

begin with the government systems of hospitals, vaccinations, written records and social care of 1000 years ago.

- *is not just* modern scientific medicine. If that were true, then epidemiology would begin with the era of germ theory, sanitation and rapid development of medical science from 150 years ago.

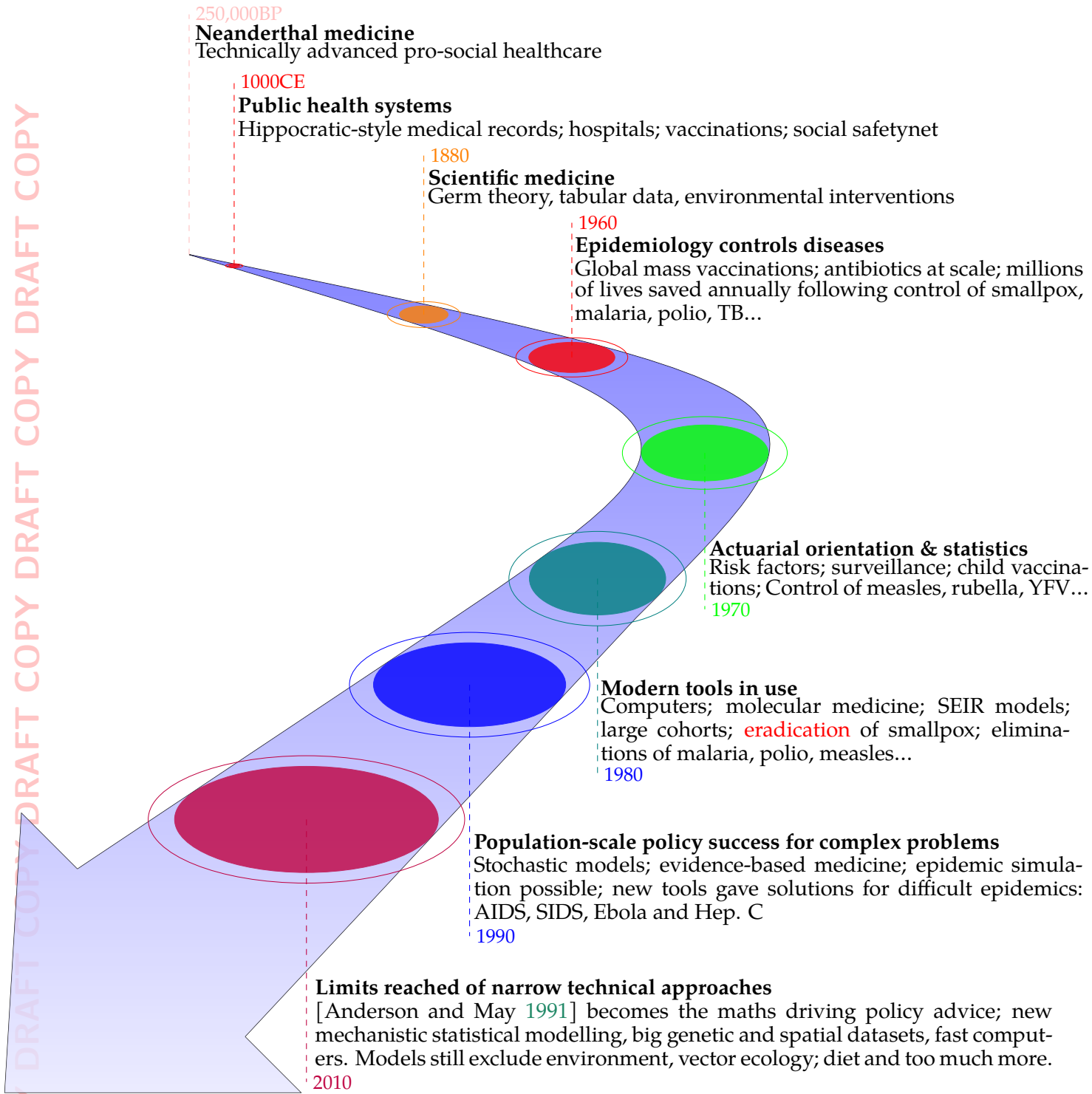
These are essential, life-saving steps towards epidemiology, but not effective disease management. Consider that despite medical progress 1900–1950, deaths from smallpox alone likely exceeded 150 million[Fenner et al. 1988], TB killed tens of millions per decade[Dye et al. 1999], malaria caused an estimated 2–3 million deaths annually throughout the period[Carter and Mendis 2002], and the 1918 influenza pandemic alone killed between 50 and 100 million[Johnson and Mueller 2002] — together well over 400 million deaths from just four diseases. Meanwhile, global infant mortality stood at 15–25% across the period, exceeding 20% at its start and still around 16% as late as 1950[United Nations Population Division 2011; Gapminder Foundation 2023]. And crucially, most of this toll predated effective medical intervention: antibiotics were not widely available until the late 1940s, meaning the great decline in mortality owed far more to improved nutrition, sanitation, and institutional structures than to medicine itself[McKeown 1976; Deaton 2013]. The toll in previous centuries was far higher still.

