RESEARCH ARTICLE

Five-Year Survival is Not a Useful Measure for Cancer Control in the Population: an Analysis Based on UK Data

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Abstract

Background: Five-year survival is an important metric for progress in cancer control broadly used both in the cancer literature and by the public. In order to assess its validity and relation to other common metrics, we analyzed the relationship between 5-year survival, incidence and mortality using publicly available cancer registry data from England and Wales. **Methods:** Five-year survival, incidence and mortality data were obtained from the online database of a registered charity, Cancer Research UK. We extracted sex-specific age-standardized mortality, incidence, and 5-year survivalfor16 types of cancer over the period from 1976 to 1995. The relationships between 5-year survival, incidence and mortality were estimated using both Pearson and Spearman correlation coefficients. **Results:** All 16cancer types showed an increase in 5-year survival for both genders from 1976 to 1995, ranging from 0.2% (pancreas and lung cancer) to 16.6% (prostate cancer) for males and 0.2% (pancreas cancer) to 16.6% (leukemia) for females. From 1976 to 1995, there was no significant correlation between changes in 5-year survival and cancer mortality for either sex (males, Pearson r=0.16, Spearman r=-0.06; females, Pearson r=-0.33, Spearman r=-0.43). A positive relationship between 5-year survival and incidence was noted among males, but not among females (males, Pearson r=0.61, Spearman r=0.53; females, Pearson r=0.03, Spearman r=0.11). However, after excluding breast and prostate cancer, the positive association became weaker and became statistically non-significant for males (Pearson r=0.47; Spearman r=0.41). **Conclusions:** Our findings suggest that there are no reliable relationships between changes in 5-year survival and cancer incidence or mortality. Increases in 5-year survival might therefore represent poor indicators of progress in cancer control at the population level. In the absence of over-diagnosis, 5-year survival might only indicate improved diagnosis and treatment in clinical practice.

Keywords: Cancer control- surveillance- incidence- mortality- 5-year survival

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Introduction

Cancer is the most common cause of death in developed countries and the second most common cause of death in developing countries (World Health Organization). It is estimated that the global burden of cancer will rise from 12.7 million cases in 2008 to 20.3 million by 2030 as a result of population growth, aging, and an increase in the prevalence of cancer-related risk behaviors (Ferlay et al., 2010; Jemal et al., 2011; Bray et al., 2012).

In the context of the increasing burden of cancer, preventive and therapeutic interventions are being developed for cancer control and evaluated for their impact on populations. Multiple indicators have been used to measure progress regarding cancer control. Cancer mortality and incidence are widely used to assess the burden of disease due to cancer. Cancer incidence is commonly defined as the number of new cases of cancer per 100,000 persons during a specific time period, while mortality is commonly defined as the number of cancer deaths per 100,000 people. Cancer mortality is often used as the gold standard measure for determining progress in cancer prevention and control as it is less subject to confounders (Arnold, 2003). Although incidence is often used to describe the burden of cancer, it might be problematic when used for comparisons across regions and time periods due to artifact effects stemming from differences in diagnostic criteria. Another common

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indicator is 5-year survival, which attempts to capture disease prognosis in terms of survival after diagnosis. The metric is defined as the proportion of cancer patients who are still alive 5 years following diagnosis. Improvements in5-yearsurvivalare commonly regarded as a utile metric for measuring progress in combating cancer (Sankaranarayanan et al., 2010; Maruvka et al., 2014; Welch et al., 2975; Karim-Kos et al., 2981). However, the utility of this measure is restricted by the potential for length time bias and lead-time bias in cancer screening (Schmidt, 2006). Moreover, the metric does not capture the impact of incomplete and poor quality incidence and follow-up data in registries.

In an analysis of registry data from the USA, changes in 5-year cancer survival were found to correlate with changes in cancer incidence, while no correlation was found between changes in5-yearsurvival and mortality (Welch et al., 2975). Based on cancer registry data from both the USA and Australia, after controlling for rising incidence, there was a highly significant correlation between changes in cancer-specific 5-yearsurvival and cancer mortality (Lichtenberg). Similarly, a negative correlation was noted between 5-year survival rates and the ratio of mortality over incidence in a separate study (Maruvka et al., 2014). Despite the disparate findings, these studies consistently demonstrate that 5-year survival may be more useful in assessing clinical management of cancer than overall progress regarding cancer control. To revisit the utility of 5-year survival as an indicator for progress, we extracted UK cancer data from online databases and investigated the relationships between changes in sex-specific 5-year survival, cancer mortality and cancer incidence.

