

Epidemiology—a science for the people

2013 is the bicentenary of the birth of John Snow (1813–58), whose elegant studies of cholera in the mid-19th century earned him iconic status among the founders of epidemiology, the basic science of public health. A series of meetings in York, Snow's birthplace, and in London, the scene of his professional triumphs, have been organised to explore his legacy. They encourage us to reflect upon the evolution, influence, and expanding scope of epidemiology as a discipline.

Over much of its early history, epidemiologists concentrated almost entirely upon human infectious diseases. The London Epidemiological Society—the first professional organisation devoted to the subject—was founded in 1850, specifically to concentrate upon epidemic diseases, and counted Snow among its members. Population studies at that time by Snow on cholera¹ and by others, such as Peter Panum on measles,² were able to infer not only the existence but also many of the properties of disease-causing microbes, before they were discovered. Subsequent studies by Louis Pasteur, Robert Koch, and their disciples—and by the virologists of later generations—confirmed these inferences, and identified the causal agents. The arguments for causality were relatively simple, and built around the postulates of Jacob Henle and Koch: isolation from cases, pure culture, and production of disease on inoculation. Much of the epidemiological work on these diseases thus focused on measuring burden, describing patterns, and attempting to understand the transmission dynamics of infectious agents.

The importance of epidemiology as a discipline was recognised with the creation of chairs and academic departments, first in postgraduate schools of public health at the Johns Hopkins School of Hygiene and Public Health in Baltimore, MD, USA, and at the UK's London School of Hygiene and Tropical Medicine, in the 1920s. Most of the work undertaken in these departments, well into the 20th century, concentrated upon infections. This is exemplified in textbooks of the era, such as Major Greenwood's *Epidemics and Crowd Diseases: an Introduction to the Study of Epidemiology* published in 1935.³ This book included lengthy descriptions of typhoid, cholera, typhus, measles, diphtheria, scarlet fever, smallpox, tuberculosis, "venereal diseases", influenza, and plague, but made only limited reference

to nutritional, occupational, and psychological causes of ill health or to cancer, and devoted but a single sentence to cardiovascular disease.

Immense changes occurred during the second half of the 20th century. There was a shift of emphasis to non-communicable diseases, which reflected the decline of many infections and an increase in heart disease and cancer in many countries. This meant a move towards trying to understand conditions that did not necessarily have a single cause, and for which Koch's postulates were inappropriate. In addition, after the UK Medical Research Council's randomised controlled trial (RCT) of streptomycin for tuberculosis, there was a rapid growth in the use of RCTs to evaluate the effectiveness of a range of interventions.⁴

By the 1960s, academic epidemiology had systematised approaches to unravel the aetiologies of many sorts of conditions and to evaluate interventions either through case-control or cohort designs, or through trials. A constellation of criteria for the inference of causality was developed,^{5,6} and a hierarchy of evidence came to be generally accepted, with greatest credence given to the RCT. Since then, much of the progress in the discipline has been in the variety of its applications and the complexity of its analytic methods. There have been notable successes in revealing the causes of certain major common diseases (eg, smoking for lung cancer and cholesterol, blood pressure, and smoking for heart disease) and in

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For John Snow bicentenary events in York see <http://www.york.ac.uk/healthsciences/john-snow-event>

For John Snow bicentenary events at the London School of Hygiene and Tropical Medicine see <http://johnsnowbicentenary.lshtm.ac.uk>



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demonstrating the effectiveness, and risks, of many interventions, notably vaccines and drugs, which have in turn guided public health policies the world over.

It has not all been smooth sailing. The identification and attribution of causal determinants has raised philosophical as well as practical problems, especially when it comes to teasing out the inter-relations between multiple determinants that are themselves correlated, or difficult to measure. The findings from some observational studies were accepted too uncritically. For example, early reports that use of hormone-replacement therapy prevented heart disease and prolonged life were later refuted by randomised trials.⁷ An awareness of problems associated with reviews that did not include the totality of the evidence led to the advent of meta-analyses, which have been important for systematic reviews⁸ on a wide range of topics. However, some systematic reviews, such as on screening for breast cancer,⁹ have been challenged.^{10,11} Epidemiologists have thus dug deeper, and studied the discipline itself by investigating the prevalence of primary outcome switching or factors associated with publication bias, deploying cohort and case-control studies on academic publications as readily as they would on people.¹² There are now several widely used conventions for promoting study rigour and grading evidence, such as Consolidated Standards of Reporting Trials (CONSORT), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), and Grading of Recommendations Assessment, Development and Evaluation (GRADE),¹³ and widespread recognition of the need for open declaration of conflicts of interest. Although still not foolproof, all these steps are part of the continuous effort to improve the self-correcting nature of science as an institution.