Then, 75 years ago, entire populations of urbanised people were made safe from deadly pathogens and behaviours. From about 1950 epidemiologists had standard scientific ways to reason about health and perform mathematical calculations. Whole societies engaged with policy and implementation arising from this reasoning. Diseases were controlled and then suppressed, en route to elimination.

Epidemiology really took off from 1950, and until about 2010 the field had clear but frequently-changing boundaries. This is classical epidemiology — take some medical data, perform calculations, produce graphs, analyse policy options, and provide advice to save lives. While this still describes epidemiology in part, the field is now a participant in something much larger.

The following diagram illustrates epidemiology progression until 2026. The dates given in the diagram are when the knowledge described is applied in widespread use, not its invention or first known use.

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One Health 2010–2026

Since about 2010, technical ability and political motivation have brought together dozens of scientific and medical fields to address what narrow epidemiology could not. The Global One Health Index [Zhang et al. 2024] tracks progress. See §4 for the current situation, including the US withdrawal from WHO in 2025.

This is the new epidemiology in 2026.

The last node in the timeline highlights advanced epidemiology, observing that progress slowed and therefore lives were being lost. During the whole of the 20th century Western societies seemed to abandon the idea of human health depending on the environment, until faced with intractable new diseases when this was embraced again.

3 What exactly is One Health?

One Health holds that population health is impacted by the environment, social activities, climate and animal health, besides the expected pathogens and medical conditions. Most of the natural and social sciences have a place in One Health, and more besides [Meisner et al. 2024].

Now we need to look at how epidemiology's familiar 20th century silo-style approach is an historical anomaly. The transition to break down these silos, is more like a reversion to the mean than a new approach. As will be shown, it is very relevant that collaboration with non-human aspects has been a normal way to improve health.

Two well-documented historical examples date from about 2300 years ago: the famous doctor Hippocrates in Kos (near modern-day Turkey), and Ashoka, king of a vast empire centred on modern-day India. Hippocrates wrote about the environment in his medical case notes (see Appendix B: *Historical steps towards epidemiology*) and King Ashoka issued edicts on the topic including the following:

Ashoka Rock Edict II, 257BCE



Everywhere, I, Ashoka, King Priyadarsi, Beloved of the Gods, have arranged for two kinds of medical treatment: medical treatment for men and medical treatment for animals. Wherever medical herbs suitable for humans or animals were not available, I have had them imported and grown. Wherever medical roots or fruits were not available, I have had them imported and grown. Along roads, I have had wells dug and trees planted for the benefit of humans and animals.

[Woolner 1924]pp. 5-6

Scientific One Health is often traced to Al-Razi of Baghdad [Tibi 2006], with the [Royal College of Physicians of Edinburgh](#) highlighting his clinical trial for distinguishing smallpox from measles [Tibi 2005] published in 900CE. Al-Razi's *Comprehensive Book of Medicine*² contains notes of his environmental engineering and animal care to prevent zoonoses and vector borne diseases.

In modern times [Schwabe 1984] published on human and animal health, often re-

² this Arabic book [al-Rāzī 1955–1971] has many thousands of pages. The Latin translation is *Liber Continens* ("Book of Everything") a collection of al-Rāzī's notebooks, clinical observations, and excerpts from foreign medical texts — all the medical knowledge he could find. *Liber Continens* was a European bestseller for centuries, the most expensive book of its time and still the only complete translation.

insufficiently integrated and non-communicable diseases largely neglected[Winkler et al. 2025]. A second line of critique, developed principally by Latin American and Global South scholars, is that One Health reproduces colonial knowledge hierarchies: it treats the health knowledge systems of the Global South as deficits to be corrected by northern science, rather than as accumulated expertise in multispecies ecological living that predates the concept[Baquero et al. 2021]. A related concern is that animal and environmental health are treated instrumentally — as inputs to human health rather than as values in their own right — meaning One Health risks propagating the same anthropocentrism it nominally challenges[Yopa et al. 2023; Van Patter et al. 2023]. Scientists arriving from outside biomedicine are therefore joining One Health at the right moment, with needed skills to help address these well-founded critiques.

In any case, One Health is the approach most of the governments and supporting organisations in the world have chosen to address our whole-ecosystem health problems.

4 One Health in 2026

To answer the question **what is One Health?** we went to a bland official definition: *One Health is a unifying approach to sustainably balance and optimise the health of humans, animals, and ecosystems through coordinated action across multiple sectors, disciplines, and levels of society* [Food and Agriculture Organization of the United Nations et al. 2025]. We found WHO’s informative [One Health fact sheet](#) and the Berlin Principles of One Health[Gruetzmacher et al. 2021] are key.

None of these really help scholars just wanting to be informed. Dissatisfied, we looked at what is unique about One Health, starting with its scope.

