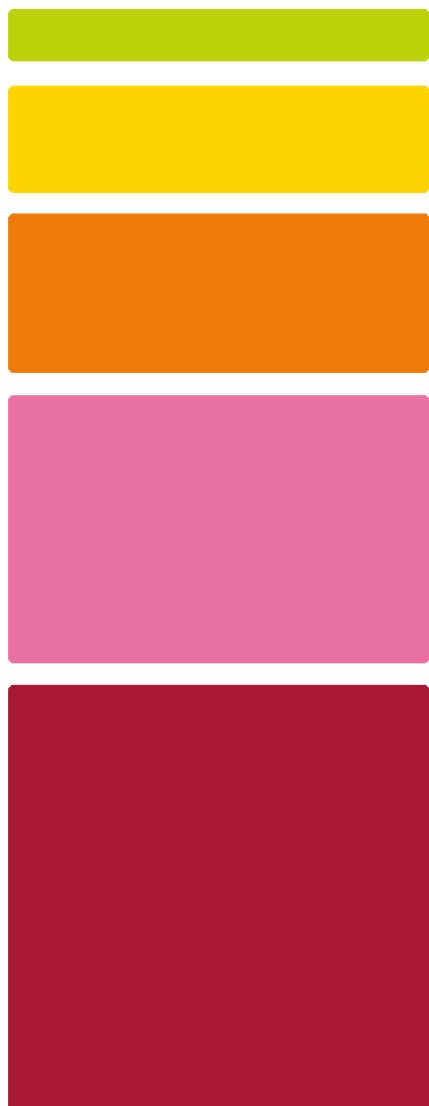

Clinical trials in cancer

Barriers in access to clinical trials, especially
in light of the Covid-19 pandemic

December 2021



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1 Introduction

The Institute of Cancer Research, London, is one of the world’s leading cancer research organisations, and is globally recognised for its work in discovering and developing new cancer treatments.

The Institute of Cancer Research (ICR) is committed as part of its mission to ensuring the results of cancer research benefit patients as quickly as possible through policy and regulatory change, including by enhancing access to high-quality clinical trials.

The ICR is concerned that barriers exist in making clinical trials of novel treatments available to as many NHS patients as possible. These issues have been exacerbated by the Covid-19 pandemic, during which many clinical research studies have been paused. However, the pandemic also stimulated innovation and opened up new ways of working which we can learn from in enhancing the systems in place for making clinical trials available for patients.

We wanted to understand the perspectives of both cancer patients and clinical researchers on the challenges in making clinical trials as widely available as possible and accelerating

the development of new treatments. In addition, we have worked with the National Institute for Health Research to collate data on the impact of the pandemic on provision of trials for cancer patients.

This briefing report summarises:

- Work commissioned by the ICR to understand the perceived barriers to expanding access to clinical trials in cancer from the perspectives of Principal Investigators and Chief Investigators.
- Work commissioned by the ICR to understand the views of cancer patients on clinical trials.
- Data from the National Institute for Health Research (NIHR), which show the impact of the pandemic on recruitment to clinical trials in cancer in England.
- Finally, we offer some recommendations for action.

Key messages

- The ICR has a vision that a suitable clinical trial should be available for every cancer patient who wants to be included in one with a particular focus on underserved groups and patients with cancers of unmet need.
- Many patients are currently missing out on being part of clinical trials even though they are typically very positive about taking part in them.
- A range of factors impede wider access to clinical trials for cancer research and treatment. We have identified barriers at all stages in the process, from initiating and setting up clinical trials through to the recruitment of suitable patients.
- Access to trials has been damaged by the pandemic. Recruitment into clinical trials for cancer in England **fell by 59% in 2020/21**, to 27,734 for the financial year 2020-21 compared with an average of 67,057 over the three years previously.



2 Barriers to participation in cancer research

Picker Institute Europe, October 2020

Clinical trial researchers across the UK shared their views on the barriers to expanding access to clinical trials of innovative new cancer treatments.

Purpose

Picker is a leading international healthcare charity that carries out research to understand individuals' needs and their experiences of care.¹ The ICR commissioned Picker to conduct qualitative research among clinical trial researchers to understand their views on the barriers to expanding access to clinical trials of innovative new cancer treatments.

