The Epidemiologic Transition Revisited: Incorporating Into This Seminal Theory What We Now Know About Cancers

Omer Gersten[1,*], Magali Barbieri[1,2], John R. Wilmoth[1]

EXTENDED ABSTRACT

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[1] Demography Department, University of California at Berkeley.
[2] Institut national d'études démographiques (INED).
[*] Author for correspondence. UC Berkeley Dept. of Demography, 2232 Piedmont Avenue, Berkeley, California 94720-2120, PHONE: (510) 643-4595 (office) or (510) 642-9800 (dept), FAX: (510) 643-8558, EMAIL: omer@demog.berkeley.edu, WEB: http://www.demog.berkeley.edu/~omer

Abstract

The conventional wisdom in the field of demography is that high-income countries have now moved beyond Omran's third stage of the epidemiologic transition and into what some have labeled a fourth stage, or even a fifth stage, of the transition. This claim is based on the premise that overall mortality trends have for some time now been driven mostly by degenerative diseases rather than infectious diseases, as the latter have reached such low levels that progress against them is unlikely to influence future trends in life expectancy. Advocates of the epidemiologic or health transition theories have long consider cancer as a "classic" example of a chronic and degenerative disease. However, relatively recent research has shown that many cancers arise from infectious sources. These infectious sources include *H. pylori*, hepatitis B and C, and the *human papillomavirus*. The findings in this paper, based on data for currently developed countries (the United States, England and Wales, France, and Japan), demonstrate that the health transition has continued to be driven in part by a decline in infectious diseases until a much later date than previously believed, at least with regard to cancer. Thus, we suggest that the populations of many high-income countries have moved only recently beyond Omran's third stage of the epidemiologic transition and that for many others this stage is still relevant and useful for explaining broad changes in contemporary mortality patterns.

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Introduction

Cancer is one of the most lethal conditions in the world, ranking second as a cause of death in the developed world in 2001 and third as a cause of death among developing nations in that same year (Garcia et al., 2007). Although the toll cancer exacts is clearly distressing, a number of countries have reported heartening trends for the condition. That is, among a number of countries, overall cancer rates have begun to decline, sometimes for the first time on record. For instance, in the United States, overall cancer mortality rates rose since the early 1900s when national mortality statistics were first collected. The death rate eventually peaked around 1990, and it has decreased steadily since then (American Cancer Society, 2009; Cole and Rodu, 1996). Similar declines in overall cancer mortality can be found in countries such as those of the European Union (Levi et al., 2004) and Japan (Gersten and Wilmoth, 2002).

Although decreasing trends in overall cancer mortality in a number of countries is certainly a positive development, for many nations cancer is becoming relatively more important because improvements in heart disease mortality have come at an even faster pace. For example, the top cause of death in Japan during 1965-1980 was cerebrovascular diseases, with malignant neoplasms the second leading cause. By 1999, however, neoplasms replaced cerebrovascular diseases as the top-ranked cause of death in Japan (Stallard, 2003). Similarly, from 1991-2006 the US death rate from cancer declined 16%, but in that same period the death rate from heart diseases declined nearly 2 1/2 times that amount (American Cancer Society, 2009).

It is not at all uncommon to find cancer-related statistics referring to overall cancer rates. Such a measure provides some understanding of the degree of progress in reducing the disease's burden. Nevertheless, over 100 different types of cancers exist, many with their own set of causes and trends, and thus site-specific cancer information is crucial for gaining a deeper understanding of these phenomena. In particular, there is a growing body of evidence suggesting that those cancers that have their main cause in infectious sources have experienced the fastest rate of decline in recent decades, whereas those caused by non-infectious factors have increased regularly, at least until the early 1990s in most high-income countries. For this reason the hierarchy of the cancer mortality burden has been completely re-ordered over time.

This shift in importance from cancers of infectious origin to those of noninfectious origin was termed a "cancer transition" by Gersten and Wilmoth (2002), who demonstrated the existence of such a phenomena in a case study of Japanese mortality trends. It remains to be seen whether this finding can be generalized to other countries. Although cancer researchers are well aware of the role of infection in cancer, there has been no systematic analysis of mortality trends due to cancers of infectious and noninfectious origin across developed nations. Documenting the generality of a cancer transition would have relevance even outside the field of cancer research. Indeed, such a finding would reinforce key aspects of Omran's original theory and challenge some more recent interpretations of the epidemiologic transition by other authors.

