1
History of a hypothesis

> The skillful doctor treats those who are well, the inferior doctor treats those who are ill.
>
> **Pien Ch'iao, Chinese surgeon (third century BC)**

A proverb's short-cut to wisdom often conceals a more circuitous route to the truth. To understand how we see the future today, it is worth looking at how we saw it in the past. Running over millennia, the recorded human history of disease prevention is a tale of hope and expectation, risk and uncertainty, truth and perception, science and superstition, power and control, individual and collective action, and of the valued present (*carpe diem*) versus the devalued future (*mañana*). The account given here, like most others, is biased towards the well-documented (in English) western world. Its purpose, however, is not to be comprehensive or categorical; rather, it is to suggest that the main ideas about prevention have a long pedigree even if, in every age and in every place, they find new interpretation.

On the preservation of health

For all biological organisms, reproductive success is measured by the number of offspring produced in the next generation. Success depends on maximizing this reproductive number in the face of adversity—including disease, injury, and death. In principle, more offspring might be produced by investing in prevention rather than treatment and cure. If the mechanism of prevention is heritable, transmissible from parent to offspring through the genome, then it would be subject to evolution by natural selection. Alternatively, or in addition, a successful preventive behaviour, once

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discovered, can be learned and memorized by others, spreading through a population as a form of cultural evolution.

There are abundant examples of prevention throughout the animal kingdom (putting aside other forms of life). Animals can anticipate the future using a mix of genetic and cultural evolution, as illustrated by behaviours that favour prevention over cure in self- and group-medicating species.[1,2] European wood ants, *Formica paralugubris*, use conifer resin to prevent bacterial and fungal infections in their nests.[3,4] Venezuelan capuchin monkeys rub millipede secretions containing insect repellent benzoquinones into their fur during the wet season peak in biting insect abundance.[5] Both are examples of prophylactic rather than therapeutic treatment in animals where prevention has been favoured as an alternative or as a complement to cure. Such observations on primates suggest that behaviours which preserve health and prevent disease have a long evolutionary and cultural history in their human descendants, spanning hundreds of thousands of years.

On that timescale, the first inferences about human preventive behaviour are relatively recent. Eating, drinking, washing, and defecating have always been essential for life; nutritious food, clean water, and safe sanitation are vital for the preservation of health and the prevention of disease.[6] The first efforts to manage the distribution of water—with dams and irrigation systems—were driven by the need to produce enough food to live in the Tigris and Euphrates (Mesopotamia, *c*.5300 BC), Nile (*c*.3300 BC) and Indus (*c*.2800 BC) river valleys. Irrigation for agriculture was the precursor to urban water and sanitation systems as small and scattered farming villages grew into conurbations, making greater demands to cooperate in providing food and water supplies and on waste management in increasingly dense, sedentary populations.[7]

Based on archaeological evidence from the third millennium BC, the Neolithic peoples of Central America (Guatemala), Europe (Orkney Islands), Mediterranean (Crete), the Middle East (Israel, Turkey), North Africa (Egypt), and South Asia (Indus valley) had the means and motives to filter and boil water, to design and build flushable cesspits and toilets, and communal drains and sewerage systems.[8] The great variety of efforts to purify water, and to remove excreta and other waste, suggest that the environmental causes of illness were understood, and understood to be preventable, with health benefits for individuals and whole communities.[9,10]

By the third millennium BC (if not before), physicians were carrying out surgery and had accumulated a rich pharmacopeia of medicinal plants

and minerals for healing. The Egyptian practice of applying a poultice of mouldy bread to an infected wound might be the first instance of antibiotic treatment. More than this, and in spite of the prevailing causal model of disease as divine punishment (penitence was cure, not prevention), doctors also gave advice on staying healthy—for instance, by washing and shaving the body to prevent conditions now known to be caused by infections.[11] There were treatments for patients and penitents; and, for some conditions at least, there were means of prevention too.

From the sixth century BC onwards, Greek philosophy sharpened the distinction between natural science and theology in pursuit of a reasoned understanding of causes and effects. Knowing the cause is a precondition for reliably preventing the effect. Health and disease were known to be associated with the physical and social environments in which people lived, and with human behaviour.[12,13] Hippocrates' (*c.*460–375 BC) *On Airs, Waters and Places* (*c.*400 BC) was a guide to preventing illness for settlers in new environments.[14] Some of the advice was common sense: houses should be built in elevated and sunny areas, avoiding marshes and malarial swamps. Some drew on prevailing aetiological theory: dietary regimens and regular exercise could maintain 'a healthy mind in a healthy body', ostensibly by keeping in balance the four humours—black bile, yellow bile, phlegm, and blood.[15] These ideas are most frequently associated with Greece, but actually co-evolved across the ancient civilized world: during the first millennium BC, humoral balance was integral to physiological models of health in contemporary Hindu (Ayurveda) and Chinese societies too.

Prevention was taken seriously by Greek physicians. According to Pliny the Elder (23–79 AD), Asclepiades of Bithynia (*c.*124–40 BC) staked his medical reputation on prevention by making a bet with [the goddess] Fortune 'that he should not be considered a doctor if ever he himself fell ill in any way'.[16] He is said to have died by falling down stairs, aged 84, thus escaping the ignominy of terminal illness, winning his bet posthumously and securing his legacy in preventive medicine.

However, prevention went far beyond the practice of physicians. Underpinning medicine, Greek democracy was an instrument of public health. Individuals and communities were empowered through participatory institutions, emphasizing education and the development of skills to maintain good health. This was 'health promotion'—enabling people to increase control over and improve their health—two thousand years before its rebranding in the twentieth century.[13] It perhaps illustrated, too, the

scale on which enabling must take place if health promotion is to succeed (Chapter 8).

Ever since people began to live in settled communities, they have been forced to relieve themselves of bodily waste, not just personally, but as whole populations. Driven by this sanitary imperative, private and communal toilets linked to drains and sewers became common from at least the third millennium BC. Between 500 BC and 500 AD, public water supply and sewage systems, albeit imperfect systems, were hallmarks of Greece and Rome.

In antiquity, risk was often seen in terms of fate and met with acceptance rather than defiance.[17] But not always: pragmatic traders—Babylonian, Chinese, Greek, and Indian, from the second millennium BC onwards—not content with the hand of fortune, also understood how to invest in prevention in the face of uncertainty and adversity.

Their understanding created foundations for the insurance industry. Risk is non-fungible, or non-transferable, for individuals. But risk can be shared among individuals in a group. So individuals exposed to losses through common risks naturally grouped together in order to aggregate the risk, put a price on it, and sell it to investors (Chapter 4).[18] Insurance is an instrument of prevention as well as cure.

For shipping, risk was not necessarily mitigated by financial compensation for loss. It was often non-financial and preventive—for example, by steering clear of sea passages known to be dangerous (which required collaboration through record keeping and the exchange of information), by arming ships as a deterrent to pirates, and by spreading risk by dividing a cargo among several vessels.

In maritime trading, 'bottomry' contracts provided loans to shipping merchants, secured on the bottom or keel of a ship. When the ship returned to port after a voyage, the loan was repaid with interest. If the shipment was lost at sea, the loan was forfeited by the guarantor. This form of insurance, in which the chance of gain and risk of loss are transferred from merchant to investor, resembles a modern catastrophe bond. It provides guarantors with incentives for prevention—invest in safe ships. Whether the idea of insurance was also applied to the risk of illness in antiquity is apparently unknown, but catastrophe bonds are one of the instruments used nowadays to protect health and life from hurricanes, epidemics, and other disasters (Chapter 4).

