Summer Training Report

TITLE:

A review study of the current trend of COVID-19 in India.

By:

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Acknowledgment

"Tell me and I forget. Teach me and I remember. Involve me and I learn."
-benjamin franklin

On the road to success, there will be many obstacles and may hinder progress but if you keep practicing and keep moving forward there's no way that anything can stop.

I want to pay my sincere gratitude to my mentor **Dr.Deepti Sharma and Abhishek Sharma** member of the department of MBA Hospital and Health Management, Indian Institute of Health Management Research, Jaipur for guidance, encouragement, and constant support at every stage of the study.

I would also like to take this opportunity to wholeheartedly thank **Dr. Abhishek Gupta** for helping me in completing project work.

TABLE OF CONTENT

ABBREVIATIONS

SARS-2	**Severe Acute Respiratory Syndrome**
COVID-19	**Coronavirus Disease**
nCoV	**Novel Coronavirus**
ARDS	**Acute Respiratory Distress Syndrome**
CT	**Computerized Tomography**
ICU	**Intensive Care Unit**
HCQ	**Hydroxychloroquine**
RNA	**Ribonucleic acid**
PPE	**Personal Protective Equipment**
MoHFW	**Ministry of Health and Family Welfare**
WHO	**World Health Organization**
ICMR	**Indian Council of Medical Research**
RBC	**Red Blood Cells**
WBC	**White Blood Cells**
PCR	**Polymerase Chain Reaction**
ALS	**Advanced Life Support**
BLS	**Basic Life Support**
ACE2 receptor	**Angiotensin-Converting Enzyme 2**

TERM PAPER

Objective:

To understand the status of India in terms of COVID-19 spread till 8th April 2020

Abstract:

The outbreak of the pandemic around the globe is alarming with the spread of novel coronavirus (COVID-19) or severe acute respiratory syndrome 2 (SARS-2). The virus seems to have been originated in bats through unknown mediator animals in Wuhan, Hubei province, China in December 2019. The infected person can potentially transmit this pathogen by inhalation or when it comes in contact with infected droplets. The infected person usually shows symptoms from 2-14 days. The usual symptoms are fatigue, sore throat, fever, cough, loss of taste, breathlessness. On most people, the disease appears to be mild, whereas in elderly patients or patients with comorbidities show severe symptoms like pneumonia or acute respiratory distress syndrome (ARDS). In some cases, people may show no symptom and is still tested with COVID-19 positive. Molecular tests are performed for the confirmation of the virus in the mucosal secretion.

Here this study is conducted to analyze different states and key districts in which India is facing a major challenge, mainly the most affected states are Mumbai, Tamil-Nadu, Delhi. Data mainly collected from secondary sources articles, journals, and websites.

COVID-19 care hospitals should be equipped with Ventilators, ICUs, and beds with assured oxygen support. The current requirement is estimated at 30-50k ventilators nationwide and about 70-100k ICU beds. Though this antimalarial drug is not yet approved by WHO but in some patients this drug was a game-changer drug and helped them cure this disease. Cost-effectiveness and easily available across India.

Introduction to Coronavirus

On 31 December 2019, several cases of pneumonia with unknown causes were reported in Wuhan city, China. The virus which caused the Pneumonia of unknown cause was then known as the novel coronavirus by Chinese authority on 7 January 2020 and was named "2019-nCOV".
These viruses belong from a large group of the virus which may show mild to moderate illness i.e common cold, cough, fever, and also show severe symptoms. This strain was not previously identified in humans and is now termed as "COVID-19 virus".

WHO on 11 March, reported the sudden increment in the number of cases outside China and WHO Director-General Dr. Tedros Adhanom Ghebreyesus declared, this disease as a pandemic. By that time approximately 118000 cases had been reported in 114 countries, along with 4291 deaths registered.

Now the European Region gets ahead with reporting 40% of globally confirmed cases by mid-March and becomes the epicenter of the outbreak. Coronavirus spreads faster than the Middle East respiratory syndrome(MERS) and SARS-CoV but has low fertility.

Special care and attention are needed by elderly patients, patients with diabetes, cardiovascular disease. Because the ongoing condition is of "public-health emergency" various medication have been used for treating the COVID-19, which consists of antimalarial drugs along with several other antiviral drugs. The standardized method for diagnosing COVID-19 is by taking a nasopharyngeal swab and then calculating reverse transcription-polymerase chain reaction.

As well, suspending travels, and attempt to decrease crowds, various measures are being taken by the country, and we are also trying to improve the production of medical supplies in all over India.

In the past two events occurred wherein crossover resulted in severe disease in humans. An exponential increase in the number of cases and studies reported an epidemic doubling time of 1.8 d.

The WHO is working around the clock since day one when the first case was reported to support countries to prepare and respond to the pandemic.

REVIEW OF LITERATURE

JOURNAL	TITLE	AUTHOR/LINK	MAIN QUESTION/ OBJECTIVE	KEY FACTS
www.elsevier.com/locate/antiviral (05 March 2020)	Antiviral Research Of chloroquine and COVID-19	Franck Touret, Xavier de Lamballerie	What is the benefit of chloroquine, in the treatment of patients infected by the novel coronavirus (SARS-CoV-2)?	For treating autoimmune diseases like lupus and rheumatoid arthritis. Its poisoning has been related to cardiovascular disorders. The prior trial assessment indicates that, to the present time, chloroquine is not proven effective in treating acute virus infections in humans. More than100 patients demonstrated that it is superior in inhibiting the aggravation of pneumonia, shortening the disease course, and improving lung imaging findings.
International Journal Of Antimicrobial Agents (31 March 2020)	Antiviral effects of chloroquine against coronavirus: What to expect for COVID-19?	Christian A. Devaux, Jean-Marc Rolain, PhilippeColson, Didier Raoult	Antiviral effects of chloroquine against coronavirus. What to accept for COVID-19?	In vitro, chloroquine and remdesivir inhibited SARS-CoV-2. For treating autoimmune diseases. A rapid decline in fever, improvement of lung &shorter recovery time, experienced by the patient.

				Sever adverse effects-retinopathy and cardiomyopathy.
International Journal of Antimicrobial Agents (31 March 2020)	Aminoquinolines Against coronavirus disease 2019 (COVID-19): Chloroquine or hydroxychloroquine	Zahra Sahraei, Minoosh Shabani, Shervin Shokouhi, Ali Saffae	To find out the effect of Aminoquinolines against coronavirus disease 2019 COVID-19.	Plays a prominent role in managing the Zika virus and SARS CoV outbreaks. It confers broad-spectrum antiviral effects by reducing pH. It alters the glycosylation of the cellular receptors of Coronavirus. HCQ is more soluble than chloroquine and shows low ocular toxicity. Other therapeutic agents: oseltamivir, lopinavir/ritonavir, ribavirin.
Diabetes & Metabolic Syndrome: Clinical Research & Reviews (May-June 2020)	Doctors and healthcare workers at the frontline of COVID-19 epidemic	Anoop Misra	What preventive measures should be taken by frontline workers dealing with COVID-19?	For treating COVID-19 patients requires training, wear PPE, ICU with ventilators. Public sector ICUs are needed up-gradation. Private sectors showed an inability in managing the patients. At the peak of the outbreak in China 1716 medical workers, came in contact with the virus.
Diabetes & Metabolic Syndrome: Clinical Research & Reviews (22 March 2020)	Chloroquine or Hydroxychloroquine is the treatment of COVID-19 with or without diabetes.	Awadesh Kumar Singh, Akriti Singh Altamash Saikh, Ritu Singh, Anoop Misra	What is the effect of chloroquine or hydroxychloroquine in treating patients of COVID-19 with or without	Chinese center for disease control and prevention showed increased mortality in people with diabetes 7.3% (overall 2.3%). So far, chloroquine was moderately efficient in chronic hepatitis c. Human research has shown a combination of HCQ plus azithromycin is highly efficient in just 3-6 days cleared nasopharyngeal carriage. It can be given in type 2 diabetes adult