The next section spells out the theoretical background more fully and is followed by a presentation of the results of our empirical analysis. The paper ends with a summary and discussion of the research and the theoretical implications of our findings.

Theoretical background

Cited over 1000 times, Omran's theory (1971) has become a classic in the field. According to Omran, nations in the second stage of the transition experience less malnutrition, childhood disease, and severe pandemics of infection compared to nations in the first stage, but infectious diseases still remain the leading cause of death. The third and last stage involves lower overall mortality, deaths concentrated at older ages, and a transition to noncommunicable and chronic ailments like "heart disease, cancer and stroke [that] replace infection as prime killers" (Omran, 1971). Writing in the early 1970s, Omran could hardly have known of the role of infection in cancer and other degenerative diseases. However, the presence of the cancer transition as we present it would be in keeping with Omran's idea of the diminishing role of infection.

In other words, the cancer trends we have been witnessing recently still reflect the playing out of a core idea of the third stage of the epidemiologic transition. Such a perspective seems to contradict the suggestion by other authors that the third stage of Omran's epidemiologic transition is less and less applicable to developed countries. Indeed, some have argued that such countries have moved on to a "fourth stage" or even a "fifth stage" of the epidemiologic transition (Feinleib, 2008; Olshansky and Ault, 1986; Rogers and Hackenberg, 1987), whereas we are suggesting that in regard to cancer mortality many countries are still in the third stage of the transition as described by Omran. By establishing a clearer empirical picture of cancer trends over several decades, we hope to enlighten this discussion.

Data and methods

Age-standardized mortality rates for the ten most deadly cancers as well as for all cancers were computed for England and Wales, France, the United States, and Japan from aggregate death counts by age, sex, and calendar year provided by the statistical offices in these countries[1]. For the first three of these four countries, the data is available at the most detailed level of the International Classification of Diseases (ICD). For Japan, the data is only available at the 3-digit level, which we regarded as sufficiently accurate for current purposes. We used data available for the period 1950-2007 for England and Wales, 1950-2005 for France, 1959-2007 for the United States, and 1951-2008 for Japan. The data span the last four or five revisions of the ICD depending on the country.

Table 3 shows the 10 cancer groups investigated here and the corresponding codes of the ICD for the 6th through 10th revisions (WHO, 1992). Age-specific mortality rates were computed for

[1] More specifically, we used data originating fro, the following institutions, in charge of collecting and distributing cause of death data: for France, the *Institut National des Etudes Economiques et Sociales* (INSEE) until 1968 and the *Institut national de la santé et de la recherche médicale* (INSERM) since then; for the United States, the National Office of Vital Statistics until 1960 and the National Center for Health Statistics (NCHS) thereafter; for England and Wales, the Office for National Statistics (ONS); and for Japan, the Vital Statistics Office of the Ministry of Health, Labour and Welfare. We are particularly grateful to France Meslé and Jacques Vallin (Institut national d'études démographiques, Paris) to have facilitated access to the French data, as well as to Shigesato Takahashi (National Institute of Population and Social Security Research, Tokyo) and Futoshi Ishii (National Institute of Population and Social Security Research, Tokyo) to have provided the Japanese data for the periods 1979-1990 and 1995-2005, respectively.

each of these ten cancer categories as well as for all cancers. Age-standardized rates were produced next, using the age structure of the U.S. population at the 2000 census (both sexes combined). Though classification changes can be very disruptive, the disease groupings used for this study appear to be highly consistent over time, except for liver cancers. Disruptions in the liver cancer mortality series are due to difficulties in determining whether a site is primary or secondary when such a specification is lacking or when the cancer is qualified as 'metastatic'. The underlying cause of death in these situations would have been coded as liver cancers in ICD-6, ICD-7, and ICD-8, but not in ICD-9 or ICD-10, with the likely result of underestimating an increasing trend in liver cancer mortality.

Results

[Please see tables and graphs on the following pages. Text for this section will be added later.]