Method

Between April and July 2020, two researchers from Picker conducted 12 semi-structured interviews by video conference to explore the views of Clinical and Principal Investigators on a range of potential barriers that might be limiting the pace and accessibility of clinical trials. Participants were from across the UK, and included people who worked in a range of cancer specialties and across different phases of clinical trials. Some participants worked solely in academia, others worked across both academic and commercially sponsored trials.

Key findings:

- There was strong support for the view that participation in clinical trials should be made available to as many cancer patients as possible and an ambition to see access expanded beyond its current level.
- Interviewees identified a range of factors that they felt impeded or prevented wider access to clinical trials for cancer patients. Barriers were identified at all stages, from the initiation and set-up of clinical trials through to the recruitment of suitable patients. There were widespread concerns over the resourcing for clinical research.
- Interviewees expressed specific concerns over the design and set-up of biomarker-driven clinical trials, which are essential for developing modern precision medicines.



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I honestly think that there should be a trial for every single patient, and that's what we should be aiming for.

2.1

Barriers to trial initiation

Interviewees felt the processes for setting up clinical trials presented a barrier to widening access:

- Trial initiation can be a slow process, with trials commonly taking one to two years to open.
- The administrative burden of sourcing funding, securing sponsorship and opening a new trial is very heavy, and some feel this burden is increasing.

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The amount of regulatory hurdles you have to go through is huge, it's slow, it's not particularly efficient. I know people have tried speeding it up in the past in order to get things done in parallel, but it's still very hard from the point of a study concept to get patients in under two years I think. It's a pretty slow process.

- The move towards precision oncology and greater use of genomic testing and biomarkers in cancer treatments is increasing the cost and complexity of setting up and running clinical trials.
- As research focuses on more targeted treatments, this can limit the range of patients for whom trials are suitable, with increased screening costs and difficulties recruiting sufficient patients. New systems and processes will be needed to ensure that clinical trials can recruit narrower groups of patients more quickly and effectively.
- The distribution of resources across the system is seen as a major barrier, with some centres at full capacity or other centres unable to offer trials because of a lack of resources. Interviewees highlighted staff shortages in specialisms supporting clinical trials, such as trial design and development specialists, trial administration, pathology and radiology.
- Regulatory barriers were seen as having less impact on the initiation of clinical trials than resource constraints – in terms of funding, staff, skills and equipment. However, achieving regulatory approval, particularly for early-phase trials, can be difficult and time consuming.

- NHS staff time must be protected for clinical research. Clinical trials are a fundamental part of cancer research, but oncologists often struggle to find the time to participate in them.
- Interviewees felt experiences during the pandemic had opened the door to faster regulatory approval, and that there was a real opportunity to drive improvements.

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I think it's going to be really important, and even more so now with Covid, that we continue to protect people working in the NHS, to be able to have time to do the trials.

2.2

Barriers to trial recruitment

Interviewees felt there were a range of barriers in being able to recruit patients to clinical trials, some of them related to access to information about trials for both patients and clinicians:

- Patients were thought to be generally positive about clinical research and often keen to participate when given appropriate information.
- However, there is a lack of information for patients on the availability and value in taking part in clinical trials, and some feel that the messaging may over-emphasise risks and that more could be done to communicate the benefits of taking part.
- Patients can be deterred from participating in clinical trials because of logistical, personal and financial considerations particularly for early-phase trials, which often take part in larger centres and may be some distance from patients' homes.
- Clinicians' awareness of clinical trials can be limited, particularly outside major centres.
- Time pressure and a perceived administrative burden discourage clinicians from discussing the possibility of taking part in a clinical trial with patients.
- Concerns over the risk and benefits as well as a patient's suitability to take part in clinical trials can also discourage clinicians from recommending patients.
- There is no centralised referral system for clinical trials which can make it more difficult to find a suitable trial for a patient.
- Information about clinical trials for patients and doctors is inadequate – existing information is difficult to locate, spread across multiple platforms, rarely up to date and often in a format that is difficult for patients to understand.
- Some would like to see clinical trials routinely considered for all cancer patients from the start of their cancer journey. More needs to be done to ensure patients have the conversation about clinical trials with their clinician earlier in their cancer journey.