			diabetes?	patients for controlling glycemia (approved in India).
Forensic Science International : Mind and Law (2020)	Caring for persons in detention suffering from mental illness during the Covid-19 outbreak	Michael Liebrenz, Dinesh Bhugra, Anna Buadze, Roman Schleifer	How to provide care for the mental illness during the COVID-19 outbreak?	Psychological care is a major challenge for many health care systems. They engage in group activities which increase in patient to patient make contact. Quarantine service and all the essential amenities isolating the suspected and their close contacts. Routine consultation of psychiatrists should be canceled to prevent the spread of infections. Provide adequate medical supplies such as masks, disinfectant & protective equipment. Avoid group interaction activities.
The Indian Journal of Pediatrics (13 March 2020)	A Review of Coronavirus Disease-2019 (COVID-19)	Tanu Singhal	A review of the global impact of this new epidemic.	Four coronaviruses namely HKU1, NL63, 229E, and OC43 cause mild respiratory diseases in humans. In the hospitalized adult patients death rate ranges from 4 to 11%. The case death rate varies from 2 to 3%. The virus enters the respiratory mucosa by angiotensin receptor 2 (ACE2). CT is more sensitive and specific with negative molecular diagnosis also.
Treatment and Research Centre for Infectious Diseases (17 February 2020)	Pathological findings of COVID-19 associated with acute respiratory distress syndrome	Z Xu MD, L Shi MD, J Zhang Ph.D., L Huang MD, C Zhang Ph.D., P Zhao MSc,	What are the pathological findings related to ARDS?	Sever condition cause massive alveolar damage and progressive respiratory failure.over activation of T cells, Th17, and high cytotoxicity of CD8 T cells, the severe immune injury in this patient. corticosteroid treatment is not regularly recommended, histological changes were

		H Liu BSc, J Song Ph.D., P Xia MSc		seen in the liver tissue, but no changes in the heart tissue.
BMJ 2020;368: m1066 doi: 10.1136 (17 March 2020)	Covid-19 and community mitigation strategies in a pandemic	Shahul H Ebrahim adjunct professor, 1, Qanta A Ahmed associate professor 2, Ernesto Gozzer associate professor 3, Patricia Schlagenhauf professor 4, Ziad A Memish professor	What should be the community migration strategies during a pandemic ?	Restrict- Mass gatherings, political events, cultural celebrations, religious gatherings, and music festivals. Restrict social contacts among people of all ages. Home quarantine decreases stress on the healthcare system. Telehealth concepts - to sorting people quarantined at home.
BioScience Trends Advance Public(2020)	Chloroquine phosphate has shown apparent efficacy in the treatment of COVID-19 associated pneumonia in clinical studies	Jianjun Gao1, Zhenxue Tian2, Xu Yang2	Chloroquine phosphate, shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicentre clinical trials.	In the testing ground, chloroquine was capable of blocking COVID-19 with a half-maximal effective concentration of 1.13 μM Chloroquine phosphate has potent action against COVID-19. Chloroquine and HCQ is an easily available and safe drug.

Methodology

1. **Research question**

- To understand the current trend of COVID-19 spread in India till 8th April 2020

2. **Specific objective:**

- To find out the number of deceased, hospitalized, recovered cases in India due to COVID-19
- To find out the fatality rate, the recovery rate of cases in different states in India
- To find out the effect of antimalarial drugs for the treatment of the patient with COVID-19

3. **Type of research method**: A review study

4. **Type of research design**: Quantitative/Qualitative, mixed-method approach

5. **Data Collection**:

Data is collected from secondary sources like journals, articles, websites, and papers.

CURRENT STATUS OF CORONAVIRUS SPREAD IN INDIA:

- The government of India planned a joint meeting with empowered groups (04 April) created for the planning and implementation of COVID-19 response actions throughout the country.
- ICMR to collaborate with the WHO solidarity trial- an international randomization trial for treating COVID-19 in hospitalized patients
- Ministry of Health and Family Welfare(MoHFW) issued a direct order for insurance cover for all healthcare workers for 90 days through – Insurance scheme for Health Workers Fitting COVID-19'

WORLD HEALTH ORGANIZATION

(WHO): 12th April 2020 (5:00 pm) following the Ministry of Health and Family Welfare

Confirmed cases: 8477
Deaths: 273
States/Union territories: 31

Based on data provided to date 08th April 2020, data analysis is performed. India has reported 5399 total cases, out of which 5215 are hospitalized, 27 deaths, and 116 patients recovered according to the data from the Health Ministry and State Governments.

Table1: *Representing Patient numbers in India on 8 April.*

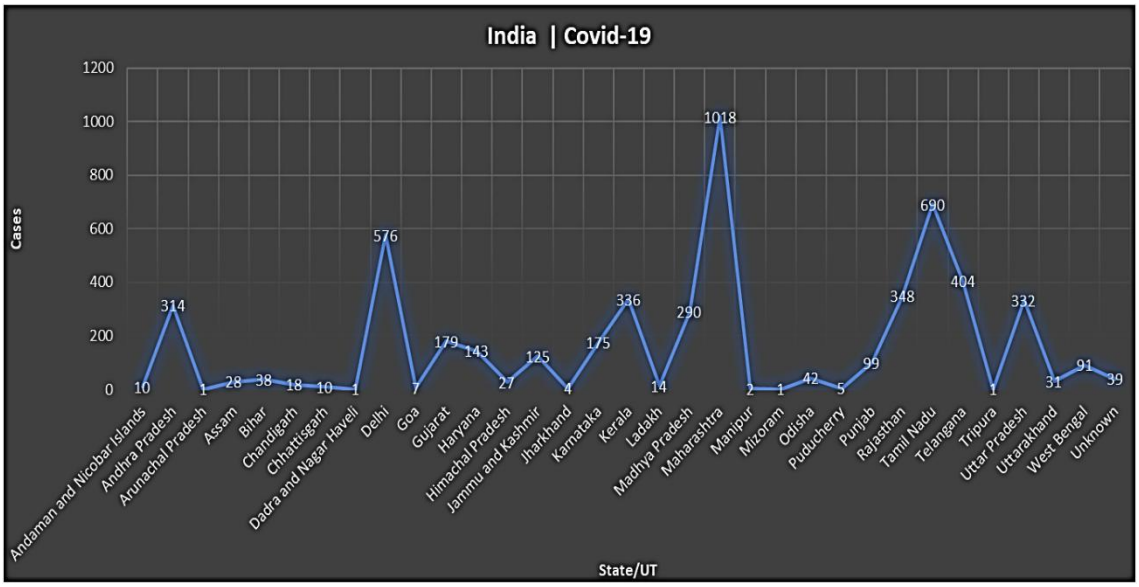
Row Labels	Count of patient number
Deceased	27
Hospitalized	5215
Migrated	1
Recovered	116
(blank)	40
Grand Total	5399

