Commentary: Civilization and peptic ulcer 40 years on

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We are happy to see the International Journal of Epidemiology reprint one of our papers\textsuperscript{1} some 40 years after publication. We are not among the deeply sceptical who would deny that understanding marches on with time. Sometimes, as with peptic ulcer, it is a slow march. Some of the mist and mystery surrounding the condition, as well as a degree of disbelief our conclusions provoked, have cleared. Points of entry to much that seemed impenetrable can be discerned.

Here we take up the editor's invitation to tell how the work came to be written. For us, the story begins in 1959, when MS received a letter from the Editor of the Practitioner. That journal planned to publish a symposium on peptic ulcer, and he hoped MS would write a review of its epidemiology. The invitation was a great surprise. We were not long out of troubles in Apartheid South Africa. With equal surprise and great good fortune MS had been appointed Lecturer in Social and Preventive Medicine at Manchester University under Professor C Fraser Brockington. Soon after moving there, ZS was appointed Research Fellow. In epidemiology, both MS and ZS were untaught novices (in the original sense). We could only assume a wand had been waved by one of the benevolent spirits whose paths we had somewhat fleetingly crossed—perhaps Jeremy Morris, or Theodore Fox at The Lancet, or Robert Platt or Douglas Black in the Manchester Department of Medicine, or Cicely Williams (discoverer of Kwashiorkor) at the School of Hygiene. We had at most a half-dozen joint or separate publications of any sort, no track record in the subject of peptic ulcer, and no knowledge of the disease beyond the requirements for the Membership of a Royal College of Physicians. Peptic ulcer was then a rarity in the Black South Africans among whom we had worked.

MS set to work on the literature, beginning with Morris’ Uses of Epidemiology\textsuperscript{2} of 1957. This treasure trove of epidemiological observations and lively ideas had entranced us, not least the idea of diseases of civilization and its identification of coronary heart disease, lung cancer and peptic ulcer as rising epidemics among males of the 20th century. He led us to an intriguing history of peptic ulcer perforations through the 19th century and into the 20th, in which Jennings\textsuperscript{3} identified three successive forms of perforated ulcer. The first, gastric ulcer in young women, appeared as a new disease in the early 19th century; by the end of the century it was disappearing only to be replaced in the 20th century first by gastric and then by duodenal ulcers predominantly in males. Next, we followed the references to Morris and Titmuss\textsuperscript{4} which had the fullest and best analysis of the vital statistics of the disorder up to that time; to the founding field studies of Richard Doll with Avery Jones et al.\textsuperscript{5,6} on the occupational epidemiology of this disease; and to much else that seemed relevant to the epidemiology of the disorder.

To examine changes over time, we assembled the mortality data of the Registrar General from Statistical Reviews 1900–1959 and the Decennial Supplements of 1921, 1931 and 1951. The cross-sectional view of mortality across each period by age were utterly confusing. Age curves criss-crossed in every direction, with no discernible consistency given no foreknowledge. Figure 1a is a greatly refined example—developed much later and much clearer for that—of what confronted us. The only conclusion one could draw was disconcerting: contrary to received opinion, there was no consistent rise in the mortality of the major persisting forms of the disease.

The notion of a rising epidemic as a disease of civilization, however, implied that it was a product of our continuously developing industrial society. Fifteen years before, Morris and Titmuss\textsuperscript{4} evidently beset in the same way by their large body of data, spoke of ‘existing confusion’, and found the results ‘surprising’ and ‘unexpected’, and reported changing and irregular patterns in the different forms of the disorder over time and among social classes. Nonetheless, their most valiant effort at analysis and interpretation indicated positive associations with the metropolitan concentration of London, with the heavy air raids over England in World War II, and with employment, and negative associations with the massive unemployment of the preceding Great Depression of the 1930s. For them, as well as for us and for many others, all this seemed to point to ready psychosocial hypotheses about causes connected with the stresses and strains of a rapidly changing society.

One day while MS was staring balefully at the mortality data as he had come habitually to do, ZS looked over his shoulder and said casually, ‘How about cohort analysis?’? In this regard, we each of us had an arrow in the quiver. Five years before, ZS had taken advantage of a pregnancy for a study leave from the Alexandra Health Centre and University Clinic in an African township outside Johannesburg.\textsuperscript{6} She elected to study under the mentorship of Sidney Kark at his new national training health centre in Durban. Among much else new to us and relevant to our work—which we were doing without any special training whatever excepting our medical degrees and internship—Sidney led her to Wade Hampton Frost’s posthumously published 1939 cohort analysis of tuberculosis.\textsuperscript{7}

MS met cohort analysis later, early in 1956 in London. Newly arrived and without employment, Dr Fox kindly suggested he might report for the Lancet and begin with the next meeting of the Royal Society of Medicine. It turned out to be a memorable...
occasion. First one heard Alice Stewart report her unpublished but now famous work on cancer in children following X-rays in pregnancy (Richard Doll and Sir Ernest Kennaway were among the commentators). RAM Case followed with his paper on ‘Cohort analysis as an historical or narrative technique’, one of the foundation works of the subject to be published later that year.

To return to peptic ulcer, MS followed the lead from ZS, wondering why, as so often, the thought had not also occurred to him. He reassembled the data in conventional form for cohort analysis i.e. 10-year date-of-birth contours (by central year of birth), with year of death along the abscissa and mortality rate along the ordinal. Alas, no evident regularities lit the bleak array of curves. Discouraged, for weeks on end MS resumed staring at the graphs whenever time allowed. Figure 1b is an example of what he had been staring at. Slowly, however, he came to think with relief that he could discern a pattern in the curves for each form of the disorder (gastric and duodenal) and for each sex. Within each cohort, but starting at different points during the 19th century according to the form of the disorder and the sex of the decedent, mortality in successive birth cohorts rose steadily and then declined.