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There are some very motivated people who will ask, and often they are the people who end up being on the clinical trials, but there are other people, your average everyday patient being referred through to cancer services with a new diagnosis of cancer, for example, who just have so many things on their mind, it just may not occur to them to even think about a clinical trial.

“ ”

You'll only get people enrolled on trials if the physician's really committed to it, because it's a huge hassle. It's just masses of work.

- Clinical trials are often seen as a last resort when standard options have been exhausted. By only testing new treatments in patients with more advanced disease we risk missing out on some of the benefits offered by these new treatments. We should be exploring ways of making trials available earlier in the treatment pathway, especially where standard treatments are not very effective.
- National variation exists in whether a patient is likely to be able to access a clinical trial – depending on the proximity to major research hospitals
- There was a view that patients recruited onto clinical trials are not representative of the patient population as a whole, in their geographic, demographic and socioeconomic profile. It was observed that patients enrolling on clinical trials tend to be wealthier and less ethnically diverse than the population as a whole. Not only does this mean that patients are missing out on the opportunity to take part in a clinical trial but the evidence base generated by a trial does not include groups for whom outcomes may vary.

“ ”

I think it's fair to say that traditionally all sorts of trials, be they cancer or not, tend to attract a certain type of population.



2.3

Biomarker-driven trials:

- Biomarkers are increasingly used to determine eligibility for clinical trials or to direct treatment within a trial.
- This is a positive step in precision medicine. However, it can result in additional barriers, especially where regulatory processes have not kept pace with the science.
- When the prevalence of a biomarker in the patient population is low, the time and financial cost of screening for trial recruitment can be prohibitive. Early screening and biomarker testing of all patients as part of their standard care could allow early identification of patients suitable for enrolment on clinical trials.
- Creation of a centralised database of patients containing biomarker information which could be used to identify eligible patients for a trial could reduce the barriers associated with the screening for biomarkers.
- The administrative burden of applying excessive, blanket regulatory standards across all biomarker research risks slowing down early-stage clinical trials and increasing costs. There are concerns that the

way regulations are being interpreted and applied risks severely hampering clinical research and disincentivising the development of biomarkers.

- Tests conducted in clinical trials at an exploratory stage to identify new biomarkers, and which have no immediate impact on decisions about patient treatment, should not need the same level of regulatory rigour as tests which directly determine a patient's treatment.

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Until we've got a system where the biomarkers are routinely available to us, and it's not complicated to identify those patients, then as I say, I tend to kind of draw the threshold at about 10%, so anything below, so there's the expectation that less than 10% of patients will have this biomarker, I kind of think, the amount of work involved actually to set the study up and run it, I'll probably only be putting two patients in maximum and therefore it's just not viable, but as I say, if we had a system whereby routine biomarkers [are available] ...

3 YouGov poll of cancer patients and their experience

YouGov, April 2020

We asked people with cancer about their experience with and attitudes towards clinical trials.

Purpose

The ICR commissioned YouGov to conduct a quantitative survey to understand the views of cancer patients on clinical trials.

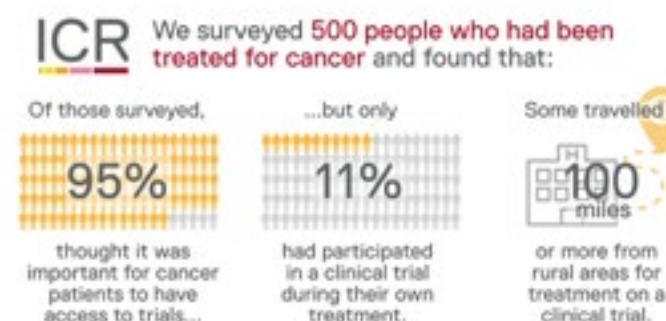
Method

In April 2020, YouGov conducted an opinion poll of patients who said they had been treated for cancer. The poll surveyed 505 people aged 25 years or more. The response rate varied by question, partly because of differences in the treatment patients had received.