References

American Cancer Society. Cancer statistics 2009: a presentation from the American Cancer Society. 2009. Atlanta, Georgia. Accessed on June 3, 2009 at: http://www.cancer.org/docroot/STT/stt_0.asp

Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res. 2008 Sep;25(9):2097-116. Epub 2008 Jul 15.

Cole P, Rodu B. Declining cancer mortality in the United States. Cancer. 1996. 78:2045-8.

Doll R. The causes of cancer. Rev Epidemiol Sante Publique. 2001 Apr;49(2):193-200.

Feinleib M. The epidemiologic transition model: accomplishments and challenges. Ann Epidemiol. 2008 Nov;18(11):865-7.

Garcia M, Jemal A, Ward EM, Center MM, Hao Y, Siegel RL, Thun MJ. Global cancer facts & figures 2007. American Cancer Society. 2007. Atlanta, Georgia.

Gersten O, Wilmoth JR. The cancer transition in Japan since 1951. Demographic research. 2002 7(5):271-306.

Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Cancer mortality in Europe, 1995-1999, and an overview of trends since 1960. Int J Cancer. 2004 Jun 10;110(2):155-69.

de Martel C, Franceschi S. Infections and cancer: established associations and new hypotheses. Crit Rev Oncol Hematol. 2009 Jun;70(3):183-94.

Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. Milbank Q. 1986;64(3):355-91.

Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. Milbank Mem Fund Q. 1971 Oct;49(4):509-38.

Parkin DM. The global health burden of infection-associated cancers in the year 2002. Int J Cancer. 2006 Jun 15;118(12):3030-44.

Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005 Mar-Apr;55(2):74-108.

Rogers RG, Hackenberg R. Extending epidemiologic transition theory: a new stage. Soc Biol. 1987 Fall-Winter;34(3-4):234-43.

Stallard, E. Diseases, chronic and degenerative. In: Encyclopedia of population. P Demeny, G McNicoll, eds. 2003 (2): 253-258. Thomson Gale: New York.

Table 1. Estimates of total worldwide cancer deaths (year 2002, both sexes)

Cancer site	Total (in 1000s)	% of total	Cumulative %
1. Lung	1178	17.4	17.4
2. Stomach	700	10.4	27.8
3. Liver	598	8.9	36.7
4. Colon/rectum	528	7.8	44.5
5. Breast	410	6.1	50.6
6. Esophagus	385	5.7	56.3
7. Cervix uteri	273	4.0	60.3
8. Pancreas	227	3.3	63.6
9. Leukemia	222	3.3	66.9
10. Prostate	221	3.3	70.2
All others	2022	29.8	100.0

Source: adapted from Parkin, Bray, Ferlay, and Pisani (2002).

Table 2. Top 10 cancers responsible for total worldwide deaths (year 2002, both sexes), by mainly infectious or mainly non-infectious etiology

Main cause(s) of cancer	
Infectious source(s)*	Non-infectious source(s)
Stomach (*Helicobacter pylori*)	Lung (smoking)
Liver (Hepatitis B and C viruses, flukes)	Colon/rectum (age, family history, lifestyle)
Cervix uteri (*Human papillomavirus*)	Breast (lifestyle, reproductive/hormonal)
	Esophagus (drinking, smoking)
	Pancreas (smoking)
	Leukemia (exposure to ionizing radiation)
	Prostate (age, family history)