CURRENT STATUS OF STATES IN TERMS OF COVID-19 SPREAD:

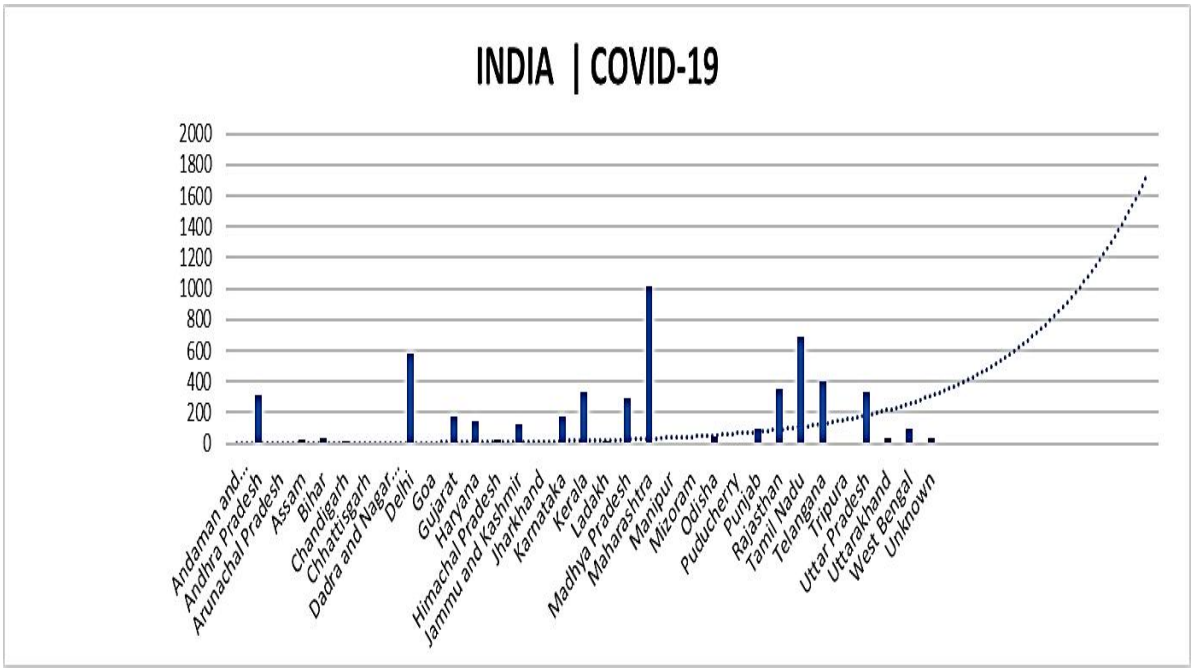
S. No.-	State/UT	Cases
1	Andaman& Nicobar	10
2	Andhra Pradesh	314
3	Arunachal Pradesh	1
4	Assam	28
5	Bihar	38
6	Chandigarh	18
7	Chhattisgarh	10
8	Dadra & Nagar Haveli	1
9	Delhi	576
10	Goa	7
11	Gujarat	179
12	Haryana	143
13	Himachal Pradesh	27
14	Jammu and Kashmir	125
15	Jharkhand	4
16	Karnataka	175
17	Kerala	336
18	Ladakh	14
19	Madhya Pradesh	290
20	Maharashtra	1018
21	Manipur	2
22	Mizoram	1
23	Odisha	42
24	Puducherry	5
25	Punjab	99
26	Rajasthan	348
27	Tamil Nadu	690
28	Telangana	404
29	Tripura	1
30	Uttar Pradesh	332
31	Uttarakhand	31
32	West Bengal	91
33	Unknown	39

Table 2: *Representing Coronavirus cases in India on 8th April 2020.*

CORONAVIRUS TREND



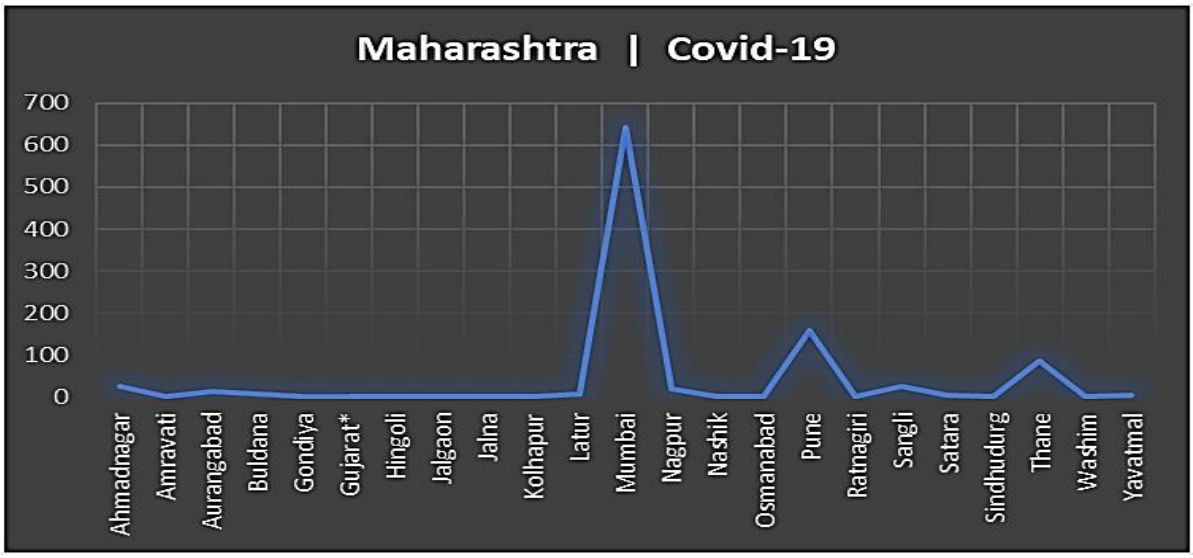
Graph 1: *Graphical representation of COVID-19 cases in India on 8th April 2020*



