Epidemiology: Study Designs

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Last update: Jun 24, 2024

Outlines

- Introduction
- Descriptive vs Analytical
- Descriptive Study Designs
- Analytical Study Designs
  - Observational
  - Experimental

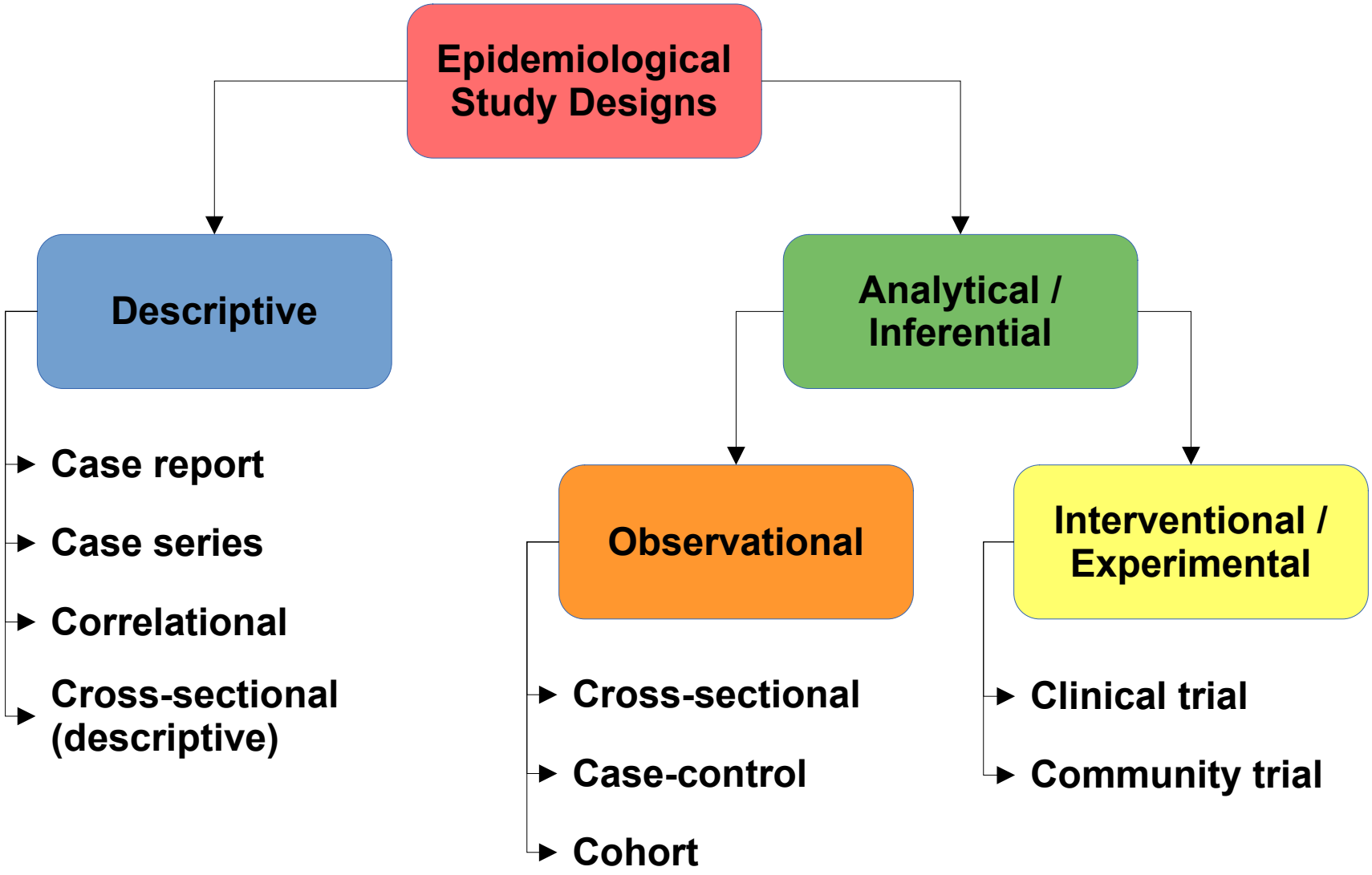
Learning outcomes

- Understand an overview of epidemiological study designs
- Differentiate descriptive and analytical designs
- Understand and differentiate different study designs

Introduction

Background

- *Quantitative* epidemiological study designs
- Research objectives → Selection of appropriate epidemiological study designs
- Determines methodology, sampling, analysis
- Varying strength of evidence



*Following the classification by Omair (2015) and Ranganathan (2019)

Table 1: The hierarchy of epidemiological study designs

Observational studies		Strength of evidence
Descriptive study designs		
Case report	Single case	
Case series	Collection of similar cases	
Correlational	Population based study - using secondary data	
Cross-sectional (descriptive)	Single sample from larger population- no comparison	
Analytical study designs		
Cross-sectional (analytical)	Single sample from larger population-compares two or more groups in the sample	
Case-control	Compares risk factors between diseased (cases) and non-diseased (controls) groups	
Cohort	Compares outcomes between groups exposed and non-exposed to a risk factor for a disease	
Interventional study		
Clinical trial	Investigator allots the subjects to different groups - intervention versus non-intervention	