What distinguishes One Health from other large-scale scientific initiatives is operational complexity: it demands integration not only of diverse scientific disciplines but also of different knowledge systems (traditional and scientific), different operational timescales (immediate clinical response alongside long-term ecological monitoring), and vastly different professional cultures, all while maintaining real-time surveillance and response capabilities. At a technical level [Oltean et al. 2025] identifies challenges to “radical multidisciplinary” merely within the United States including recording individual health in a compatible way with measurements about rivers. Politically, [Lee and Brumme 2023] discusses scope and scale, including who is paying for One Health and who is making the rules. We conclude that while One Health shares common features with the IPCC, national combined science organisations and large space programmes, it exceeds them all in complexity and vastness.

We identified some defining characteristics of One Health:

- Singular focus on improving collective health of humans, animals and ecosystems.
- Urgent, due to emerging diseases, vulnerable populations, and accelerating an-

thropogenic behaviour.

- Slow, due to so many organisations needing to work together for the first time.
- Systemic, needing to study and make changes in systems of systems of systems.
- Highly political, due to impacts on national wellbeing, wealth, prestige and competitiveness and the power imbalance disfavouring the global South.
- Deciding things hitherto unknown: what should we be counting? What are the official numbers of these things?
- Especially harmed by US actions: many, arguably most, of the hundreds of the targeted multilateral treaties, organisations and science collaborations have to do with One Health.

In many ways the global discussion has only just started. Multi-disciplinary questions are being addressed at the regional and country grouping level though, including things such as:

- What standards can we agree on for measuring the deluge of data from -omics and real-time observations?
- Who is going to fund surveillance and ongoing measures which are less visible than emergency response?
- Which sentinel species should we surveil for chemical pollution, cancer and obesity?
- Which changes in farming practices can stop specific vectors increasing their range?
- What preventative measures should we deploy right now against zoonotic spillover of prion diseases?
- Should we prioritise AMR reservoirs in ecosystems over humans?
- What plant species best reverse urban deforestation to slow emerging diseases?

There seems a great deal of One Health activity in regions with uneven development, indicated by progress papers in e.g. China[Gao et al. 2025; Wei et al. 2025], South America[Manterola et al. 2024] and others. Developed countries including in Europe are highly vulnerable but have been slower to operationalise One Health at the national level, with a 2025 EU/EEA study finding that cross-sectoral collaboration still requires “incremental steps” to become sustainable[Kuhn et al. 2025]. Low middle-income countries carry the highest burden of the threats One Health was built to address: zoonotic disease, vector-borne illness, and antimicrobial resistance. These countries have the greatest incentive and the sharpest operational experience[Yopa et al. 2023]. The Global One Health Index[Zhang et al. 2024] confirms this pattern across 195 countries, finding that LMIC regions are ahead of many wealthier counterparts in building the inter-sectoral governance and field surveillance capacity.

The complexity above is real, but individual contributions do not need to be complex. One Health advances when specialists share what they already know in forms that modellers can use. Here are concrete starting points:

Starting in One Health

One Health needs scholars who can communicate a rate or a dataset, and also, scholars with a question, a method, or factual evidence. The following applies to both.

- **Find a model that needs parameters from your knowledge.** One Health models are often open: search for models in your disease area and read the parameter tables. Domain data is weakest when you see “assumed,” “estimated from literature,” or given suspiciously round values.
- **Are your measurements model-ready?** Expressing a measurement as a rate requires four things: a numerator, a denominator, a population definition, and a time period. “*Mean 14 bites per person per night, July, 28°C, semi-urban Burkina Faso*” is immediately usable. “*High biting activity in summer*” is not, however, if that is the historical evidence over the last 200 years then that could be crucial, and you can seek help to transform it from field observation to model parameter.
- **Is your data interoperable?** One Health data must flow between clinical systems (which expect **FHIR** or **OMOP** formats), ecological databases (such as **GBIF** for species occurrence), and epidemiological surveillance feeds. If your measurements use non-standard species names, informal geographic identifiers, or units that do not match surveillance case definitions, they will be unusable. Ask your collaborators early what format they need.
- **Decide whether you are contributing data, analysis, or interpretation.** Epidemiological models produce numbers, but numbers do not speak to policymakers. Sociologists, anthropologists, historians and political scholars supply the behavioural and institutional parameters that no field trial can measure directly. These include compliance rates under different governance structures, trust dynamics affecting vaccine uptake, the organisational conditions under which inter-agency surveillance actually functions. In modelling, these are often parameters where a small change gives entirely different policy recommendations.
- **For historians, your data predates the models.** Epidemiological models require validation, and the most demanding validation test is fitting to an outbreak that has already ended and whose outcome is known. Historical epidemic records are cited in this paper ([Yi 2015], [Johnson and Mueller 2002], [Snow 1855] and more) These are the longest out-of-sample test sets available to modellers and can be hugely valuable. The historical question and the modelling question should be designed together, not retrofitted.