Some of the wisdom of Ancient Greece found continuity in Classical Rome, as recorded in practice and proverb. Galen (129–*c*.210 AD), 'first

among doctors' in the opinion of Emperor Marcus Aurelius, was renowned for his discoveries in anatomy and physiology to inform medical treatments. But he also taught that a physician's priority was to keep people in good health. Galen's physiological model of good health expanded the Greek theory of balancing humours by regulating the 'non-naturals' (as Arab scholars later called them). The non-naturals or necessities to be regulated were air, food and drink, sleep and wakefulness, motion and rest, evacuation and repletion, and the passions of the mind, with occasional add-ons including baths, exercise, and sex.[19]

Galen believed in good health and well-being for all, founded not merely on philosophy and medicine but also on the physical constructs of urban life: gymnasia, aqueducts, bath houses and communal toilets, streets and public meeting places. His *Hygiene* (or *On the Preservation of Health*) identified education as vital to learning what was harmful and what was beneficial for health. To the extent that the theory and its practice were beneficial, they did not significantly lengthen life expectancy, which in the Roman Empire was typically 20–30 years from birth. Military campaigns carried an obvious risk of disease and injury for adult males, but death rates were far higher in children under five years old.[20] Nevertheless, Galen's synthesis of medical practice in general, and of prevention in particular, had wide appeal and astonishing longevity—influencing health and medicine globally for more than a thousand years.

Greco–Roman progress in science and medicine slowed in Europe with the decline of the western Roman empire from the fourth century AD but continued to flourish in the east. Roman and Byzantine Constantinople became a centre for experimentation and empirical observation. Constantinople, situated at the junction between Europe and Asia, also served as a conduit for Greek and Roman thought into the Islamic world where it developed through cross-fertilization with Indian and Persian medicine.

The Islamic Golden Age (*c.*750–1258) produced a succession of polymaths who expanded the concepts and methods of disease prevention and treatment. An array of Arabic medical texts offered technical solutions for environmental pollution and the management of municipal waste. Rhazes (854–925) studied the effects of diet, hygiene, climate, and seasonality on health. Avicenna's (980–1037) encyclopaedic *Canon of Medicine* (1025), published at the turn of the first millennium, synthesized more than a thousand years of medical practice from the Egyptian, Greek, Roman, Indian, Christian, Jewish, and Islamic worlds. The *Canon* was as much a treatise on

prevention as on cure, for the dual 'goal of medicine is keeping health and returning it while having disease'.[21]

That which preserveth health is more excellent

Mediaeval Christian Europe (500–1000), maligned as the Dark Ages, was not so dark as commonly portrayed. Instances of scientific censorship in the Middle Ages were outnumbered by examples of the Roman Catholic Church acting as custodian, funder, and promoter of mediaeval intellectual advancement. This was neither doctrinally inconsistent nor scientifically prejudicial: as Aristotle (384–322 BC) had concluded much earlier, if the natural world was governed by God's laws, then studying nature would be one way to understand His purpose. Gaining that understanding may not have been motivated by an earthly need for innovation, but it certainly permitted it. Mediaeval agriculture, for example, was a beneficiary: productivity increased with the development of heavy ploughs, crop rotation, and watermills. Besides, the Church's mission was also to serve the needs of the poor, and the remedies for poverty were secular as well as spiritual.

In terms of public health in Europe, the Middle Ages were bracketed by two major pandemics of plague (later known to be caused by the flea-borne bacterium, *Yersinia pestis*)—the Plague of Justinian in 542 and the Black Death in 1348, with frequent smaller outbreaks in between. The high burden of sickness and death caused by plague, leprosy, and other contagious diseases was a powerful impetus to seek pragmatic solutions. There was no medical cure for plague so the best tactic was prevention: known or suspected cases, and people who had been in contact with them, were isolated (e.g. for 40 days, 'quarantine') to stop the spread of disease.

Plague and leprosy were not the only targets for disease control. Motivated by the need to curb contagion more generally, public officials created a system of sanitary controls, using surveillance stations, isolation hospitals, and disinfection procedures. Efforts to improve sanitation included the development of pure water supplies, garbage and sewage disposal, and food inspection. Before national public health services were created, the value of personal and public hygiene was understood, if not diligently practised, by citizens and by local authorities alike.

From the early Middle Ages onwards, Latin and Greek translations of Islamic medical texts, including Avicenna's *Canon*, began to appear in

Europe. In this convergence of western and eastern thought, the idea of prevention resurfaced—for instance, in Henry de Bracton's *On the Laws and Customs of England* (*c*.1240). Once again, we read that 'it is better and more useful to meet a problem in time than to seek a remedy after the damage is done'.

Despite the advances made in the millennium since Galen, the task of the physician was still to maintain health by regulating the non-naturals, keeping the body in good 'temperament' and with an optimal 'complexion'.[22] Some facets of fourteenth-century health care were decidedly modern, such as attending to the particular requirements of each patient. Because complexion was known to differ among individuals, a satisfactory health regime would have to be tailored to individual needs, at least for those who could afford them. Thus, twenty-first century personalized or precision medicine, as it is now called, has a history of at least 700 years. Furthermore, the concept of prevention was applied to groups of people as well as to individual patients. Among these public health initiatives, regular prophylactic venesection (blood-letting) was prescribed for entire monastic communities, and healthy regimens were suggested for defined categories of vulnerable people—children or the elderly, or those living in unhealthy environments.

As the western world emerged from the Middle Ages, Galen's legacy was subjected to increasingly critical examination. Roger Bacon's (*c*.1219–92) *Greater Work* (*Opus Maius*), for instance, challenged conventional medical theories with experimental science. Doctors, he argued (after Horace), should take nothing on authority, specifically church authority; they should instead do their own empirical research.

Whether or not Bacon's advice was followed, the view that prevention trumps cure travelled more or less unscathed through the European Renaissance. Erasmus of Rotterdam (1466–1536), humanist scholar of classical antiquity (who was inclined to overlook advances made in the Middle Ages), reinforced the notion in his book of proverbs (the *Adages*) first published in 1500.[23] He is credited with stating that prevention is better than cure but he did not actually go that far. A more accurate translation of his Latin text is: 'It is better to treat at the beginning of illness than at the end' (*Adage* 1.ii.40). This falls short of true (primary) prevention because the emphasis is on the early diagnosis and treatment of illness, not on removing the underlying cause.

Other contemporary writers did promote strict prevention. One of them was Thomas Cogan who, echoing Avicenna's *Canon*, wrote in 1612: 'The art

of Physicke hath two principall parts; the one declaring the order how health may be preserved: the other setting forth the meanes how sicknesse may bee remedied. Of these two parts that is more excellent which preserveth health and preventeth sicknesse.'[15,24]

An ounce of prevention

Prevention is better than cure, but not at any price. This insightful qualification was perhaps first made explicit in Benjamin Franklin's 'an ounce of prevention is worth a pound of cure' (1736), which has been widely generalized from his investigation of fire safety in Philadelphia. Because the costs of early versus late intervention are now quantified, at least metaphorically, this rendition of the proverb turns conventional wisdom into a conditional hypothesis. It is pedantic, of course, to ask whether the cost–benefit ratio is actually 1:16 (ounces in a pound); but it is sensible to ask, in general, whether benefits exceed costs, and under what circumstances.

Franklin's application to fire insurance had a long pedigree. The idea of insuring against risk had been in practical use for millennia (e.g. bottomry contracts already mentioned), including ways of insuring against fire. In AD 67, Nero had allegedly fiddled while Rome burned. He may well have dithered during the conflagration, but he undertook a costly rebuilding of the city thereafter, driven by imperial vanity but guided by, among other practicalities, fire precautions. According to Tacitus, 'from the ashes of the fire rose … a city made of marble and stone with wide streets … and ample supplies of water to quell any future blaze'.[25] New houses had to be built with fire walls, Rome acquired a fire department, and debris from the fire was used to fill nearby malarial swamps.