The shift in emphasis towards the logic of problem-solving has made epidemiology increasingly relevant and important, far beyond its original home territory. Although much of the early epidemiological literature dealt with human disease,^{3,5,14} its methods are now applied to a range of species,^{15,16} and not only to disease in the conventional sense of that word. The links between physical and mental illness, and social pathology, are still being elucidated, and the language and tools of epidemiology have been used increasingly in the social sciences. This is particularly clear in the

field of criminology, which focuses upon risk factors for being either a victim or a perpetrator of crime, and in which "clinical" trial methods are being applied to evaluate different interventions at both the individual sentencing and community levels.¹⁷⁻¹⁹ Similar methods are being used to assess teaching in an effort to determine education policy less on the basis of politics and more on evidence.^{20,21} The complexity and controversial nature of economic and development policies have led to increasing application of cluster or individually randomised controlled trials in assessments of financial and development interventions,^{22,23} including microfinance, crop failure insurance, and business training.^{24,25} Infectious disease concepts have been used to understand the failures of financial systems.²⁶ There are calls for formal evaluation of public policies in general,²⁷ with epidemiological approaches making a major contribution. The No Child Left Behind Act in the USA specifically supports the use of randomised controlled trials in education, and a recent Cabinet Office paper discusses how the same methods could be applied more broadly in the UK, describing recent policy RCTs of expensive "back to work" interventions and simple comparisons of different forms of tax reminder letter.²⁸

Much of epidemiology concerns the evaluation of absolute and relative risks of particular outcomes associated with, or attributable to, various factors. The fact that the methods for making such inferences were developed so thoroughly in the context of research on human diseases may reflect the special importance placed on human health by society and by the agencies that fund scientific research. The acceptance of intervention studies might have been facilitated by the proximity of medicine to the experimental biological sciences. Whatever the course of their development, it is to our advantage that these methods be applied as broadly as possible to a wide range of societal, as well as individual, human ills. If one wants to know what makes Olympic champions, or suicide bombers, or whether a restorative justice regimen reduces recidivism, the basic logic and methods are effectively the same as those used to determine why certain people develop arthritis, and to assess how best to treat them. The differences lie in the nature, collection, and validation of the data on appropriate relevant variables.

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In the health arena many problems remain—the causes of multiple sclerosis, Parkinson's disease, prostate cancer, to name a few—and new interventions will continually need to be evaluated (eg, is a universal test-and-treat policy cost effective for reducing the incidence of HIV infection). New infections will continue to emerge, the spread of which will require monitoring. There will be increasing emphasis upon mega cohorts and mega trials, and the availability of large electronic datasets, including genetic data, will uncover new associations. Given its immense political implications, there will be a need for more studies of the effects of climate change on populations, one of the greatest problems facing our species. Although the terminology may differ according to the domain in which they are used, epidemiological methods and analysis of large datasets will be applied increasingly in the social and economic sciences—to everything from learning disabilities and poverty to crime and ecological or social disruption.

Once taught only at the postgraduate level in schools of public health, epidemiology was introduced into the curriculum of most medical and veterinary schools in recent decades, and has more recently been introduced into some undergraduate programmes. We believe this does not go far enough. The tools of epidemiology help us answer the most important applied questions that science can explore: what does good and what does harm in the world around us? These issues extend beyond the concerns of researchers and policy makers themselves. The public have an interest in what works, and reports on the risks and benefits of various policies and behaviours are prevalent in mainstream media, although evidence indicates that many of these reports provide misleading or naive overinterpretations of research, to an audience who are often ill-equipped to spot flaws.²⁹ There is a need to increase the scientific literacy of the population and to assist the public in interpreting evidence for and against different interventions and policies. Given the power of epidemiological methods in the assessment of human experience and endeavour, and its implicit role in so many discussions and decisions at the core of the everyday lives of all people, one might ask whether the subject should now be introduced as an obligatory part of the general science curriculum in secondary schools. We think so.