Materials and Methods

Data sources

Five-year survival, incidence and mortality data were obtained from the online databases of Cancer Research UK, a major cancer research charity, which compiles and summarizes epidemiological data from the Office for National Statistics (ONS) (Quinn and Britain, 2001) and original studies (Quaresma et al., 2015). The ONS is a UK government organization that gathers and publishes population, economic and societal indexes for the country. All reported data are age-standardized to the 2013 European standard population (The Office of National Statistics, 2013).

We extracted sex-specific data for 20 cancer site types, including the esophagus, stomach, colon, rectum, pancreas, larynx, lung, malignant melanoma, breast, cervix, uterus, ovary, prostate, testis, bladder, kidney, brain, non-Hodgkin's lymphoma, multiple myeloma, and all leukemias. Five-year survival and mortality data are presented for both England and Wales in the Cancer Research UK website for 1971-2011. The database also presents incidence data for 1975-2011. However, survival data for some cancer types were not available for 1996-2000, 2001-2003, and 2005-2009.In addition, survival data for malignant melanoma, testicular cancer, non-Hodgkin's lymphoma, and multiple myeloma were not available in Wales. Since our study analyzed combined data for England and Wales, we ultimately only utilized survival data for 16 cancer types for 1976-1980, 1981-1985, 1986-1990, and 1991-1995, and incidence and mortality data for 1976-1995.

Statistical analysis

Data were analyzed using IBM SPSS 19.0 (Armonk, New York, USA). All tests were two-tailed and at 0.05 significance level. We adopted a statistical analysis plan similar to that utilized in an earlier investigation (Welch et al., 1975). First, for each cancer type, we estimated the absolute change in 5-year survival rates from 1976-1980 and 1991-1995. We made the same calculation for incidence and mortality rates from 1976-1995. Pearson correlation measures were used to analyze the relationship between changes in 5-year survival and changes in incidence and mortality. In nonparametric analyses, Spearman correlation measures were used to account for possible extreme outliers for certain observations. Second, we repeated the analysis across different time periods - i.e. 1981-1985 versus 1991-1995, and 1986-1990 versus 1991-1995. Since breast and prostate cancer are particularly subject to potential over-diagnosis and survival bias due to screening (Esserman et al., 2009), we repeated the analysis after excluding these two cancer types.

Results

Summary of changes in incidence, mortality, and 5-year survival

All 14 cancer types showed an increase in 5-year survival for both genders from 1976 to 1995, ranging from 0.2% (pancreatic and lung cancer) to 16.6% (prostate cancer) for males and 0.2% (pancreatic cancer) to 16.6% (leukemia) for females. During this time interval, there was an increase in male esophageal, prostate, kidney and brain cancer mortality and a decrease in the mortality for six male cancer types. Similarly, female esophageal, lung, bladder and kidney cancer exhibited a rise in mortality, while other female cancer types showed a decline. Incidence for male stomach, pancreatic, laryngeal, and lung cancer and for female stomach, rectal, and cervical cancer declined, while all other cancer types saw an increase in incidence (Table 1).

Five-year survival, mortality and incidence from 1976 to 1995

Overall trends showed a poor relationship between absolute change in 5-year survival and cancer mortality from 1976-1995 for both genders (Figure 1). Consistent with this observation, there was no significant correlation between changes in 5-year survival and cancer mortality for any specific cancer type among either gender (males, Pearson r=0.16, Spearman r=-0.06; females, Pearson r=-0.33, Spearman r=-0.43) (Table 2).