Key findings:

- Patients are missing out on being part of, and hearing about, clinical trials even though there is a high inclination to take part in them.
- We need to make sure that suitable clinical trials are available for as many cancer patients as possible who want to be included on one, particularly for cancers of unmet need.
- The majority of cancer patients surveyed (95%) believe it is important for cancer patients to receive access to treatment through clinical trials.
- However, only 11% of cancer patients surveyed who received treatment for their cancer have been part of a clinical trial.
- Some 63% of cancer patients said they would consider receiving treatment as a part of a clinical trial as an alternative to standard treatment options.
- We need to make sure that all patients are aware of the clinical trial options available to them.

- Only 35% of cancer patients surveyed heard about clinical trials during their cancer treatment.
- Of the patients who did hear about clinical trials, 70% of them received this information from their main doctor or specialist in charge of their treatment.
- Only 5% of cancer patients who heard about clinical trials found out about them through their own online research.
- Patients should be able to access suitable trials wherever they are treated – whether in a cancer unit or a specialist cancer centre, and whatever part of the country they live in.
- Of the patients with cancer who took part in a clinical trial, the largest proportion of them (44%) travelled between five and 10 miles from their home to the location of the trial.
- The distances people travelled to take part in a clinical trial varied – those living in urban areas on average travelled between 10 and 20 miles, whereas patients living in rural areas travelled on average between 20 and 50 miles. A few patients living in rural areas reported travelling between 100 and 200 miles for trials.



Note: All figures, unless otherwise stated, are from YouGov Plc. Total sample size was 505 UK adults who have been diagnosed with cancer. Fieldwork was undertaken between 1st - 5th April 2020. The survey was carried out online. The figures are unweighted.

4 Recruitment to clinical trials for cancer in England

Data from the NIHR Clinical Research Network², September 2021

We analysed data from the NIHR Clinical Research Network to understand how Covid-19 has impacted UK cancer trials.

Purpose

The Covid-19 pandemic had a significant impact on clinical research across the UK, including work under way at the ICR. We have analysed data from the NIHR to demonstrate the scale of the impact of the pandemic on clinical trials for cancer.

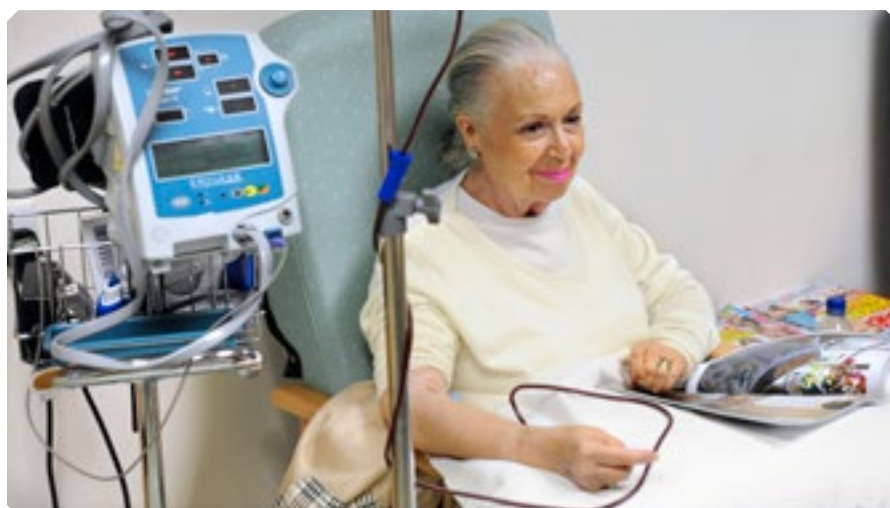
Method

The NIHR provided the ICR with data on recruitment to clinical trials in England for cancer for each of the four financial years 2017-18 to 2019-20, with data also broken down by sub-specialty. Data was provided for both non-commercial and commercial trials. The pandemic began to take effect on the NHS by mid-March 2020, and continued to do so in some from throughout 2020-21. To investigate the impact of the pandemic on clinical trials for cancer, we compared recruitment for the financial year 2020-21 with the recruitment average for the three years before the pandemic.

