Cancer mortality does not differ between migrants and Danish-born patients

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ABSTRACT
INTRODUCTION: The aim of this study was to compare cancer mortality among migrant patients with cancer mortality in Danish-born patients.

MATERIAL AND METHODS: This was a historical prospective cohort study. All non-Western migrants (n = 56,273) who were granted a right to residency in Denmark between 1 January 1993 and 31 December 1999 were included and matched 1:4 on age and sex with Danish-born patients. Cancer patients in the cohort were identified through the Danish Cancer Registry and deaths and emigrations through the Central Population Register. Using a Cox regression model, mean sex-specific hazard ratio (HR) for all-cause mortality were estimated by ethnicity; adjusting for age, income, co-morbidity and disease stage.

RESULTS: No significant differences were observed in mortality for gynaecological cancers between migrant women (HR = 1.12; 95% confidence interval (CI): 0.70-1.80) and Danish-born women. Correspondingly, migrant women (HR = 0.76; 95% CI: 0.49-1.17) showed no significant differences in breast cancer mortality compared with Danish-born women. Regarding lung cancer, neither migrant women (HR = 0.79; 95% CI: 0.45-1.40) nor men (HR = 0.73; 95% CI: 0.53-1.14) presented statistical variances in mortality rates compared with Danish-born patients. Similarly, for colorectal cancer, migrant women (HR = 0.64; 95% CI: 0.27-1.55) and men (HR = 1.58; 95% CI: 0.75-3.36) displayed no significant differences compared with Danish-born patients.

CONCLUSION: Different trends were observed according to cancer type, but cancer mortality did not differ significantly between migrants and Danish-born patients. This may imply that the Danish health-care system provides equity in cancer care.

TRIAL REGISTRATION: not relevant.

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Immigrants and descendants comprise 9.5% of the Danish population [1]. The focus of this study was on refugees and family-reunited immigrants. Refugees enter Denmark as quota refugees or spontaneous asylum seekers. Denmark receives approximately 500 quota refugees annually under an agreement between the Danish State and the United Nations High Commissioner for Refugees (UNHCR); asylum seekers arrive by their own means. Family reunited immigrants arrive in Denmark independently and rely entirely on their family when establishing their new life. In this paper, “migrants” refer to all groups of foreign-born individuals.

Cancer mortality patterns among migrants are not well investigated in a European context. The relatively few studies, which mainly derive from the UK, show contrasting mortality patterns for migrants and ethnic minorities compared with local born citizens [2-6]. Mortality is, among other determinants, related to stage at diagnosis and access to cancer treatment. Several studies have shown that migrants and ethnic minorities have a tendency towards late-stage diagnosis compared with local born citizens – also in the population of this study [5-7]. Stage at diagnosis is related to participation in screening and access to primary care. Indeed, studies show that migrants and ethnic minorities have lower screening participation rates than rates observed among local born persons. This also applies to Denmark [8]. Moreover, based on the US literature, ethnic minorities are likely to experience a number of obstacles when accessing cancer treatment; these obstacles are often related to financial barriers [9, 10].

To our knowledge, similar studies on ethnic inequalities in cancer mortality are not available from the Scandinavian free-access health-care systems. However, migrants may experience a number of informal barriers to hospital care related to language, newness and cultural factors in a socialised health-care system [11]. Consequently, we wished to study differences in mortality between migrants and Danish-born patients after adjusting for stage at diagnosis. We considered mortality a clinical proxy for access to cancer treatment upon diagnosis in a free-access health-care setting such as Danish health care. Our hypothesis was that even in a free-access health-care setting like the Danish system, migrants may experience a higher mortality than Danish-born patients due to informal problems in accessing cancer diagnosis and treatment.

MATERIAL AND METHODS
Study population
The study cohort was obtained through the Statistical Department at The Danish Immigration Service. Migrants
who obtained residence permission as refugees or through family reunification in Denmark from 1.1.1993 to 31.12.1999 were included. In total, 84,379 individuals were identified in this period. Individuals who were below 18 years of age (n = 18,861) when they obtained residence permission were excluded. A Danish-born reference population (with Danish-born parents) was identified through Statistics Denmark and matched 4:1 on an individual level with regard to age and sex through a random sampling procedure. The final study cohort counted 56,273 migrants (controls: 225,090). The study cohort, exclusion processes and matching procedures have previously been described in more detail [12].