- **Find your organisations.** The Quadripartite [Joint Plan of Action](#) lists national focal points; most countries now have a designated One Health coordinator in the ministry of health or agriculture. Discipline-specific networks exist including veterinary One Health platforms, One Health entomology groups, and climate-health working groups within UNEP. These are the places where modellers and domain scholars actually meet and where data-sharing agreements get negotiated.

5 Conclusion

Epidemiology has embraced a wide range of sciences because today's health threats are more complex and amplified by anthropogenic activity. By addressing the health needs of entire ecosystems the hope is that ill-health in the broadest sense can be addressed, because it is now clear that unless the plants and animals are healthy the humans won't be either. The resulting scientific collaboration is still recognisable as epidemiology because that is where its measurables and methods come from, and therefore also its language of communication: rates of health and disease; expected impact of society-wide interventions, and causal information.

One Health brings together clinical knowledge, standardised surveillance data, mathematical modelling, and the environmental and animal systems that drive the health of human populations. The progression from Hippocrates' case notes to Kermack and McKendrick's differential equations, to the inclusion of today's rule-based and agent-based simulations correlates with the embrace of new sources of data and new forms of scientific thinking.

This is where scholars from other fields become essential. An ecologist who can identify sentinel species, an historian who documents evidence of plagues down the ages, a veterinarian who knows the dynamics of a zoonotic reservoir, a climate scientist who can quantify vector range expansion, and a sociologist who can explain collective human responses to health pressures — each brings variables and rates that epidemiological models need.

The [2025 World Health Statistics Report](#) [WHO 2025a] show that health progress has been derailed, worsened by instability around the US withdrawal from WHO and the multilateral health system (Appendix D: *US withdrawal from WHO and One Health*). And yet global commitments to One Health have increased, and the [current WHO work programme](#) aims to dramatically accelerate progress by the end of 2026. Regional bodies across Africa, Asia and Latin America are building new collaborative structures.

One Health is hugely ambitious, involves most of the natural and social sciences, and has made very uneven progress. But the mathematical and organisational tools now exist to make it work, and the scientific workforce is expanding to include people never previously considered epidemiologists. Whether the 2030 WHO report is happier reading will depend in large part on how quickly these new scholars find their

way into the collaboration.

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Appendices

Appendix A Cheatsheet glossary for non-epidemiologists

This cheatsheet explains a minimum subset of the language of epidemiology for scholars in a hurry. Better glossaries are available³.

Health related states or events This is a clumsy term, but it means “everything epidemiology studies”. That covers infectious diseases such as measles, non-infectious diseases such as diabetes, violence [Ransford et al. 2025] and even online misinformation [Gavric et al. 2025]. Epidemiologists are not just disease detectives, although they certainly are that.

Outbreak A sudden increase in cases of a disease above what is normally expected in a defined area. An outbreak is the unit of alarm and is what triggers an epidemiological investigation. Outbreaks can be as small as two linked cases of a rare disease or as large as the initial wave of a pandemic.

Surveillance The ongoing, systematic collection and analysis of health data to detect outbreaks, monitor trends and guide interventions. Surveillance ranges from hospital reporting systems to wastewater sampling and sentinel veterinary networks.

Incidence The number of *new* cases of a disease in a population over a defined time period. Usually expressed as a rate: cases per 1000 person-years, or per 100,000 per month. Incidence tells you how fast people are becoming ill.

Prevalence The *total* number of existing cases (new and ongoing) at a given point in time or over a period. A disease with short duration has low prevalence even if incidence is high; a chronic disease accumulates prevalence even when few new cases arise.

Relative Risk The ratio of incidence in an exposed group to incidence in an unexposed group. If farmworkers exposed to a pesticide have twice the cancer incidence of unexposed workers, the relative risk is 2.0. This is the most intuitive way to express how much a risk factor matters.

Confidence Interval A range of values within which the true value is likely to fall, given the observed data, and most numbers in epidemiology come with one. A 95% confidence interval means if the study were repeated many times, 95% of the calculated intervals would contain the true value. Confidence intervals appear on virtually every number in epidemiology.

Cohort Study A study that follows a group of people over time, comparing those exposed to a risk factor with those not exposed, to see who develops disease. Cohort studies establish temporal sequence which is why they provide stronger evidence of causation than cross-sectional snapshots.

³ from e.g. the US CDC[Disease Control and Prevention 2024], WHO[WHO 2004], Johns Hopkins School of Public Health[Public Health 2018] and even an EU food safety One Health glossary.

Case-Control Study A study that starts with people who have a disease (cases) and people who do not (controls), then looks backwards to compare their exposures. Faster and cheaper than cohort studies, especially for rare diseases, but more susceptible to bias in how controls are selected and exposures recalled.

Rates Epidemiology requires counting things over time, or per 1000, or some similar measure. The *incidence rate* is how many new cases there are, while *prevalence rate* is the total number of sick people. *Case fatality rate* is the number of people who die once diagnosed. *Infant mortality rate* and *maternal mortality rate* are common examples among many more. A Dutch epidemiologist wrote a children's book called *Daddy counts sick people* that sums it up.