There is evidence of a positive association between changes in5-year survival and incidence for males, but not for females (Figure 2). This positive association for males was confirmed through statistical analyses, although

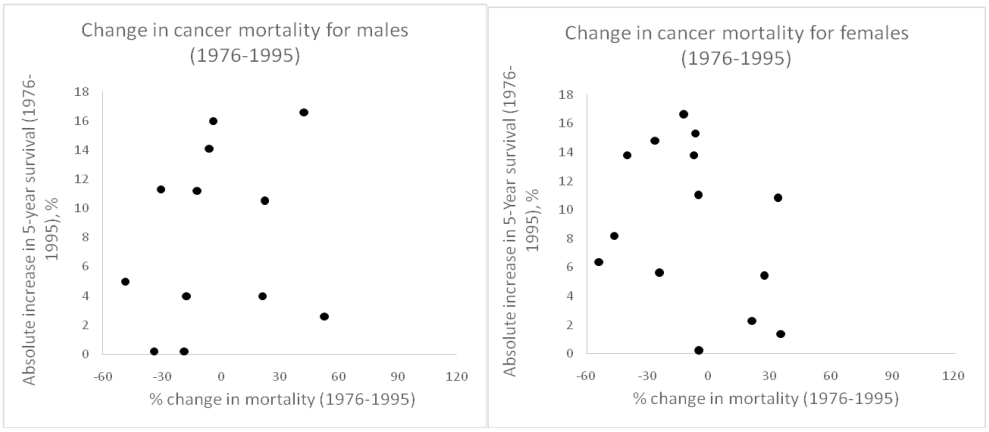

Figure 1. Relationship between the Change in 5-Year Survival and the Change in Mortality for 16 Types of Cancer in England and Wales

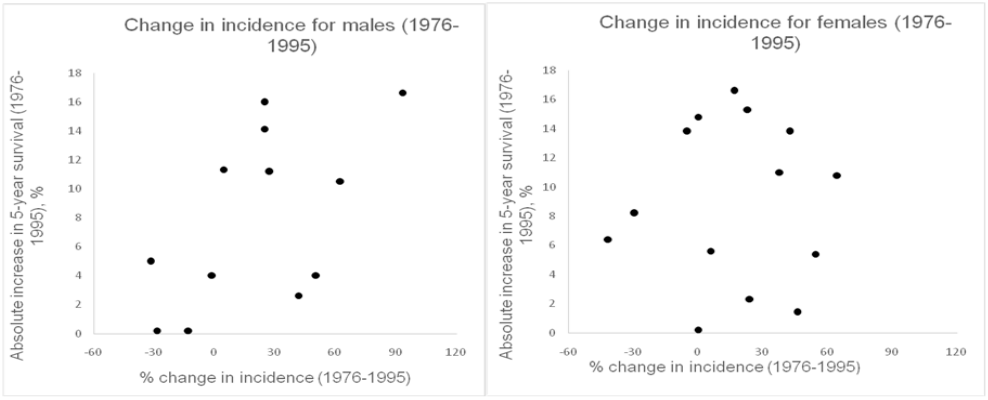

Figure 2. Relationship between Change in 5-Year Survival and the Change in Incidence for 16 Types of Cancer in England and Wales

Table 1. Changes in 5-Year Survival, Mortality, and Incidence for 16 Types of Cancer in England and Wales

Site	5-year Survival, %				Absolute increase 5-year% in Survival,		Change (1976-1995),%			
	1976-1980		1991-1995				Mortality		Incidence	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
Esophagus	3	6	5.6	8.3	2.6	2.3	53	20.9	41.6	23.9
Stomach	5	6	10	12.4	5	6.4	-48.6	-54.1	-31.7	-41.7
Colon	28	28	42.1	42.8	14.1	14.8	-5.6	-26.7	24.8	0
Rectum	29	31	40.3	44.8	11.3	13.8	-30.6	-40.5	4.3	-5
Pancreas	2	2	2.2	2.2	0.2	0.2	-18.3	-5.1	-13.4	0
Larynx	58	-	62	-	4	-	-17.2	-	-1.7	-
Lung	5	4	5.2	5.4	0.2	1.4	-34	35	-28.6	45.9
Breast	-	59	-	72.8	-	13.8	-	-8	-	42.5
Cervix	-	54	-	62.2	-	8.2	-	-46.8	-	-29.5
Uterus	-	65	-	70.6	-	5.6	-	-24.4	-	5.7
Ovary	-	44	-	59.3	-	15.3	-	-7.1	-	23
Prostate	37		53.6		16.6		42.6		93.2	-
Bladder	53	48	64.2	59	11.2	11	-11.8	-5.7	26.9	37.7
Kidney	31	29	41.5	39.8	10.5	10.8	22.4	33.3	62.1	64.5
Brain	9	10	13	15.4	4	5.4	21.3	26.7	50	54.3
All leukemias	16	17	32	33.6	16	16.6	-3.9	-12.5	24.7	16.7