A century before Franklin, John Winthrop, Governor of Boston, Massachusetts, had in 1631 outlawed the building of homes with wooden chimneys and thatched roofs, which were recognized fire hazards. In Great Britain, the fire insurance industry was given a boost by the Great Fire of London in 1666. In the aftermath of the fire, the Rebuilding Act of 1667 was designed to prevent future disasters. Among other safety features, it required houses to have brick fronts, to be of equal height, and to have signs fixed to a wall rather than hanging over the street. Buildings had to be registered with city authorities and were checked against regulations by city surveyors.

Franklin's contribution in the 1750s was to set up one of America's first voluntary fire services (the Union Fire Company, also known as 'the Bucket Brigade'). But he also realized that, if fire is inevitable, and the timing and identity of victims are unpredictable, then it should be possible to set a premium for safety, affordable for everyone, based on the pooling of risk. He therefore established in 1751 the first colonial insurance company, the *Philadelphia Contributorship for the Insurance of Houses from Loss by Fire*. The *Contributorship* put a price on prudence, offering mutual insurance plans, 'whereby every man might help another, without any disservice to himself'. In gambling against ill fortune, this was a triple win: insurance gave peace of mind in the face of a fire risk, and of course it provided financial compensation for losses in the event of fire. But it also encouraged prevention: by inspecting properties to be insured, by setting premiums based on risk assessment, and by rejecting buildings that were not constructed to specified standards.

The categorical 'a stitch in time saves nine', attributed to astronomer Francis Baily (1797), also set costs against benefits. In fact, the original, less confident version is better: 'a stitch in time *may* save nine' properly captures the uncertainty associated with investing in the future. Like Erasmus' *Adages*, this form of the proverb calls for early diagnosis of an existing problem, rather than true prevention (no stitch needed at all). These different shades of proverbial wisdom highlight the question, still relevant today, of whether to invest in prevention proper (primary prevention), or to make do with early diagnosis (secondary prevention). The answer to the question depends on the costs and benefits of each strategy.

The eighteenth-century growth of experimental medicine led to improvements in the means of prevention, as well as creating better treatments. John Pringle's *Observations on the Diseases of the Army* (1752) spoke to problems of hospital ventilation and camp sanitation by advancing rules for proper drainage and latrines, and the avoidance of marshes. He insisted on sanitary measures that reduced the rate of typhus and dysentery, diseases that killed more soldiers than military conflict.

James Lind's *Treatise on the Scurvy* (1754) described his discovery that lemon juice prevented this severe skin and skeletal disease among British sailors (lime juice works too, hence 'limeys'). He did not need to know that scurvy was caused by vitamin C deficiency (vitamins were not discovered until 1912 and vitamin C not until 1928). He just needed to be able to design, carry out, and interpret his prototype of the controlled clinical trial.

Lind's study had its roots in the early seventeenth century. In 1601, Captain James Lancaster gave lemon juice to sailors on four ships, but not on another three 'control' ships. All the crew of the first four ships stayed healthy, whereas 110 of 278 men died of scurvy on the other three. In 1747, Lind extended the experiment by giving citrus fruits to scurvy patients who were cured in a few days. The British Navy adopted the policy in 1795 and eliminated scurvy entirely. In 1865, the British Board of Trade did the same for the merchant navy, with the same results. The time from discovery to full implementation in merchant and defence navies was 264 years.[26]

Variolation, the inoculation with smallpox virus to protect against severe disease later in life, was used in China from around 1000 AD. But it was Mary Wortley Montagu (1689–1762) who in 1721 famously introduced variolation to the western world.[27] She had observed the practice and its prophylactic power in Ottoman Turkey. Variolation clearly carried the risk of causing a severe episode of smallpox (with approximately a 2% chance of death), but Montagu nevertheless had her son (in Constantinople) and daughter (in England) inoculated. In August 1721, seven prisoners awaiting execution at Newgate Prison made their own calculation of risk when offered the chance to undergo variolation instead of execution. All were inoculated, all survived, and all were released.[28] The way they eventually died is not known, but it was probably not from smallpox. Setting the certainty of hindsight against the uncertainty of foresight, Benjamin Franklin greatly regretted that he had not made the same calculation on behalf of his own son. Four-year-old Francis Franklin died of smallpox in Boston in 1736 when inoculation was, on balance, probably worth the risk.[29]

After investigations in the 1760s and 1770s by physicians in England and Germany, in 1796, Edward Jenner 'vaccinated' an eight-year-old boy with pus from the hand of a milkmaid infected with the related cowpox virus (*vacca*, the cow). Jenner then boldly demonstrated that the boy was immune to challenge with smallpox infection. Farmers knew from practical experience that a mild episode of cowpox was protective against smallpox, but Jenner made the point experimentally and almost incontrovertibly (his study design would not satisfy modern standards of inference or ethics).

The road from smallpox variolation to vaccination is well known in the history of prevention. But variolation was not the only form of immunization with a long tradition. Cutaneous leishmaniasis is a skin disease caused by protozoan parasites in the genus *Leishmania* and transmitted by bloodsucking phlebotomine sandflies. Familiar in antiquity from North Africa across the Middle East to India, leishmanial lesions were

variously known, with their geographical identifiers, as buttons (Basra), boils (Aleppo, Baghdad, Delhi, Jericho) and sores (Balkh, Oriental). For centuries, Bedouin, Kurdistani, and other tribal societies had practised leishmanization, the deliberate exposure of children to the parasite by the bite of a sandfly or the inoculation of infectious exudate from an active skin lesion. As with variolation, the aim was to produce a self-healing sore, which would be followed by long-lasting immunity. Immunity would protect against later disfiguring lesions on the face and other exposed parts of the body, especially crucial for the marriage prospects of a young woman.[30]

These advances in the scientific understanding of prevention, from lime juice to vaccination, needed a favourable medical, social, economic, and political environment for their application. Like anyone offering the next big idea, Pringle, Lind, Jenner, and other eighteenth-century pioneers had to overcome the scientific scepticism of their peers, plus the predictable opposition of those with vested interests, such as doctors making money out of risky variolation rather than the safer alternative, vaccination.

But there were larger societal forces at work. Through a succession of social revolutions between 1775 (America) and 1848 (Europe), these forces would help to create a more favourable environment for public health. In revolutionary late eighteenth-century Europe and America, the fortunate few in authority faced mounting pressure from the discontented many living in feudal poverty. In America, Thomas Jefferson (1743–1826) put health in context: in his view, despotism produced disease and democracy liberated health.[31] Out of the French revolution (1789–99) emerged the belief that healthy citizenship was a human right. And Europe's democratic advances leading up to the revolutions of 1848 provided the backdrop to advances in public health: medical police (Central Europe), statistical analysis of mortality (France), poor relief (Scotland), the provision of infirmaries (Ireland), and sanitation (England and Wales).[32]

Preventive police and the sanitary idea

In nineteenth-century Europe, the use of the word 'sanitation' made it clear that water and sewage were viewed as principal determinants of health and hygiene, even though citizens were more concerned then, as they are today, about privacy, comfort, odour, and the physical removal of urine and faeces (Chapter 7).[33,34] Unearthing the remnants of historical sanitation systems has drawn attention to the technology, but the implications for social

organization are at least as important: advances in sanitation were products of early Indus valley culture, Greek democracy, Roman administration, and European Enlightenment humanitarianism.

