



# Survival of European adolescents and young adults diagnosed with cancer in 2000–07: population-based data from EUROCARE-5

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## Summary

**Background** Data from EUROCARE have consistently shown lower survival for adolescents and young adults (AYAs; aged 15–24 years) than for children (0–14 years) for most cancers that affect both groups, and modest survival improvements up to 2000–02. AYAs have longer survival than that of adults for most cancers. We used the latest definition of AYAs (aged 15–39 years) and provided estimates of 5-year relative survival for European AYAs with cancer diagnosed in 2000–07, compared with children and adults (40–69 years) with cancer, and assessed survival improvements over time.

**Methods** We analysed data from population-based cancer registries of 27 European countries participating in EUROCARE-5. We used the so-called complete method to estimate 5-year, population-weighted relative survival for 19 cancers affecting AYAs and children, and for 27 cancers affecting AYAs and adults. We assessed relative-survival differences between children versus AYAs, and between AYAs versus adults, using the Z test. We used the period approach to estimate 5-year relative survival over time for children and AYAs, and used a generalised linear model to model survival time trends (1999–2007) and to assess the significance of changes over time.

**Findings** We analysed 56 505 cancer diagnoses in children, 312 483 in AYAs, and 3 567 383 in adults. For all cancers combined, survival improved over time for AYAs (from 79% [95% CI 78.1–80.5] in 1999–2002 to 82% [81.1–83.3] in 2005–07;  $p < 0.0001$ ) and children (from 76% [74.7–77.1] to 79% [77.2–79.4];  $p < 0.0001$ ). Survival improved significantly in children and AYAs for acute lymphoid leukaemia ( $p < 0.0001$ ) and non-Hodgkin lymphoma ( $p < 0.0001$  in AYAs and  $p = 0.023$  in children). Survival improved significantly in AYAs only for CNS tumours ( $p = 0.0046$ ), astrocytomas ( $p = 0.040$ ), and malignant melanomas ( $p < 0.0001$ ). Survival remained significantly worse in AYAs than in children for eight important cancers: acute lymphoid leukaemias, acute myeloid leukaemias, Hodgkin's lymphomas, non-Hodgkin lymphomas, astrocytomas, Ewing's sarcomas, and rhabdomyosarcomas ( $p < 0.0001$  in all cases), and osteosarcomas ( $p = 0.011$ ).

**Interpretation** Notwithstanding the encouraging results for some cancers, and overall, we showed poorer survival in AYAs than in children for the eight important cancers. Recent European initiatives to improve outcomes in AYAs might reduce the survival gap between children and AYAs, but this reduction can only be verified by future population-based studies.

**Funding** Italian Ministry of Health, European Commission.

## Introduction

No internationally agreed definition exists for adolescents and young adults (AYAs) for cancer purposes; age ranges of 15–24 years and 15–29 years (at cancer diagnosis) have been used. EUROCARE<sup>1</sup> has shown that AYAs (aged 15–24 years) have poorer survival than children (aged 0–14 years) for most cancers that affect both groups, and survival improvements up to 2000–02 were modest. Additionally, AYAs (aged 15–29 years) have better survival than adults for most cancers.<sup>2</sup> Poorer survival in AYAs than in children has been attributed to various factors including no or few clinical trials conducted in AYAs, the dearth of specific treatment guidelines, differences in cancer biology, variations in the pharmacokinetics of chemotherapeutic agents, and delays in diagnosis and treatment.<sup>3–7</sup> AYAs with cancer are, in many ways,

neglected by both paediatric and adult oncologists, yet effective disease management necessitates a multiprofessional approach incorporating expertise from both specialties.<sup>8</sup> To improve cancer outcomes for AYAs, various initiatives—including promoting collaboration between paediatric and adult oncologists, developing national policies for managing AYAs with cancer, and setting up specific treatment units—have been implemented in several European countries<sup>8</sup> and worldwide.<sup>9</sup>

In the present EUROCARE-5 study, we used the latest definition of AYAs (age 15–39 years) proposed by the US National Cancer Institute<sup>10</sup> and accepted by the European Network for Cancer in Children and Adolescents (ENCCA) to provide population-based analyses of 5-year relative survival for European AYAs with cancer,

Lancet Oncol 2016; 17: 896–906

Published Online

May 26, 2016

[http://dx.doi.org/10.1016/S1470-2045\(16\)00162-5](http://dx.doi.org/10.1016/S1470-2045(16)00162-5)

