Study Design

Dr Myo Myo Mon
MBBS; MMedSc (PH);
MSc (Epidemiology); PhD (Epidemiology)
Deputy Director/Head, Epidemiology Research Division
Department of Medical Research (HQ

Choice of Study Design

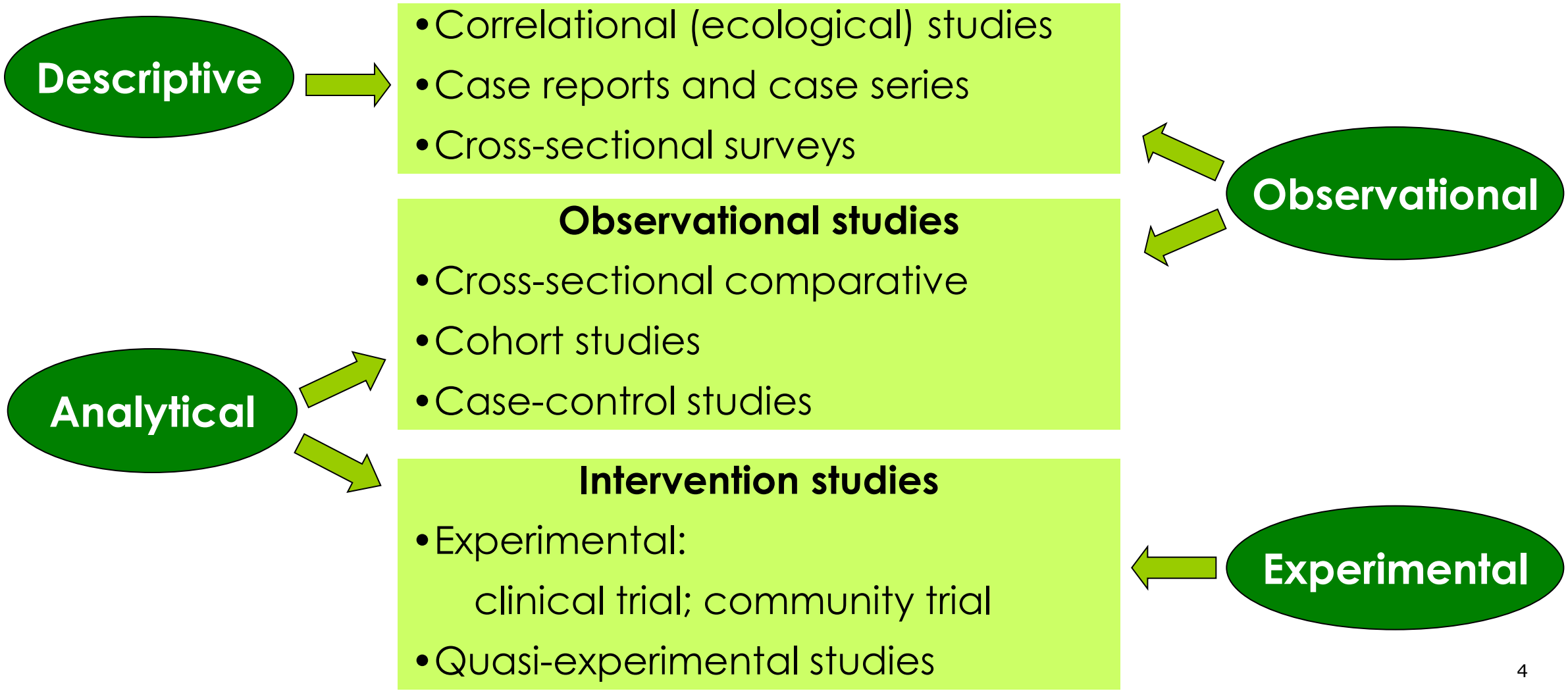
The choice of study design is mainly determined by:

- Objectives of the study
- Available resources
- Time frame

Objective and study design

Knowledge Gap	Objective	Study Design
Magnitude & distribution	To quantify the magnitude and distribution of a health state/event	Descriptive
Causes	To compare groups to elicit the causes/risk factors	Analytical
Solutions	To assess the efficacy of drugs, treatments, interventions	Experimental

Study design: Overview



Descriptive studies

To describe the general characteristics of the distribution of a disease, particularly in relation to **person, place and time** by making all measurements on **a single occasion**

- Correlational (ecological) study
- Case reports and case series
- Cross-sectional surveys

Correlational studies

- Use data from whole population
- Data often readily available (secondary data)
- Compares frequencies of disease (or other characteristics) across these population at same time
- Compares frequencies in the same population across different points in time
- May be useful in suggesting hypotheses
- Cannot be used to test hypotheses of association

Example: Correlation between dietary fat intake and breast cancer by country
J Natl Cancer Inst 80:802-814, 1988

Case reports and case series

- Detailed report of one or a series of patients
- Describe clinical characteristics of a well-defined group of patients without comparison group (e.g., pts. with a certain disease)

CDC. Pneumocystis pneumonia -- Los Angeles. *MMWR* 1981; 30:250-2.

Initial report of five cases of pneumocystic pneumonia in previously healthy, homosexual men.

JOURNAL ARTICLE

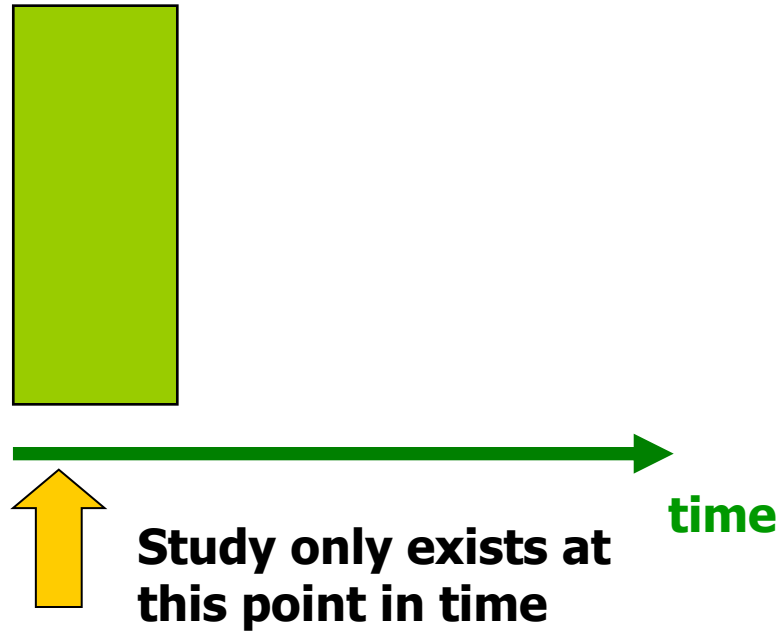
Pneumocystis Pneumonia — Los Angeles

Morbidity and Mortality Weekly Report
Vol. 30, No. 21 (June 5, 1981), pp. 250-252

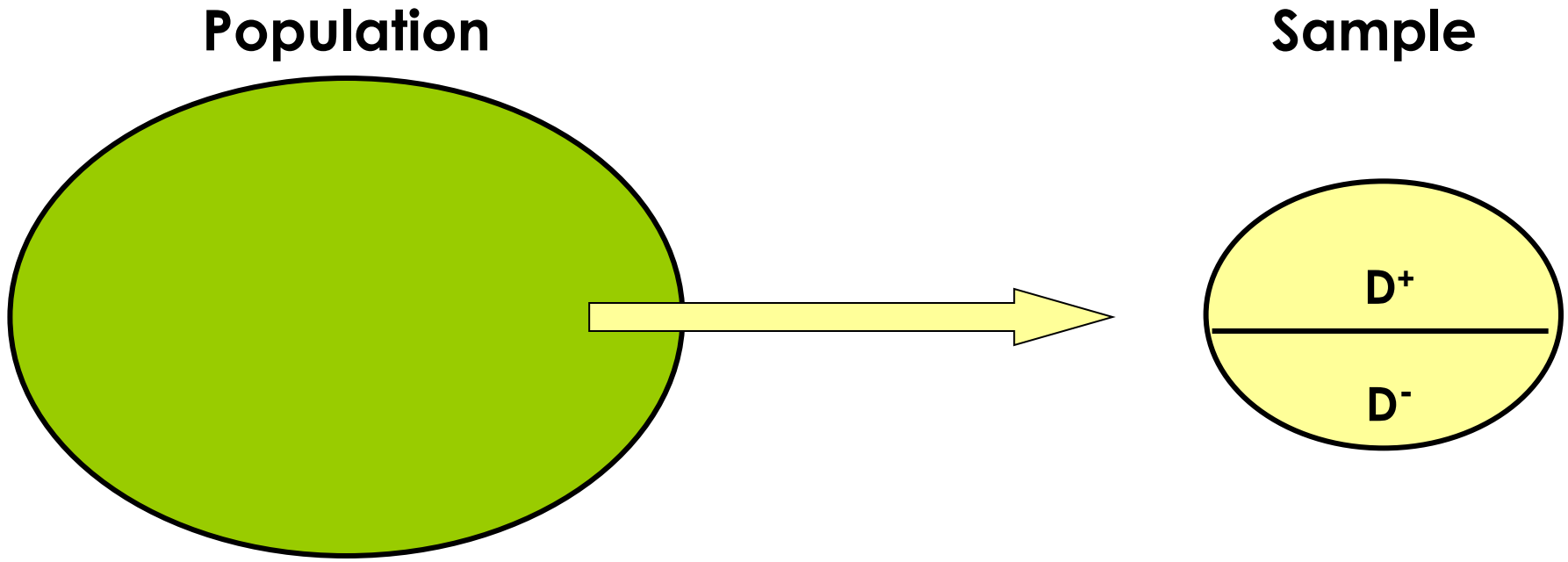
Published by: Centers for Disease Control & Prevention (CDC)
Stable URL: http://www.jstor.org/stable/23295554
Page Count: 3

