Bitesize Epidemiology for General Awareness of All Students – II*

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This is the second part of a two-part series article. Recently, we have been in the middle of a difficult time due to the Covid-19 pandemic. Pandemics or global epidemics are not new to humankind; they have occurred many times in history. The discourse of epidemiology describes mainly the causal factors which need to be mitigated to prevent or combat the effects of epidemics. In epidemiology, we are not concerned for a person, but rather every individual globally, to make life healthier for all. In this article, we will discuss the basics of epidemiological practice that scientists have used for centuries to prevent epidemics with great results. Overall, we plan for better global health aided by epidemiology.

A Summary of Part One and Why It Requires a Reading

Students are advised to look at part one of this article (Bitesize Epidemiology for General Awareness of All Students–I, Resonance, Vol.28, No.3, pp.411–432, 2023.) series first before commencing their journey on the application of epidemiology in disease control—the theme of this (second) part of the article series. From the first part, students would get an idea of the discourse of epidemiology, the history of epidemiology and concepts associated with the epidemiological approach. These concepts are required to understand the subsequent sections discussed below better.

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**Figure 1.** Disease timeline, disease and outcome [2] [25–27].

### 1. Natural History of Disease Timeline

The natural history of a communicable disease refers to the sequence of events in the progression of a disease over a period of time in a person who is not receiving treatment. Events that occur in the natural history of a communicable disease are grouped into four stages: exposure, infection, infectious disease and, finally, outcome (*Figure 1*).

### Stage of susceptibility/exposure:

The process begins with the exposure to or accumulation of factors (microbes in case of infectious diseases, carcinogens like asbestos fibres or tobacco in case of cancer) sufficient for the disease process to begin in a susceptible host.

### Stage of subclinical disease/infection:

After the disease process has been triggered by the entry of the pathogen in the host body, which has begun multiplication, pathological changes start occurring. The time of exposure to onset of disease symptoms, is called the incubation period for infectious diseases, and the latency period for chronic diseases. During this stage, disease is said to be asymptomatic (no symptoms) or inapparent.

### Stage of infectious/clinical diseases:

The onset of symptoms marks the transition from subclinical to clinical disease. Most diagnoses are made during this stage while the illness ranges from asymptomatic to mild to severe to fatal. This range is called the spectrum of disease.

### Stage of outcome/recovery, disability or death:

At this stage the disease may result in recovery, disability, or death of the patient. For example, a child who fully recovers from a diarrhoeal disease, or is paralyzed from poliomyelitis, or dies from malaria, is in the stage of outcome.
2. Concepts of Disease Occurrences

A critical boundary of epidemiology is the lack of randomness in disease manifestation in a population. Instead, the presence of risk factor distribution patterns in a population drives the disease’s prevalence in some community members. Thus, an important aim of epidemiology is to identify the factors that put some members at greater risk than others. Again, we are restricting discussion in this section primarily to infectious diseases for simplification.

2.1 Epidemiologic Triad of Disease Causation

Among the different proposed models, the epidemiologic triad or triangle is the traditional and simplest model for infectious disease causation (Figure 2). The triad comprises an external agent, a susceptible host, and an environment that brings the host and agent together. This model proposes that the complex interaction and interrelation between the agent and the susceptible host in the presence of environmental factors that support the transmission of the agent from a source to that host causes the disease. The balances and interactions between these three components differ for each disease. Thus assessment of all three components and their interactions aid in the development of appropriate, practical, and effective public health measures to control or prevent disease. Various important components of causation are listed below.

Figure 2. (a) A model that shows the agent, host, and environment as having equal influence. (b) A model that shows that the agent and host are variables dependent on each other and the environment.
(a) Agent

Agent refers to an infectious microorganism or pathogen—a virus, bacterium, parasite, or other microbes. The presence of the agent, along with factors like the organism’s pathogenicity (the potential of an infectious organism to induce disease), [28] and infectiousness (expressed as the ratio: number infected/number susceptible and exposed) that needs to be in sync, cause the manifestation of the disease.

Characteristics of pathogens that make them favorable epidemiologic agents are as follows: [29]

- **Easy spread, entry, and survival through environments**: Number of organisms released by the infected host, resistance to the physical environment (e.g., heat, UV, moisture), ability to multiply within the environment and ability to infect intermediate host or insect vector.

- **Compatibility for initiation and development of infection**: Host range of organisms, genetic makeup and antigenic diversity, the infectivity of the organism, the pathogenicity of the organism, adherence of agent to host surface, self-defence measures in an agent, Number of organisms entering the host and the portal of entry, enzymes involved in spread through tissues [30].