All-cause Mortality The death rate from every cause combined, measured across a defined population and time period. Because it makes no attempt to assign a cause, it is immune to the misclassification and coding errors that affect cause-specific rates. This makes it both the most reliable single number in epidemiology and a powerful check on interventions: if a drug, vaccine or public health programme truly works, it should eventually show up as a reduction in all-cause mortality. If all-cause mortality is unchanged while a cause-specific rate falls, deaths may be displaced to other causes or the intervention may be causing harm that the targeted measure conceals.

Reproductive Number (R or R_0) This is just a number not a rate: the average number of new infections caused by one case of the disease. The bigger R , the more infectious the disease: winter flu is 0.9-2.1 people on average, while measles is 12-18 people.

Anthropogenic Caused by human activity, typically used in a negative sense such as pollution, climate change and ecocide. If it wasn't for anthropogenic pressures maybe we wouldn't need One Health.

Pathogen A virus, bacteria, parasite or fungus that causes disease in a host human, animal or plant. The pathogen infects the host, and is a microorganism.

Reservoir This is any place or thing where a pathogen can survive ready to infect. Examples include: rabies and ebola persist in bat populations; legionella bacteria live in water systems; malaria parasites and measles viruses live in human hosts. When conditions are right the pathogen exists in numbers ready for an epidemic. This is why eradicating a disease is so difficult.

Vector a living organism that transmits pathogens from an infected host or the environment to a host. Examples are ticks, mosquitoes, fleas, flies and rats. The vectors may feed on blood, or leave infected faeces for humans to touch. Warmer climates increase vector activity and therefore disease risk. If there were no reservoirs there would be nothing for the vectors to transmit.

Natural history The progression of a disease process in an individual over time, as understood by medical and biological science. For example the natural history of measles includes its various stages (incubation, fever period, rash stage, and recovery); its complications (swelling of the brain, pneumonia, death etc); transmission characteristics; and prognoses.

Sentinel species These are organisms that signal the presence of pathogens before they affect humans, because in some sense they are in the same environment as humans. For example, beehives sicken from agricultural pesticides that will, years later, cause Parkinson's in humans. Domestic pets suffer from cancer or obesity before their owners succumb to the same lifestyle causes. And many plants become visibly ill from air pollution in a matter of weeks.

Control Reducing disease to an acceptable level in one geographic area, perhaps by a vaccination campaign or reducing breeding places for particular insects. The disease will continue to circulate.

Suppression Reducing the number of cases to very low levels, often through multiple aggressive interventions. "Aggressive" here means "very keen, well-funded or even mandatory". Examples are mass testing and COVID-19 lockdowns. The disease will continue to exist and may bounce back once measures are stopped.

Elimination Reducing disease in a particular geographic area, usually a country or region. This requires ongoing surveillance (that is, constant testing but not mandatory testing) and usually mass vaccinations, and often high levels of hospital care during the elimination. The disease will still exist, and needs to be addressed whenever surveillance shows an outbreak is occurring.

Eradication Totally erasing the disease from the world, except in laboratory jars. This is very difficult and rare, and has only happened in the case of one and almost two diseases ever: **Smallpox**, and almost **Dracunculiasis** (sometimes **Guinea-worm**). In the theme of One Health, we could add the disease **Rinderpest**, a cattle disease that has been eradicated and therefore cannot mutate and harm other species including humans.

-demic words An *endemic* disease is constantly present in a particular population, like baseline seasonal flu in winter in temperate countries. An *epidemic* is a sudden, large increase in a disease beyond what is expected, confined to a particular geographic region. A *pandemic* is an epidemic in many regions or multiple continents, potentially global. The Greek *dēmos* means "people", so none of these apply to non-human animals or to plants.

Zoo-words A *zoonosis* is a disease can spread from non-human animals to humans, for example rabies from a dog bite. There are hundreds of *zoonoses*, comprising a majority of infectious diseases in humans. *Zoonotic spillover* is the first occasion when all the factors align and a disease has changed enough to jump from animals to humans. *Zoodemic* is expected disease, equivalent to endemic in humans. Non-human animals have *epizootic* and *panzootic* events, corresponding to epidemics and pandemics. Unsurprisingly, *zōon* means "animal" in Greek.

Phyto-words A *phytopathogen* is a pathogen that causes disease in plants. An *epiphytotic* is a plant disease outbreak affecting many plants across a wide area, the plant equivalent of an epidemic. *Epiphytology* is the study of epiphytotics and *panphytotics*, analogous to epidemiology. Well-known historical epiphytotics include the Irish Potato Famine (1840s), caused by the water mould *Phytophthora infestans*, and the chestnut blight that wiped out American chestnut tree in the early 20th century. The word pattern holds across the three pillars of One Health:

epi- (upon) + the population type (*dēmos* = people, *zōon* = animal, *phyton* = plant).