Cross-sectional studies

- Observe prevalence of a disease and other characteristics in a well-defined population
- Can be usually performed in a short time
- Measure at a single point in time
- Association can be investigated
- Causality usually cannot be inferred
- Can be useful for generating hypotheses



Basic design of Cross-sectional study



Example: Prevalence data on overweight and obesity using measured Ht. & Wt. in National Health and Nutrition Examination Survey (NHANES)

Dhital et al. BMC Pediatrics (2017) 17:101
DOI 10.1186/s12887-017-0858-0

BMC Pediatrics

RESEARCH ARTICLE Open Access

Molecular epidemiology of Rotavirus causing diarrhea among children less than five years of age visiting national level children hospitals, Nepal

Subhash Dhital[1*], Jeevan Bahadur Sherchand[2], Bharat Mani Pokhrel[2], Keshab Parajuli[2], Niranjan Shah[2], Shyam Kumar Mishra[2], Sangita Sharma[2], Hari Prasad Kattel[2], Sundar Khadka[1], Sulochana Khatiwada[3], Narayan Parajuli[4] and Basistha Rijal[2]

Abstract

Background: Rotaviruses are the major cause of diarrhea among the infants and young children all over the world causing over 500,000 deaths and 2.4 million hospitalizations each year. In Nepal Rotavirus infection positivity rates ranges from 17.0 to 39.0% among children less than 5 years. However, little is known about the molecular genotypes of Rotavirus prevailing. The objective of this study was to estimate the burden of Rotavirus gastroenteritis and determine the genotypes of Rotavirus among children less than 5 years.

Methods: The cross sectional study was conducted from January to November 2014 among children less than 5 years old visiting Kanti Children's Hospital and Tribhuvan University Teaching Hospital.
Rotavirus antigen detection was performed by Enzyme Linked Immunosorbent Assay (ELISA) using ProSpecT Rotavirus Microplate Assay. Among the Rotavirus antigen positive samples, 59 samples were used for Rotavirus RNA extraction. Multiplex PCR was performed to identify G type comprising G1-G4, G8-G10 and G12 and P type comprising P[4], P[6], P[8], P[9], P[10], and P[11].

Results: A total of 717 diarrheal stool samples were collected from patients ranging from 10 days to 59 months of age. Rotavirus antigen positive was found among ($N = 164$)22.9% of patients. The highest number of the diarrhea was seen in January. Molecular analysis of Rotavirus genotypes revealed that the predominant G-Type was G12 (36%) followed by G9 (31%), G1 (21%), G2 (8.6%). The predominant P- type was P6 (32.8%) followed by P8 (31%), P10 (14.8%), P4 (14.8%). A total of seven G/P type combinations were identified the most common being G12P [6] (35.8%), G1P [8] (15.1%), G9P [8] (15.1%).

Conclusion: Rotavirus diarrhea is, mostly affecting children from 7 to 24 months in Nepal, mostly occurring in winter. The circulating genotypes in the country are found to be primarily unusual genotypes and predominance of G12P[6]. It is recommended to conduct genotyping of Rotavirus on large samples before starting vaccination in the country.

Keywords: Rotavirus, Diarrhea, Nepal

Lin et al. BMC Public Health 2015, 15:3
http://www.biomedcentral.com/1471-2458/15/3

BMC Public Health

RESEARCH ARTICLE Open Access

Screening for pulmonary tuberculosis in type 2 diabetes elderly: a cross-sectional study in a community hospital

Yung-Hsiang Lin[1], Chia-Pei Chen[1], Pao-Ying Chen[1], Jui-Chu Huang[1], Cheng Ho[1], Hsu-Huei Weng[2,4], Ying-Huang Tsai[3,4] and Yun-Shing Peng[1*]

Abstract

Background: Tuberculosis is one of the major infectious diseases in Taiwan. It has an especially high prevalence in diabetes patients, in whom it is usually asymptomatic and are more likely to result in drug-resistant tuberculosis. The aim of the study was to aggressively screen high risk diabetic elderly, identify the prevalence of tuberculosis and its determinants.

Methods: Type 2 diabetes patients aged over 65 years were enrolled. They received chest X-rays, blood tests and the questionnaires to assess their medical history and symptoms. Suspicious cases were referred to the pulmonary or infectious disease outpatient clinics. Pulmonary tuberculosis was confirmed by sputum culture. Variables between groups were analyzed by Student *t* test, Chi-square test or Fisher's exact test. Risk factors were assessed using univariate logistic regression and multiple logistic regression.

Results: A total of 3,087 patients participated this screening program and 7 patients screened positive for pulmonary tuberculosis. Another 5 patients were being under treatment when participating screening program. The prevalence rate was 3.89 per thousand people. The patients with male gender, smoking, liver cirrhosis or subjective body weight loss were associated with an increased risk of tuberculosis significantly. Subjective body weight loss (OR: 6.635 [95% CI: 2.096-21.007]), liver cirrhosis (OR: 10.307 [95% CI: 2.108-50.395]) and history of smoking (OR: 3.981 [95% CI: 1.246-12.718]) are independent risk factors. Among all 73 patients with active tuberculosis or tuberculosis history, they tended to be male, lower body mass index (BMI), more smoking history, more alcohol consumption, more family history of tuberculosis, higher low density lipoprotein (LDL), and less hypertension. However, there was no significant difference in the glycated hemoglobin (HbA1c) levels between the tuberculosis group and non-tuberculosis group.

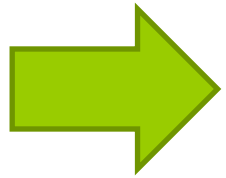
Conclusions: Active screening program is helpful in detecting pulmonary tuberculosis in elderly diabetes patients. Subjective body weight loss, smoking and liver cirrhosis are independent risk factors

Uses of Descriptive Studies

Correlational (ecological) study

Case reports and case series

Cross-sectional studies



- Health care planning
  - Prioritization
  - Target population
  - Resource allocation
- Trend analysis
  - Seasonal variation
  - Epidemic
- Clues about cause

Analytic studies

To examine the relationships between exposure and disease status (or health outcome) in order to judge whether a particular exposure causes or prevents disease

Exposure

- Alcohol consumption
- Raw hamburger
- Smoking

Health Outcome

- Breast Cancer
- E. Coli
- Lung Cancer

Cross-sectional Comparative Studies

Cohort Studies

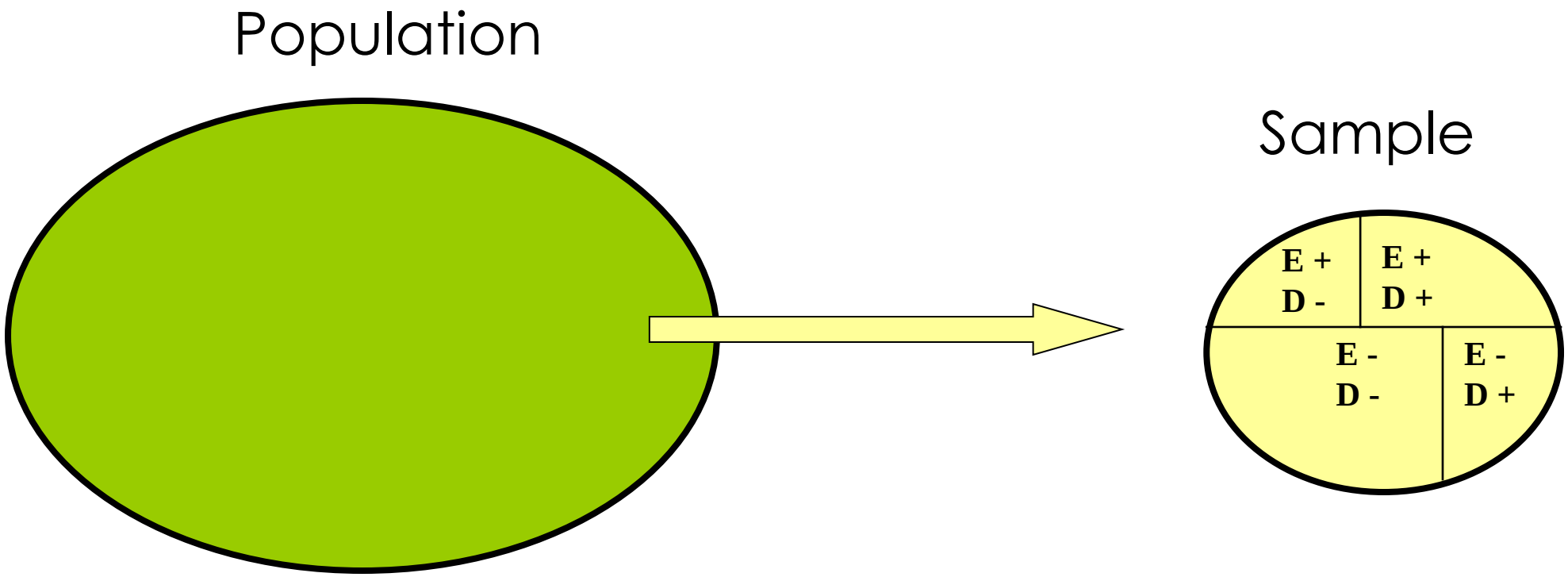
Case-Control Studies

Cross-sectional comparative studies

Measure health states & determinants at the same time and relate them in a population