Consequent to the latter, the huge increase in life expectancy enjoyed by people in the industrialized world since the eighteenth century is among the most remarkable biological events in human history.[35] No one living in Europe in the 1700s could have foreseen that life expectancy would increase so rapidly above the centuries-long norm of 20–40 years, more than doubling within two centuries. Within the changing social environment, the factors that lay behind the increase were cleaner water, safer sanitation, a more reliable supply of high-quality food, and a revolution in microbiology. Technological advances were coupled with accelerating economic growth, suggesting (but not proving) that there were mutually reinforcing, positive feedbacks between processes affecting health and the economy (Figure 1.1).

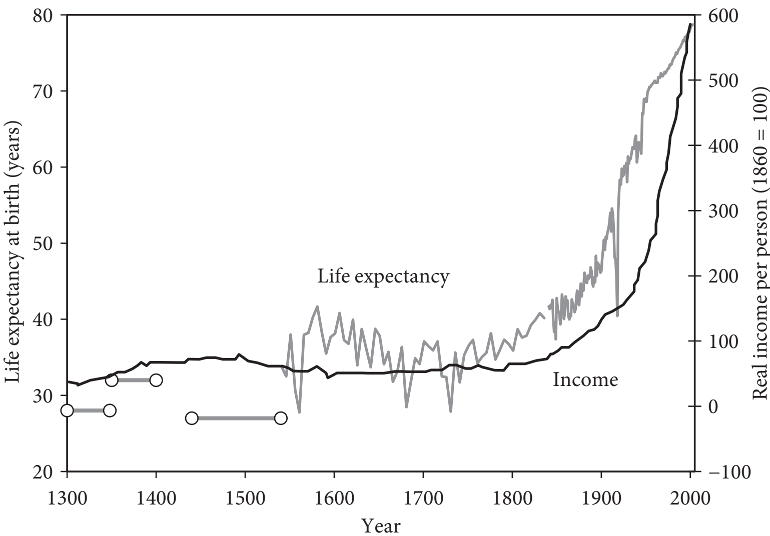

Figure 1.1 Up to 1800, life expectancy from birth in England and Wales was under 40 years (grey lines) but it more than doubled between 1800 and 2000. Income per person (black line) also accelerated sharply after 1800, suggesting that there was positive feedback between processes affecting health and the economy, although a third factor could have contributed to both.

Adapted with permission from Dye, C. (2010). 200 years in the history of longevity. *The Biologist*. 57 (3): 127–30.

The rise in life expectancy, driven mainly by the prevention of childhood infectious diseases, began a worldwide epidemiological and demographic transition. As a higher proportion of children survive to adulthood, parents choose to have smaller families. As infectious diseases wane, they are replaced by the chronic, non-communicable diseases typical of adulthood in larger, older populations. In Europe, North America, and other parts of the industrialized world, this transition took place over centuries. In some low- and middle-income countries, large reductions in mortality and fertility have taken place over just a few decades.[36]

The nineteenth-century sanitation 'revolution' was so-called, not because it was quick (it spanned the long life of Queen Victoria, 1819–1901) but because it was a national engineering project with effects that were ultimately enormous.

In England, Edwin Chadwick (1800–90), more than anyone else, put health in the broader social, economic, and environmental context. Passionate about state intervention for social good, Chadwick has been called the founder of English public health, though he and his collaborators, notably Thomas Southwood Smith, were products of the prevailing, and for them enabling, humanitarian outlook.[31] Elsewhere in Europe, others such as Rudolph Virchow (1821–1902) also championed the cause.

Chadwick pursued his mission partly through his role as a junior member of the Poor Law Commission of 1832. He became the main architect of the new Poor Law of 1834. The principle of the law was to make the conditions under which public relief could be given so unpleasant that most would refuse to request it. Popular objections to the law were understandable; as its administrator, Chadwick was said to be the most hated man in England.[32]

And yet his efforts delivered many benefits: the Commission stipulated that children should not work more than six hours a day and that employers should be held responsible for accidents in the workplace.[37] The work of the Poor Law Commission was followed by the Registration Act of 1836, which launched a public vaccination service in England. Under the first Vaccination Act, smallpox vaccination (replacing risky variolation) was at first optional (1840) and later made compulsory (1853).

But Chadwick's focus was on sanitation and what it could achieve. The stench of ordure and refuse was not new; it had long been a scourge of urban life in Europe,[38] but Chadwick skilfully advanced the case for hygiene in the face of complex sanitary politics. *The Means of Insurance against Accidents* (1828) developed his 'sanitary idea' for nationwide improvements to water

supply and waste removal. His 1829 paper on 'Preventive Police' was an enquiry into 'the removable antecedents of crime'. This was a justification of state-controlled social welfare,[31] and a forerunner to Henry Rumsey's (1809–76) *Essays on State Medicine* (1856), which was, in effect, a practical guide for interventionists and preventionists: investigation, regulation, and prosecution carried out by the medical police.[39–41] Chadwick's crowning glory was his magisterial three-volume, systematic geographical study of health as a basis for action, the *Report on The Sanitary Condition of the Labouring Population of Great Britain* (1842).[8] The aims and methods of the *Report* were informed by, and in turn influenced, similar analyses in France and America, such as the sanitary reports for New York and Massachusetts, published, respectively, in 1845 and 1850.

The 1838 report of the Poor Law Commission promoted, once again, the view that prevention is better than cure: 'the expenditures necessary to the adoption and maintenance of measures of prevention would ultimately amount to less than the cost of the disease now constantly engendered'.[8] Inspired by Jeremy Bentham's (1748–1832) utilitarian ('felicific') calculus, Chadwick estimated 'that this expense [incurred by manual removal of decomposing refuse] may be reduced to one-twentieth or to one-thirtieth, or rendered inconsiderable, by the use of water and self-acting means of removal by improved and cheaper sewers and drains'. He went on to calculate, in an analysis of the kind still done today, 'that by the combinations of all these arrangements, it is probable that the full ensurable period of life, an increase of 13 years at least, may be extended to the whole of the labouring classes'.[42] Thirteen years was a big increase; retrospectively, that estimate looks justified by the remarkable growth in life expectancy (Figure 1.1).

The ensuing Public Health Act of 1848 was the first occasion on which a British government took national responsibility for the health of its citizens. Taking responsibility in this way inevitably provoked debate about whether preventive policing was in the public interest or an infringement of personal liberty. Sanitary engineering for better health was popular; sanitation as an instrument of social engineering much less so. The indomitable Chadwick personified the division of opinion. To enthusiasts, he was a pioneer of social reform; to dissenters, he was an agent of political oppression.[31,43]

In parallel with the 1848 Public Health Act, London's Metropolitan Sewer Commission (1848) made household sewer connections compulsory—relieving houses of the reek of cesspits but transferring the problem of pollution to the River Thames. The transition from cesspits to open sewers and faecally polluted rivers played out in different ways across Europe.[38] To

remedy the Great Stink emanating from the Thames, the 1852 Metropolis (London) Water Act required all private water companies to move their intakes upstream and to install mechanisms for filtration. In fact, the private water companies were already investing in filtration systems to purify their water supplies, though they acted with varying speed and efficiency. That variation between water companies allowed physician John Snow (1813–58) to test his theory that cholera was caused by a water-borne infection rather than an air-borne miasma. During the first seven weeks of London's 1854 epidemic, Snow found that the number of cholera cases per capita was about eightfold higher in districts supplied by the Southwark and Vauxhall Water Company (intake downstream, poor filtration) as compared with those supplied by the Lambeth Waterworks Company (intake upstream, improved filtration).[44,45]

As part of the effort to curtail a cholera outbreak in the Golden Square district of London during 1854, Snow famously removed the handle of the Broad Street pump which, it was later discovered, dispensed water contaminated with the faeces of a choleric infant. Handles had previously been removed from pumps during cholera outbreaks in the United States. Snow's action in Broad Street actually had no discernible effect on the Golden Square outbreak, which was already in decline. But it was powerfully symbolic of a general truth about cholera: it is a water-borne disease.[45] Indeed, disabling the pump was just one of several precautions taken against cholera (liming of the streets was another) because local authorities remained unconvinced of Snow's argument. The eminent physician William Farr (1807–83) was not convinced until 1866. And, despite the Public Health Act of 1875, sewage pollution of the Thames continued until the 1880s. Definitive proof of the cause of cholera awaited experimental microbiology.