Appendix B Historical steps towards epidemiology

This appendix explains and expands on the arrow timeline diagram in [What is epidemiology not just?](#) The question at each point is **can epidemiology be done?** — specifically, is it possible to model disease? The US CDC Field Manual[Hedberg and Maher 2024] describes how data for modelling must have consistent definitions, time-based rates and completeness. These three requirements have not been met in human history until very recently.

Ancient medicine: records, but still partly mystical. The Ancient Egyptians of 4000 years ago kept extensive medical, pharmaceutical and surgical records but felt that magic and medicine were indistinguishable. About 2600 years ago Sushruta of India was an exceptionally skilled surgeon. His work Samhita[Suśruta 1907] understands infection and is highly rational, but still has categories for supernatural causality.

Ancient scientific medicine: data but no rates. Hippocrates was a doctor who wrote about epidemics and the environment[Hippocrates 1849b], and a theoretician who explicitly rejected mystical/religious explanations even for then-inexplicable illnesses such as epilepsy. His case notes[Hippocrates 1849a] (c. 400BCE) are so accurate that medical anthropology has established which two Plasmodium parasite species caused malaria in his patients[C. B. Cunha and B. A. Cunha 2008]. But they do not contain rates. Al-Razi of Baghdad[Tibi 2006] produced the most extensive case notes of the ancients, but even his data is not sufficiently regular to model. In the Song dynasty China (960–1279CE), records describe 293 epidemic instances across 12 diseases with state-funded hospitals, social distancing and mobile medical care[Yi 2015]. A century later in the Ming dynasty there was methodical vaccination[Kaitai 1590 CE–]. This data also fails the CDC requirements for epidemiology. In summary: **more than two and a half millennia of medical records, and none suitable for modelling.**

Tabular data arrives, 1750–1855. James Lind’s controlled scurvy trial[Lind 1753] produced the first data tables[[Scurvy Dataset 2023](#)] usable for statistical calculation. Post-revolution France mandated standardised death certificates in 1792[Assemblée législative nationale 1792], and Europe-wide standards followed in 1855 — at last we can calculate rates. John Snow’s cholera investigation[Snow 1855] produced tempo-spatial tables[[SnowData Package Manual 2023](#)] suitable for modelling.

The first epidemic model, 1927. Kermack and McKendrick[Kermack and McKendrick 1927] published the SIR model, applying chemical mass-action kinetics to human populations (see Appendix C: [Minimum requirement: mathematics](#)). [Anderson and May 1991] later linked compartmental models to empirical data from many diseases, making epidemiology intimately connected with modelling. From this point on, mathematical models and policy could inform each other.

The first modern-style blinded trial, 1948. The same UK Medical Research Council

who funded the current paper also conducted the first published randomised controlled clinical trial[UK Medical Research Council 1948], into Tuberculosis. The 1948 data can be used today[UK MRC 2024] but curiously, there is no evidence of Kermack-style modelling being used or discussed.

This brings us to 1950, after which epidemiology was applied in fully modern ways as discussed in the main paper.

Appendix C Minimum requirement: mathematics

C.1 Foundation: From Chemistry to Epidemiology

This appendix is aimed at scientific scholars with a quantitative background. Others may find the conceptual framing in *What is epidemiology not just?* sufficient.

The mathematical foundations of epidemiology come directly from chemical kinetics. There are three fundamental concepts:

1. **The Master Chemical Equation:** A system of differential equations describing how reaction rates relate to concentrations over time while preserving mass. Though reactions at the molecular level are inherently random, with vast numbers of particles the deterministic approximation holds remarkably well.
2. **Gillespie's Stochastic Algorithm:** Addresses the computational challenges when particle numbers are small (such as reactions within a single cell, or the initial "spark" of an outbreak). This discrete, probabilistic approach computes individual particle interactions using the rate constants from the master equation.
3. **Exponential Distributions:** Both deterministic and stochastic approaches assume reaction waiting times follow exponential distributions—a simplification that proves computationally tractable even when not entirely realistic.

C.2 Deterministic Models: The SIR Framework

In 1927, Kermack and McKendrick[Kermack and McKendrick 1927] published the foundational SIR (Susceptible-Infected-Recovered) model, treating populations as chemical reactants. For large populations, individual randomness averages to smooth, continuous curves:

1. Calculates when the next event occurs (τ)
2. Determines which reaction happens (infection or recovery)
3. Updates population counts
4. Repeats

Unlike ODEs which give a single trajectory, Gillespie produces a distribution of possible futures. Outbreaks are uncertain, and a probability distribution informs the discussion of what to invest, when and where.