Example: A comparative study on knowledge about reproductive health among urban and rural women of Bangladesh
J family reprod health 9(1): 2015; 35-40

Cross-sectional comparative studies



Cohort studies

- An "observational" design comparing individuals with a known risk factor/exposure with others without the risk factor/exposure
- Classify on basis of presence or absence of exposure → follow up to determine the development of disease
- Best observational design

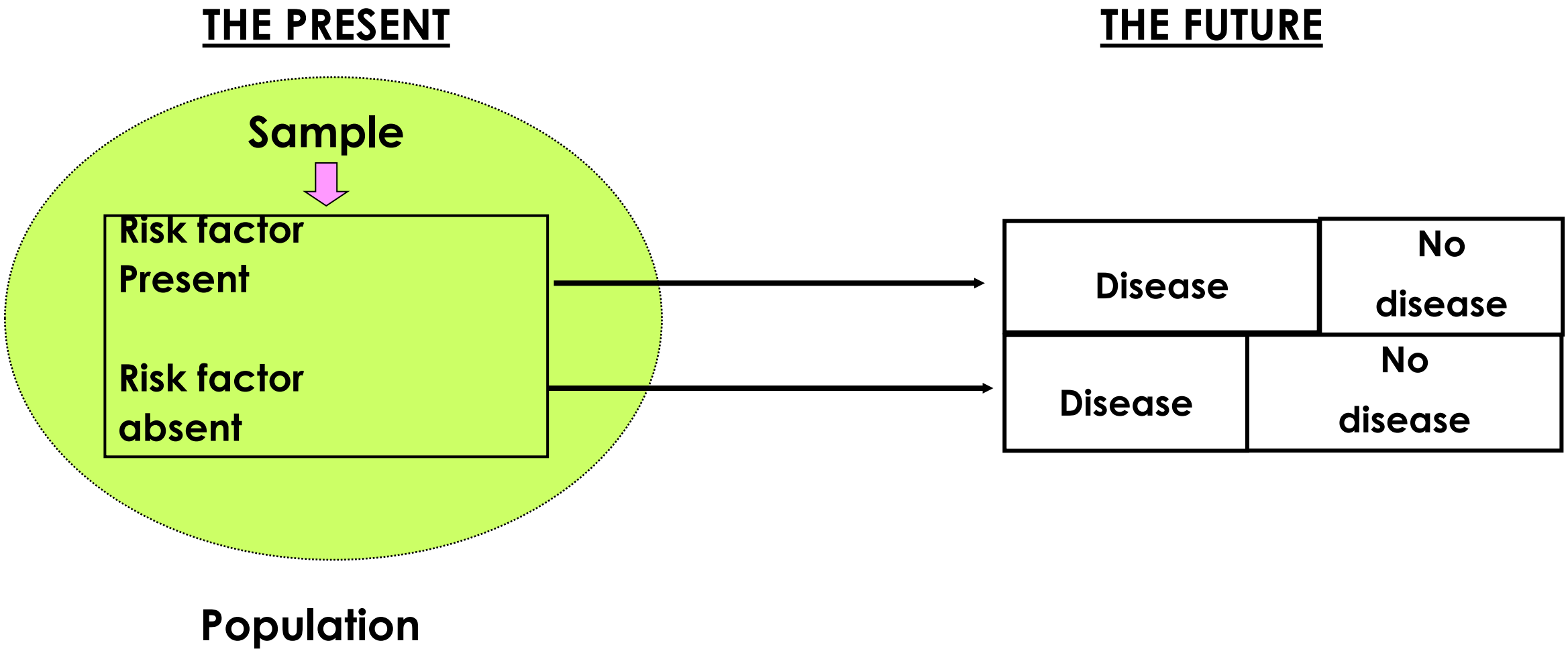
- **Temporal relationship → can establish causal association**
- **Suitable for rare exposures**
- **Not suitable for rare outcomes**

Sources of Cohort

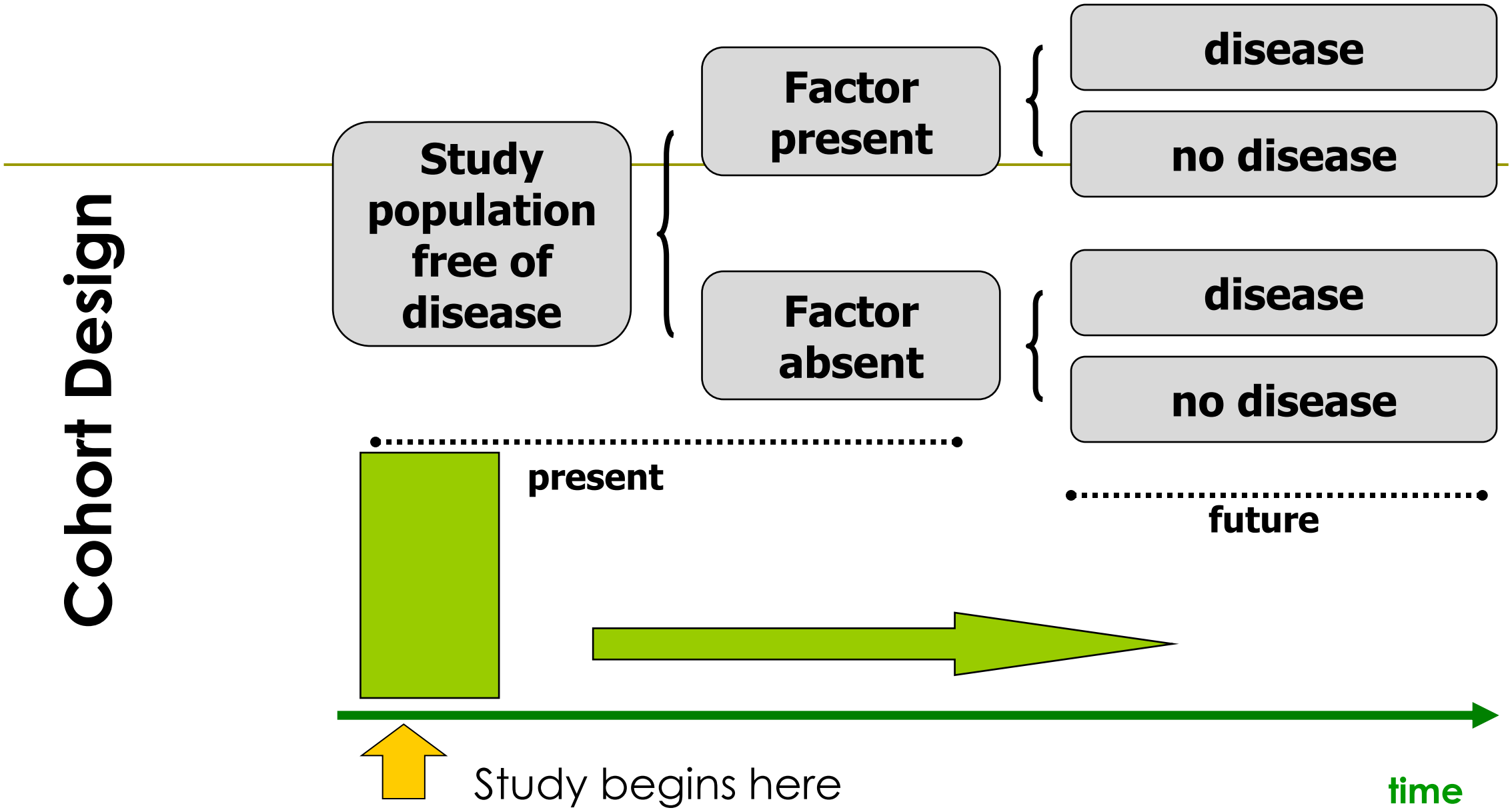
- General population
- A group known to have a high incidence of disease
- Persons who can be followed up easily

  (*e.g.* doctors, nurses, or other employees)

Cohort studies



Cohort Design



Cohort studies - Example

Ranch Hand Study

Exposed group: 1,264 Air Force servicemen who sprayed agent orange during Vietnam War, 1962-1971

