TO DO IN THE FUTURE?**

We know that there are many initiatives ongoing that could help provide more opportunities for teenagers and young adults to access clinical trials, and many will also need time to bed down. Together, they may help make a difference.

We are also aware that there are broader changes happening; from the expansion in knowledge about genetics and the links to disease to different models for research and development, and initiatives such as Open-Lab supported by Glaxo-Smith-Kline and the Structural Genomics Consortium. We, as will many, have an interest in these and we hope to continue our discussions with experts to find out about the opportunities that these may bring for teenagers and young people with cancer.

We want to see these issues discussed at a UK, European and International level and will do all we can to help promote debate and influence changes to practice. By bringing together experts to agree on the key actions for all the stakeholders involved we hope this has helped all those stakeholders consider this issue further, and we will continue to work with the NCRI and others to track improvements to clinical trial access for young people with cancer.
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You can find out more about Teenage Cancer Trust from our website: www.teenagecancertrust.org
APPENDIX 1: LIST OF SOURCES FOR FIGURE 2

- Academy of Medical Sciences, A new pathway for the regulation and governance of health research, 2011
- Commons Select Committee, Committee to inquire into clinical trials and disclosure of data, 13 December 2012
- Department for Business, Innovation & Skills, Office for Life Sciences, Strategy for UK Life Sciences, 2011
- Department for Business, Innovation & Skills, Office for Life Sciences, Life Sciences Strategy: One Year On, 2012
- Department of Health, The UK Strategy for Rare Diseases, 2013
- Department of Health, Government Response to the House of Commons Science and Technology Inquiry into Clinical Trials, 2013
- MHRA, Revision of the Clinical Trials Regulation, Available at url: www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Legislation/RevisionoftheClinicalTrialsLegislation/index.htm
- Science and Technology Committee, Clinical trials: summary, 2013
- EUROPA Press Release: Statement by Health Commissioner Tonio Borg following the vote in Parliament on the Clinical Trials Regulation, 2 April 2014
- European Commission, Better, faster treatment for children with cancer, 1 February 2014
- National Institute for Health and Care Excellence Press release, NICE publishes new standards to improve care and young people with cancer, 26 February 2014
- Health Research Authority, HRA Assessment and Approval, Available at url: www.hra.nhs.uk/about-the-hra/our-plans-and-projects/assessment-approval
REFERENCES

i  Cancer Research UK ‘Teenage and Young Adult Cancer Stats report’, March 2013

ii  Hough, R ‘Outcomes of Teenagers and Young Adults on the UKALL 2003 Paediatric Trial for Children and Young People with Acute Lymphoblastic Leukaemia’, 2003

iii  Whelan. J. and Fern, L. Poor rates of accrual of teenagers and young adults into clinical trials in the UK, Lancet Oncology 2008; 9 (4), 306-307

iv  O’Hara, C, Moran, A ‘Survival in Teenagers and Young Adults with Cancer – a comparative report comparing TYA cancer survival with that of children aged 0 to 14 years and adults aged 25 to 49 years and looking at difference in survival by gender’ 2012

v  Rago, L and Santoso, Chapter 6: Regulation: History, Present and Future, Undated

vi  HM Government, Investing in UK Health and Life Sciences, 2011


ix  Cancer Research UK, Teenage & Young Adult Cancer: Cancer Statistics Key Facts, January 2014

x  Teenage Cancer Trust, Facts and statistics

xi  Cancer Research UK, Teenage & Young Adult Cancer: Cancer Statistics Key Facts, January 2014

xii  Cancer Research UK, Teenage & Young Adult Cancer: Cancer Statistics Key Facts, January 2014

xiii  Fern LA., Lewandowski J., Coxon K., Whelan J.S. Available, accessible, aware, appropriate, and acceptable: a strategy to improve participation of teenagers and young adults in cancer trials. Lancet Oncology2014 (15) 8, e341 - e350

xiv  Fern LA., Lewandowski J., Coxon K., Whelan J.S. Available, accessible, aware, appropriate, and acceptable: a strategy to improve participation of teenagers and young adults in cancer trials. Lancet Oncology 2014 (15) 8, e341 - e350

Hough, R 'Outcomes of Teenagers and Young Adults on the UKALL 2003 Paediatric Trial for Children and Young People with Acute Lymphoblastic Leukaemia', 2003

National Cancer Research Institute, Cancer Research Spend in the UK 2002-2011: An overview of the research funded by NCRI Partners, 2013


Asselin, BL, Gaynon, P and Whitlock, JA. Recent advances in acute lymphoblastic leukaemia in children and adolescents: An expert panel discussion, Current opinion in Oncology, 2013 (25) 3

European Commission, Q&A: New rules for clinical trials conducted in the EU, 2nd April 2014


Cancer Research UK, Teenage & Young Adult Cancer: Mortality Statistics, February 2014

Great Ormond Street Hospital for Children, NHS Foundation Trust, Press Release: ICH research highlights unmet needs of children and young people with cancer and challenges public policy, 20 February 2013

National Cancer Research Institute, NCRI Teenage & Young Adult Clinical Studies Group, Annual Report 2012/13

Health Research Authority, HRA Assessment and Approval, Available at url: www.hra.nhs.uk/about-the-hra/our-plans-and-projects/assessment-approval


Tres Cantos Open Lab Foundation, available at url: www.openlabfoundation.org
