ICR The Institute of Cancer Research

PhD Project Proposal

Funder details

Studentship funded by: NIHR

Project details

Project title: Late-effects of paediatric cancer treatment

Supervisory team

Primary Supervisor: Amy Berrington

Associate Supervisor(s): Aislinn Macklin-Doherty

Secondary Supervisor:

Divisional affiliation

Primary Division: Genetics and Epidemiology

Primary Team: Clinical cancer epidemiology

Site: Sutton

Project background

Each year approximately 2000 children are diagnosed with cancer in England and they receive a range of treatments including surgery, chemotherapy, radiotherapy, immunotherapy, and stem cell/bone marrow transplants. These treatments are continuously evolving with important changes in the last decades including the introduction of proton therapy and increased use of multi-modal treatment with anthracyclines. With significant improvements in survival there is a need to understand the long-term effects of these treatments. We have previously shown that anthracyclines increase the risk of breast cancer (1). The children who receive both radiotherapy and anthracyclines have an especially high risk of developing breast cancer. In a related study we found that children who received methotrexate had an increased risk of meningioma (2). However, other changes, such as reductions in radiation doses and field sizes and the introduction of proton therapy have likely reduced the risk of radiation-related cancers. The full impact of the variety of changes in radiotherapy and chemotherapy on long-term side-effects is not yet known but the NHS national radiotherapy dataset and systemic anticancer dataset provide a unique opportunity to study this question using real world data.

Project aims

- Establish a real world dataset by developing standardised methodology to utilize the national radiotherapy dataset and systemic anti-cancer dataset and other national linkages to summarize childhood cancer treatments in England over time and according to geography and socio-economic status.
- Assess trends in the risk of subsequent malignancies in childhood cancer patients in England compared to the risks in the general population.
- Assess the risk of subsequent malignancies in childhood cancer patients in relation to specific treatments including anthracyclines and modern radiotherapy, and the combination of these treatments for potential interactions.

Research proposal

The project will use state-of-the-art causal inference and quantitative bias assessment methodology (3) and leverage real world data from linked NHS datasets. The PhD candidate will use advanced epidemiological methods and these rich resources to explore the long-term outcomes after radiotherapy and chemotherapy for childhood cancer to provide real world evidence on the risks and benefits in the general population.

Study Populations

The National Radiotherapy Dataset (RTDS) was established in England in 2009 to collect consistent and comparable data from all providers of NHS-funded radiotherapy (4). It contains clinical information on the primary disease being treated, modality and intent of treatment, dose and fractionation. The Systemic Anticancer Dataset (SACT) (5) includes all chemotherapy agents, number of cycles and doses and other treatments was established in 2012 and has been mandatory since 2014. These treatment datasets will be linked to the National Cancer Registration and Hospital Episode Statistics to provide comprehensive treatment and outcome information for all childhood cancer patients in England with an expected cohort of approximately 40,000 patients diagnosed since 2009.

Impact

The purpose is to advance our understanding of the risk of subsequent cancers from modern radiotherapy and chemotherapy treatments used for childhood cancer. These results can inform guidelines for surveillance or screening strategies for patients who received these treatments.

"The studentship/position is funded by the NIHR Health Protection Research Unit in Radiation Threats and Hazards. The Health Protection Research Units are NIHR's flagship research partnerships between Universities and UKHSA, focused on the highest priority challenges in public health. From 1st April 2025, the HPRU in Radiation Threats and Hazards, led by Imperial College London, will seek to advance understanding of ionising and non-ionising radiation and health and delivery direct impact on policy to improve the long term health of the nation."

Literature references

[1] Veiga LH, Curtis R, Morton LM, Withrow DR, Howell R, Smith S, Weathers R, Oeffinger K, Moskowitz CS, Henderson T, Arnold M, Gibson T, Leisenring W, Neglia JP, Turcotte LM, Whitton JA, Robison LL, Armstrong GT, Inskip PD, Berrington de Gonzalez A (2019). Breast cancer risk after childhood cancer according to radiation dose to the breast and anthracyclines: a report from the Childhood Cancer Survivor Study. JAMA Pediatrics, 173(12):1171-9.

[2] Withrow DR, Anderson H, Armstrong GT, Hawkins M, Journy N, Neglia JP, de Vathaire F, Tucker MA, Inskip P, Brenner A, Berrington de Gonzalez A, Veiga L (2022). A pooled analysis of subsequent meningioma tumors following childhood cancer treatment. JAMA Oncology, 8: 1756-64.

[3] Berrington de González A, Richardson DB, Schubauer-Berigan MK, editors (2024). Statistical methods in cancer research, Volume V. Bias assessment in case–control and cohort studies for hazard identification (IARC Scientific Publications No. 171). Lyon, France: International Agency for Research on Cancer.

[4] Sandhu, S. et al. (2023) 'Cohort profile: radiotherapy dataset (RTDS) in England', BMJ Open, 13(6), p. e070699. Available at: https://doi.org/10.1136/bmjopen-2022-070699.

[5] Bright CJ, Lawton S, Benson S, Bomb M, Dodwell D, Henson KE, McPhail S, Miller L, Rashbass J, Turnbull A, Smittenaar R (2020). Data Resource Profile: The Systemic Anti-Cancer Therapy (SACT) dataset. Int J Epidemiol, 49(1):15-15l.

Candidate profile

Note: the ICR's standard minimum entry requirement is a relevant undergraduate Honours degree (First or 2:1).

Pre-requisite qualifications of applicants: Master in Epidemiology, Public Health, Data Science or related field; or equivalent experience in these areas.

Intended learning outcomes:

- Develop expertise in real world evidence and causal inference methodology.
- Critically read and analyse scientific literature, fostering a deep understanding and the ability to integrate current research with historical perspectives.
- Develop hypotheses that build upon existing knowledge.
- Apply rigorous epidemiological methods for study design, data generation, analyses and interpretation, accounting for potential biases.
- Learn to work in a collaborative research environment, leveraging the support of internal teams and external collaborators to enhance research outcomes.
- Communicate research goals, methods, results and implications in both writing and orally.
- Understand and adhere to the ethical considerations and guidelines pivotal in research involving human samples and data.

Advertising details

Project suitable for a student with a background in:

- ☐ Biological Sciences
- ☐ Physics or Engineering
- ☐ Chemistry
- ☒ Maths, Statistics or Epidemiology
- ☐ Computer Science