Chapter 14 Field Epidemiology

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As of Epidemiology (14)

Field Epidemiology

- Applied work
  - To identify public-health problems in a community
  - Intervention to prevent/reduce harms from those problems.
- Much of that involves outbreak investigation
  - To tackle the result of an infectious disease
  - To reveal environmental contaminants or shared chronic disease risk factors leading to an excess of a specific disease
  - Which includes some unique types of studies

Surveillance

- Regular, systematic collection and analysis of data related to disease
- Key source information on the incidence and prevalence of disease at population level
- Various types, but in any of those, case definition (or reporting criteria) is very important.
  - John Graunt's "*Bills of Mortality*" in 1665, first regular collection of surveillance data, compared the frequency of causes of death in different years, seasons, and sociopolitical events.
  - Passive surveillance: Collecting regular or frequently recurring data on a health condition, examples shown below
    - Vaccine Adverse Event Reporting System (VAERS)
    - USCDC's reportable (notifiable) infectious diseases (eg. Hepatitis A, chlamydia, acute flaccid paralysis[急性弛緩性麻痺])
    - Infectious Diseases Surveillance (Japan) https://id-info.jihs.go.jp/en/surveillance/index.html https://id-info.jihs.go.jp/surveillance/idss/nesid-program-summary/nesid_en.pdf
  - Active surveillance: Health department-initiated data collection typically in the beginning of disease outbreak + Routine collection of national survey data, examples shown below
    - Census
    - National Health and Nutrition Examination Survey (NHANES) by USCDC
    - National Health and Nutrition Survey (Japan) https://www.nibn.go.jp/eiken/kenkounippon21/en/eiyouchousa/
- Over time, case definition can be updated. Thus when sudden change in the pattern is observed, paying attention to whether it's apparent one due to the change in case definition or not.

Case definition / Syndromic surveillance

- Three types in case definitions
  - **Definite** case definitions: Known to have the disease under surveillance (it means definitely diagnosed and reported by health professionals)
  - **Suspected** case definitions: With symptoms or exposures highly suggestive of the disease but without a definitive diagnosis
  - **Probable** case definitions: With symptoms being potentially compatible with the disease and a suspected epidemiologic link with exposure, but a diagnosis is less certain
- A new type of surveillance, increasingly used in field epidemiology "*Syndoromic surveillance*"
  - Passive or active collection of data on collections of symptoms or other nondiagnostic markers suggesting an important change in disease frequency
  - (eg.) The collection of data on influenza-like illness at **sentinel sites**, which are a set of clinics chosen to report regularly on the syndrome (including fever and cough) in EU https://www.ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/facts-sentinel-surveillance
  - (eg.2) Monitoring of sales of OTC anti-diarrheal medications
  - (eg.3) Real time monitoring of Internet searches or social mediia posts related to flu-like symptoms

Seroprevalence Surveys

- Additional information for infectious diseases from targeted seroprevalence surveys to estimate the prevalence of current infection or the prevalence of a biomarker for past infection.
- Often conducted only once.
- The estimation of population prevalence depends on sampling methods: Requiring representative sample.
- Key measures
  - Immunity (antibody = IgG) to specific antigen from serum or plasma (extracted from blood)
- Getting blood samples from a population representative cross-section is challenging. Getting blood samples in health care setting is much easier, but patients may not represent a general population.
- Values
  - Assessing vulnerability of a population (low immunity means high vulnerability)
  - Finding susceptible subgroups in a population
  - Setting priorities for vaccination
- It can also provide the estimates of past prevalence from serum samples even if the definitive diagnosis requires red blood cells as in malaria.
  - Nakazawa M et al. (1994) Differential malaria prevalence among villages of the Gidra in lowland Papua New Guinea. *Trop Geogr Med* 46(6): 350-4.
- Also useful for the situation where there are many asymptomatic patients who did not go to any medical facilities as in the case of COVID-19 (but effective only after considerable part of population got infected, partly because extremely high specificity of testing is necessary in low prevalence situation)

Bias in Surveillance Data

- Random sampling of the population vs Targeted oversampling of specific groups
  - To monitor seasonal flu, hospitals or nursing homes are used as sentinel sites, where flu-like symptoms are more likely to be identified there. But the patients diagnosed in sentinel sites do not represent a whole patients in a population. Many people with flu-like symptoms do not seek health care. The changes of patients in sentinel sites show an overall trends.
  - During the early periods of COVID-19 pandemic, seroprevalence survey was designed to estimate total infection rate in the population and thus needed random sampling from the population.
- Under pandemic situation, people who had ever experienced plausible symptoms were more likely to participate in serosurveys (a kind of selection bias), resulting in overestimate of the population prevalence (as suspected in a study conducted in Kobe 2020). https://doi.org/10.1016/j.cegh.2021.100747
  - In Wuhan city, all the residents were checked by RT-PCR to get the exact prevalence after all symptomatic patients disappeared. Such a whole population study is almost impossible in other countries.