females did not demonstrate a similar relationship (males, Pearson r=0.61, Spearman r=0.53; females, Pearson r=0.03, Spearman r=0.11).

Five-year survival, cancer mortality and incidence from 1981 to 1995 and from 1986 to 1995

The absolute change in 5-year survival showed no

Table 2. Correlation between the Change in 5-Year Survival and the Change in Mortality and Incidence for 16 Types of Cancer in England and Wales (1976-1995)

	Correlation with change in 5-year	survival (1976-1995)		
	Pearson r		Spearman r	
		All cancer types		
	Males	Females	Males	Females
Change in mortality	0.16	-0.33	-0.06	-0.43
Changein incidence	0.61*	0.03	0.53**	-0.11
	Excluding breast and	prostate cancer		
	Males	Females	Males	Females
Change in mortality	-0.04	-0.34	-0.2	-0.43
Change in incidence	0.47	-0.04	0.41	-0.14

*P, 0.012; **P, 0.036

Table 3. Correlation between the Change in 5-Year Survival and the Change in Mortality and Incidence for 16 Types of Cancer in England and Wales (1981-1995)

	Correlation with change in 5-year	survival (1981-1995)		
	Pearson r		Spearman r	
		All cancer types		
	Males	Females	Males	Females
Change in mortality	0.32	-0.24	0.21	-0.4
Change in incidence	0.65*	0.2	0.53**	0.16
	Excluding breast and	prostate cancer		
	Males	Females	Males	Females
Change in mortality	0.09	-0.23	0.09	-0.36
Change in incidence	0.42	0.06	0.44	-0.02

*P, 0.007; **P, 0.033

Table 4. Correlation between the Change in 5-Year Survival and the Change in Mortality and Incidence for 16 Types of Cancer in England and Wales (1986-1995)

	Correlation with change in 5-year	survival (1986-1995)		
	Pearson r		Spearman r	
		All cancer types		
	Males	Females	Males	Females
Change in mortality	0.38	-0.15	0.34	-0.41
Change in incidence	0.78*	0.32	0.65**	0.19
	Excluding breast and	prostate cancer		
	Males	Females	Males	Females
Change in mortality	0.05	-0.11	0.22	-0.33
Change in incidence	0.51	0.2	0.55***	0.01

*P, 0.000; **P, 0.007; ***P=0.04

correlation with changes in mortality for either males or females from1981-1995 (males, Pearson r=0.32, Spearman r=0.21; females, Pearson r=-0.24, Spearman r=-0.4) (Table 3). Similar results were obtained for the relationship from 1986-1995 (Table 4).

A positive relationship between changes in5-year survival and incidence was noted for males both from 1981 to 1995 (Pearson r=0.65, Spearman r=0.53) and from 1986 to 1995 (Pearson r=0.78, Spearman r=0.65). However, we did not observe such a finding among females during either time interval.

Other analyses

Since over-diagnosis and population aging may inflate both incidence and 5-year survival statistics, we performed repeated our analyses after excluding the two most over-diagnosed cancer types, breast cancer for females and prostate cancer for males (Table 2-4). Consistently, all positive associations between 5-year survival and cancer incidence were weaker than before and became statistically non-significant, except that from 1986-1995.

Discussion

Concerns remain for the utility of different indicators

for assessing progress regarding cancer control. One major contemporary question considers the value of 5-year survival as a population metric for cancer progress. Our findings show that 5-year survival in cancer is not associated with changes in mortality, which is consistent with an earlier finding based on registry data from the USA (Welch et al., 2000).

