Are data from general practices suitable for survival analyses in the field of breast cancer? A retrospective study conducted in the United Kingdom, France and Germany

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Abstract. The aim of the present study was to investigate the suitability of data obtained from general practices in the UK, France, and Germany for survival analyses in the field of breast cancer (BC). This study included women diagnosed with BC between 2004 and 2008 in 416, 322 and 210 general practices in the UK (n=4,085), France (n=1,198) and Germany (n=2,934), respectively. The outcomes of the study were the mean duration of follow-up in years and the proportion of participants followed for at least 5 years. The mean duration of follow-up was 7.5-9.6 years in the UK, 7.4-8.8 years in France and 6.3-8.5 years in Germany. The proportion of patients followed for at least 5 years was 80-91% in the UK, 68-78% in France, and 55-76% in Germany. The data obtained in general practices in the UK appeared to be more suitable for survival analyses in the field of BC when compared with those obtained in France and Germany.

Introduction

Breast cancer (BC) is the most frequent cancer in women and the second most common cancer in the general population worldwide, with approximately two million new cases in 2018 (1). BC mortality rates have recently decreased in high-income countries, and this declining trend is likely explained by the early detection and improved treatment of this cancer (2). The average 5-year survival rate for women with invasive BC is about 90%, and, since BC is considered a chronic condition, and since this disorder has a substantial impact on health (3,4), the long-term follow-up of patients with BC is of particular importance.

The management of BC survivors is multidisciplinary and involves a wide range of health professionals (e.g., physicians, nurses, psychologists). The specialist in charge of BC management can be either the oncologist or the gynecologist, depending on the country in question (5-7). Although the specific role of general practitioners (GPs) in the care of individuals with BC is not well defined, the importance of GPs has increased steadily in recent years. A cross-sectional questionnaire study including 317 GPs from Norway reported that 17 and 62% of them provided follow-up care to women with BC on a regular basis less than and more than five years after treatment respectively (8). More recently, a survey of 740 cancer patients showed that a substantial proportion of them visited GP practices for several reasons (e.g., blood test, complaints and side effects, comorbidities) during their cancer therapy, and that 54% of participants reported being satisfied with their primary care physician (9). These studies have advanced our knowledge about the role played by GPs in the management of people affected by BC.

Epidemiological studies using survival analyses may benefit from data obtained from GP practices. However, in order to be methodologically valid, these studies require the survival time to be similar to the follow-up time. Unfortunately, little is known about the duration of follow-up in BC patients in GP practices after the diagnosis of cancer, and it is possible that BC survivors change doctors more frequently than people with other conditions (e.g., osteoporosis, diabetes, hypertension). This may be due to several reasons, such as the primary care physician's lack of experience with cancer or his/her lack of empathy (10,11).

Therefore, the goal of this study was to investigate the suitability of data obtained from general practices in the UK, France, and Germany for survival analyses in the field of BC.

Materials and methods

Database. This retrospective study was based on data from the Disease Analyzer database (IQVIA). This database compiles demographic, clinical, and pharmaceutical data obtained in

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an anonymous format from the computer systems used in clinical practices (2). The quality and accuracy of the data (e.g., diagnoses, drug prescriptions) are regularly assessed by IQVIA. Using prescription statistics for several drugs and age groups for several diagnoses, the Disease Analyzer database was shown to be representative of clinical practices in Germany (12). Finally, this database has already been used for several studies focusing on BC (13,14).

Patients and outcomes. This study included data obtained from women diagnosed for the first time with BC (International Classification of Diseases, 10th revision: C50) between 2004 and 2008 in 416, 322, and 210 GP practices in the UK, France, and Germany respectively (index year). Women were selected only if they had not been diagnosed with another cancer (C00-C99) (Fig. 1).

The outcomes of the study were the mean duration of follow-up in years and the proportion of women with BC followed for at least five years. These outcomes were studied in different age subgroups (i.e., ≤50, 51-60, 61-70, >70 years).

Statistical analysis. The present retrospective study used descriptive statistics only. Differences in the mean follow-up time between the three countries were tested using Kruskal-Wallis tests (data were not normally distributed). $P<0.05$ was considered to indicate a statistically significant difference. All analyses were carried out using SAS 9.4 (SAS Institute, Cary, USA).