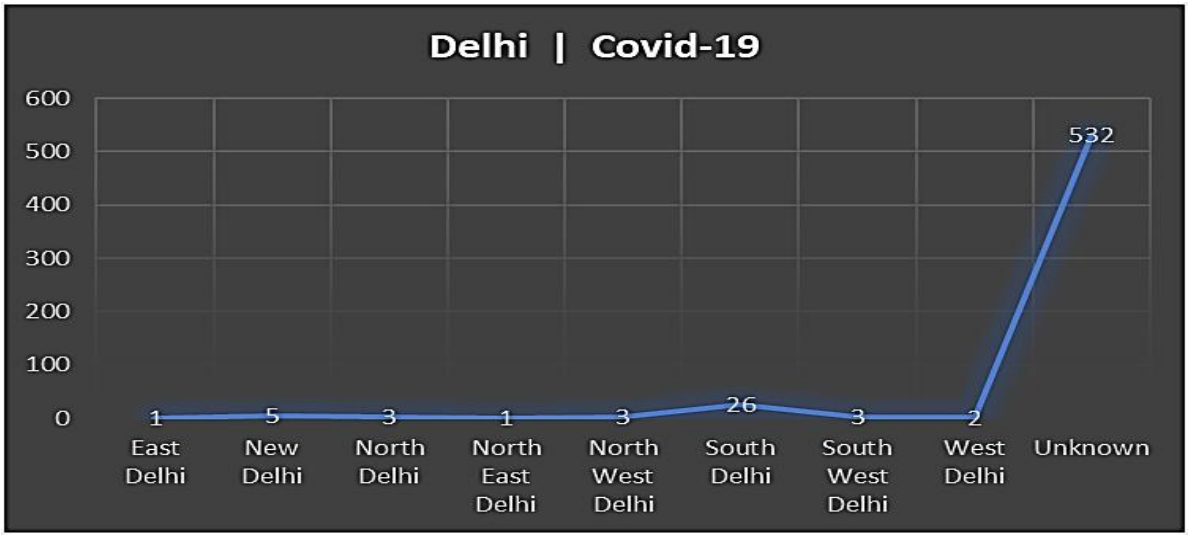
Graph 2: *Bar graph representing COVID-19 cases*

The country is seeing a spurt in the number of cases with 1,018 cases in Maharashtra was the worst-hit state, followed by Tamil Nadu at 690 and Delhi at 576, Telangana at 364 and Kerala at 336. Followed by Rajasthan, Andhra-Pradesh, Uttar Pradesh.

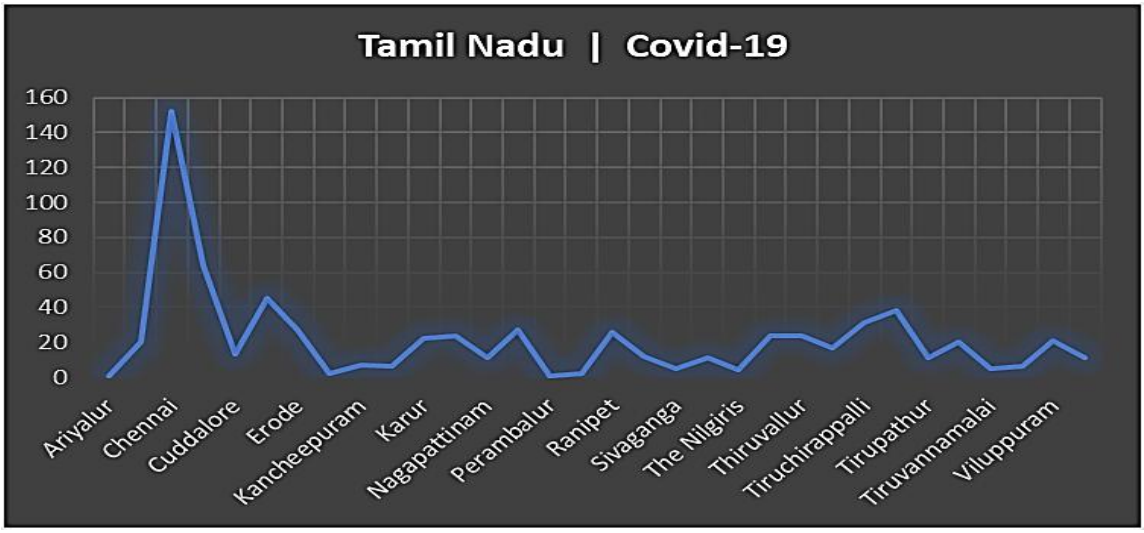
Key states and districts in India facing a major challenge:



Graph 3: *Representing COVID-19 cases in Maharashtra*

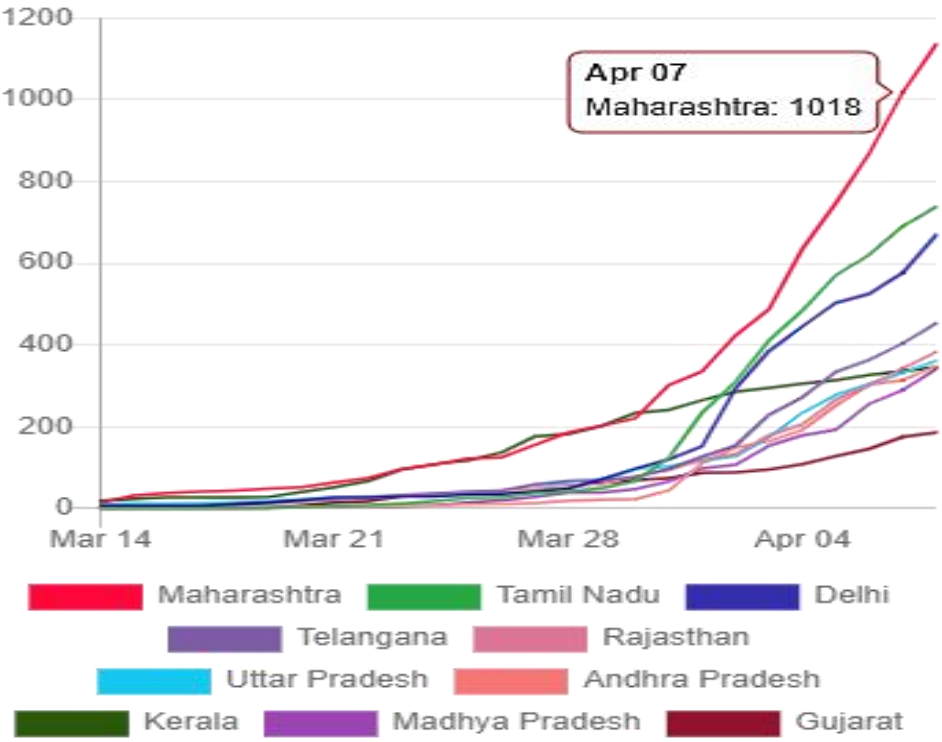


Graph 4: *Representing COVID-19 cases in Delhi*



Graph 4*: Representing COVID-19 cases in Tamil Nadu*

Maharashtra reported the highest number of cases, with Mumbai alone having 643 cases, followed by Pune 159. Tamil Nadu reported 690 cases, where Chennai reported with 152 cases. The number of cases in the capital has risen to 576.