- **Production of clinical disease**: The virulence of the organism, invasiveness of the organism [31], production of endo- and exotoxins [16], and immunopathologic potential [32] are the critical points to be considered.

(b) Host

Host refers to the human who can manifest the disease. Prognosis of the disease depends on the exposure, susceptibility, and response of the host, which is influenced by various factors (called the ‘clinical illness promotion factors’ [33] intrinsic to the host).

We list below some host factors that make the host a favourable target for infectious agents [34].

- **Factors leading to exposure**: Personal habits such as hygiene,
drug usage, or sexual promiscuity; behavioural, nutritional, and cultural habits; degree of crowding; occupational exposure risks (military recruits, hospital workers, etc.); socioeconomic status and privileges (lower socioeconomic status increases exposure risk to respiratory and enteric infectious diseases due to hygienic practices. E.g., increased tuberculosis severity in the Black population in the USA); environmental contamination; travel to susceptible regions with a high prevalence of disease/health effects [35], etc.

- **Factors leading to clinical illness of the exposed**: Susceptibility and response to an agent are influenced by genetic composition, nutritional and immunologic status, anatomic structure, presence of other conditions or medications, and psychological makeup. The entry sites are critical factors, as those sites close to vital organs or that permit easy access to the invasion of the bloodstream may result in more severe and complicated infections. Age (highest mortality from infection in early life and old age when the immune defence is immature or deteriorating), presence of other chronic diseases like HIV and administration of immunosuppressants are important determinants of the frequency and severity of clinical illness.

(c) **Environment**

Refers to the extrinsic factors that provide the setting for the agent-host interaction and opportunity for exposure. Environmental factors include physical factors such as geology and climate, biological factors such as insect vectors, and socioeconomic factors such as crowding, sanitation, and the availability of health services. Climate also is an important factor in the transmissibility of agents to the host (warmer climates facilitate enteric pathogen transmission, while cooler climates favour respiratory tract infections). The macro or micro-environmental setting also influences clinical disease occurrence and patterns. E.g., In hospitals, patients with chronic illnesses undergoing immunosuppressive treatments commonly manifest particular skin, wound, and urinary infections by antibiotic-resistant bacteria [35].

Susceptibility and response to an agent are influenced by genetic composition, nutritional and immunologic status, anatomic structure, presence of other conditions or medications, and psychological makeup.

Due to the non-applicability of the agent-host-environment model in the case of many non-infectious diseases, many multifactorial causation models have been proposed.
**Figure 3.** Causal pies are pie charts with each component cause as a slice. Slice A is in each pie. Slice B is only in pies 1 and 2. Slice C is only in pies 1 and 3. Adapted from [36].

### 2.2 Causal Pies and Component Causes

Due to the non-applicability of the agent-host-environment model in the case of many non-infectious diseases, many multifactorial causation models have been proposed. One such model—Causal Pies—was proposed by Rothman in 1976 [36]. It depicted an individual disease-causing factor called ‘component cause’ as a piece of a pie that includes intrinsic host factors as well as the agent and the environmental factors of the agent-host-environment triad. After all the pieces of a pie fall into place, the pie is complete, and disease occurs. The complete pie depicting a causal pathway is called a sufficient cause, while a component that appears in every pie or pathway and without which the disease does not occur is called a necessary cause (*Figure 3*).

### 3. The Chain of Infection

For an infectious agent to spread and cause disease, several intermediate stages are necessary. The complete process is called the chain of infection, and it consists of six steps (*Figure 4*). When all six links of this chain are intact, infection occurs. By breaking this chain, the spread of infection can be stopped [37].

#### 3.1 Causative Agent

The pathogenic microorganism capable of causing an infection is known as the causative agent (bacteria, viruses, fungi, or parasites).
3.2 Infectious Reservoir

A reservoir of infection is the source from which infection can spread. Infectious reservoirs act like vessels or habitats that provide an environment to enable the causative pathogen to survive, persist, and multiply, and from where it can infect a host or target species. The pathogen can rely on a species or group of species to sustain it indefinitely. This ecological community that allows the pathogen to persist is essential for its maintenance and is hence also called a maintenance host. Epidemiology study is motivated by the need to control disease in the particular population or population subset (called the ‘target population’) that gets targeted or infected by the pathogen [40].

To meet the definition of a reservoir of infection, a maintenance host or community must have an infection pathway to the target, either directly or via additional host species [38]. An example of reaching the target indirectly is *Clostridium botulinum*, whose natural habitat soil acts as its reservoir. But the actual source of most botulism infections is improperly canned foods contaminated with *C. botulinum* spores [39].