Preventive microbiology

Anton van Leeuwenhoek (1632–1723) had seen 'animalcules', including bacteria, through his new microscope in the 1670s but microbiology did not start to benefit from microscopy for another two centuries.

Louis Pasteur (1822–95) and Robert Koch (1843–1910) were twin peaks in the nineteenth-century landscape of microbiology. Their work began an explosion in the discovery of microorganisms as the causative agents of infectious diseases. These discoveries led in turn to new options for the prevention (vaccines, infection control) and treatment (antibiotics) of specific

infectious diseases—and moves towards the greater medicalization of public health.[46]

Pasteur's experimental tests of germ theory (first postulated in the sixteenth century) rapidly generated germ facts. Techniques for staining bacteria made them observable under a light microscope. 'Pasteurization' sterilized fermenting liquids by heat-killing microorganisms. Inoculation experiments with killed or attenuated bacteria and viruses produced prototype vaccines against anthrax, chicken cholera, and rabies. Koch's focus was on microbiology to improve public health measures, including sanitation.[47] Based on his work with anthrax, he devised a set of widely used criteria (Koch's postulates) for inferring that a particular microorganism caused a particular disease. The microorganism must be found in diseased but not healthy persons; cultured from a diseased person; cause disease when inoculated into a healthy person; and be recovered from that person. These criteria guided his work to identify the bacteria that caused cholera (as proposed by Filippo Pacini in 1854) and tuberculosis (TB). Experimental microbiology was extended to insect-borne diseases too. Patrick Manson (1844–1922) demonstrated in 1877 that *Culex* mosquitoes are vectors of filarial worms (*Wuchereria*) and Ronald Ross (1857–1932) in 1897 that *Anopheles* mosquitoes transmitted malaria parasites (*Plasmodium*).

The rapid discovery of antibacterial agents gave many more options for treatment: antitoxin or serum therapy for diphtheria (1890), arsenic-derived salvarsan for syphilis (1911), and the true antibiotics (derived from bacteria and fungi) penicillin (1928), sulphonamides (1935), streptomycin (1944), cephalosporins (1945), and tetracycline (1948). But the options for prevention multiplied too, with vaccines for human cholera (1885), typhoid (1896), TB (1921), yellow fever (1936), whooping cough (1939), and Japanese encephalitis (1944).

The causes of the causes

This proliferation of vaccines and antibiotics provided medical reinforcements in the front-line fight against infectious diseases, backed up by large-scale public health measures, and underpinned by improving social and economic conditions. In the first half of the twentieth century, infectious diseases were clearly in decline, but which of these factors was responsible?

The most debated framing of that question was due to a professor of social medicine, Thomas McKeown (1912–88), who observed between the

1950s and 1970s that 'health has advanced significantly only since the late eighteenth century and until recently owed little to medical advances'.[48] McKeown argued that the medical profession had attributed too much of the health benefits to its own work—curative medicine—and commandeered disproportionate resources to do so.[48,49] He pointed instead to the effects of market-based economic growth, the rise in living standards, improved nutrition (the basis of host resistance to infection), and, to a lesser extent, municipal sanitation.[50,51]

Just after World War II, when McKeown began to develop his ideas, recently discovered medical treatments could not possibly account for the decline in infections observed over the preceding decades. The mortality rate from TB in England and Wales had fallen from 320/100,000 population in 1870 to 57/100,000 in 1944 (i.e. by about 80%) when the first TB drug, streptomycin, became available (the BCG vaccine, created in 1921, was not efficacious against infectious pulmonary TB in adults).[52] Deaths from diphtheria, scarlet fever, and pneumonia had also declined before the discovery of antitoxin, sulfa drugs, and penicillin.[53] In McKeown's view, too much credit went to treatment and too little to prevention.

The shortcomings of McKeown's own analyses and conclusions are now well known; he probably overstated the benefits of economic growth and understated the impact of public health measures, especially sanitation.[50] But his question was crucial and stimulated many subsequent investigations, which refined and revised his theory. Samuel Preston (1943–) elevated the role of public health technologies, including water and sanitation, in preventing infections and enhancing life expectancy.[48,54] Robert Fogel (1926–2013) described the positive association between health (measured by height) and nutrition running over two centuries.[55,56] Fogel also saw positive feedbacks between health and human capital: he argued that better nutrition enabled people to grow bigger, stronger, and perhaps smarter, which further boosted income, productivity, and health (Figure 1.1).[57,58]

At the time of McKeown's analysis, preventive measures, whether more (sanitation) or less direct (nutrition), had taken effect over decades. Vaccines and antibiotics had had far less time to make an impact. It is clear now, however, that antibiotics have been responsible for dramatic reductions in mortality (cure), if not the incidence of disease (prevention). For instance, TB deaths per capita declined at only 2%–3%/year in England and Wales between 1870 and 1944. But, thanks to streptomycin, isoniazid, and other TB drugs, the TB death rate dropped far more quickly from the 1940s

onwards—by more than 80% within the decade 1946–55 (>15%/year; Figure 1.2).[52]

Other analyses have also revealed that relatively slow gains were made from prevention. In the United States during the 1990s, the preventive measures then in place were extending life expectancy by 18–19 months, less than half as much as the prolongation of life from curative measures, roughly 44–45 months.[59] By these criteria, cure was better than prevention.McKeown had fashioned his argument around the decline in infectious diseases, which were slowly being replaced by chronic, non-communicable diseases in aging populations—the joint epidemiological and demographic transition. Chronic diseases presented the same question about prevention versus treatment, albeit in a new context. Geoffrey Rose's (1926–93) influential *Strategy of Preventive Medicine* (1992)[60–62] drew

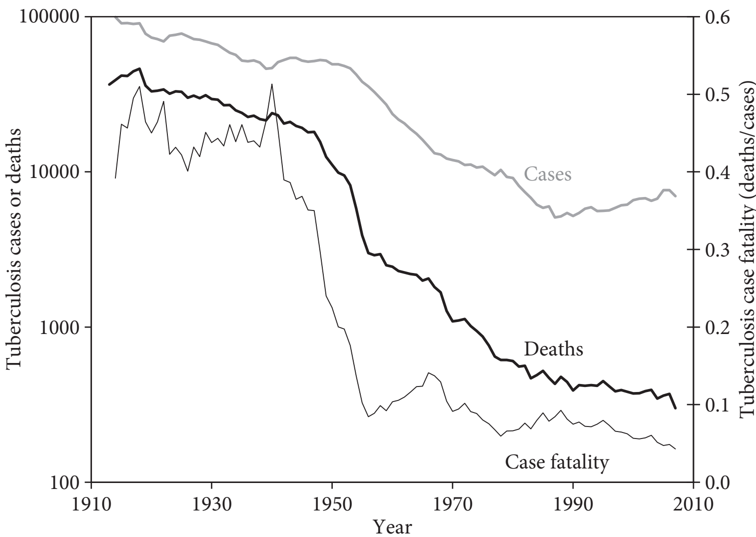

Figure 1.2 Trends in tuberculosis (TB) cases and deaths (left axis) and case fatality (right axis) in England and Wales, 1913–2007. Like other infectious diseases, TB was in decline long before the discovery of antibiotics. From the 1940s onwards, curative drugs greatly accelerated the decline, especially of case fatality (proportion of patients who die), far exceeding the effects of earlier preventive measures. Drug treatment also interrupted transmission and was therefore a means of prevention.

