

National Disease Registration Service (NDRS) summary of the BENCHISTA paper on stage at diagnosis and international survival variation in childhood tumours

Background:

- [NDRS](#) in NHS England, as the national cancer registry, collects diagnosis, treatment and outcome data on cancer patients in England.
- The BENCHISTA project aims to explore whether international variation in childhood cancer survival might be explained by differences in stage at diagnosis. The project does this by analysing stage at diagnosis (based on the internationally agreed Toronto guidelines), non-stage prognostic factors, treatment modalities and relapse.
- The retrospective cohort includes six childhood solid tumours – neuroblastoma, medulloblastoma, Ewing sarcoma, rhabdomyosarcoma, osteosarcoma, and Wilms tumour – diagnosed between 2014 and 2017.
- 9,883 cases from 23 European countries, Australia, Brazil, Canada, and Japan were included in the survival analysis. Overall stage completeness was 93%.
- Three-year overall survival in Europe was Wilms tumour 95%, neuroblastoma 83%, medulloblastoma 79%, Ewing sarcoma 78%, rhabdomyosarcoma 77%, osteosarcoma 75%.
- European countries were grouped geographically as in EURO CARE studies, therefore England is part of the ‘UK and Ireland’ group. The main comparator in this project is Central Europe (Austria, Belgium, France, Germany, Switzerland, and the Netherlands).
- NDRS are members of the Project Working Group, submitted data and have provided clinical and analytical expertise.

Publications:

This briefing is about the forthcoming BENCHISTA paper focussing on international survival variation in childhood cancer (expected 9 February 2026).

In addition to the analysis carried out by BENCHISTA for this paper, NDRS did further analysis internally to provide insight into possible reasons for variation in outcome where it was observed. We have also provided feedback on manuscript drafts including suggestions on interpretation of results.

Previous BENCHISTA publications:

- [Cancer data quality and harmonization in Europe: The experience of the BENCHISTA Project – International Benchmarking of Childhood Cancer Survival by Stage](#) - Frontiers Oncology August 2023
- [International benchmarking of stage at diagnosis for six childhood solid tumours \(the BENCHISTA project\): a population-based, retrospective cohort study](#) - Lancet Child and Adolescent Health February 2025.

Further site-specific papers and a paper on variation in child health practices are also planned.

Key findings in the BENCHISTA paper which focusses on survival variation, from a 'UK and Ireland' perspective:

- Significant survival differences were not found between geographical areas for Wilms tumours and osteosarcoma either when adjusting by age group only or when adjusting by age group and stage.
- Significant survival differences were not found between the UK & Ireland and Central Europe for rhabdomyosarcoma.
- Significant survival differences were not found between the UK & Ireland and Central Europe for medulloblastoma. Additional sensitivity analysis was completed for medulloblastoma due to the high proportion of cases in the UK & Ireland with a missing stage. This reported a slight increase in the probability of death when re-allocating the missing stage cases in different scenarios, however all remained non-statistically significant.

Our interpretation

We think cases with a missing stage are biased towards negative CSF results. This is supported by the reported survival of cases with a missing stage. 3-year OS for cases with an unknown stage in the UK & Ireland was 85% (95% CI 73%-92%). This is comparable to the M0 category (3-year OS 87%, 95% CI 79%-92%).

- For neuroblastoma a significantly higher risk of death was found for the UK & Ireland. However, after adjustment for stage the difference in survival for neuroblastoma lost significance.

Our interpretation

We already know from the stage at diagnosis paper that patients in the UK & Ireland had a higher probability of been diagnosed at a metastatic stage when compared to Central Europe.

- For Ewing Sarcoma a significantly higher risk of death was found for UK and Ireland relative to Central Europe. Adjusting for stage had little impact on the significance. This suggests that other factors, may underlie these differences. The survival differences were however, confined to cases with metastatic disease at diagnosis only.

Our interpretation

Survival for patients with localised disease is in line with other areas. 3-year OS for the UK & Ireland is 86% (95% CI 77%-91%) compared to 87% (95% CI 82%-91%) for Central Europe. 3-year OS for metastatic disease was 36% (95% CI 23%-49%) in the UK & Ireland compared to 71% (95% CI 61%-79%) in Central Europe (NB: Germany did not contribute patients to the Ewing sarcoma cohort).

In view of these findings, we performed an internal analysis of the English Ewing metastatic patients recruited to this study and were surprised to observe the majority (>70%) had bone / bone marrow metastases. This is higher than the expected bone / bone marrow incidence of ~20% of those with metastatic disease. Bone/bone marrow metastases have significantly worse outcome than those with lung only metastases. We believe this is likely a major contributor to the explanation for worse survival in the UK.

In this context, it is important to acknowledge the limitation of Toronto staging at differentiating between different metastatic groups with very different treatment and outcomes.

Further investigation is also required to determine whether differences in treatment that may contribute to the differences observed.

The BENCHISTA dataset does not allow a comparison of the different types of metastatic Ewing sarcoma across the participating countries so we don't know how comparable the English and UK data are with central Europe. It is also unclear whether the unexpectedly high proportion of bone / bone marrow metastases in England is a statistical blip confined to the years of the BENCHISTA cohort or a systemic problem of more advanced disease in the UK compared to central Europe.