Key findings:

- Total recruitment into clinical cancer trials in England between the financial year 2017-18 and 2020-21 was just over a quarter of a million (228,905). Recruitment into non-commercial cancer trials was far greater than into commercial trials; over this time period non-commercial research recruited around 13 times (12.7) more patients than commercial trials.
- Annual recruitment into clinical trials for cancer showed a steady increase in the three years before the pandemic, from 61,810 in the financial year 2017-18 to a peak of 71,709 in the financial year 2019-20.
- Compared with the combined average of the three years before the pandemic (67,057) in the financial year 2020-21 recruitment fell dramatically to 27,734 – a fall of 59%.
- Recruitment into clinical trials across the years from the financial year 2017-2018 to the financial year 2020-2021 varied significantly by cancer sub-specialty. The highest recruitment was seen in trials for breast cancer and lung cancer, and the lowest in brain cancer and skin cancer. There were different patterns in recruitment across the cancer sub-specialties over the four years.
- In the financial year 2020-21 recruitment fell across all cancer sub-specialties analysed except for brain cancer and radiotherapy.

For further information, please see Appendix 1.



5 Actions

The ICR will continue to build on the evidence base summarised in this report and use it to seek to influence relevant policy and decision makers. The ICR has a vision that a suitable clinical trial should be available for every cancer patient who wants to be included in one. We would like to see a particular focus on under-served groups and cancers of high unmet need.

Actions we believe should be taken:

1 Co-ordination and availability of information about clinical trials:

We believe the Government should co-ordinate all information about clinical trials in an easily accessible format for patients and doctors. The Department of Health and Social Care, devolved administrations, and trials centres and registries should work together to create a system for providing information on trials that has a single, clear point of entry and which is accessible and easy operable by the public, clinicians and researchers.

2 Integrating clinical trials into routine clinical practice:

The NHS should integrate clinical trials for cancer much more closely into the patient care pathway. Doctors should give patients information about clinical trials much earlier in the patient journey. The NHS could screen patients at or shortly after diagnosis to understand the molecular profile of their cancer, aim to identify more people eligible for clinical trials, and make trials available at earlier stages in their treatment pathways.

3 Improving regulation of clinical trials:

We need streamlined and risk appropriate regulations on clinical trials to allow them to be set up more quickly, and especially to accelerate the initiation of trials with scientifically innovative designs, such as those driven by biomarkers. The Medicine and Healthcare products Regulatory Agency (MHRA) and Health Research Authority (HRA) should continue to review the approval and regulation of clinical research, seeking to learn lessons from the pandemic and from their international equivalents.

“““

The ICR has a vision that a suitable clinical trial should be available for every cancer patient who wants to be included in one.

4 Protected research time:

We need to ensure that there is ring-fenced time for clinicians to conduct research and that trial administration is adequately resourced and provided. In order to progress cancer research and continue to provide good services, NHS clinicians should be allowed adequate time to conduct research and deliver clinical trials separate to the provision of care, so as not to spread their capacity too thinly. Trial administration should not fall on clinicians. Clinical trials are a fundamental part of cancer research and improving the lives of patients.

5 Equalising resources:

We need to address the unwarranted variation that patients face across the UK in access to the latest trials, technologies and approaches. Lack of up-to-date equipment, trained staff or support for clinical trials restricts access to cancer clinical trials in many parts of the country. That results in some patients having to travel long distances for access to the highest-quality care or latest trials.

6 Innovative clinical trial design:

There is a need to test drugs in smarter, faster, more efficient trials to generate the required standard of evidence more quickly. The ICR supports greater use of innovative trial designs such as basket, umbrella and multi-arm, multi-stage trials (MAMS) where patients are stratified by their specific tumour profile rather than simply their broad cancer type and stage, and the design can be modified according to how early participants have responded. Adaptive platform trials which allow evaluation of multiple interventions, and the flexibility of using interim evaluations to drop ineffective interventions early, as well as swift addition of new promising interventions during the trial should also be encouraged. We support the MHRA's ambition to create a world-class regulatory system, and are committed to working with regulatory partners to ensure clinical research is safe and benefits patients. However, it is essential that the regulatory system keeps pace with advances in science, especially on the use of biomarkers and clinical trial methodologies and supports innovation in research.