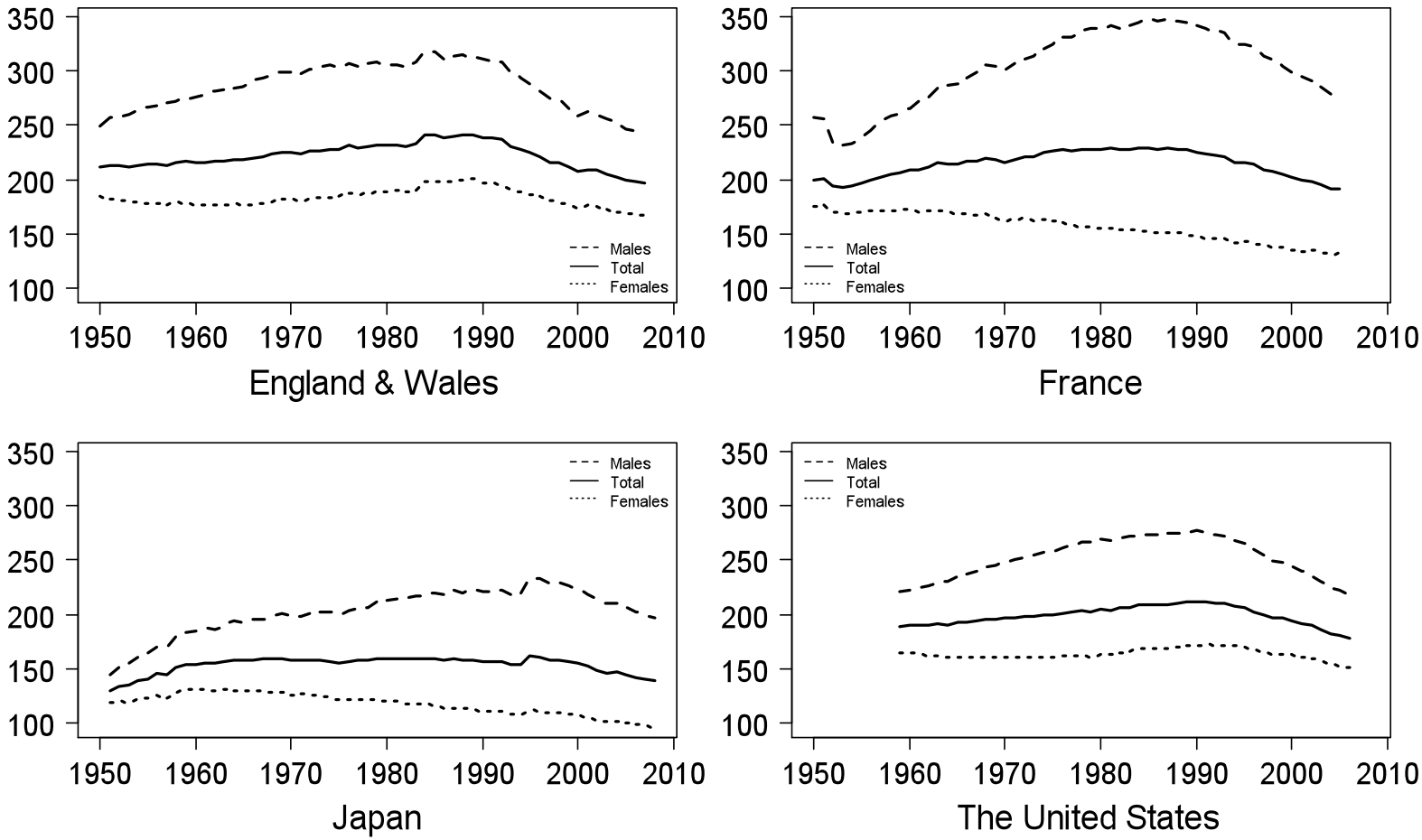
* For cancers of the stomach, liver, and cervix uteri, it is estimated that infection accounts for 64%, 84%, and 100%, respectively, of worldwide cancer deaths at those sites (Parkin, 2006).

Table 3. ICD codes for cancers included in this analysis, 6th through 10th revisions

Type of cancer (by site of primary tumor)	**6th ICD**	**7th ICD**	**8th ICD**	**9th ICD**	**10th ICD**
All sites	140-205	140-205	140-209	140-208	C00-C97
Breast	170	170	174	174	C50
Colo-rectum	153, 154	153, 154	153, 154	153, 154	C18-C21
Esophagus	150	150	150	150	C15
Leukemia	204	204	204-207	204-208	C90-C95
Liver, gallbladder, bile ducts	155,156	155,156	155, 156	155, 156	C22-C24
Pancreas	157	157	157	157	C25
Prostate	177	177	185	185	C61
Stomach	151	151	151	151	C16
Trachea, bronchus, lung	162, 163	162, 163	162	162	C33-C34
Uterus	171-174	171-174	180-182	179-182	C53-C55, C58