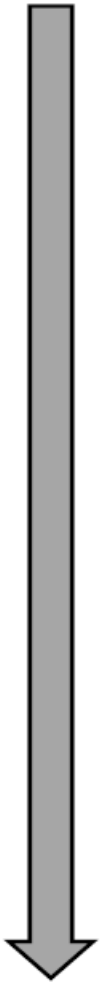


*Table from Omair, 2015

Descriptive vs Analytical

Descriptive Epidemiology

- It is a "*descriptive study of the occurrence of disease and other health-related characteristics in human populations*." (*A Dictionary of Epidemiology, 6th ed*. Porta, 2016)
- It deals with *what* (disease description), *how much* (counts, rates), and *patterns*. (*The CDC Field Epidemiology Manual*. Fontaine, 2018)
- Patterns of data in terms of *time*, *place*, *person*. (Fontaine, 2018)

Time

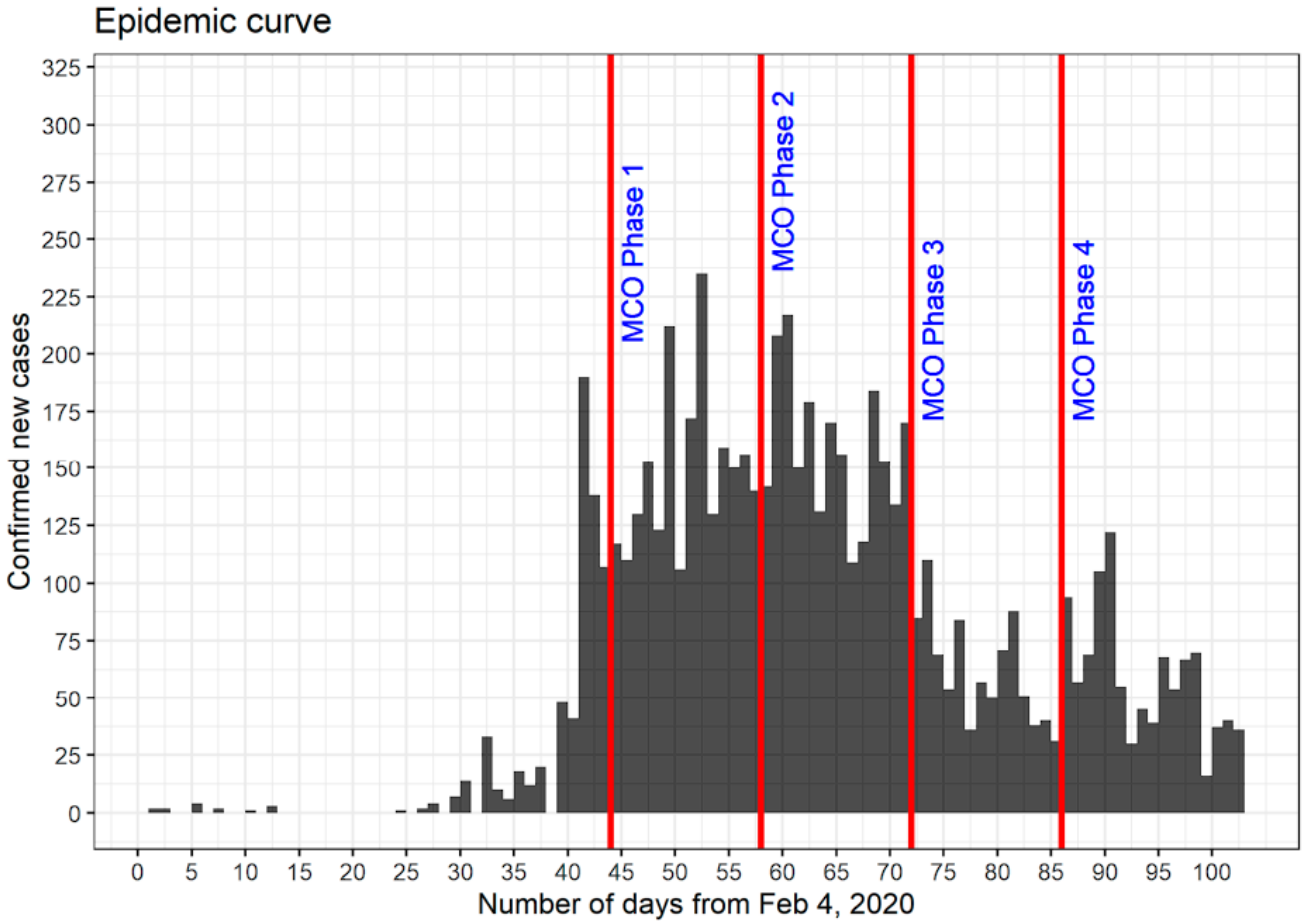


Figure 2. Epidemic curve between day 1 (4 February 2020) and day 102 (16 May 2020) for Malaysia.

