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Age-specific cancer rates: A bird’s eye view on progress

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ABSTRACT

Purpose. We aim to shed light on progress in cancer medicine through studying time trends in age-specific rates of cancer incidence and mortality over the last quarter century.

Methods. We analyzed age-specific incidence and mortality rates of all cancer sites combined using the high-quality population-based databases of Denmark, Finland, Norway, Sweden and The Netherlands for the period 1990-2016.

Results. Over these 26 years, cancer incidence rates increased in all investigated countries irrespective of age by about 22%. In contrast, cancer mortality rates decreased across all ages, also by about 22%, except ages 80+ in Denmark, Norway and Sweden, where they remained unchanged. This pattern is consistent with earlier diagnoses and more effective treatments of cancer.

Conclusions. This bird’s-eye view on cancer reveals substantive progress in cancer medicine.

Word count: 127

Keywords: Age-specific rates; Cancer incidence; Cancer mortality; Time trends; European cancer registries
INTRODUCTION

Great progress may happen under the radar. Just as we have seen major improvements in cardiovascular medicine without a single magic bullet, so there can be marked progress in cancer medicine through incremental advances.

Recognizing such progress requires a suitable perspective. Cancer risk is sensitive to competing risks, and does not reveal at what age cancer occurred. Indeed, cancer risks may well have increased because of the massive reduction in cardiovascular mortality over the last half century [1, 2]. Papers looking at (lifetime) cancer risk continue to paint a mixed picture of progress in cancer medicine [3]. Meanwhile, time trends in age-standardized cancer mortality rates seem favorable, at least for some cancers [4].

To take a bird’s-eye view on any progress made in cancer medicine, we charted trends in age-specific rates of cancer incidence and mortality for a set of countries with high-quality data spanning a quarter of a century.

MATERIAL AND METHODS

We retrieved population-based data from cancer databases of Denmark, Finland, Norway, Sweden and The Netherlands. The data originates from the national cancer registries and causes of death registries of each country. The Nordic Cancer Registries are known for their completeness and accuracy through time [5, 6]. Except for the oldest old, high sensitivity and high positive predictive values over age and over calendar time have been demonstrated [7]. Data used were cancer incidence and mortality by age for all sites (ICD-10 CXX.X+ D09.0-1+D30.1-9+D35.2-4+D41.1-9+D32-33+D42-43+D44.3-5+D45-46+D47.0-1, 3-9). We analyzed data for persons aged 50 to 85+ in 5-year age groups from 1990 until 2016 for the total population and separately by sex for each country.
These data are freely available under the NORDCAN Database [8] and The Netherlands Comprehensive Cancer Organization (IKNL) Database [6]. We computed age-specific rates (events per 100,000 person-years) of cancer incidence and mortality on a log scale for each calendar year and country. Due to the population covering nature of these registries, the large numbers, and the descriptive nature of this work, we did not calculate p-values and confidence intervals.

RESULTS

Age-specific cancer incidence rates increased for all ages for all countries, typically by about 22%. Age-specific cancer mortality rates generally decreased by the same amount (Fig.1). These changes resulted from a steady progress over the study period (Supplementary Material Fig.S1 and Fig.S2). The only exception to this pattern was cancer mortality at ages 80+ in Denmark, Norway and Sweden, which remained constant.
Figure 1. Comparison of age-specific cancer rates on logarithm scale of all sites ICD-10 CXX.X+D09.0-1+D30.1-9+D35.2-4+D41.1-9+D32-33+D42-43+D44.3-5+D45-46+D47.0-1,3-9 (top panel: incidence; bottom panel: mortality) in Denmark, Finland, Norway, Sweden and The Netherlands in 1990 (light gray line) vs. 2016 (dark gray line). Source: NORDCAN Database (www-dep.iarc.fr/NORDCAN/english/frame.asp) and IKNL Database (www.cijfersoverkanker.nl).

Repeating the analysis by sex, we found that the general pattern held for both females and males. However, females saw a greater increase in incidence (with the exception of Sweden) while males saw a greater mortality reduction (Fig. 2). Where age-specific cancer incidence increased most dramatically, for instance for Dutch and Norwegian females, the reduction in age-specific cancer mortality was negligible. Where increases in age-specific cancer incidence were small, such as for Dutch and Finnish males, the drop in age-specific cancer mortality was large. For Swedish females
the changes were small overall. Thus, the overall divergence between cancer mortality and cancer incidence was broadly robust to variations in the levels of cancer incidence and mortality.