Infectious reservoirs can be humans, other animals, inanimate objects like medical equipment, or the environment.
(a) Human Reservoirs

A human reservoir can be an infected, diseased individual or a carrier. Often, the reservoir hosts do not get the disease carried by the pathogen and thus remain asymptomatic carriers [37]. Many commonly known infectious outbreaks began with human carriers, the most popular example being the case of Typhoid Mary; the nickname was given to the cook Mary Mallon, who was an asymptomatic carrier of the disease pathogen, *Salmonella typhi*, and had unintentionally infected dozens of people, leading to an alarming surge of typhoid fever in early 1900s New York. [41–42].

(b) Animal Reservoirs

Zoonosis refers to an infectious disease that is transmitted from animals (non-human vertebrate animals) to humans. Commonly known zoonotically transmitted diseases induced by direct or indirect exposure of humans to infected animals include brucellosis (cows and pigs) [43], anthrax (sheep) [44], plague (rodents, fleas) [45], and rabies (bats, raccoons, dogs, and other mammals) [46].

Recent infectious diseases in humans, including HIV/AIDS, Ebola infection, and SARS, are also thought to have emerged from animal hosts. Most animal pathogens can infect multiple host species, and ‘pathogen spillover’ from one host species to another is common [47]. The persistence of the pathogen in multi-host systems makes the identification of infection reservoirs all the more crucial [40].

(c) Environmental Reservoirs

Plants, soil, and water in the environment are also reservoirs for many infectious agents. Additionally, a surprising number of inanimate objects, especially when left uncleaned or in unsanitary conditions, become reservoirs for various microbes. An interesting example is a 2010 case of ‘Saxophone Lung’, which described a man with pneumonitis. The source of the infection was
unknown until it was discovered that his saxophone reed was positive for the pathogenic moulds *Ulocladium botrytis* and *Phoma sp.* due to lack of cleaning [48].

Similar reports of patients that played the saxophone, trombone, and clarinet suddenly presenting with a persistent cough, wheezing, and/or shortness of breath led researchers to conclude that woodwind instruments, when not cleaned properly, can harbour bacteria and fungi, leading to sudden allergic reactions due to repeated exposure to the mould colonising the instrument.

### 3.3 Path of Exit

The path or portal of exit refers to the route by which a pathogen leaves its reservoir. It generally refers to the site where the microorganism grows and is localised. Common sites of exit associated with human reservoirs include skin, mucous membranes, and the respiratory, gastrointestinal, and genitourinary tracts [37].

For example, influenza viruses and *Mycobacterium tuberculosis* exit through the respiratory tract, *Vibrio cholerae* through faeces, and some bloodborne agents can even exit by crossing the placenta from mother to foetus (examples: rubella, syphilis, toxoplasmosis). Others can escape through cuts or needles in the skin (hepatitis B) or blood-sucking arthropods (malaria) [2].

### 3.4 Mode of Transmission

For the infection of a new host to occur, there must be an opportunity for a susceptible host to be exposed to the infectious agent (contact between the agent and the host) via a particular mode of transmission [7].

Transmission can occur through direct contact or droplet spread from an infected patient or indirect contact where the pathogen is transmitted through a contaminated intermediate (airborne or carried by vectors) [37]. Certain pathogens may use multiple transmission routes from the reservoir to the host.

One vital factor that influences the severity of a disease is the
infective dose, which is the number of units of the infectious agent required to produce the disease [7].

3.5 Path of Entry

The portal of entry is how a pathogen enters a susceptible host. The portal of entry must provide access to tissues where the pathogen can multiply or a toxin can act. Infectious agents may use the same portal to enter a new host that they used to exit the source host. For example, the influenza virus exits the respiratory tract of the source host and enters the respiratory tract of the new host. Some pathogens that cause gastroenteritis have a ‘faecal-oral’ route because they exit the source host through faeces, then get carried via inadequately washed hands to a vehicle such as food, water, or utensil, and enter a new host through the mouth [7].

3.6 Susceptible Host

The final step in the infection chain is for the pathogen to infect a host organism that is susceptible to disease. The infectious agent, after establishing itself in a new individual and ensuring the survival of its species, needs to constantly find and infect new susceptible individuals. Infectivity, the ability of an infectious agent to cause new infection in a susceptible host, is measured by the proportion of susceptible individuals that develop the infection after exposure to the pathogen [7].

