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Comments on the paper *"On prognosis"* by William Farr: a forgotten masterpiece

The many contributions of William Farr, the "father of sanitary science" (Newsholme 1899), to the development of classical epidemiology (the study of disease incidence) are widely acknowledged (Susser & Adelstein 1975). Farr's role in the genesis of clinical epidemiology (the study of disease outcomes) is not so well known. It is hoped that by reprinting Farr's 1838 paper *"On prognosis"* this imbalance will be remedied. Farr published the paper in the British Medical Almanack, a journal which is not readily accessible to epidemiologists. Its existence was noted by medical historians such as Garrison (1929), Shryock (1979) and Eyler (1979), but it was not included in the collection of Farr's work edited by Humphreys (1885).

"On prognosis" is an extension of the second of two papers published in the Lancet in 1835 (Farr 1835), based on lectures on "hygiene" given by Farr at his home in Grafton Street, London. In this paper Farr quoted extensively from books I and III of "Epidemics" by Hippocrates. He tabulated, by day of disease, the crises of 41 cases of disease listed by Hippocrates. For comparison he did the same for the crises of 297 cases of typhus reported by Latham. Farr complimented Hippocrates for including information on whether crises ended in death or recovery, which Latham omitted. Farr comments:

> "Whatever the Hippocratic doctrine (of critical days) may be, it is certain that in this country, in France, and in Germany, few diseases terminate of particular days, or at one period; *but I shall be able to show you that the termination or crisis of several, and probably every disease, takes place according to a* determined *law, which may at any time deduced, when observations are sufficiently exact and numerous* (emphasis added)."

Farr's paper begins with quotations from another Hippocratic work, Prognostics, on the definition of prognosis and its importance to the work of the physician. However Farr does not follow his illustrious predecessor in describing the clinical signs of impending death. He emphasises the need for statistical estimates "in collective masses". This application of the law of large numbers, especially in the context of therapeutics, had been proposed earlier by Laplace (1814), and popularised by Louis (1835). It was subsequently decried by Bernard (1966), and was not generally accepted until well into the 20th century.

In the main body of his paper Farr reviews the data then existing on the prognosis for various diseases, and the factors which influence disease outcome. The statistics cited by Farr are of considerable historical interest and are remarkable in the detail provided. Where, in this information age, can one find a table like that which Farr derived from the statistics on the prognosis of diseases in the Madras Army?

Farr was the first to distinguish between two measures of the tendency of a disease to destroy life: the ratio of the number of deaths to the number of cases in a given period; and the ratio of the number of deaths to the number of patient-years of sickness when patients are followed up to death or recovery. The first of these Farr calls simply "mortality", the second the "relative force of mortality". The current terms for these two measures are the case-fatality rate and the hazard rate. It is remarkable that the distinction between the two did not re-enter epidemiological parlance until the middle of the 20th century (Elandt-Johnson 1975).

In his analysis of the effect of age on the case-fatality rate for small pox Farr uses the approach developed by the actuary T.R. Edmonds, which assumes a log-linear relationship after the age of 10, i.e., the first difference of the logarithm of the rate is constant with age. Neither Edmonds nor Farr provide details on the method used to estimate this relationship. Today we would use least squares regression. The method of least squares to estimate the coefficients of a linear equation was introduced by Legendre in 1805, but Farr was not apparently aware of the technique. It is possible that Farr used the method outlined in Table 1 to analyse the small pox data.

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Table 1 Log-linear regression of case-fatality of small pox on age: comparison of Farr's estimate with least squares (Data from the London Small Pox Hospital, 1780–99 and 1826–35)

Age group	Log (fatality%)	Model	Farr's estimate	L.S. estimate
10–20	$y_1 = 1.367$	a-2b	24.7	24.4
20–30	$y_2 = 1.532$	a-b	33.1	32.9
30–40	$y_3 = 1.668$	a	44.4	44.3
40–50	$y_4 = 1.766$	a+b	59.7	59.8
50–	$y_5 = 1.900$	a+2b	80.1	80.6

Farr's estimate of $b = (y_4 + y_5 - y_1 - y_2)/6 = 0.128$.
Farr's estimate of $a = (y_1 + y_2 + y_3 + y_4 + y_5)/5 = 1.647$

As seen, Farr's estimates are very close to the least squares estimates. Thus Farr found a method of estimating a linear regression equation 50 years before Galton. However, later in the paper when analysing the cholera data from Vienna Farr uses the simpler method of interpolating logarithmically between the first and last age groups.

But without doubt the most innovative part of Farr's paper is his use of a double-decrement life table, with illness terminating by recovery or death, to estimate the recovery and death rates by period of disease in patients with small pox. It was not until 1926 that Greenwood used single decrement life tables to estimate the natural duration of cancer. Even to this day no-one, to my knowledge, has used a double decrement table to estimate recovery rates and death rates in communicable disease. The idea of a competing risk between recovery and death, the former increasing and the latter decreasing with duration of disease, was a conceptual breakthrough. Of course Farr knew nothing about bacteria and immunity, but it is only recently that immunologists have used predator-prey models to simulate the competition between antigens and antibodies (Bell 1973).

William Farr was the son of a farm labourer. He was largely self-taught. The little formal education he received was paid for by a retired cab-driver named Pryce, to whom epidemiologists should be eternally grateful.

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