Study Designs for Field Epidemiology

- **Field trials**: Randomized trials for preventive measures
- **Community intervention trials**: Conducted at the level of an entire community (unit of random assignments is community)
- Both recruit healthy individuals, not patients. Usually large study size
- Vaccine trials require a huge study size, because (1) the most severe outcomes of infection tend to be rare (2) assessment of (rare) adverse events is needed
- A further challenge of preventive trials
  - Distinction between individual-level effects and community-level or population-level effects
  - (eg.) **Spillover effect**: Vaccine is expected to reduce the chance that an individual who received vaccine gets infected, ideally reduce the duration of infectiousness even if they get infected (direct effect = **vaccine efficacy**). Vaccinating one individual can reduce the risk of infection in surrounding others (spillover effect)
  - Combination of direct effect and spillover effect is called as **vaccine effectiveness**.
- To assess vaccine efficacy, field trial is appropriate, but to assess spillover effect and vaccine effectiveness, community intervention trial is needed, though observational data also provides important information about spillover effect and vaccine effectiveness

Outbreak Investigations

- When active or passive surveillance detects an unexpected (unusual) increase in the number of cases of disease, outbreak investigations start.
- Initial goal: To determine whether the detected increase represents real increase in cases of the disease or not. If it's a real increase, to determine whether the cause of the increase is increased transmission of an agent or not.
  - Many apparent disease clusters are simply the result of a chance aggregation of cases.
  - Artificial increases in reported cases can also occur due to the change of reporting system / methods / lab techniques.
- Next step: To enumerate the full extent of the outbreak, by refining case definition, implementing active surveillance (so-called *shoe-leather epidemiology*) through knocking on doors and traveling to factories, farms, food-processing plants, and other spots where the epidemic may have originated. Or by cohort or case-control study, hypothesis on the cause of epidemic is tested
- To prevent person-to-person transmission of infectious agents, identifying the cases and their contacts is important. It's possible by **contact tracing** in the early stage of outbreak.

Steps of outbreak investigations

- The ***CDC Field Epidemiology Manual*** (it's sold as a book, expensive) outlines 9 key steps https://www.cdc.gov/field-epi-manual/php/about/index.html
  1) Prepare for fieldwork
  2) Confirm the diagnosis and outbreak
  3) Identify and count cases
  4) Describe the data in terms of person, place, and time
  5) Assess potential control measures to implement immediately
  6) Formulate and test hypotheses for additional measures
  7) Plan systematic studies
  8) Interpret, make recommendations, and monitor for future outbreaks
  9) Communicate findings

(cf.) Studies needed in the beginning of COVID-19 pandemic

- Lipsitch M et al. (2020) Defining the epidemiology of COVID-19 — studies needed. *New England Journal of Medicine*, 382: 1194-6. https://www.nejm.org/doi/full/10.1056/NEJMp2002125
- To answer 4 critical questions (full spectrum of diisease severity, transmissibility, who are infectors, underlying risk factors of severe illness and death), the following studies were needed.

Evidence needed	**Study type**
No. of cases, including milder ones	Syndromic surveillance + targetted viral testing
Risk factors and timing of transmission	Household studies
Severity and attack rate	Community studies
Severity “pyramid”	Integration of multiple sources and data types
Risk factors for infection and severe outcome, including death	Case-control studies
Infectiousness timing and intensity	Viral shedding studies

Contact tracing

- To reduce R_t less than 1, the combination of isolating infected patients and quarantining contacts with them can be effective to cut short an outbreak.
- For that, identification of cases and their contacts are needed.
- It’s usually done by contact tracing, where health department personnel (in Japan, it was mostly public health nurses) contacting reported cases or their families or doctors to obtain key information about their disease experience.
- **Forward** contact tracing: Obtaining much information from known cases about where they have been and who they may have come in contact with while infectious, to identify potentially infected but presymptomatic individuals → They are informed of potential exposure and get support for quarantine and symptom monitoring
- **Reverse** contact tracing: Obtaining much information from known cases about where or from whom they may have been infected, to identify locations with a high potential to support transmission (so-called “clusters” in Japan).
- In USA, mostly forward contact tracing was done.