“Susceptibility refers to the ability of an exposed individual (or group of individuals) to resist infection or limit disease as a result of their biological makeup” [49]. The communicable period (or duration of infectiousness) is the time interval during which the infected host, ill or not, eliminates an agent to the environment and new susceptible individuals can become infected [7].

The success of the invasion of the causative agent depends on multiple factors influencing the target host, including both innate genetic factors as well as acquired factors. These include age, genetics, sex, population groups, nutritional status, previous exposure to this agent, and consequently, the presence or absence
of pre-existing immune resistance following exposure or vacci-
nation.

An example of genetic influence on host susceptibility to infec-
tious agents is the partial malaria resistance seen in heterozygous
carriers of the autosomal recessive disease, sickle cell anaemia.
Individuals from sub-Saharan Africa, where a high proportion
of people are born with sickle cell anaemia, bear a genetic mu-
tation in the beta globin gene that encodes the beta subunit of
haemoglobin. Those with homozygous mutations suffer from
sickle cell anaemia. But the carriers who are heterozygous for the
mutated gene are not only safe from the disease but also surpris-
ingly exhibit partial protection against severe Plasmodium falc-
parum infection and hence are less susceptible to malaria com-
pared to people with normal haemoglobin [50].

4. Measures of Spread

4.1 Morbidity and Mortality

To estimate the severity of the spread of infectious disease, certain
epidemiological parameters are used to measure the impact of a
disease on public health. Two common measures frequently used
for epidemiological surveillance are ‘morbidity’ and ‘mortality’.
These parameters describe the progression and severity of a dis-
ease and are useful tools to learn about risk factors of illnesses
and compare and contrast health events between different popu-
lations. While similar and often related, morbidity and mortality
are not identical. Morbidity is related to the rate at which the pop-
ulation is catching the disease. In contrast, mortality refers to the
rate at which deaths are recorded in that population caused by the
said disease.

4.2 $R_0$ (R Naught)

$R_0$ is an important parameter associated with infectious disease
epidemiology. It is a quantitative term that measures the con-
tagious nature of the disease and thus is very useful for drawing
remedial measures. The value of $R_0$ indicates the average number of people who will contract a contagious disease from one person with that disease. It is a population average number that can assume any value. One assumption taken while calculating $R_0$ is that the population has no innate immunity against the pathogen; the pathogen is of a novel type. $R_0 < 1$ indicates that the disease will fade away on its own as one person is affecting less than one person. An example is the MERS epidemic, which had $R_0$ 7.5, which died down by itself. But the Spanish flu of 1918 had an $R_0$ of 2.2, thus it spread unchecked to almost 1/3rd of the global population. SAER-CoV2 has $R_0$ value between 2 and 3. Generally speaking, any pathogen with $R_0 > 1$ could spread unchecked in a population and would need urgent preventive measures.

### 4.3 Population Attributable Risk (PAR)

A measure of the public health impact that is used frequently is the attributable proportion (also known as attributable risk percent or population attributable risk, i.e., PAR). PAR is a measure of the public health impact of a causative factor. It is the proportion of the incidence of a disease in a population (exposed and unexposed) that can be attributed to a particular risk factor. It can also be looked at as the proportion of disease in the exposed group that could be prevented by eliminating the risk factor.

PAR is calculated by subtracting the incidence in the unexposed from the incidence in the total population (exposed and unexposed) and is usually expressed as a percentage. The PAR% is calculated by dividing the population attributable risk (PAR) by the incidence in the total population and then multiplying the product by 100 to obtain a percentage [52].

Example: The lung cancer mortality rate among persons who smoked 1–14 cigarettes per day was 0.57 lung cancer deaths per 1,000 persons per year. In another study on smoking and lung cancer, the lung cancer mortality rate among non-smokers was found to be 0.07 per 1,000 persons per year.

Therefore, attributable proportion or $\text{PAR} \% = (0.57 - 0.07)/0.57$
× 100% = 87.7%. We know that a causal relationship exists between cigarette smoking and lung cancer. Provided that the people in the study are comparable, we can assume that roughly 88% of lung cancer among smokers might be attributable to their smoking. The remaining 12% of the lung cancer cases may have occurred even without the risk factor of 1–14 cigarettes a day [2].

4.4 Other Measures

(i) Efficacy: The extent to which an intervention does more good than harm under ideal circumstances (examples: a clinical trial to test a drug or vaccine).

(ii) Effectiveness: An assessment of whether an intervention does more good than harm when provided under the usual circumstances of healthcare practice (not under perfectly controlled experimental conditions) [53].