*Figure from Musa et al., 2021

Place

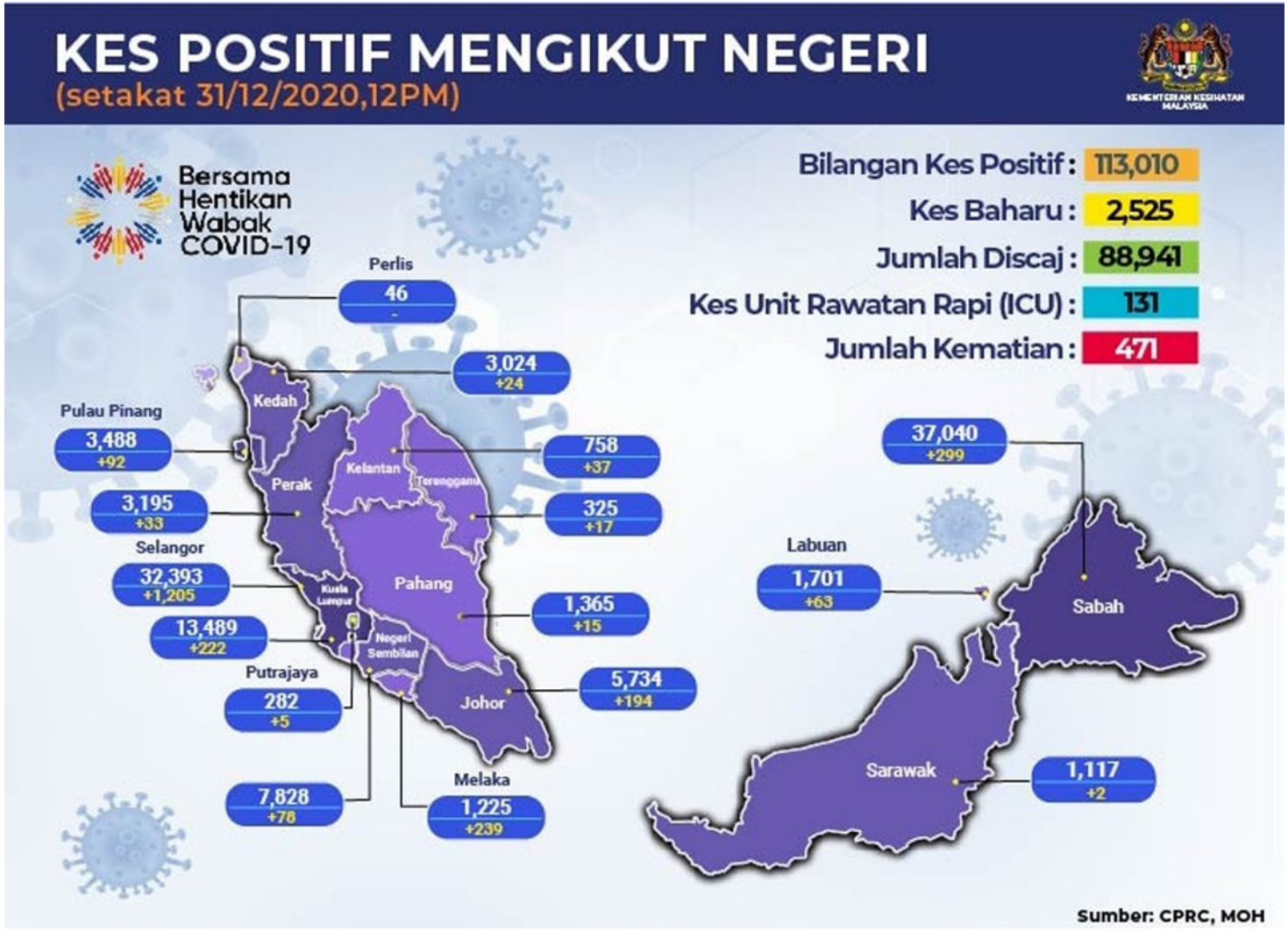


*Figure from covid-19.moh.gov/my

Person

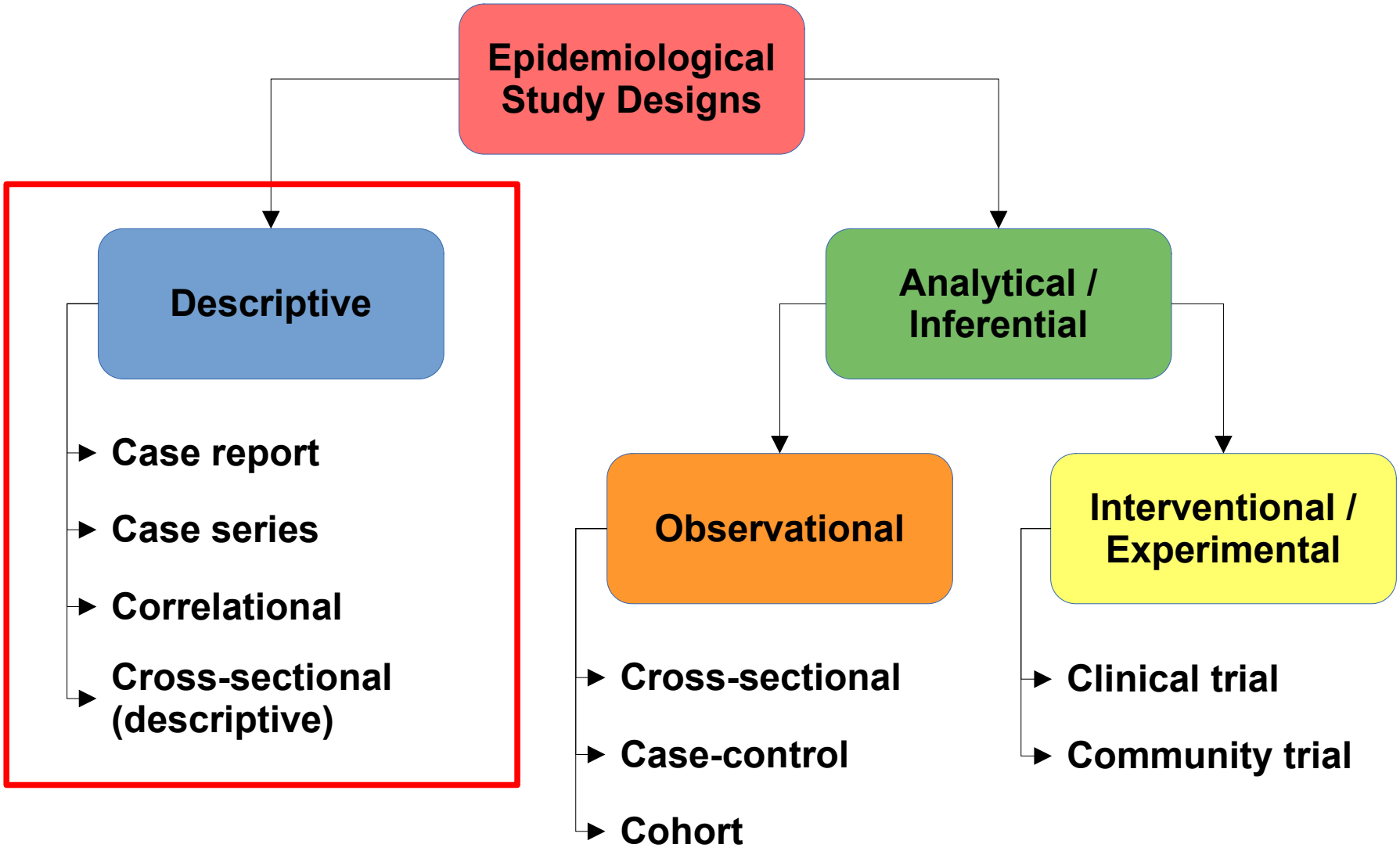
*Figure from covid-19.moh.gov/my

Descriptive vs Analytical

Aspect	Descriptive	Analytical
Aim	Describe	Determine, Explain
RQs	When? Where? Who?	How? Why?
Hypothesis	Generate	Test, Prove
Comparison Group	No	Yes
Data	Observation	Observation or Intervention

*Omair (2015), *CDC PH 101 Series* (CDC, 2018), Ranganathan (2019)

Descriptive Study Designs



*Following the classification by Omair (2015) and Ranganathan (2019)

Case Report

- Single case
- Abnormal / Atypical / Unexplained / Unexpected outcomes – undocumented side-effect of a treatment
- New disease / phenomenon – COVID-19
- Generate hypothesis for exposure-outcome association
- Lowest level of evidence

Case Report

Ischemic stroke after AstraZeneca (Covid-19) vaccination

Muath A. Alammar, MD, PhD.

ABSTRACT

يعتبر التطعيم ضد فيروس كورونا (كوفيد ١٩) استراتيجية وقائية فعالة لوقف جائحة هذا الفيروس ، التقارير الطبية عن الإصابة بتجلط الدم لدى متلقي اللقاح أثارت اهتمام الناس واتخذت بعض الدول الاوربية قرار بإيقاف مؤقت لهذا اللقاح ، لا يزال غير واضح ما إذا كانت الإصابات ناتجة بالفعل عن اللقاحات أم هي مجرد صدفة ، إن خطورة الأحداث لا سيما في الشباب والذين ليس لديهم تاريخ مرضي بأمراض مزمنة في السابق تستحق مزيداً من البحث للوصول إلى نتيجة نهائية ، في هذا التقرير نقدم حالة مماثلة أصيب فيها المريض بسكتة دماغية بعد وقت قصير من تلقيه للجرعة الأولى من اللقاح.