To emphasize the obscurities of the repeated patterns as we then saw them, one need only say that for a longish time Abe Adelstein (then statistician to the department and our close friend and adviser on things numerical and much else) and, ironically, also ZS, wondered if the patterns MS perceived were possibly illusory. After much cogitation, MS settled on a different way of arranging the data, namely in age contours with birth

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**Figure 1** Death rates from duodenal ulcer in males, England and Wales, 1900–77. Reprinted from Susser M J Chronic Dis 1982;35:29–40 with permission from Elsevier Science
year on the abscissa so that cohorts are read vertically upward
from the abscissa across successive age contours (Figures 2a,b).
This device at last made clear the pattern of waxing to a peak for
late 19th century births, and then waning through the births of
the 20th century.

All will understand by now, in the light of theoretical and
technical work on cohort analysis (for instance, by MacMahon
and Terry in 1958 and many authors since), that inference
from it is subject to confounding. In part this arises because
generally the cohort approach must be an ecological analysis,
but centrally because of the structural and unbreakable linkage
between any two of the three variables of birth date, age,
and date of observation. Forty years ago, we certainly did not
ourselves understand all this. Intuitively, we did understand the
need for both external validation of the interpretation and tests
of alternative explanations by all means possible.

MS’s review for the Practitioner, with no more than a mention
of the mortality trend, was published with the symposium in
1961. We did report on the new format in London later that
year at the annual meeting of the Society for Social Medicine
(the annual gathering of the then modest numbers of enthusi-
asts engaged in the subject). There we were heartened, in
the face of doubt and questioning, by the endorsement of our
analysis by Richard Doll, the pre-eminent epidemiologist in the
field.

While the search for validation proceeded we deferred further
publication. The few previous intimations of a decline in mor-
tality or morbidity had been attributed either to the widespread
use of gastrectomy or to such other interpretations as selective
survival and diagnostic fashion. We had collected morbidity data
from several sources, however (the national sickness survey, the
British Army, Navy and Air Force morbidity records, hospital
admissions, and prevalence rates in cross-sectional field surveys
separated by several years). All conformed with the pattern of
recent decline cohort by cohort. These findings we reported
only briefly in the Discussion section of the now reprinted

![Figure 2](image-url)
article. For a final test, namely, a prediction of a continuing decline in mortality shifts in social class, we had to await the next census report on occupational mortality of 1971.11

In the meanwhile Sonnenberg12 had applied cohort analysis to national mortality data sets from many European countries to show similar declines, as others did earlier for morbidity data in England and the US. Yet in conversation with MS as late as 1978, two leading internists from a leading American medical school were incredulous, even dismissive, of our account of the history of peptic ulcer and its decline. We cannot deny a degree of satisfaction, not we hope smug, from the present state of the matter.

References
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3 Jennings D. Perforated peptic ulcer; changes in age incidence and sex-distribution in the last 150 years. Lancet 1940;i:444–47.
4 Morris JN, Titmuss RM. Epidemiology of peptic ulcer, vital statistics. Lancet 1944;i:841–45.

Commentary: Helicobacter as the ‘environmental factor’ in Susser and Stein’s cohort theory of peptic ulcer disease

Barry Marshall

I am not certain how I became aware of the paper by Susser and Stein in Lancet of 1962, I suppose it was from references in another article on peptic ulcer.1 It did amaze me that 20 years before the discovery of Helicobacter pylori the idea of a cohort effect in peptic ulcer had been considered, and various predictions made. Although brilliantly correct about an environmental effect peaking near the turn of the century, Susser and Stein still exhibited some of the tunnel vision regarding ‘stress’ in all its forms as a peptic ulcer aetiology. One of their hypotheses for changes in ulcer mortality involved urbanization stress, its subsequent ‘tolerance’ by communities and, more recently, increased affluence lowering the global urbanization stress level.

Susser and Stein’s first point was that gastric ulcer perforations in young women were a new disease in the beginning of the 19th century, but a peak of the same disease in older women (the same cohort) occurred in the latter half of the 19th century. According to the original authors, the female epidemic related to ‘acute gastric ulcers’ of the cardia, a disease characterized by lack of scarring at the ulcer base and location in the top half of the stomach. Similar perforation increases, but for duodenal ulcer in young to middle-aged men, and for gastric ulcer in older men, were later reported.

In the 20th century however, most of the interesting ulcer mortality related to pylor-duodenal ulcers, and occurred in men. Gastric ulcer mortality peaked in the early 1950s and duodenal ulcer mortality peaked in the late 1950s. Of secondary interest is the fact that the supposed ‘executive ulcer’ never really existed in that no socioeconomic gradient existed for duodenal ulcer in the early 20th century, and its actual predilection for the working classes was well documented after 1940.

To explain some of these observations, we might try to place H. pylori into the above scenario. Although it is difficult to determine the prevalence of H. pylori in previous generations, some assumptions can be made based on the observed age-related sero-epidemiology in the US and from biopsy surveys of Estonians and Japanese in the past 50 years.2,3

First, we may assume that H. pylori was ubiquitous at the turn of the 20th century. Faecal-oral contamination of the water supply was present, families were large, children shared beds and in-house piped running water was uncommon so washing...