Ethnicity and socioeconomic position
We divided migrants into three regional categories reflecting the largest regions of origin in the study population: 1) Eastern Europe (including Former Yugoslavia); 2) The Middle East (including North Africa) and 3) Other non-Western countries. We based our definition of geographical areas on WHO guidelines [13]. Income was used as a proxy for socioeconomic position. Data on income were obtained from Statistics Denmark and divided into three categories. Information on income is updated annually on 31 December. All cancer patients in the study had a registered income during the study period.

Cancer diagnosis
By use of the personal identification numbers, the study population was cross-linked to the Danish Cancer Registry from where we obtained data on all cases of first primary cancers diagnosed between 1.1.1994 and 31.12.2007. Tumours in the registry are classified according to the International Classification of Diseases (ICD-10). We only included the most prevalent cancer types: colorectal cancers (C18-C20), breast cancer (C-50), gynaecological cancers (C53-C56) and lung cancer (C-34). In total, 437 migrants and 2,599 controls had received one of these cancer diagnoses during the study period. We followed migrants and controls from the time of diagnosis to the first of the following events: a) death; b) end of study (31.12.2007); or c) first registered emigration date (they were not included again if they later returned to Denmark). To identify fatalities, we cross-linked our cancer cohort to population data from the Central Population Registry, which contains data on all registered deaths during the study period. In total, 126 migrants and 757 controls in the cancer cohort died from 1 January 1994 to 31 December 2007. Table 1 shows the characteristics of the cancer cohort included in the study by cancer type.

Disease stage
Information on disease stage was also obtained from the Danish Cancer Registry. From 1 January 1994 to 31 December 2003, disease stage was classified into one of four categories: 1) local; 2) regional spread; 3) metastatic; or 4) unknown. From 1 January 2004 to 31 December 2007, disease stage was recorded according to the tumour-node-metastasis (TNM) classification of malignant tumours [14]. As we used data from before 1 January 2004, we decided also to classify TNM stages into the four above-mentioned disease stage categories in our analysis.

Co-morbidity
We used the summary measure developed by Charlson et al [15] to describe co-morbidity. The index takes into account both the number and seriousness of co-morbid diseases. It includes 19 severe medical conditions each weighted according to its potential for influencing mortality, with scores ranging from one to six. As previously done, we grouped patients into three co-morbidity scores: 0 (none); 1 (medium); ≥ 2 (high) [16]. As our analyses were based on primary cancers only, no cancers were included in the index. In order to identify co-morbidities, we linked the personal identification numbers of the cancer cohort to the Danish National Patient Register obtaining all records on inpatient hospitalisations from 1 January 1994 to 31 December 2007. Any co-morbidities (based on ICD-10 diagnoses) leading to inpatient hospitalisation up to one year before the cancer diagnosis was included in the co-morbidity score. For patients diagnosed in 1994, co-morbidity score was based only on any in- or outpatient hospital contacts from 1 January 1994 until diagnosis of first primary cancer implying that their index is based on data from < 1 year.

Statistical analysis
For each cancer type, we estimated the mean HR and 95% confidence interval (CI) for migrants compared with their Danish-born controls using a Cox regression model (in SAS version 9.1), which was fitted separately for men and women. The Cox regression analysis implies a continuous adjustment for age in the model. The HR was analysed by region of origin and adjusted for disease stage, co-morbidity and income. Table 2 shows both the adjusted HR and unadjusted HR estimates.

Ethics
The Danish Data Protection Agency has approved the study. Further ethical approval regarding registry-based research is not required in Denmark. The data set was made available and analysed in an anonymous form by remote online access to the data set stored at Statistics Denmark.

Trial registration: not relevant.
RESULTS

Table 2 shows HR for cancer mortality by region of origin and sex adjusted for stage at diagnosis, co-morbidity and income. Danish-born patients formed the reference group.