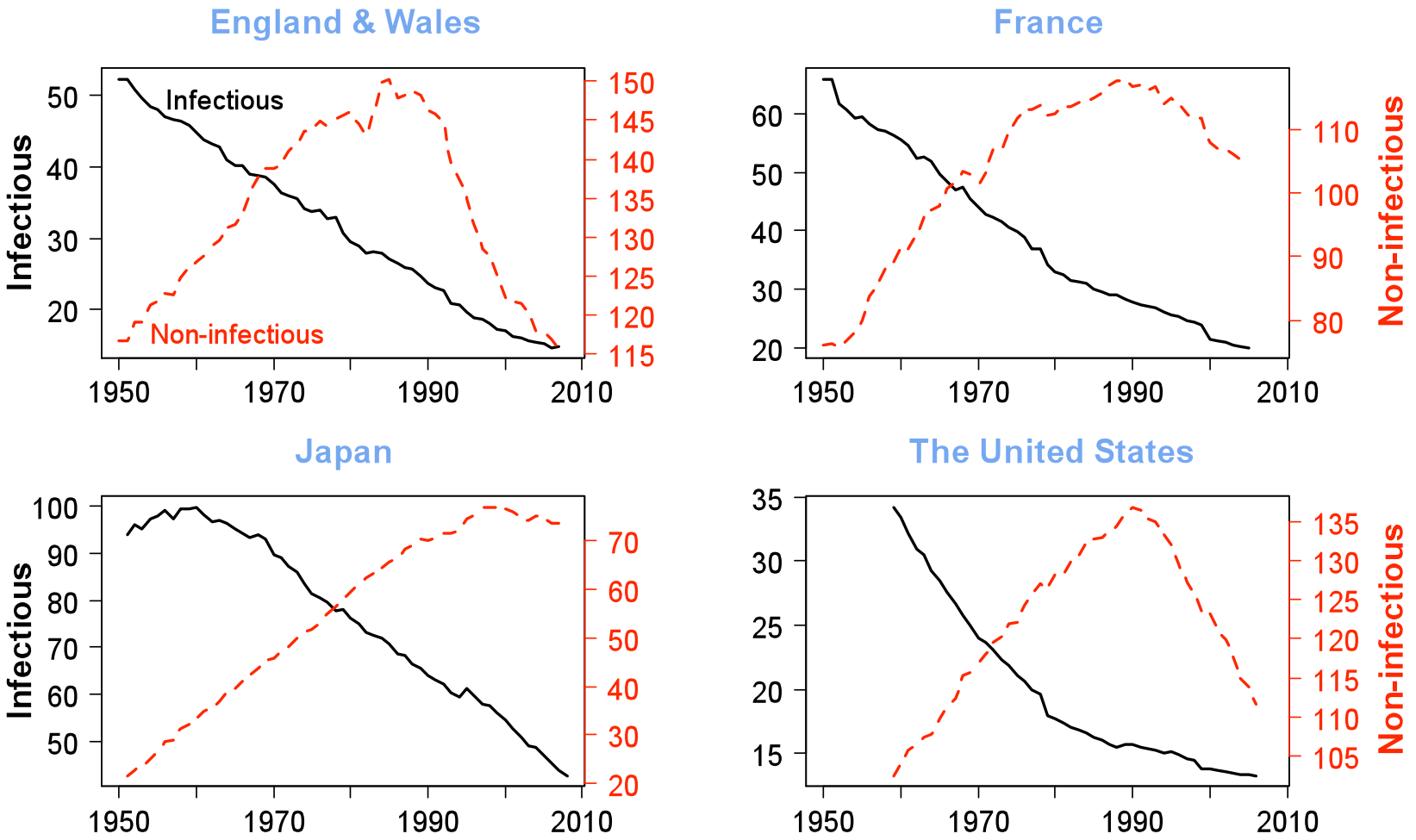
Note: ICD stands for International Classification of Diseases.
Source: WHO, 1992.

Figure 1. *Age-standardized mortality rates from all cancers (per 100,000), by sex, year, and country*



Note: The standard age structure is that of the United States, both sexes, at the 2000 census.

Figure 2. *Age-standardized mortality rates (per 100,000) for selected cancers of infectious and non-infectious origin by sex, year, and country*



Note: the standard age structure is that of the United States, both sexes, at the 2000 census.