7 Biomarker driven clinical trials:

We need efficient smarter clinical trials, which stratify patients based on the molecular and genetic profile of their disease to ensure treatments are targeted to those most likely to benefit. It should become standard within the NHS to perform molecular profiling on all cancers at the point of diagnosis to help guide treatment and clinical trial participation – ensuring that the cost of screening cost does not disincentive the establishment of biomarker-driven trials. Genomics England's plans to provide more widespread genome sequencing of cancer patients could help to address this issue in the future.

8 Clinical research funding:

The Government needs to create a simpler system for funding NHS clinical trials in the UK as current complexities are causing delays to setting up trials. Clinicians currently have to apply for 'excess treatment cost' (ETC) funding to cover the cost of additional activities in trials, such as biomarker or diagnostic tests, where they are not already commissioned by the NHS. NHS England should commit to covering these costs in trials to encourage innovation and expand access to trials for patients.

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Appendix:

Recruitment to clinical trials in England 2017-18 to 2020-21

Table 1:

Total recruitment by cancer specialty by financial year, commercial and non-commercial (England)

	FY17-18	FY18-9	FY19-20	FY20-21	Total
Non-commercial	56,863	61,902	67,752	25,737	212,254
Commercial	4,947	5,750	3,957	1,997	16,651
Total	61,810	67,652	71,709	27,734	228,905

- In total recruitment into clinical cancer trials in England between 2017-8 and 2020-21 was just over a quarter of a million (228,905).
- Across all years, total recruitment into non-commercial cancer trials in England was far greater than into commercial trials. In the last four years together non-commercial research has recruited around 13 times (12.7x) more patients than commercial trials.

Table 2:

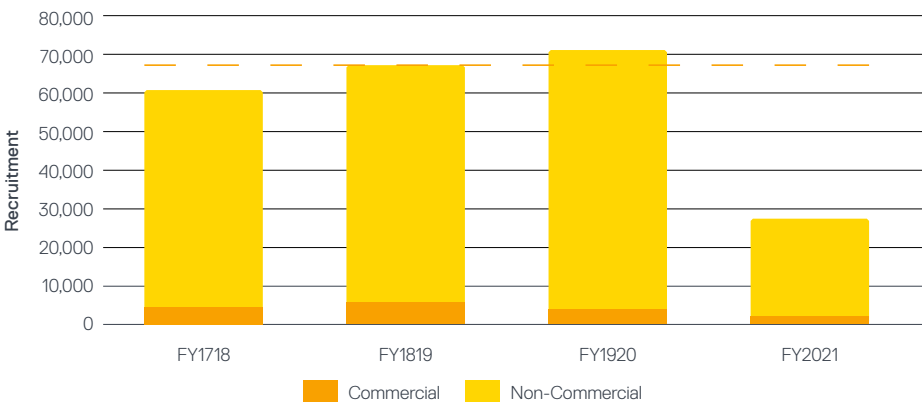
Total recruitment by cancer specialty by financial year, commercial and non-commercial (England)

Cancer subspecialty	Avg. recruitment FYs2017-20	Recruitment FY2020-21	% change
Brain cancer	567	727	+28
Breast cancer	13510	7401	-45
Colorectal cancer	11327	986	-91
CYP*	1968	1700	-14
Gynaecological cancers	5099	3450	-32
Haematology	8330	1858	-78
Head & neck cancer	1878	630	-66
Lung cancer	13276	8158	-38
Sarcoma	1361	319	-77
Skin cancer	1510	835	-45
SPCPS**	7352	1302	-82
Upper GI***	3659	1669	-54
Urology	8559	1219	-86
Primary Care	4579	2022	-56
Radiotherapy	393	869	+121

* Children and Young People's (CYP) Cancer
** Supportive and Palliative Care, Psychosocial oncology and Survivorship
*** Upper Gastrointestinal Cancer

Graph 1:

Total recruitment by cancer specialty by financial year, commercial and non-commercial (England)