Vaccination against SARS-COV-2 is considered an effective preventive strategy to halt COVID-19 pandemic. Reports of thromboembolic events in vaccine recipients has jolted some of the European countries to pause the vaccination process temporarily. It is still unclear whether the events are actually due to the vaccines or it is just a coincidence. The gravity of events particularly in young and previously normal patients merits further research to reach some conclusion. Here we present a similar case who sustained ischemic stroke shortly after receiving the first dose of his vaccine.

Vaccination against SARS-CoV-2 has been an important breakthrough to manage the COVID-19 pandemic. To date, 4 vaccines has been approved by the European Medical Agency based on randomized controlled trials: Pfizer/BioNTech, Moderna, AstraZeneca, and Janssen.[1] By the June 14, 2021 approximately 2.4 billion doses of vaccines have been administered worldwide (COVID-19 Vaccinations - Statistics and Research - Our World in Data).

Unusual thromboembolic events were reported in patients who received vaccination against COVID-19.[2] Based on these preliminary reports of thromboembolic events, some European countries paused Oxford AstraZeneca COVI-19 vaccination.[3] Here we present a case of ischemic stroke post Oxford AstraZeneca COVID-19 vaccination. Is the vaccine responsible for ischemic stroke in this patient or it is mere a coincidence is yet to be determined?

Case Report. A 43-year old male patient presented with right-sided sudden onset, upper, and lower limb weakness of the body after 3 days of receiving the first dose of AstraZeneca vaccine against COVID-19

Case Series

- Many cases (from three to 100 cases) (Sayre et al., 2017; Omair, 2015)
- A collection (series) of cases with similar findings / outcomes
- Generate more viable hypothesis for exposure-outcome association
- Stronger evidence than a case report – case reports

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

Nina H. Schultz, M.D., Ph.D., Ingvild H. Sørvoll, M.D., Annika E. Michelsen, Ph.D., Ludvig A. Munthe, M.D., Ph.D., Fridtjof Lund-Johansen, M.D., Ph.D., Maria T. Ahlen, Ph.D., Markus Wiedmann, M.D., Ph.D., Anne-Hege Aamodt, M.D., Ph.D., Thor H. Skattør, M.D., Geir E. Tjønnfjord, M.D., Ph.D., and Pål A. Holme, M.D., Ph.D.

SUMMARY

We report findings in five patients who presented with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first dose of the ChAdOx1 nCoV-19 adenoviral vector vaccine against coronavirus disease 2019 (Covid-19). The patients were health care workers who were 32 to 54 years of age. All the patients had high levels of antibodies to platelet factor 4–polyanion complexes; however, they had had no previous exposure to heparin. Because the five cases occurred in a population of more than 130,000 vaccinated persons, we propose that they represent a rare vaccine-related variant of spontaneous heparin-induced thrombocytopenia that we refer to as vaccine-induced immune thrombotic thrombocytopenia.

Case Report / Series

Advantages	Disadvantages
• Easy to conduct • Low cost • Good starting point to generate hypothesis • Provide detailed information about the case(s) • Allow studies into conditions that could be unethical to perform by other study designs	• Findings could be due to chance – not the real association • Incidental findings – maybe due to other factors, not the one hypothesized • Absence of comparison group • Poor generalizability

Correlational

- a.k.a Ecological study
- Used when individual level data not available – population level / aggregate data
- Secondary data from databases, hospital records
- Study population-level associations between exposure-outcome
- Serve as hypothesis generating steps

Environmental Science and Pollution Research (2022) 29:16667–16677
https://doi.org/10.1007/s11356-021-16876-x

RESEARCH ARTICLE

Correlation between environmental factors and COVID-19 indices: a global level ecological study

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Received: 8 July 2021 / Accepted: 30 September 2021 / Published online: 15 October 2021

Abstract

This global level ecological study aimed to investigate the correlation between environmental factors and the COVID-19 indices. This survey is an ecological study, so all studied variables are aggregate variables. To collect the variables in the study, a data set was provided, which includes the information of each country based on the cumulative deaths, case fatality rate, recovery rate, and the number of performed COVID-19 tests. Scatter plots of environmental factors for the studied countries were drawn based on cumulative incidence rate of cases, cumulative incidence rate of death, tests, recovery rate, and case fatality rate of COVID-19. Furthermore, Spearman correlation coefficient was also used to verify the correlation between environmental factors and indicators related to COVID-19. The results of this ecological study showed that among all countries surveyed, Montenegro (60,310.56 per million) and Luxembourg (54,807.89 per million) had the highest cumulative incidence rates of COVID-19 cases, when Tanzania (8.42 per million) and Vietnam (13.78 per million) had the lowest cumulative incidence rates of COVID-19. In addition, in this study, it was shown that the cumulative incidence rate of cases, the cumulative incidence rate of deaths, and performed COVID-19 tests had significant direct correlations with the access to drinking water and the access to sanitation services ($p < 0.001$). The findings of the present study showed an inverse correlation between the mortality rate due to unhealthy water consumption, poor health status, and a positive correlation between access to drinking water and health services with the cumulative incidence and mortality rates of COVID-19. The differences between our findings and many other studies could be due to the ecological nature of the study. Nevertheless, our findings will help health policymakers to develop timely strategies to reduce the mortality and incidence rate of COVID-19.