No significant differences were observed in mortality for gynaecological cancers between migrant women in total (HR = 1.12; 95% CI: 0.70-1.80) and Danish-born women. Trends were seen in different directions according to regional origin, but no migrant groups experienced significant differences in breast cancer mortality compared with Danish-born patients.

Likewise, for breast cancer, migrant women in total (HR = 0.76; 95% CI: 0.49-1.17) showed no significant differences in mortality compared with Danish-born women. Again, trends were seen in different directions according to regional origin, but no migrant groups experienced significant differences in breast cancer mortality compared with Danish-born patients.

For lung cancer, both migrant women (HR = 0.79; 95% CI: 0.49-1.29) showed no significant differences in mortality compared with Danish-born women. Trends were seen in different directions according to regional origin, but no migrant groups experienced significant differences in breast cancer mortality compared with Danish-born patients.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
 & Female & & Male & \\
 & migrants & Danish-born & migrants & Danish-born \\
\hline
Colorectal cancer & & & & \\
Eastern Europe origin, % (n) & 60.0 (21) & 65.8 (25) & 20.0 (7) & 10.5 (4) \\
The Middle East origin, % (n) & 20.0 (7) & 23.7 (9) & 20.0 (7) & 20.0 (10) \\
Other non-Western origin, % (n) & 20.0 (7) & 30.6 (86) & 0.4 (1) & 36.9 (98) \\
Total deaths, % (n) & 2.9 (1) & 2.9 (1) & 77.1 (27) & 77.1 (27) \\
Emigrations, % (n) & 77.1 (27) & 69.0 (194) & 63.1 (167) & \\
Population at study end, % (n) & 100 (35) & 100 (281) & 100 (38) & 100 (265) \\
Median age at diagnosis, yrs (range) & 53.1 (45.1-69.1) & 60.8 (49.4-71.2) & 65.1 (52.7-72.4) & 65.6 (52.8-72.8) \\
Median age at study enda, yrs (range) & 30.6 (86) & 62.6 (54.1-75.5) & 68.7 (55.8-76.4) & 69.1 (56.1-76.3) \\
Median follow-upb, yrs (range) & 2.9 (1) & 4.9 (1.4-7.7) & 77.1 (27) & 3.1 (1.5-6.5) \\
\hline
Lung cancer & & & & \\
Eastern Europe origin, % (n) & 79.2 (19) & 81.4 (57) & 4.2 (1) & 10.0 (7) \\
The Middle East origin, % (n) & 4.2 (1) & 8.6 (6) & 66.7 (16) & 67.0 (126) \\
Other non-Western origin, % (n) & 16.6 (4) & 63.4 (135) & 0.0 (0) & 36.9 (98) \\
Total deaths, % (n) & 66.7 (16) & 67.2 (47) & 2.8 (2) & 60.0 (21) \\
Emigrations, % (n) & 4.2 (1) & 0.0 (0) & 0.0 (0) & 10.0 (7) \\
Population at study end, % (n) & 29.1 (7) & 30.2 (21) & 100 (24) & 100 (213) \\
Median age at diagnosis, yrs (range) & 53.1 (45.1-69.1) & 60.8 (49.4-71.2) & 65.1 (52.7-72.4) & 65.6 (52.8-72.8) \\
Median age at study enda, yrs (range) & 30.6 (86) & 62.6 (54.1-75.5) & 68.7 (55.8-76.4) & 69.1 (56.1-76.3) \\
Median follow-upb, yrs (range) & 2.9 (1) & 4.9 (1.4-7.7) & 77.1 (27) & 3.1 (1.5-6.5) \\
\hline
Breast cancer & & & & \\
Eastern Europe origin, % (n) & 56.1 (101) & 56.1 (101) & 18.9 (34) & 18.9 (34) \\
The Middle East origin, % (n) & 18.9 (34) & 18.9 (34) & 25.0 (45) & 25.0 (45) \\
Other non-Western origin, % (n) & 25.0 (45) & 25.0 (45) & 13.3 (24) & 13.3 (24) \\
Total deaths, % (n) & 13.3 (24) & 18.4 (215) & 0.6 (1) & 18.4 (215) \\
Emigrations, % (n) & 13.3 (24) & 18.4 (215) & 0.6 (1) & 18.4 (215) \\
Population at study end, % (n) & 86.1 (155) & 81.3 (945) & 86.1 (155) & 81.3 (945) \\
Total, % (n) & 100 (180) & 100 (1,164) & 100 (180) & 100 (1,164) \\
Median age at diagnosis, yrs (range) & 46.9 (40.8-57.5) & 56.1 (55.3-68.1) & 50.7 (42.9-63.4) & 64.1 (54.0-71.7) \\
Median age at study enda, yrs (range) & 51.8 (44.5-60.2) & 64.2 (57.7-70.4) & 55.0 (46.5-67.8) & 65.4 (56.1-73.5) \\
Median follow-upb, yrs (range) & 3.6 (1.9-7.2) & 1.5 (0.7-3.2) & 4.7 (2.2-7.4) & 0.9 (0.6-2.7) \\
\hline
Gynaecological cancers & & & & \\
Eastern Europe origin, % (n) & 62.3 (56) & 62.3 (56) & 14.4 (13) & 14.4 (13) \\
The Middle East origin, % (n) & 14.4 (13) & 14.4 (13) & 23.3 (21) & 23.3 (21) \\
Other non-Western origin, % (n) & 23.3 (21) & 23.3 (21) & 24.4 (22) & 24.4 (22) \\
Total deaths, % (n) & 24.4 (22) & 19.9 (97) & 5.6 (5) & 1.6 (8) \\
Emigration, % (n) & 24.4 (22) & 19.9 (97) & 5.6 (5) & 1.6 (8) \\
Population at study end, % (n) & 70.0 (63) & 78.5 (383) & 70.0 (63) & 78.5 (383) \\
Total, % (n) & 100 (90) & 100 (488) & 100 (90) & 100 (488) \\
Median age at diagnosis, yrs (range) & 49.1 (41.5-64.6) & 49.1 (41.5-64.6) & 53.56 (44.8-66.6) & 53.56 (44.8-66.6) \\
Median age at study enda, yrs (range) & 53.56 (44.8-66.6) & 53.56 (44.8-66.6) & 50.2 (40.2; 65.1) & 50.2 (40.2; 65.1) \\
Median follow-upb, yrs (range) & 5.2 (1.62-7.99) & 5.2 (1.62-7.99) & 4.8 (2.20-7.91) & 4.8 (2.20-7.91) \\
\hline
\end{tabular}
\caption{Characteristics of the cancer patient populations (colorectal cancer, lung cancer and breast cancer) included in the study. Migrants and their age- and sex-matched Danish-born controls are distributed by sex.}
\end{table}