Outbreaks vs Epidemics vs Pandemics

- For a given population and time frame, the occurrence of more cases of disease than expected defines an **outbreak**.
- The number of cases that constitutes an outbreak can vary.
  - *Yersinia pestis*, the bacterium causing the plague, is fairly common in prairie dogs in some areas of the American Southwest. Human cases are so rare that a single reported case can trigger the outbreak investigation.
  - Influenza cases occur at fairly predictable levels following seasonal pattern (It peaks January or February in Northern hemisphere). Only if the cases exceeds expected range for a given time of year (high in flu-season), it is considered as outbreak.
- Large outbreaks are typically called **epidemics**. No specific threshold.
- When an epidemic has spread across the border, it is **pandemic**. No specific threshold. Since 2005, WHO has used PHEIC rather than pandemic. Recent PHEICs in 2023 include poliovirus, COVID-19, mpox. Poliovirus PHEIC is ongoing since 2014.
- Over a long period of time, an infectious disease occurs with a known and predictable pattern and the average incidence within an expected range, it is considered as **endemic** (in other words, average R_t over a long period exceeds 1).

Point-Source, Common-Source, and Propagated Epidemics

- Surveillance data can be useful in hypothesizing the likely source or mode of infection.
- First step is to plot the data gathered as an **epidemic curve**. Plot the number of new cases with time of symptom onset (or diagnosis).
- Shape of epidemic curve suggests
  - **Point-source** epidemic: Rapid increase in cases followed by a gradual diminution of the outbreak (**Figure 14.1 = Figure 2.1**), where a single source transmits disease to all affected individuals, usually during a brief time period, as observed in cholera epidemic around Broad Street Pump in 1854, in food poisoning of restaurant patrons ate contaminated meal, and in cancer among the survivors of atomic bomb in Hiroshima and Nagasaki in 1945.
  - **Common-source** epidemic: The source of exposure persists, the epidemic curve remains high. Peaks may occur irregularly. As in the epidemics caused by persistent water pollution or air pollution.
  - **Propagated** epidemic: Infection is transmissible directly person-to-person. Recurrent peaks of increasing size until herd immunity, depletion of susceptible individuals, or reduced contact halts transmission. Examples are flu-epidemics and COVID-19 pandemic. As shown in **Figure 14.2** (hysteria in elementary school children), it can occur within very short time.

Control of Infectious Disease Outbreaks

- After identifying causal agent, source of exposure, route of transmission, field epidemiologists must make decisions about how to control transmission.
- Goal: Ending the outbreak.
- When an outbreak is caused by a new agent (emerging disease), no prior threshold. When the outbreak has ended is difficult to determine.
- Three main targets
  - **Reducing infectious contacts**: By isolation, quarantine, social distancing, physical barriers such as mosquito net or face masks
  - **Reducing the per contact transmission probability**: By pharmaceutical interventions such as prophylaxis and/or non-pharmaceutical interventions such as condoms, handwashing, sanitation measures
  - **Reducing the number of susceptible individuals**: By vaccination. Through the outbreak, infection-induced immunity can also decrease the number of susceptible individuals, but it’s not considered as control approach.

Herd immunity threshold by vaccination

- (Also partly addressed in Chapter 13)
- If vaccine would be available, R_t depends on **vaccine efficacy** (V_e) and **coverage** (V_c)
  - $R_t = R_0 (1 – V_e V_c)$
    $\leftrightarrow R_t/R_0 = 1 - V_e V_c \leftrightarrow V_c = (1 - R_t/R_0)/V_e$
  - $R_t < 1 \leftrightarrow V_c > (1 – 1/R_0)/V_e$ [14.1]
  - When R_0 is large, to succeed in curtailing the epidemic, high efficacy and coverage are needed (If R_0 is 10 and V_e is 95%, V_c has to be larger than 95% needed to reduce R_t below 1; (1 – 1/10)/0.95 = 0.947… ≈ 0.95)
  - In the case of measles, R_0 is 15. Even if V_e is 100%, V_c has to be larger than 93% to reduce R_t below 1; (1 – 1/15)/1 = 0.933… ≈ 0.93
  - If R_0 is 2 and V_e is 65% (based on COVID-19 in 2020), V_c needs to be larger than 77% to reduce R_t below 1; (1 –1/2) /0.65 = 0.769… ≈ 0.77.
- The same relationship may stand for not only vaccination but also naturally acquired immunity after infection. Vaccine efficacy corresponds to the proportion of immunized by single infection and coverage corresponds to the proportion of people ever infected and recovered (**herd immunity threshold**)