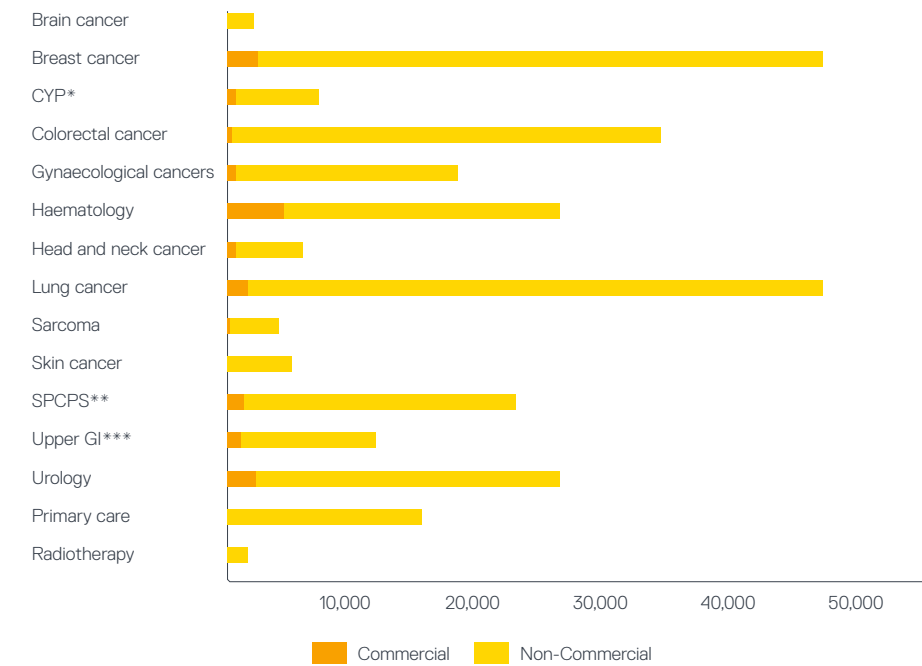


- Recruitment into clinical trials in England for all types of cancer show some variability in the three financial years before the pandemic, ranging from 61,810 in 2017-8, to a peak of 71,709 in 2019-20.
- The first UK reported death in the UK due to Covid-19 was reported to be on 5 March 2020, with people being asked to work from home where possible on 16 March 2020. This meant that the last month of 2019-20 and effectively the whole of 2020-21 would have been during the pandemic in some form of lock down.
- Compared to a combined average of the previous 3 financial years before the pandemic (67,057), in 2020-21 recruitment fell dramatically to 27,734 a fall of 59%.
- Across all years, total recruitment into non-commercial cancer trials in England was far greater than into commercial trials (see above). Compared to a combined average of the previous 3 financial years before the pandemic, in 2020-21 the fall in recruitment in non-commercial trials and commercial trials was the same at 59%.

Graph 2:

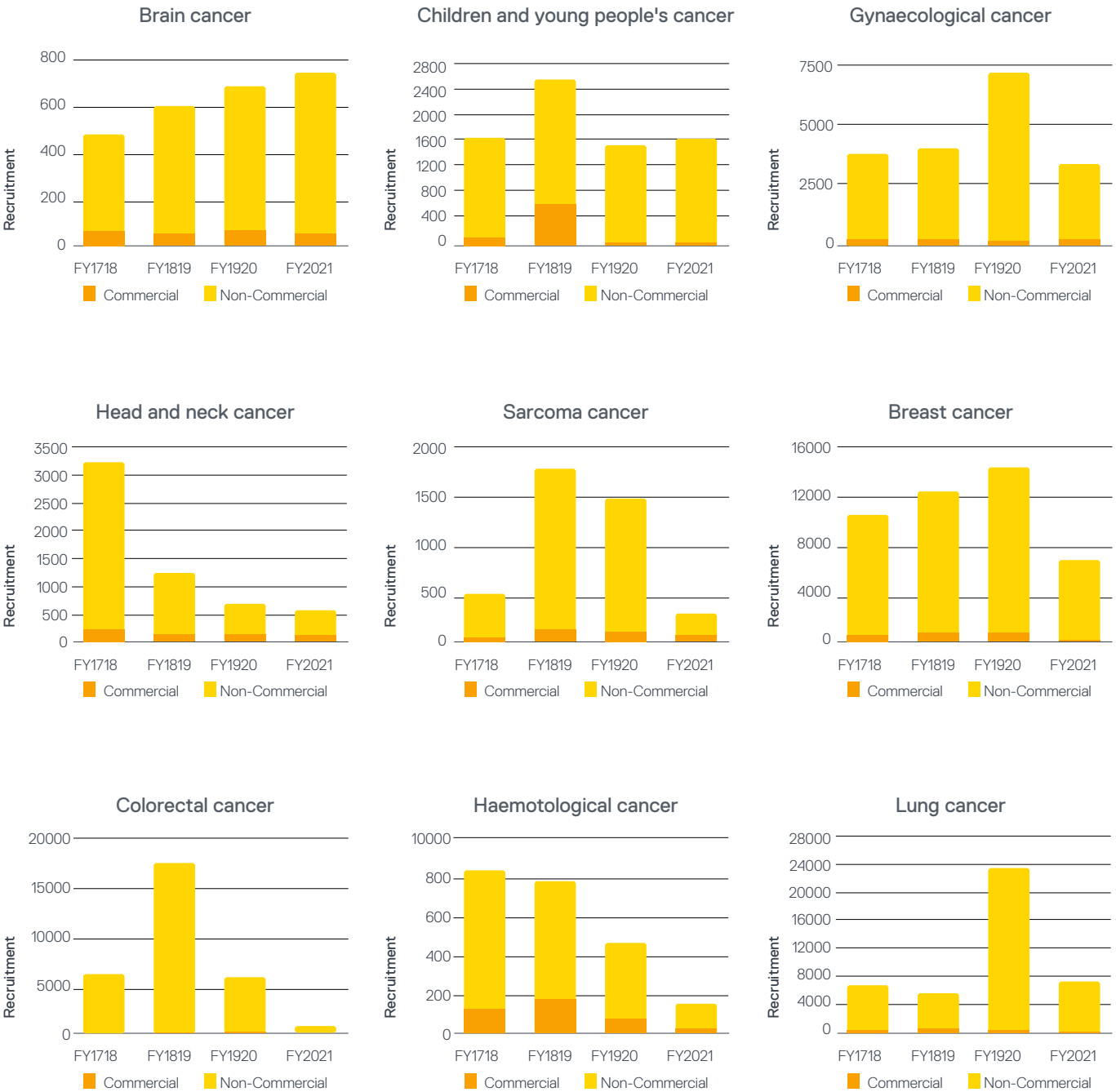
Total recruitment for financial year 17-18, 18-19, 19-20, 20-21 by cancer subspecialty, commercial and non-commercial (England)

* Children and Young People's (CYP) Cancer
** Supportive and Palliative Care, Psychosocial oncology and Survivorship
*** Upper Gastrointestinal Cancer



- The total recruitment into clinical trials in England for all types of cancer across the four financial years 2017-2018 to 2020-2021 varied significantly by the cancer subspecialty.
- The highest recruitment was seen in trials for breast cancer, lung cancer and colorectal cancer. The lowest recruitment was seen in brain cancer and radiotherapy.

Graph 3: Total recruitment by cancer subspecialty by financial year, commercial and non-commercial (England)



- Further analysis reveals different patterns in recruitment rates by cancer subspecialty over the four years from 2017-2018 to 2020-2021.
- For example CYP, colorectal cancer, sarcoma, and primary care all show peak recruitment during 2018-9.
- Lung cancer, Breast cancer, Gynaecological cancer, SPCPS and Upper GI shows a peak in recruitment during 2019-2020.
- Trends are likely to be due to changes in non-commercial trials are these far outnumber commercial trials.
- Compared to a combined average of the previous three financial years before the pandemic, in 2020-21 recruitment fell across all sub-specialties analysed except for brain cancer and radiotherapy, for overall recruitment.

References

1. Person centred care to deliver high-quality healthcare experiences (picker.org)
2. Research activity data provided by the National Institute for Health Research, Clinical Research Network's Business Intelligence team using the CRN's Open Data Platform. Contact inforequest@nih.ac.uk for more information.