Our findings highlight the potential limitations of using 5-year survival as a population measure for cancer progress. Mortality, incidence and 5-year survival play important roles in analyzing the current burden of cancer and allocating resources for cancer control (Vostakolaei et al., 2010). They are cited in reports as comprehensive indicators of progress against cancer. These approaches posit that progress would correlate with increases in 5-year cancer survival and decreases in mortality and incidence. In contrast to these assumptions, our analysis shows that increases in 5-year survival were not associated with changes in cancer mortality or incidence for either males or females in the UK. Mortality is regarded as the most robust measure of progress against cancer (Sondik, 1990). It is thus risky to use improved survival alone to monitor progress regarding cancer treatment and control.

Increased 5-yearcancer survival, as observed in 1975-1995 registry data from England and Wales, may have been due to several factors. First, improvements in social environments, such as better health, employment and education, may have contributed to an extension of survival (Wang and Guo, 2012). Second, this extension may reflect advances in oncology which have made primary and secondary interventions more

successful in prolonging life with cancer (Altekruse et al., 2012). Third, early detection and screening may push back the time of diagnosis and thereby increase 5-yearsurvival due to lead-time bias. This would represent early diagnosis without a change in the course of disease such that patients are observed at earlier stages in the disease process and therefore appear to live for a longer period post-diagnosis. In this regard, 5-yearsurvival may not provide evidence for progress against cancer, or even for improvements in clinical management.

Realizing that indolent cancers might be more subject to lead-time bias, we repeated our analyses after excluding prostate and breast cancer, which are subject to screening procedures with relatively low specificity and are therefore commonly over-diagnosed. However, results for the relationship between 5-year survival and mortality did not change, whereas the positive relationship between 5-year survival and incidence became statistically non-significant. Widespread population screening with mammography and prostate specific antigen testing has contributed to an accentuation of lead-time bias and over-diagnosis of breast and prostate cancer (Borre et al., 2011). The rate of over-diagnosis ranges from 23% to more than 60% for prostate cancer, and10% to 30% or more for breast cancer (Etzioni et al., 2013). Logically, the number of cancer cases diagnosed should not impact survival. The positive correlation between 5-year survival and incidence may reflect the impact of changes in clinical practice such as diagnosis of subclinical cases, leading to early diagnosis of some cancer types. This suggestion is strengthened by the observation that the correlation became statistically non-significant after the exclusion of breast and prostate cancer. In this regard, we suspect that over-diagnosis may be inflating the relationship between incidence and 5-year survival.

Consequently, due to the potential for over-diagnosis, lead-time bias, and length time bias, the utility of 5-year survival as a benchmark might be restricted to the clinical management of cancer (Lichtenberg). It can be particularly useful in clinical trials comparing various cancer therapies (Arnold, 2003). Moreover, the value of this measure further diminishes with regard to commonly indolent cancers such as breast cancer, prostate cancer, and thyroid cancer (Welch et al., 2011). Researchers, policy makers and the media should therefore avoid using 5-yearsurvival data alone to evaluate progress in cancer control. Five-year survival data may, ideally, only complement mortality and incidence data at the population level.

This study is subject to a number of limitations. Certain cancer types and data before 1971 and after 1995 were excluded from our analyses because of the focus on data available for both England and Wales. This exclusion may limit the validity of our findings, particularly because we did not use more recent statistics that might have better quality. It may have been advantageous to analyze these relationships using data from an older age group less prone to over-diagnosis. Older patients are generally diagnosed using routine tests and procedures that show greater specificity in detecting cancer. Limiting analyses to this cohort may produce a more definitive answer regarding the utility of 5-year survival.

Our findings suggest that there are no reliable relationships between changes in 5-year survival and cancer incidence or mortality. An increase in 5-year survival does not correspond to a significant reduction in mortality. 5-year survival may not signify progress in cancer control at the population level and may only indicate improved diagnosis and treatment in clinical practice. Even this relationship will hold only in the absence of over-diagnosis.

Competing Interests

We have read and understood the Chinese Journal of Cancer policy on declaration of interests and declare that we have no competing interests.

Authors' Contributions

SQL, XFP, HJL, YYW, and CXY designed the study and performed data analysis. SQL, XFP, MSK, and QPX prepared the manuscript.

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