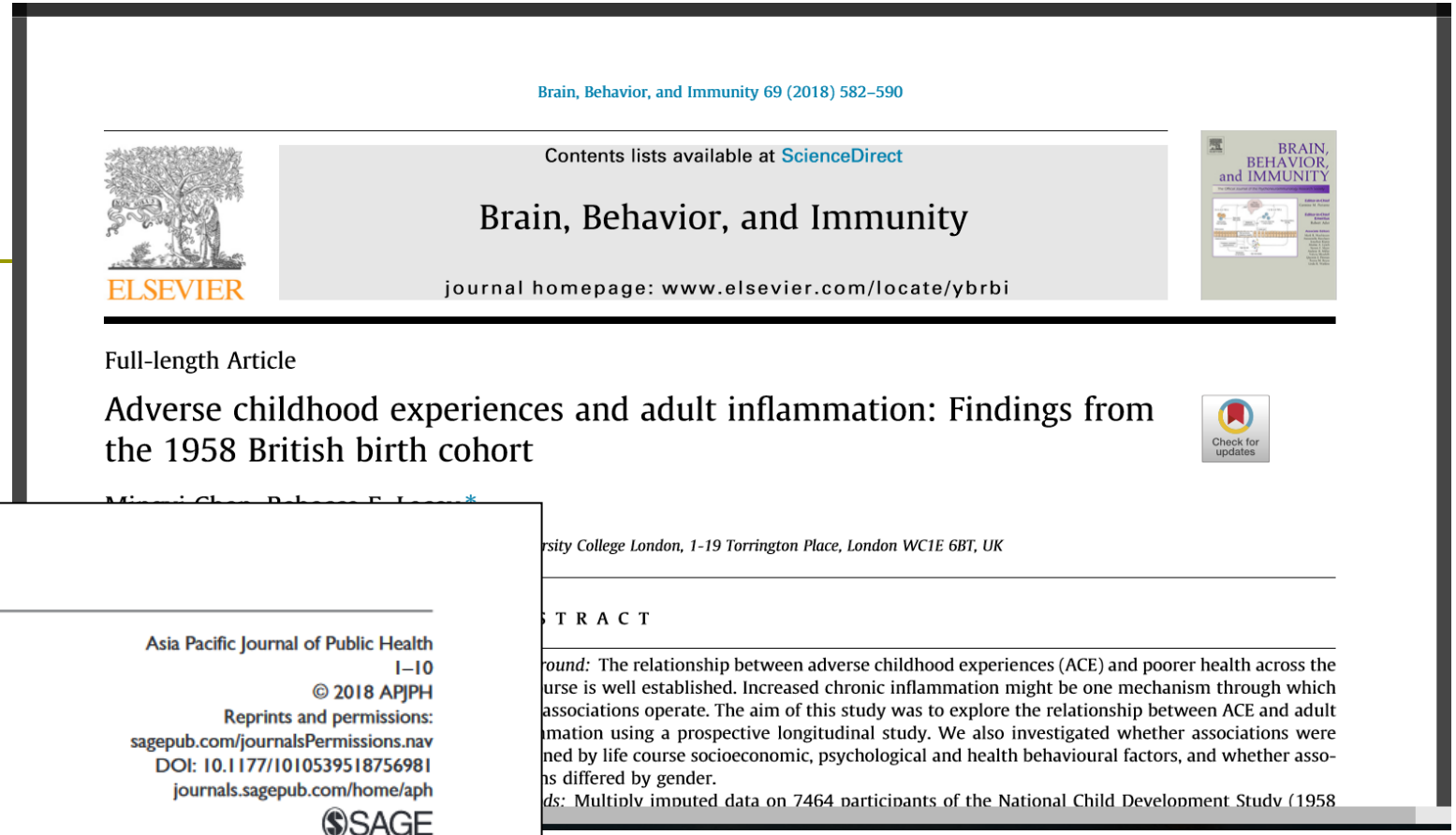
Unexposed group: 1,264 Air Force servicemen who flew other missions during Vietnam War

Outcomes of interest: cancer, post traumatic stress, adverse pregnancy outcomes etc.

Examples of Cohort Studies

- Adverse childhood experiences and adult inflammation: findings from the 1958 British birth cohort
- Effects of initial body mass index and weight change on all-cause mortality: A 10-year cohort study in Korea
- Factors associated with maternal depression in the Maldives: a prospective cohort study
- Hepatitis E virus infection in HIV infected patients: a large cohort study in Yunnan Province, China

Examples of Cohort Studies



Brain, Behavior, and Immunity 69 (2018) 582–590

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Full-length Article

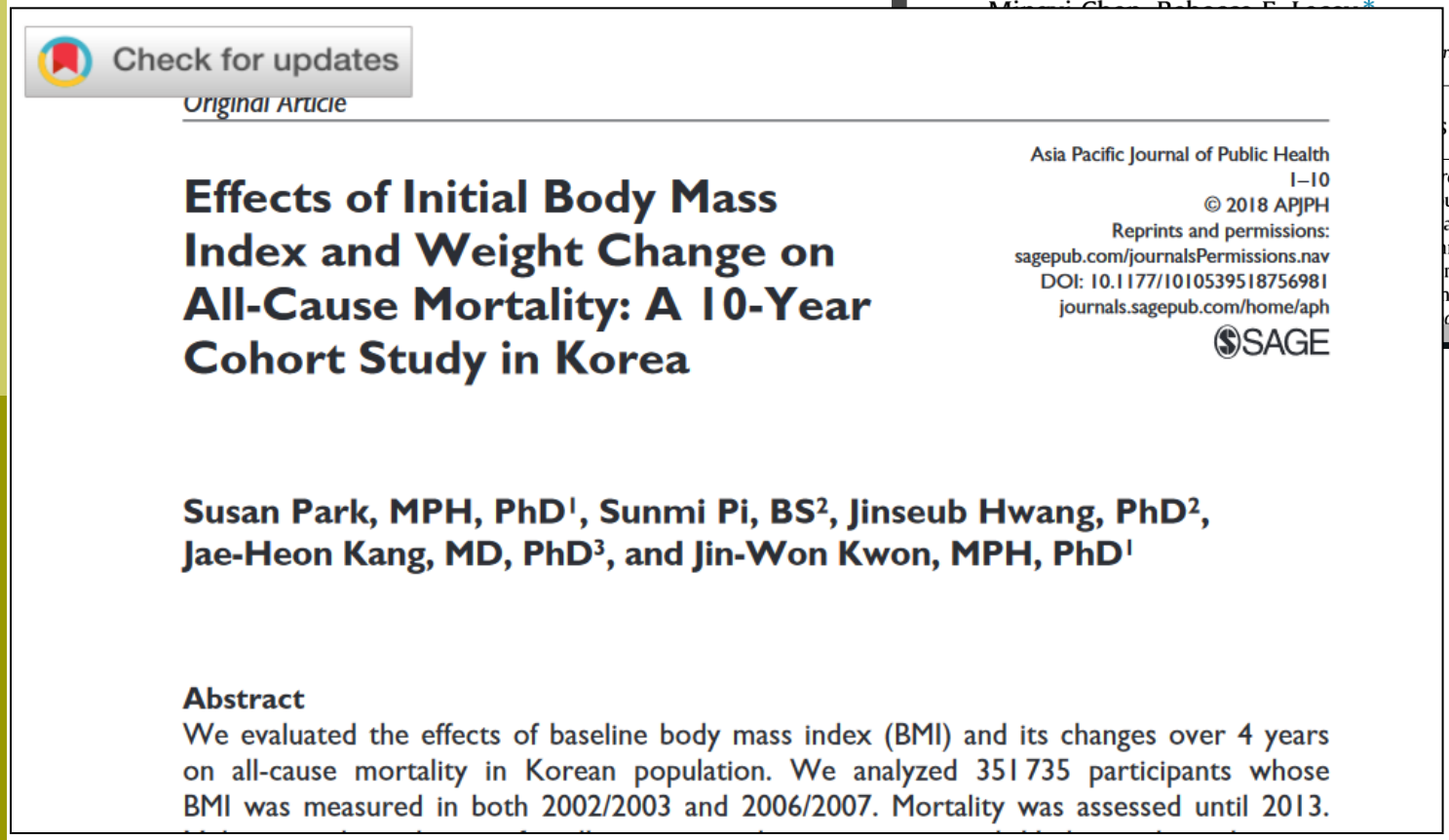
Adverse childhood experiences and adult inflammation: Findings from the 1958 British birth cohort

rsity College London, 1-19 Torrington Place, London WC1E 6BT, UK

STRACT

round: The relationship between adverse childhood experiences (ACE) and poorer health across the urse is well established. Increased chronic inflammation might be one mechanism through which associations operate. The aim of this study was to explore the relationship between ACE and adult mation using a prospective longitudinal study. We also investigated whether associations were ned by life course socioeconomic, psychological and health behavioural factors, and whether asso- s differed by gender.

ds: Multiply imputed data on 7464 participants of the National Child Development Study (1958