Graph 5: *Trend analysis of the COVID-19 pandemic in India*

DISCUSSION

The strategy recommended for hospitals treating cases with COVID-19:

- There should be ambulances identified specifically for transporting COVID-19 suspected patients or those who have developed complications.
- Currently, there are two types of ambulance – ALS (with ventilators) and BLS (without ventilators). However, this must be ensured that strict adherence to cleaning and decontamination protocols should be followed.
- The ambulance staff should be trained and oriented about the symptoms of COVID-19 (fever, cough, and difficulty in breathing).
- Two sets of appropriate **PPEs** provided for medium and low-risk healthcare workers (it contained an N95 respirator mask for medium-risk workers and a surgical mask for low-risk workers). The two surgical masks should be provided to every inpatient and one for every outpatient.
- COVID care hospitals should be equipped with ICUs, Ventilators, and beds with Oxygen support. The current requirement for ventilators is estimated at 30-50K nationwide and about 70-100K ICU beds.

- Hospitals should have separate areas for the suspect and confirmed cases.
- A separate block of the hospitals should be preferable with separate entry/exit.
- Patients having mild symptoms should be admitted to **COVID CARE CENTRE** (hotels/lodges/hostels), moderate symptoms admitted to **DEDICATED COVID HEALTH CENTRE,** and sever in **DEDICATED COVID HEALTH CENTRE** with ICU facility.
- There is no particular treatment for disease caused by a novel coronavirus. However, many of the symptoms could be treated by anti-malaria (chloroquine or HCQ) or anti-viral drugs and are based upon the patient's clinical condition.

Lockdown strategies for severely affected states:

- India, begin its 21-day lockdown which started midnight on March 24 involved shutting down offices, public gathering, and asking everyone to stay home.
- Chief ministers of Maharashtra, Punjab, Delhi, and other states have asked to extend the lockdown period till April 31st.
- So, we should use all our public health resources in isolating and tracing people who have been first and second contacts.
- Locale sanitization of the area by authorities.
- Door-to-door health check-up of everyone living in the area.
- Launch a massive education campaign for educating people in the affected places, so that they inform if they feel any symptoms, instead of hiding it.
- Ministers should prepare their priority areas once the lockdown is lifted, for sustaining economic growth.
- The government must increase the production of PPEs, gloves, mask for healthcare workers plus frontline workers.
- Mass screening camps at bus stands, railway stations, college, and school campuses and in other public spaces should be performed.

All Industrial and private establishment shall remain closed.

Exceptions. (During lockdown)

- Ration shops (groceries, fruits and vegetables, dairy, meat, and fish) home delivery may be preferred to minimize the movement of individuals.

- Bank, Insurance offices, ATMs
- Petrol pumps, LPG, Petroleum, and gas retail
- Telecommunication Networks, internet services, broadcasting, and cable services.
- Pharmaceuticals, medical equipment will be delivered through E-commerce.
- Power generation, transmission and distribution units, and services
- Warehousing services and Cold storage
- All means of transport services will remain closed except- essential goods.
- All other businesses will remain closed.

FATALITY RATE AND THE RECOVERY RATE IN INDIA

This is the recovery rate of India till 8th April 2020.

- The fatality rate in India is 0.51
- The recovery rate in India is 2.15

Formula:

Fatality rate: (total deaths/ total cases)*100

Recovery rate: (total recovered/total cases)*100

Role of Anti-Malarial Drugs in Treating COVID-19 Patients:

A suspicious case is characterized as one with cough, sore throat, fever, breathlessness, or giving travel history to China or different parts of the world.

Diagnosis is done by conducting a particular molecular test on respiratory samples (sputum, throat swab, nasopharyngeal swab).

In severe cases, the virus may present in stool and blood.

Research conducted on chloroquine and hydroxychloroquine in vitro

In an experimental research study, chloroquine inhibits the replication of intracellular microorganisms in vitro.

Endosomal pH rises and interferes with glycosylation of protein of the SARS-CoV receptor and hence prevent viral infections. It also inhibits quinone

reductase-2 that makes it a broad anti-viral agent. Hence chloroquine plays a role in the treatment of coronavirus.

Chloroquine changes the pH of lysosomes and inhibits cathepsins, which leads to the formation of the autophagosome which splits COVID-19 spike protein.
Chloroquine prevents its attachment to the target cells, by interfering with glycosylation of the ACE2 receptor.
Chinese scientists found out the chloroquine effect in vitro to be very impressive in slowing viral duplication.
The mechanism of action and structure of HCQ is as same as chloroquine. Some data have shown HCQ efficacy is high and much safer than chloroquine as it has less risk of retinal toxicity.

The **second human study** conducted in an open-label, non-randomized trial (n=36) conducted in Marseille, France, Gautret et al. discovered that HCQ and combination of HCQ and azithromycin are highly efficient in just 3-6 days in cleaning nasopharyngeal carriage which is measured by PCR.
HCQ functioning was considerably higher in patients with symptoms as compared to asymptomatic patients.

Contraindications:

- Some precautionary measures should be taken when you use these drugs, keep an eye on hematological parameters (RBC, WBC, Platelet count)
- Check hepatic and renal functions.
- Hypoglycemia should be checked for diabetic patients, among patients with the use of chloroquine/HCQ.
- Chloroquine has not been contraindicated in pregnancy.

LIMITATIONS

In India, the coronavirus cases are setting new records daily.
Ministry of Health and Family Welfare(Government of India)

COVID-19 INDIA as on15 June 2020, 08:00 IST (GMT+5:30)
Active Cases: 153106

Cured/Discharged:169797

Deaths:9520

The drawback of this study is that it is based on earlier data and as we can see we have reached in the top 4 positions in terms of COVID-19 cases. The suggestions which are given based on April month data are still helpful in breaking the COVID-19 chain if followed correctly.

CONCLUSION

As we all are aware of the new community health condition threatening the globe with the outbreak of novel coronavirus or SARS-2.

A significant number of cases are reporting daily in India with 5399 cases reported on April 8th, 2020. The country is seeing several cases with 1,018 cases in Maharashtra was the worst-hit state, followed by Tamil Nadu at 690 and Delhi at 576, Telangana at 364, and Kerala at 336.

Maharashtra reported the highest number of cases, with Mumbai alone having 643 cases, followed by Pune 159. Tamil Nadu reported 690 cases, where Chennai reported with 152 cases. The number of cases in the capital has risen to 576.

Specified ambulances should be used for transporting COVID-19 suspected patients. The ambulance staff should be trained and oriented about the symptoms of COVID-19.

Fully equipped hospitals should be used in treating COVID-19 patients. Hospitals should have separate areas for the suspect and confirmed cases.

The recovery rate and fatality rate till 8th April in India is estimated to be 2.15 and 0.51. Maybe the Government will extend the lockdown by arguing that it is necessary to “flatten the curve” of infections. This may be partially true, in absence of lockdown, there would have been an upsurge in the number of cases and difficult for us to break the “community transmission” or stage-3 this when the source of infection cannot be located because several areas got affected. This happens when a patient positive despite no exposure to an infected person nor any travel history.

But we cannot stop the production of essential commodities like the production and distribution of medicines, medical equipment, fruits, vegetables, etc.

So, by continuing the lockdown government should increase tracing people who have been first and second contacts. Sanitize the hotspot areas. Door-to-door health check-up of everyone living in the area.

Mass screening camps at bus stands, railway stations, college, and school campuses and in other public spaces should be performed.

The Proof of chloroquine and HCQ is limited but seeing the agreeable risk-benefit balance of chloroquine and HCQ, we can use this for treatment of the current pandemic COVID-19 outbreak.