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We declare that we have no conflicts of interest.

- 1 Snow J. On the mode of communication of cholera. London: John Churchill, 1855.
- 2 Panum PL. Observations made during the epidemic of measles on the Faroe Islands in the year 1846, trans Hatcher AS. New York: F H Newton, 1940.
- 3 Greenwood M. Epidemics and crowd diseases: an introduction to the study of epidemiology. London: Williams and Norgate, 1935.
- 4 Streptomycin in Tuberculosis Trials Committee. Streptomycin treatment of pulmonary tuberculosis: a Medical Research Council investigation. *BMJ* 1948; **2**: 769–82.
- 5 MacMahon B, Pugh TF, Ipsen J. Epidemiologic methods. Boston: Little Brown and Company, 1960.
- 6 Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965; **58**: 295–300.
- 7 Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002; **288**: 321–33.
- 8 Peto R. Why do we need systematic overviews of randomized trials? *Stat Med* 1987; **6**: 233–40.
- 9 Gotzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database Syst Rev* 2009; **4**: CD001877.
- 10 US Preventive Services Task Force. Screening for breast cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009; **151**: 716–26.
- 11 Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet* 2012; **380**: 1778–86.
- 12 Song F, Parekh S, Hooper L, et al. Dissemination and publication of research findings: an updated review of related biases. *Health Technol Assess* 2010; **14**: iii, ix–xi, 1–193.
- 13 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; **64**: 383–94.
- 14 Lilienfeld DE. Definitions of epidemiology. *Am J Epidemiol* 1978; **107**: 87–90.
- 15 Wilesmith JW, Wells GA, Cranwell MP, Ryan JB. Bovine spongiform encephalopathy: epidemiological studies. *Vet Record* 1988; **123**: 638–44.
- 16 Timmermann V, Borja I, Hietala AM, Kirisits T, Solheim H. Ash dieback: pathogen spread and diurnal patterns of ascospore dispersal, with special emphasis on Norway. *EPPO Bulletin* 2011; **41**: 14–20.
- 17 Bell CC, Mock L, Slutkin G. The perceptions of victimization and perceptions of job neighbourhood safety in a social service agency and the need for screening. *J Nat Med Assoc* 2002; **94**: 602–08.
- 18 Wortley R, McFarlane M. The role of territoriality in crime prevention: a field experiment. *Security J* 2011; **24**: 149–56.
- 19 Bird SM, Goldacre B, Strang J. Give judges evidence on which to base sentencing. *BMJ* 2011; **342**: 335.
- 20 Torgerson C. Education research, call for controls. *Science* 2011; **333**: 1220.
- 21 Banerjee A, Cole S, Duflo E, Linden L. Remedying education: evidence from two randomized experiments in India. *QJEcon* 2007; **123**: 1235–64.
- 22 Ranson MK, Sinha T, Chatterjee M, et al. Equitable utilisation of Indian community based health insurance scheme among its rural membership: cluster randomised controlled trial. *BMJ* 2007; **334**: 1309.
- 23 Deaton A. Instruments of development: randomisation in the tropics, and the search for the elusive keys to economic development. *Proc Br Acad* 2008; **162**: 123–60.
- 24 Banerjee A, Duflo E. Poor economics: barefoot hedge-fund managers, DIY doctors and the surprising truth about life on less than \$1 a day. London: Penguin, 2012.

- 25 Karlan D, Appel J. More than good intentions: improving the ways the world's poor borrow, save, farm, learn, and stay healthy. New York: Plume Books; 2012.
- 26 Haldane AG, May RM. Systemic risk in banking ecosystems. *Nature* 2011; **469**: 351–55.
- 27 Oxman AD, Bjørndal A, Becerra-Posada F, et al. A framework for mandatory impact evaluation to ensure well informed public policy decisions. *Lancet* 2010; **375**: 427–31.
- 28 Haynes L, Service O, Goldacre B, Torgerson D. Test, learn, adapt: developing public policy with randomised controlled trials. London: Cabinet Office, 2012.
- 29 Cooper BEJ, Lee WE, Goldacre BM, Sanders TAB. The quality of the evidence for dietary advice given in UK national newspapers. *Public Underst Sci* 2011; **21**: 664–73.