Original Article

Asia Pacific Journal of Public Health
1–10

DOI: 10.1177/1010539518756981
journals.sagepub.com/home/aph
SAGE

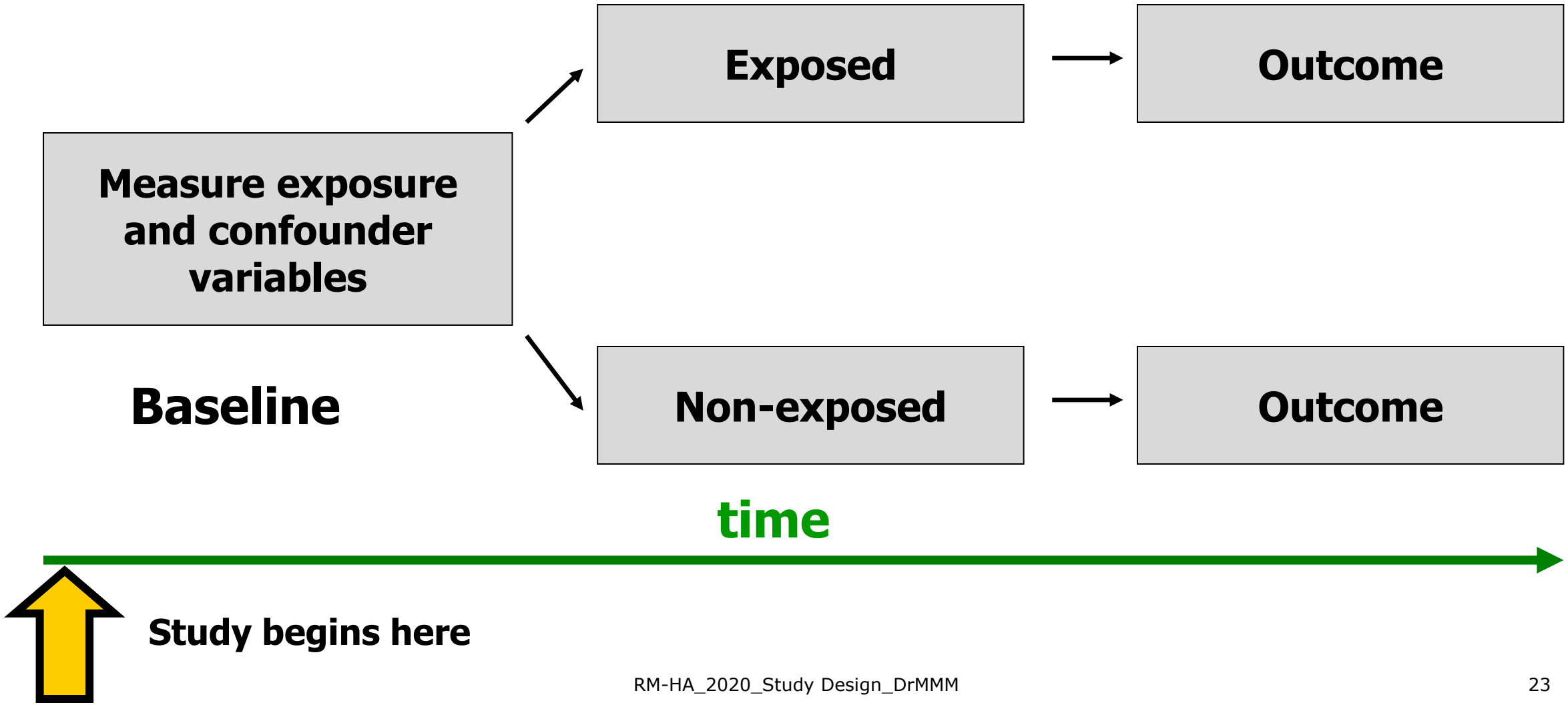
Effects of Initial Body Mass Index and Weight Change on All-Cause Mortality: A 10-Year Cohort Study in Korea

Susan Park, MPH, PhD[1], Sunmi Pi, BS[2], Jinseub Hwang, PhD[2], Jae-Heon Kang, MD, PhD[3], and Jin-Won Kwon, MPH, PhD[1]

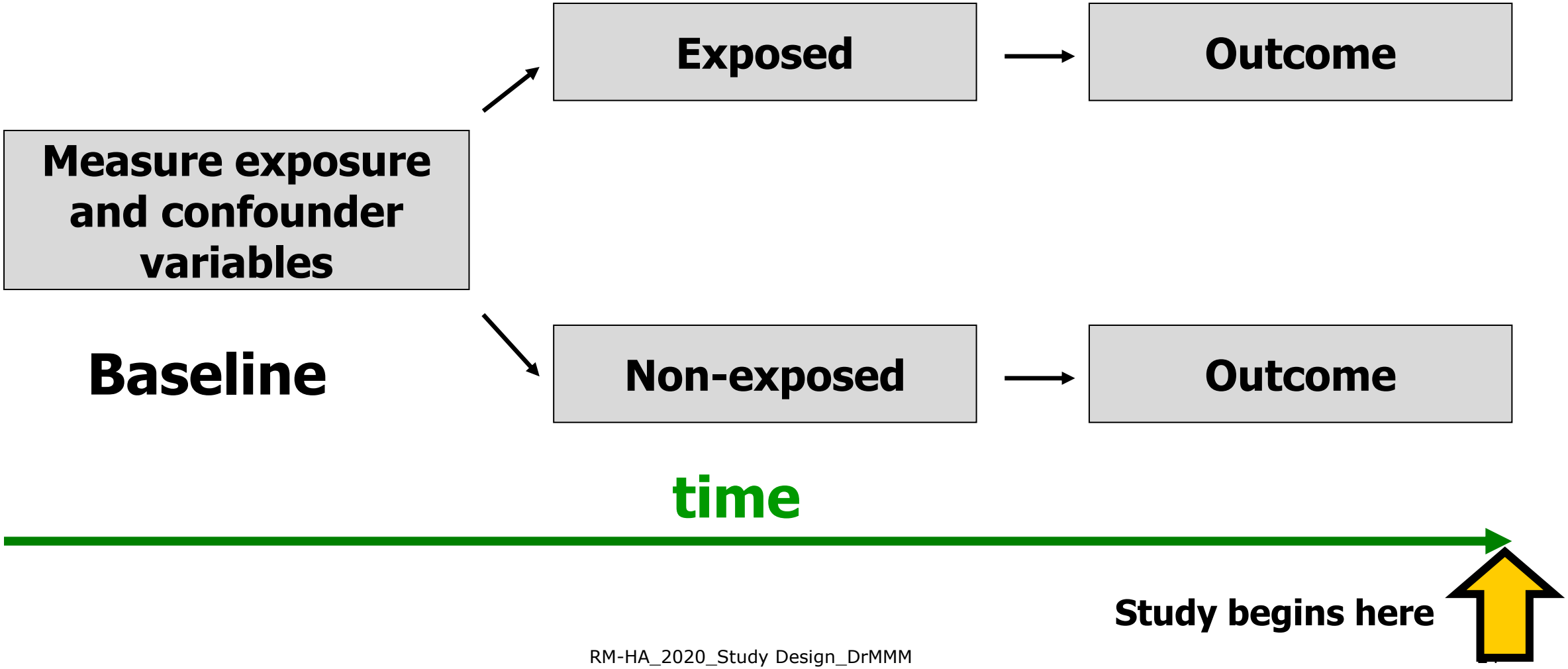
Abstract

We evaluated the effects of baseline body mass index (BMI) and its changes over 4 years on all-cause mortality in Korean population. We analyzed 351 735 participants whose BMI was measured in both 2002/2003 and 2006/2007. Mortality was assessed until 2013.

Prospective Cohort Study



Retrospective Cohort Study



Cohort Study

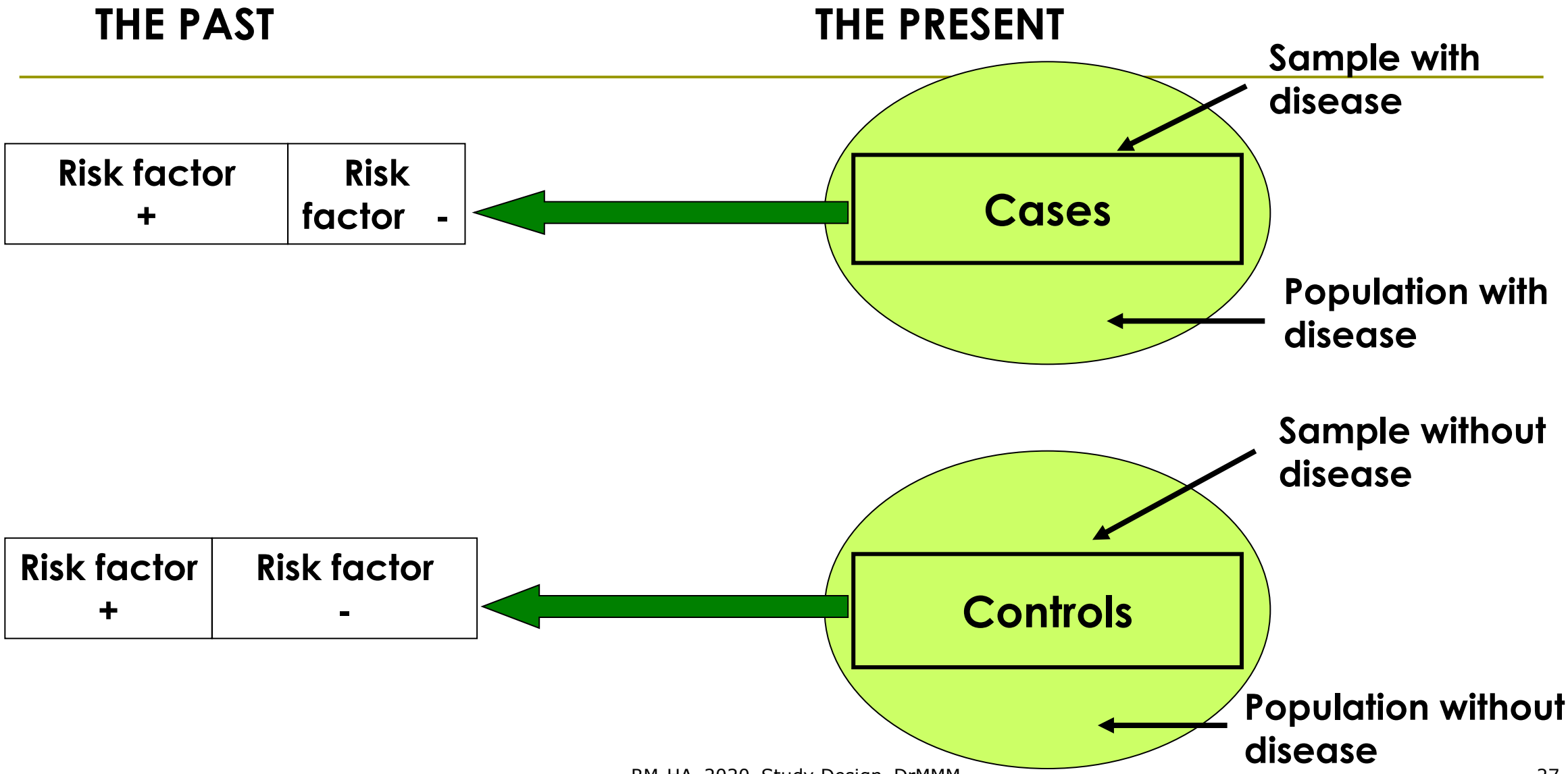
- **Strengths**
  - Exposure status determined before disease detection
  - Subjects selected before disease detection
  - Can study several outcomes for each exposure