The outcomes of chloroquine and HCQ is more promising in treating COVID-19 than the earlier trial of drugs in other viral diseases.

The Above-Mentioned drugs are safe, easily available, and are of low cost, and generally available in countries with malaria.

HCQ is much more soluble than chloroquine shows low ocular toxicity.

Since HCQ blocks the potassium channel and potentially prolonged heartbeat it may result in arrhythmia, cardiac arrest, and sudden death. So, patients must be constantly monitored and patient with cardiac disease, the renal disease should not be given this line of treatment.

The line of treatment must depend upon the severity and health condition of the patient.

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Title:

Epidemiology: The Basic Science of Public Health

Report on an online course offered by

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

COURSE DESCRIPTION –

The word epidemiology is derived from the Greek word epidemic, where Epi=upon, demos= people, and logos= study or science. This course focuses on the population level and rather than the individual level. It covers the health events occurring in the population not only disease distribution and causation. By identifying risk factors of chronic diseases, it provides new opportunities for prevention, treatment design by improving the efficiency of health-related services.

To better understand this course, it is first useful to review some of the basic histories of the field. The first known epidemiologist was Hippocrates (460-375 B.C). He considered the relationship between habit, body, weather, and disease.

Initially, the main focus was on infectious diseases and epidemics in the mid-1800s. By the mid-1950s it started to focus upon conditions that are linked with disease. During the 1960s the focus was on the community level. Then, in the late 1980s, epidemiology focused on how to control or minimize health problems.

OBJECTIVES OF THE COURSE –

- Define Epidemiology
- Describe how epidemiology supports improving the public's health
- Relate the mission of public health to the population perspective on health outcomes
- Historic development of epidemiology
- Differentiate the following measures: Prevalence, Risk, Rates, and Odds
- Calculate the following measures: Prevalence, Risk, Rates, and Odds
- Define the concept of Person-Time and able to apply in its calculations
- Interpret the Prevalence, Odds, Rates, Risks, within the context of public health research
- Describe the difference between experimental and non-experimental (observational) study design
- List two different units of analysis
- Explain the purpose of randomization
- Characterize randomized control trial and clinical cross over study design

- Define blinding, equipoise, placebo, and intention to treat
- Define the different types of measures of association

Risk, Rate, Odds, and Prevalence ratios

Risk, Rate, Odds, and Prevalence difference

- Recognize which measure of frequency and association are used with study design
- Interpret both statistically significant and non-statistically significant measures of association and their confidence intervals
- Define causality and causal inference
- Describe the nine Bradford Hill criteria and give examples of each
- Conclusion

Course Content-

WEEK 1

- Introduction, History of Epidemiology

WEEK 2

- Understanding Measures of Disease Frequency
- Introduction to disease frequency
- Definitions of disease frequency

WEEK 3

- Study Designs
- Experimental study design
- Study design
- Studies

WEEK 4

- Measures of Association
- Confidence Interval

WEEK 5

- Causality

WEEK 6

- Conclusion

Methodology-

- Video lectures

  This program consists of a six-week course module. The video lectures were held by the professionals working in the epidemiology department in Global public health and clinical associate professor at North Carolina Institute.

The sessions were divided into introduction, measures of disease or health outcome occurrence followed by study designs, measures of association, and then lastly an overview of causal inference and the Bradford Hill guidelines.

- Additional reading materials:

Reading materials were provided usually at the end of the session. Materials usually comprised of topics that were taught by the professor for the given session.

- Assignments:

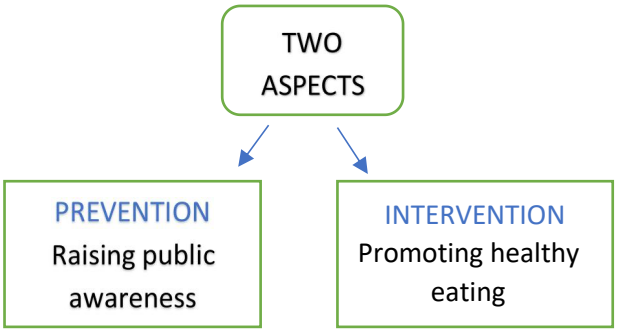
  Assignments were given at the end of the session, mainly consisting of a quiz that was graded and must score 80% grade to clear the quiz.

KEY LEARNINGS –

Week 1

Epidemiology – **"**The study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems". John M. Last (1988)

The Snow was the first person who mapped cases of the disease. His work generally considered as the beginning of epidemiology.



Three Levels of Public Health Prevention –

Primary prevention	It may decrease the risk of health outcomes. Ex. Vaccination
Secondary Prevention	It aims to treat the disease early, which may cure disease. Ex. Early-stage of Cancer
Tertiary prevention	The main aim is to prevent damage from the disease. Ex. Diabetes and heart disease.

Interventions –

1. **Individuals-** Changing individual risk factors or behavior.
2. **Structural –** Making Physical, Social, or Economic changes in the environment.

<u>Week 2</u>

Measures of Health Outcome Frequency –

Health Outcome – It includes diseases, illness, conditions, disorders, symptoms, behavior, risk factors and injuries, and as well as healthy behavior. Ex. Eating fruits and vegetables, No smoking habit.

Prevalence – Proportion of defined population that has the health outcome. Cases were diagnosed before the beginning of the study. Quantifies the burden on the population.

$$\text{Prevalence} = \frac{\text{No. of people with the disease}}{\text{No. of people in the total study population}}$$

Numerator: Prevalent cases (all the cases at the given time)

Denominator: Total study Population

- Prevalence is a cross-sectional measure.
- Prevalence is a period specified.

Two types of Prevalence Measurements –

- **Point Prevalence –** Prevalence at one point in time. Ex. Do you currently have ulcers?
- **Period Prevalence –** No. of people with the health outcome over a specific time, divided by the number of populations during that time.

Ex. Have you had asthma during the past few years.

Risks – It measures the number of new cases that develop among populations at risk.

$$\text{Risks} = \frac{\text{Incident cases}}{\text{Total number of individuals at risk}}$$

Numerator: New cases

Denominator: Study population at risk at the beginning of the study follow-up.

- Define the study population.
- Specified period.

Rates – Measures the event of new cases of the disease in a population.

$$\text{Rates} = \frac{\text{New or Incident cases}}{\text{Person- time}}$$

- The denominator is not fixed

Person- Time: Period when each person remains at risk for health outcome and understudy observation. years, months, days.

Peron-Time stop:

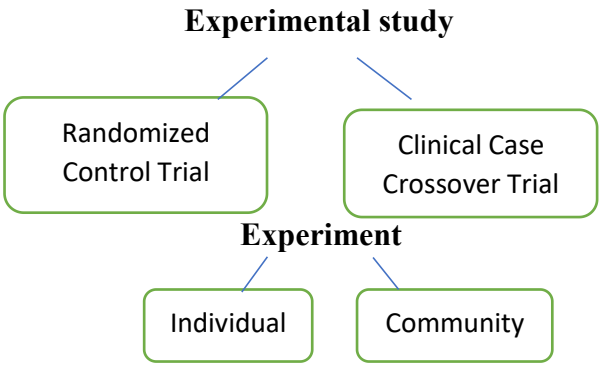
- Death
- Leaving the study
- Develops the health outcome during the study.
- Unable to follow-up

Week 3

Types of Study Designs –

Experimental study design: In experimental study design the investigator usually determines who will get exposed and who will not. This exposure or intervention is randomly allocated.