\textsuperscript{a) End of follow-up is defined as 1 of the 1st of the following events: death, end of study (31.12.2007), or first registered emigration date (individuals were not included again if they later returned to Denmark).}

\textsuperscript{b) The median follow-up is counted from date of diagnosis to date of study end.}
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95% CI: 0.45-1.40) and men (HR = 0.73; 95% CI: 0.53-1.14) in total presented no statistical variances in mortality rates compared with Danish-born patients. Uniform, non-significant tendencies were seen across sex and regional origin towards a lower mortality compared with Danish-born patients.

Regarding colorectal cancer, HRs showed that in total migrant women (HR = 0.64; 95% CI: 0.27-1.55) and men (HR = 1.58; 95% CI: 0.75-3.36) displayed no significant differences in mortality compared with their Danish-born counterparts. Trends were seen in different directions according to sex.

DISCUSSION

We studied all-cause mortality in a cohort of 3,044 cancer patients based on a total cohort of 281,363 individuals. Our hypothesis was that migrants’ cancer mortality was higher than Danish-born patients’ mortality due to inequalities in access to cancer care. Tendencies in cancer mortality varied with cancer type and ethnic background. However, our hypothesis was not confirmed in that cancer mortality was not significantly higher among migrants than among Danish-born patients in any of our analyses.