C.4 Agent-Based and Rule-Based Approaches

Classical SIR models assume homogeneous mixing: every susceptible person has equal contact probability with every infected person. Humans are not chemical molecules, so this assumption often fails due to:

- Spatial structure (geographical spread)
- Heterogeneous contact networks (households, workplaces, schools)
- Individual variation (age, immunity, behaviour)
- Vector-borne diseases (mosquitoes, ticks)
- Environmental factors (temperature, land use, animal reservoirs)

This is the big problem with compartmental models. Where there are four compartments, we can write ODEs for each of the possibilities. But consider malaria, for example, where a mosquito may be infected or uninfected, just like a human. This means that we have to additional S and I compartments for mosquitoes, meaning four more ODEs. This continues for every new variable we introduce: bednets yes/no, age old/young/middle, and so on. This is a combinatorial explosion and quickly becomes impossible. One Health has a huge scope that makes this problem even worse.

There are two ways of approaching this:

Agent-Based Modeling: Represents each human, animal, or pathogen as a discrete entity with individual state variables. Agents interact according to specified rules, generating emergent population-level patterns. Computationally intensive and therefore subject to different, combinatorial explosion at a higher limit than ODEs. It does capture heterogeneity and spatial structure.

Rule-Based Modelling: Rather than enumerating every possible combination of states, rule-based models define *interaction rules* that fire when their conditions are met. For example: *IF human is within 10m of infected mosquito AND mosquito bites, THEN human becomes exposed at rate β* . Adding a bednet doesn't require rewriting the model, it adds

a rule: *IF human has bednet, THEN bite rate is reduced by factor δ* . Each new variable adds rules, not compartments, so the combinatorial explosion is avoided.

The Kappa (κ) rule based modelling system[W. Waites et al. 2021] formalises this approach. Agents are defined by their internal state (infected, symptomatic, carrying a genetic trait) and interact through rules that modify those states. The simulator KaSim computes the stochastic dynamics. Our group has applied this to COVID-19 transmission dynamics[W. Waites et al. 2022] and to reconstructing a large epidemic in a structured community using a stochastic graph rewriting system[William Waites et al. 2022]. Current work investigates how hidden genetic reservoirs in malaria interact with surveillance bias, involving an unmanageable number of ODE compartments but which is naturally expressed as a small set of rules.

Both approaches extend beyond the chemical kinetics analogy, though they retain the probabilistic foundations. They are essential for One Health modeling where traditional epidemiology (humans only) must integrate with veterinary surveillance, vector ecology, climate drivers, and land-use patterns.

Even if an overly complex model is computable, the results may not be useful. For this reason, epidemiologists emphasise selecting only relevant parameters to avoid obscuring useful results in the noise. This also helps the combinatorial problem, even with ODEs.

C.5 Parameter Estimation and Model Calibration

All models require parameter values (β , γ , contact rates, etc.). These are estimated through:

- **Fitting to outbreak data:** Using statistical methods (maximum likelihood, Bayesian inference) to find parameters that best match observed case counts
- **Contact studies:** Measuring actual human interaction patterns through surveys or digital tracking
- **Laboratory measurements:** Determining pathogen characteristics (infectivity, survival times)
- **Sensitivity analysis:** Testing how results change across plausible parameter ranges

One Health makes these challenges more difficult. Human disease parameters are often difficult to find, and animal reservoir dynamics, vector behavior under climate change, and cross-species transmission rates tend to be much more sparse. Model uncertainty quantification becomes critical.

Parameter estimation is one of many places in epidemiology where Bayes' Theorem is important. Bayes says $P(A|B) = \frac{P(B|A)P(A)}{P(B)}$, and in parameter estimation we can think of this as *Posterior = (Likelihood \times Prior) / Evidence*, which is very helpful for solving the inverse parameter problem — there is an event happening and we can measure what is happening but we don't know how likely the input parameters are.

Bayes is also helpful for selecting between models with different numbers of parameters, probabilistic forecasting and updating estimates in real time (because Bayes algorithms are constantly updating themselves with the information from the previous step anyway.) The specific application of Bayes to epidemiology is a large subject and it is sufficient to know that it underpins much of what happens with data and parameters outside the models.

C.6 Policy implications of models

Mathematical models inform public health decisions:

- Epidemic forecasting (hospital capacity planning)
- Intervention evaluation (vaccination strategies, lockdowns)
- Scenario analysis (what-if questions about policy choices)
- Resource allocation (where to deploy limited supplies)

Models can only formalise assumptions, making the reasoning explicit and testable. In One Health, models must now integrate across timescales (hours for clinical response, years for ecological change), spatial scales (subcellular to continental), and knowledge systems (laboratory virology, traditional veterinary practice, indigenous land management). This is where mathematical epidemiology is challenged to meet the complexity of real-world health systems, and the data which all the new scholars are bringing with them.

C.7 Causal inference

The models above — SIR, Gillespie, rule-based — are all *mechanistic*: they encode assumptions about how transmission works. But how do we know those assumptions are correct? When a model includes a parameter β for infection rate, we need to know what *causes* infection at that rate. In traditional epidemiology, establishing causation from observational data was the central unsolved problem for decades.