Ex. Developing a new drug.



Individual- In this study, some participants are assigned in exposed and some are unexposed.
Unit of analysis- Individual level

Community- One or more communities are assigned to an exposed and remaining unexposed.
Unit of analysis- Community level

Non-Experimental or Observational study: Investigator usually does not determine the exposure.
Ex. Health status of the people working in coal mines.

Randomized Control Trial- Intervention groups and Control groups should be comparable in all aspects. Ex. The proportion of males and the age distribution should be similar in both groups.

Crossover Clinical Trial- In this trial subjects switch from one treatment to another after a certain period.

- Wash-out period (no treatment is given during this period).
- Shorter interventions are preferred.

Epidemiology vocabulary-

Equipoise: Genuine uncertainty about the benefits/harms of treatment or exposure.

Placebo: Treatment that appears identical to the real treatment.

Compliance/Adherence: Weather or not participants follow treatment recommendations.

Intention-to-treat analysis: When subjects are analyzed according to their treatment.

Cohort Studies-A group of persons sharing common characteristics Ex. Geographic location, occupation, race, gender, ethnicity, socioeconomic status

- Cohort study track patients over time.
- The selected subjects should be free from the outcome at the study onset.
- The exposure precedes the outcome.

Basic design: It begins with a well-designated source population. Then this sample is assessed and a person who already has the outcome of interest is then removed.
Ex. For a study of prostate cancer, we will not include women.
A cohort study is the best method for associating cause and effect when exposure and treatment cannot be controlled by the investigator but when we want to be certain that the exposure preceded the outcome.

For Calculating Risk: the total number of disease-free persons in the cohort will come in the denominator

Calculating Rate: we only count person-time at risk in the denominator

Cohort study population:

1. **Open study population:**
    - Join at any point, within limitations
    - Person-time
    - Less prone to the problem with the sample size
2. **Closed study population:** Closed to new participants

Two types of Cohort studies-

Retrospective	Prospective
The cohort is formed in the past Study often use to measure occupational exposure Such as- Cancer or other chronic measures	Study starts now and goes into the future Investigator obtain baseline exposure data in real-time and then follow the cohort member measure the exposure of health outcome.

Advantage-

- Directly estimates rate and risk
- Good for rare exposures
- Good for multiple outcomes
- Provides evidence of temporality between exposure and outcome

Disadvantage-

- Time-consuming
- Expensive
- Resource-intensive
- Inefficient for rare outcomes
- Loss to follow-up

Case-Control Study Design- It is an efficient method for studying rare diseases (prevalence of less than 10%)

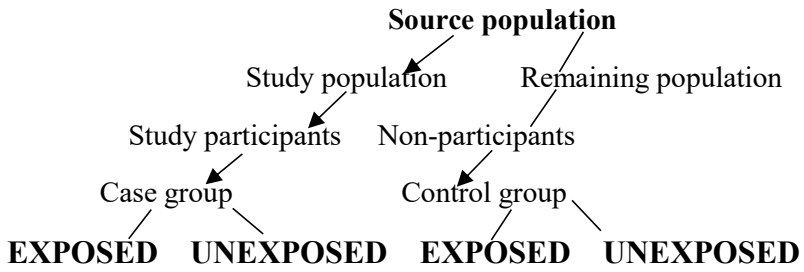
Researchers select a group of individuals with disease or health outcome known as cases. Individuals without disease known as controls.

Key Steps for Case-Control Studies:

1. **Define and select cases:** Cases are selected from the groups that have a disease or health outcome.
    - Determine the diagnostic criteria (i.e. fever, ulcer, nausea, vomiting)
    - Incident cases are preferable (prevalent cases are influenced by the duration of disease).

2. **Define and Select Controls:** Controls are the non-cases that are representative of the same source population that of cases.
    - Multiple controls per case (statistical power)
    - Multiple control groups (consistency=credibility)
3. **Compare Exposure Prevalence:** Measure and compare the exposure prevalence in the controls Vs cases.
    - The investigator arbitrary decide how many controls will be selected to compare with the cases.

Odds Ratio- Odds of exposure for cases ▭ odds of exposure for controls



Matching- Matching means that for every case, there is at least one control who has the same or similar values of the matching variable. It may be by sex, age, race, group, etc.

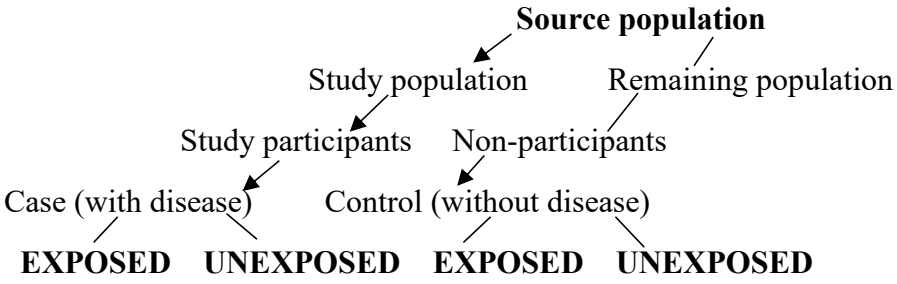
Advantage-

- Take less time
- Use fewer resources and money
- Can examine multiple exposures
- Likely to be replicable in other populations
- If sampled accurately odds ratio provides an estimate of risk and rate ratio

Disadvantage-

- Some possible biases in the selection of subjects, measurement of exposures, and analysis
- No direct estimate proxy for risk or rate ratio

Cross-Sectional Studies- In this type of study the exposure and outcome are studied at the same time with the specified study population.



Example- Road traffic accidents occurring because of using cell phones is increasing day by day, so research conducted for checking the prevalence of talking or texting among driving.

Study: distracted drivers

Population base: 3 cities in Mexico

With a systemic sampling methodology, 7940 drivers and their vehicles were observed from 2011 to 2012. So, the overall prevalence of mobile phones uses while driving was 10.8%.

- Describes the occurrence of health outcomes or exposure in the population.
- The measure used to describe the occurrence is the prevalence.

Prevalence = $\frac{\text{No. of people with health outcome}}{\text{Total number of the study population}}$

Denominator: prevalent + non-prevalent cases

Prevalence = Rate * Average duration

- Describes the prevalence of health outcome or disease in the specified population over a specified period.
- Obtain data on the prevalence of exposure and the health outcome.

Limitations-

- Prevalence is influenced by the (incidence) rate and duration of a health outcome.
- Interpreting cross-sectional studies

  Antecedent-consequent bias (chicken Vs egg)

- Not sure that the exposure preceded the disease

Advantage-

- Estimates the occurrence of risk factors or health outcome in a population
- Surveillance of changing behavioral risk factors and long-lasting diseases
- Data on the prevalence of exposure and health outcome

Ecologic Studies- Ecologic studies use a group level of measurement. Here exposure or the health outcome data is collected at the group level, not at an individual level.
Example: yearly average air pollution air concentration in different cities and their relationship with lung cancer.