Our study adds to the scarce European literature on migrant cancer patients’ mortality using the unique Danish national registries including the Danish Cancer Registry, which has a high degree of completeness and validity of diagnoses and is generally considered of sound quality [17]. The study also has several limitations. Firstly, although it is based on a relatively large cohort of migrants, the absolute numbers of deaths were small in our analysis. Secondly, our results might be affected by unregistered remigration, which can skew the estimates; however, we do not know the extent of this phenomenon in the population. Thirdly, we used all-cause mortality instead of cause-specific mortality. We did this because in the Danish Cancer Registry causes of death are obtained from death certificates, which may be inaccurately reported, i.e. the primary cancer site is not always listed, but rather the site of metastasis or recurrence.

As all analysis results were statistically insignificant, we do not know if our findings are due to small numbers or an indicator of equity in access to cancer treatment in Denmark. If we assume that the observed tendencies are valid, then our results may be supported by several explanations: i) Studies from the US show ethnic inequalities in treatment provision [9, 10]; however, the Danish health-care system is a socialised, tax-financed system that provides free of charge access to the vast majority of health services including primary care and

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>The Middle East</th>
<th>Eastern Europe</th>
<th>Other non-Western</th>
<th>Total migrants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>n (n) a</td>
<td>HR (95% CI)</td>
<td>n (n) a</td>
</tr>
<tr>
<td>Gynaecological</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>1.45 (0.48-4.42)</td>
<td>16 (50) 0.514</td>
<td>1.19 (0.68-2.08)</td>
<td>4 (22) 0.533</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>1.14 (0.50-2.63)</td>
<td>6 (54) 0.753</td>
<td>0.69 (0.39-1.22)</td>
<td>15 (121) 0.203</td>
</tr>
<tr>
<td>Colorectal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>– 0 (27) –</td>
<td>0.77 (0.29-2.09)</td>
<td>6 (45) 0.613</td>
<td>0.30 (0.04-2.33)</td>
</tr>
<tr>
<td>Males</td>
<td>– 0 (28) –</td>
<td>1.58 (0.75-3.36)</td>
<td>10 (54) 0.232</td>
<td>– –</td>
</tr>
<tr>
<td>Both sexes</td>
<td>– – –</td>
<td>1.21 (0.67-2.19)</td>
<td>16 (99) 0.523</td>
<td>– – –</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>– 0 (34)</td>
<td>0.85 (0.46-1.58)</td>
<td>14 (74) 0.610</td>
<td>0.53 (0.12-2.40)</td>
</tr>
<tr>
<td>Males</td>
<td>0.58 (0.19-1.77)</td>
<td>4 (26) 0.341</td>
<td>0.82 (0.53-1.25)</td>
<td>39 (76) 0.347</td>
</tr>
<tr>
<td>Both sexes</td>
<td>– – –</td>
<td>0.83 (0.58-1.18)</td>
<td>53 (195) 0.304</td>
<td>0.61 (0.24-1.58)</td>
</tr>
</tbody>
</table>

CI = confidence intervals; HR = hazard ratio.

a) n = number of migrant deaths; (n) = number of deaths among Danish-born controls.

TABLE 2

Adjusted mean hazard ratios of cancer mortality estimated by region of origin. Hazard ratios are adjusted for age, disease stage, co-morbidity and income. Danish-born controls form the reference group. Analyses are based on data from the 1.1.1994-31.12.2007 period from the Danish Cancer Registry.
hospital treatment. This also includes free of charge interpreter services, which most likely enhances treatment compliance. ii) Still, informal barriers to access including language and communication problems as such may hamper migrants’ access to health-care services. However, a recent Danish study of cancer patients found no differences for migrants compared with Danish-born patients in perceived emotional support delivered by health-care professionals at the largest oncology department in Denmark [18]. In this context, emotional support is hypothesised to be of importance to treatment compliance. iii) Lastly, cancer treatment in Denmark is widely performed according to uniform guidelines, which may further help prevent inequality in the treatment given.

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LITERATURE
18. Kristiansen M, Thernhall-Thomsen T, Krasnik A. The benefit of meeting a