Keywords COVID-19 · Coronavirus · Environmental factors · Ecologic study

Correlational

Advantages	Disadvantages

• Easy to conduct and low cost – utilize available data
• Enables analysis when individual level data are not available
• When measuring individual level data is not practical – pollution index in an area
	• Ecological fallacy / bias:
	  • maybe due to other factors, not the one hypothesized
	  • group level data might not reflect individual level data
	• Difficulty to adjust for confounders
	• Cause-effect / temporal ambiguity
	• Weak generalizability

Cross-sectional (descriptive)

- a.k.a cross-sectional survey / prevalence study
- A representative sample from A population
- Establish prevalence of the disease in the population
- Allows prevalence estimation + 95% CI
- Can intermediate step to estimate the severity of the problem before conducting a proper analytical cross-sectional
- Also common to have both descriptive and analytical components

OPEN ACCESS
doi: 10.31729/jnma.6421

Depression among Online Respondent Oral Healthcare Workers during COVID-19 Pandemic: A Descriptive Cross-sectional Study

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ABSTRACT

Introduction: COVID-19 outbreak brought unprecedented pressure on dental and oral health care workers leading to increased depression. This study aimed to find the prevalence of depression among online respondent oral healthcare workers during the COVID-19 pandemic.

Methods: A descriptive cross-sectional study was conducted from 24 June 2020 to 13 July 2020 among oral health care workers in a tertiary care centre. Ethical approval was taken from the Ethical Review Board (Reference number: 2710). Convenience sampling method was used. The data were collected using a questionnaire through Google Forms. Point estimate and 95% Confidence Interval were calculated.

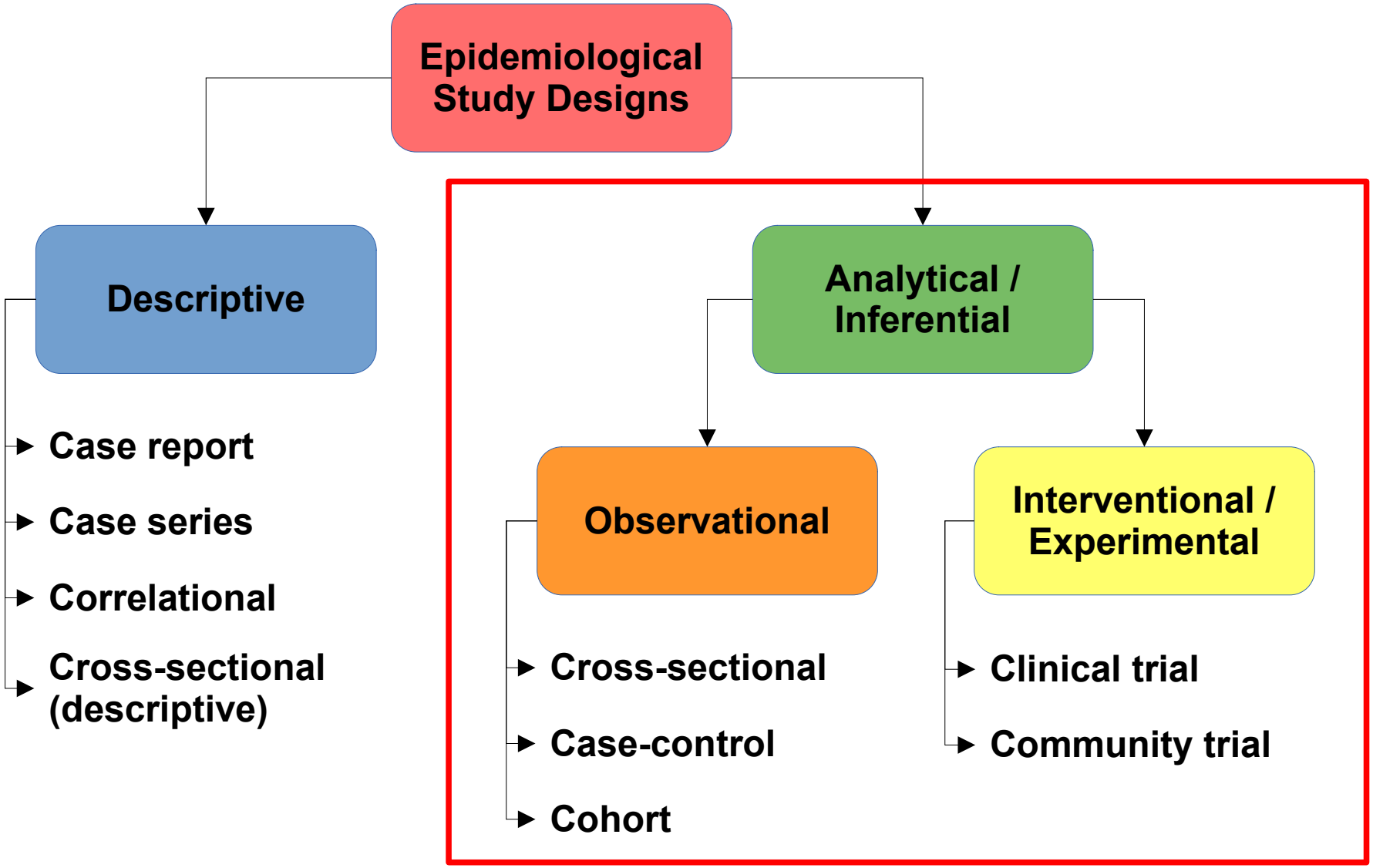
Results: Among 133 oral health care workers, the prevalence of depression was found to be 29 (21.80%) (14.78-28.82, 95% Confidence Interval).