Results

The study included 4,085 women from the UK, 1,198 from France, and 2,934 from Germany (Table I). The mean age was 60.0 years (SD=4.7 years) in the UK, 61.7 years (SD=12.6 years) in France and 62.5 years (SD=12.4 years) in Germany. The mean duration of follow-up was 7.5-9.6 years in the UK, 7.4-8.8 years in France and 6.3-8.5 years in Germany ($P<0.03$) (Fig. 2). The proportion of patients followed for at least five years was 80-91% in the UK, 68-78% in France, and 55-76% in Germany (Fig. 3). Women aged >70 had the shortest duration of follow-up.

Discussion

This is the first study investigating the suitability of data obtained in general practices for survival analyses in the field of BC. We found that a substantial proportion of participants with this cancer were followed for less than five years in France and Germany. Therefore, the data obtained from general practices in these two countries may not be appropriate for survival analyses in the context of BC. By contrast, more than 80% of BC patients were followed for at least five years in the UK.

Survival analyses, also known as time-to-event analyses, are a branch of statistics focusing on data where the dependent variable is the time until the occurrence of an event of interest (e.g., death, metastasis, depression). One major characteristic of survival analyses is that data are usually censored, meaning that the information about the survival time of some individuals is incomplete (15). Although there are several statistical methods that take censoring into account, censored

Table I. Baseline characteristics of study patients.

Variables	UK	France	Germany
Total n	4,085	1,198	2,934
Age in years, mean (SD)	60.0 (4.7)	61.7 (12.6)	62.5 (12.4)
Age, years			
≤50	27.8	22.4	18.8
51-60	26.2	26.4	22.9
61-70	21.9	23.2	30.9
>70	24.1	28.0	27.5
Year of initial diagnosis (index year)			
2004	19.7	12.8	23.2
2005	19.9	18.8	20.2
2006	20.5	22.8	19.2
2007	19.2	22.8	18.8
2008	20.7	22.8	18.6

SD, standard deviation.

samples can undermine the findings of survival analyses, and one should bear in mind that not all data are suitable for this type of analysis.

There are several hypotheses that could explain why the mean duration of follow-up was relatively short and the proportion of participants followed for more than five years relatively low in general practices in Germany. For example, a recent study including 464 Danish GPs reported substantial variation in empathy between physicians, and this variation was significantly associated with several factors, such as the physician-patient relationship and physicians' interactions with their colleagues (11). Since the diagnosis of BC has major psychological effects (16), women with BC may be more likely than women with other chronic conditions (e.g., osteoporosis, hypertension, diabetes) to change doctors when they identify a lack of empathy in their physician. Another survey of primary care physicians showed that lack of formal training with regard to cancer was a problem for almost half of the responders (47%) when treating cancer survivors (10). Therefore, a lack of experience with BC may sometimes motivate general practitioners to refer women suffering from this condition to other primary care physicians or specialists (e.g., gynecologists, oncologists). In addition, the occurrence of complications requiring specialized care may explain the discrepancy between the proportion of participants with BC who were followed for at least five years in general practices in both Germany and France (i.e. <80%) and the proportion of BC survivors five years after cancer diagnosis (i.e. >80%) (17). For example, a prospective study of Canadian women with BC estimated that the prevalence of bone metastases is around 6.5% five years after BC diagnosis (18), while heart failure and cardiomyopathy are frequent after adjuvant therapy for this cancer (19).