For instance, vaccine efficacy and vaccine effectiveness measure the fraction of reduction or lowering in the risk of infection cases among individuals who have already been vaccinated. Vaccine efficacy/vaccine effectiveness (VE) gives a ratio that is measured by calculating the risk of disease among vaccinated and unvaccinated persons and determining the percentage reduction in the risk of disease among vaccinated persons compared to unvaccinated persons.

\[ VE = 1 - \frac{\text{Risk of disease in the vaccinated group}}{\text{Risk of disease in the unvaccinated group}} \text{ or } VE = 1 - \text{Risk ratio.} \]

The higher the percentage reduction of illness in the vaccinated group, the greater the vaccine efficacy/effectiveness. Hence a VE of 90% indicates a 90% reduction in disease occurrence among the vaccinated group or a 90% reduction from the number of cases that could have been expected if the group had not been vaccinated [2].

Efficacy refers to the extent to which an intervention does more good than harm under ideal circumstances.

The science of epidemiology is concerned with minimising the impact of pathogens/adverse effects on public health.
5. Implications for Public Health

The science of epidemiology is concerned with minimising the impact of pathogens/adverse effects on public health. Effectively designing interventions aims at controlling/eliminating the causative agent/health effectors at the source of transmission, protecting portals of entry, and increasing host defences.

 Interruption of direct transmission can be achieved by simple acts such as isolating infected individuals (quarantine) to prevent spread, promoting handwashing and cleanliness to prevent faecal-oral routes of infections, using mosquito repellents to prevent vector-borne diseases, and so on.

 Strategies to protect portals of entry, the most common being skin and mucous membranes of the respiratory, digestive, or urogenital tract, can be as easy as using mosquito nets and covered clothing, wearing masks and gloves to prevent contact with droplets of secretions from infected patients, etc.

 Interventions seeking to enhance a host’s defences depend on susceptibility to different infections. The most effective method of building host defence is through vaccinations that promote the development of specific antibodies to protect against different pathogens. Consumption of vitamin-enriched functional foods, personal hygiene, and lifestyle choices (diet, exercise, alcohol/substance abuse, etc.) all contribute to an individual’s immune strength against infectious agents.

 In the non-communicable disease and social ailment front, epidemiological data are used to make laws targeted at the reduction of smoking and banning it altogether in some countries for those below 21 years many countries. Student councillors are now very common in many schools in developing nations, advising students to cope with stress, which often leads to incidences like mass shootings or suicide.

 Epidemiology is needed for educating and planning public health responses and interventions, not only during epidemics and pandemics but even during normal times, and thus plays the role of an
integral base of public health. Epidemiological science and statistics provide a foundation for implementing measures concerning public health issues such as sanitation, clean water supply, maternal and child health, etc. However, human social values shape the system and carry the implementation process forward into society by defining objectives for the healthcare system and finding ways to implement health goals within a social structure. The process is then executed to eliminate health and social problems, resulting in economic, political, and ideological transitions within the government, nations, and the world. Therefore, epidemiology is not applicable only during epidemics but for the public’s daily needs and well-being [2].

6. Concluding Note and Challenges Ahead

We conclude our discussion with some aspects of the current Covid-19 pandemic. Unlike any other pandemic, as discussed above, Covid-19 is still a developing situation, and there is much left to learn. Covid-19 disease is caused by many strains of double-stranded RNA virus SARS-CoV2, and epidemiological parameters for these pathogens are being studied at this very moment, worldwide [54]. As epidemiological parameters for Covid-19 are still being worked out, we do not have a Covid-19 eradication plan ready in hand yet. But what we have is a set of vaccines that have been developed in record time to counter this threat. These vaccines give partial to near complete protection against Covid-19 disease caused by all isoforms of SARS-CoV2 [55]. Therefore, universal vaccination is the only way to contain the disease. Such vaccination drives are in progress in India and all other countries worldwide. Additionally, we need to follow all basic health measures that have been mapped out based on the information on Covid-19 we have in hand. We hope that in the near future, we can determine, with full certainty, the source, reservoir, transmissibility, and risk of SARS-CoV2 from ongoing investigations. We can then plan for a robust scheme to mitigate the issues associated with the transmission of the virus and prevent the disease from spreading ever again. Until then, we must
follow widely accepted social distancing, mask mandate, and universal vaccination initiatives.

Thus, epidemiology could help us build a better place to live, free from any threats to public health. It has emerged as an indispensable interdisciplinary platform for those who not only care about their personal health but are also willing to work towards better global health.

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Suggested Reading


