

Commentary: Liver cancer and the epidemiological and cancer transition theories

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The article by Shibuya and Yano¹ in this issue investigates the most common form of liver cancer in Japan, hepatocellular carcinoma (HCC). Using log-linear Poisson regression models and addressing the problem of non-identifiability, the authors attempt to tease out the influence of age, period, and cohort effects on HCC mortality. An important conclusion of the article is that HCC death rates are highest in cohorts born around 1930. Another conclusion at the opposite end of the spectrum also deserves to be stressed. That is, the lowest levels of HCC belong to the most recent cohorts. Hepatitis is spread by infection, and steep declines of HCC are expected in 5–10 years in Japan largely because of the widespread vaccination for hepatitis B virus and more recently instituted programs screening donated blood (to be used in transfusions) for hepatitis C virus. Exploiting what is known about the successfully implemented public health efforts that have benefited more recent cohorts to try to make firmer predictions of future death rates would make an additional useful contribution.

In providing a context for the Shibuya and Yano piece, it is useful to consider an extension of the epidemiological transition theory proposed by Gersten and Wilmoth.² They advance the idea of a ‘cancer transition’, the notion that for the cancers that drive overall trends it is those with declining death rates that have their origin mainly in infectious sources, whereas those with increasing death rates have their origin primarily or entirely in non-infectious causes. In essence, there is something of a small-scale epidemiological transition within the broad category of cancers. The cancer transition theory applies at the very least to Japan and probably to other developed nations as well. The cancer transition concept is strengthened by Shibuya and Yano’s finding that liver cancer, which often has an infectious origin, is expected to decline soon.

Arguably the most important feature of Omran’s original theory is that developed countries have mostly made the transition from a health burden mainly comprising acute, infectious diseases (e.g. tuberculosis, smallpox, cholera) to chronic and degenerative ones (e.g. heart disease, stroke, cancers). This shift in disease burden largely characterizes a move from the second to the third and last stage of the epidemiological transition.³ Despite the citation of cancers as a typical third stage, non-communicable disease, we are now more fully aware of the heterogeneity of cancer causes and the fact that some have their source primarily in infection. For instance *Helicobacter pylori*—a bacterium discovered in the early 1980s—can almost be considered a necessary but not sufficient cause of stomach cancer. While a small portion of those infected with the bacterium eventually develop the disease, very few who have stomach cancer do not also have *H. pylori*. In other examples, certain

strains of the sexually transmitted human papilloma virus are main causes of cervical cancer and hepatitis B and C viruses play major roles in the onset of liver cancer. With their root in non-communicable sources, these cancers are not classical chronic and degenerative diseases. Nevertheless, like other chronic and degenerative diseases, stomach, liver, and cervical cancers take years to develop, progressively worsen, strike at older ages, and have death rates that vary relatively little from year to year.

Many experts now observe that with regard to these cancers the traditional line between infectious and non-infectious disease has been blurred. The analysis need not stop here. It is possible to draw on Omran’s framework to conceptualize which cancers become more or less prominent over time. While over a hundred cancers exist, often only a fraction of them account for most of the cancer disease burden in a given country. Lung, stomach, and liver cancers are examples of those that usually drive overall cancer rates. On the one hand, as mentioned before, cancers of the liver, stomach, and cervix mainly derive from an infectious root. On the other, the causes of breast, lung, pancreatic, and colorectal cancer are, as far as is known, entirely or largely non-infectious in nature. The increasing death rates in this latter set of cancers are tied to personal behaviours such as smoking and dietary habits, and other changes that are correlated with economic development. It is precisely those cancers with a root mainly in infection that are declining or that are expected to decline and those with a non-communicable root that are on the increase. This ‘cancer transition’, then, is similar to the broader epidemiological transition from acute and infectious diseases to chronic and degenerative ones. The cancer transition reaffirms the usefulness of Omran’s original framework and poses a challenge to those who would claim that in various ways developed countries have moved beyond the framework.

Lastly, it is interesting to note the parallel between the cohort effect mentioned in Shibuya and Yano’s paper and *H. pylori* infection rates in Japan. As regards HCC, cohorts born in the 1930s were young adults during the period after the Second World War. It has been hypothesized that the depressed conditions following the war contributed to a rise in methamphetamine drug use, especially among young men. Sharing needles to inject the drug intravenously is likely to spread hepatitis in this group resulting in HCC death rates evident years later. Regarding *H. pylori*, it is acquired mainly in childhood and partly spread in settings characterized by food scarceness, poor sanitation, and a low standard of living. Those born during and shortly after the Second World War appear to have the highest rates of infection.⁴ Thus, despite the different mechanisms of transmission, the compromised conditions created by the Second World War and its aftermath seem to have played a major role in cohort HCC and *H. pylori* infection rates. Japan’s rapid development after the war is linked to

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decline in hepatitis and *H. pylori* infection, but an increase in other risk factors for a variety of cancers.

References

- ¹ Shibuya K, Yano E. Regression analysis of trends in mortality from hepatocellular carcinoma in Japan, 1972–2001. *Int J Epidemiol* 2005;**34**:397–402.
- ² Gersten O, Wilmoth JR. The cancer transition in Japan since 1951. *Demogr Res* 2002;**7**:271–306. Available at: <http://www.demographic-research.org>.
- ³ Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q* 1971;**49**:509–38.
- ⁴ Replogle ML, Kasumi W, Ishikawa KB *et al.* Increased risk of *Helicobacter pylori* associated with birth in wartime and post-war Japan. *Int J Epidemiol* 1996;**25**:210–14.