Epidemiologists famously found it difficult to say that smoking causes cancer because a randomised controlled trial would be unethical. All the scientists and statisticians could do was *observe correlations*, but in order to mathematically prove causation something else was needed. Judea Pearl called this the “Causality Crisis” [Pearl and Mackenzie 2018], arguing that the delay in officially concluding that smoking causes lung cancer was a failure of mathematical vocabulary.

Pearl’s do-calculus goes beyond the conditional probability of statistics which states $P(\text{Cancer} \mid \text{Smoking})$, or “What is the probability of cancer among people who happen to smoke?” This is vulnerable to hypotheses such as a gene for smoking — if such a thing existed it might influence both the desire to smoke and the risk of cancer.

With Pearl’s **do-operator** we can instead ask a counterfactual question: “What would the probability of cancer be if we forced the entire population to smoke, regardless of their genetic predisposition?” or $P(\text{Cancer} \mid do(\text{Smoking}))$. Pearl showed that using a Directed Acyclic Graph (DAG) and the Front-Door Criterion, one could mathematically prove the causal link using observational data alone by looking at intermediate variables like tar deposits.

This matters directly for One Health modelling. When an epidemiological model includes environmental variables — climate data, land use change, pesticide exposure — the causal relationships between these variables and disease outcomes are rarely established by experiment. Pearl’s framework provides the mathematical tools to identify causal effects from observational data, which is often all we have when working across disciplines and scales. Later work, especially [Jaber et al. 2022], has allowed computation of the more realistic scenario of an incomplete causal diagram — precisely the situation facing any One Health modeller combining data from multiple fields.

Appendix D US withdrawal from WHO and One Health

Epidemiology is inherently political in its goals, and One Health even more so. In 2025 the US withdrew from WHO[Buse et al. 2025], formally completed in January 2026. This is a destabilising blow and the impacts have been discussed in the literature. To illustrate that the first concern is not funding, consider that the US was absent from the first-ever adoption of One Health into international law:

- The WHO Pandemic Agreement is a global treaty on pandemic prevention, preparedness and response
- Launched in response to failures exposed by COVID-19
- Article 1(b) defines One Health, and Articles 4 and 5 discuss land use, food systems, wildlife, antibiotic use etc
- Passed in May 2025 by 124 countries (with 11 abstentions and 0 objections) at the 78th World Health Assembly[WHO 2025b]

This is not an own goal, but an everyone-goal. Viruses do not respect borders, meaning the US cannot isolate itself in reality by isolating itself politically.

Science community responses range from *...an attack on multilateralism and its institutions that develop and implement global rules, standards and norms ...modelling studies across various disease control programmes indicate potential adverse health effects for millions.:[Franz and Bozorgmehr 2025]* to *One Health cannot function when its largest funder walks out mid-crisis[Ortiz-Prado et al. 2025]*. In January 2026 *Nature* published the first of a four-part series on the destruction the US has already caused by the withdrawal[Nature 2026].

There are many complexities. As to health-related aid for developing countries, African voices have been consistent that a return to pre-Trump aid is not desirable even if it were possible:

Any continuing or new donor initiative cannot take the same inefficient approach as before. Donors should invest in underlying healthcare systems to make vertical programmes, targeting specific populations or diseases ...How the global public understands and talks about aid – as charity instead of reparation for colonial era and contemporary injustice – also needs to change. Aid often comes with conditions, including requiring aid recipients to source goods and services from the donor country. Donor countries often benefit as much if not more than recipients, as aid supports their own economies and access to markets and global political influence.

— [Mudide et al. 2025]

The funding is of course significant at least in the short term. The United States provides 42% of all international health assistance among major donor governments [Kaiser Family Foundation 2025], including through programmes such as USAID as well as WHO. No countries or organisations have indicated they will make up the shortfall. Some replacement funding has been mobilised (much of it from China), but as of January 2026 there does not seem to be any coordinated plan for how health progress is to be made.

In February 2026 the situation escalated from disengagement to active opposition: the US Department of Health and Human Services proposed spending \$2 billion per year to build a US-run rival to WHO, duplicating the global disease surveillance and outbreak response functions the US once accessed through WHO at a fraction of the cost [Sun and Bogage 2026]. This moves beyond withdrawal towards constructing a parallel system outside multilateral governance.

Nevertheless, there have been some rapid changes. Global health is becoming more multilateral, and peak bodies seem even more focussed on One Health. This urgent and scathing statement from November 2025 captures the mood, going head-to-head with the US approach:

We hereby reaffirm our commitment to advancing the One Health approach ...high burdens of zoonotic disease outbreaks ...persistence of neglected zoonoses ...irrational uses of antibiotics in health care and agriculture ...requiring whole-of-government, whole-of-society approaches, including the effective engagement of the private sector.

— the **Quadripartite Statement of peak bodies in Africa**

Similar political statements come from the European Union representatives [EJP 2026], and the African Union [AU-IBAR 2025]. The Association of Southeast Asian Nations