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attention to the importance of considering risk across whole populations. Taking high blood pressure as a 'risk factor' for stroke, Rose pointed to the potential benefits of changing the behaviour of many people at low risk of illness rather than, or in addition to, targeting a few individuals at high risk. In doing so, his analysis also drew attention to some of the perennial challenges of prevention. Because most diseases are unevenly distributed in populations, population-wide interventions may bring large benefits to an entire population but small benefits to most individuals. For the latter, even a small cost of participation, or a small risk that treatment is harmful, could outweigh the benefits, discouraging compliance.

The investigation of social and economic factors that influence health has a long tradition.[48] Initiatives, such as the World Health Organization (WHO)'s Commission on the Social Determinants of Health (2008), have driven action on 'the causes of the causes'[63] from an explicitly ideological position. In the view of this Commission, health inequalities are unfair and putting them right is a matter of social justice.[64] That ethical position echoes the constitution of WHO where 'the highest attainable standard of health is one of the fundamental rights of every human being'.[65] A weakness of the ideological approach, however, lies in an unwillingness to understand alternative values and viewpoints, when progress actually hinges on such an understanding.[66] To make ideology work, it must be turned into instruments of enticement (carrots: financial and other rewards) or censure (sticks: laws, regulations, social customs), or both.[67] Broadly speaking, the enticements are to promote health, the censures are to prevent illness, but both have leverage (Chapter 6).

There are other reasons why the case for investing in the social, economic, and environmental determinants of health needs to be carefully constructed: although these factors account for as much as 45%–60% of the variation in health in populations around the world (Preface), the benefits of tackling them compared with, say, vaccination or reducing blood pressure, are generally less certain and realized over longer timescales. Despite much promotion, action on the social determinants of health has been less effective than hoped. Successes have been local rather than global, for various reasons: an inward-looking medical focus on health service coverage, commercial conflicts with health, and an equity agenda that does not necessarily appeal to the public or to policymakers.[66]

The questions at the heart of the McKeown debate—prevention versus treatment, market economics versus publicly funded state

intervention—remain alive and relevant today. These questions apply just as much to environmental health risks as to those linked to society and the economy.[68]

Environmental becomes existential

As the human population surpassed three billion around 1960, it was becoming clear that none of the earth's life support systems would be free from human influence. The airs, waters, and places of Hippocrates' world were largely fixed sources of risk or benefit to health. Now all natural resources were being shaped by human activity, in all parts of the planet, with big consequences for health and well-being.

Rachel Carson's (1907–64) *Silent Spring* (1962) was a gospel for the new age of concern about mankind's impact on the environment. Carson persuaded a worldwide audience that the indiscriminate use of pesticides was not only poisoning the environment: it was also poisoning people.

Carson contributed to the invention of 'environment' as a political force. *Silent Spring* was a potent influence on a succession of international conferences that made the connection, systematically and systemically, between environment and health. The United Nations Conference on the Human Environment (Stockholm, 1972) proclaimed that 'Man is both creature and moulder of his environment'. The ensuing Stockholm Declaration listed the preventable environmental risks to physical, mental, and social health, specifically 'dangerous levels of pollution, disturbances to the ecological balance of the biosphere, and the depletion of irreplaceable resources'.

The impetus generated in Stockholm was maintained by the 1987 Report of the World Commission on Environment and Development (also known as 'the Brundtland Commission'), which proposed that sustainable development should 'meet the needs of the present without compromising the ability of future generations to meet their own needs'.[69] This definition of sustainability, still used today, laid down a criterion for investing in *Our Common Future*, and for preserving the health and well-being of future generations. As in the Stockholm conference, the Brundtland Commission took a systemic, holistic view of development by framing poverty, inequality, and environmental degradation as interdependent challenges.

The goal of the Earth Summit (Rio de Janeiro, 1992) was to promote international cooperation on the environment after the end of the Cold War. Its main product, the *Rio Declaration on Environment and Development*,

embraced the precautionary principle, which had previously been central to the *Montreal Protocol on Substances that Deplete the Ozone Layer* (1987). In the face of future uncertainty, the precautionary principle looks, at first sight, like a strong argument for prevention.[70] Whereas physicians treating individual patients are under oath to 'above all, do no harm',[71] the precautionary principle says, in effect, 'above all, *allow* no harm'. Both principles aim to avoid errors in the face of uncertainty. However, both are ambiguous in practice because decisions, whether they concern the well-being of individuals, populations, or the environment, should balance costs against benefits. For the precautionary principle, to propose safeguards for prevention is not likely to be persuasive unless the benefits (time-discounted and risk-adjusted) outweigh the costs.

Against this historical background, it is widely recognized that the social, economic, environmental, and ethical factors affecting health are interdependent. And yet, in practice, each of these preventable risks to health has been pursued separately, championed, for example, by different intergovernmental organizations: poverty (World Bank), environment (United Nations Environment Programme), food (Food and Agriculture Organization), zoonotic diseases (World Organisation for Animal Health), and health services (WHO).

While specialization gave energy and identity to each technical domain, it neglected the benefits of synergy and connectivity. At the end of the twentieth century, it was time to draw together the separate strands of development to create a comprehensive programme for human health and well-being. 'Ecological public health'[72] might, by cross-linking causes and effects, reinvigorate the agenda for prevention in the twenty-first century—the age of sustainable development.

Prevention for sustainable development

Now, early in the twenty-first century, the United Nations has already set two successive sets of goals based on two different propositions for development: the Millennium Development Goals (MDGs 2000–15) and the Sustainable Development Goals (SDGs 2016–30).[73] The SDGs, more than the MDGs, are a potentially powerful force for prevention.

Three of the eight MDGs were linked to health, focusing on mothers, children, and infectious diseases. The health goals were treated separately from each other and from the other five. They were each to be achieved

through top-down, prescriptive, time-limited programmes targeting major causes of illness and death in low- and middle-income countries. Not all goals were met but substantial gains were made: the number of people living in extreme poverty; the malaria, TB, and under-five mortality rates; and the maternal mortality ratio all fell by about one-half or more between 1990 and 2015.[74]

The success of these targeted health programmes was attributed to the provision of medical technologies such as vaccines and drugs. But these successes also relied on functioning health services, run by skilled health workers with health information systems, supply chains, and financing and governance mechanisms. Health gains also depended on social, economic, and environmental factors that lie outside the control of the health sector, such as female education and fertility, family income, and access to safe water and sanitation.[74] This restatement of root causes was integral to the MDG upgrade—the fully comprehensive 2030 Agenda for Sustainable Development.[74] Linked to that Agenda, the 17 SDGs open up new opportunities for development in general and for prevention in particular, tackling the root causes of ill health on all temporal and spatial scales.[75,76]

The transition from MDGs to SDGs requires a cultural change that could take a generation or more. The transition has, in effect, rekindled the McKeown debate. Some experts have argued for maintaining the momentum achieved under the targeted approach. The Copenhagen Consensus Center published in 2015 *The Nobel Laureates' Guide to the Smartest Targets for the World*, still arguing for specific objectives to maximize impact, such as 'lower chronic child malnutrition by 40%', and 'increase immunization, reduce child deaths by 25%'. This chimes with the views of some health professionals who believe that the 'unfinished agenda' of child survival is best served by doing more of what the MDGs prescribed: investing in the immediate benefits of primary health care, rather than in the less certain and slowly realized benefits of, for instance, female education.[77] The argument to 'create fair employment and good work for all'[64] as a basis for better health presents a far greater challenge than, say, 'vaccinate all girls aged 12–18 years against human papilloma virus to protect them from cervical cancer'.[78] In fact, the two approaches should be complementary rather than mutually exclusive, as envisioned by the 2030 Agenda to achieve the SDGs. There is no need, in principle, to choose between prevention and cure, but limited resources might force a choice in practice (Chapter 3).