- **Limitations**
  - Expensive and time-consuming
  - Inefficient for rare diseases or diseases with long latency
  - Loss to follow-up

Case-control studies

- An "observational" design comparing exposures in disease cases *vs.* healthy controls from same population
- Diseased people **(cases)** are compared with non-diseased people **(controls)** to determine if the two groups differ in the proportion of persons exposed to a specific factor
- Exposure data collected **retrospectively**
- Most feasible design where disease outcomes are rare

Case-control studies



Sources of Cases

Should have standardized selection criteria from a well-defined population

- Hospital patients
- Case registry (e.g. cancer registry)
- Death certificates
- Population

Sources of Controls

Representative of the source population from which the cases derived

- Population-based controls
- Hospital-based controls

Examples: case-control study

- Case-control study of IM vitamin K and newborns with childhood leukaemia
- Asbestos exposure, cigarette smoking and death rates

Tony Nengom et al. BMC Pediatrics (2017) 17:109
DOI 10.1186/s12887-017-0862-4

BMC Pediatrics

RESEARCH ARTICLE Open Access

Assessment of cardiac function in children with congenital adrenal hyperplasia: a case control study in Cameroon

J . Tony Nengom[1*], S. Sap Ngo Um[1,2], D. Chelo[1,2], R. Mbono Betoko[1], J. Boombhi[1,3], F. Mouafo Tambo[1,4], A. Chiabi[1,4], S. Kingue[1,3] and P. Koki Ndombo[1,3]

Abstract

Background: High level of androgens found in congenital adrenal hyperplasia (CAH) seems to have a deleterious effect on heart function. We therefore evaluate cardiac function of children with CAH in comparison with a healthy group.

Methods: We carried out a case-control study in the single endocrinology unit of the Mother and Child Center of Chantal Biya's Foundation. Cases were matched for age and genotypic sex to 2 healthy controls. We analyzed the ejection fraction (LVEF), fractional shortening and left ventricular mass; output and cardiac index; E and A waves velocities, E/A ratio and the mitral deceleration time and diameter of the left atrium; tricuspid annular plane systolic excursion and pulmonary artery systolic pressure were also measured.

Results: We included 19 patients with a median age of 6.26 ± 3.75 years and 38 controls stackable distribution. The left ventricular mass of cases was greater than that of controls. A case of reversible cardiomyopathy on hormone replacement therapy was found.
For the cases, the average ejection fraction was 71.95 ± 7.88%; the average fractional shortening was 40.67 ± 7.02%. All these values were higher than those of controls, although the difference was not statistically significant. Diastolic left ventricular function was more impaired among the cases.
Right ventricular function was similar in both groups. These abnormalities were highly correlated to the late age at diagnosis and duration of treatment.

Conclusion: This study shows an altered cardiac function in CAH compared to healthy control and highlights importance of an early diagnosis of cases, a tight control of androgens levels and a regular monitoring of cardiac function.

Keywords: Cardiac function, Congenital adrenal hyperplasia, Children

Case-Control Study

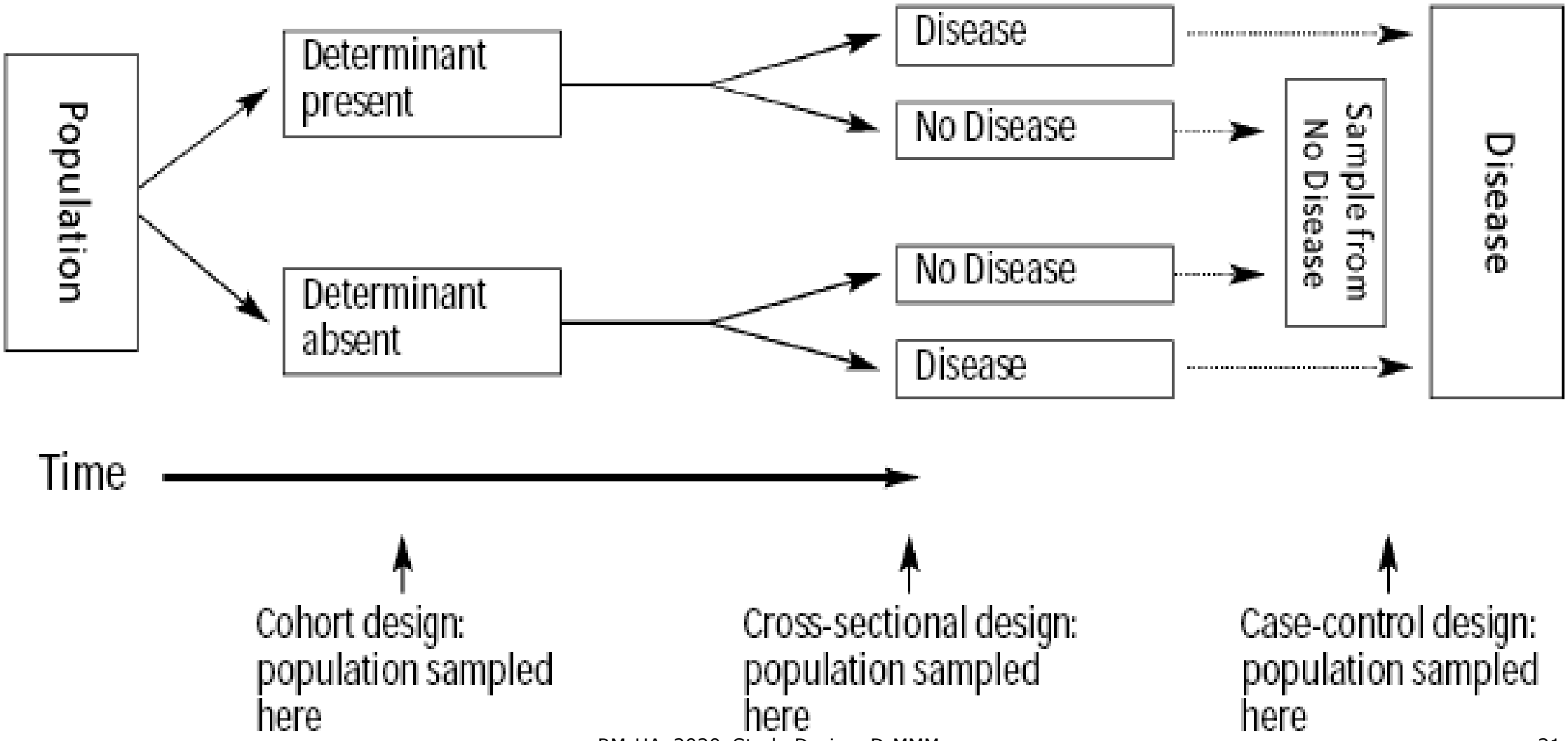
Strengths

- Less expensive & time consuming
- Efficient for studying rare diseases

Limitations

- Inappropriate when disease outcome for a specific exposure is not known at start of study
- Exposure measurements taken after disease occurrence
- Disease status can influence selection of subjects

Overview of Analytical Studies



Intervention or Experimental Studies

- Similar to cohort study, except that exposure is allocated by the investigator
- Investigator can control the exposure
- Subjects are followed up to determine if (when) they develop the outcome
- Allocation is best done using a randomization procedure
- Clinical trials are most well known experimental design
- "Treatment group" and "comparison group"