Conclusions: The prevalence of depression among oral health care workers was lower than similar studies done in similar settings.

Cross-sectional

Advantages	Disadvantages
• Easy to conduct – no follow-up • Low cost, limited resources • Exposure-outcome is determined at the same time • Can collect many variables at the same time • Can be analytical when exposure and outcome association is determined • Allow studies into conditions that could be unethical to perform by other study designs	• Unable to establish cause-effect / temporal relationship • Only provides a snapshot at a point of time • Not suitable to study rare conditions • May have weak generalizability

Analytical Study Designs



*Following the classification by Omair (2015) and Ranganathan (2019)

Observational Study Designs

Cross-sectional (analytical)

- Cross-section / snapshot of population at a single time point
- Comparison element (vs descriptive version of cross-sectional study)
- Exposure and outcome are measured simultaneously at the same time
- Temporality (cause → effect relationship) cannot be determined
- Determine association, not causation / risk

Cross-sectional (analytical)

Advantages	Disadvantages
• Study multiple exposures and outcomes • Determine prevalence • Easy to conduct – no follow-up • Low cost, limited resources • Exposure-outcome is determined at the same time • Allow studies into conditions that could be unethical to perform by other study designs • Starting point for prospective studies – potential associated factors	• Unable to establish clear cause-effect / temporal relationship • Only provides a snapshot at a point of time • Cannot determine risk • Not suitable to study rare conditions • Survival bias – not picked up given snapshot nature of CS study

Case-control

- Backward-directed study, retrospective nature
- Suitable for rare diseases
- Identiy individuals with an outcome / medical condition (CASE) and matching individuals without the medical condition (CONTROL)
- Retrospectively go through the records to identify exposures / associated factors of the medical condition by comparison across case-control
- Allow case-control matching for factors that might influence the exposure / outcome (e.g. age, gender, sociodemographic factors)

Case-control

Advantages	Disadvantages
• Study multiple exposures • Easy and quick to conduct • Low cost, limited resources • Best for rare diseases • Suitable for disease with long latent period • Smaller sample size • Allow studies into conditions that could be unethical to perform by other study designs • Starting point for prospective studies – potential associated factors • Case-series can be turned to case-control study	• Difficult to identify matching control – suitable matching variables unknown • Bias in determination of exposures, cases and controls (outcomes) are known to investigators • Sampling bias – case vs control come from different population subgroups • Recall bias – cases might recall exposure better • Unable to establish causation – cannot determine risk, only association • Not suitable for rare exposures • Cannot determine prevalence and incidence • Limited to one outcome

Cohort

- “cohort” is a group of people being exposed to the same risk factor
- Follow-up exposed cohort vs unexposed cohort over a period of time, then compare the outcome
- Both cohorts have not developed the outcome at the start of followup!
- To some extent, resembles clinical trial – only exposure is natural
- Two types:
  - Prospective
  - Retrospective