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## Research in context

### Evidence before this study

There is no internationally agreed definition of adolescents and young adults (AYAs) for cancer purposes; age ranges of 15–24 years and 15–29 years (at cancer diagnosis) have been used. The US National Cancer Institute proposed defining AYAs as those aged 15–39 years at diagnosis. The European Network for Cancer in Children and Adolescents has adopted this definition and is promoting its use in Europe. Less is known about factors that affect cancer incidence, outcomes, and quality of life in AYAs than other age groups. Furthermore AYAs with cancer have not had the same mortality reduction seen in recent years in younger and older patients with cancer (for some cancers). To try to improve outcomes for AYAs with cancer, various initiatives—including the promotion of collaboration between paediatric and adult oncologists, development of national policies for managing AYAs with cancer, and setting up of AYA-specific treatment units—have been implemented in several European countries. Over the past 5 years population-based analyses of incidence and outcomes for AYAs with cancer have been completed in France, the Netherlands, and the UK. However, the latest survival analysis for Europe as a whole was provided by EURO CARE-4 for patients aged 15–24 years who were diagnosed in 1995–2002.

### Added value of this study

The present EURO CARE-5 study provides the latest population-based, 5-year relative survival estimates for European AYAs (aged 15–39 years at diagnosis) compared with children (0–14 years) and adults (40–69 years), diagnosed with cancer in 2000–07. The study also provides survival time trends (1999–2007) for AYAs and children, and assesses whether survival improvements in AYAs still lag behind those in children; and, for the first time to our knowledge, analyses survival differences between AYAs and adults. We found that survival improved during the study period for both AYAs and children

with cancer in Europe, and that survival improvements were similar in both these age categories. This finding contrasts with previous results that AYAs lag behind children in terms of survival improvement. However, survival remained significantly worse in AYAs than in children for acute lymphoid leukaemia, acute myeloid leukaemia, Hodgkin's lymphoma, non-Hodgkin lymphoma, astrocytoma, Ewing's sarcoma of bone, rhabdomyosarcoma, and osteosarcoma; and for acute myeloid leukaemia, soft-tissue sarcomas, and fibrosarcomas, survival remained unchanged for AYAs over the study period. These findings are in line with data from earlier time periods (1995–2002).

### Implications of all the available evidence

AYAs have worse survival than children for many cancers affecting both groups, justifying initiatives to improve outcomes for adolescents and young adults. For cancers affecting AYAs and children, it has been suggested that AYAs should be treated in an integrated paediatric–adult multidisciplinary setting. This integration would increase the likelihood of inclusion in clinical trials, and improve family and social support. For AYAs with acute lymphoid leukaemia, data clearly indicate that although tumour biology is relatively unfavourable in this group, application of paediatric treatment protocols is feasible and improves outcomes. However, robust evidence that regimens used to treat children actually benefit AYAs is only available for acute lymphoid leukaemia. Thus, further studies are needed to understand why survival improvements in AYAs lag behind those in children for many important cancers affecting both. The time of these analyses (patients diagnosed in 2000–07, and followed up until at least the end of 2008) pre-dates implementation of European initiatives to improve outcomes, and thus provides important baseline data to evaluate whether initiatives will lead to improved survival in European AYAs with cancer.

compared with survival in children (aged 0–14 years) and adults (aged 40–69 years). We also present time trends in 5-year relative survival for cancers typically occurring in AYAs and children, to assess whether survival improvements in the older age group still lag behind those in children. The time period of our analyses pre-dates implementation of the European initiatives to improve outcomes for AYAs, and thus provides an important baseline from which to assess the effectiveness of these initiatives.

## Methods

### Study design and data collection

We used data provided by European population-based cancer registries participating in EURO CARE-5.<sup>11</sup> Registries provided information on the site and morphology of each cancer diagnosed, which was coded according to the International Classification of Disease for

Oncology third revision (ICD-O-3).<sup>12</sup> Data for AYAs and for adults were provided by 97 of the 99 cancer registries contributing to the EURO CARE-5 adult database.<sup>13</sup>

Data for cancers in children were supplied by 72 of the 74 cancer registries contributing to the EURO CARE-5 childhood database.<sup>14</sup> These registries were the same as those that provided data for AYA and adult cancers for 21 of 27 countries (Finland, Iceland, Norway, Sweden, Ireland, Northern Ireland, Scotland, Austria, Belgium, Netherlands, Switzerland, Croatia, Malta, Portugal, Slovenia, Bulgaria, Estonia, Latvia, Lithuania, Poland, and Slovakia). For the remaining six countries (England, France, Germany, Italy, Spain, and Wales), data from specialised childhood registries were used instead, which were generally national (in one case supranational, the England and Wales childhood cancer registry) rather than the several subnational registries used for adult cancers, maximising population coverage. Preliminary

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