Types of experiments

- Clinical trials

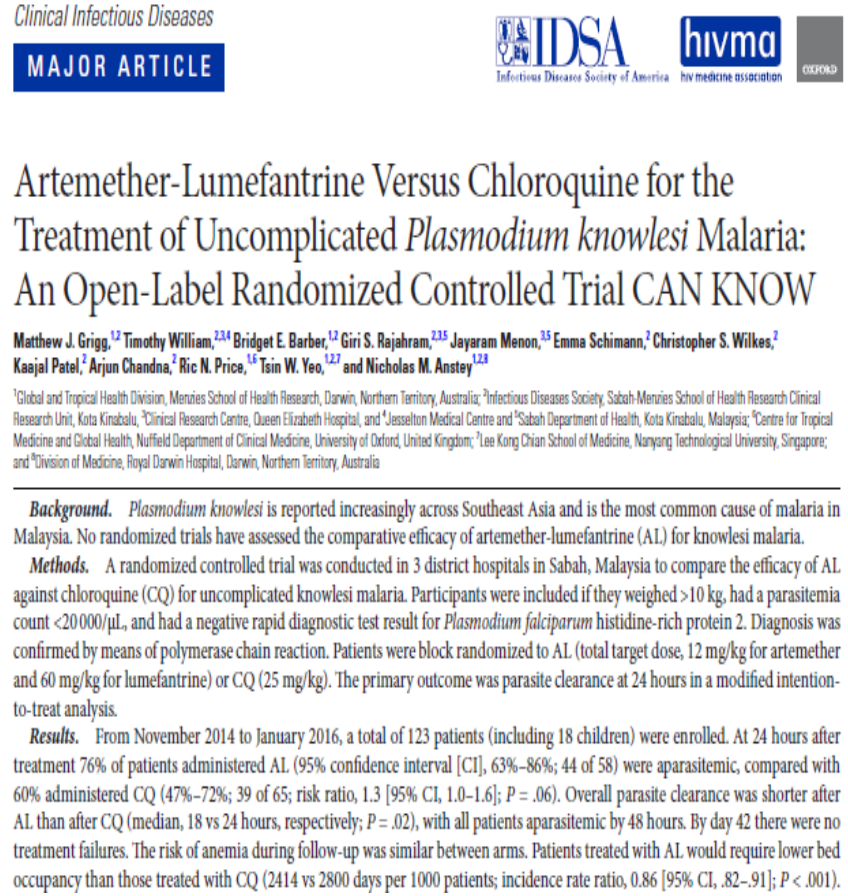
  Trials or intervention is applied to individuals (patients, students, workers)

- Community trial

  Trials on individual community (schools, worksites, communities)

Randomized controlled trial (RCT)

- A design with subjects randomly assigned to "treatment" and "comparison" groups
- Provides most convincing evidence of relationship between exposure and effect
- Not possible to use RCTs to test effects of exposures that are expected to be harmful, for ethical reasons
- **The "gold standard" of research designs**



Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Artemether-Lumefantrine Versus Chloroquine for the Treatment of Uncomplicated *Plasmodium knowlesi* Malaria: An Open-Label Randomized Controlled Trial CAN KNOW

Matthew J. Grigg,[1,2] Timothy William,[2,3,4] Bridget E. Barber,[1,2] Giri S. Rajahram,[2,3,5] Jayaram Menon,[3,5] Emma Schimann,[2] Christopher S. Wilkes,[2] Kaajal Patel,[2] Arjun Chandna,[2] Ric N. Price,[1,6] Tsin W. Yeo,[1,2,7] and Nicholas M. Anstey[1,2,8]

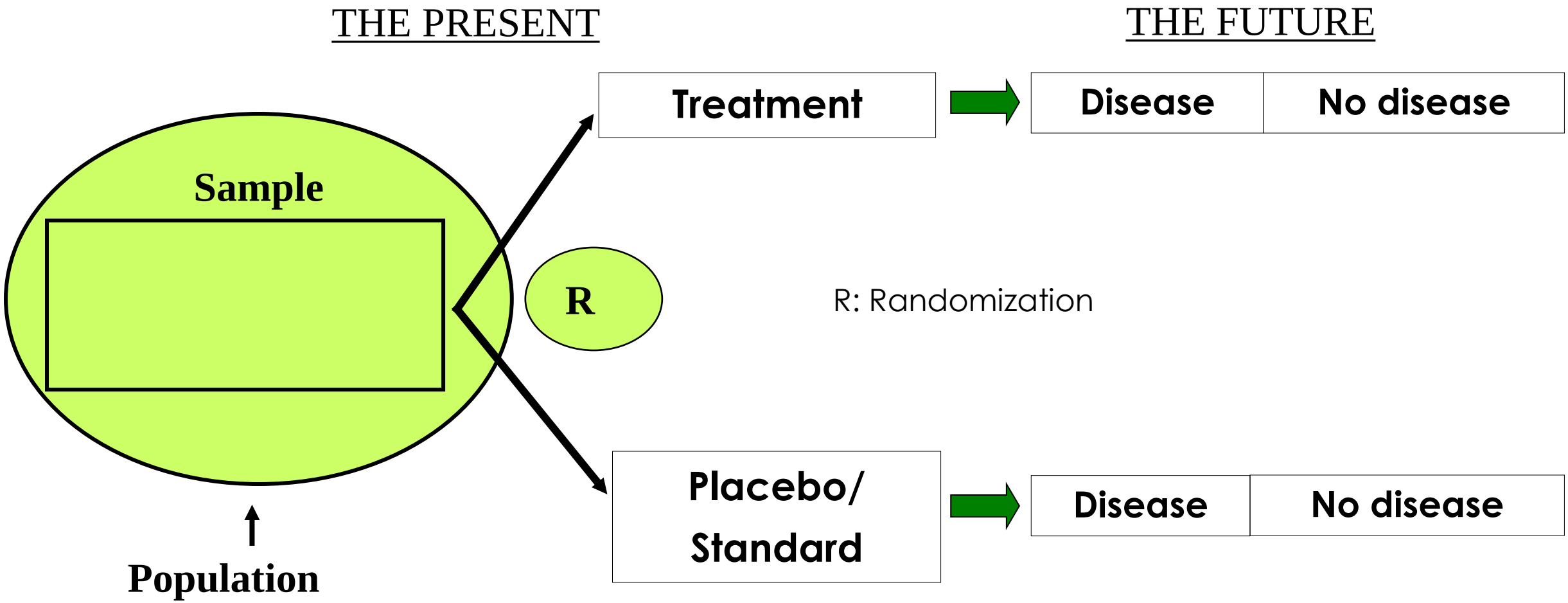
[1]Global and Tropical Health Division, Menzies School of Health Research, Darwin, Northern Territory, Australia; [2]Infectious Diseases Society, Sabah-Menzies School of Health Research Clinical Research Unit, Kota Kinabalu, [3]Clinical Research Centre, Queen Elizabeth Hospital, and [4]Jesselton Medical Centre and [5]Sabah Department of Health, Kota Kinabalu, Malaysia; [6]Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, United Kingdom; [7]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; and [8]Division of Medicine, Royal Darwin Hospital, Darwin, Northern Territory, Australia

Background. *Plasmodium knowlesi* is reported increasingly across Southeast Asia and is the most common cause of malaria in Malaysia. No randomized trials have assessed the comparative efficacy of artemether-lumefantrine (AL) for knowlesi malaria.

Methods. A randomized controlled trial was conducted in 3 district hospitals in Sabah, Malaysia to compare the efficacy of AL against chloroquine (CQ) for uncomplicated knowlesi malaria. Participants were included if they weighed >10 kg, had a parasitemia count <20 000/μL, and had a negative rapid diagnostic test result for *Plasmodium falciparum* histidine-rich protein 2. Diagnosis was confirmed by means of polymerase chain reaction. Patients were block randomized to AL (total target dose, 12 mg/kg for artemether and 60 mg/kg for lumefantrine) or CQ (25 mg/kg). The primary outcome was parasite clearance at 24 hours in a modified intention-to-treat analysis.

Results. From November 2014 to January 2016, a total of 123 patients (including 18 children) were enrolled. At 24 hours after treatment 76% of patients administered AL (95% confidence interval [CI], 63%–86%; 44 of 58) were aparasitemic, compared with 60% administered CQ (47%–72%; 39 of 65; risk ratio, 1.3 [95% CI, 1.0–1.6]; $P = .06$). Overall parasite clearance was shorter after AL than after CQ (median, 18 vs 24 hours, respectively; $P = .02$), with all patients aparasitemic by 48 hours. By day 42 there were no treatment failures. The risk of anemia during follow-up was similar between arms. Patients treated with AL would require lower bed occupancy than those treated with CQ (2414 vs 2800 days per 1000 patients; incidence rate ratio, 0.86 [95% CI, .82–.91]; $P < .001$).

Randomized controlled trial (RCT)



Community trial

- trials on communities rather than patients
- usually quasi-experimental

  (absence of randomization (or) control)
- usually test of preventive measures

Examples:

- Iron-fortified salt and anemia in the community
- Impregnated bed net and malaria morbidity

Lu et al. BMC Public Health (2015) 15:33
DOI 10.1186/s12889-015-1401-6

BMC Public Health

RESEARCH ARTICLE Open Access

Community-based interventions in hypertensive patients: a comparison of three health education strategies

Chu-Hong Lu[1,2†], Song-Tao Tang[2†], Yi-Xiong Lei[1], Mian-Qiu Zhang[2], Wei-Quan Lin[1], Sen-Hua Ding[2] and Pei-Xi Wang[1*]

Abstract

Background: Community-based health education programs may be helpful in improving health outcomes in patients with chronic illnesses. This study aimed to evaluate community-based health education strategies in the management of hypertensive patients with low socioeconomic status in Dongguan City, China.

Methods: This was a randomized, non-blinded trial involving 360 hypertensive patients enrolled in the community health service centre of Liaobu Town, Dongguan City, China. Participants were randomized to receive one of the three community-based health education programs over 2 years: self-learning reading (Group 1), monthly regular didactic lecture (Group 2), monthly interactive education workshop (Group 3). Outcomes included the changes in the proportion of subjects with normalized blood pressure (BP), hypertension-related knowledge score, adherence to antihypertensive treatment, lifestyle, body mass index and serum lipids.