The principal new goal for health, SDG 3, aims 'to ensure healthy lives and promote well-being for all at all ages'. Universal Health Coverage (UHC), seen as central to achieving SDG 3, means that all individuals and communities receive the health services they need without suffering financial hardship.[79] However, it is under the umbrella of UHC, sitting mainly within the health sector, that 96% of health funding is invested in treatment and only 4% in prevention (Preface, Chapter 3). The advantage of UHC is that it responds to the huge demand for health services: at least half of the world's population still do not have full coverage of essential health services. The disadvantage is that it places less emphasis on tackling the preventable, root causes of ill health, which reside in the other 16 SDGs.

Pay now, live later?

From ancient sanitary systems to contemporary development goals, the circumstances of disease prevention have changed radically over five millennia. The number of people on Earth has increased by a factor of a thousand (from about 7 million to 7 billion); lifespan has more than doubled; the principal causes of death have shifted from infectious diseases in young populations to chronic diseases in aging populations; there is vastly greater understanding of the causes and effects of illness and death, opening up an array of opportunities for intervention; the practice of public health, and the need for collective action, now occur on greatly expanded geographical (from provincial to planetary) and temporal scales (from weeks to centuries).

And yet the underlying principles of prevention—whether applied to personal, social, economic, or environmental health—have remained the same. Throughout history, aspirations to good health have faced the down-to-earth reality that benefits usually come at a cost—hope is free, but expectation has a price tag.

This historical overview, like most others concerning public health, has centred on Europe. But the conditions for staying healthy are the same everywhere: prevention (of any kind of adverse event) should hold most appeal when a reasoning decision maker is asked to pay a small amount while healthy, for an intervention of proven efficacy, against the likely occurrence, in the near future, of an event that is perceived to be serious, such as grave personal illness. Those who pay for prevention want to be assured that the benefits will go to the intended recipients, especially when contributing

to collective action for the common good. They should be more willing to pay in advance when avoiding future harm also comes with immediate benefits—such as fresh airs, clean waters, and safe places.

If there is a choice between acting sooner (prevention) or later (treatment and cure), under what conditions will those who have the power to decide favour the former over the latter? By understanding these conditions, is it possible to shift the balance towards staying healthy, or becoming even healthier? Informed by the past, the next step is to lay out a logical framework for investigating prevention—a theory of thinking ahead (Chapter 2).

Summary

The main ideas about preventing illness run through the whole of human history even if, in every age and in every place, they find new interpretation. Spanning 5,000 years, this chapter reveals prevention's common themes, including the following: illnesses have preventable causes (Neolithic filtration and boiling of water); the choice of prevention over cure is conditional on the balance of costs and benefits, where the benefits depend on the risk, timing, and severity of the hazard (shipping insurance, from 4000 BC); prevention is about improving health, not merely avoiding illness (Ancient Greece); prevention is for communal as well as personal health (Roman aqueducts and communal toilets); prevention is at a premium in the absence of a cure (fourteenth-century plague); the costs and benefits of prevention can be calculated and used to make choices about health (Franklin on fire insurance, Chadwick on sanitation); and the immediate, preventable causes of illness (diet, tobacco) depend, in turn, on deeper causes, in societies, economies, and environments (Hippocrates to the SDGs).

References

1. de Roode JC, Lefevre T, Hunter MD. Self-medication in animals. *Science* 2013; *340*: 150–1.
2. Shurkin J. Animals that self-medicate. *Proceedings of the National Academy of Sciences of the United States of America* 2014; *111*: 17339–41.
3. Castella G, Chapuisat M, Christe P. Prophylaxis with resin in wood ants. *Animal Behaviour* 2008; *75*: 1591–6.
4. Brütsch T, Chapusiat M. Wood ants protect their brood with tree resin. *Animal Behaviour* 2014; *93*: 157–61.

5. Zito M, Evans S, Weldon PJ. Owl monkeys (*Aotus* spp.) self-anoint with plants and millipedes. *Folia Primatologica (Basel)* 2003; *74*: 159–61.
6. World Health Organization (WHO) and United Nations Children's Fund. *Progress on Drinking Water, Sanitation and Hygiene: 2017 Update and SDG Baselines*. Geneva: World Health Organization; 2017.
7. Mithen S. *Thirst: Water and Power in the Ancient World*. London: Weidenfeld and Nicholson; 2012.
8. Rosen G. *A History of Public Health*. New York: MD Publications; 1958.
9. Wilson A. Drainage and sanitation. In: Wikander Ö, ed. *Handbook of Ancient Water Technology (Technology and Change in History)*. Leiden: EJ Brill; 2000: 151–79.
10. Tankersley KB, Dunning NP, Carr C, Lentz DL, Scarborough VL. Zeolite water purification at Tikal, an ancient Maya city in Guatemala. *Scientific Reports* 2020; *10*: Article number: 18021.
11. Rochberg F. Science and Ancient Mesopotamia. In: Taub AJL, ed. *The Cambridge History of Science*. Cambridge: Cambridge University Press; 2018: 7–28.
12. Kleisiaris CF, Sfakianakis C, Papathanasiou IV. Health care practices in ancient Greece: The Hippocratic ideal. *Journal of Medical Ethics and History of Medicine* 2014; *7*: 6.
13. Tountas Y. The historical origins of the basic concepts of health promotion and education: The role of ancient Greek philosophy and medicine. *Health Promotion International* 2009; *24*: 185–92.
14. Porter D. *Health, Civilisation and the State: A History of Public Health from Ancient to Modern Times*. Abingdon: Routledge; 1999.
15. Hill Curth L. Lessons from the past: Preventive medicine in early modern England. *Medical Humanities* 2003; *29*: 16–20.
16. Brand N. *The Concept of the* Sanus Homo *in the* De Medicina *of Celsus*. Stellenbosch: University of Stellenbosch; 2007.
17. Haueter NV. *A History of Insurance*. Zurich: Swiss Reinsurance Company Ltd; 2017.
18. Buckham D, Wahl J, Rose S. The evolution of insurance. In: *Executive's Guide to Solvency II*. Cary, North Carolina: SAS Institute Inc.; 2010: 1–9.
19. Jacquart D. Anatomy, physiology, and medical theory. In: Lindberg D, Shank M, eds. *The Cambridge History of Science*. Cambridge: Cambridge University Press; 2013: 590–610.
20. Hin S. Mortality. In: *The Demography of Roman Italy: Population Dynamics in an Ancient Conquest Society (201 BCE–14 CE)*. Cambridge: Cambridge University Press; 2013: 101–71.
21. Kelishadi R, Hatami H. Avicenna as the forerunner of preventive medicine: On the occasion of 1032nd birth anniversary of Avicenna (22 August 980). *International Journal of Preventive Medicine* 2012; *3*: 517–19.
22. Sairisi NG. *Medieval and Early Renaissance Medicine: An Introduction to Knowledge and Practice*. Chicago: University of Chicago Press; 1990.
23. Barker W. *The Adages of Erasmus*. Toronto: University of Toronto Press; 1500.
24. Cogan T. *The Haven of Health*. London: Roger Ball; 1612.

