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Rare cancers are not so rare: The rare cancer burden in Europe

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ABSTRACT

Purpose: Epidemiologic information on rare cancers is scarce. The project Surveillance of Rare Cancers in Europe (RARECARE) provides estimates of the incidence, prevalence and survival of rare cancers in Europe based on a new and comprehensive list of these diseases.
Materials and methods: RARECARE analysed population-based cancer registry (CR) data on European patients diagnosed from 1988 to 2002, with vital status information available up to 31st December 2003 (latest date for which most CRs had verified data). The mean population covered was about 162,000,000. Cancer incidence and survival rates for 1995–2002 and prevalence at 1st January 2003 were estimated.
Results: Based on the RARECARE definition (incidence <6/100,000/year), the estimated annual incidence rate of all rare cancers in Europe was about 108 per 100,000, corresponding to 541,000 new diagnoses annually or 22% of all cancer diagnoses. Five-year relative survival was on average worse for rare cancers (47%) than common cancers (65%). About 4,300,000 patients are living today in the European Union with a diagnosis of a rare cancer, 24% of the total cancer prevalence.
Conclusion: Our estimates of the rare cancer burden in Europe provide the first indication of the size of the public health problem due to these diseases and constitute a useful base for further research. Centres of excellence for rare cancers or groups of rare cancers could provide the necessary organisational structure and critical mass for carrying out clinical trials and developing alternative approaches to clinical experimentation for these cancers.

1. Introduction

There is no internationally agreed definition of rare cancers. In Europe rare diseases are often defined as those with a prevalence of <50/100,000.[1] In the US, the Orphan Drug Act defined rare diseases as those affecting <200,000 persons.[2] However, a recent analysis of rare cancers in the US employed the definition of <15 incident cases per 100,000 per year.[3]

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A major problem with rare cancers is that their overall burden on society has not been adequately estimated, although they are thought to constitute a major public health problem.[4–6] Rare cancers are often inadequately diagnosed and treated[4] in relation both to lack of knowledge and lack of clinical expertise. Improving the quality of care for these cancers is a public health priority. One way of doing this would be to use a similar approach to that used for rare childhood cancers: concentrate treatment at specialised centres, and recruit most patients diagnosed to clinical trials.[5] However this requires a huge organisational effort; and for the rarest cancers it will always be impossible to recruit sufficient patients to perform standard clinical trials. Thus new approaches to obtaining evidence on treatment efficacy need to be developed.[6]

The project Surveillance of Rare Cancers in Europe (RARECARE) collected data on cancers from 89 population-based cancer registries (CRs) in 21 European countries, making it possible to study the epidemiology of these cancers as a whole in a large and heterogeneous population. Working from this database and the literature, a RARECARE working group produced a new list of cancers and developed a new definition of rare cancers (http://www.rarecare.eu).

This paper delineates the burden of these cancers in Europe, providing estimates of the incidence, prevalence and survival of rare cancers diagnosed from 1988 to 2002, based on the RARECARE definition and list.

2. Materials and methods

RARECARE gathered data on cancer patients diagnosed from 1978 to 2002 and archived in population-based CRs, all of which had vital status information available up to at least 31st December 2003. For 11 countries, the CRs covered the entire national population (Austria, Iceland, Ireland, Malta, Norway, Slovakia, Slovenia, Sweden, Northern Ireland, Scotland and Wales); the other countries do not have national cancer registration and were represented by regional CRs covering variable proportions of their national populations. The mean population covered, over the period 1995–1999, was about 162,000,000, corresponding to 39% of the population of countries participating in RARECARE and 32% of the European Union (EU27) population.

Systematic data checks were performed to detect errors, inconsistencies or unusual combinations of site, morphology, sex and age at diagnosis.[7,8] Only a negligible proportion (0.14%) of cases had major errors and had to be excluded.[7] RARECARE collected data from 89 CRs; however the present paper considered data from 76 CRs, excluding CRs which did not classify cancers according to the third edition of the International Classification of Diseases for Oncology (ICD-O-3),[9] and also those which collected data on childhood cancers only.

2.1. Incidence

The incidence analysis only considered cases incident in the more recent 1995–2002 period. Specialised CRs and some non-specialised CRs, with information available only for some anatomical sites were excluded. This criterion implied restricting the incidence analyses to 4,048,903 cases from 64 CRs.

Incidence rates were estimated as the number of new cases occurring in 1995–2002 divided by the total person-years in the general population (male and female) in each CR area, over the same period. The expected number of new cases per year in EU27 in 2008 was also estimated, assuming that incidence rates in Europe were same as those in the RARECARE sample.

2.2. Prevalence

CRs that started up recently do not have records of longer-term cancer survivors diagnosed before start up, resulting in underestimation of prevalence. To estimate prevalence, we therefore used data from CRs able to provide cases for the relatively long period 1988–2002; only 22 CRs fulfilled this condition. We calculated the number of prevalent cancers in 2008 and prevalence per 100,000 at the index date of 1st January 2003. The counting method,[10] based on CR incidence and follow-up data, was applied to CR data from 1988 to 2002. The completeness index method[11] was used to estimate the complete prevalence and involved adding the estimated surviving cases diagnosed prior to 1988 to those counted in 1988–2002. The total number of prevalent cases in the EU27 in 2008 was estimated assuming the same prevalence as in the RARECARE sample. Overall, 4,302,067 cancer cases were used to produce the prevalence estimates.

2.3. Survival

Data from all 76 CRs (including specialised registries) were used to produce survival estimates. We used the cohort approach[12] to estimate survival for patients diagnosed in 1995–1999 and followed-up until at least the end of 2003, enabling estimation of 5-year survival. A total 2,708,344 cases were used for the analysis. We estimated relative survival[12], the ratio of observed survival to the expected survival in the general population of the same age and sex, to correct for deaths from causes other than the cancer under investigation.

2.4. List of cancers and definition of rare cancers

The present analyses are based on the new list of cancer types provided by RARECARE. The list was produced by a group of pathologists, haematologists, clinicians and epidemiologists and emerged after a consultation process during which the developing list and its rationale were available at http://www.rarecare.eu. The list, endorsed by major European cancer organisations, is organised into three tiers as exemplified in Table 1. The bottom tier corresponds to the WHO names of individual cancer entities (http://www.iarc.fr/en/publications/pdfs-online/pat-gen/) and their corresponding ICD-O-3[9] codes. Bottom tier entities were grouped into categories (middle tier) considered to require similar clinical management and research. Middle tier entities were grouped into general categories (top tier) considered to involve the same clinical expertise and patient referral structure.