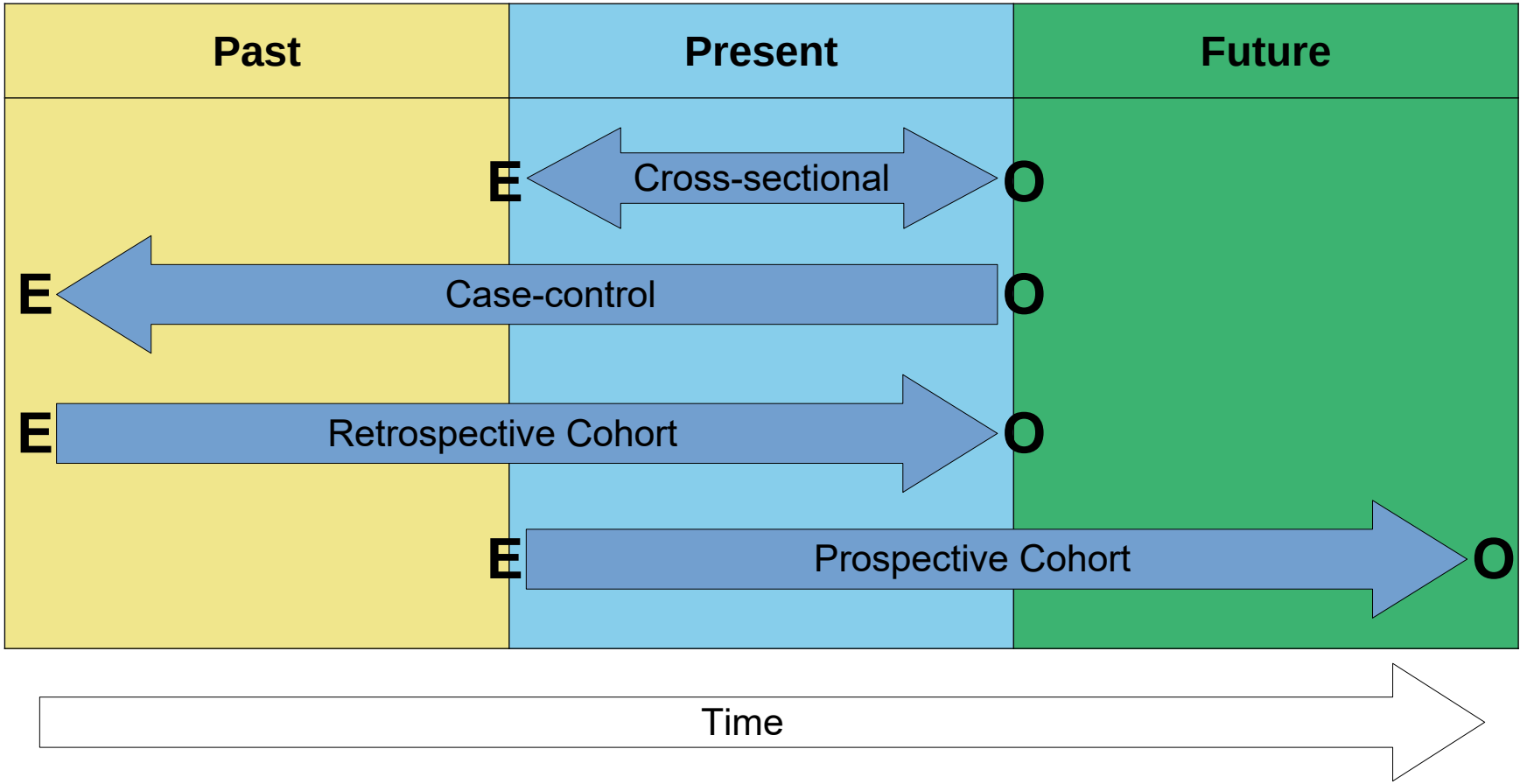
Prospective vs Retrospective

- Prospective
  - New data
  - Follow-up after the start of study for a specified period of time
- Retrospective
  - Records for other purposes
  - Medical records, registry data

Cohort

Advantages	Disadvantages
• Study multiple outcomes • Strongest evidence out of all observational studies • Determine incidence • Can determine causality / temporal relationship – allows determination of risk • Can evaluate multiple outcomes for a single exposure • Suitable for rare exposures	• More expensive • Longer time to complete • Larger sample size • Not suitable for rare diseases • Loss to followup bias • Misclassification bias • Unknown confounders other than the exposure that cause the outcome • Limited to one exposure

CS vs CC vs Cohort



*Modified based on Figure 1 in Levin (2006); E = exposure, O = outcome

Interventional Study Designs

Interventional Study

- a.k.a. Experimental study
- It tests a new treatment/intervention on a selected group of patients
- Intervention study = Trial
- Intervention = “Exposure” that is controlled by the investigators, not natural
- Two types:
  - Clinical trial
  - Community trial

Clinical vs Community Trials

- Clinical trial:
  - Individuals are assigned to treatment / control groups
- Community trial:
  - Communities are assigned to treatment / control groups
  - Communities: villages, schools, districts etc.

Study Designs

- Randomized controlled trial
- Non-randomized controlled trial
- Interventional study without concurrent controls
- Before–after (pre–post) study
- Crossover study
- Cluster randomized trial

Randomized controlled trial

- Strongest design
- Features:
  - "randomized": Random assignment to treatment/control (randomization)
  - "controlled": Control group
- Randomization – cancel out all external factors except the intervention that affect the outcome
- Control – to compare against a baseline without intervention, ascertain the effect of intervention

Randomized controlled trial

- Other considerations to improve the validity of RCT:
  - Allocation concealment
  - Blinding
  - Intention-to-treat analysis
  - Ensure compliance
  - Minimize dropouts
  - Adequate sample size

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Acknowledgments

Dr Anis Kausar Ghazali, Lecture note: Observational Study Design

Dr Siti Azrin Ab Hamid, Lecture note: Experimental Study Design