Results: After the 2-y intervention, the proportion of subjects with normalized BP increased significantly in Group 2 (from 41.2% to 63.2%, p<0.001), and increased more substantially in Group 3 (from 40.2% to 86.3%, p<0.001), but did not change significantly in Group 1. Improvements in hypertension-related knowledge score, adherence to regular use of medications, appropriate salt intake and regular physical activity were progressively greater from group 1 to group 2 to group 3. Group 3 had the largest reductions in body mass index and serum LDL cholesterol levels.

Conclusion: Interactive education workshops may be the most effective strategy in community-based health promotion education programs for hypertensive patients in improving patients' knowledge on hypertension and alleviating clinical risk factors for preventing hypertension-related complications.

Keywords: Community-based intervention, Health education, Hypertension, Blood pressure, Serum lipids

Background

Hypertension is a serious public health concern. More than one-quarter of the adult population over the world has hypertension, a significant health burden in many countries [1,2]. As a major chronic non-communicable disease, hypertension is the most important risk factor for cardiovascular and kidney diseases, stroke and premature death if not detected early and treated appropriately. The estimated prevalence of hypertension in China is 22% in Chinese adult population, corresponding to about 200 million hypertensive patients [3,4]. Targeted interventions for patients with hypertension to control blood pressure are needed to improve health related quality of life and reduce hypertension-related complications and mortality in China.

Health education may result in lifestyle modifications and increase adherence to antihypertensive medications to improve effective blood pressure (BP) control in

20_Study

OPEN ACCESS Freely available online PLOS | MEDICINE

Effect of Household-Based Drinking Water Chlorination on Diarrhoea among Children under Five in Orissa, India: A Double-Blind Randomised Placebo-Controlled Trial

Sophie Boisson[1]*, Matthew Stevenson[1], Lily Shapiro[1], Vinod Kumar[2], Lakhwinder P. Singh[2], Dana Ward[3], Thomas Clasen[1]

1 Department of Disease Control, Faculty of Tropical and Infectious Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom, **2** Indian Institute of Health Management Research, Jaipur, India, **3** Population Services International, New Delhi, India

Abstract

Background: Boiling, disinfecting, and filtering water within the home can improve the microbiological quality of drinking water among the hundreds of millions of people who rely on unsafe water supplies. However, the impact of these interventions on diarrhoea is unclear. Most studies using open trial designs have reported a protective effect on diarrhoea while blinded studies of household water treatment in low-income settings have found no such effect. However, none of those studies were powered to detect an impact among children under five and participants were followed-up over short periods of time. The aim of this study was to measure the effect of in-home water disinfection on diarrhoea among children under five.

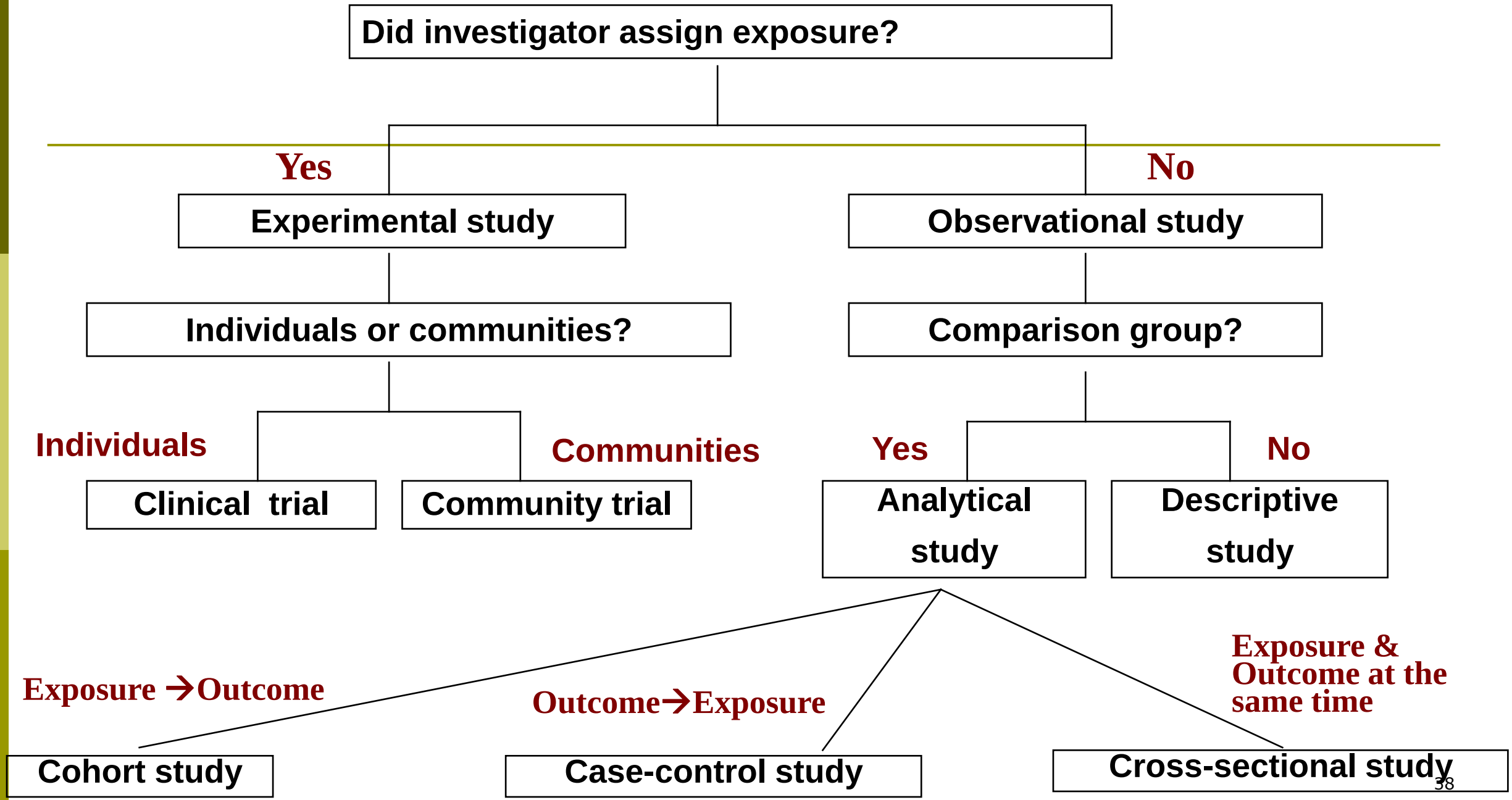
Methods and Findings: We conducted a double-blind randomised controlled trial between November 2010 and December 2011. The study included 2,163 households and 2,986 children under five in rural and urban communities of Orissa, India. The intervention consisted of an intensive promotion campaign and free distribution of sodium dichloroisocyanurate (NaDCC) tablets during bi-monthly households visits. An independent evaluation team visited households monthly for one year to collect health data and water samples. The primary outcome was the longitudinal prevalence of diarrhoea (3-day point prevalence) among children aged under five. Weight-for-age was also measured at each visit to assess its potential as a proxy marker for diarrhoea. Adherence was monitored each month through caregiver's reports and the presence of residual free chlorine in the child's drinking water at the time of visit. On 20% of the total household visits, children's drinking water was assayed for thermotolerant coliforms (TTC), an indicator of faecal contamination. The primary analysis was on an intention-to-treat basis. Binomial regression with a log link function and robust standard errors was used to compare prevalence of diarrhoea between arms. We used generalised estimating equations to account for clustering at the household level. The impact of the intervention on weight-for-age z scores (WAZ) was analysed using random effect linear regression.

Over the follow-up period, 84,391 child-days of observations were recorded, representing 88% of total possible child-days of observation. The longitudinal prevalence of diarrhoea among intervention children was 1.69% compared to 1.74% among controls. After adjusting for clustering within household, the prevalence ratio of the intervention to control was 0.95 (95% CI 0.79–1.13). The mean WAZ was similar among children of the intervention and control groups (−1.586 versus −1.589, respectively). Among intervention households, 51% reported their child's drinking water to be treated with the tablets at the time of visit, though only 32% of water samples tested positive for residual chlorine. Faecal contamination of drinking water was lower among intervention households than controls (geometric mean TTC count of 50 [95% CI 44–57] per 100 ml compared to 122 [95% CI 107–139] per 100 ml among controls [$p<0.001$] [$n=4,546$]).

Conclusions: Our study was designed to overcome the shortcomings of previous double-blinded trials of household water treatment in low-income settings. The sample size was larger, the follow-up period longer, both urban and rural populations were included, and adherence and water quality were monitored extensively over time. These results provide no evidence that the intervention was protective against diarrhoea. Low compliance and modest reduction in water contamination may have contributed to the lack of effect. However, our findings are consistent with other blinded studies of similar interventions and raise additional questions about the actual health impact of household water treatment under these conditions.

Trial Registration: ClinicalTrials.gov NCT01202383

Please see later in the article for the Editors' Summary.


Did investigator assign exposure?
Yes
No
Experimental study
Observational study
Individuals or communities?
Comparison group?
Individuals
Communities
Yes
No
Clinical trial
Community trial
Analytical study
Descriptive study
Exposure →Outcome
Outcome→Exposure
Exposure & Outcome at the same time
Cohort study
Case-control study
Cross-sectional study

Rating evidence

- Systematic reviews
- Randomized clinical trials
- Non-randomized clinical trials
- Cohort study
- Case-control study
- Cross-sectional study
- Ecological study

Thank You