25. Facts and Details. Nero, Christians, the Great Fire, the rebuilding of Rome and his death. 2019. factsanddetails.com/world/cat56/sub368/entry-6271.html (accessed 7 January 2021).
26. Rogers EM. *Diffusion of Innovations*. 5th edn. New York: Free Press; 2003.
27. Weiss RA, Esparza J. The prevention and eradication of smallpox: A commentary on Sloane (1755) 'An account of inoculation'. *Philosophical Transactions of the Royal Society B* 2015; 370.
28. Grundy I. *Montagu, Lady Mary Wortley*. Oxford: Oxford University Press; 2004.
29. Best M, Katamba A, Neuhauser D. Making the right decision: Benjamin Franklin's son dies of smallpox in 1736. *Quality and Safety in Health Care* 2007; *16*: 478–80.
30. Handman E. Leishmaniasis: Current status of vaccine development. *Clinical Microbiology Reviews* 2001; *14*: 229–43.
31. Porter D. *Health, Civilization and the State: A History of Public Health from Ancient to Modern Times*. London and New York: Routledge; 1999–01.
32. Hamlin C, Sheard S. Revolutions in public health: 1848, and 1998? *BMJ* 1998; *317*: 587–91.
33. Lutz W. Global Sustainable Development priorities 500 y after Luther: *Sola schola et sanitate*. *Proceedings of the National Academy of Sciences of the United States of America* 2017; *114*: 6904–13.
34. Black M, Fawcett B. *The Last Taboo: Opening the Door on the Global Sanitation Crisis*. London: Earthscan; 2008.
35. Dye C. 200 years in the history of longevity. *The Biologist* 2010; *57*: 127–30.
36. Dye C. After 2015: Infectious diseases in a new era of health and development. *Philosophical Transactions of the Royal Society B: Biological Sciences* 2014; *369*: 20130426.
37. Bloy M. Edwin Chadwick (1800–1890). 2002. http://www.victorianweb.org/history/chad1.html (accessed 7 January 2021).
38. van Oosten R. The Dutch Great Stink: The end of the cesspit era in the pre-industrial towns of Leiden and Haarlem. *European Journal of Archaeology* 2016; *19*: 704–27.
39. Acheson RM. Henry Wyldbore Rumsey and the case for state medicine. *Public Health* 1988; *102*: 217–25.
40. Watkins DE. *The English Revolution in Social Medicine, 1889–1911*. London: University of London; 1984.
41. Simon J. *English Sanitary Institutions, Reviewed in their Course of Development, and in some of their Political and Social Relations*. London: Cassell & Company; 1890.
42. Chadwick E. *Report on the Sanitary Conditions of the Labouring Population of Great Britain: A Supplementary Report on the Results of a Special Inquiry into the Practice of Interment in Towns*. London: Poor Law Commissioners; 1843.
43. Joshi P. Edwin Chadwick's self-fashioning: Professionalism, masculinity, and the Victorian poor. *Victorian Literature and Culture* 2004; *32*: 353–70.
44. Tynan N. Nineteenth century London water supply: Processes of innovation and improvement. *The Review of Austrian Economics* 2013; *26*: 73–91.

45. Smith GD. Commentary: Behind the Broad Street pump: Aetiology, epidemiology and prevention of cholera in mid-19th century Britain. *International Journal of Epidemiology* 2002; *31*: 920–32.
46. Worboys M. Public and environmental health. In: Pickstone PBJ, ed. *The Cambridge History of Science*. Cambridge: Cambridge University Press; 2009: 141–64.
47. Ullmann A. Pasteur–Koch: Distinctive ways of thinking about infectious diseases. *Microbe* 2007; *2*: 383–7.
48. Szreter S. The population health approach in historical perspective. *American Journal of Public Health* 2003; *93*: 421–31.
49. McKeown T. *The Role of Medicine: Dream, Mirage, or Nemesis?* London: Nuffield Provincial Hospitals Trust; 1976.
50. Szreter S. Rethinking McKeown: The relationship between public health and social change. *American Journal of Public Health* 2002; *92*: 722–5.
51. Link BG, Phelan JC. McKeown and the idea that social conditions are fundamental causes of disease. *American Journal of Public Health* 2002; *92*: 730–2.
52. Dye C. *The Population Biology of Tuberculosis*. Princeton: Princeton University Press; 2015.
53. Bynum LJ. Riding the waves: Optimism and realism in the treatment of TB. *Lancet* 2012; *380*: 1465–6.
54. Preston SH. *Mortality Patterns in National Populations: With Special Reference to Recorded Causes of Death*. New York: Academic Press; 1976.
55. Fogel RW. *The Escape from Hunger and Premature Death, 1700–2100: Europe, America and the Third World*. Cambridge: Cambridge University Press; 2004.
56. Deaton A. The great escape: A review essay on Fogel's 'The Escape from Hunger and Premature Death, 1700–2100'. *Journal of Economic Literature* 2006; *44*: 106–14.
57. Fogel RW. Health, nutrition, and economic growth. *Economic Development and Cultural Change* 2004; *52*: 643–58.
58. Deaton A. *The Great Escape. Health, Wealth, and the Origins of Inequality*. Princeton and Oxford: Princeton University Press; 2013.
59. Bunker JP, Frazier HS, Mosteller F. Improving health: Measuring effects of medical care. *Milbank Quarterly* 1994; *72*: 225–58.
60. Rose GA. *Rose's Strategy of Preventive Medicine: The Complete Original Text*. Oxford: Oxford University Press; 2008.
61. Charlton BG. A critique of Geoffrey Rose's 'population strategy' for preventive medicine. *Journal of the Royal Society of Medicine* 1995; *88*: 607–10.
62. Rose G. Strategy of prevention: Lessons from cardiovascular disease. *British Medical Journal (Clinical Research Edition)* 1981; *282*: 1847–51.
63. Marmot M. Social determinants of health inequalities. *Lancet* 2005; *365*: 1099–104.
64. Marmot M. *Fair Society, Healthy Lives: The Marmot Review*: *Strategic Review of Health Inequalities in England Post-2010*. London: Marmot Review Team.
65. World Health Organization. *Constitution of the World Health Organization*. Geneva: WHO; 2006.

66. Rasanathan K. 10 years after the Commission on Social Determinants of Health: Social injustice is still killing on a grand scale. *Lancet* 2018; *392*: 1176–7.
67. de Sadeleer N. *The Principle of Prevention. Environmental Principles: From Political Slogans to Legal Rules*. Oxford: Oxford University Press; 2002.
68. Colgrove J. The McKeown thesis: A historical controversy and its enduring influence. *American Journal of Public Health* 2002; *92*: 725–9.
69. World Commission on Environment and Development. *Our Common Future*. Oxford: United Nations World Commission on Environment and Development (WCED); 1987.
70. Greenhalgh T, Schmid MB, Czypionka T, Bassler D, Gruer L. Face masks for the public during the covid-19 crisis. *BMJ* 2020; *369*: m1435.
71. Smith CM. Origin and uses of *primum non nocere*—above all, do no harm! *Journal of Clinical Pharmacology* 2005; *45*: 371–7.
72. Lang T, Rayner G. Ecological public health: The 21st century's big idea? *BMJ* 2012; *345*: e5466.
73. United Nations. *The Sustainable Development Goals Report*. New York: United Nations; 2018.
74. Dye C. Expanded health systems for sustainable development. *Science* 2018; *359*: 1337–9.
75. International Council for Science (ICSU). *A Guide to SDG Interactions: From Science to Implementation*. Paris: ICSU; 2017.
76. Nilsson M, Griggs D, Visbeck M. Map the interactions between Sustainable Development Goals. *Nature* 2016; *534*: 320–2.
77. Bryce J, Victora CG, Black RE. The unfinished agenda in child survival. *Lancet* 2013; *382*: 1049–59.
78. National Health Service. Who should have the HPV vaccine? 2017. https://www.nhs.uk/conditions/vaccinations/who-should-have-hpv-cervical-cancer-cervarix-gardasil-vaccine (accessed 7 January 2021).
79. World Health Organization. Universal health coverage (UHC). 2019. https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc) (accessed 7 January 2021).