Primary spontaneous pneumothorax: to pleurodesis or not?

Published Online
February 18, 2013
[http://dx.doi.org/10.1016/S0140-6736\(13\)60285-8](http://dx.doi.org/10.1016/S0140-6736(13)60285-8)
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Pneumothorax refers to air in the pleural cavity and can be spontaneous or traumatic. Traumatic pneumothorax occurs because of direct or indirect trauma to the chest (including iatrogenic causes). Spontaneous pneumothorax occurs without preceding trauma or obvious precipitating cause, and is subdivided into primary and secondary. Secondary spontaneous pneumothorax occurs as a complication of an underlying pulmonary disorder, most often chronic obstructive pulmonary disease, whereas primary spontaneous pneumothorax affects people who do not have clinically apparent lung disease. The yearly incidence of secondary spontaneous pneumothorax is 6·3 per 100 000 in men and 2·0 per 100 000 in women, whereas that of primary disease is 18·0–28·0 per 100 000 in men and 1·2–6·0 per 100 000 in women.¹

The course of spontaneous pneumothorax is variable, and the recurrence rate is 25–54%; presence of lung disease is a major determinant of recurrence.^{1–3} Although primary spontaneous pneumothorax arises in patients without clinically apparent lung disease, most patients have emphysema-like changes, which can be shown by high-resolution chest CT.⁴ Bense and coworkers⁵ noted emphysema-like changes (blebs and bullae) bilaterally distributed in the upper lung zones in 22 of 27 (81%) non-smoking patients presenting with primary spontaneous pneumothorax, but no such changes were reported in healthy, never-smoker controls.⁵ The emphysema-like changes score of the affected lung was high in individuals with recurrent primary spontaneous pneumothoraces.⁶ The size and number of bullae (as detected by high-resolution CT), and body-mass index of less than 18·5 kg/m² are predictors of recurrence of primary spontaneous pneumothorax, but age, sex, and smoking status are not.^{4,7,8}

Emphysema-like changes can be assessed during thoracoscopy in accordance with the Vanderschueren

classification (stage 1=normal pleura, stage 2=pleural adhesions, stage 3=blebs <2 cm, stage 4=bullae >2 cm).⁹ A systematic review showed that recurrence of spontaneous pneumothoraces was significantly more common after video-assisted thoracic surgery than after limited thoracotomy, because of inadequate exposure of the chest cavity and less resection of emphysema-like changes.^{10,11} Loubani¹² and colleagues reported significantly higher recurrence in patients who underwent thoracoscopic staple bullectomy alone than in those who received bullectomy and tetracycline pleurodesis; this finding was attributed to the probable control by pleurodesis of many blebs that were difficult to resect.¹² Tschopp and coworkers¹³ showed that thoracoscopic talc poudrage achieved 95% recurrence prevention; however, when bullae >2 cm were noted during thoracoscopy and left alone, four of ten patients experienced recurrence, and two of four needed surgery.¹³ The role of emphysema-like changes as a cause of primary spontaneous pneumothorax is debatable, because macroscopic emphysema-like changes were not noted during thoracotomy or thoracoscopy in about 50% of patients.¹⁴ Pleural porosity was proposed as another cause. Noppen and colleagues¹⁵ reported abnormal parenchymal lesions that were detected only by autofluorescence thoracoscopy after aerosolised inhalation of fluorescein. These parenchymal lesions were present exclusively in patients with primary spontaneous pneumothoraces, and were noted in areas of the lung that seemed normal during white light thoracoscopy.¹⁵

In *The Lancet*,¹⁶ Jin-Shing Chen and colleagues randomly assigned patients with first episodes of primary spontaneous pneumothorax to simple aspiration via a pigtail catheter (n=108) or catheter drainage followed by minocycline pleurodesis (n=106); interventions were administered immediately after radiographic confirmation of complete lung expansion and