Our findings indicate that, although the data obtained from general practices are important for the improvement
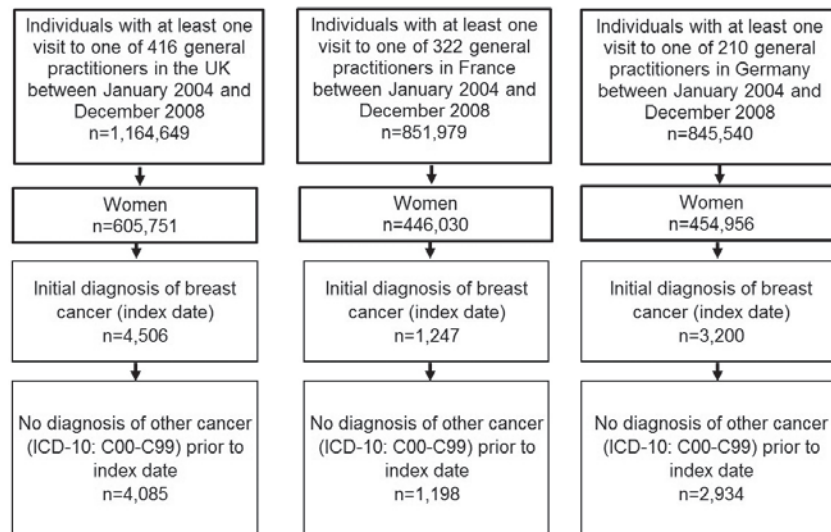
Figure 1. Flowchart presenting the methodology involved in the selection of study patients.
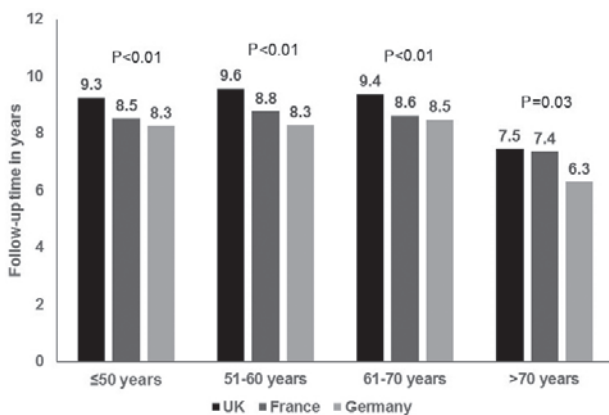

Figure 2. Mean duration of follow-up in patients with BC in the UK, France and Germany. BC, breast cancer.
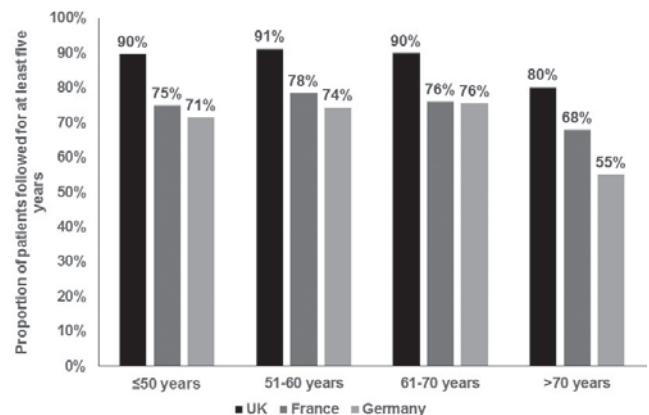

Figure 3. Proportion of patients with BC in the UK, France and Germany followed for at least 5 years. BC, breast cancer.

of our understanding of the epidemiology of BC, one major point should be considered before conducting survival analyses using these data. Researchers should ensure that the mean follow-up of patients is sufficient and that it is not vastly different from the mean survival time. If this is not the case, it may affect the validity of studies with long-term outcomes, such as mortality at five years or metastases at 10 years. Since a substantial proportion of the individuals censored may have simply changed doctors, using an unique personal identification number for each patient may help overcome this issue in the future (20). Finally, further research is needed to gain a better understanding of the factors that may impact the follow-up of BC survivors in general practices in Europe and other areas of the world.

The major strengths of this study are the use of data from three countries and the number of patients available for analysis. However, the results of this study should be interpreted in light of several limitations. Firstly, if a participant visited another GP, this visit would not have been documented in the database and this participant would have been censored. Secondly, there was no information on the factors that potentially impacted the follow-up of women with BC (e.g., lack of empathy displayed by the primary care physician, a physician's lack of experience with cancer, development of complications). Finally, it is possible that there were differences in terms of data completeness between the UK, France, and Germany, which could explain the discrepancy in the findings that were observed between these three countries.

Overall, the data obtained from general practices in France and Germany may be inappropriate for survival analyses in the field of BC. Future studies are needed to corroborate or refute the present findings and to investigate the potential factors impacting the follow-up of women with BC in general practices.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

LJ designed the study, interpreted the data, and drafted and revised the manuscript. KK conceived and designed the study, performed statistical analysis, interpreted the data, and revised the manuscript. MK and GH interpreted the data, and revised the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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