Ecologic Fallacy- an association between exposure and the health outcome at a group level is true at the individual level

Advantage-

- Group-level data is publicly available. Ex. Census data
- Lower cost, convenient
- Evaluating the Impact of community-level interventions. Ex. Fluoridation of water, seatbelt laws
- Maximize exposure differences between communities. EX. Cities, countries
- Studying the effects of short-term variations in exposure within the same communities.

Limitations-

- Ecologic fallacy
- Exposure precedes outcome.
- Migration can bias the interpretation of data

Group-level data (ecologic studies)	**Individual level data** (cohort, case-control, cross-sectional)
The average exposure of group not individuals.	Provides information on exposure of each Individual.
Knows health outcome of group	Individual exposers to those who became

but do not know exposures of diseased and those who do not.
individuals who became diseased.

Week 4

Measures of association- Compare measures of disease occurrence in two different groups, the exposed group, and unexposed group.

Comparison can be made by:

- Division (ratio affect measures)
- Subtraction (difference effect measures)
- The ratio measures indicate the relative strength of the association between exposure and the disease compared with the absence of exposure or less exposure, this is of greater interest when we are trying to understand the cause of the disease or health outcome.
- In contrast, different measures sometimes called attributable risk. The difference measure tells us whether the exposure or risk factor is associated with many health outcomes cases or a small number of cases.

Relative Risk- Any ratio measure of the effect that approximates risk. This is not a precise measure.

More precise- Rate ratio, Risk ratio, and odds-ratio

- Risk Ratio (RR) = $\frac{\text{risk in the exposed}}{\text{risk in the unexposed}}$
- Rate Ratio (IRR) = $\frac{\text{rate in the exposed}}{\text{the rate in the unexposed}}$
- Odds Ratio (OR) = $\frac{\text{odds in the exposed}}{\text{odds in the unexposed}}$
- Prevalence ratio(PR) = $\frac{\text{prevalence in the exposed}}{\text{Prevalence in the unexposed}}$

- Risk difference (RD) =

  risk of disease in the exposed - risk of disease in the unexposed

- Rate difference (IRD) =

  Rate of disease in the exposed - rate of disease in the unexposed

Two by Two Table- **diseased** **non-diseased** **total**

Exposed	**a**	**b**	**(a+b)**
Non-exposed	**c**	**d**	**(c+d)**

Risk ratio= Risk exposed= a/(a+b)

Risk unexposed= c/(c+d)

Exposed	A	Person-years
Non-exposed	C	Person- years

Rate difference= (Incidence rate exposed) – (Incidence rate unexposed)

a/ (total person-time exposed) – c/(total person-time unexposed)

Rate Ratio= a/(total person-time exposed) ⏚ c/(total person-time unexposed)

Odds Ratio-

	Case	control	total
Exposed	A	B	(a+b)
Non exposed	C	D	(c+d)
	(a+c)	(b+d)	N

OR = 1: No association

OR > 1: Positive association

OR< 1: Negative association

$$\frac{\text{Odds of being exposed in cases}}{\text{Odds of being exposed in controls}} = \frac{(a/c)}{(b/d)}$$

Odds ratio= (a*d)/(b*c)

We cannot calculate the rate or risk directly in the case-control study. Under certain conditions, we can obtain a valid estimate of the risk ratio, rate ratio by using the odds ratio.

Interpretation of Measures of Association-

- If risk rate = 1: No association
- If the risk ratio or rate ratio > 1: (+) Risk in exposed is greater than the risk in unexposed.

- If the risk ratio or rate ratio < 1: (-) Risk in exposed is lower than the risk in unexposed.
- If risk difference= 0 : No association
- If risk difference > 0 : (+) Risk in exposed is greater than in unexposed.
- If risk difference <0 : (-) Risk in exposed is lower than in unexposed.

Measures of association and study design

	Prevalence ratio, difference	**Odds ratio, difference**	**Risk ratio, difference**	**Rate ratio, difference**
Study design	Cohort (at baseline or for non-outcome variable)	Cohort	Cohort	Cohort
	Cross-sectional	Cross-sectional		
		Case-control		
		Experimental	Experimental	Experimental
	Ecologic	Ecologic	Ecologic	Ecologic

Confidence Interval (CI)- Statistical construct that provides us with information about a range in which a true value lies with a certain degree of probability.

- Information about the direction and strength of the effect.
- 95% is the commonly used confidence interval.

The mathematical formula for the 95% confidence interval

=Measure of association ± (1.96 * standard error of the point estimate)

The point estimate will always be somewhere between the upper and lower confidence intervals.

p-value- Probability that tells you to weather the study results are consistent with being due to chance.

- The 95% CI has a relationship with the p-value
- If a 95% CI does not include the null value, it may be called “statistically significant”
- When the p-value is less than alpha (usually0.05), maybe “statistically significant”

- When we receive statistically significant results, we reject the null hypothesis, no association between exposure and outcome.

The confidence interval tells us **more information** than a p-value:

- Tells us the magnitude of the association between exposure and outcome.
- Tells us about the precision of the estimate that we obtained: narrow CI: more precise

Statistical significance Vs clinical relevance-

A result may be statistically significant if the large sample size is used, and not significant if the small significant size is used.

A null value for ratio measures is 1 and for difference, the measure is 0.

<u>Week 5</u>

Causality- "An event, condition or characteristic that preceded the outcome or disease event and without the event either would not be occurred at all or would not have occurred until some later time". -Rothman and Greenland

- Inferred: casual inference
- Counterfactual model (what would have the chances of lung cancer if smoking had not occurred)
- Casualty is not determined by anyone's factors, but the conclusion builds on the evidence.

Causal association Vs Spurious association-

Events depend upon the the occurrence of other events	bias, variables

Bradford Hill Criteria-

1. **Strength of association:** strong risk factor. Measured by ratio, risk, odds.
   Ex. A strong association between smoking and heart disease or lung cancer.
2. **Consistency:** Reproducibility of results. Use to rule out another explanation.
   Lack of consistency leads to a lack of association.
   Greater consistency, more likely a causal relation.

3. **The specificity of association:** If a single risk factor consistently relates to a single effect, then it plays a causal role. Ex. Bacterial diseases
4. **Temporality:** Essential for causality. Exposure's present must precede the outcome. Lack of temporality rules out casualty.
5. **Biological gradient:** Dose-response, dose increases the risk of disease increases
6. **Plausibility:** Support from a science laboratory. Experimental evidence increases confidence in conclusions.
7. **Coherence:** New data should not expose the current evidence.
8. **Experimental evidence:** Well-controlled study, randomized trials, altering cause alters the effect.
9. **Analogy:** Identifies other similar factors as possible causes. Weaker criterion.

Week 6

Conclusion-

In this course, I learned more about epidemiology, about its history. The measures of disease or health outcome occurrence followed by study designs, measures of association, and then lastly an overview of causal inference and the Bradford Hill guidelines.

This can be applied in the different fields of public health including nutrition Health behavior, health policy, environmental science