Figure 2. Gender based age-specific cancer rates on logarithmic scale of all sites ICD-10 CXX.X+D09.0-1+D30.1-9+D35.2-4+D41.1-9+D32-33+D42-43+D44.3-5+D45-46+D47.0-1,3-9 (top panel: incidence; bottom panel: mortality) in Denmark, Finland, Norway, Sweden and The Netherlands in 1990 (light gray line) vs. 2016 (dark gray line). Source: NORDCAN Database (www-dep.iarc.fr/NORDCAN/english/frame.asp) and IKNL Database (www.cijfersoverkanker.nl).

DISCUSSION AND CONCLUSION

We here show marked and opposite changes in age-specific cancer incidence and mortality rates. Age-specific all-cause cancer mortality rates declined dramatically: a change in the log cancer
mortality rate from 6.5 to 6.25 implies a reduction from 665 events per 100,000 person-years to 518 per 100,000, while a change in the log cancer rate from 7 to 6.75 implies a reduction from 1097 events per 100,000 person-years to 854 per 100,000 (a 22% reduction in both cases). Simultaneously, age-specific cancer incidence rates increased by about 22% over the same period. This pattern was observed across all countries and almost all ages, and was robust to variability in overall levels of cancer incidence and mortality across sexes.

The only exception to the described pattern was that cancer mortality increased at ages 80+ in some countries. Possible explanations include people aged 80+ being (deemed) unfit for treatment, and multimorbidity or interacting causes of death giving variability in cause-of-death classifications that do not reflect genuine differences [9, 10].

The potential ways in which age-specific cancer incidence may correlate with age-specific cancer mortality are charted in Table 1.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better treatment through earlier diagnosis</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Better treatment only</td>
<td>=</td>
<td>↓</td>
</tr>
<tr>
<td>More tumors</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Higher detection rates and hence more accurate death certificates</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>
Table 1. Causal table: Potential mapping of increasing age-specific cancer incidence into age-specific cancer mortality. Better treatment through earlier diagnosis is the only mechanism that can explain the age-specific patterns observed by itself, i.e. increase in age-specific incidence and decrease in age-specific mortality.

Cancer incidence may increase because more persons get a tumor. Ceteris paribus, cancer mortality is then expected to go up. Also, cancer incidence may increase due to higher detection rates when screening or awareness programs are rolled out. Increased detection may lead to cancer being more often than before listed as the underlying cause of death. In this case, age-specific cancer mortality is expected to go up, or at least stay the same.

Could deaths that were previously classified as cancer deaths now be classified under other causes? This too is unlikely in the light of higher cancer detection rates and higher incidence rates, as well as an increasing awareness that cancer may be the underlying cause of death if for instance a hospitalized patient dies of pneumonia; if anything, the reverse trend could be expected. In this light, the reduction in cancer mortality is especially substantial.

Cancer mortality could also decrease because of improved effectiveness in treatment alone, irrespective of earlier diagnosis. Indeed, improved treatment effectiveness could be explained by recent cohorts reaching a certain age in better overall health than previous cohorts, making them able to withstand harsher treatment, for instance more rounds of chemo-therapy, which may improve their survival. Increasing cancer incidence could then be explained as a mere detection phenomenon, not reflecting any real changes. We would then conclude that cancer medicine has made no progress.

Yet the most likely explanation linking increased cancer incidence to decreased cancer mortality is more effective treatment and earlier diagnosis. Treatments have become more effective through scientific discovery and innovation: as science progresses and treatment protocols are updated, cancer
mortality falls. Another possibility is that while treatment effectiveness per se remained unchanged, earlier diagnosis makes the cancer easier to treat (e.g. before metastasis has occurred) perhaps aided by a cohort effect of improving overall health. Such a situation would allow patients to withstand treatment, thus improving their survival. A favorable interaction of these factors is perhaps the most likely explanation.

Indeed, over the last decades, the major determinants in cancer mortality reduction for men were a decline in lung and other tobacco-related cancers, together with a fall in gastric cancer, and a more recent fall in colorectal cancer [11]. In women, relevant contributions came from a persistent decline in cervical cancer and a fall in breast cancer mortality, particularly in Northern and Western Europe [11]. These declines are due to earlier diagnosis, although the fall in breast cancer mortality is mainly due to improved treatment [12]. These findings support the idea that our findings are genuine.

We conclude that our analysis most likely reflects unambiguous, substantive progress in cancer medicine. Over the last decades, major systemic changes have been implemented in cancer health care, such as screening programs, public awareness programs, doctor’s awareness programs, cancer registries, protocols and cancer plans, and centralization of treatment. It is tantalizing to see how the combination of these changes and great differences between specific cancers add up to a remarkably uniform change in age-specific rates: incidence is up by about 22%, mortality is down by about 22%. While the countries in this study are all high-resource countries, the potential unveiled here is probably general.

Word count: 1386 (without references)
REFERENCES


